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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 31-12-2016

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FUNDING

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

CITATION

The suggested citation for this report is as follows:

ANZLT Registry Report 2016
Australia and New Zealand Liver Transplant Registry
Brisbane, QLD, AUSTRALIA
Editors: S.V. Lynch, G.A. Balderson

STATISTICAL METHODS

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

ACKNOWLEDGMENT

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

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Preface

We are pleased to present the 28th Report of the Australia and New Zealand Liver Transplant Registry (ANZLTR). This report contains data to the 31st December 2016 and analyses the cumulative data since the establishment of the first liver transplantation unit in Australia or New Zealand in 1985.

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

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

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

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

Comments are always welcome and should be forwarded to the Coordinating Centre at the contact information listed on the front page as should requests for further copies of this Report. The report is now also available on the ANZLTR public web site 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 2016, 5553 orthotopic liver transplants (OLT) were performed in Australia and New Zealand on 5136 patients, 4246 adult patients [83%] and 888 children (< 16 years) [17%]. The median age of all recipients was 48.9 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. Three hundred and thirty-six new patients were transplanted in 2016 compared with 295 in 2015.

7. The trend to increasing age of adult recipients in recent years continued and the overall adult median age is now 51.9 years. The median age of new adult recipients in 2015 -16 was 56.4 years.

8-9. In 2016, there was an increase in the number of transplants with 57 more performed [373 vs 316]. Split grafts continue to make a significant contribution to the total number of paediatric transplants performed providing 33 of 64 [62%] of deceased donor grafts in 2016 and 294 of 1012 [29%] overall. In children, other reduced size grafts have been used in 419 [41%] cases including 82 living donor grafts. One child has been treated with liver cell implantation. Of adult patients, 338 have received reduced size grafts - 294 split liver grafts (including one as auxiliary graft), 30 other reduced size grafts (one as auxiliary graft) and 14 living donor grafts. Four domino transplants of a whole liver have been performed.

10-11. Overall, chronic viral hepatitis (CVH) is the most common primary indication for liver transplantation. In children biliary atresia (BA) is the most common primary disease. In adults chronic hepatitis C [CVH : HCV] is the primary disease in 22.4% of recipients and chronic hepatitis B [CVH : HBV] in 5.6%. Full details of specific diagnoses categories by age group are listed in the Appendices for – Metabolic disorders (Appendix II), Other diseases (Appendix III) and Fulminant Hepatic Failure (Appendix IV).

12-15. The number of patients transplanted with non-alcoholic fatty liver disease [NAFLD/NASH] as the primary diagnosis continued to increase with 28 [10%] of new patients transplanted in 2016 bringing the total to 156. The proportion of adult patients transplanted with a primary diagnosis of chronic viral Hepatitis B, C or B/C/D fell in 2016 compared with the previous eras but the number of patients with a primary diagnosis of hepatocellular carcinoma [HCC] increased and accounted for 20% in 2016. 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 2016 was 38%.

16. Overall one year patient survival of all patients is 90% at one 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 30 years post-transplant.

17. Whilst older children had superior early survival than infants and babies, long term survival is similar. Older adult recipients had poorer longer term outcomes.

18-19. Patient survival in later cohorts show continued improvement in outcome for the first 10 years compared with earlier cohorts. This is seen in both children and adults. One year patient survival in 2015-16 cohort was 95% for all patients [98% for children, 95% for adults].

20. In both children and adults, there are worse early outcomes in patients receiving a deceased donor reduced size graft as their primary graft compared with split liver graft or whole liver grafts. Split liver grafts and whole livers have similar early outcomes in both children and adults.

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21. Smaller children and babies weighing < 8 kg at the time of transplant had inferior early survival compared to heavier children but similar long term results.

22. Adult patients transplanted for biliary atresia or hepatitis virus co-infections had the best longer term survival while those whose primary disease was primary biliary cirrhosis or primary sclerosing cholangitis or Hepatitis C have significantly lower long term survival rates.

23. In children, patient survival was similar for all disease groups though lower in patients whose primary disease was malignancy. There were no differences in survival between adults and children transplanted for fulminant hepatic failure [acute and sub-acute] with overall five year survival of 76%.

24. Recent cohorts of adult patients with a primary diagnosis of hepatitis B continue to show a significantly improved survival. Adult patients with hepatitis C as primary disease show some improvement in survival in more recent cohorts. Patients transplanted for malignancy continue to have a poor outcome but some improvement in longer term outcome is seen in patients transplanted since 2000.

25-26. Overall graft survival was 86% at one year and 77% at five years with significantly better graft survival longer term in children. Graft survival was significantly worse in second grafts in both children and adults. Third grafts in adults have better outcomes than in children.

27. Overall split liver grafts have similar graft survival to whole liver grafts. Reduced grafts have lower graft survival in the early post-transplant years in both children and adults.

28. Graft survival has increased significantly over time for all deceased donor grafts.

29-30. Vascular complications and rejection were the commonest indications for retransplantation. 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 six months of transplant. Deaths from early graft failure were due to poor or no early graft function. By one year malignancy and graft failure from recurrent disease or chronic rejection cause most deaths. Deaths due to de novo malignancy and chronic rejection are increasing with longer survival times.

35. There was an large increase in the number of cadaveric donors in 2016 to 334 with 367 grafts transplanted from deceased donors. The number of livers split to produce two transplantable grafts was 33 in 2016. Seventeen liver grafts donated after cardiac death were transplanted. The number of people on the waiting list at 31 December 2016 was lower than the number on the waiting list at 31 December 2015.

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

37. One hundred patients [82 children, 18 adults] have now received a living donor graft with six performed in 2016. In 93 patients the living donor graft was a primary graft, in six as a second and one as a third graft. The median age of the donors was 33.8 years with a range of 18.3 to 54.5 years. Four adult grafts were domino whole liver graft.

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Summary

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38. Waiting list activity for 2016 shows the number of patients listed for transplantation continued to increase with 161 remaining on the waiting list at 31 December 2016. Patient delistings due to death, becoming too ill or tumour [HCC] progression accounted for 6% of all delistings. Three hundred and seventy-three patients were transplanted [60%]. Forty-five patients were listed as urgent in 2016 [20 with initial listing as Category 1 and 25 Category 2]. Nineteen [95%] of Category 1 and 24 [100%] of Category 2 patients had a positive outcome.

39-40. Median waiting times varied across the blood groups. Blood group O patients had the longest waiting times to transplant but similar waiting times to B 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 1182 patients (23%) had a liver cancer at the time of transplantation with HCC being the most common (95%). Four hundred and forty-three patients (9%) were transplanted for liver cancer, 739 patients (14%) had liver cancer as a secondary or incidental diagnosis, of which 167 (23%) were undiagnosed prior to transplantation. Three of 1182 patients had both primary and secondary liver cancers and 3 had multiple secondary or incidental liver cancers.

Post transplant 145 (12%) of pretransplant cancers recurred and 131 (11% of those with cancer at transplantation) died as a result of recurrence.

42-43. Actuarial patient survival was 50% 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.

44-48. In patients with liver cancer as a secondary diagnosis, 20 year patient survival was 40%. Seventy-one [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.

Incidence of liver cancer at time of transplantation continues to increase, climbing from 303 to 821 over the last decade.

48-54. Four hundred and twelve de novo non-skin types of cancer developed in 381 (7%) of patients. Thirty patients developed more than one de novo non-skin cancer.

Adult recipient cancer is being more commonly diagnosed from 10 years post transplantation.

The three most common categories of de novo non-skin cancer were cancers of the alimentary tract 144 (35%), lymphoma 107 (26%) and genitourinary 63 (15%).

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

55. Seven hundred and twenty-three (14%) developed a first skin cancer, with a peak of 1-3 years after transplantation, with 343 going on to develop multiple types of skin cancer. Forty-five patients developed 52 melanomas.

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Section 1

Demographic Data

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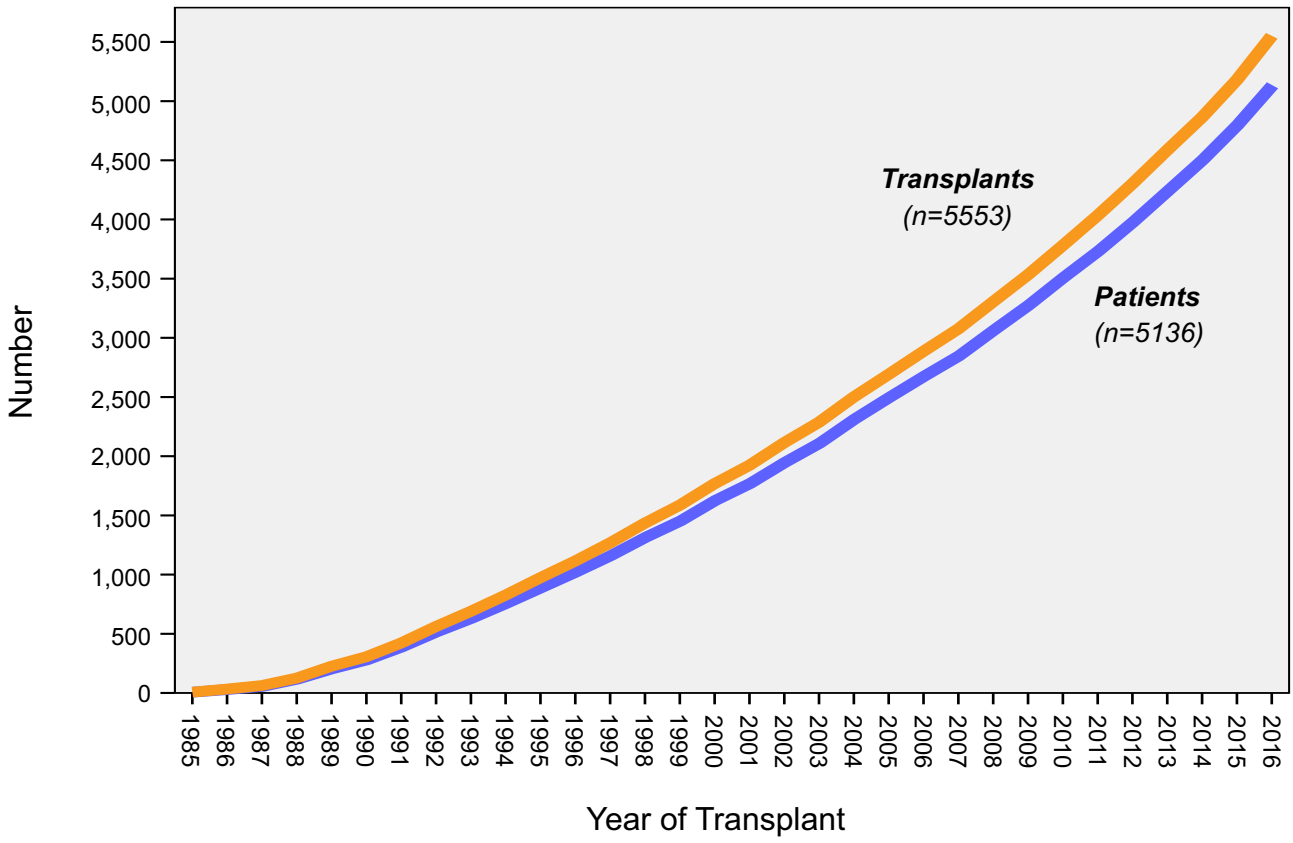
Cumulative Number of Patients & Transplants



Summary Statistics by Age and Gender

ALL PATIENTS TRANSPLANTED

	Children [<16y]	**Adults**	**Total**
Patients	888	4246	5134
Age			
Mean ± SD	4.5 ± 4.5y	49.5 ± 11.7y	41.7 ± 20.2y
Median	2.4y	51.9y	48.9y
Range	24d -15.9y	16.0 - 73.1y	24d - 73.1y
Gender			
Female	457 (52%)	1438 (34%)	1895 (37%)
Male	431 (48%)	2808 (66%)	3239 (63%)
Surviving	727 (82%)	2973 (70%)	3700 (72%)

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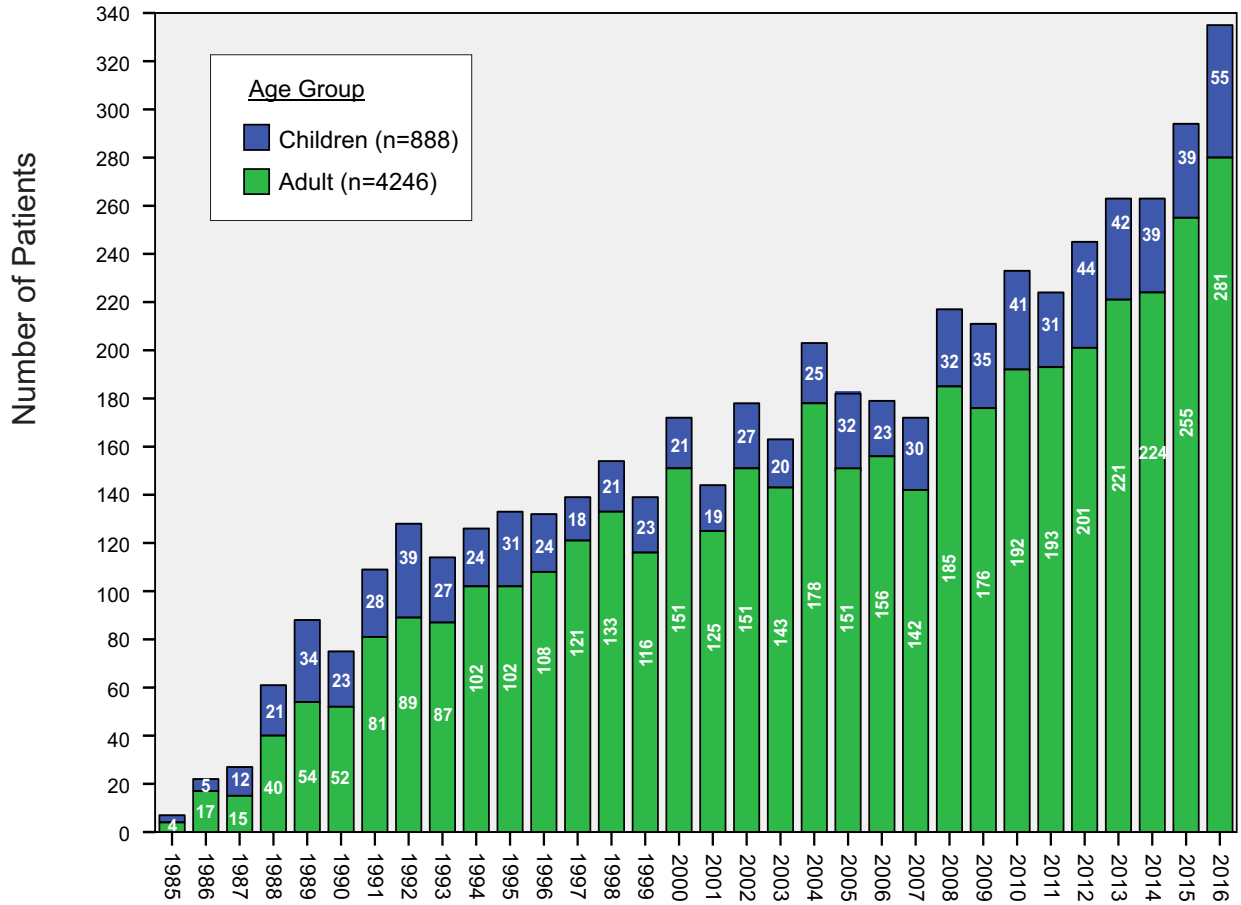
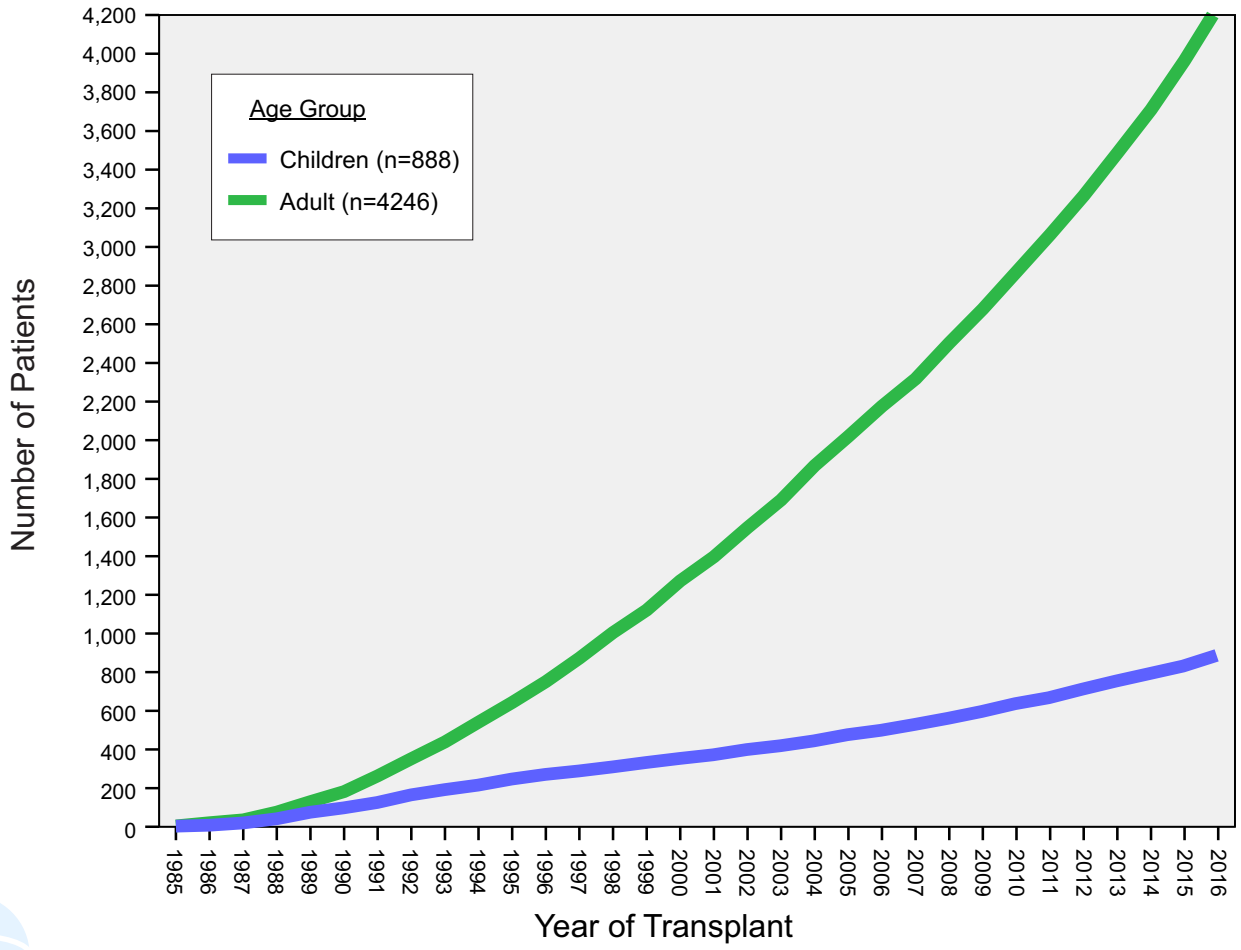
Number of New Patients Transplanted by Year



Cumulative Number of New Patients Transplanted



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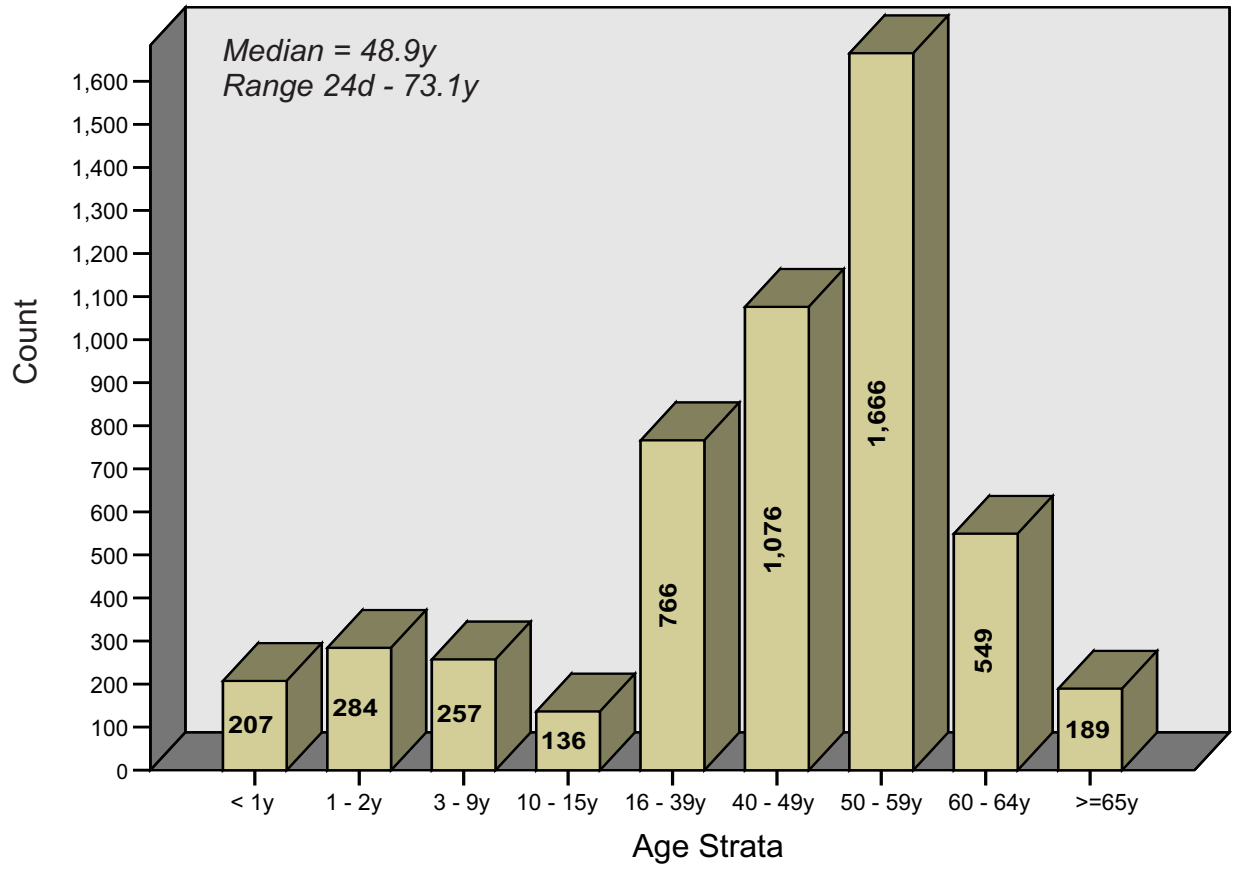
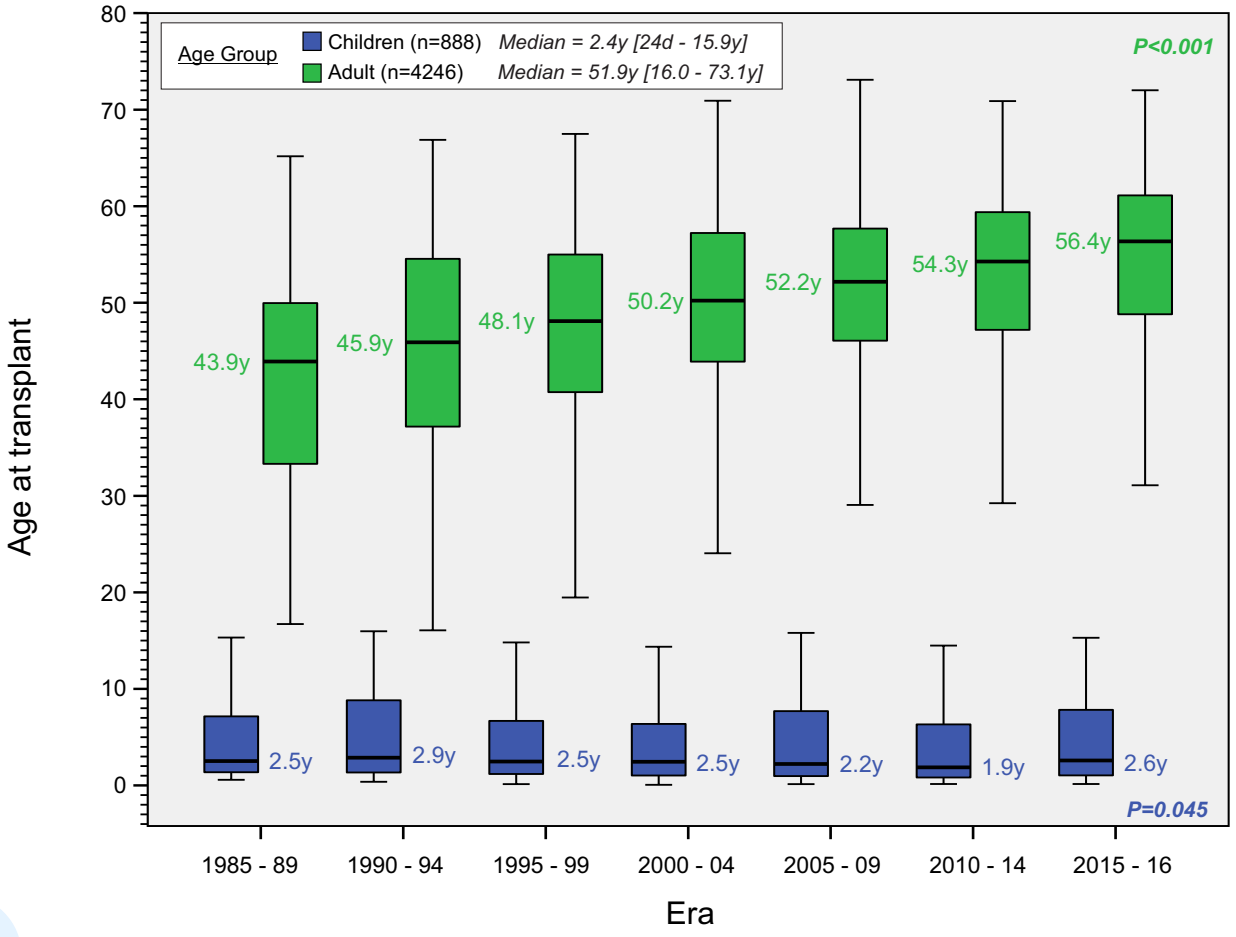
Number of Recipients by Age at Primary Transplant N=5134



Age at Primary Transplant by Era



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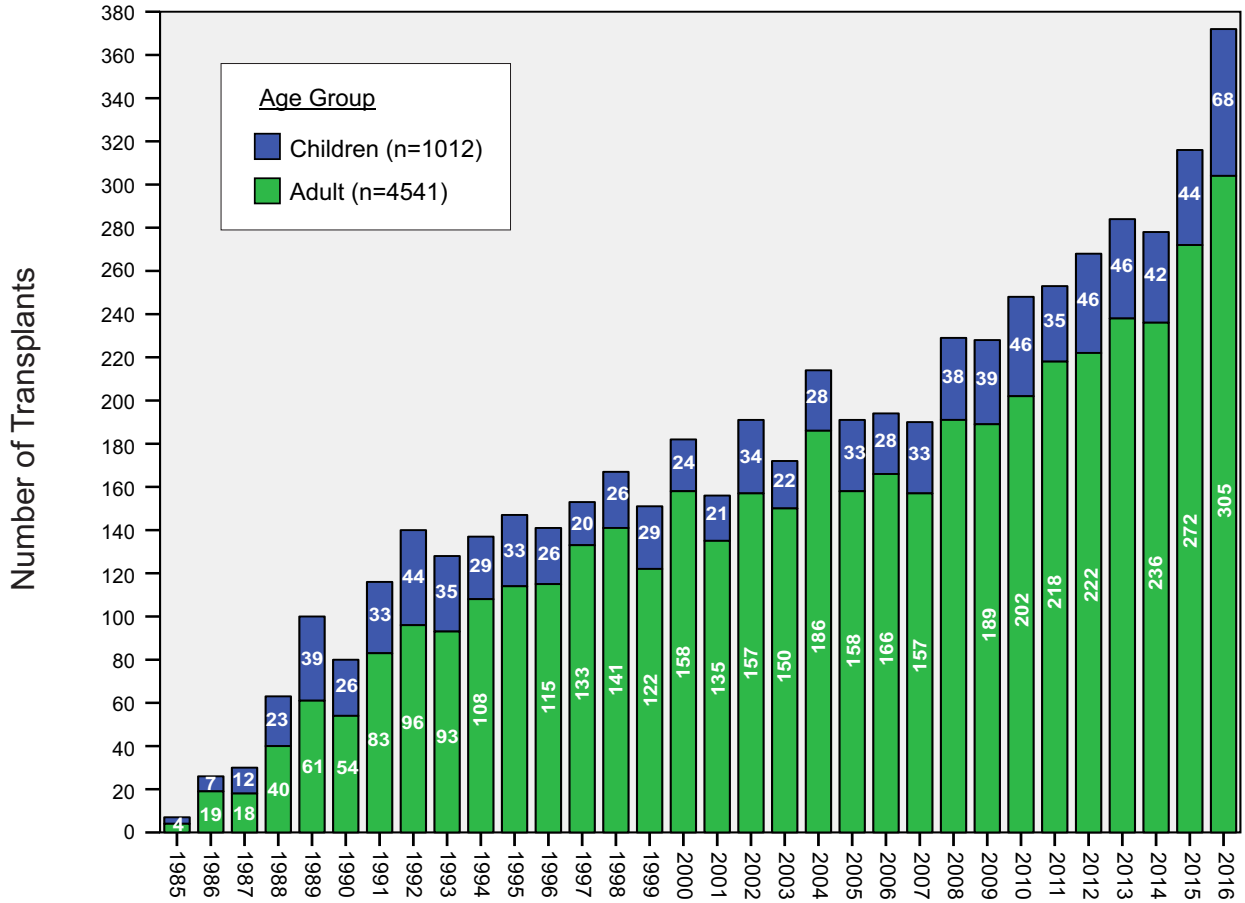
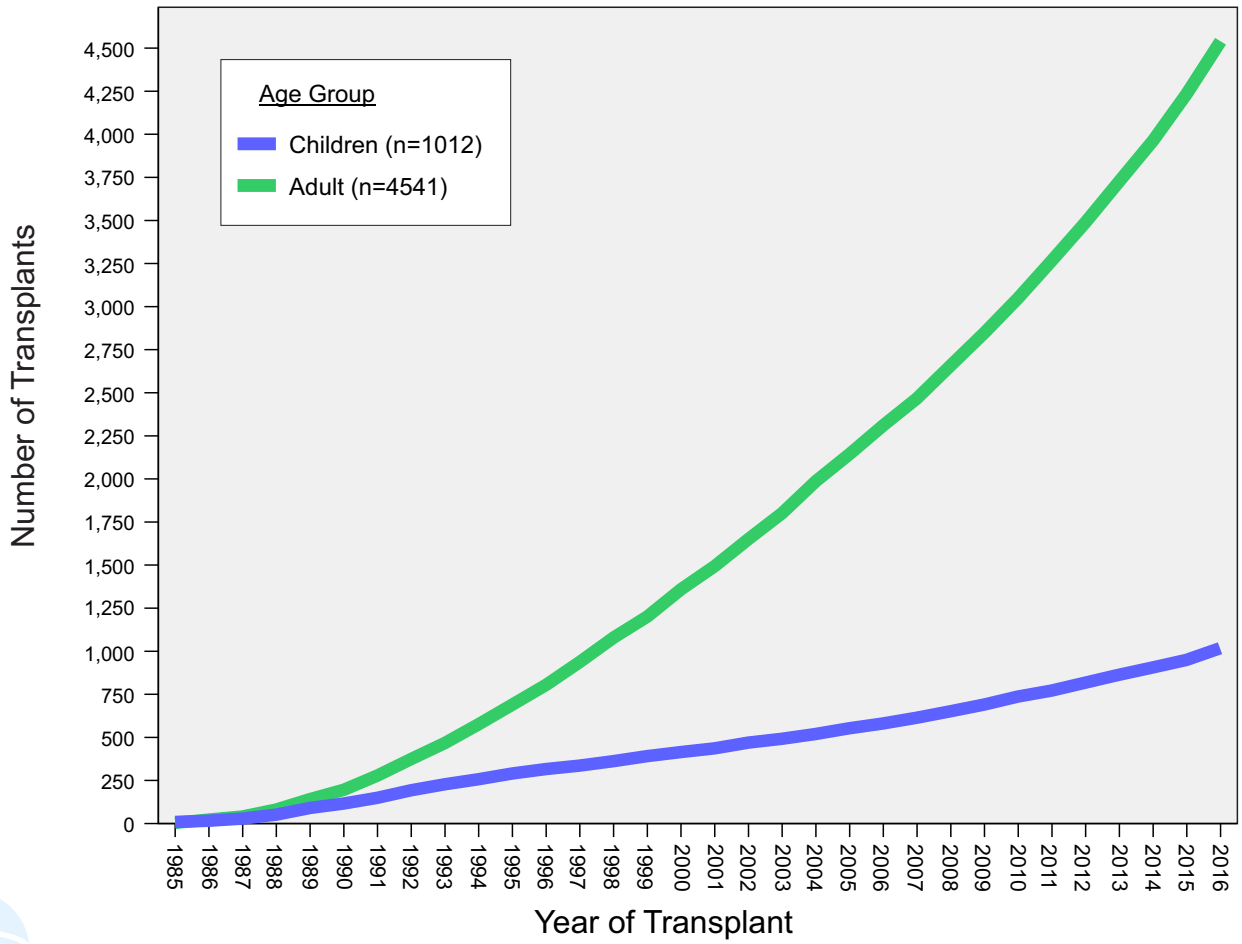
Number of Transplants by Year



Cumulative Number of Transplants



Type of Graft by Year
Split vs Reduced vs Whole

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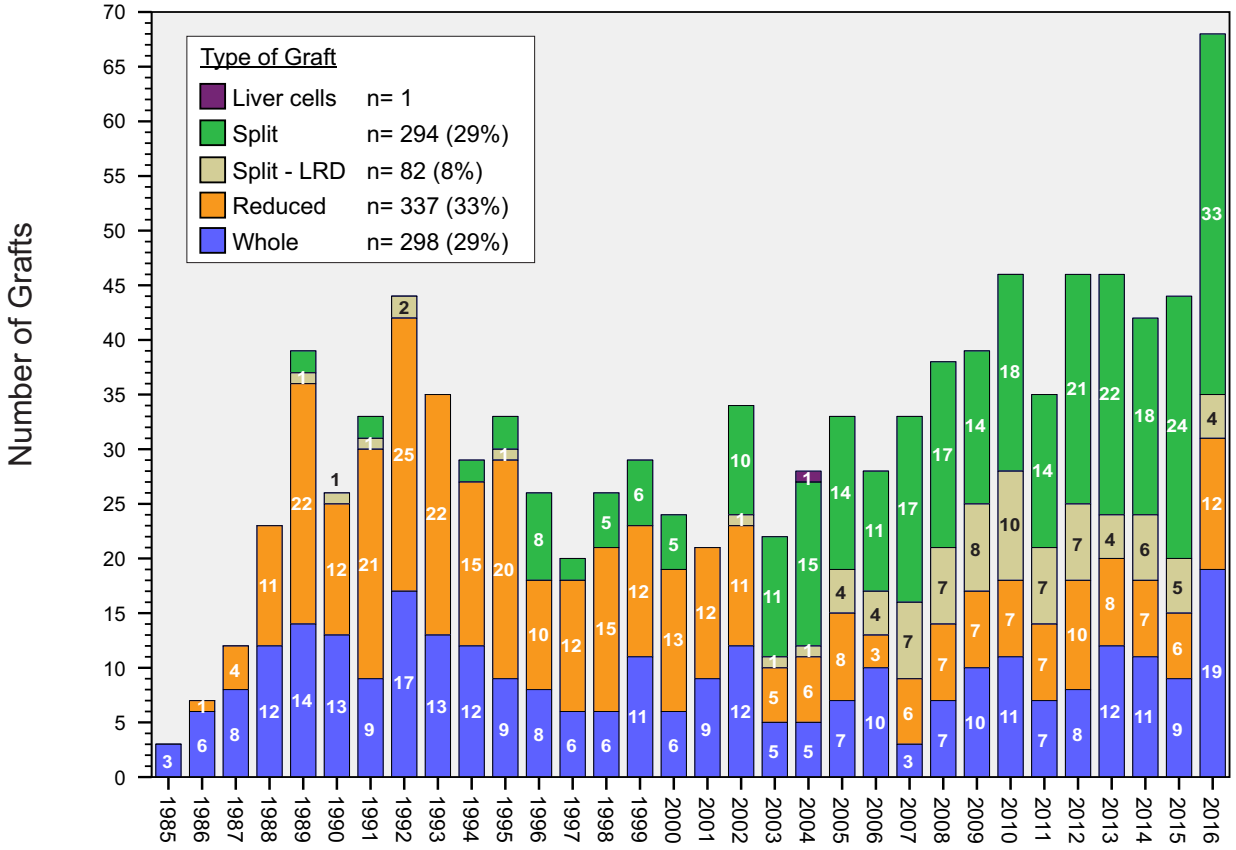
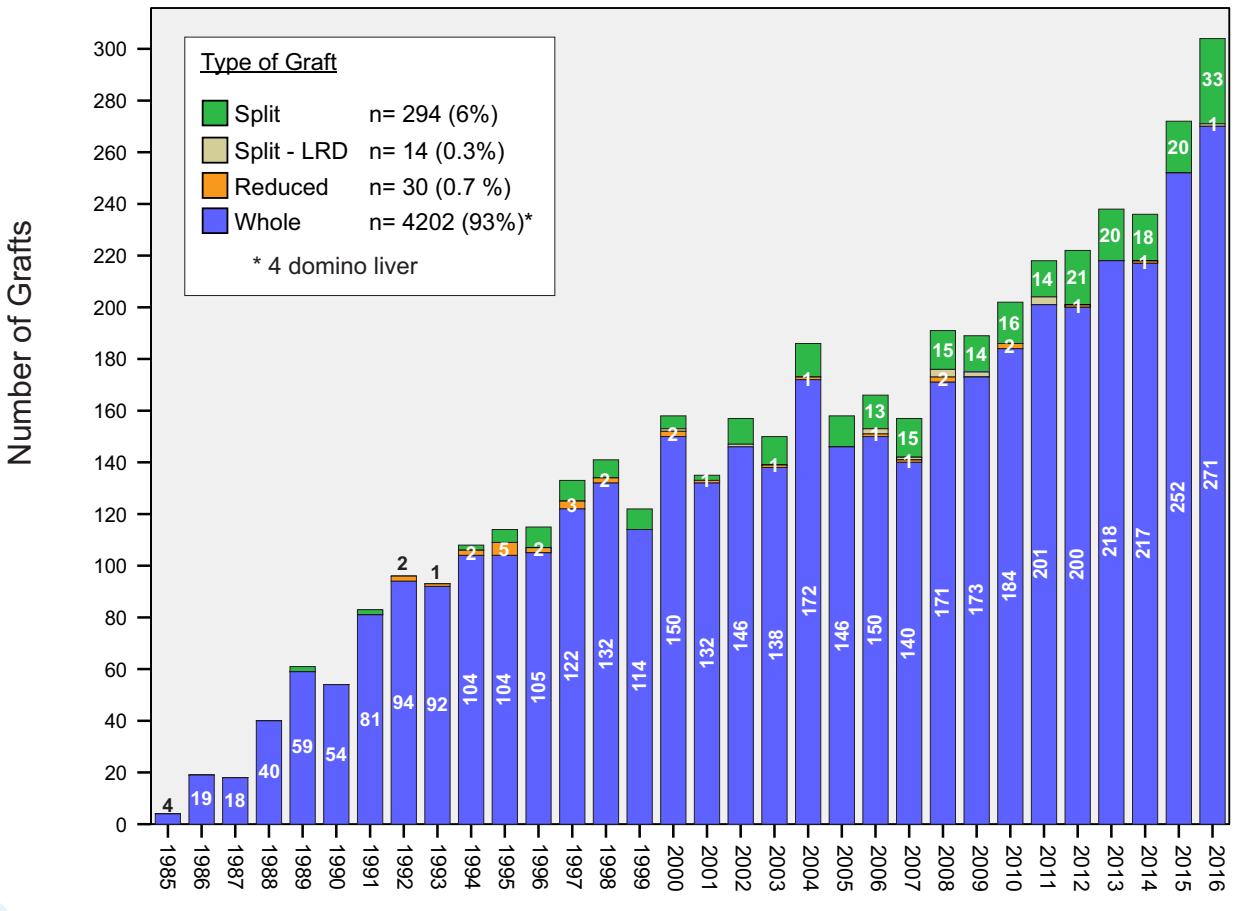
Children (N = 1012)



Adults (N = 4541)



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Section 2

Primary Diagnosis

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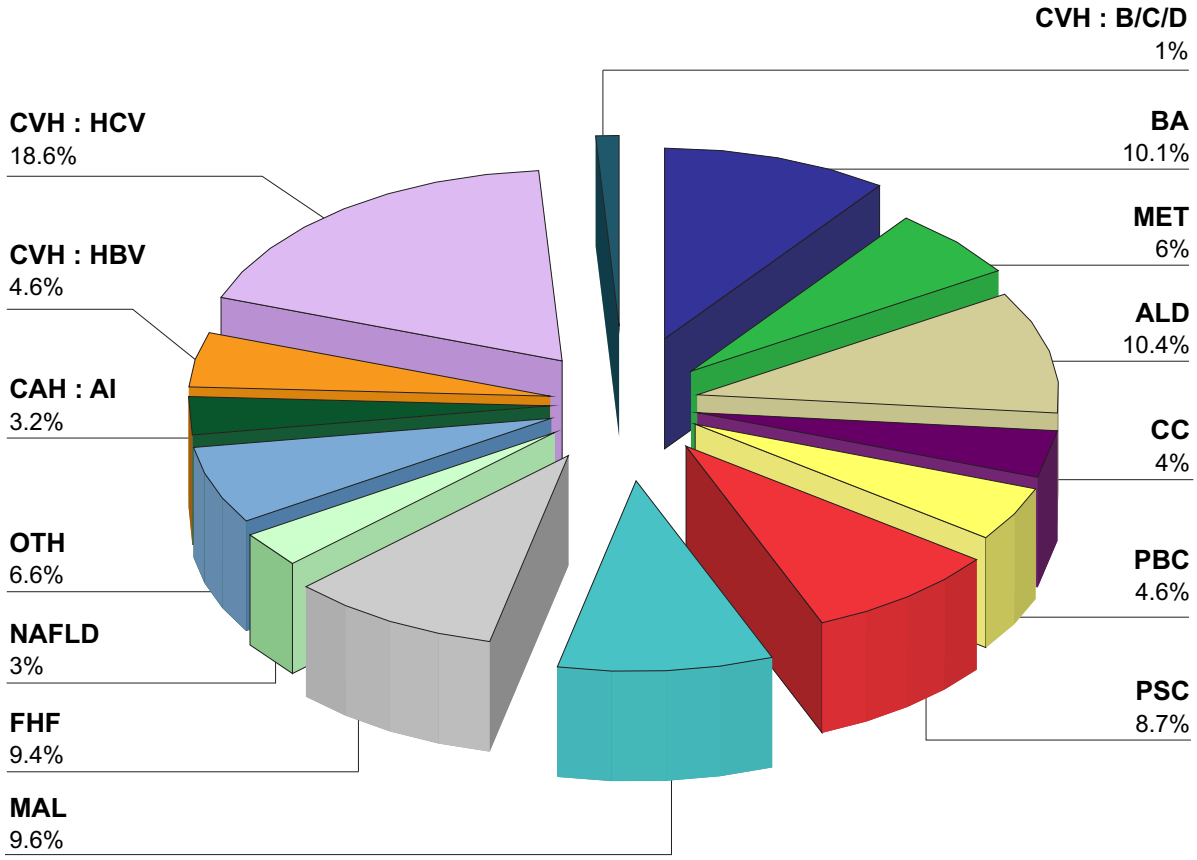
Primary Diseases of All Recipients



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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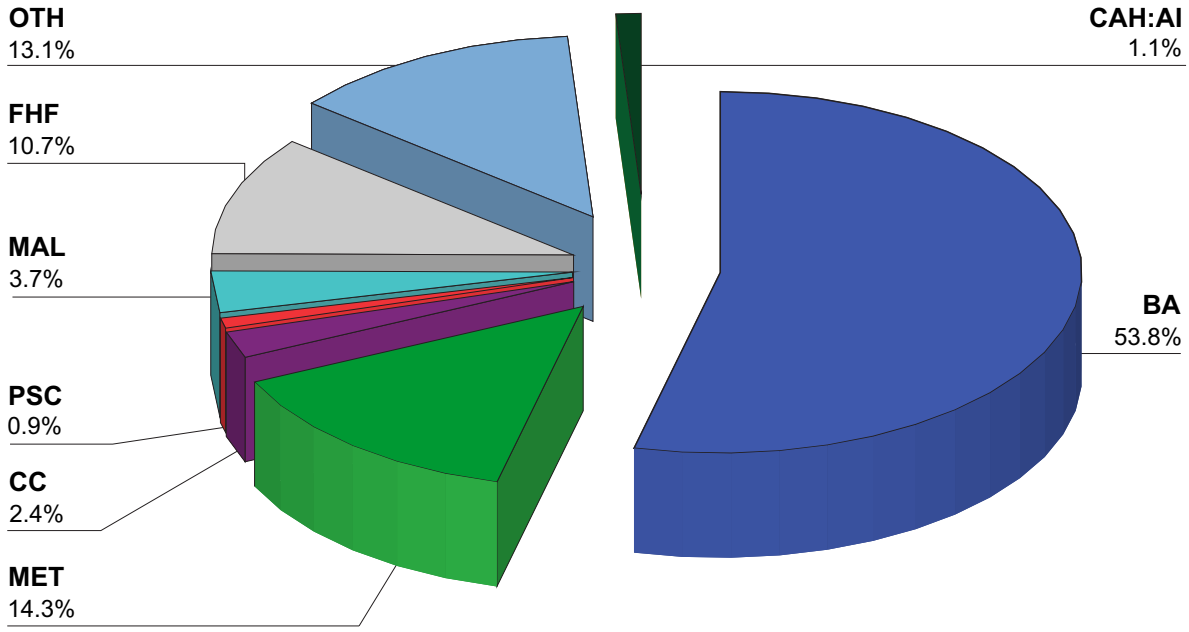
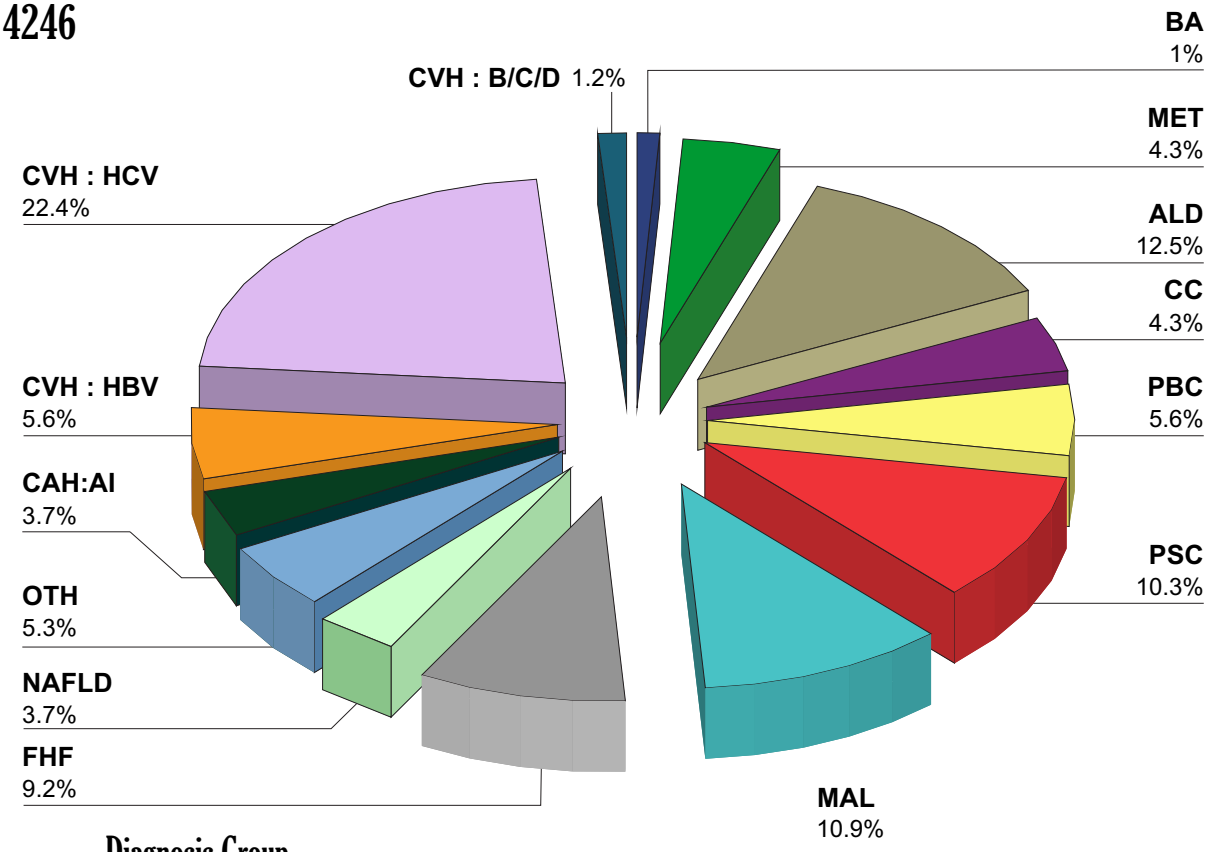
Primary Diseases of Children
N =888



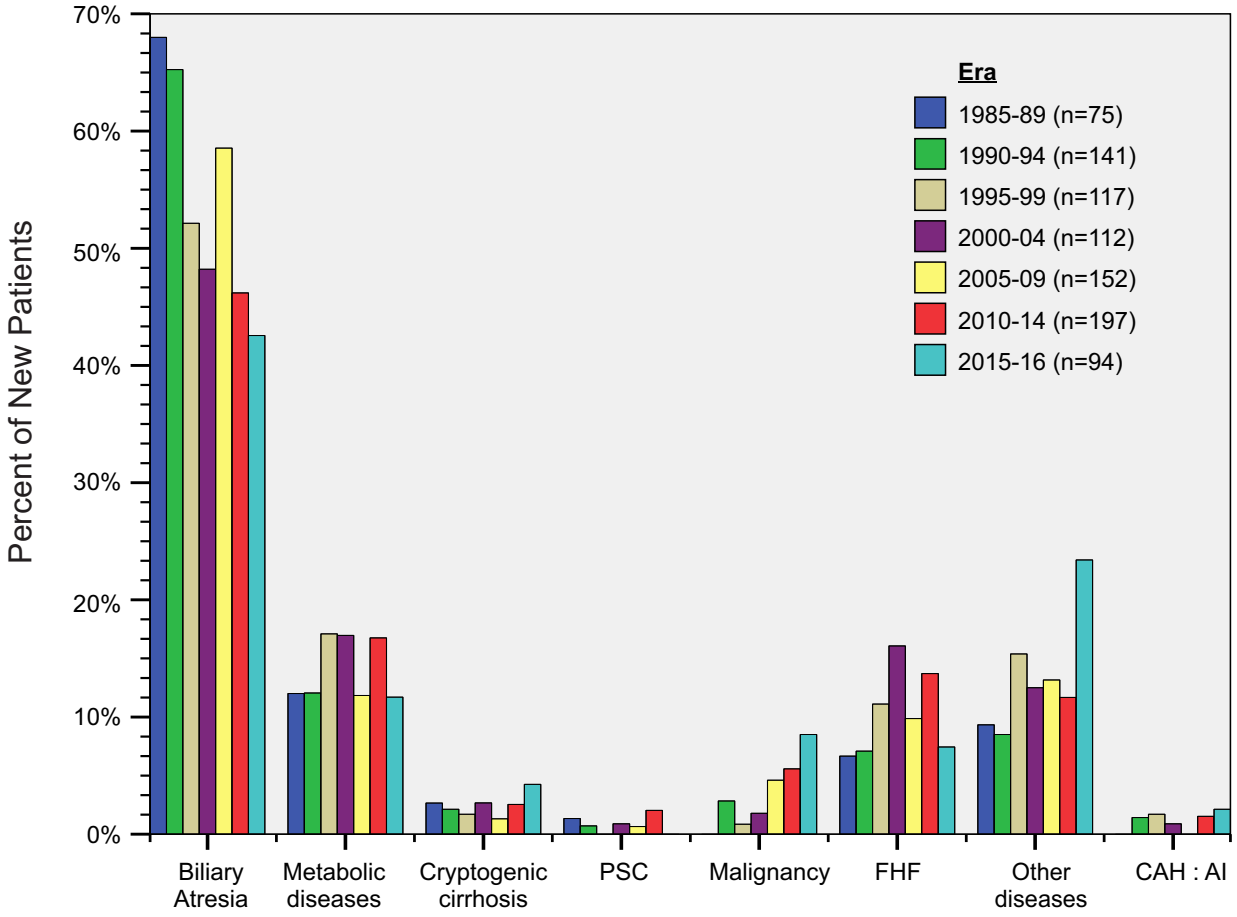
Primary Diseases of Adult Recipients
N = 4246



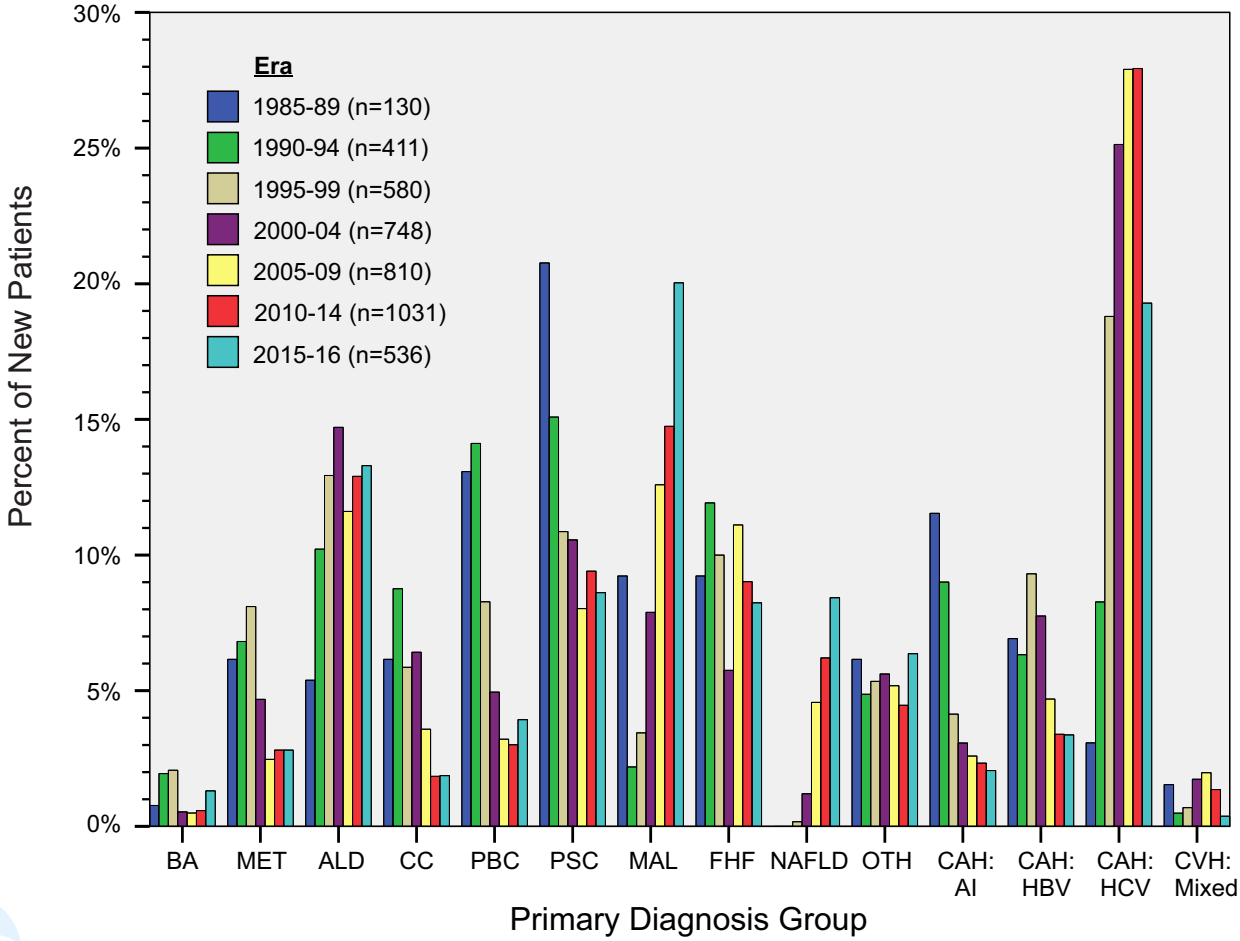
Diagnosis Group

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

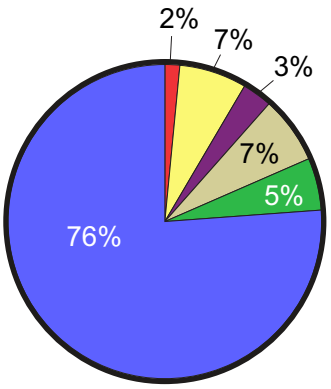
Children (N=888)



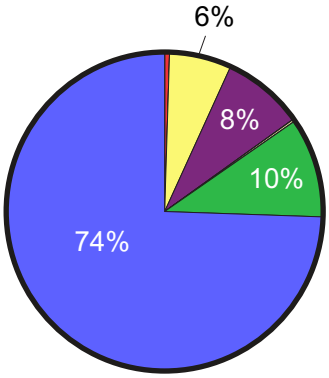
Adults (N = 4246)



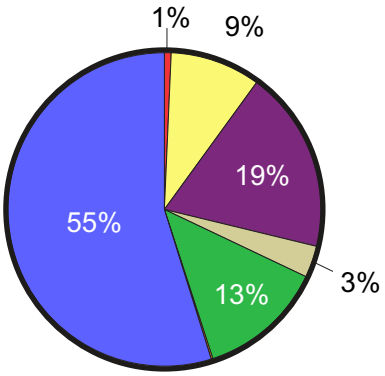
1985 - 89
(n=130)



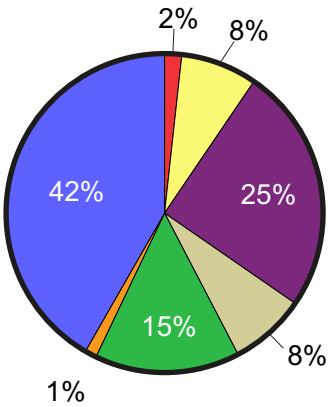
1990 - 94
(n=411)



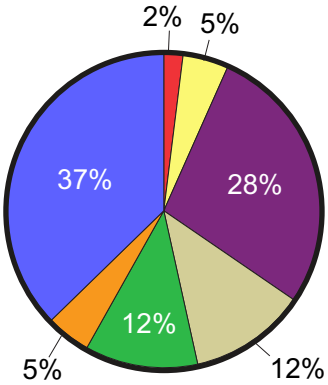
1995 - 99
(n=580)



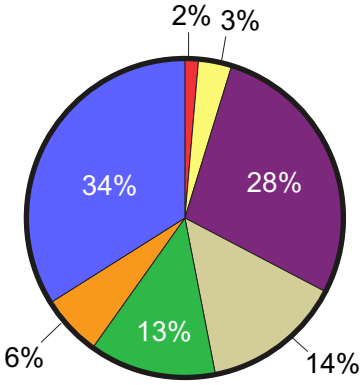
2000 - 04
(n=748)



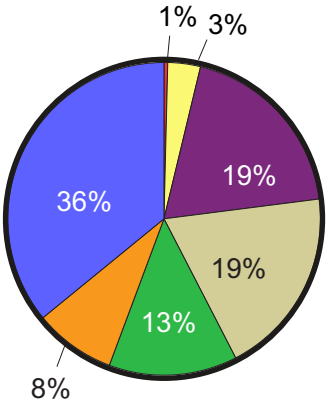
2005 - 09
(n=810)

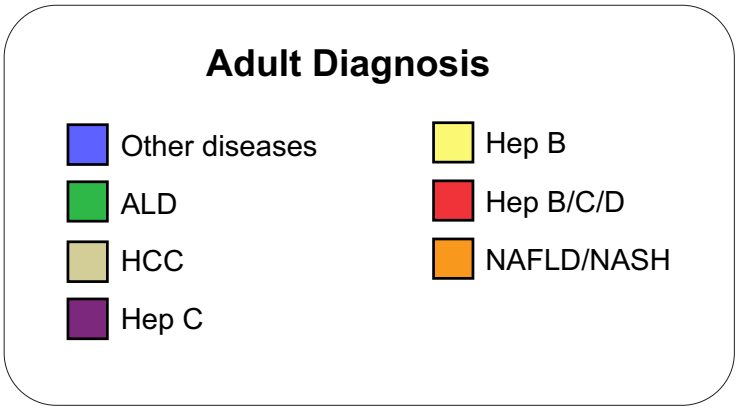


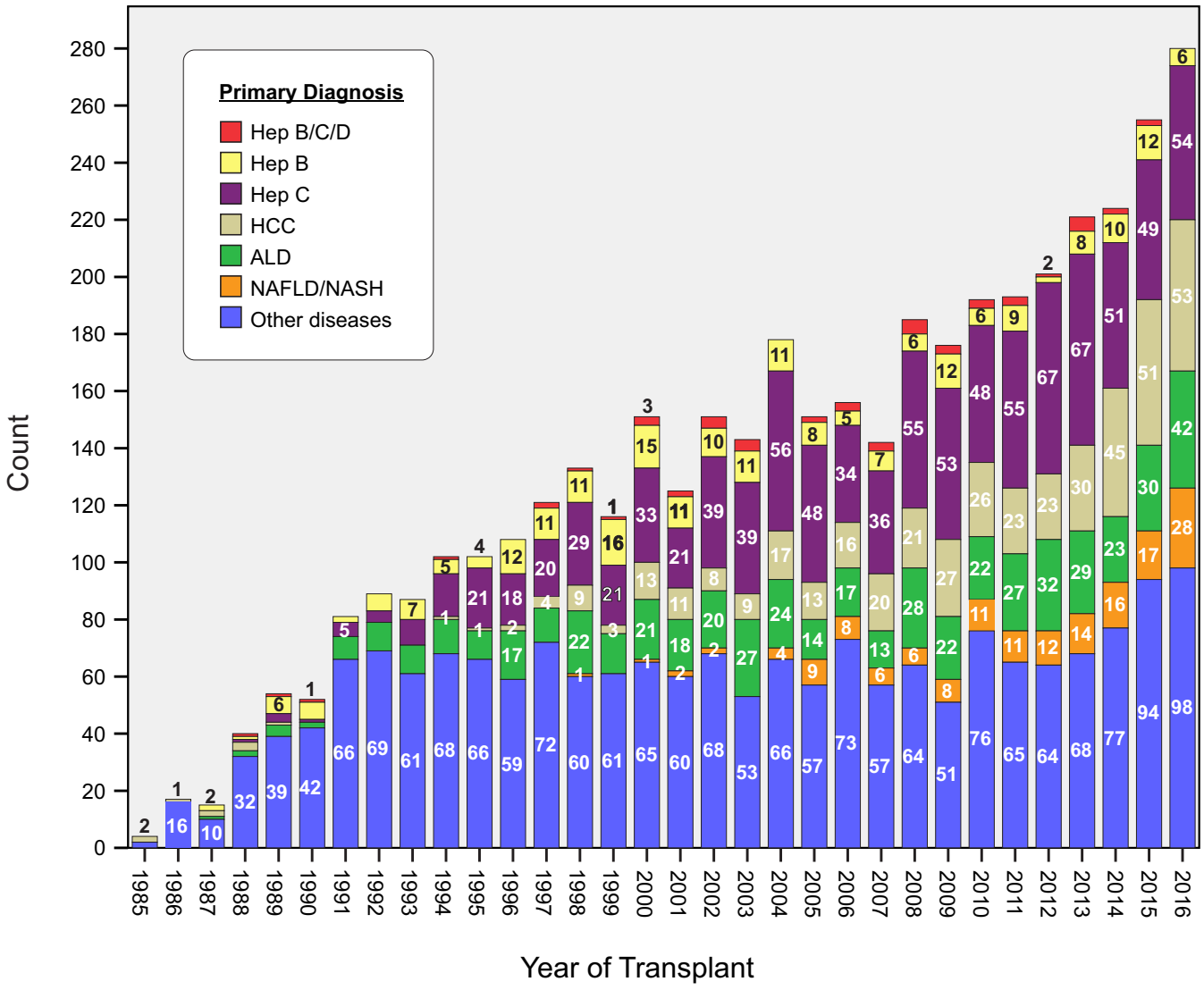
2010 - 14
(n=1031)



2015-2016
(n=536)







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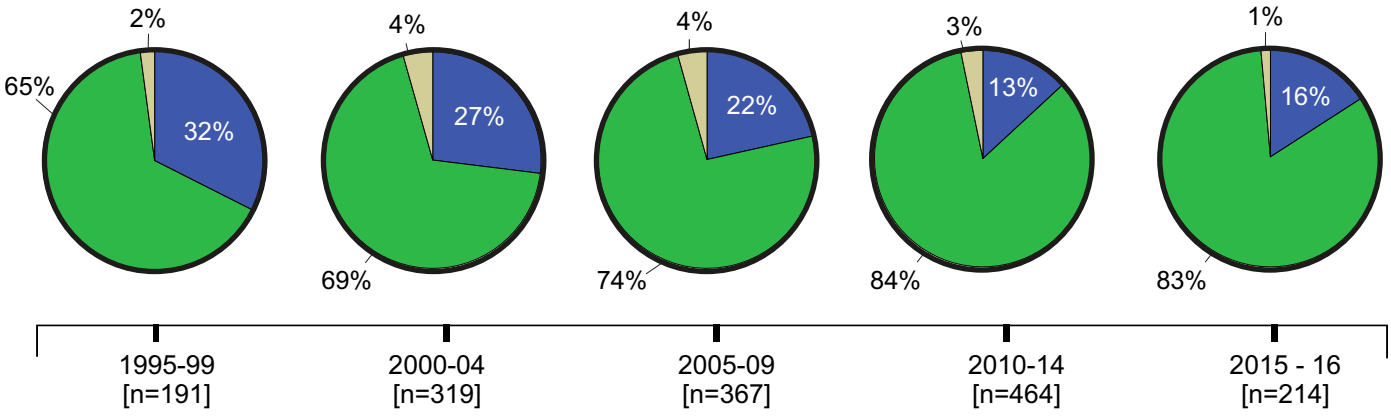
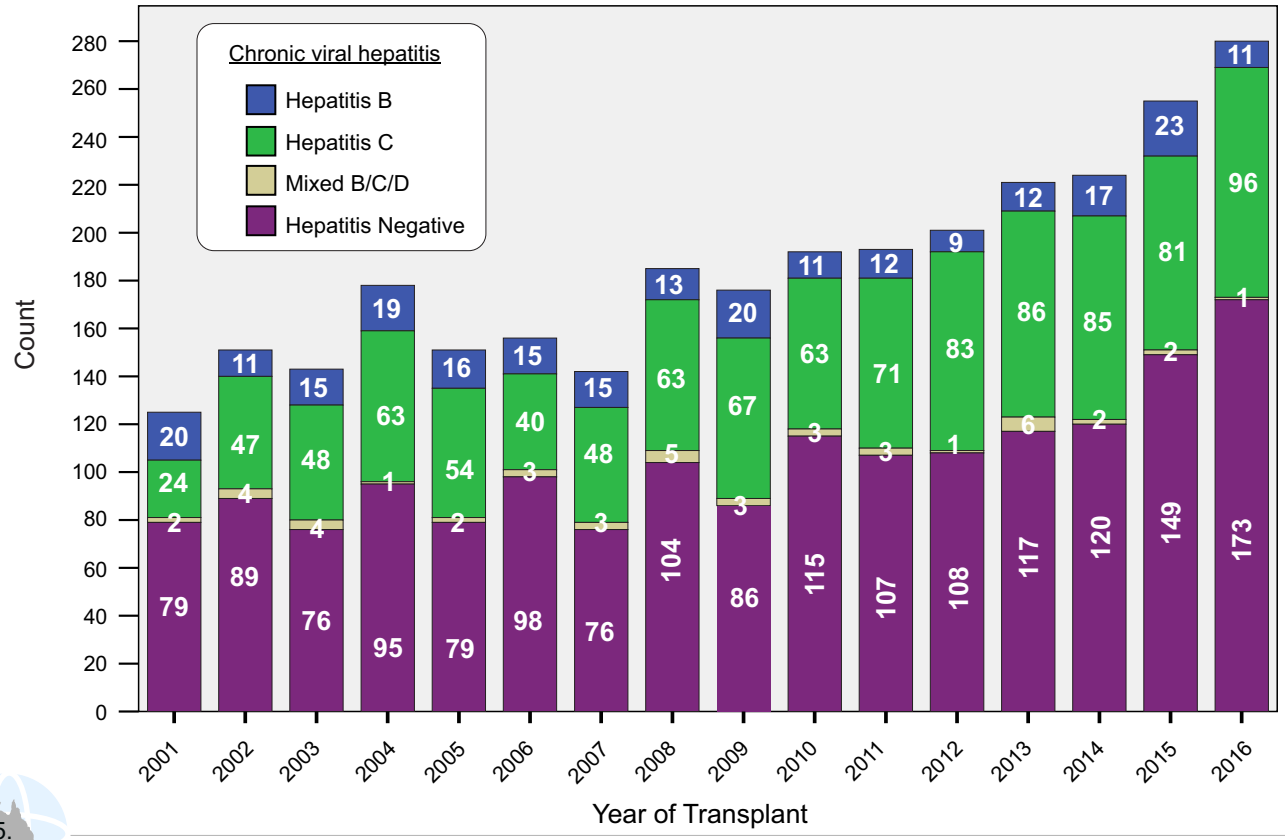
Chronic Viral Hepatitis as Primary or Secondary Diagnosis in Adult Patients

Primary Diagnosis	n =	Secondary / Tertiary diagnosis: Hepatitis C	Hepatitis B	Hepatitis B,C	HCC	NAFLD	ALD
Hepatitis C	952		7		302	10	257
Hepatitis B	238	2			99	2	7
Hepatitis BD/BC/BCD	53				10		8
HCC + cirrhosis	435	232	106	7		20	101
ALD	533	31	3		70	18	
NAFLD	156	1	2		38		15
Other	1879	17	9		62	4	23
TOTAL	4246						

Type of Chronic Viral Hepatitis in Adult Patients by Era



Hepatitis Diagnosis



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Section 3

Patient Survival

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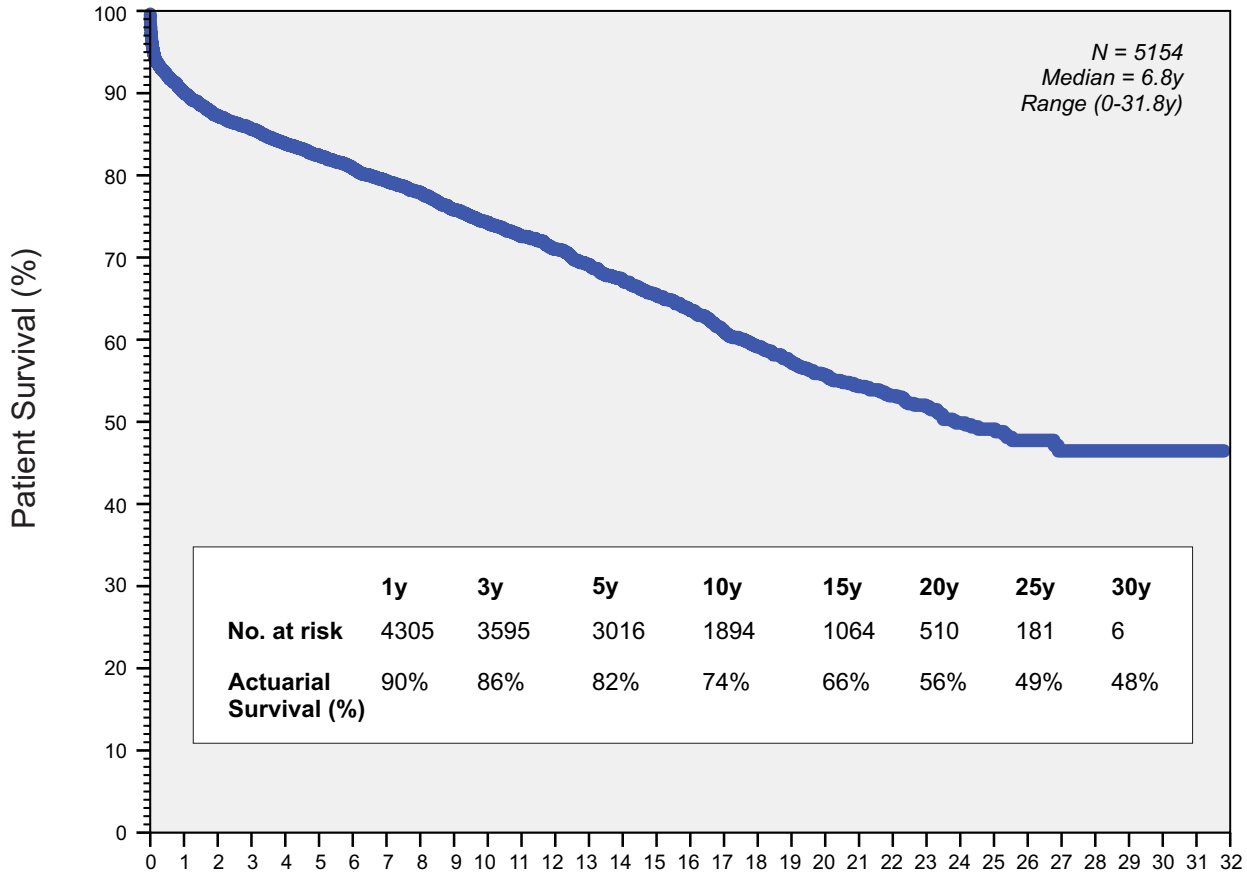
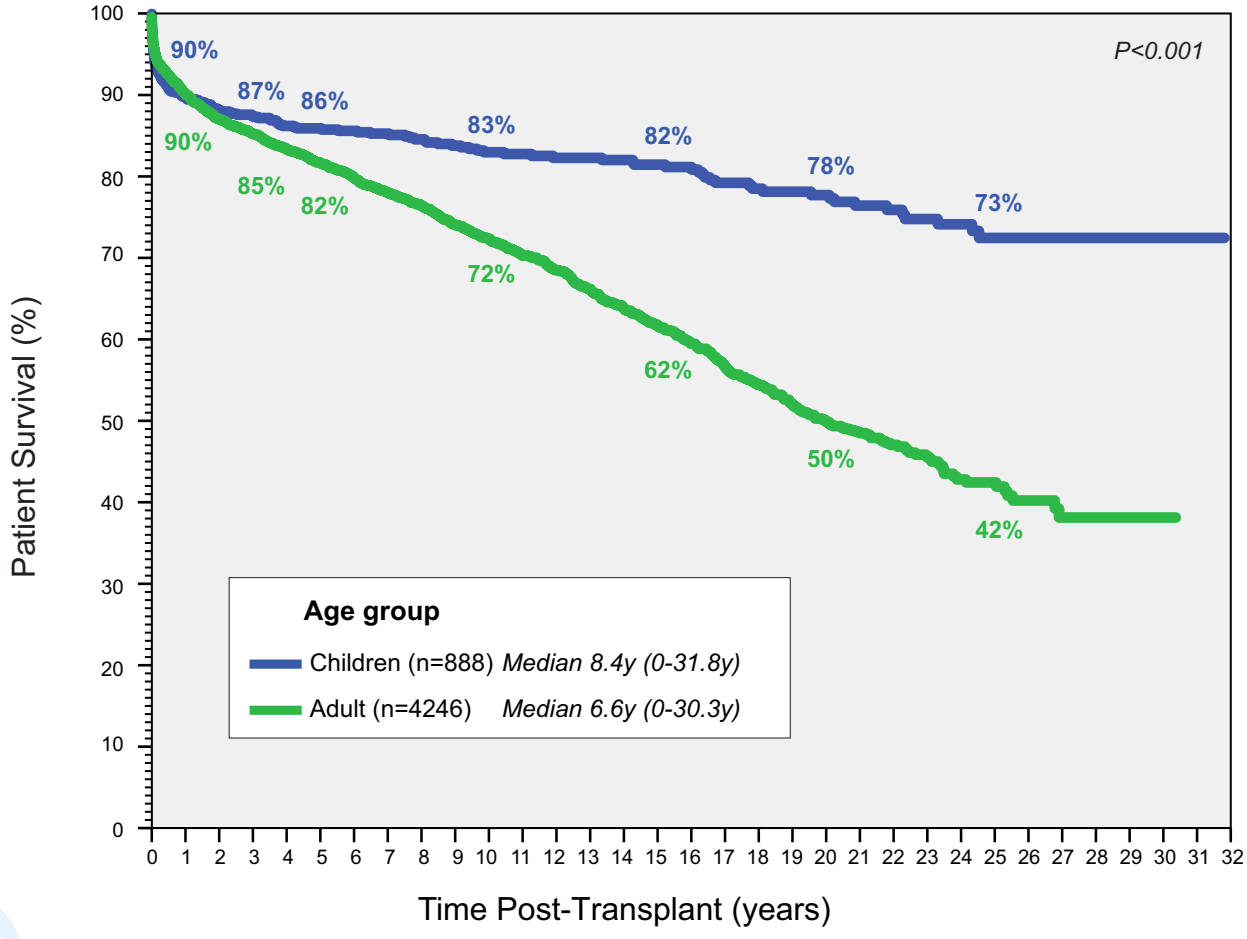
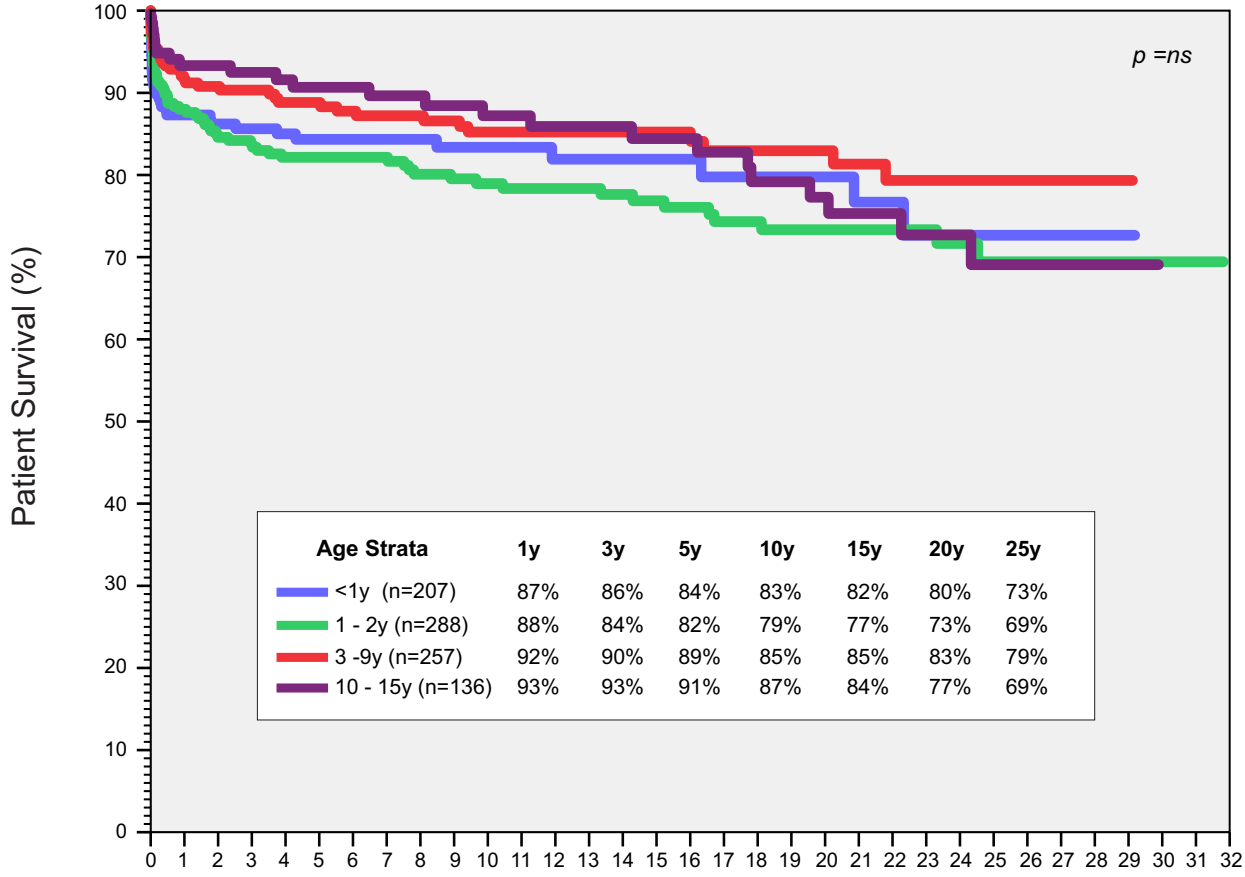
Patient Survival Post Transplant



	1y	3y	5y	10y	15y	20y	25y	30y
No. at risk	4305	3595	3016	1894	1064	510	181	6
Actuarial Survival (%)	90%	86%	82%	74%	66%	56%	49%	48%

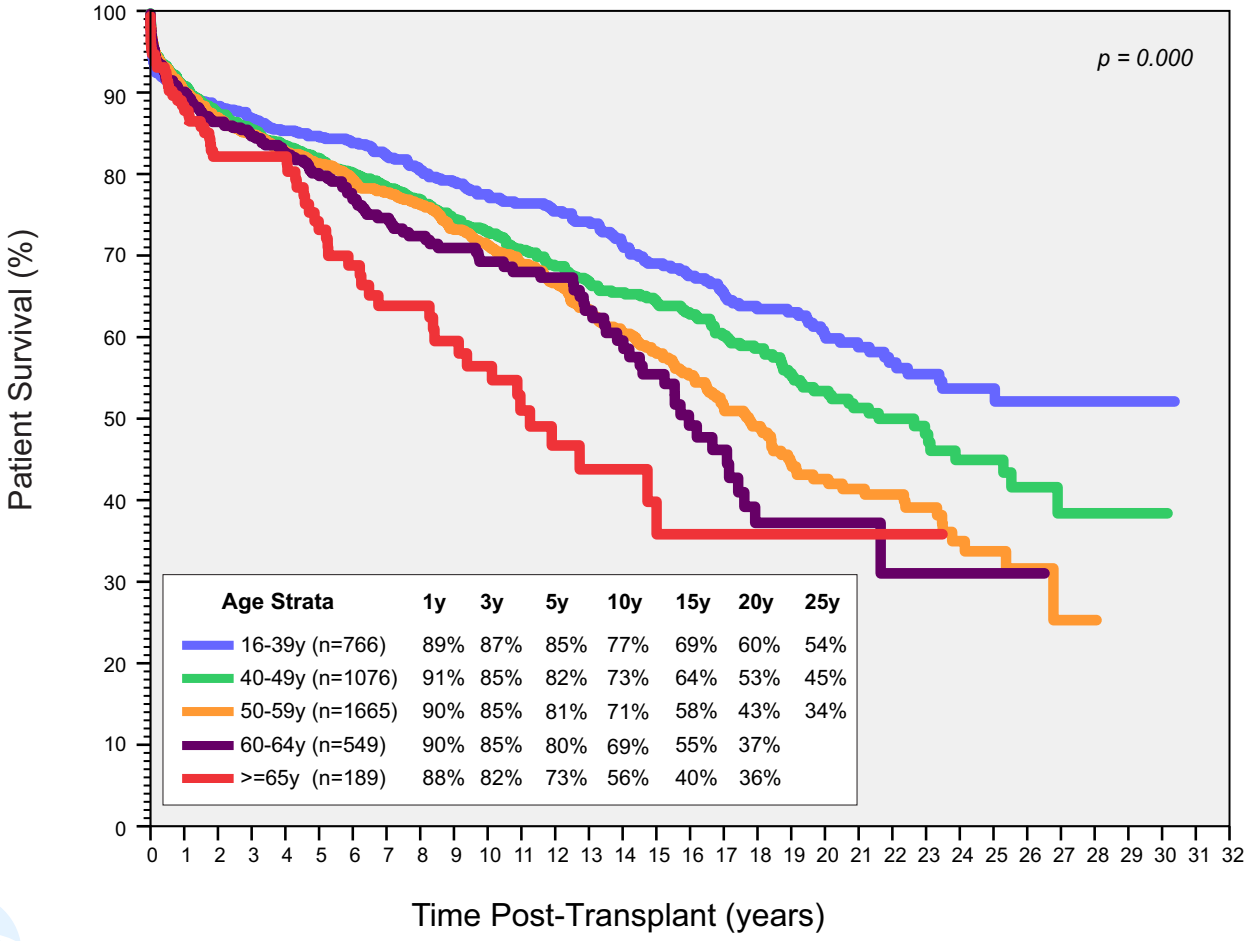


Children (N = 888)



Age Strata	1y	3y	5y	10y	15y	20y	25y
<1y (n=207)	87%	86%	84%	83%	82%	80%	73%
1 - 2y (n=288)	88%	84%	82%	79%	77%	73%	69%
3 -9y (n=257)	92%	90%	89%	85%	85%	83%	79%
10 - 15y (n=136)	93%	93%	91%	87%	84%	77%	69%

Adults (N = 4246)



Age Strata	1y	3y	5y	10y	15y	20y	25y
16-39y (n=766)	89%	87%	85%	77%	69%	60%	54%
40-49y (n=1076)	91%	85%	82%	73%	64%	53%	45%
50-59y (n=1665)	90%	85%	81%	71%	58%	43%	34%
60-64y (n=549)	90%	85%	80%	69%	55%	37%	
>=65y (n=189)	88%	82%	73%	56%	40%	36%	

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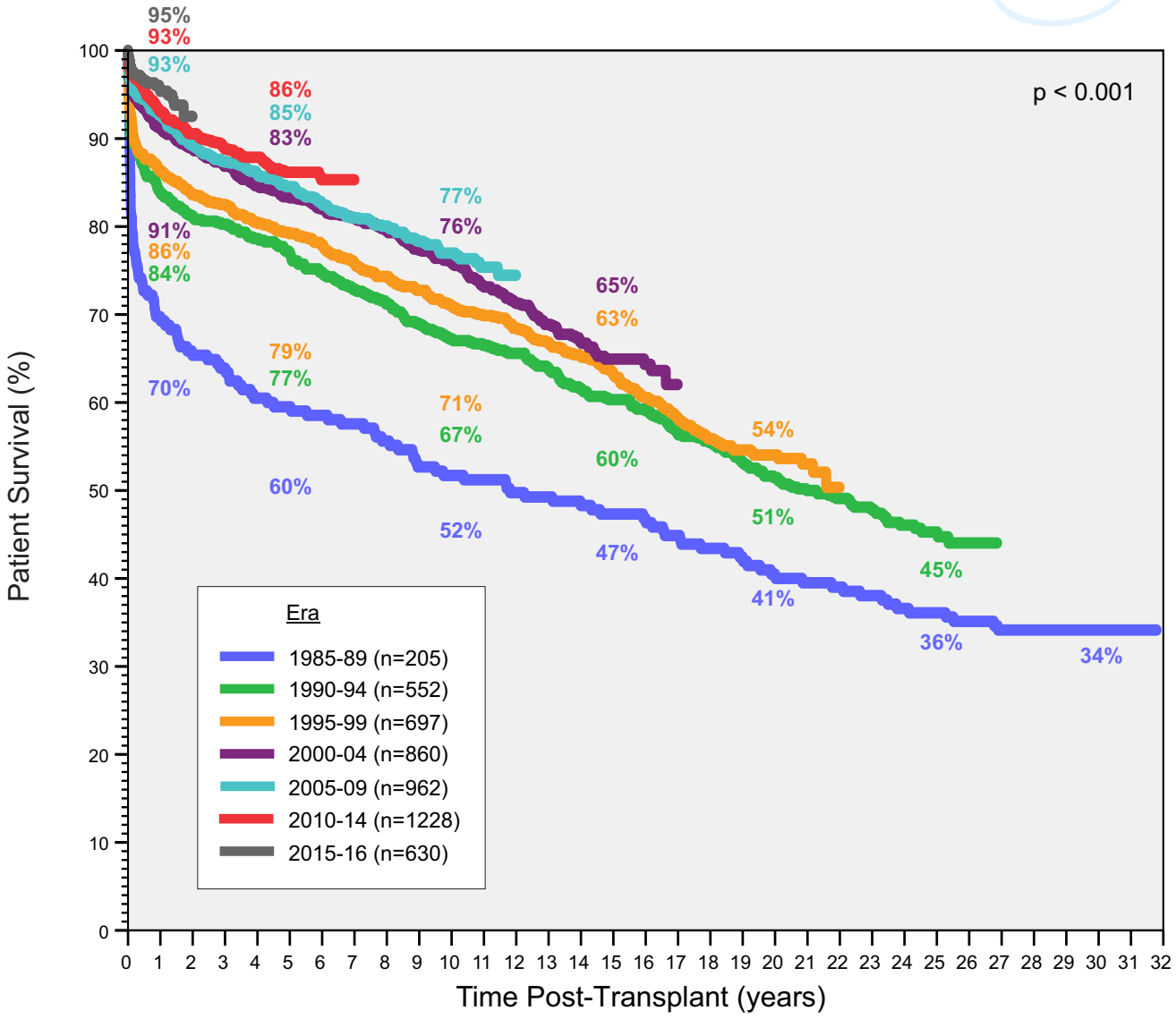
All Patient Survival by Year of Transplant



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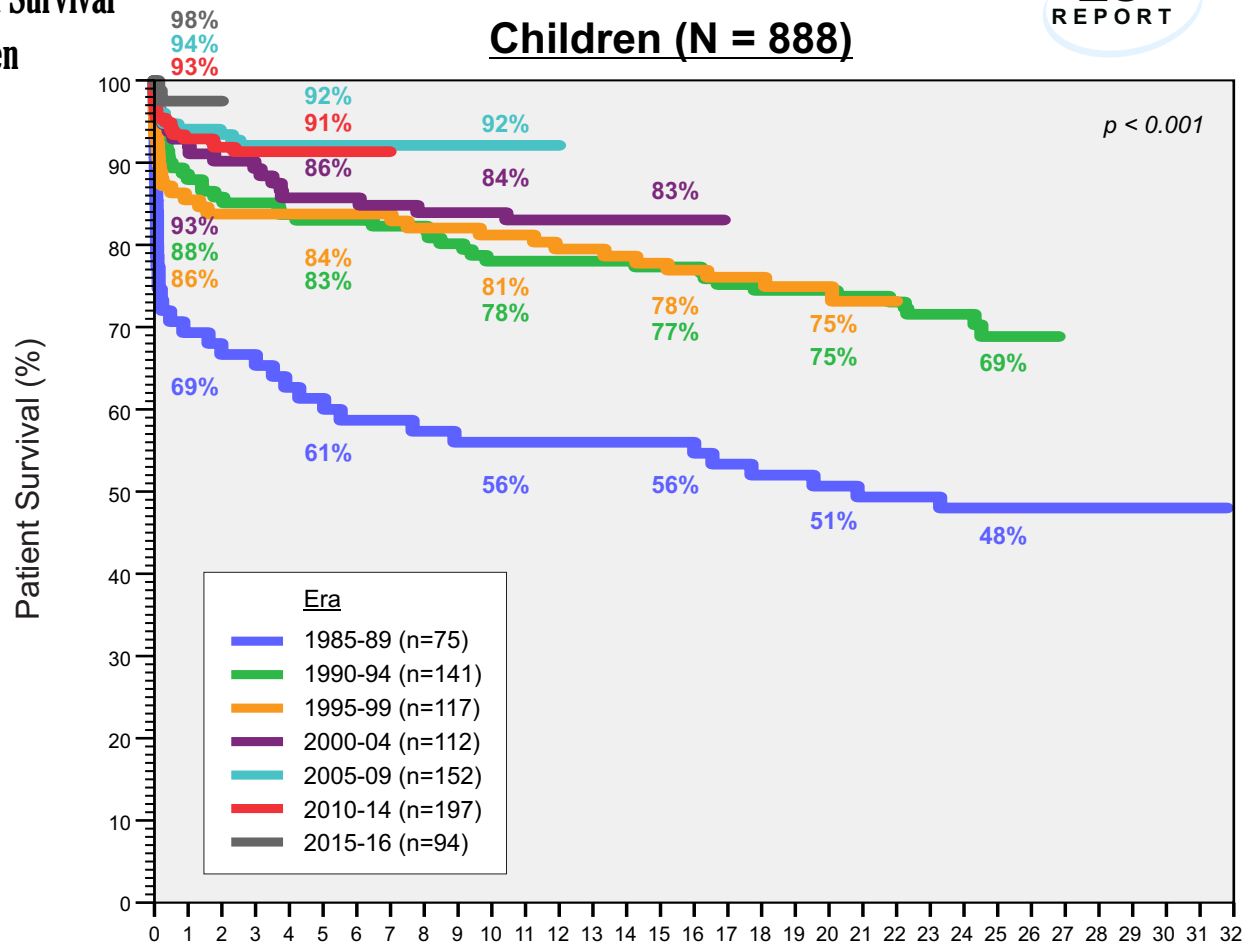
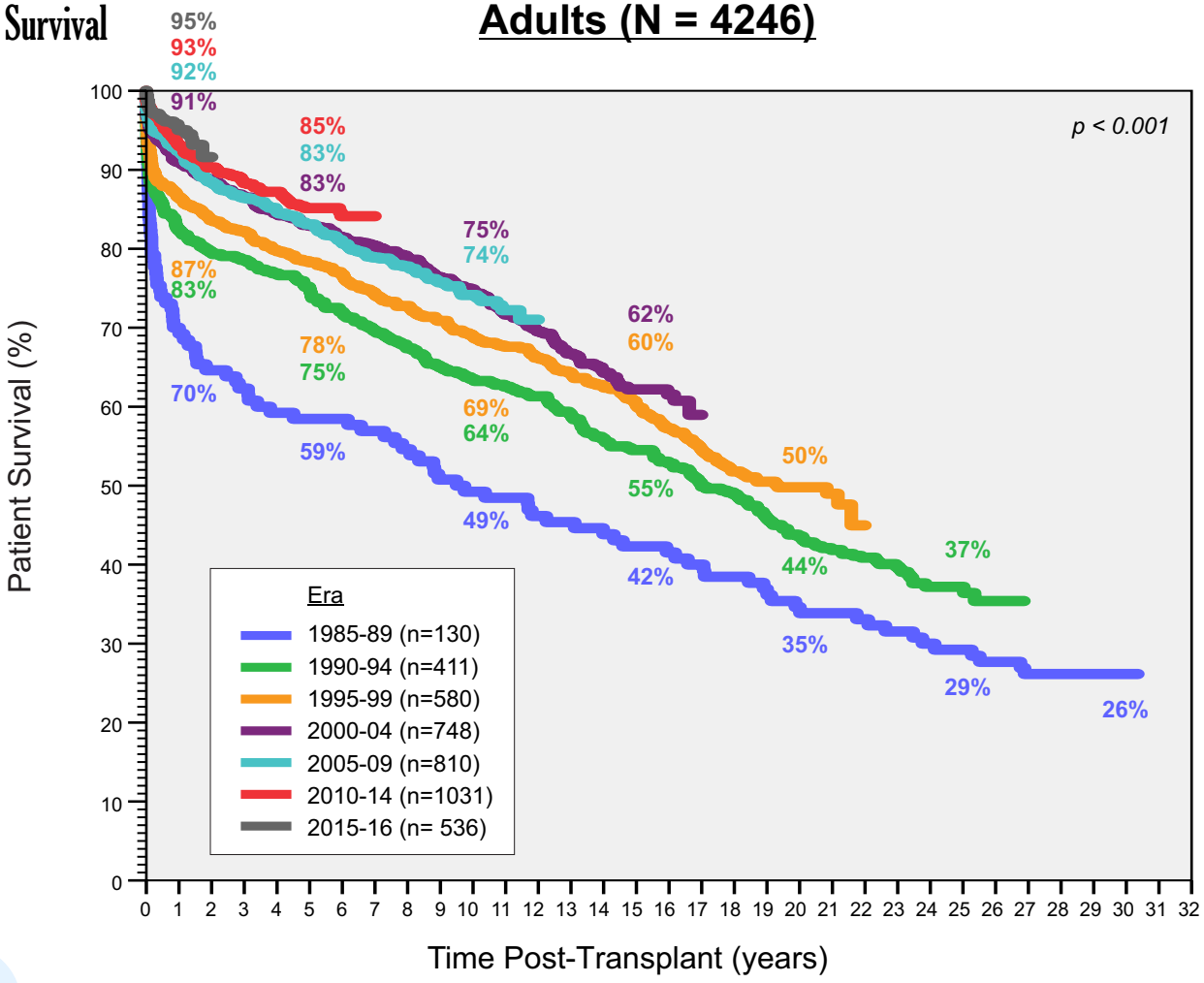
Patient Survival Children



Patient Survival Adults



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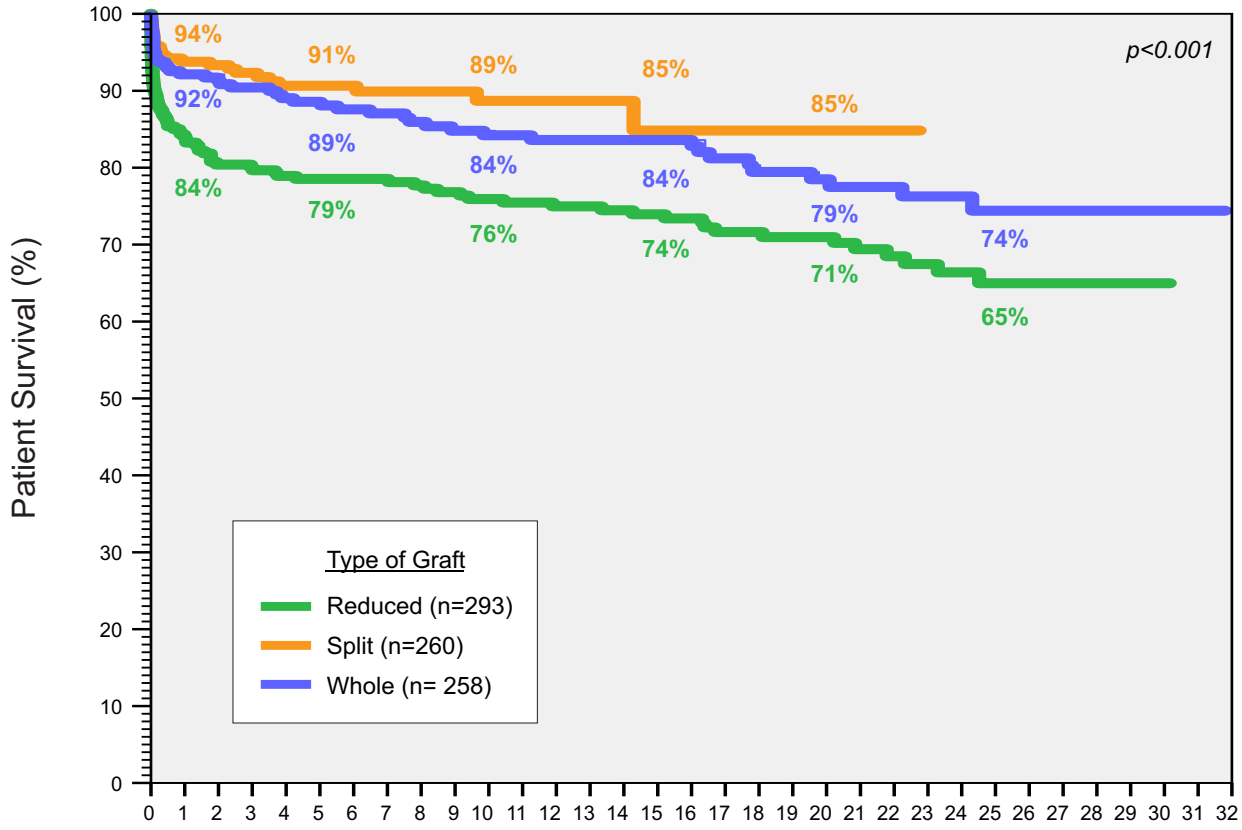
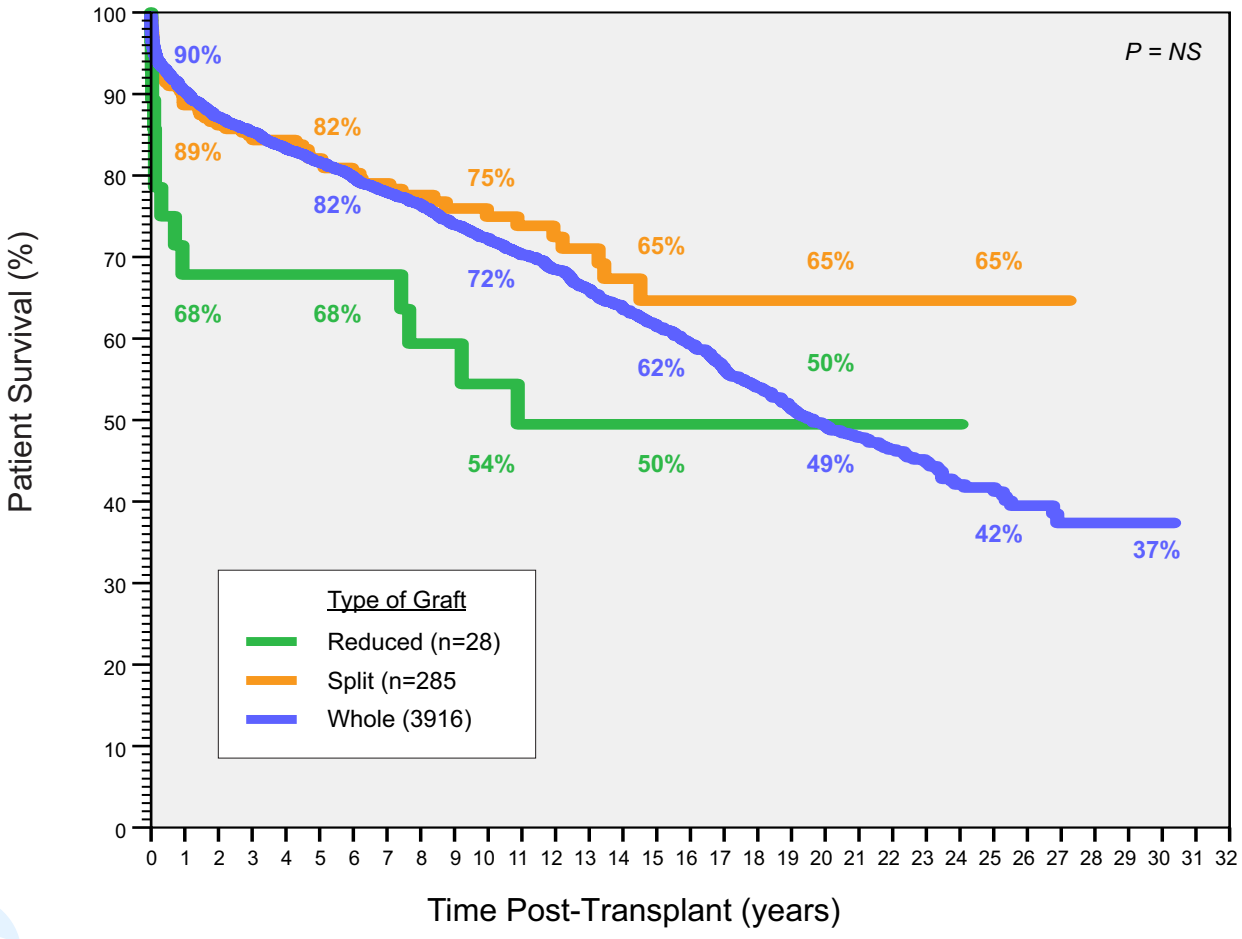
Patient Survival by Type of Primary Graft [deceased donors]

Children (N = 811)



Adults (N = 4229)



Patient Survival by Weight - Children

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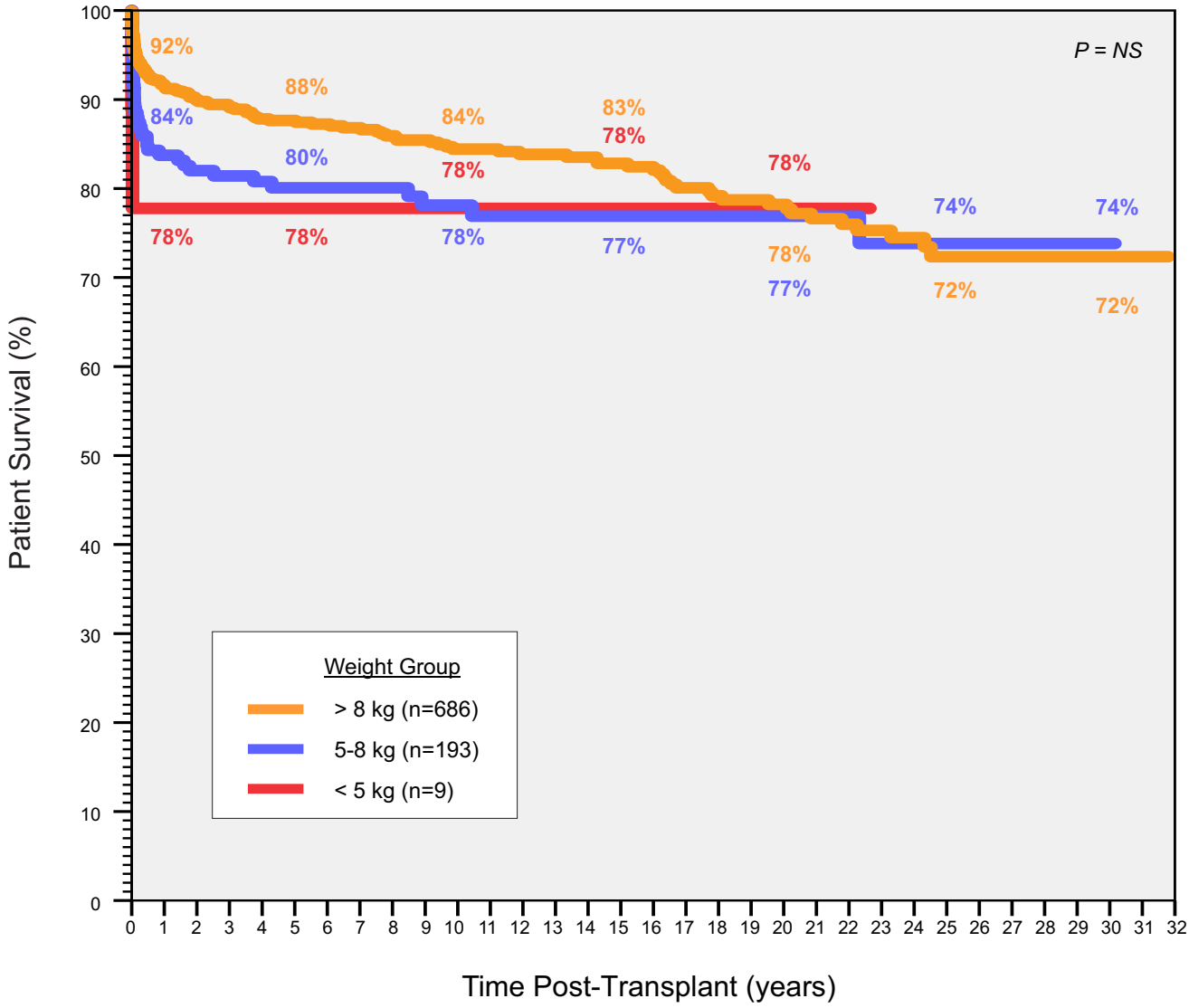

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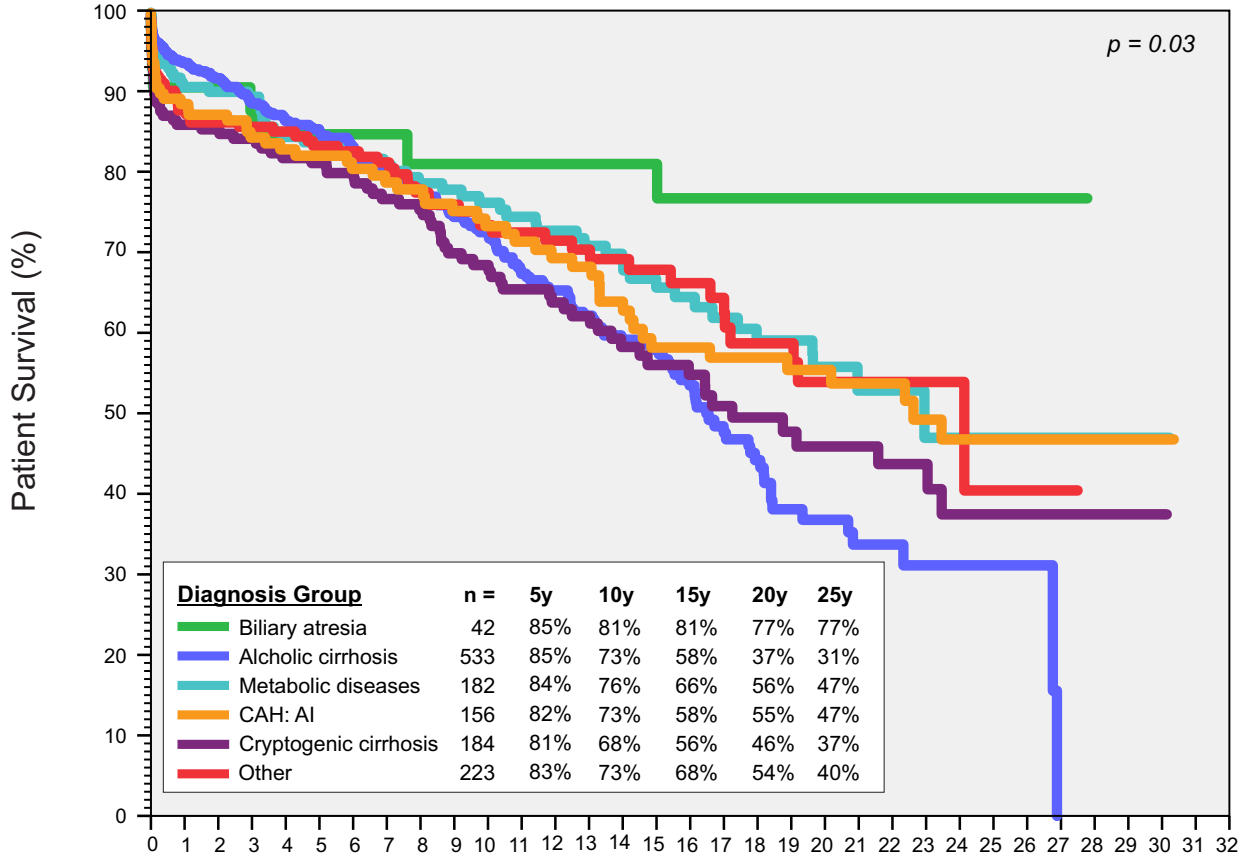
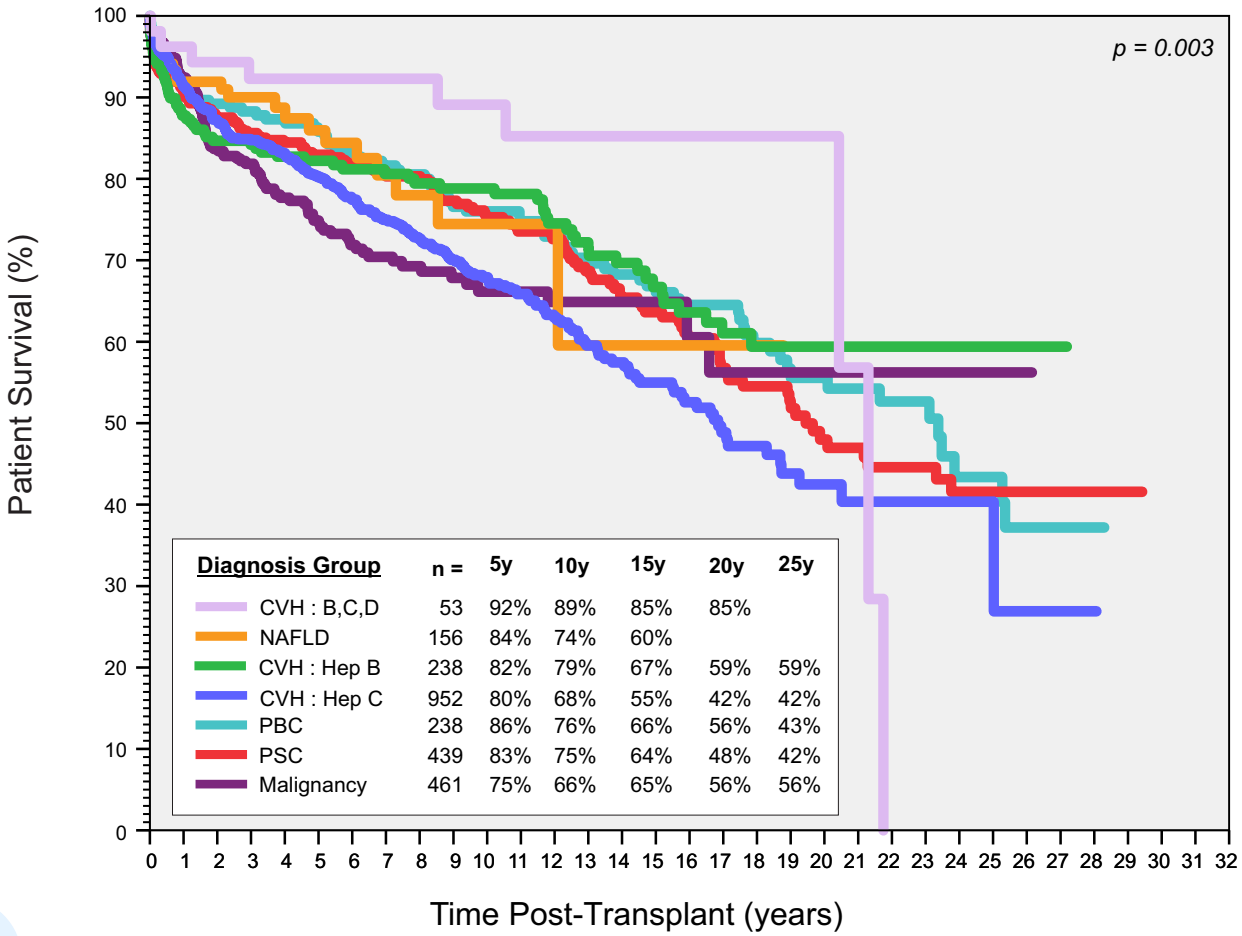
(1) Adults [excluding FHF] (N = 1320)



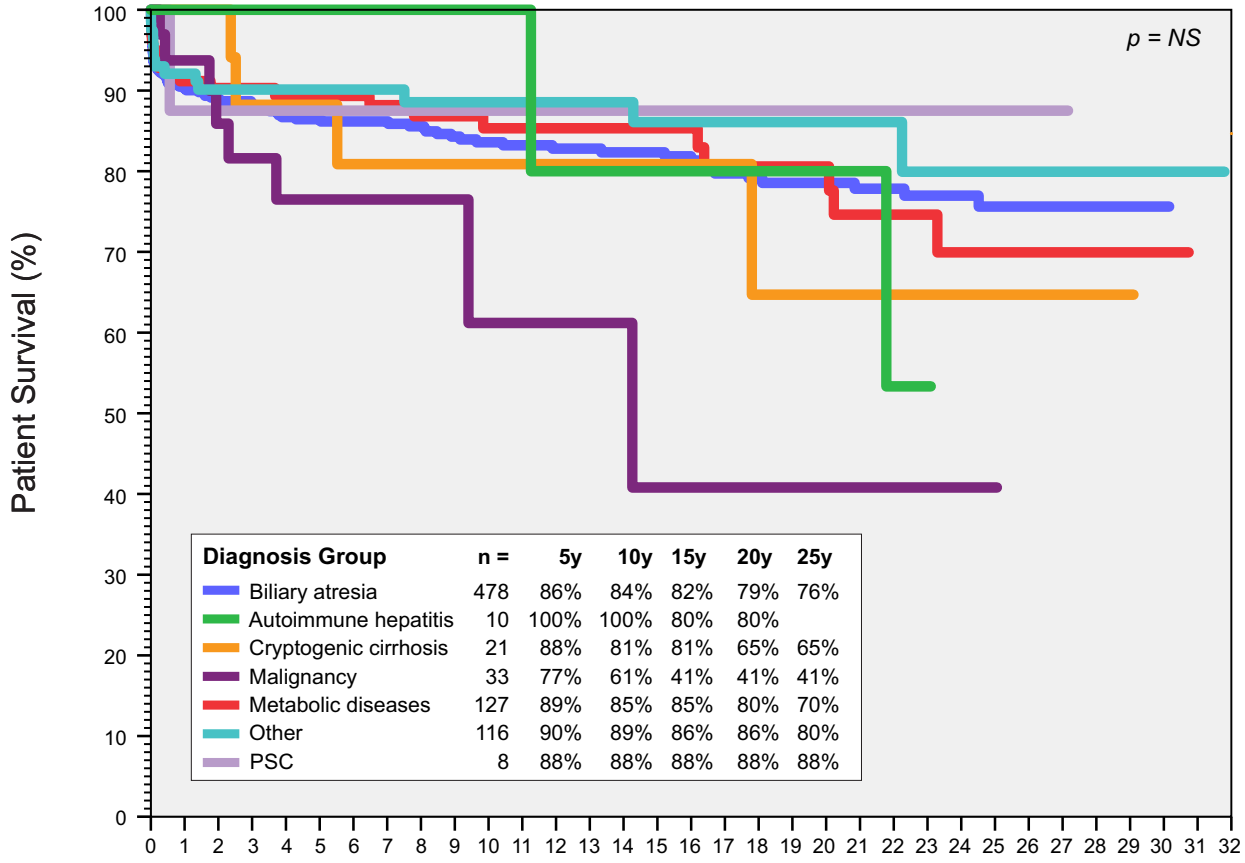
Diagnosis Group	n =	5y	10y	15y	20y	25y
Biliary atresia	42	85%	81%	81%	77%	77%
Alcholic cirrhosis	533	85%	73%	58%	37%	31%
Metabolic diseases	182	84%	76%	66%	56%	47%
CAH: AI	156	82%	73%	58%	55%	47%
Cryptogenic cirrhosis	184	81%	68%	56%	46%	37%
Other	223	83%	73%	68%	54%	40%

(2) Adults [excluding FHF] (N = 2537)

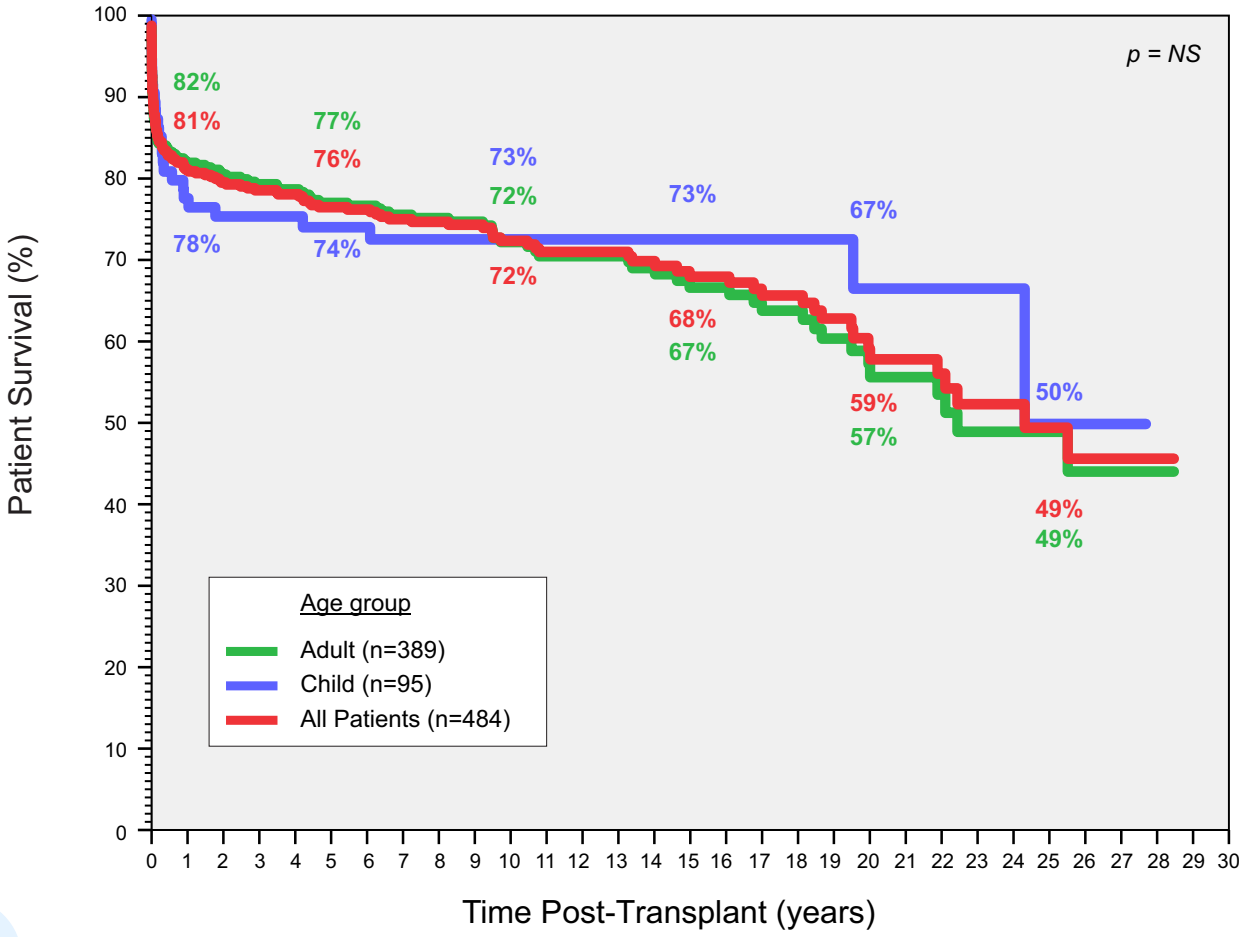


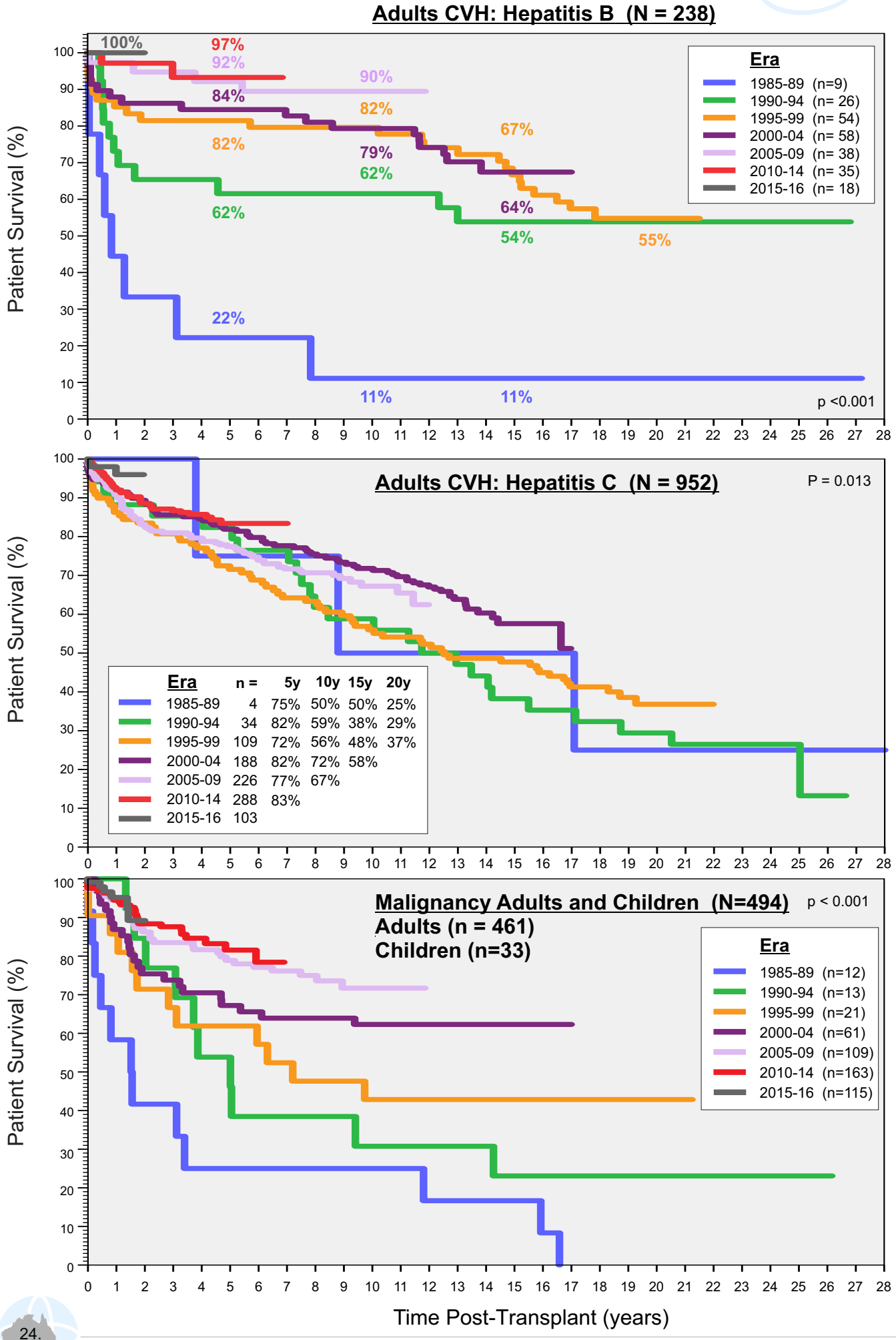
Diagnosis Group	n =	5y	10y	15y	20y	25y
CVH : B,C,D	53	92%	89%	85%	85%	
NAFLD	156	84%	74%	60%		
CVH : Hep B	238	82%	79%	67%	59%	59%
CVH : Hep C	952	80%	68%	55%	42%	42%
PBC	238	86%	76%	66%	56%	43%
PSC	439	83%	75%	64%	48%	42%
Malignancy	461	75%	66%	65%	56%	56%

(3) Paediatric recipients [excluding FHF] (N = 793)



(4) Fulminant hepatic failure (N = 484)





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Section 4

Graft Outcome

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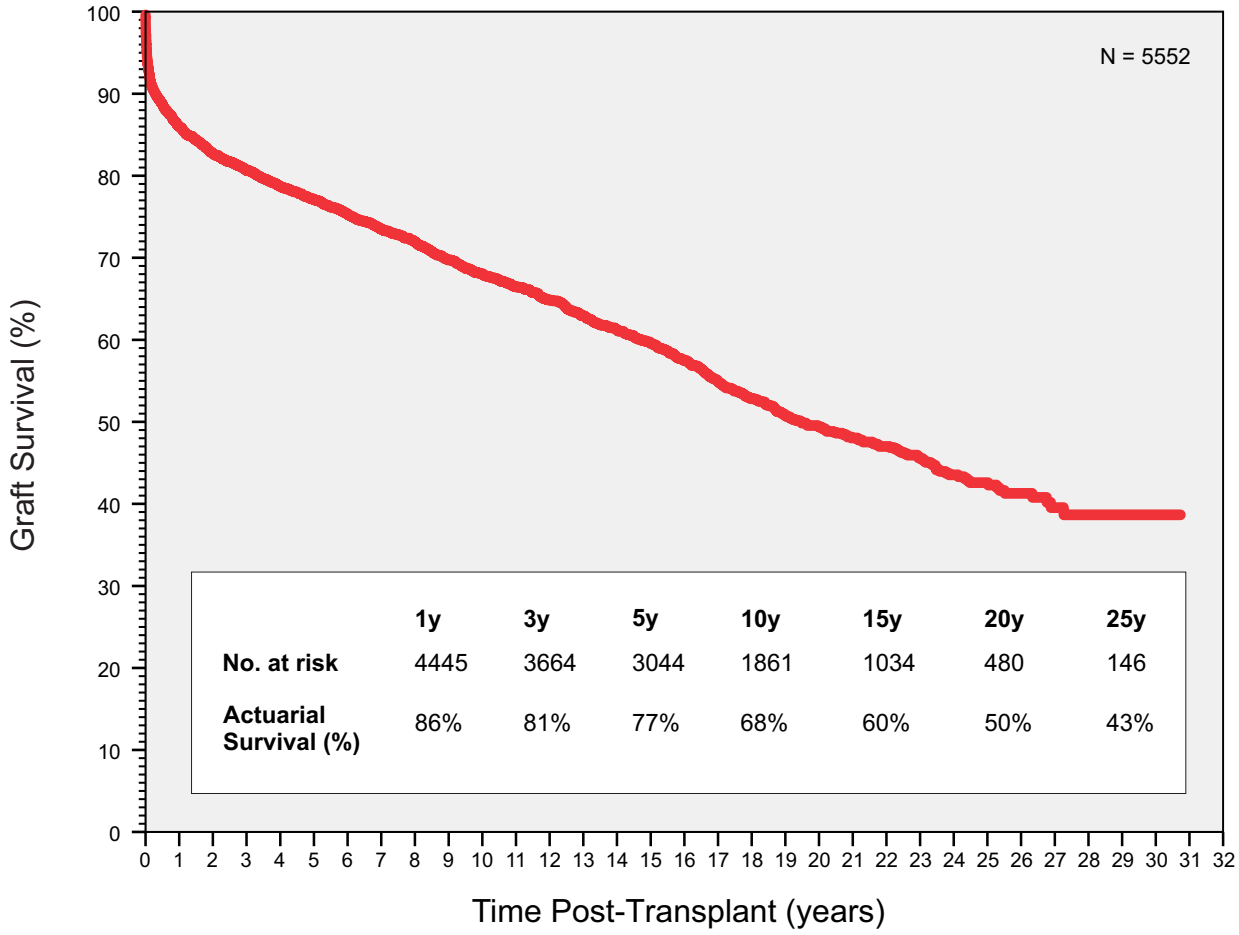
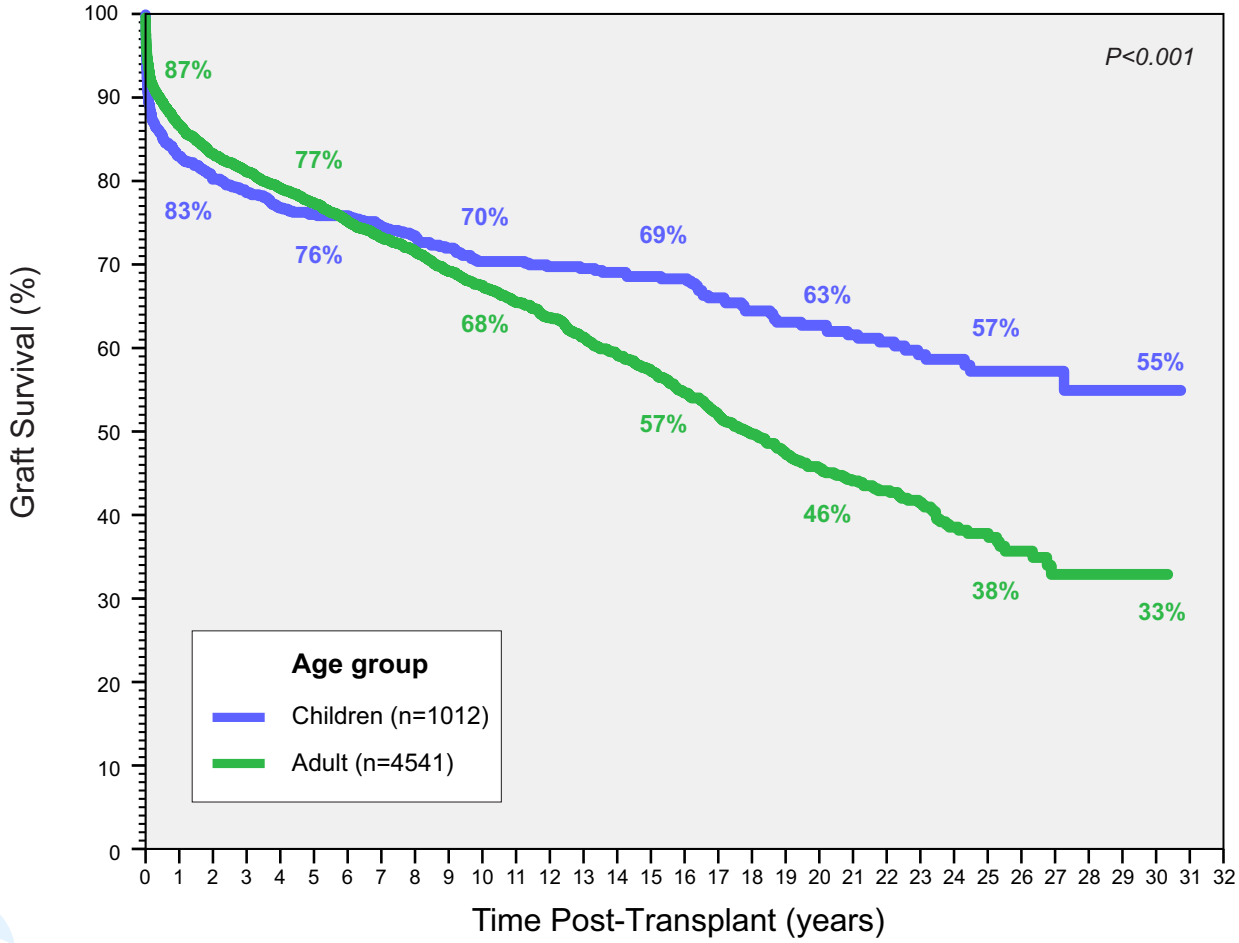
Graft Survival All Grafts

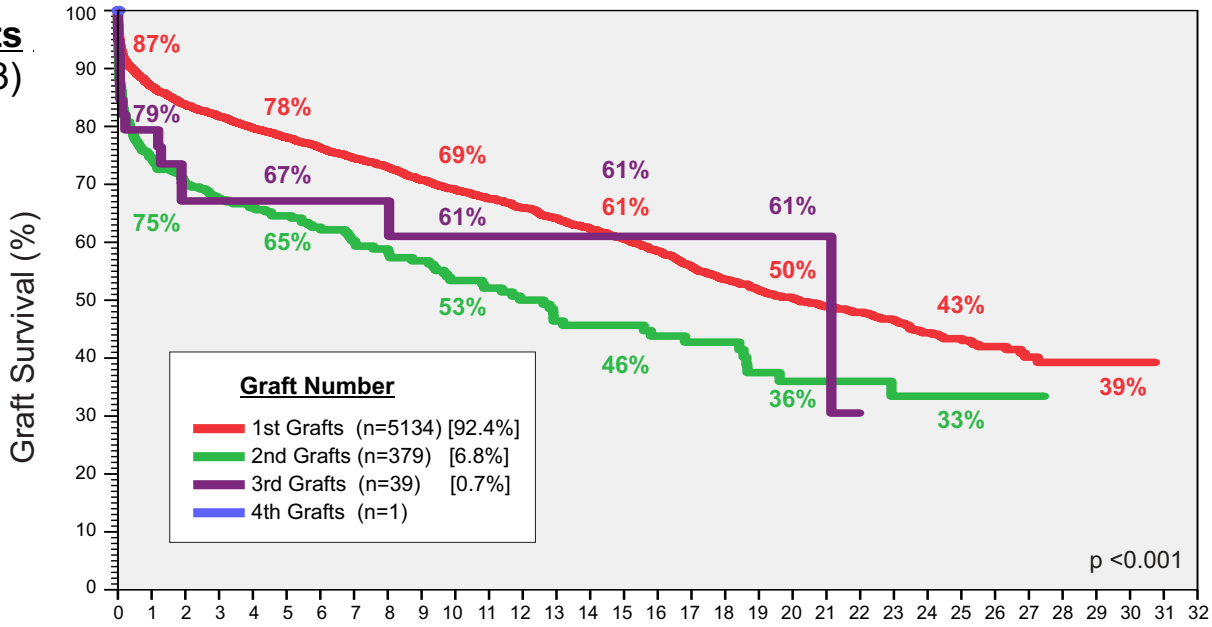


	1y	3y	5y	10y	15y	20y	25y
No. at risk	4445	3664	3044	1861	1034	480	146
Actuarial Survival (%)	86%	81%	77%	68%	60%	50%	43%

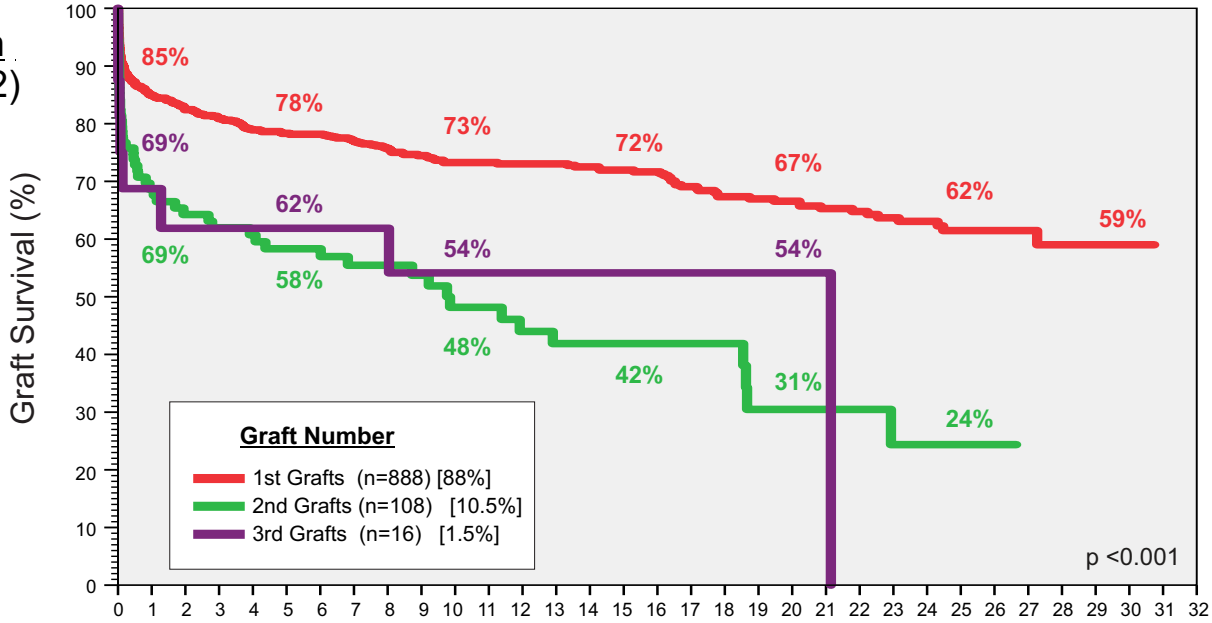
Graft Survival by Age Group



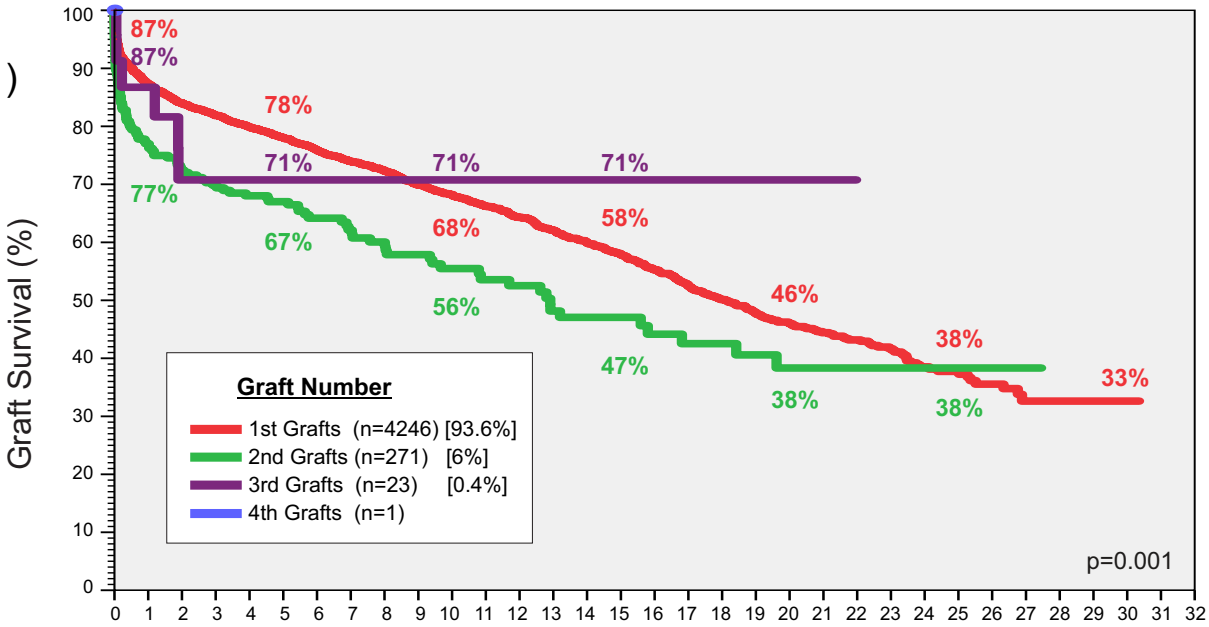
All Grafts
(N= 5553)



Children
(N= 1012)



Adult
(N= 4541)



Time Post-Transplant (years)

Graft Survival by Type of Graft [Deceased Donors]

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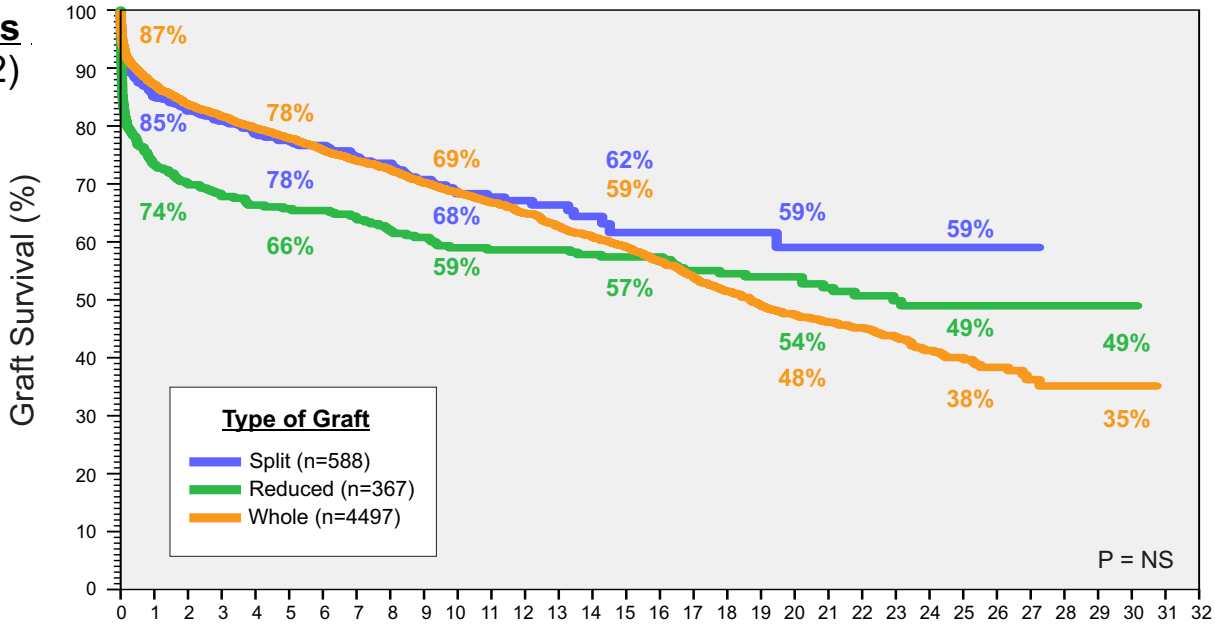
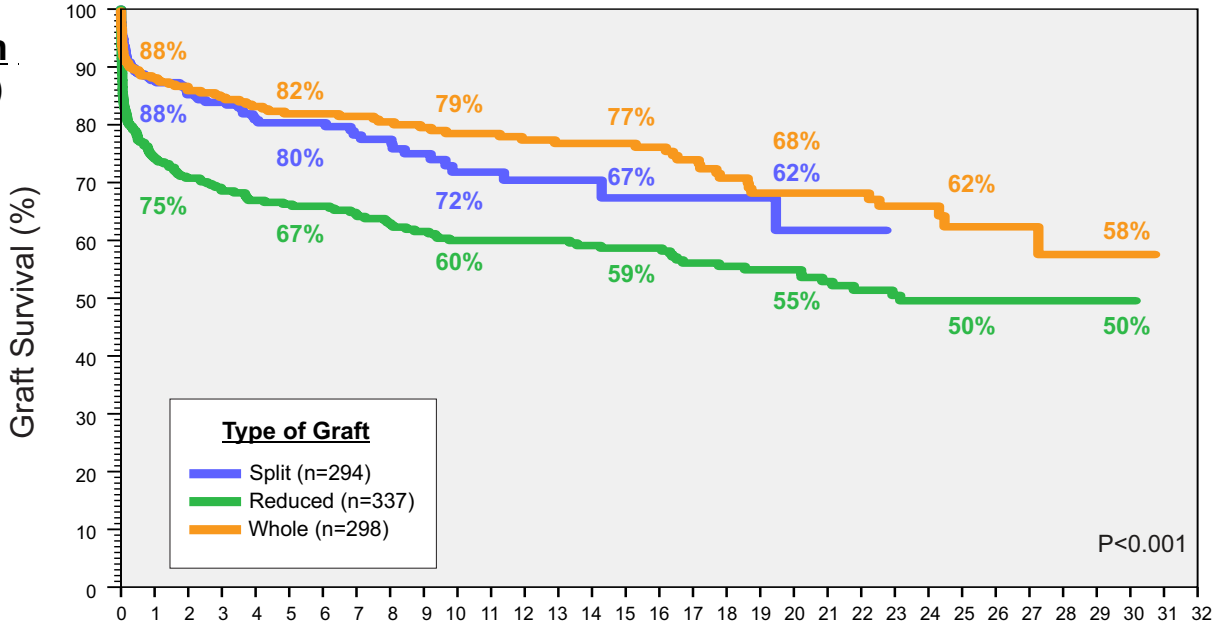
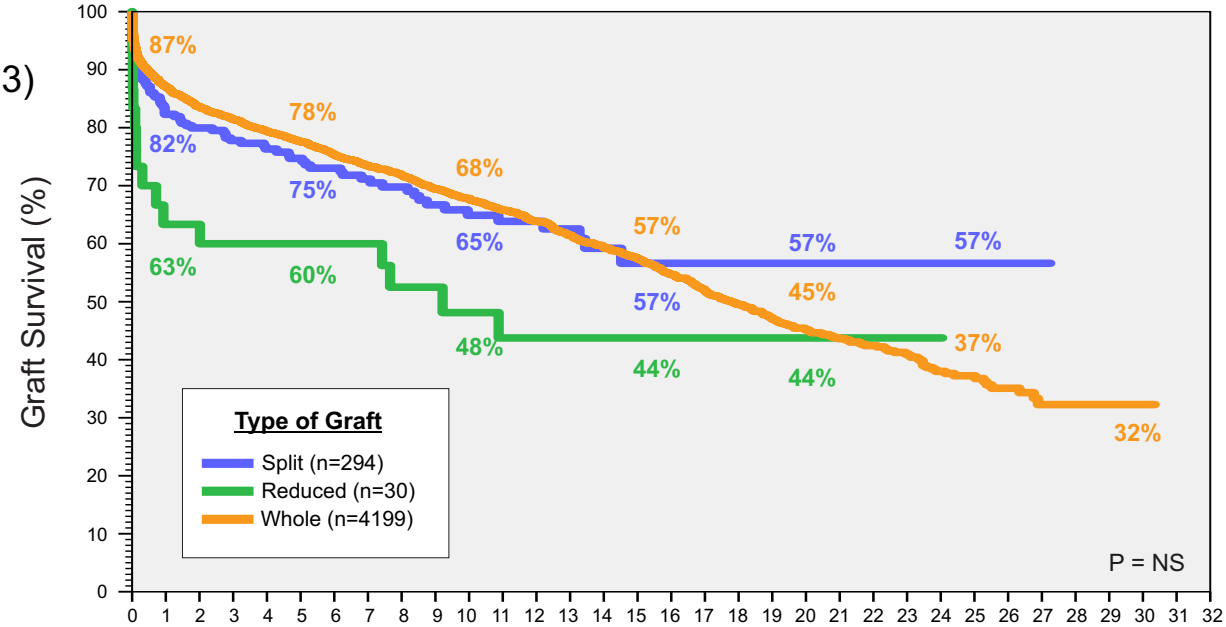
All Grafts
(N= 5452)



Children
(N= 929)



Adult
(N= 4523)



Time Post-Transplant (years)

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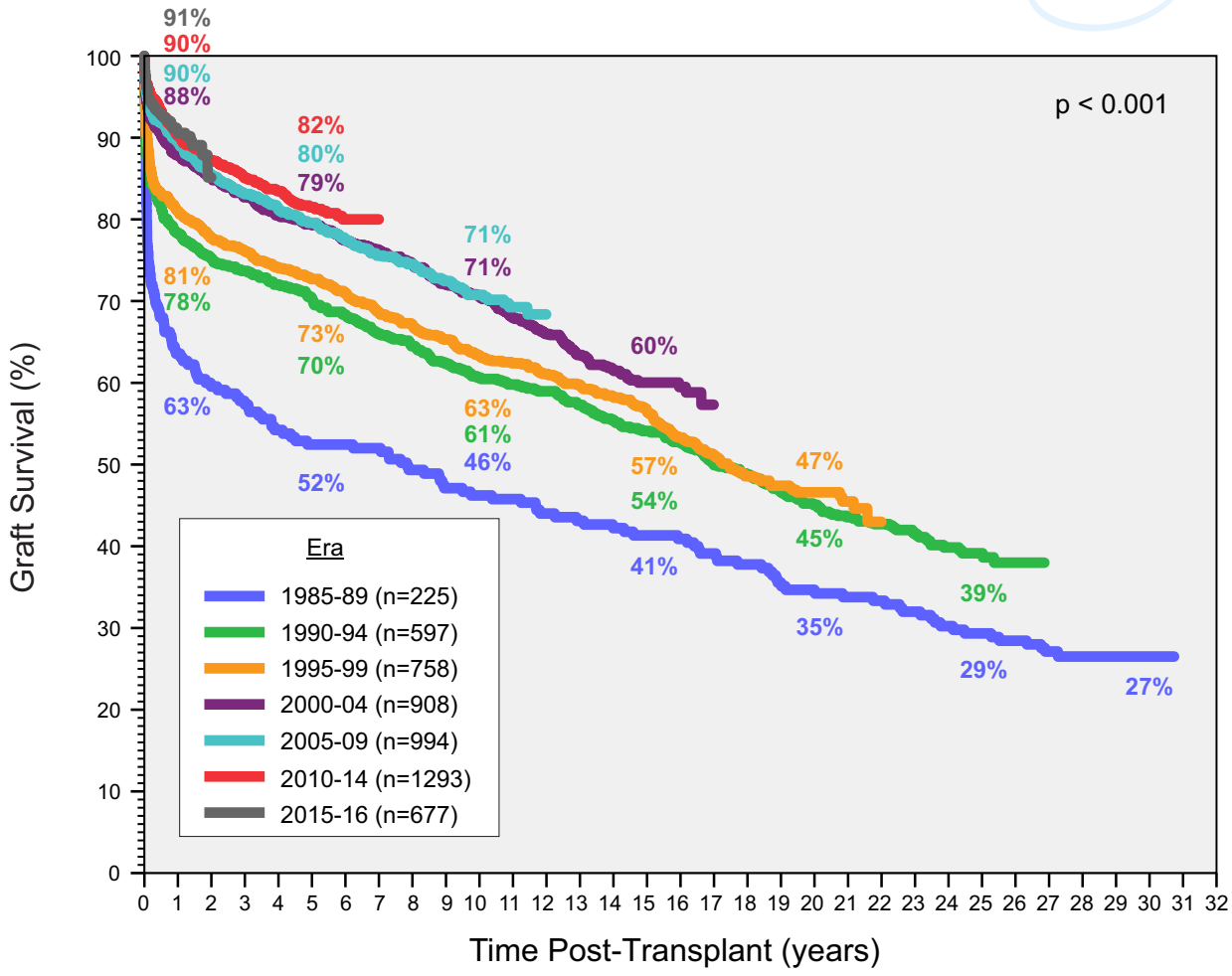
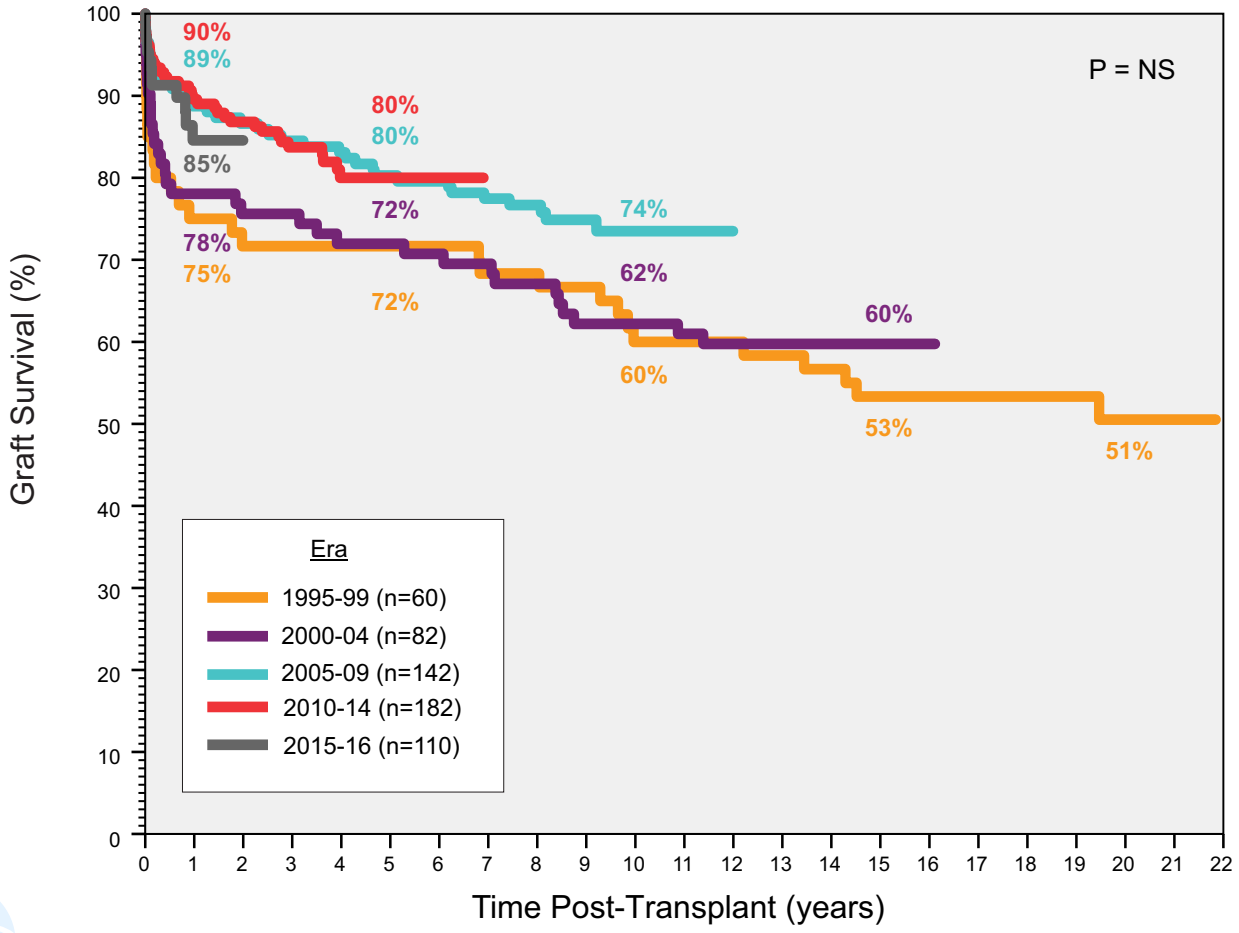
All Deceased Donor Grafts Survival by Year of Transplant



Deceased Donor Split Liver Grafts by Era



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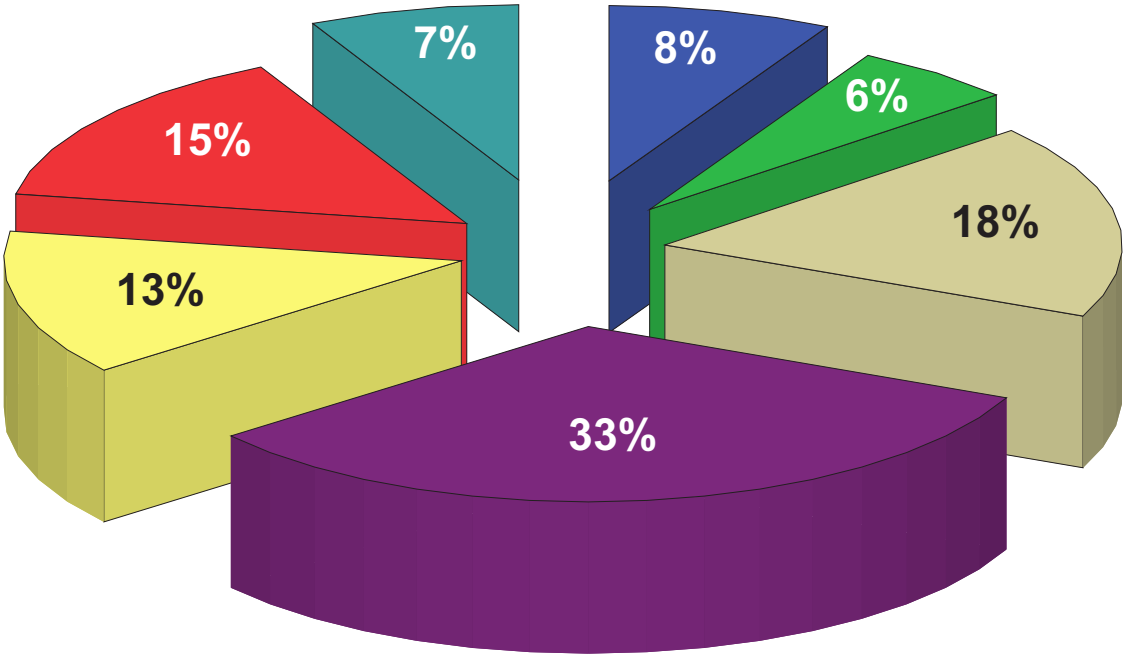
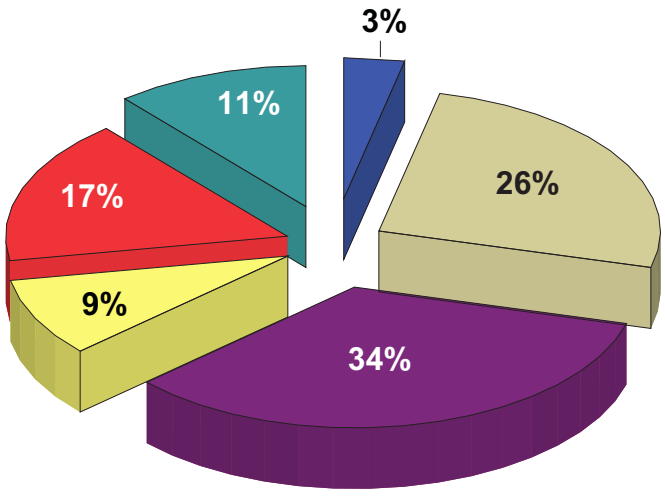
Indication for Retransplantation

N = 417 *(379 2nd grafts, 39 3rd grafts & 1 4th graft)*

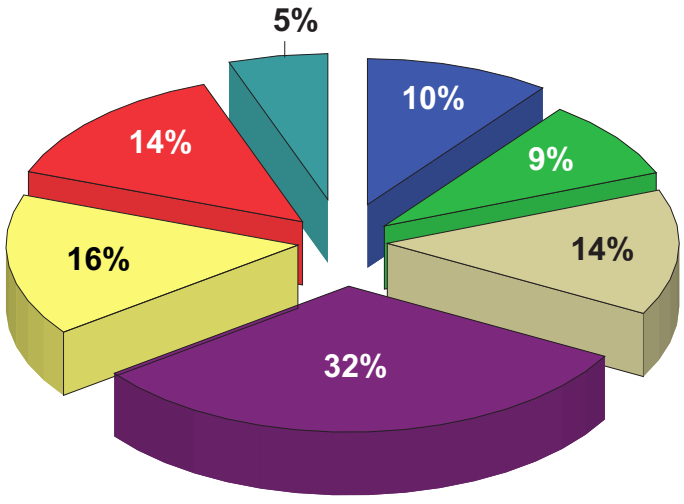


Age Group

Children
(n= 144)



Adults
(n= 273)



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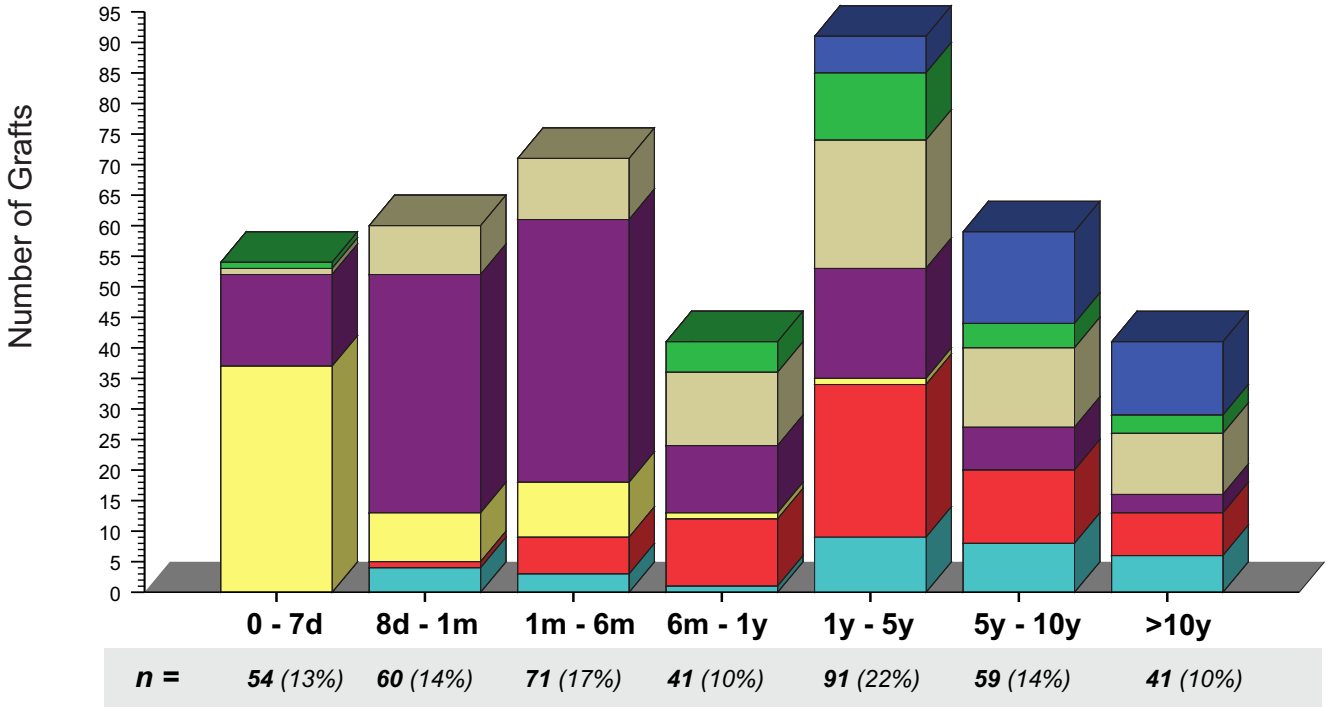
Indication for Retransplantation

N = 417 *(379 2nd grafts, 39 3rd grafts & 1 4th graft)*

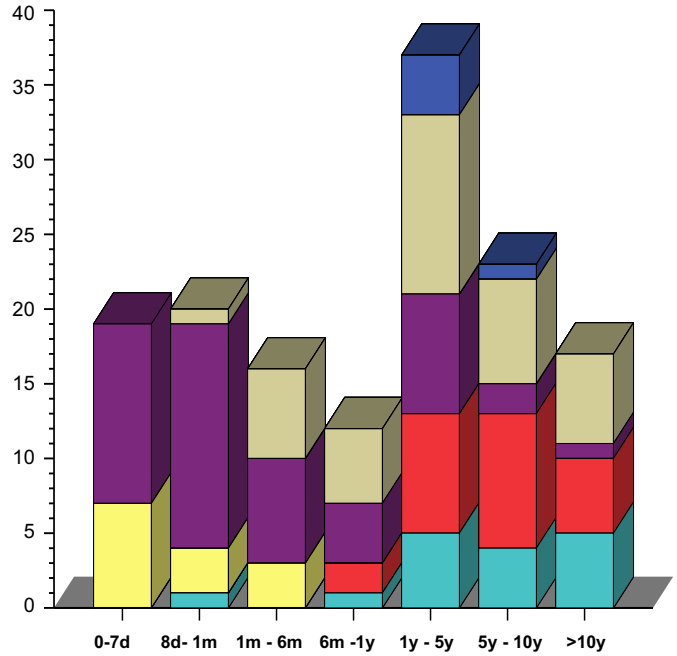


	0 - 7d	8d - 1m	1m - 6m	6m - 1y	1y - 5y	5y - 10y	>10y
n =	***54*** *(13%)*	***60*** *(14%)*	***71*** *(17%)*	***41*** *(10%)*	***91*** *(22%)*	***59*** *(14%)*	***41*** *(10%)*

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

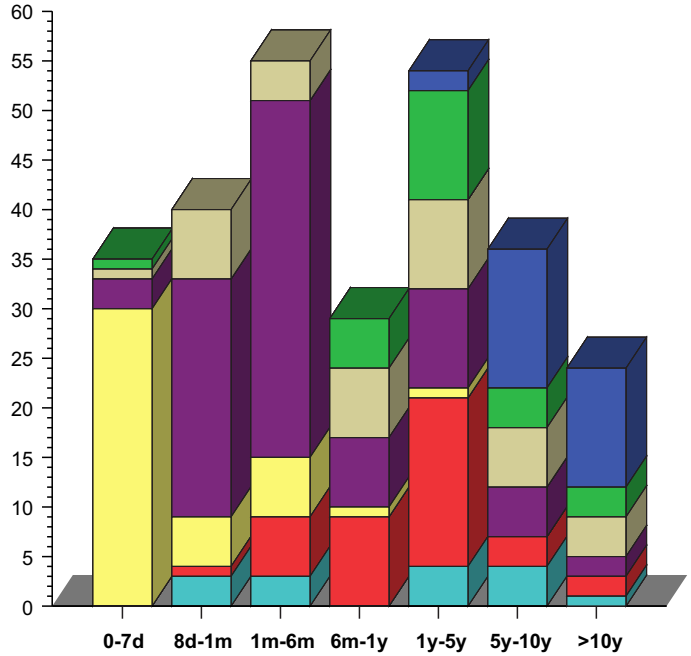
Recurrent HBV /HCV | Vascular | Biliary

Children (n=144)



	0-7d	8d- 1m	1m - 6m	6m -1y	1y - 5y	5y - 10y	>10y
n =	***19*** *(13%)*	***20*** *(14%)*	***16*** *(11%)*	***12*** *(8%)*	***37*** *(26%)*	***23*** *(16%)*	***17*** *(12%)*

Adults (n=273)



	0-7d	8d-1m	1m-6m	6m-1y	1y-5y	5y-10y	>10y
n =	***35*** *(13%)*	***40*** *(15%)*	***55*** *(20%)*	***29*** *(11%)*	***54*** *(20%)*	***36*** *(13%)*	***24*** *(9%)*

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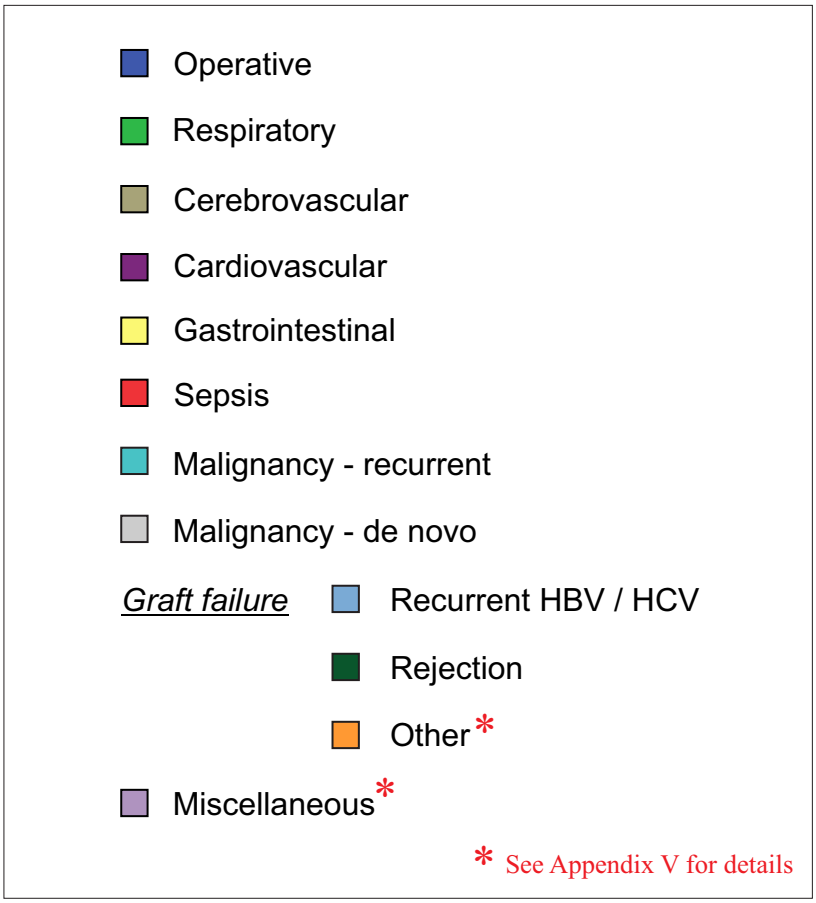
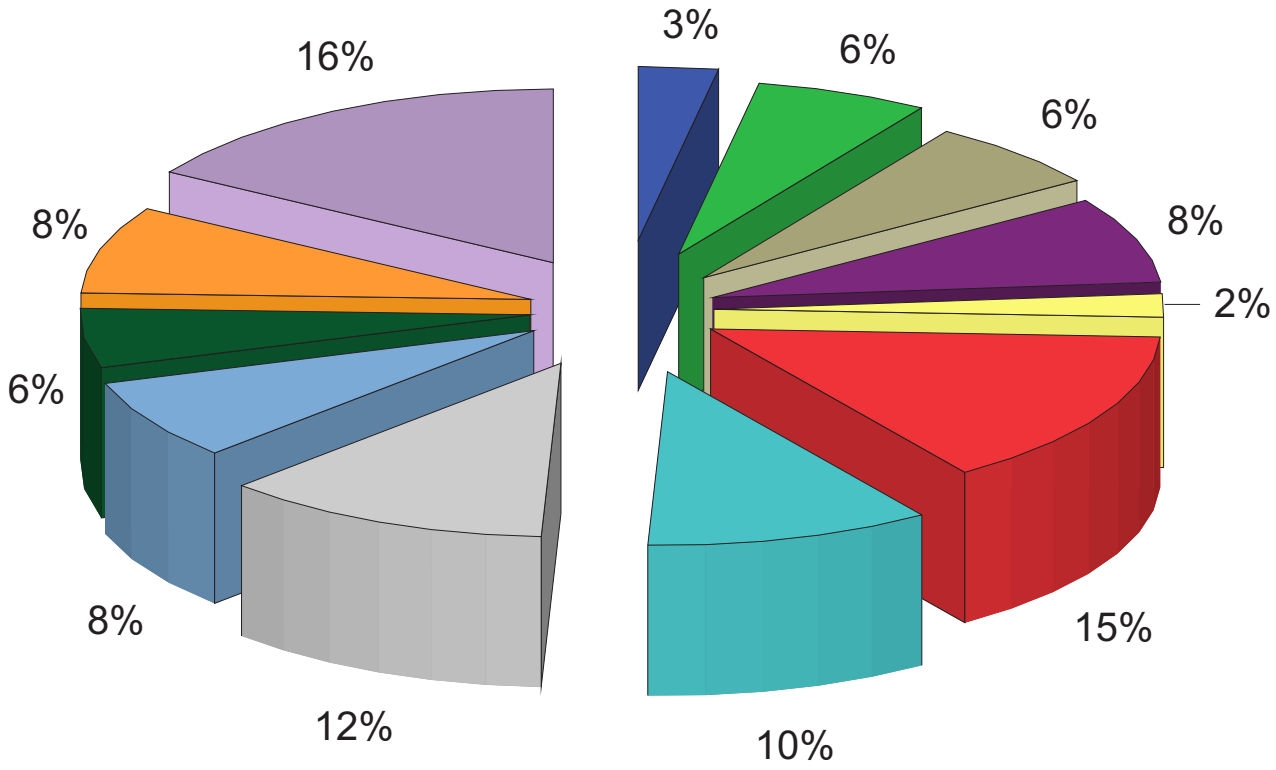
Section 5

Cause of Patient Death

All Patients (N = 1434)





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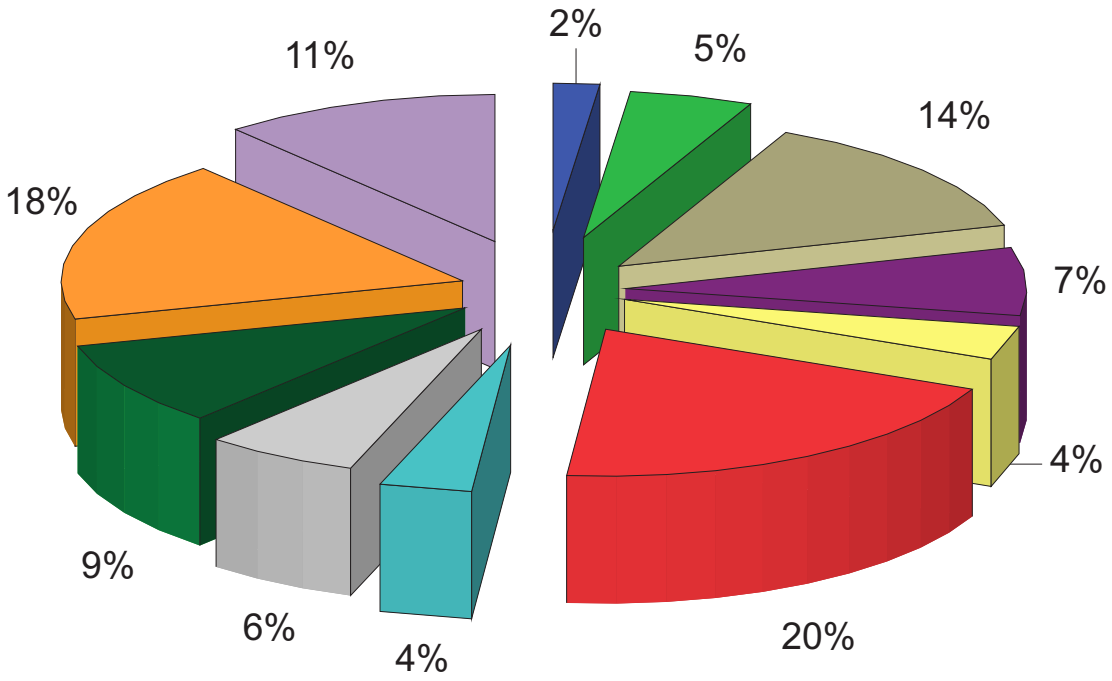
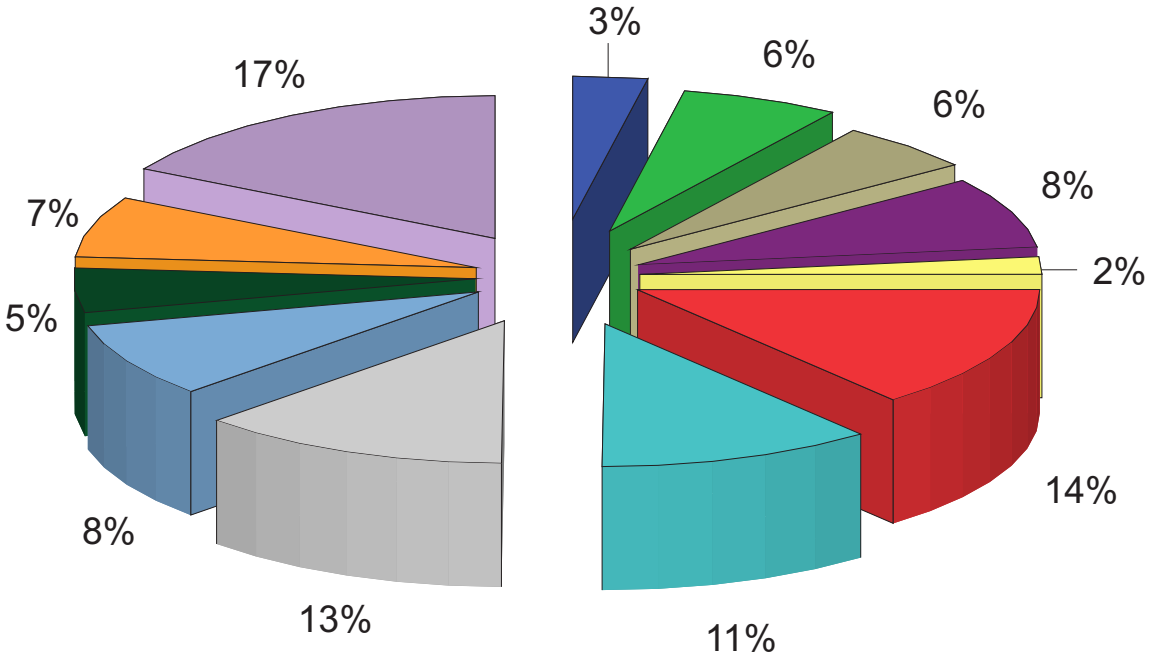
Causes of Death in Children
N =161



Causes of Death in Adult
N = 1273



- 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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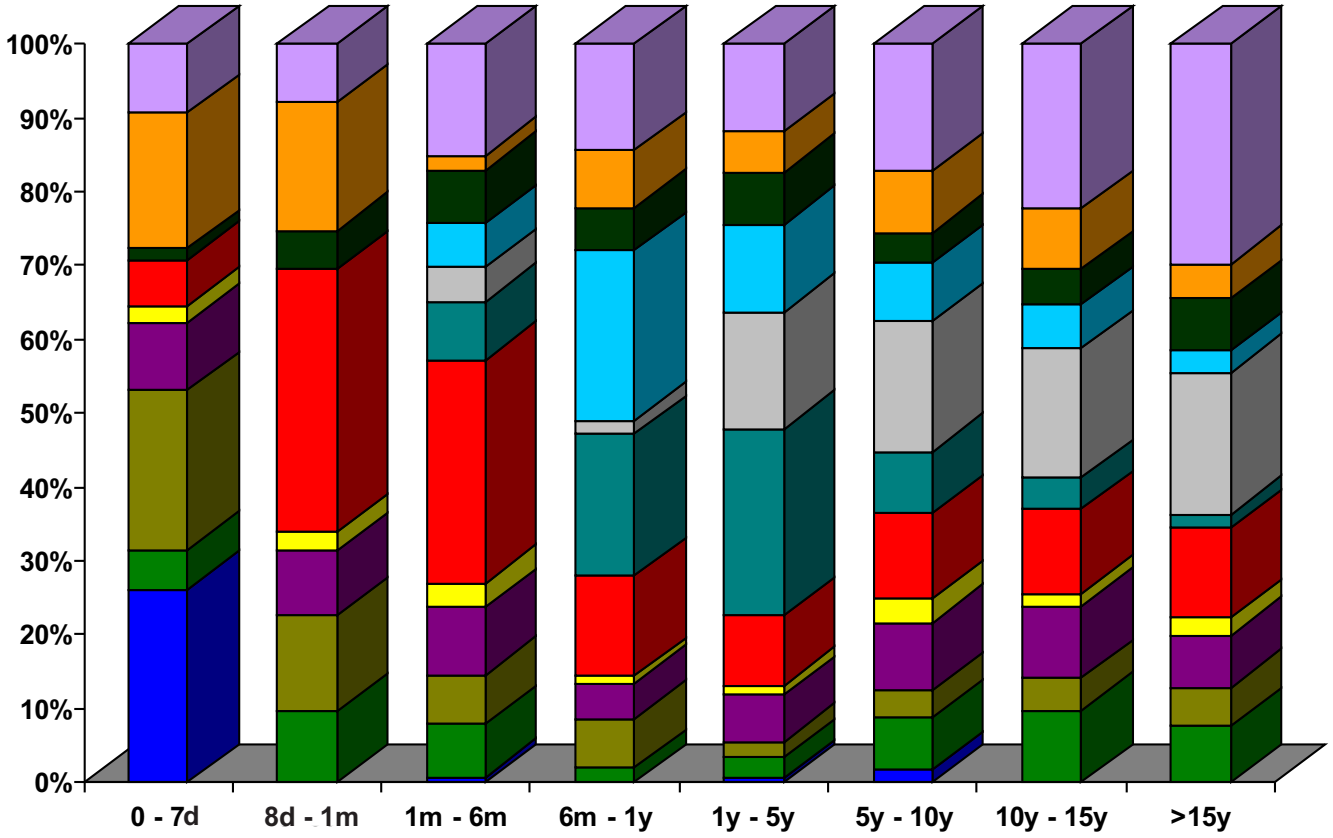
Cause of Death by Time Post Transplant



	0 - 7d	8d - 1m	1m - 6m	6m - 1y	1y - 5y	5y - 10y	10y - 15y	>15y
n =	***130*** *(9%)*	***115*** *(8%)*	***152*** *(11%)*	***104*** *(7%)*	***328*** *(23%)*	***250*** *(17%)*	***184*** *(13%)*	***171*** *(12%)*

- 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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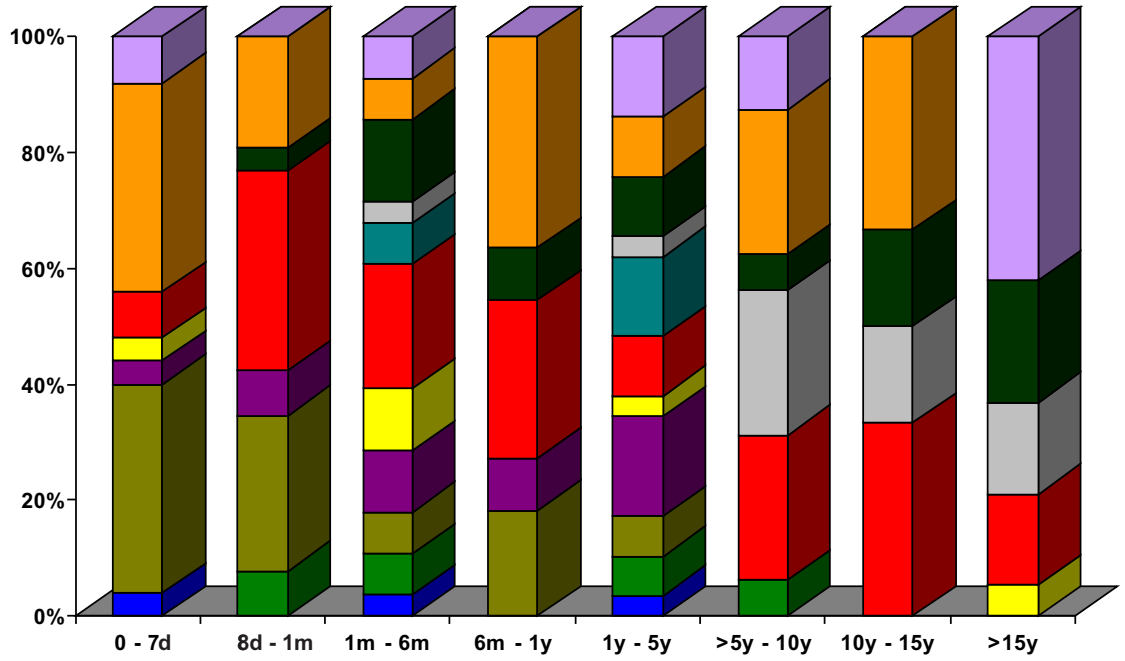
Cause of Death by Time Post Transplant

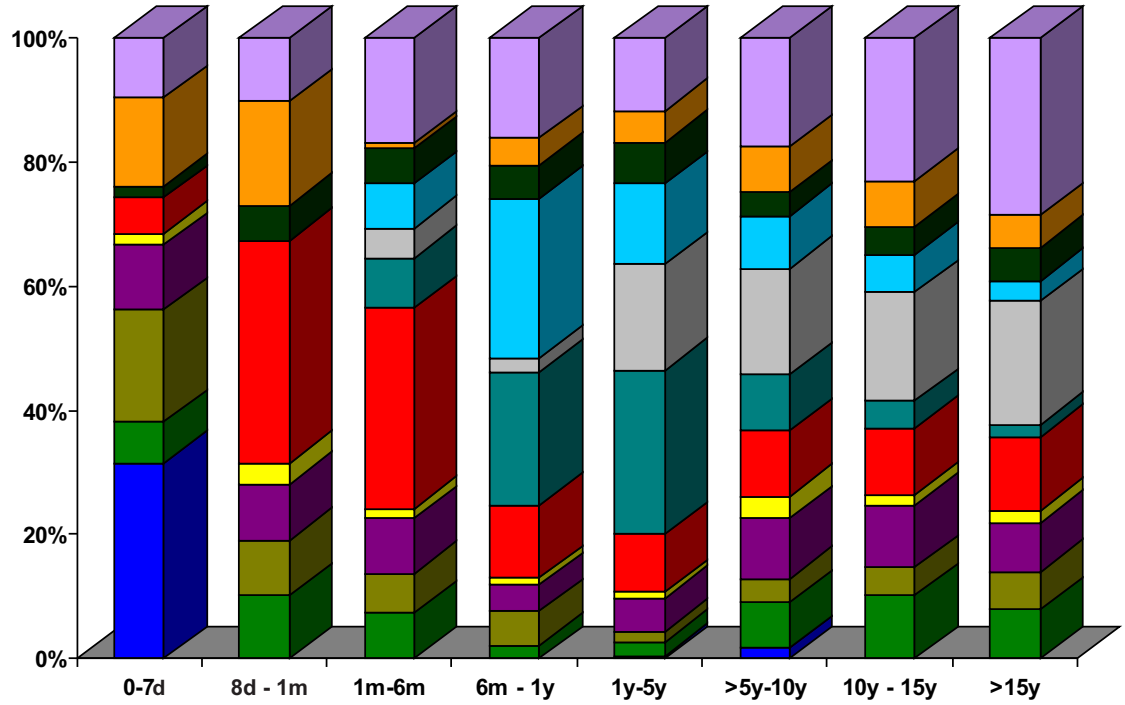
Children (N=161)



	0 - 7d	8d - 1m	1m - 6m	6m - 1y	1y - 5y	>5y - 10y	10y - 15y	>15y
n =	***25*** *(16%)*	***26*** *(16%)*	***28*** *(17%)*	***11*** *(7%)*	***29*** *(18%)*	***16*** *(10%)*	***6*** *(4%)*	***20*** *(12%)*

Cause of Death by Time Post Transplant

Adult (N=1273)



	0-7d	8d - 1m	1m-6m	6m - 1y	1y-5y	>5y-10y	10y - 15y	>15y
n =	***105*** *(8%)*	***89*** *(7%)*	***124*** *(10%)*	***93*** *(7%)*	***299*** *(24%)*	***234*** *(18%)*	***178*** *(14%)*	***151*** *(12%)*

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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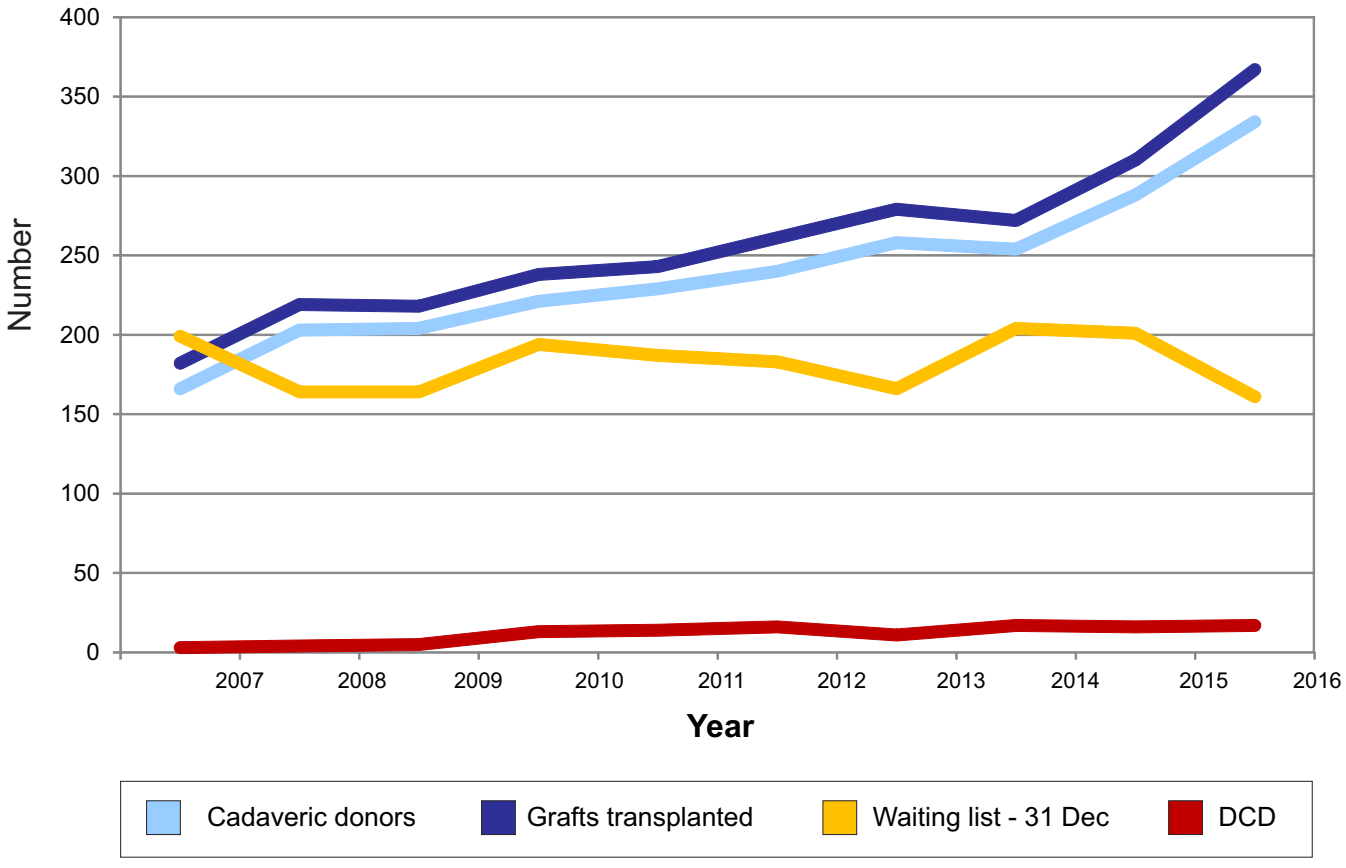
Deceased Donation by Year

	QLD	NSW/ACT	VIC/TAS	SA/NT	WA	NZ	TOTAL
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
2016	69	74/12	61/4	28/4	33	51	334

Grafts from deceased donors



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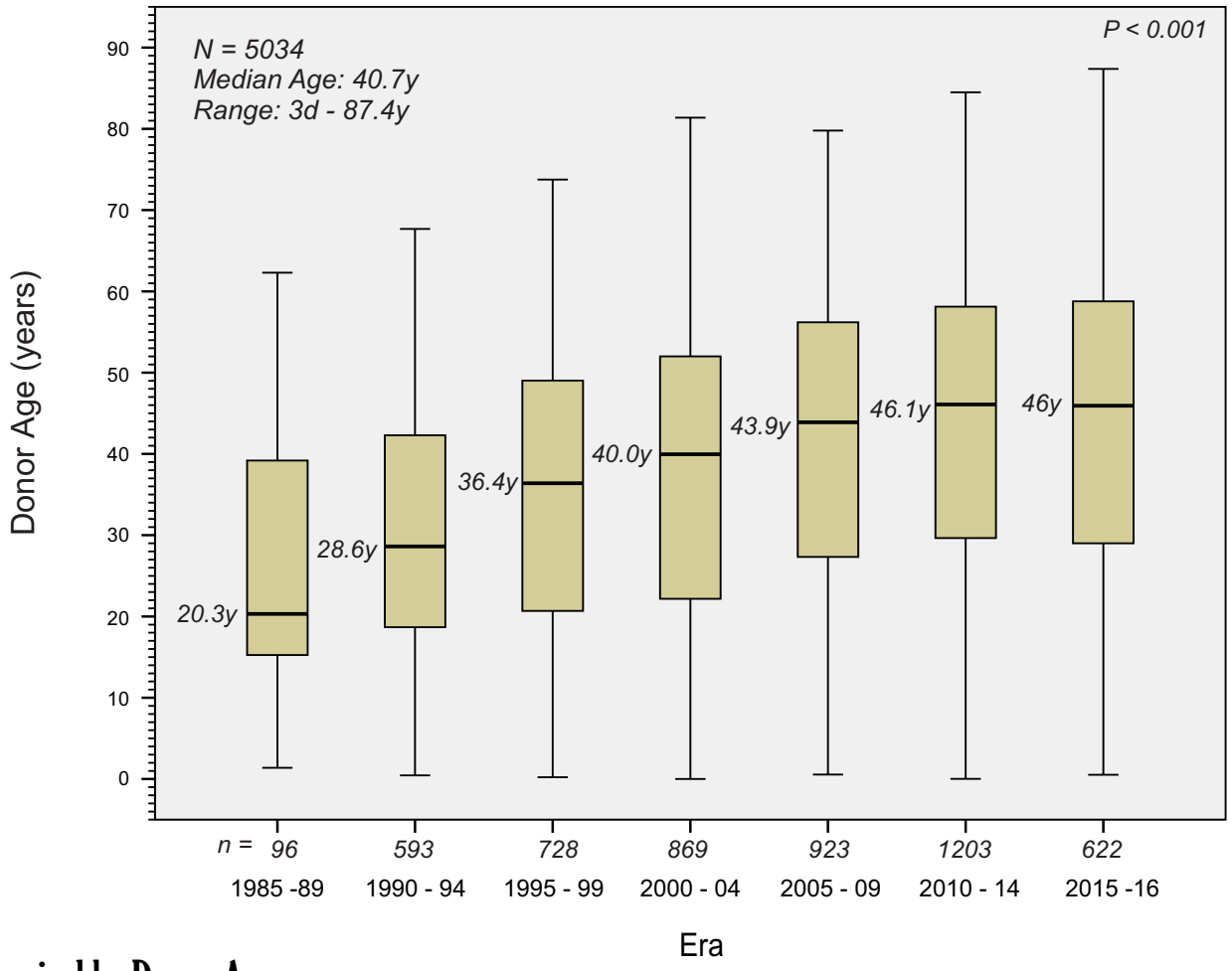
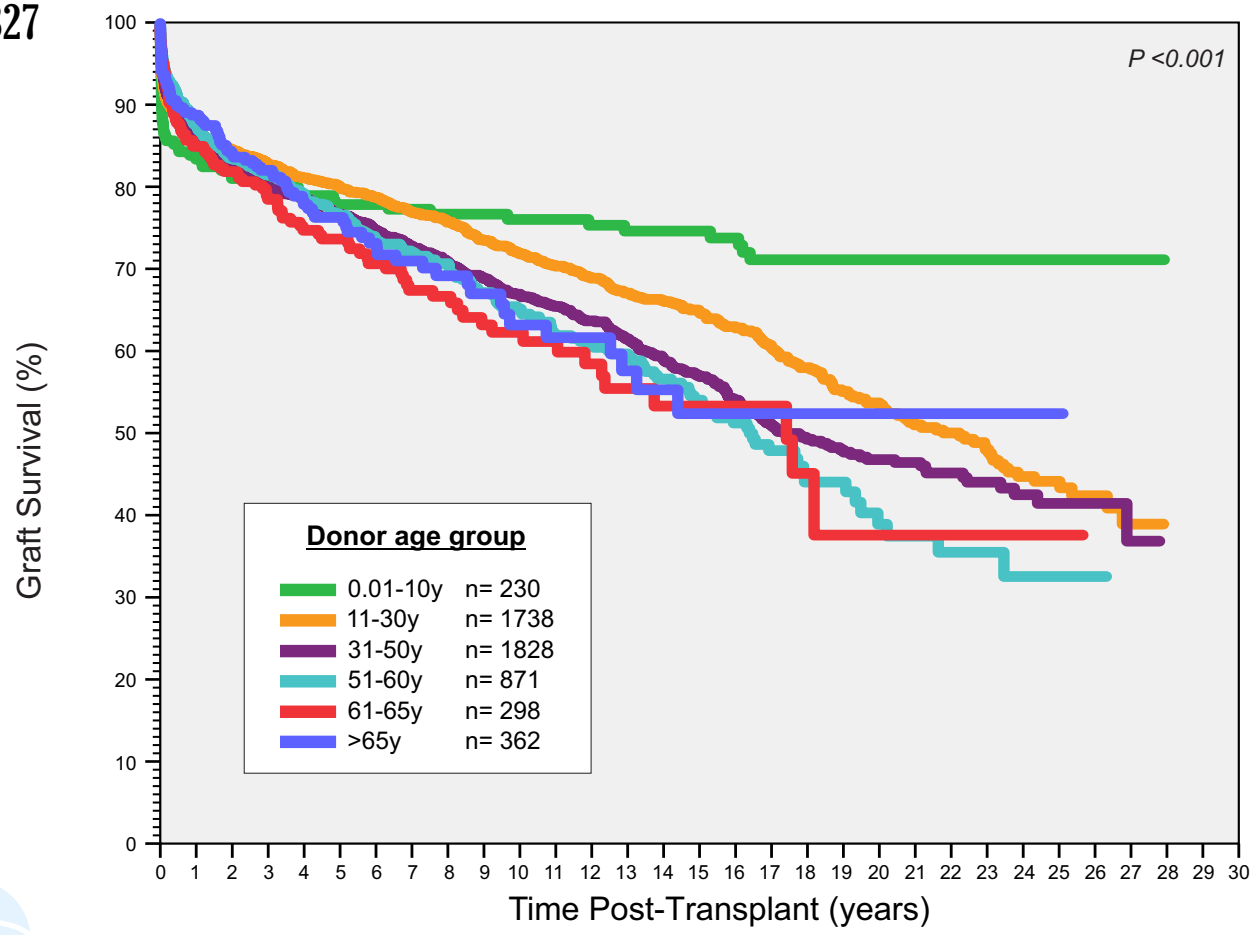
Donor Age by Era
N = 5034



Graft Survival by Donor Age
N = 5327



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Section 7

Living Donor Transplantation

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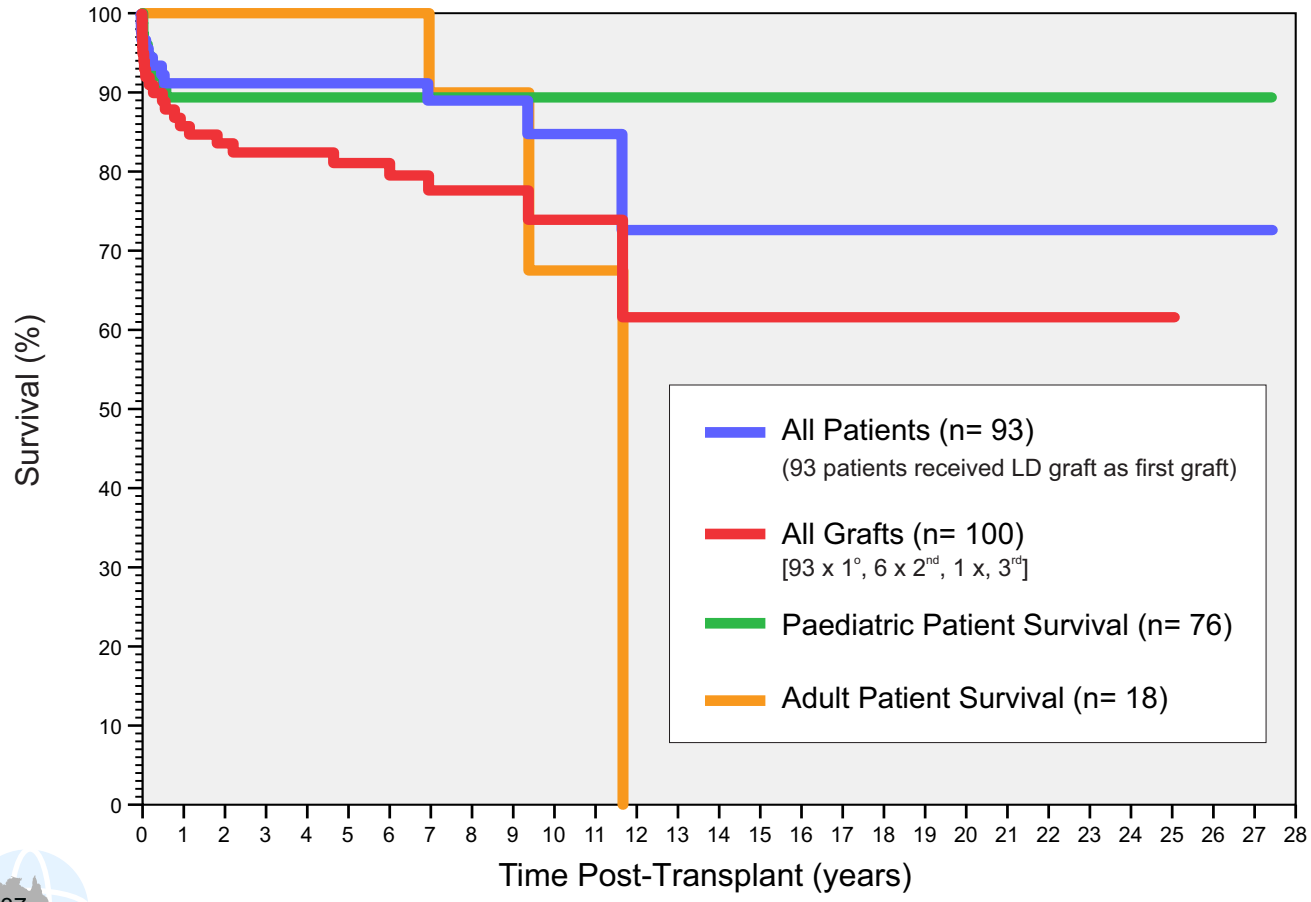
Living Donor Transplantation
N = 100

	Recipient Age Group		
	Child [n=82]	Adult [n=18]*	All [n=100]
Donor gender	-	-	-
Male	45	12	57
Female	37	6	43
Donor age	-	-	-
Median	34.5y	31.7y	33.8y
Range	19.0 - 54.5y	18.3 - 54.4y	18.3 - 54.5y
Donor relationship	-	-	-
Mother	22	-	22
Father	35	-	35
Son	-	5	5
Daughter	-	1	1
Grandmother	1	-	1
Grandfather	1	-	1
Sister	-	3	3
Brother	2	3	5
Aunt	8	-	8
Uncle	2	-	2
Family friend	7	1	8
Cousin	4	-	4
Spouse	-	1	1

* *4 x whole liver domino transplant*



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Section 8

Waiting List

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Waiting List Activity
[Data 1/1/12 - 31/12/16]

Activity	2012	2013	2014	2015	2016				
Listed at 1 January	192	186	164	206	211	-	TOTAL 2016	Adult	Paediatric
Activated	351	360	407	404	-	406			
TOTAL	**543**	**546**	**571**	**610**	**211**	**406**	**617**	**531**	**86**
	OUTCOME					OUTCOME			
Transplant	**268 [50%]**	**284 [52%]**	**278 [49%]**	**316 [52%]**	**127**	**246**	**373 [60%]**	**304 [57%]**	**69 [80%]**
Delisted	**89 [13%]**	**98 [18%]**	**87 [16%]**	**83 [14%]**	**39**	**44**	**83 [13%]**	**78**	**5**
Died on list	29	26	18	21	0	12	12	12	0
Too sick	16 } 8%	11 } 10%	10 } 8%	5 } 7.5%	3	4	7 } [6%]	7 } 6%	0
Tumour progression	10	16	15	20	9	8	17	17	0
Improved	17	24	18	17	14	11	25	21	4
Other	17*	21*	26*	20*	13	9	22*	21	1
Active at 31 Dec	186 [34%]	164 [34%]	206 [36%]	211 [34%]	45	116	161 [26%]	149	12

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

Outcome of Initial Urgent Listing

OUTCOME	CATEGORY 1						
	2012 (n=16)	2013 (n=19)	2014 (n=8)	2015 (n=25)	2016 N=20	Adult n=14	Paediatric n=6
TRANSPLANTED	11 } 81%	11 } 74%	6 } 88%	21 } 88%	17 } 95%	11	6
IMPROVED	2	3	1	1	2	2	-
DIED / TOO SICK	3	5	1	3	1	1	-
OTHER TREATMENT	-	-	-	-	-	-	-

OUTCOME	CATEGORY 2						
	2012 (n=19)	2013 (n=29)	2014 (n=22)	2015 (n=22)	2016 N=25	Adult n=17	Paediatric n=8
TRANSPLANTED	14 } 86%	22 } 89%	18 } 95%	20 } 95%	21 } 100%	14	7
IMPROVED	3	4	3	1	3	3	
DIED / TOO SICK	1	2	-	-	-	-	-
OTHER TREATMENT	1 active 31/12/12	1 active 31/12/13	1 active 31/12/14	1 active 31/12/15	1 active 31/12/16		1 active 31/12/16

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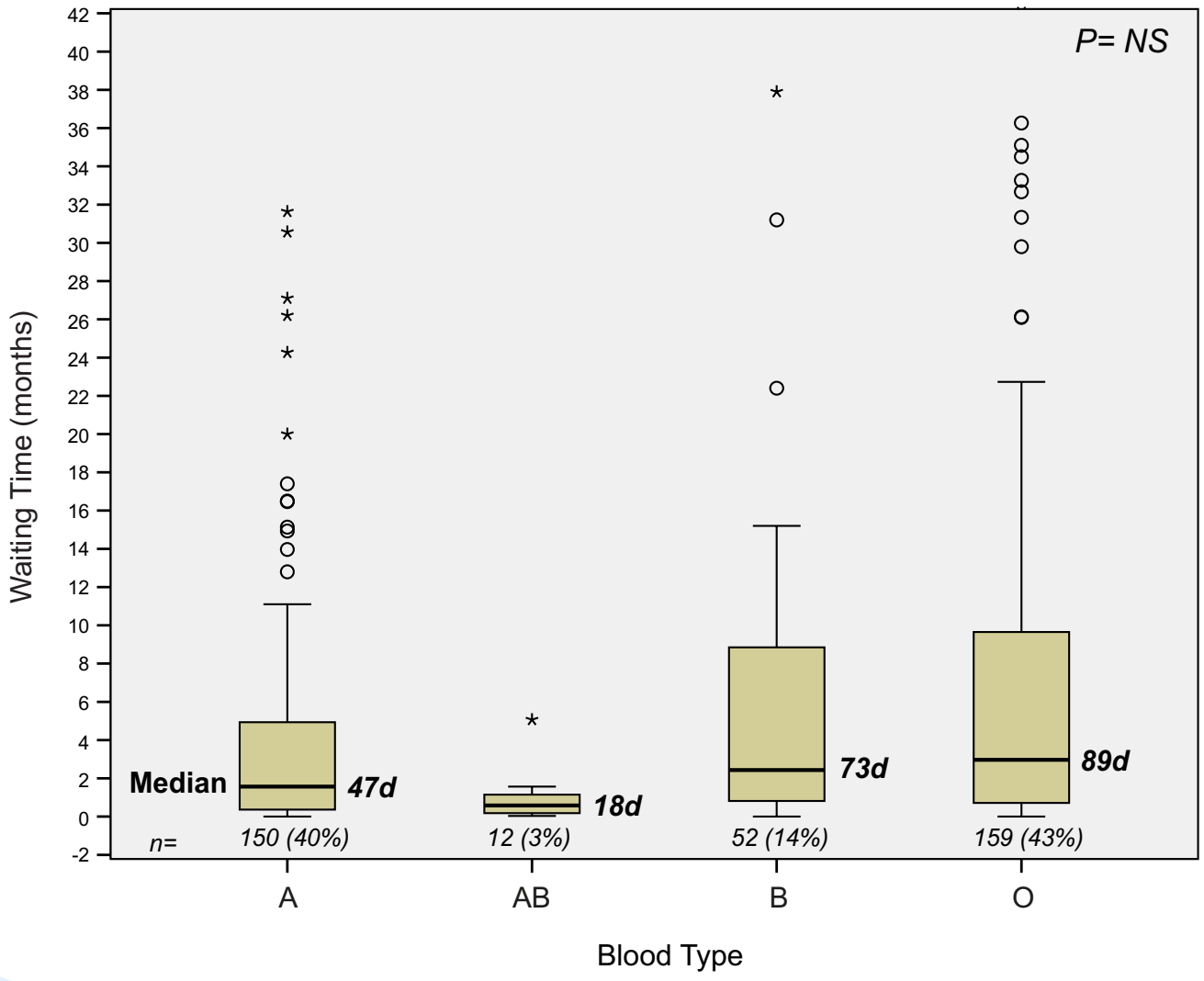
Outcome by Blood Group

	Blood Group				
	A	O	B	AB	TOTAL
n=	227 (37%)*	282 (46%)	84 (14%)	24 (4%)	617
Not transplanted	77	123	32	12	244
Transplanted	150 (66%)**	159 (56%)	52 (62%)	12 (50%)	373 (61%)

* *% of total number listed*

** *% of blood group*

Waiting Time to Transplant 2016



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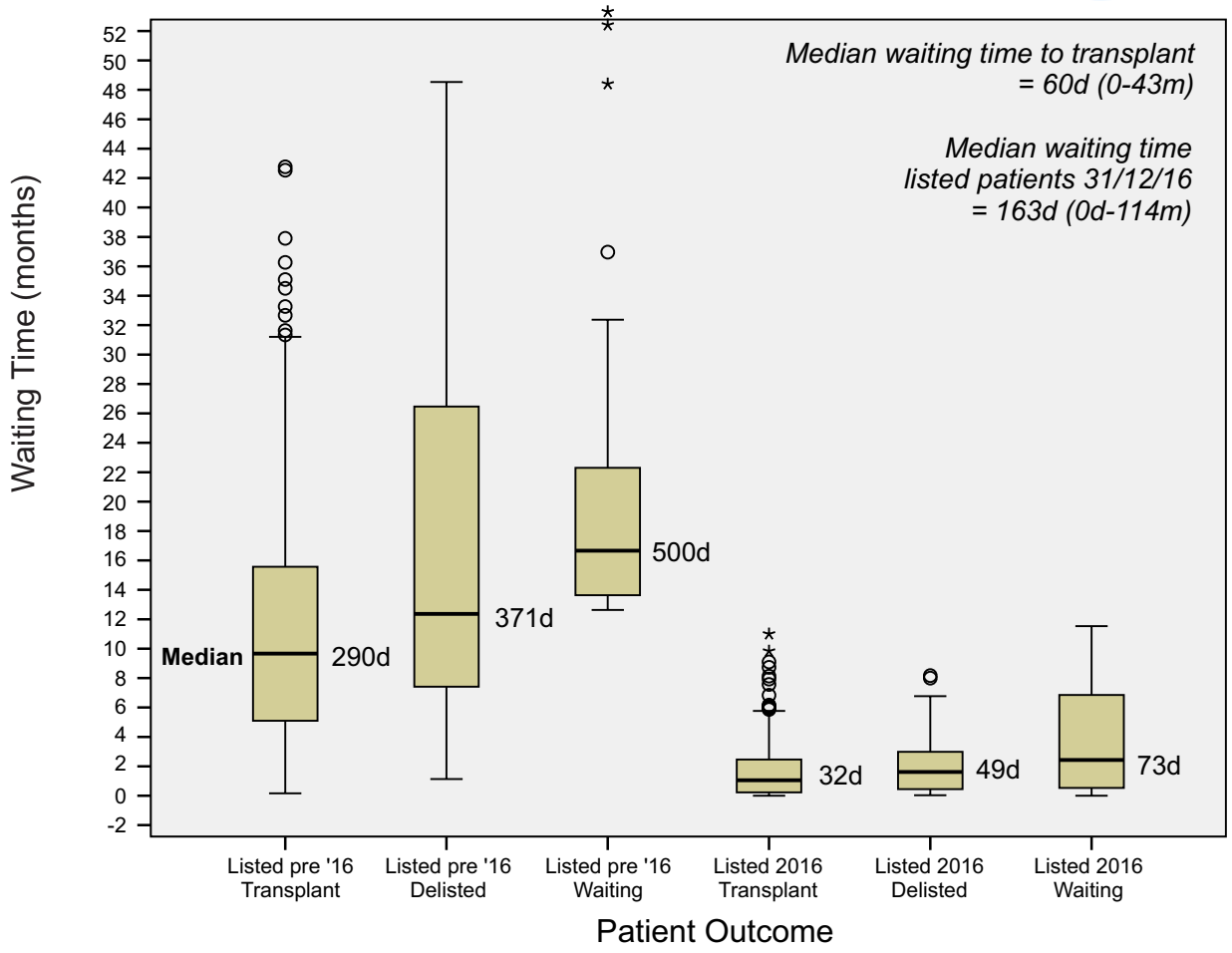
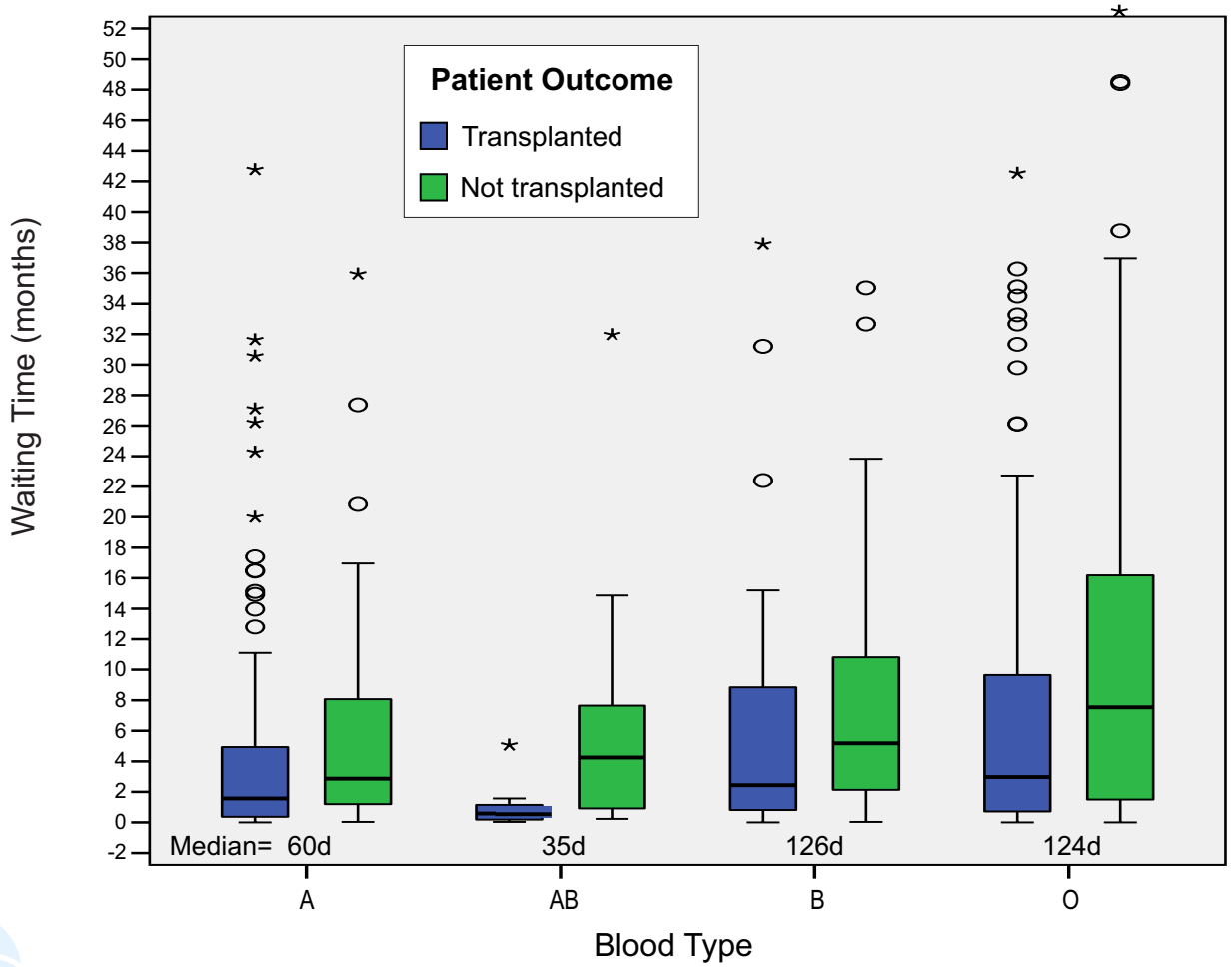
Waiting Time by Outcome



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 = 5136

At Tx	Total number pts. transplanted = 5136
Liver Cancer as indication for Transplant	443 (9%) 446 Ca
Liver Ca as a Secondary Diagnosis	739 (14%) 742 Ca
Total	1182* (23%)
Post Tx	
Recurrent Liver Ca	145 (3% of all pts, 12% pts with Ca at Tx)
De Novo Ca	381 (7%) 412 Ca
Skin Ca	723 (14%)
Total	1249 (24%)
Multiple Cancer types (non skin and skin)	343 (7% of all pts)
Multiple non skin cancers	104 (2% of all pts)
Developed non skin Ca < 90days	10

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

Liver Cancer as Primary Diagnosis
N = 443/5136 (9%)

TYPE OF CA	No	DIED	DIED OF THIS CA
HEPATOCELLULAR CA	391	94	46 (12%)
HEPATOBLASTOMA	29	5	4 (14%)
FIBROLAMELLAR	7	5	2 (29%)
EPITHELOID HAEMANGIOENDOTHELIOMA	5	0	0
CHOLANGIOCARCINOMA	5	2	1 (25%)
CARCINOID	4	4	4 (100%)
HEPATOCELLULAR MALIGNANT NEOPLASM	1	0	0
ANGIOSARCOMA	1	1	1 (100%)
GASTRINOMA	1	1	1 (100%)
PANCREATIC ISLET CELL	1	1	1 (100%)
ERYTHROID LEUKAEMIA	1	1	1 (100%)
TOTALS	**443* (9% of pts)**	**111 (25% of those with PCa)**	**61 (14% of those with PCa)**

* 3 pts had two primary liver cancers

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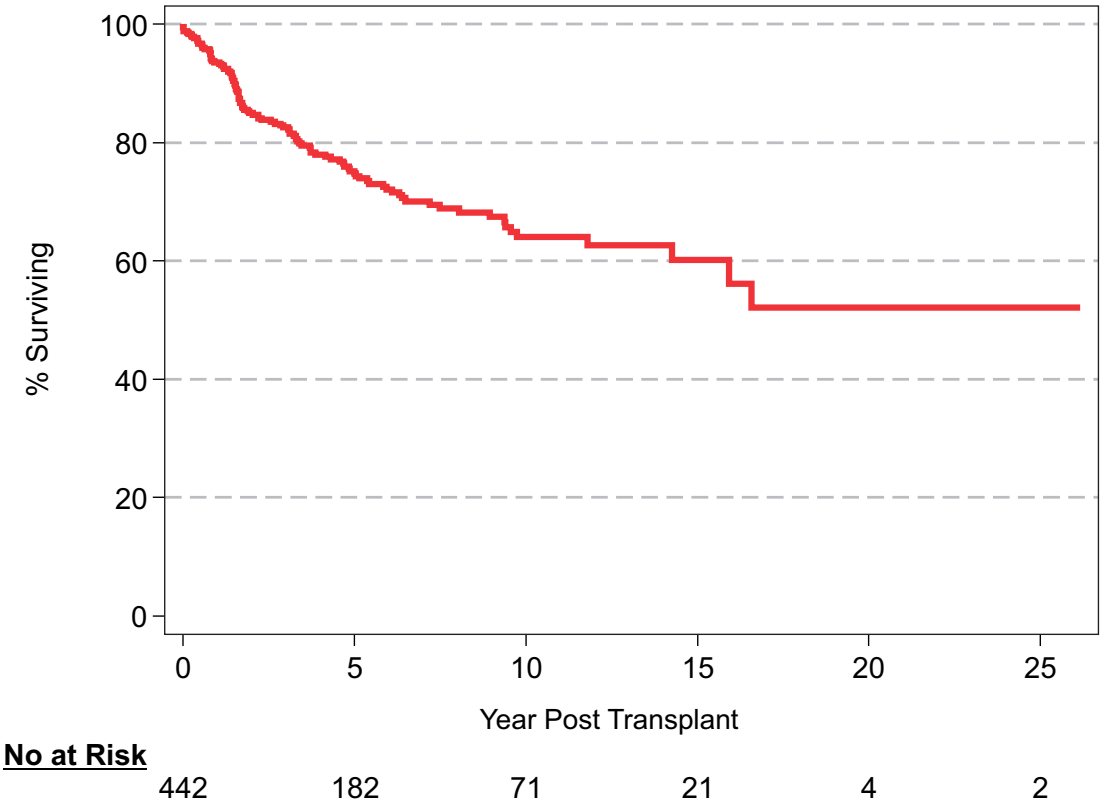
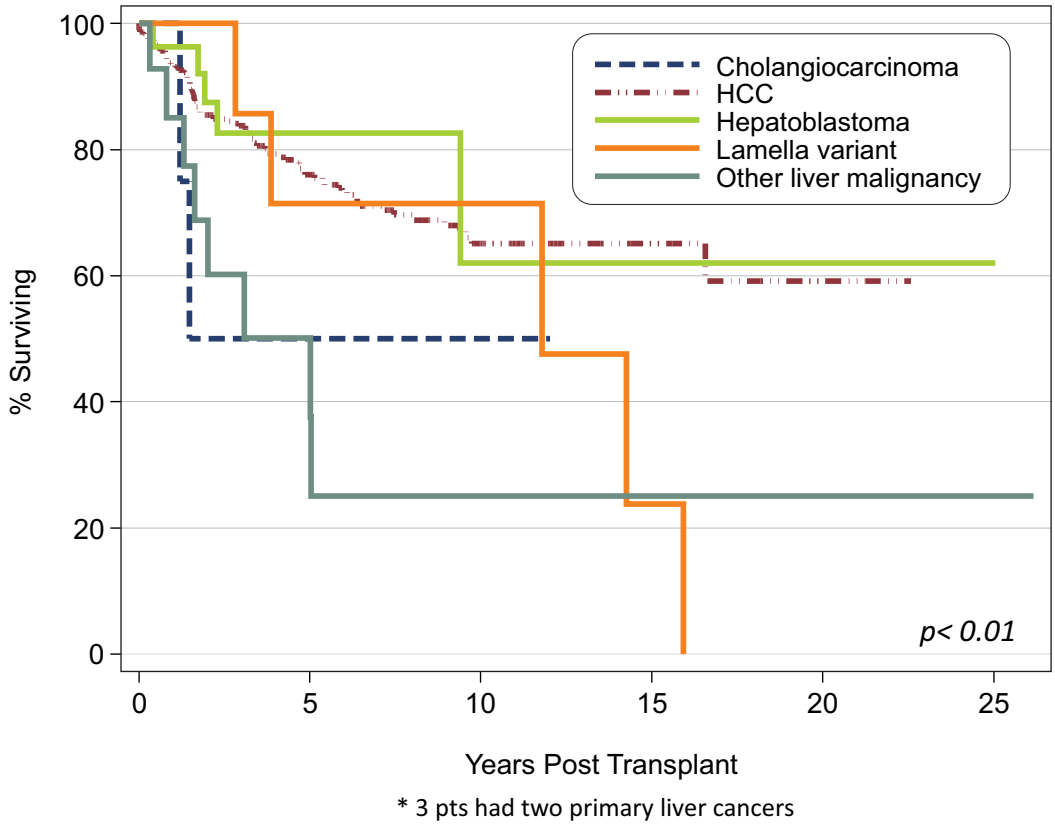
Overall Survival
Primary Liver Cancer
N =443/5136 (9% of pts transplanted)



Overall Survival
Primary Liver Cancer
N=443*/5136 (9%)



* 3 pts had two primary liver cancers

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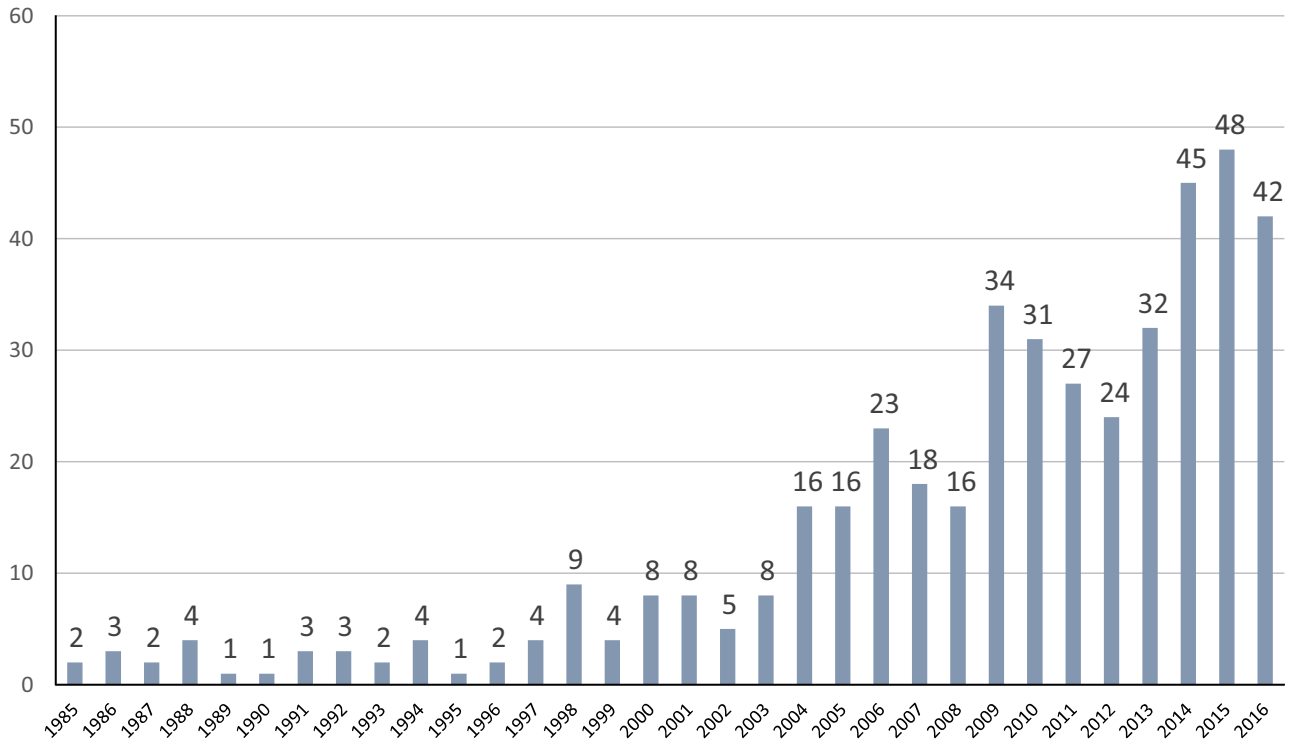
Primary Liver Cancer
Actuarial Survival Summary
N = 443/5136 (9%)

		1yr	5yr	10yr	15yr	20yr	25yr
HCC (n=391)	n	328	158	64	18	3	
	%	93	75	64	64	59	
Hepatoblastoma (n=29)	n	24	15	4	3	2	1
	%	96	82	61	61	61	61
Other (n=14)	n	12	5	2	2	2	1
	%	92	54	27	27	27	27
Fibrolamellar (n=7)	n	7	6	4	2		
	%	86	71	71	24		
CC (n=5)	n	4	2	2			
	%	100	33	33			

Primary Liver Cancer Incidence
N=443/5136 (9%)



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Liver Cancer as a Secondary Diagnosis
N = 739/5136 (14% pts)

	No	Died	Died of This Cancer
HEPATOCELLULAR CA*	687	163	48 (7%)
CHOLANGIO CA	40	32	20 (50%)
OTHER	8	6	3 (38%)
FIBROLAMELLAR	4	0	0
HEPATOBLASTOMA*	3	1	0
Total	**742* Ca in 739 pts**	**202 (28% of pts with SCa)**	**71 (10% of pts with SCa)**

* 3 patients had 2 secondary cancers

Overall Survival
Liver Cancer as a Secondary Diagnosis
N = 739/5136 (14% pts)

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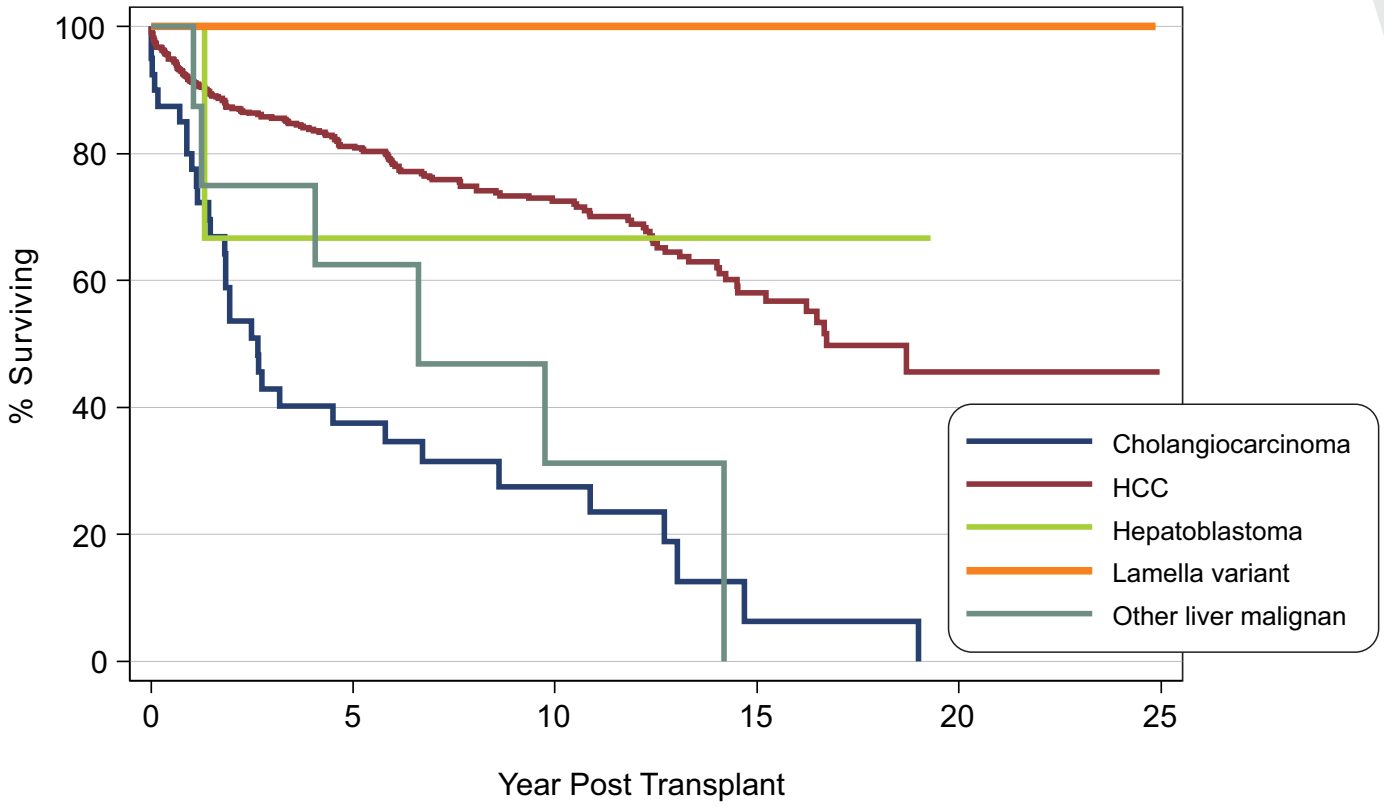
Liver Cancer as a Secondary Diagnosis
N= 739/5136 (14% pts)



Secondary Liver Cancer - Actuarial Survival Summary
N =739/ 5136 (14%)

		1yr	5yr	10yr	15yr	20yr
HCC (n=687)	n	502	275	148	38	5
	%	90	79	71	54	39
CC (n=40)	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=3)	n	3	3	2	2	
	%	67	67	67	67	

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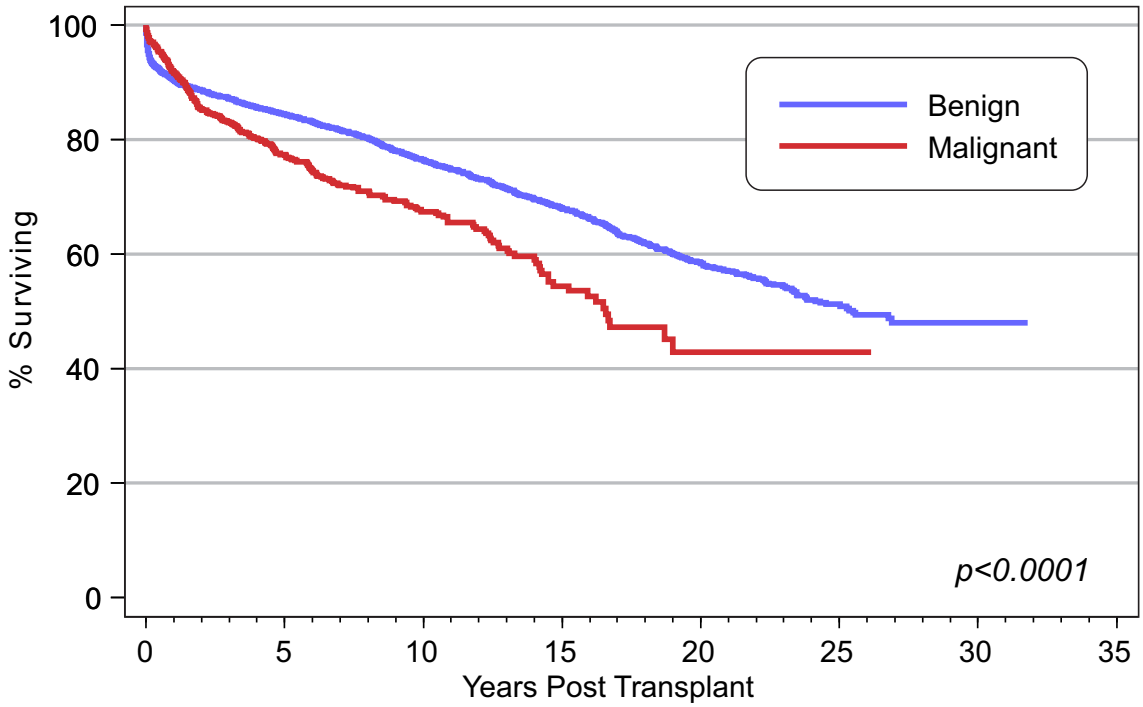
Liver Cancer - (Primary or Secondary Diagnosis)
N = 1182/5136 (23%)

TYPE OF CA	No.	DIED	DIED OF THIS CA
HEPATOCELLULAR CA*	1077	257	94 (9%)
CHOLANGIOCARCINOMA*	42	32	20 (48%)
HEPATOBLASTOMA*	32	6	4 (13%)
FIBROLAMELLAR	10	5	2 (20%)
EPITHELOID HAEMANGIOENDOTHELIOMA	7	1	1 (17%)
ADENOCARCINOMA	5	4	1 (20%)
CARCINOID	4	4	4 (100%)
ANGIOSARCOMA	2	2	2 (100%)
GASTRINOMA	1	1	1 (100%)
PANCREATIC ISLET CELL	1	1	1 (100%)
ERYTHROID LEUKAEMIA	1	1	1 (100%)
HEPATOCELLULAR MALIGNANT NEOPLASM (NOS)	1	0	0
TOTALS	**1188* Ca in 1182 pts**	**314 (27%of those with Ca)**	**131 (11% 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 =5136



Number at risk

Benign	3918	1657	501	6
Malignant	1174	237	10	0

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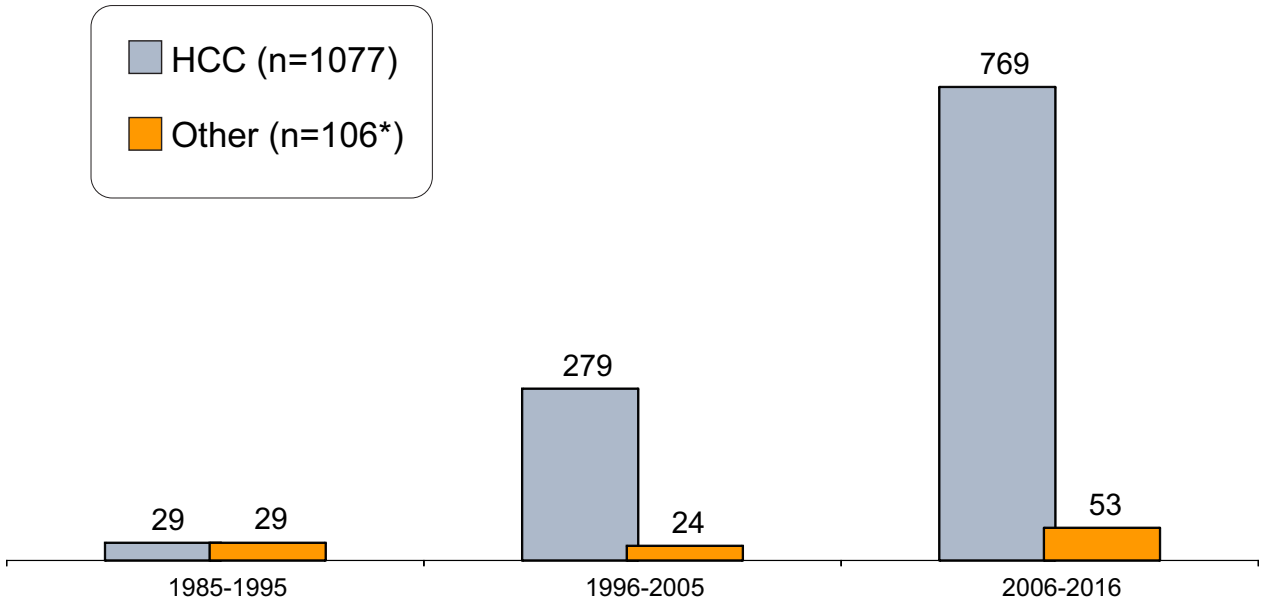
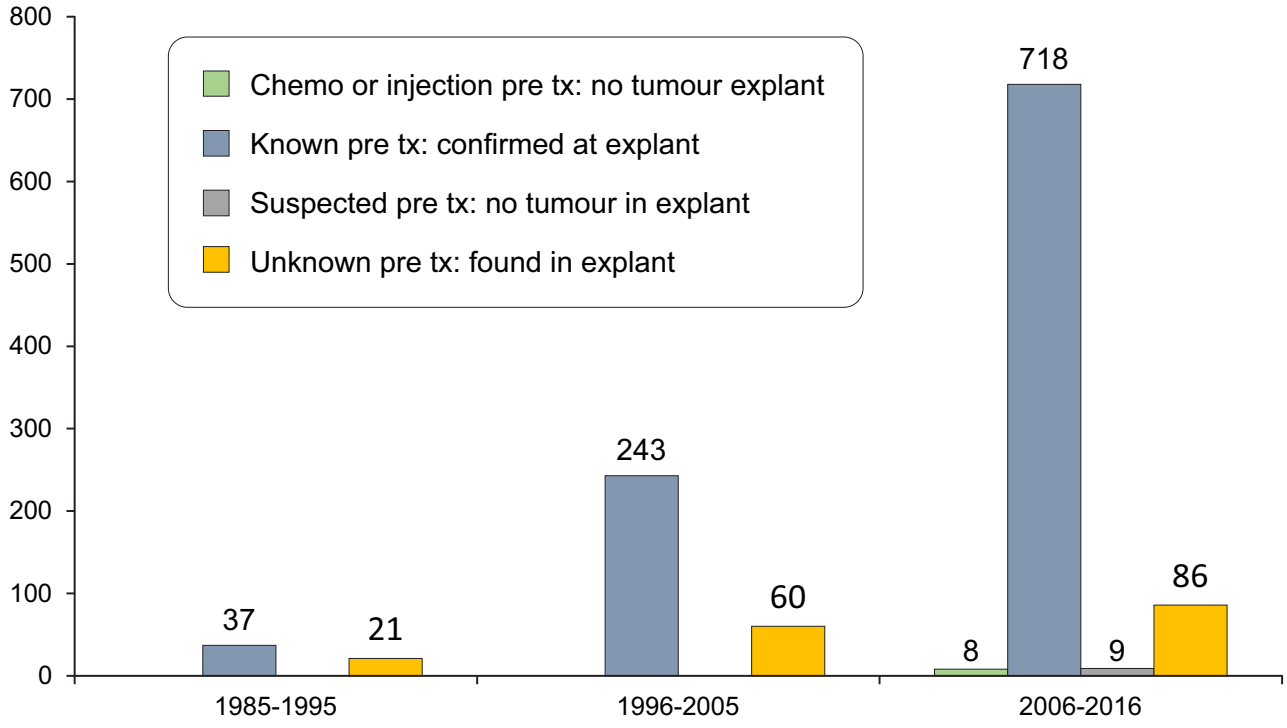
Liver Cancer at Transplantation
N = 1182/5136 (23%)



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

HCC at Transplantation



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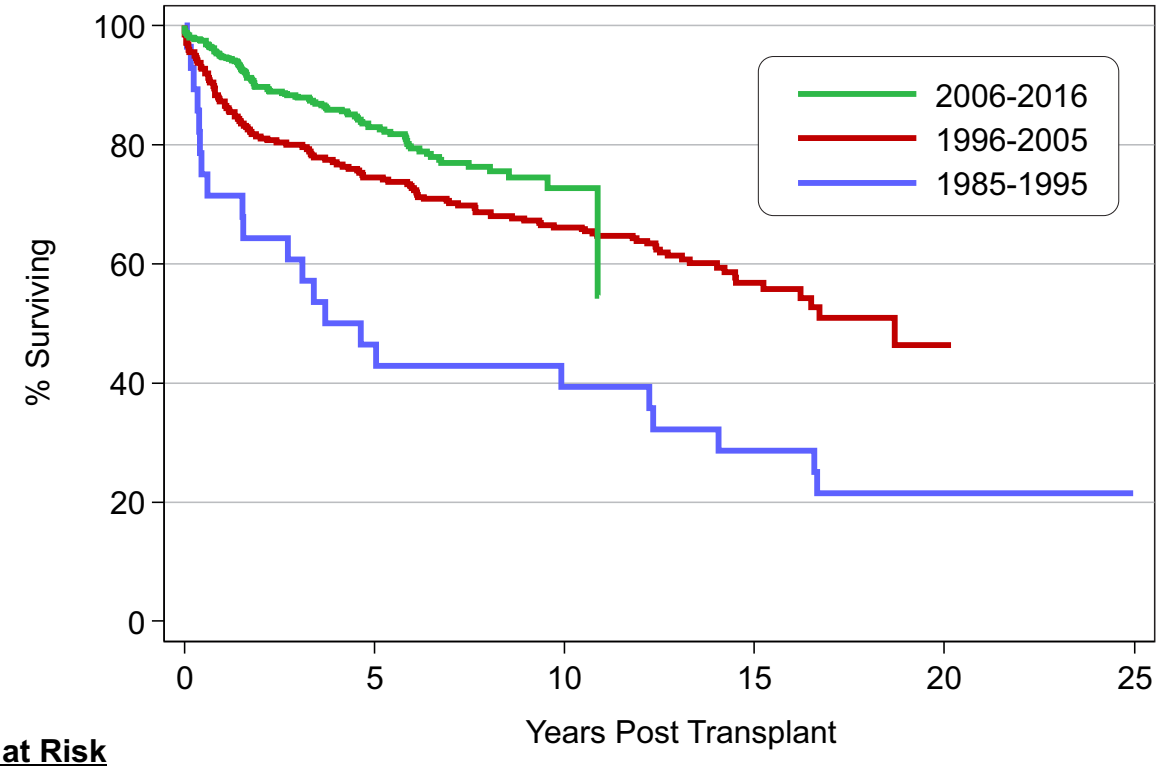
HCC vs Era (Primary and Secondary Indication)



No at Risk						
1985-1995	28	13	11	8	6	0
1996-2005	275	205	182	59	1	0
2006-2016	764	256	27	0	0	0

De Novo Non Skin Cancer
N = 381/5136 (7%)

	No	Male	Female	Age of pts (yrs)	Time to diagnosis (mths)	Died of This Cancer
Alimentary*	144	107	37	13 – 83 (m 59)	3 – 316 (m 78)	66 (45%)
Lymphoma*	107	63	44	1– 80 (m 50)	1 – 283 (m 66)	39 (37%)
Genitourinary*	63	40	23	21 – 82 (m 61)	2 – 350 (m 81)	5 (9%)
Breast	28	-	28	30 – 74 (m 55)	11 – 282 (m 95)	10 (37%)
Respiratory	39	30	9	29 – 75(m 60)	1 – 278 (m 97)	29 (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%)
Miscellaneous	6	3	3	59 – 73 (m 67)	34 – 235 (m 96)	2 (20%)
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
Bone	1	1	-	62	17	0
Total	***381 ca in 412 pts**	**259**	**153**	**1 – 83 (m 67)**	**1 – 350 (m 72)**	**160 (42% of pts with Ca)**

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

m=median

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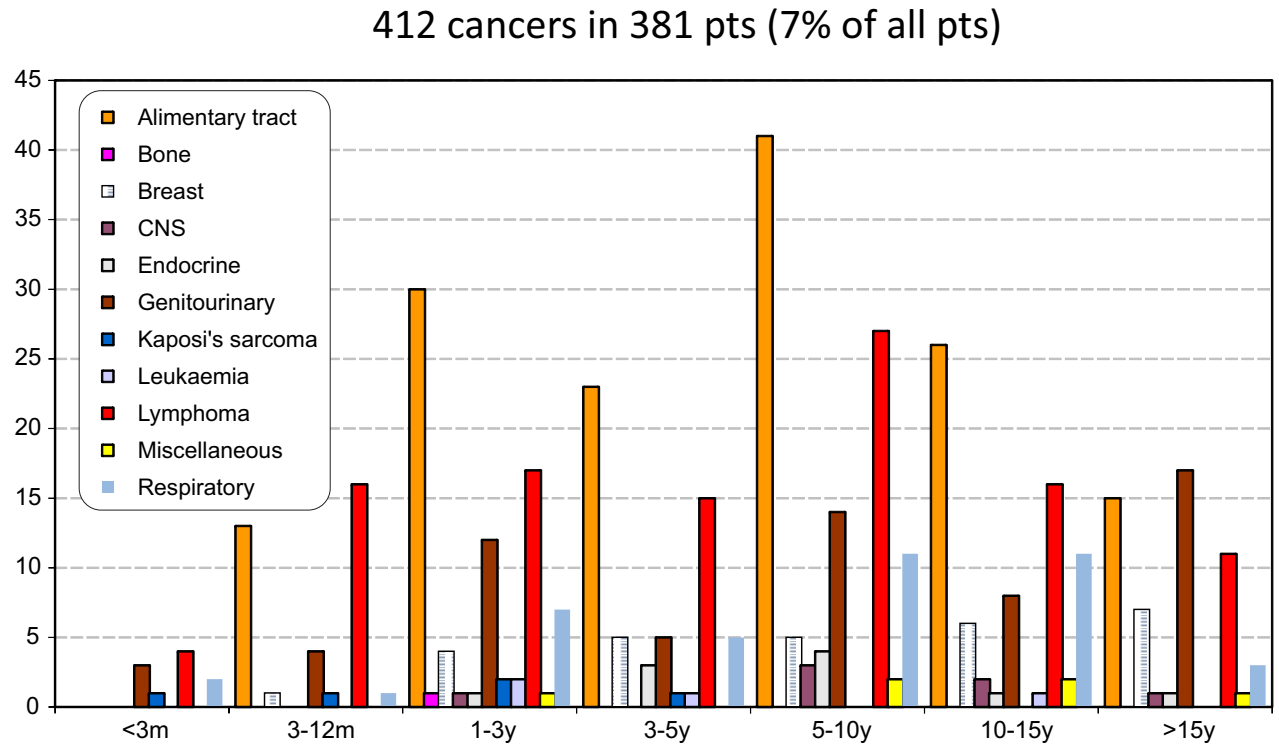
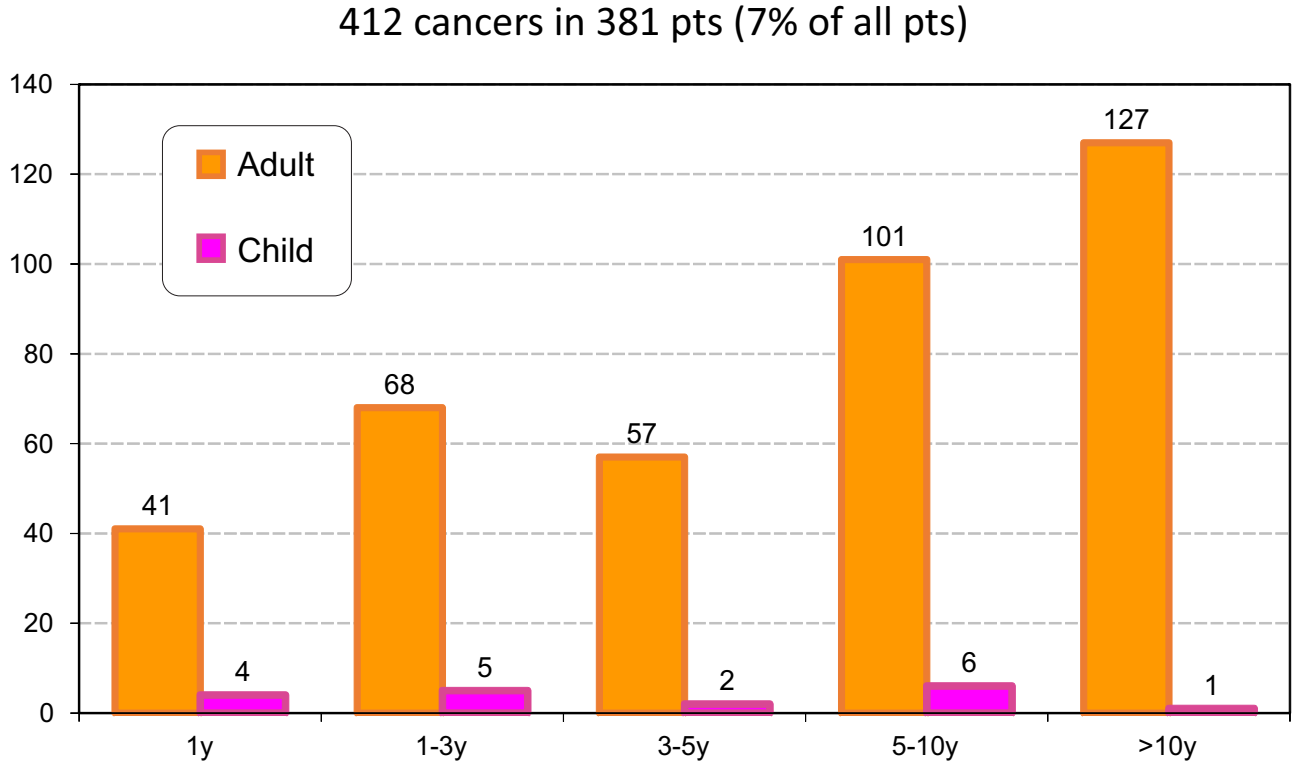
Time to Diagnosis of De Novo Non Skin Cancer (3m - >15y)
N = 5136



Time to Diagnosis of Any Non Skin Cancer (3m - >10y)
N = 5136



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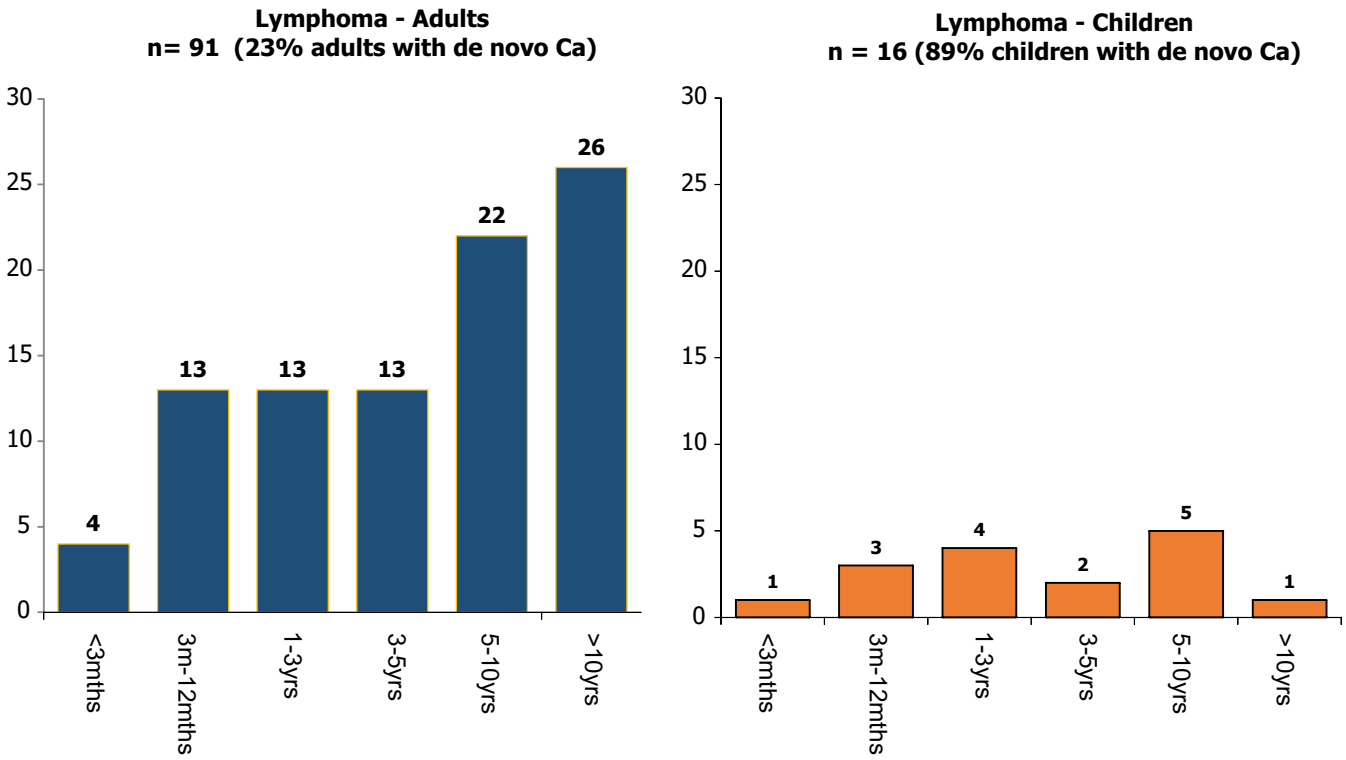
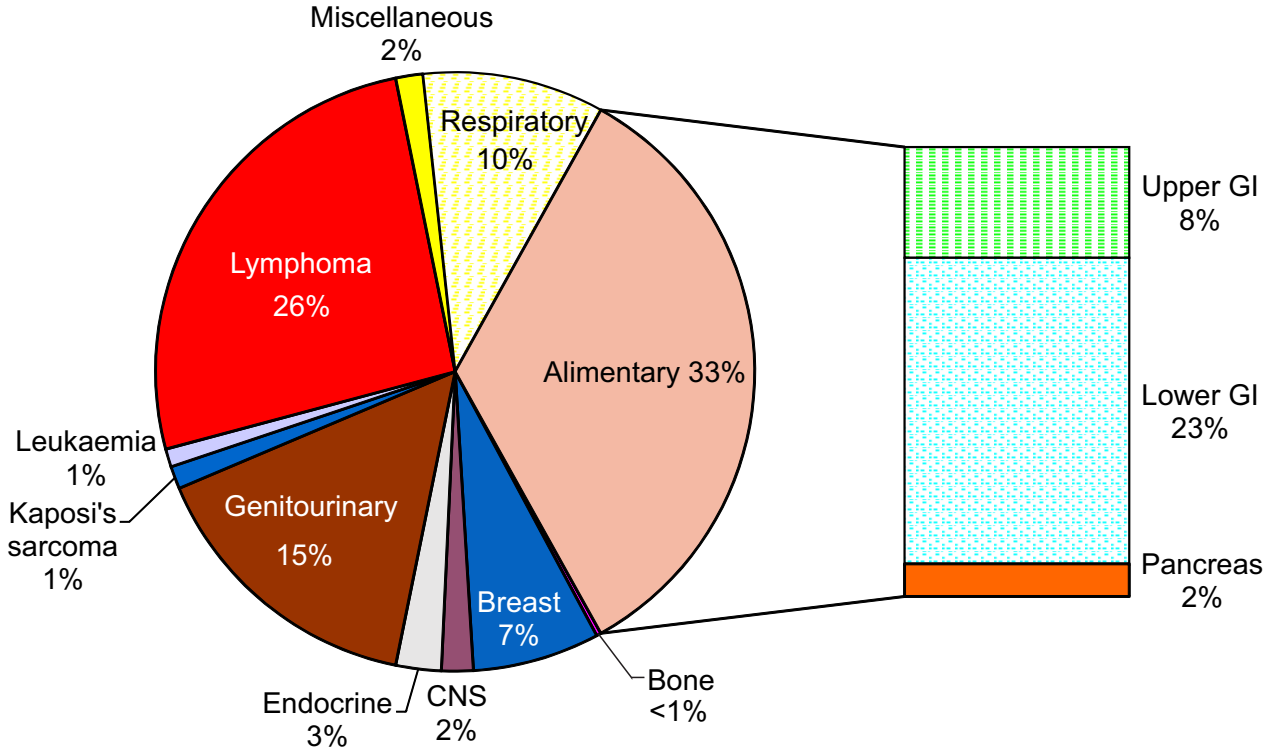
Time to Diagnosis of Lymphoma (3m - >10yrs)



De Novo Non Skin Cancer
N = 381/5136 (7%)



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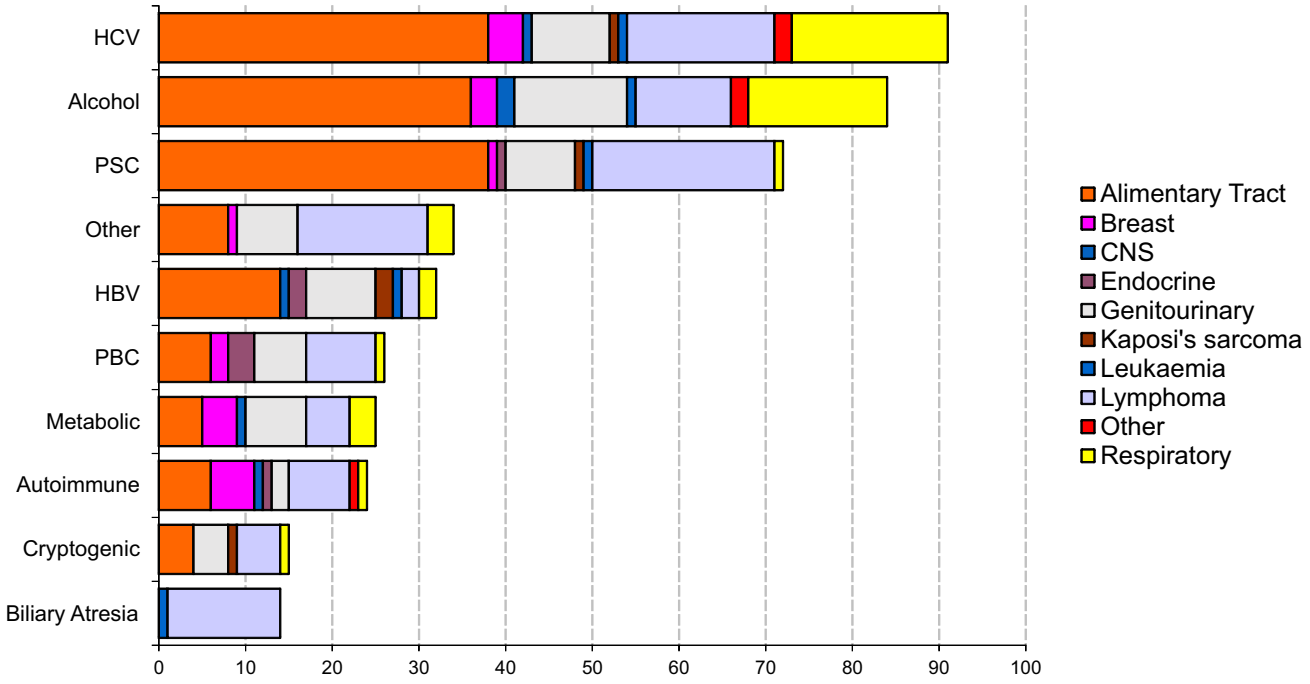
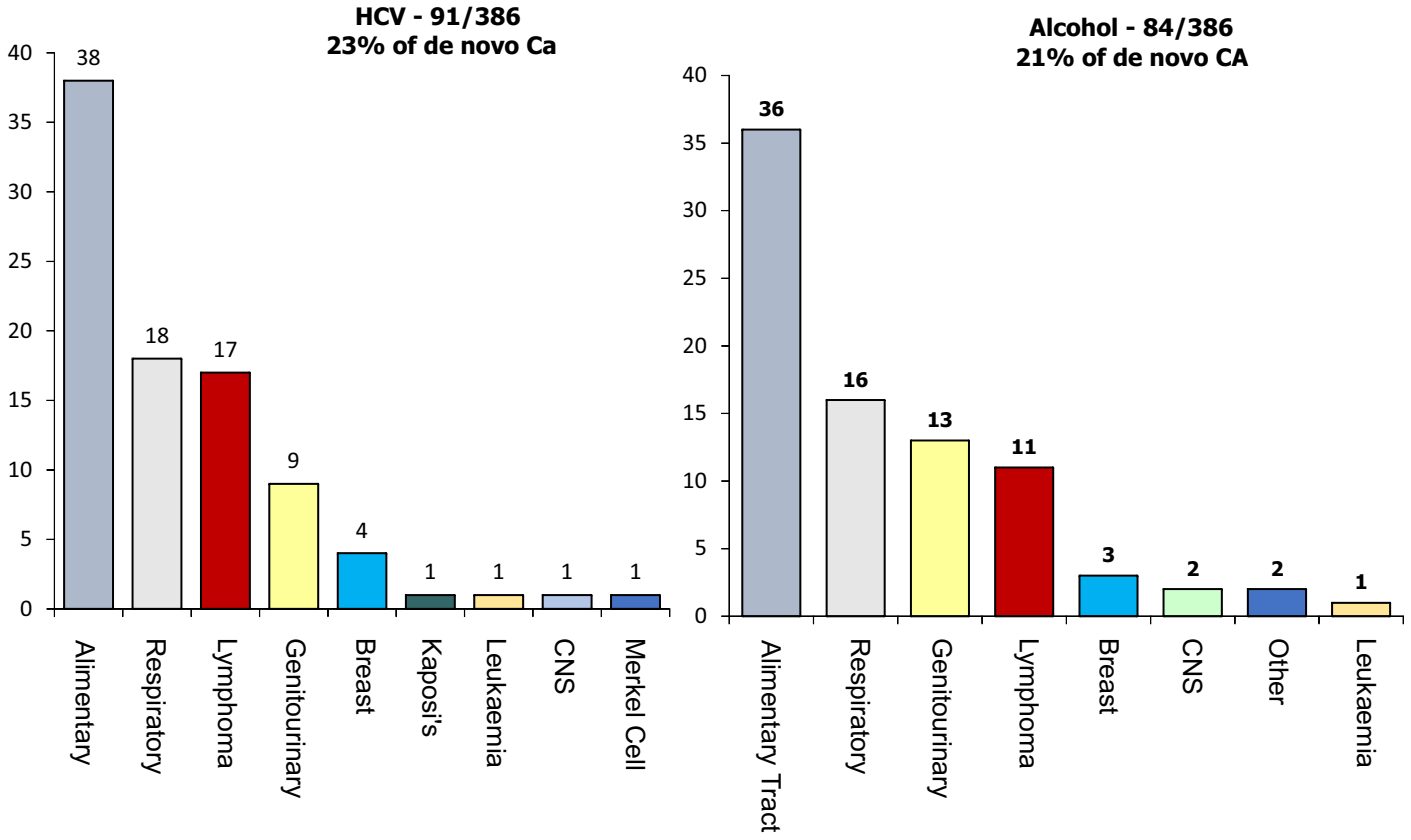
Pre Transplant Disease and De Novo Non Skin Cancer
N = 381/5136 pts (7%)



Pre Transplant Disease and De Novo Non Skin Cancer
N = 386 (413 Ca)/5136 pts (7%)



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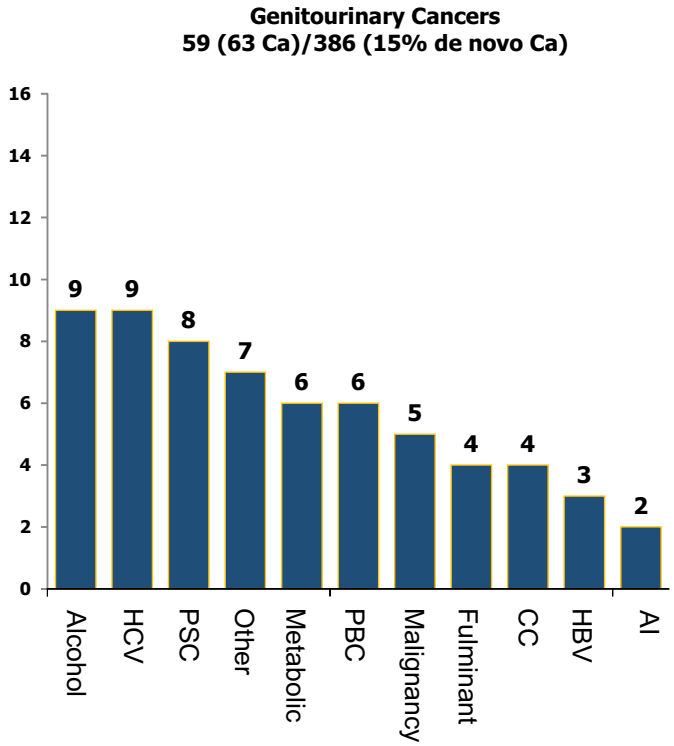
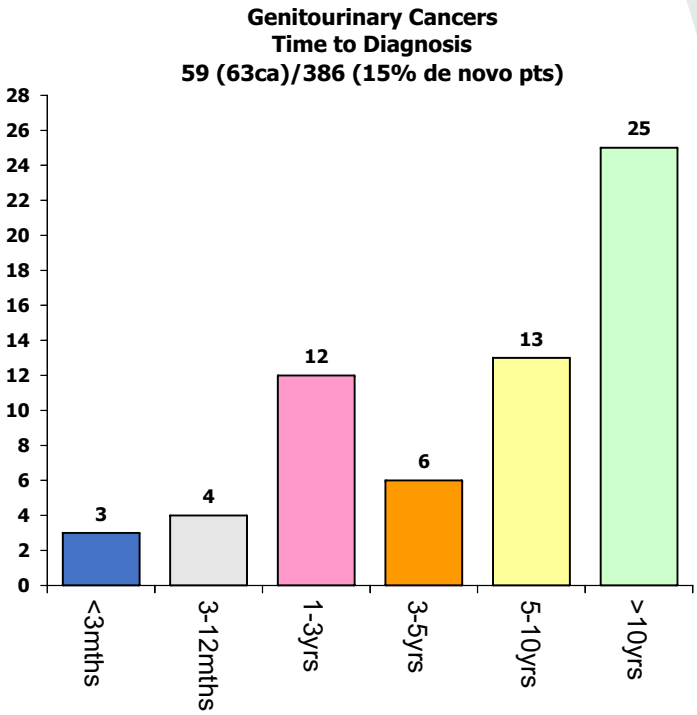
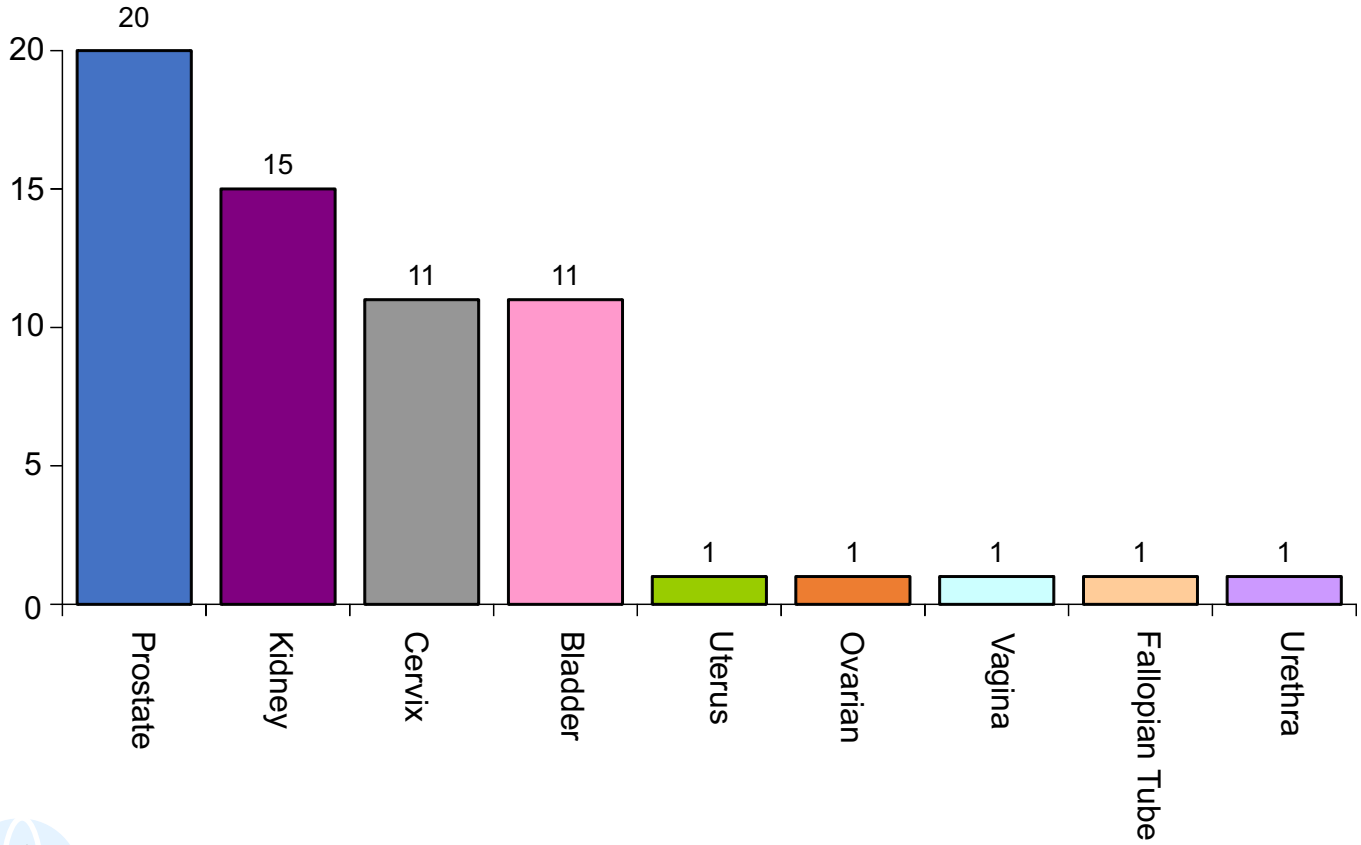
Pre Transplant Primary Liver Disease and - De Novo Non Skin Cancer
N = 381 (412 Ca)/5136 pts (7%)





De Novo Non Skin Cancer - Genitourinary Tract Incidence
N = 59/381 cancers (15%)



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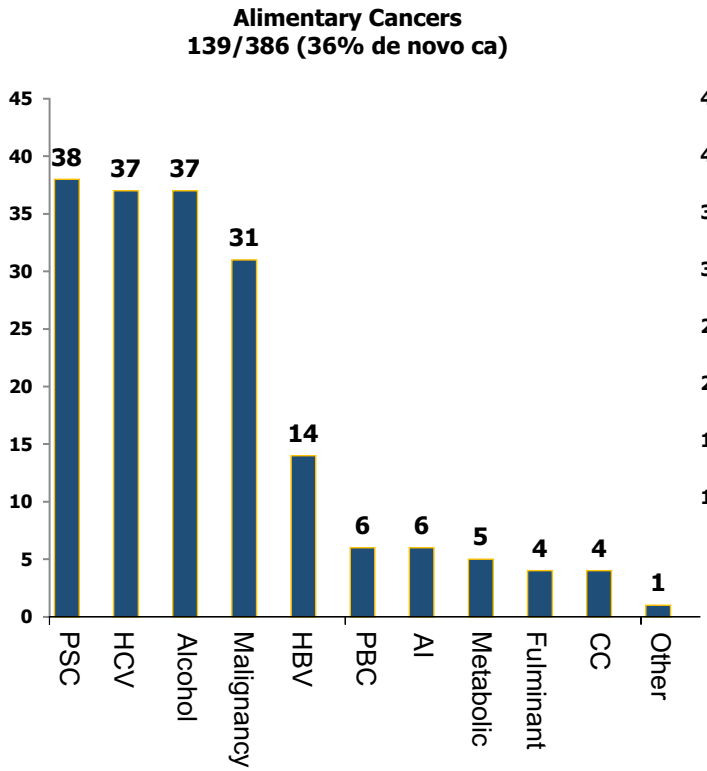
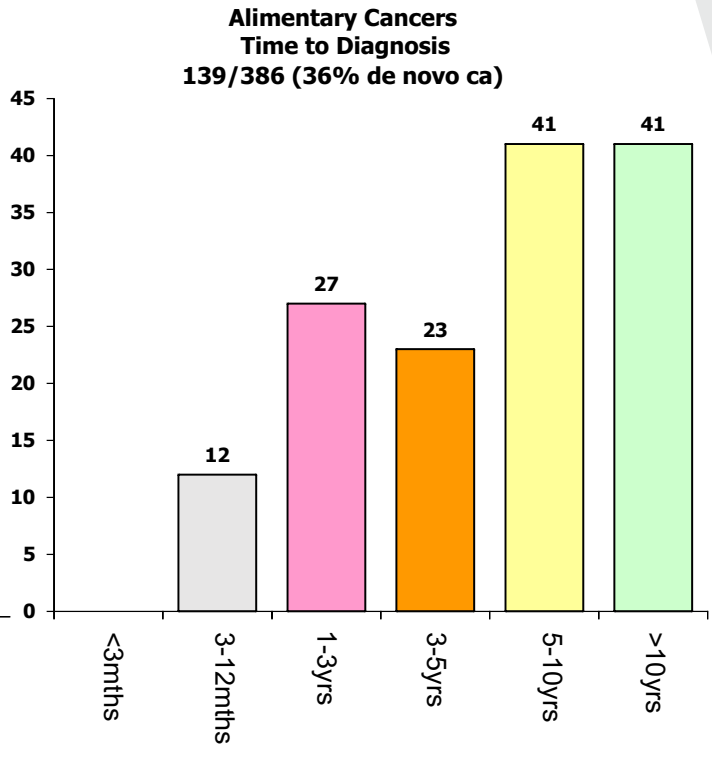
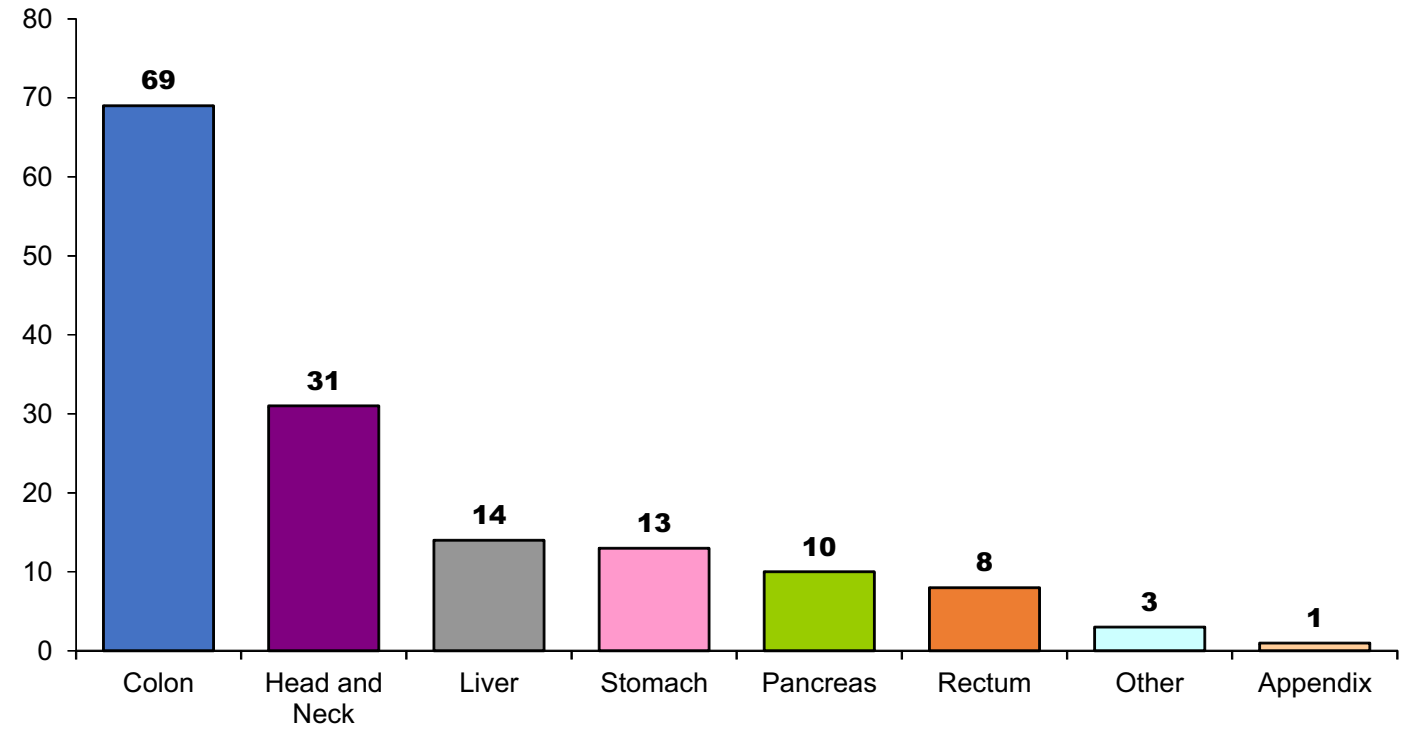
Pre Transplant Primary Disease and – Alimentary Cancer
N = 381 (412 Ca)/5136 pts (7%)





De Novo Non Skin Cancer - Alimentary Tract Incidence
N = 144/412 cancers (35%)



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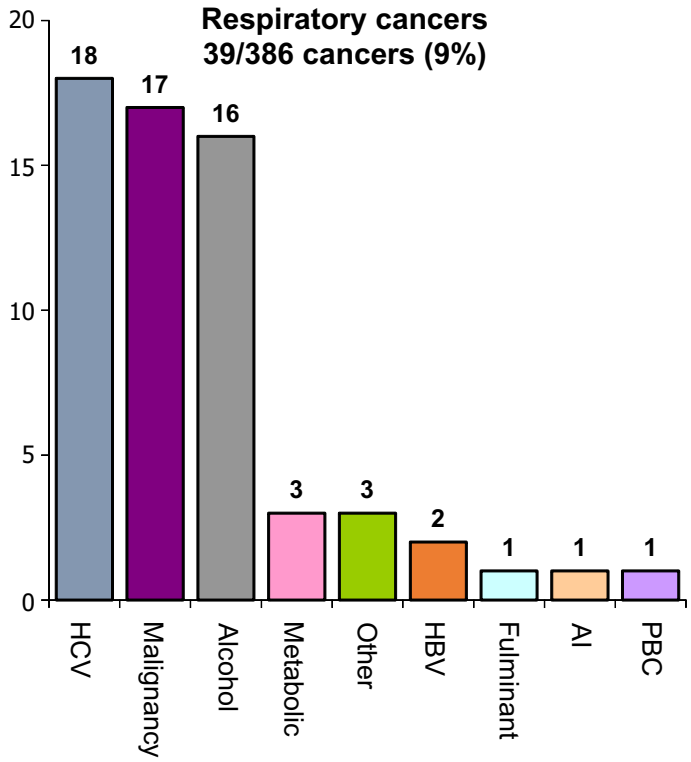
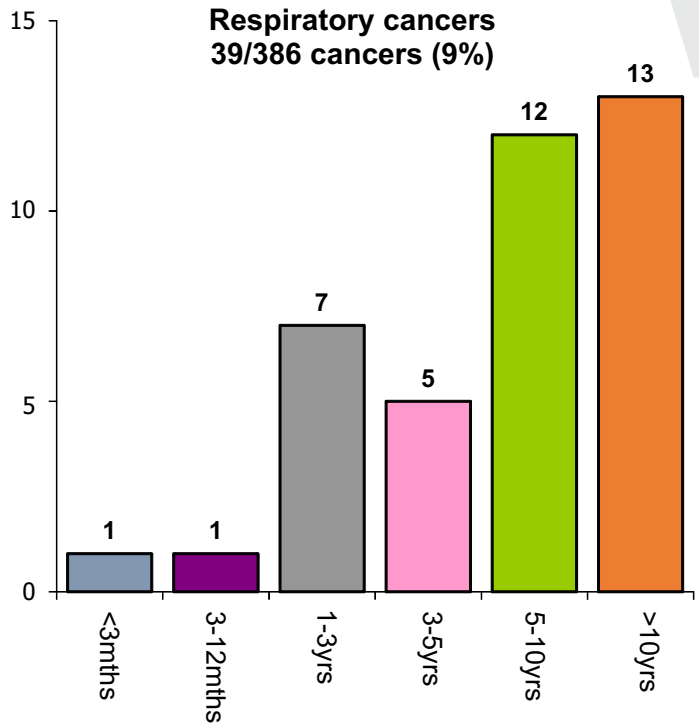
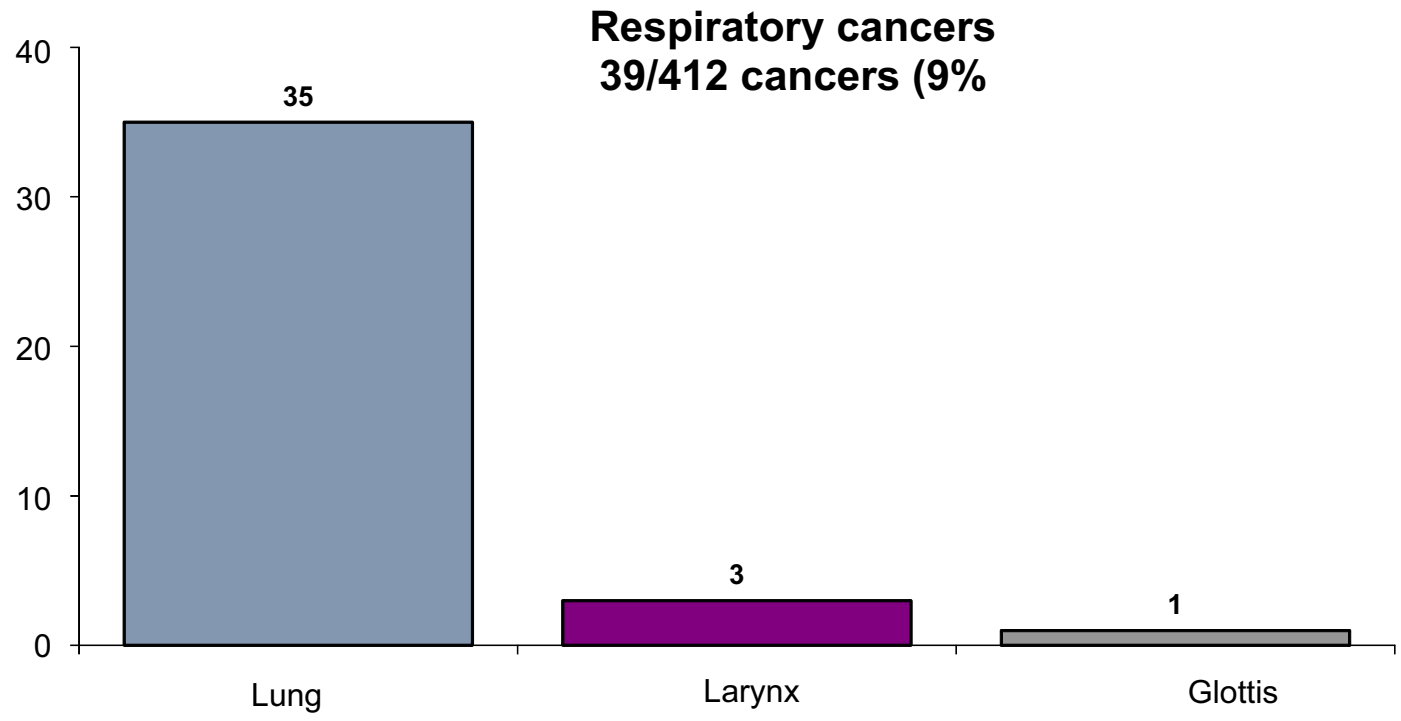
De Novo Non Skin Cancer - Respiratory Cancer Incidence





De Novo Non Skin Cancer - Respiratory Cancer Incidence



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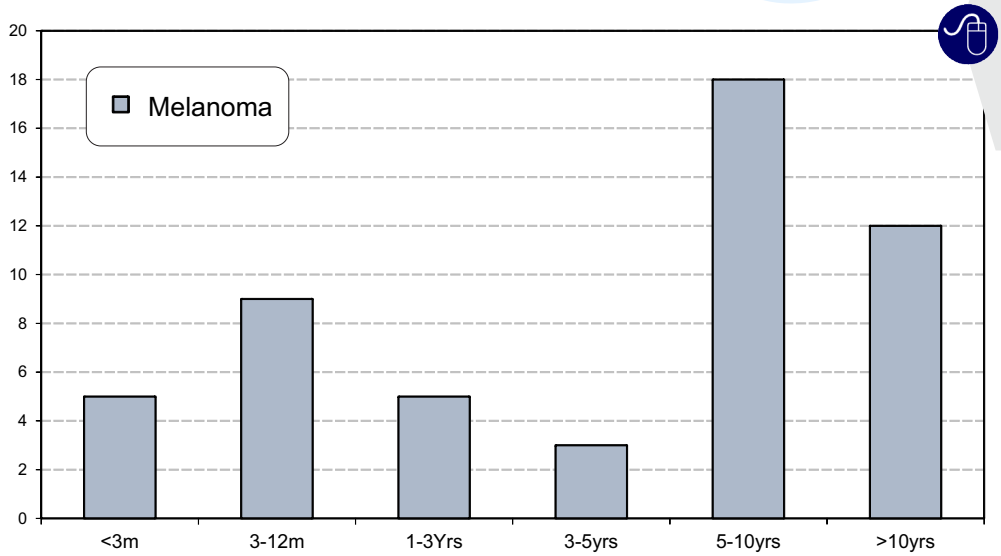
Time to Melanoma Skin Cancer Development Post Tx.

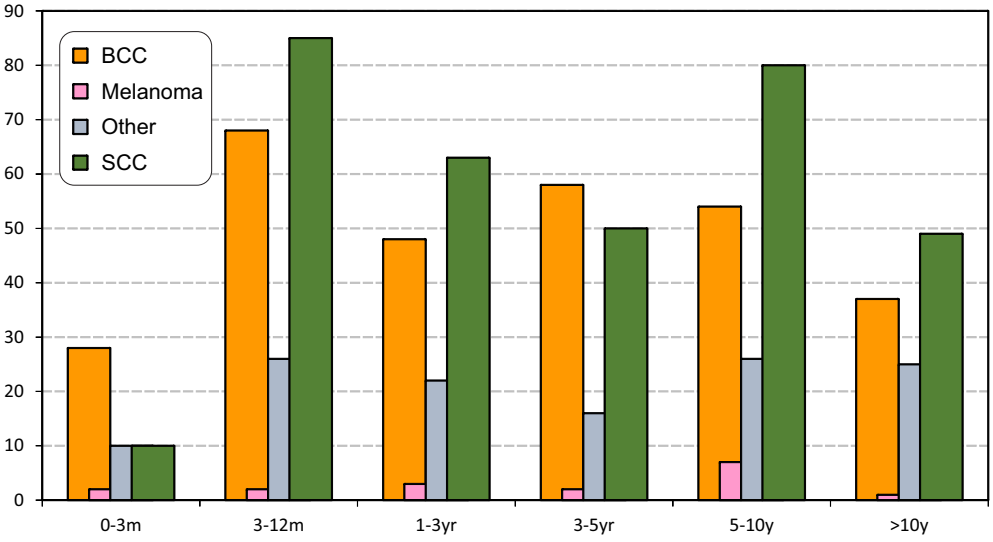
N =5136

52 (0.9% of all pts)



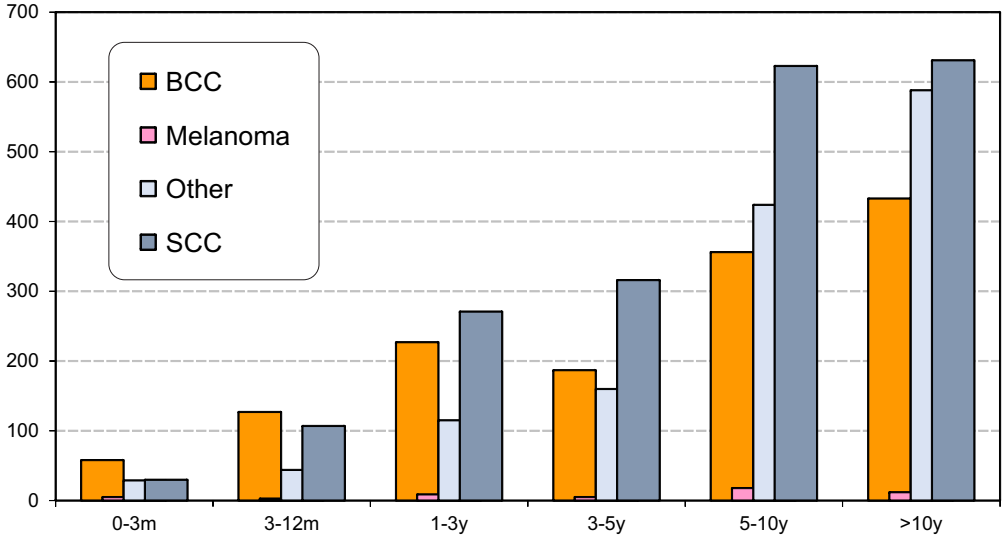
Time to 1st Skin Cancer Development

723/5136 (13% of all pts)



Time to Multiple Skin Cancer Development

343/723*/5136 (6% of all pts)



723 pts developed skin cancer post Tx. 343 have multiple skin cancer types.

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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
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

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	53	**92**
Crigler-Najjar	11	1	**12**
Familial amyloid polyneuropathy	0	39	**39**
Glycogen storage disease	4	7	**11**
Haemochromatosis	3	31	**34**
Homozygous hypercholesterolemia	7	2	**9**
Idiopathic copper toxicosis	1	0	**1**
Indian childhood cirrhosis	1	0	**1**
Other*	17	7	**24**
Primary hyperoxaluria	9	8	**17**
Tyrosinemia	6	0	**6**
Urea cycle disorders**	22	4	**26**
Wilsons disease	8	30	**38**
Total	**127**	**182**	**309**

* *Maple syrup urine disease 5*
Amyloidosis 2
Bile acid transport disorder 3
Protein C deficiency 2
Propionic acidemia 4
Methylmalonic acidemia 2
Familial immunodeficiency
Mitochondrial disease
Porphyria 3
Niemann-Pick disease

** *OTC deficiency 14*
Citrullinemia 5
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	35	9	**44**
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	22	**24**
Choledocal cyst	2	2	**4**
Cholestatic disease-Other	4	9	**13**
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**
Hereditary haemorrhagic telengectasia / OWRD	0	6	**6**
Neonatal hepatitis	4	0	**4**
Nodular regenerative hyperplasia	0	6	**6**
Polycystic liver disease	0	24	**24**
Polycystic liver and kidney disease	2	19	**21**
Progressive familial intrahepatic cholestasis (PFIC)	23	5	**28**
Secondary biliary cirrhosis	3	19	**22**
Secondary biliary cirrhosis - hepatolithiasis	0	4	**4**
Secondary biliary cirrhosis - cystic fibrosis	15	22	**37**
Other - specify#	15	28	**43**
Total	114	223	**337**

*Vanishing bile duct syndrome*
Haemangiotelangiectasia
Veno-occlusive disease
Chronic active hepatitis A
Non-cirrhotic portal hypertension
Kassabach-Merritt syndrome
Arterial-venous malformation
Oriental cholangio hepatitis
Liver trauma
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	18	**26**
Acute - α-1 -AAT	2	0	**2**
Acute autoimmune hepatitis	0	9	**9**
Acute unknown / unspecified	48	99	**147**
Acute - paracetamol	4	21	**25**
Acute - other drugs	3	29	**32**
Acute herbs / mushrooms	1	11	**12**
Acute - hepatitis A	1	3	**4**
Acute - hepatitis B	0	70	**70**
Acute - hepatitis non A-G	15	21	**36**
Acute - hepatitis E	0	1	**1**
Acute - other virus	1	1	**2**
Acute - post liver resection/trauma	1	3	**4**
Subacute - Budd Chiari	1	2	**3**
Subacute - Wilson's	2	5	**7**
Subacute autoimmune hepatitis	2	21	**23**
Subacute - drug / herbs	1	16	**17**
Subacute - unknown / unspecified	5	29	**34**
Subacute - hepatitis A	0	2	**2**
Subacute - hepatitis B	0	20	**20**
Subacute - hepatitis non A-G	0	6	**6**
Total	**95**	**389**	**484**

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Appendix V

ANZLTR Causes of Patient death

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

Miscellaneous	Children	Adult	
Multiorgan failure	10	82	92
Renal failure	1	37	38
Graft vs Host disease	-	6	6
Social *(accident, suicide,non-compliance, Rx withdrawn)*	1	21	22
Sudden death *(cause unknown)*	3	37	40
Other *(hyperkalaemia,motor neurone disease diabetes complications, drug reaction, progression FAP essential thrombocythemia)*	3	32	35
TOTAL	18	215	233