Australia & New Zealand
Liver and Intestinal Transplant Registry

Report on liver and intestinal transplantation activity to 31/12/2018

30th
ANNUAL REPORT
ANZLITR

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1 Preface

We are pleased to announce the new name of our Registry to reflect the inclusion of intestinal transplantation data alongside Australian and New Zealand liver transplantation data. The Registry is now known as the Australia and New Zealand Liver and Intestinal Transplant Registry (ANZLITR) and a new logo has been developed to reflect this.

The 30th Annual Report of the Australia and New Zealand Liver and Intestinal Transplant Registry contains liver and intestinal transplantation data to 31st December 2018 and analyses the cumulative data since the establishment of the first liver transplant units in Australia and New Zealand in 1985. The format of the annual report has been revised to include information about the history of the registry, analysis methodology, new areas of analysis including additional detailed graft survival analyses, commentary alongside the figures and tables to assist with interpretation and understanding, an intestinal transplantation section, glossary and a list of publications that have utilised the ANZLITR data. The report can be downloaded from the ANZLITR website: https://www3.anzltr.org/ A limited number of hard copies are produced each year. Requests for hard copies may be made via the website or through your local liver transplantation unit.

In 2018, the ANZLITR secretariat moved from Princess Alexandra Hospital in Brisbane to Austin Health in Melbourne. We would like to thank Glenda Balderson (prior Registry Manager) and Professor Stephen Lynch (prior Director) for their significant contribution to the ANZ Liver Transplant Registry over many years. Michael Fink is the new Director and Mandy Byrne is the Registry Manager. Formal Human Research and Ethics approval for the Registry was obtained in 2019.

We thank the staff at all the liver transplantation units who contribute their data by direct entry into the ANZLITR database. The Liver Transplantation Cancer Registry is based at Royal Prince Alfred Hospital, Sydney. We acknowledge the continued contribution of Pamela Dilworth, Program Manager, and Marie Mulhearn in the maintenance of the Liver Transplantation Cancer Registry and preparation of the cancer report for the ANZLITR Annual Report.

We are grateful to the Australian Government and the Organ and Tissue Authority for the ongoing financial support of the Registry. We also thank Astellas Pharma Australia Pty Ltd for additional financial support. We thank the Australian and New Zealand Organ Donor Registry for their collaboration and provision of deceased donor data.

We welcome any feedback or suggestions regarding the ANZLITR Annual Report.

Finally, we would like to acknowledge all the patients and their families that have been involved in the liver and intestinal transplantation program and organ donation over the years.

Mr Michael Fink
Ms Mandy Byrne

2 Executive Summary

Annual waiting list mortality has decreased from a peak of 11.3% in 2008 to 2.7% in 2018. One of 15 patients listed as category 1 and none of 13 patients listed as category 2 in 2018 died waiting.

There has been a progressive increase in liver transplantation from deceased donors since 2007, predominantly comprising brain dead donors, including donors aged over 60 years, with a modest increase in donation after circulatory death donors. Living donor liver transplantation accounts for 1.7% of transplants performed.

In 2018, 369 liver transplants were performed in 356 patients. Between 1985 and 2018, 6,259 transplants were performed in 5,786 patients, including 1,110 transplants in 977 children and 5,149 transplants in 4,809 adults. Between 2007 and 2018, there was a 95% increase in the number of patients transplanted per year. Paediatric age at transplant has decreased progressively and adult recipient age has increased progressively over time. Split liver transplantation is the dominant form of liver transplantation in children (55% in 2018) and whole liver transplantation is the dominant form of liver transplantation in adults (92% in 2018).

The commonest indication for transplantation in children is biliary atresia and in adults is hepatitis C virus cirrhosis until 2014, after which hepatocellular carcinoma has become the commonest indication. The proportion of patients transplanted primarily for hepatitis C has decreased from 33.8% in 2012 to 13.3% in 2018.

The 1-, 3-, 5- and 10-year patient survival in recent years for paediatric patients was 97%, 97%, 91% and 92%, respectively. Children transplanted with a split or living donor graft had slightly superior patient survival to those transplanted with a whole graft and those transplanted with a reduced graft had inferior survival ($P < 0.001$).

The 1-, 3-, 5- and 10-year patient survival in recent years for adult patients was 95%, 91%, 85% and 73%, respectively. Patient survival in adults reduced progressively with increasing age ($P < 0.001$), varied significantly by primary disease ($P = 0.038$), with poorer outcomes for hepatitis C virus and alcoholic cirrhosis, and has improved over time for hepatitis B ($P < 0.001$) and more recently for hepatitis C virus cirrhosis ($P = 0.016$).

The 1-, 3-, 5- and 10-year graft survival in recent years for paediatric patients was 91%, 90%, 83% and 81%, respectively. The 1-, 3-, 5- and 10-year patient survival in recent years for adult patients was 91%, 86%, 81% and 69%, respectively. Graft survival varied significantly by era of transplant (better outcome in more recent era ($P < 0.001$), age group (better outcome in children, $P < 0.001$), graft number ($P < 0.001$), graft type in children (poorer outcome with reduced grafts, $P < 0.001$), donor age (better outcome with younger donors, $P < 0.001$), donor cause of death (poorer outcome from donors who died of stroke, $P < 0.001$), shipping of grafts (better outcome with livers that were not shipped from another unit, $P < 0.001$), cold ischaemia time (better outcome with cold ischaemia time < 442 mins, $P < 0.001$) and recipient urgency (poorer outcome for category 1 recipients, $P = 0.001$).

The commonest indications for retransplantation were vascular problems (30%), rejection (17%), primary non-function or initial poor function (14%) and recurrent disease (14%). The commonest causes of death were malignancy (23%), sepsis (13%), multi-organ failure (8%) and cardiovascular disease (8%).

3 Australia and New Zealand Liver and Intestinal Transplant Registry Information

3.1 Australia and New Zealand Liver and Intestinal Transplant Registry Overview

The Australia and New Zealand Liver and Intestinal Transplant Registry (ANZLITR) is a collaborative effort of the liver transplantation units in Australia (Adelaide, Brisbane, Melbourne, Perth, Sydney) and New Zealand (Auckland). The Australian Intestinal Transplant Service, co-located with the Victorian Liver Transplant Unit, offers an intestinal transplant service to Australian and New Zealand paediatric and adult patients. The ANZLITR Management Committee is comprised of the Registry Director, the Registry Manager and the director of each liver transplant unit. The Management Committee oversees all activities associated with the registry, including database design, data collection, analysis, reporting and approval of research utilising Registry data.

The Registry contains de-identified data on all liver and intestinal transplantation activity across Australia and New Zealand since the first liver transplant in 1985. Data are collected and entered into the Registry by a data manager/ transplant nurse employed by each Liver Transplant Unit. Data include:

- demographics on patients placed on the liver and intestinal transplant waiting lists
- information at time of listing for transplant such as diagnoses, medical and laboratory information and urgency category
- date patient listed on transplant waiting list (full collection from 2004, partial collection prior to 2004)
- information about the transplant such as date, graft number, type of graft, donor source, serology and operative information
- information about the outcome of the transplant such as the status of the graft, patient status, cause of patient death
- information about patients delisted without transplantation, including reason for delisting
- donor information – deceased (from 1989 onwards) and living donors
- cancer after transplantation

3.2 History of the Australia and New Zealand Liver and Intestinal Transplant Registry

Since the first Queensland liver transplant in 1985, data have been collected on all liver transplants in Australia and New Zealand. New South Wales data collection commenced in 1986. Victoria performed their first liver transplant in 1988, South Australia and Western Australia, in 1992 and New Zealand, in 1998. The first intestinal transplant in Australia and New Zealand was performed by the Australian Intestinal Transplant Service in Melbourne in 2010.

In 1988, the three established liver transplants units in Australia (New South Wales, Queensland and Victoria) agreed to combine their liver transplant data into a central database to provide an overall report on liver transplantation and outcomes. In 1999, when New Zealand commenced liver transplantation, all Australian and New Zealand units agreed to collaborate and contribute their data to a combined registry and this was named the Australia and New Zealand Liver Transplant Registry (ANZLTR).

The initial liver transplantation data reporting was undertaken by Professor A.G.R. Sheil at Royal Prince Alfred Hospital in Sydney in the late-eighties. In the 1990s, reporting of liver transplantation activity alternated between Royal Prince Alfred Hospital in Sydney and Princess Alexandra Hospital in Brisbane.

Initial funding for the data collection from 1988 to 2000 was by the liver transplant units. In May 2001, at the Australian Health Ministers' Advisory Council meeting, the Registry was formalised and funding from the Commonwealth Government was provided for the first time. This included funding for a part-time data manager and production costs of the Annual Report. An ANZLTR Management Committee was formed, comprising the head or a senior consultant from each of the liver transplant units and the ANZLTR data manager.

In 2003, the Management Committee decided to move to a web-based format and the liver transplant units provided the funds for the development of a web-based database. The electronic Registry was established and managed by Ms. Glenda Balderson (Registry Manager) and Professor Stephen Lynch (Registry Director) at Princess Alexandra Hospital in Brisbane. After importation of historical data, near real time data collection began in January 2004. Collection of all new listings and outcome data commenced at this time.

In 2007-08, the Commonwealth Funding Agreement was extended to include the costs of the web-based program hosting, software development and maintenance, and funds for each unit to assist with data entry services. Currently the ANZLITR is fully funded by the Organ and Tissue Authority (OTA), Australian Government.

In August 2018, the coordinating centre moved to Austin Health in Melbourne. Mr Michael Fink commenced as the Registry Director and Ms. Mandy Byrne as the Registry Manager. Formal Human Research and Ethics (HREC) approval for the Registry was obtained in 2019 under the National Mutual Acceptance scheme.

The Liver Transplantation Cancer Registry was established alongside the liver transplantation data collection by Professor A.G.R. Sheil at Royal Prince Alfred Hospital in Sydney in the mid-eighties. The Liver Cancer Registry is still hosted and managed at Royal Prince Alfred Hospital and they prepare the cancer report for the ANZLITR Annual Report.

3.3 Australia and New Zealand Liver and Intestinal Transplant Registry Application

The ANZLITR database consists of an on-line data registry application which is hosted on an Australian based server cloud platform (Digital Pacific), with a Linux operating system and a web-based application using a Postgres database repository. High level security is maintained including high level user authentication, firewall protection and an intrusion prevention software framework.

Access to this system is strictly controlled and only authenticated users are allowed access to the application. Users from each liver transplant unit only have full access to data relevant to their own patients.

3.4 Australia and New Zealand Liver and Intestinal Transplant Registry Website

The ANZLITR website is accessible to the public via the following address: https://www3.anzltr.org/
The website provides:

- an overview and history of the Registry
- a list of participating centres
- copies of Annual Reports
- links to international liver transplant registries, organ donation website in ANZ and other useful sites
- contact information

3.5 Funding of the Registry

The ANZLITR is funded by the Australian Government Organ and Tissue Authority.
Additional funding has been received from Astellas Pharma Australia Limited.

3.6 Registry Secretariat

Registry Manager Ms Mandy Byrne
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Email: mandy.byrne@austin.org.au
c/o Victorian Liver Transplant Unit,
Austin Health,
145 Studley Road,
Heidelberg, Australia.
PO Box 5555, Victoria, 3084

3.7 Registry Management Committee

Director	Mr Michael Fink, Austin Health
Manager	Ms Mandy Byrne, Austin Health
New South Wales	Professor Geoff McCaughan, Royal Prince Alfred Hospital and Westmead Children's Hospital
Queensland	Dr Peter Hodgkinson, Princess Alexandra Hospital and the Queensland Children's Hospital
South Australia	Dr John Chen, Flinders Medical Centre
Victoria	Professor Robert Jones, Austin Health and The Royal Children's Hospital
Western Australia	Professor Bryon Jaques, Sir Charles Gairdner Hospital
New Zealand	Professor Stephen Munn, Auckland City Hospital and Starship Children's Hospital

3.8 Participating Centres

Australian National Liver Transplant Unit (NSW)

Royal Prince Alfred Hospital
Missenden Road
Camperdown NSW 2050

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

Queensland Liver Transplant Service

Princess Alexandra Hospital
Ipswich Road
Woolloongabba QLD 4102

Queensland Children's Hospital
Stanley Street
South Brisbane QLD 4101

South Australian Liver Transplant Unit

Flinders Medical Centre
Flinders Drive
Bedford Park SA 5042

Victorian Liver Transplant Unit

Australian Intestinal Transplant Service
Austin Health
Studley Road
Heidelberg VIC 3084

The Royal Children's Hospital Melbourne
Flemington Road
Parkville VIC 3052

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

Starship Children's Hospital
Park Road
Auckland, New Zealand

4 Methodology

4.1 Data Collection and Preparation

Data are entered into the web-based Registry by data managers / transplant nurses at each Liver Transplant Unit in near real time. The Registry Manager undertakes regular data validation and cleaning steps to ensure data are accurate. Data are downloaded from the Registry to construct the analysis dataset after all validation and cleaning has been undertaken.

4.2 Waiting Lists

Comprehensive wait list data are available from 1 January 2004. The wait list dataset contains all patients who are added to the wait list for a liver or intestinal transplant. Listing can occur in patients who have or have not had a prior liver transplant.

At the end of each year, the outcome of each listing is categorised as transplanted; wait list mortality (patient died whilst wait listed or within one year of delisting for reasons other than transplantation); delisted without transplant (patient condition improved; patient too sick for transplant but still alive one year after delisting; other reasons); listed at end of year.

4.3 Liver Transplant Wait List Dataset (5,243 listings)

Comprehensive wait list data including listing and delisting date and delisting outcome are available from 1 January 2004. There are data on 5,243 wait listings from this date.

4.4 Liver Transplant Recipient Datasets

In order to ensure a consistent process for analysis, three datasets have been constructed from the transplant recipient data, as listed below.

4.4.1 Demographics Dataset (5,786 patients)

The demographic analysis dataset is based on the first liver transplant in Australia or New Zealand for each patient. Three patients had their first liver transplant overseas so their first liver transplant in Australia or New Zealand (their second graft) has been used for demographic data analysis.

4.4.2 Patient Survival and Initial Diagnosis Dataset (5,783 patients)

The patient survival analysis dataset only includes patients who had their first transplant in Australia or New Zealand. The three patients who had their first liver transplant overseas are excluded from this dataset.

4.4.3 Graft Survival Dataset (6,259 transplants)

All Australian and New Zealand transplants are included in this dataset. Patients who have had a prior transplant overseas have their first graft in Australia or New Zealand recorded as graft 2.

Both deceased and living donor grafts are included in this analysis, unless otherwise specified.

4.5 Liver Donor Datasets

4.5.1 Deceased Liver Donors (5,676 deceased donors; 6,025 transplants)

The Australian and New Zealand Organ Donor Registry (ANZOD) provides the ANZLITR with deceased donor data for analysis. Collection of deceased donor information commenced during 1989. There is no deceased donor information on 127 grafts from 1985 to 1989.

Deceased donor data are available on 5,676 donors. In addition to 5,327 whole livers, 349 donated livers were split, resulting in a total of 6,025 grafts.

4.5.2 Living Liver Donors (107 living donors)

Data on 107 living liver donors are collected in ANZLITR.

4.6 Intestinal dataset

The intestinal dataset includes data on all 15 wait-listed patients (the first listing was in 2007) and all seven transplanted patients (the first intestinal transplant was performed in 2010). Patients requiring both liver and intestinal transplants are included in both the liver and intestinal datasets.

4.7 Patient Age Groups

Paediatric patients are defined as less than 16 years old and adults are 16 years and older.

4.8 Survival Curves

4.8.1 Patient Survival

Patient survival is based on patients who had their first liver transplant in Australia or New Zealand (ie. Graft 1). Patients are classified as either alive (censored as of 31 December 2018) or dead. Patients may have undergone retransplantation in the time period. Retransplantation is not considered an event and the patient is not censored at retransplantation for patient survival analysis.

4.8.2 Graft survival

Graft survival is based on patients who had a liver transplant in Australia or New Zealand (i.e. any graft number). Grafts are classified as either functioning (censored as of 31 December 2018) or failed (due to death or re-transplantation).

4.9 Statistical Analysis

Statistical analyses were undertaken using IBM SPSS Statistics 26.

The log-rank (Mantel-Cox) test was used to compare the survival distributions of samples in Kaplan-Meier survival curve analysis.

The independent-samples Kruskal-Wallis test was used to determine if there is a significant difference in the distribution of age across the eras.

Receiver operating characteristic analysis of cold ischaemia time in relation to graft loss within 1 year was performed and the Youden-J statistic was calculated to determine the optimal cut off for the categories of cold ischaemia time.

Multivariate Cox regression using the backward stepwise method was used to determine independently significant variables that were associated with graft survival after living donor liver transplantation. Of a list of potentially significant variables, the following variables with a P value of < 0.1 on univariate analysis were included in the multivariate analysis: transplant era, listing urgency, listing medical condition, listing albumin and transplant albumin.

P values < 0.05 were considered significant.

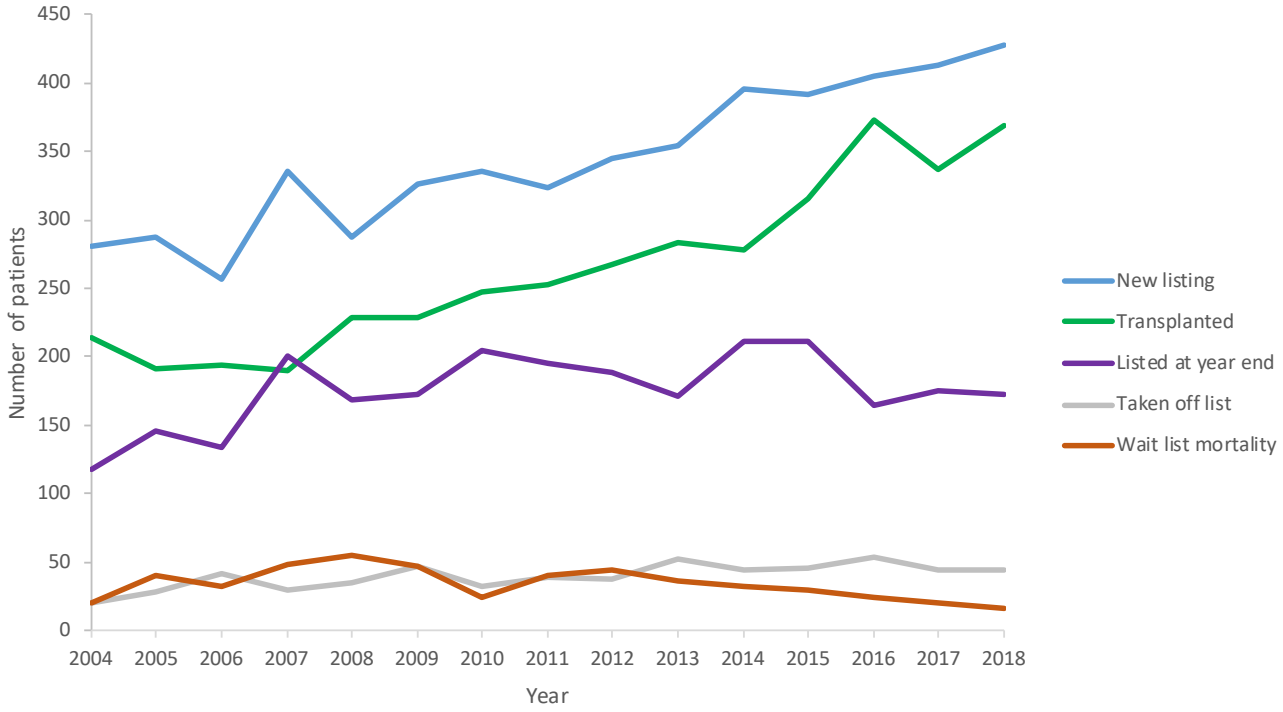
5 Liver Transplant Waiting List

5.1 Waiting List Activity

There has been a steady increase in the number of new listings on the liver transplant waiting list, increasing 52% from 2004 to 2018 (281 to 427, Figure 1). There has been a 72% increase in the number of liver transplants performed from over the same time period (214 to 369). There were 172 people on the waiting list for a liver transplant at the end of 2018. This number has remained fairly stable over recent years despite an increase in the number of transplants performed as the number of new patients listed has increased.

The annual waiting list mortality has progressively decreased from a peak of 11.3% in 2008 to 2.7% in 2018.

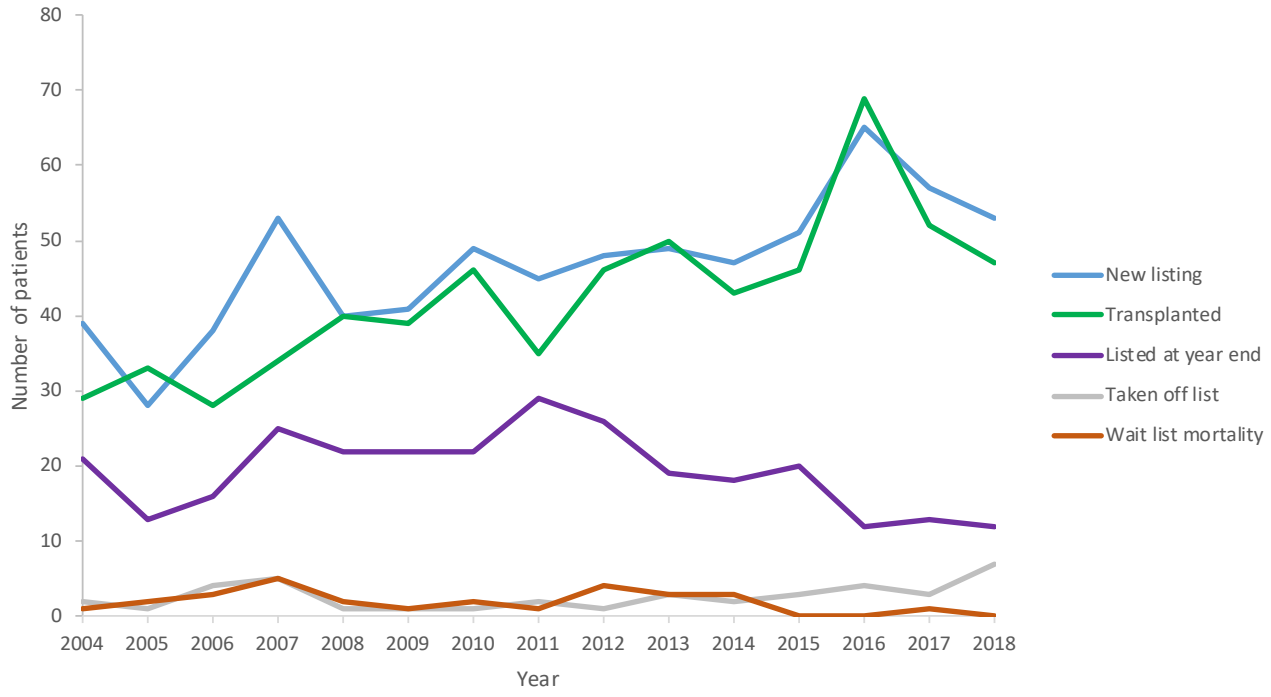
Figure 1. Liver transplant waiting list activity – all patients



5.2 Paediatric Waiting List Activity

There has been an increase in the number of new paediatric listings with the number of paediatric transplants following this trend (Figure 2). There has been a 62% increase in paediatric transplants from 29 in 2004 to 47 in 2018. The waiting list mortality has been low over the whole period and there has only been one death over the last 4 years. The number of patients still listed at the end of each year has gradually decreased from 21 in 2004 to 12 in 2018.

Figure 2. Paediatric liver transplant waiting list activity

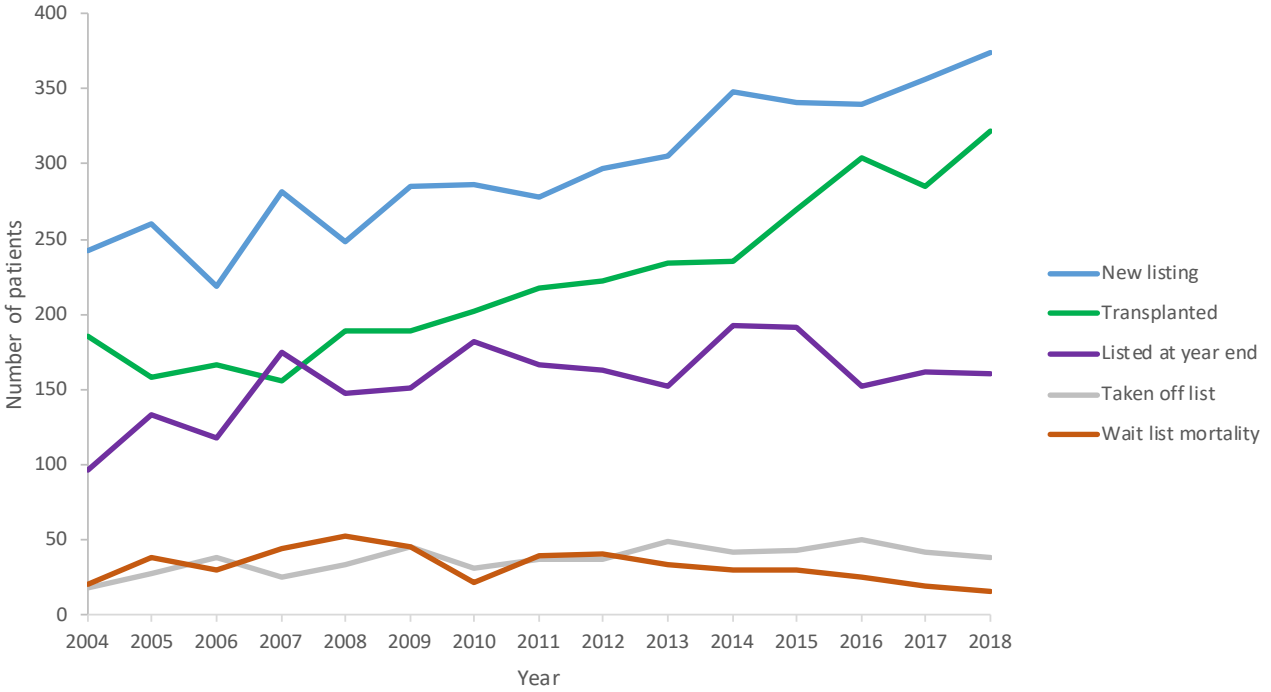


5.3 Adult Waiting List Activity

There has been a 55% increase in the number of adults listed for liver transplant from 242 in 2004 to 374 in 2018 (Figure 3). The number of adults transplanted has increased 74% from 185 in 2004 to 322 in 2018. The number of adults remaining on the waiting list at the end of the year has stabilised around 160 after peaking at 193 in 2014.

The adult wait list mortality peaked at 12.5% in 2008 and has fallen to 3% in 2018.

Figure 3. Adult liver transplant waiting list activity



5.4 Urgent Waiting List Activity

Certain categories of patients have a high risk of dying waiting for liver transplantation and a short window of opportunity for transplantation. A system of organ sharing between units in Australia and New Zealand has been developed by the Liver and Intestinal Transplant Advisory Committee of the Transplantation Society of Australia and New Zealand. The guidelines can be viewed via the following address:
https://www.tsanz.com.au/organallocationguidelines/index.asp

Urgent cases are flagged in the waiting list as Category 1 and Category 2.

Category 1 patients are defined as patients suitable for transplantation with acute liver failure who are ventilated and in an ICU at risk of imminent death. When such patients are listed, allocation to them is mandatory.

Category 2 patients are defined as listed below. When a donor liver becomes available, discussion occurs between the urgent listing unit and the local retrieving unit to determine optimal allocation.

- Category 2a. Patients suitable for transplantation with acute liver failure from whatever cause who are not yet ventilated but who meet the King's College criteria. This includes patients who have acute liver failure because of vascular thrombosis in a liver allograft. In addition, this category includes paediatric candidates with severe acute or chronic liver disease who have deteriorated and are in a paediatric intensive care unit.
- Category 2b. Paediatric patients suitable for transplantation who suffer from severe metabolic disorders or hepatoblastoma (after initial treatment) for whom a limited time period exists during which liver transplant is possible.
- Category 2c. Patients awaiting combined liver-intestinal transplantation by the National Intestinal Transplantation programme in Victoria.

Good outcomes have been achieved for patients listed as urgent category 1 and 2 (Figures 4 and 5). In the last four years, the category 1 waiting list mortality was between 7 and 11% and there was no waiting list mortality for category 2.

Figure 4. Urgent category 1 waiting list outcomes

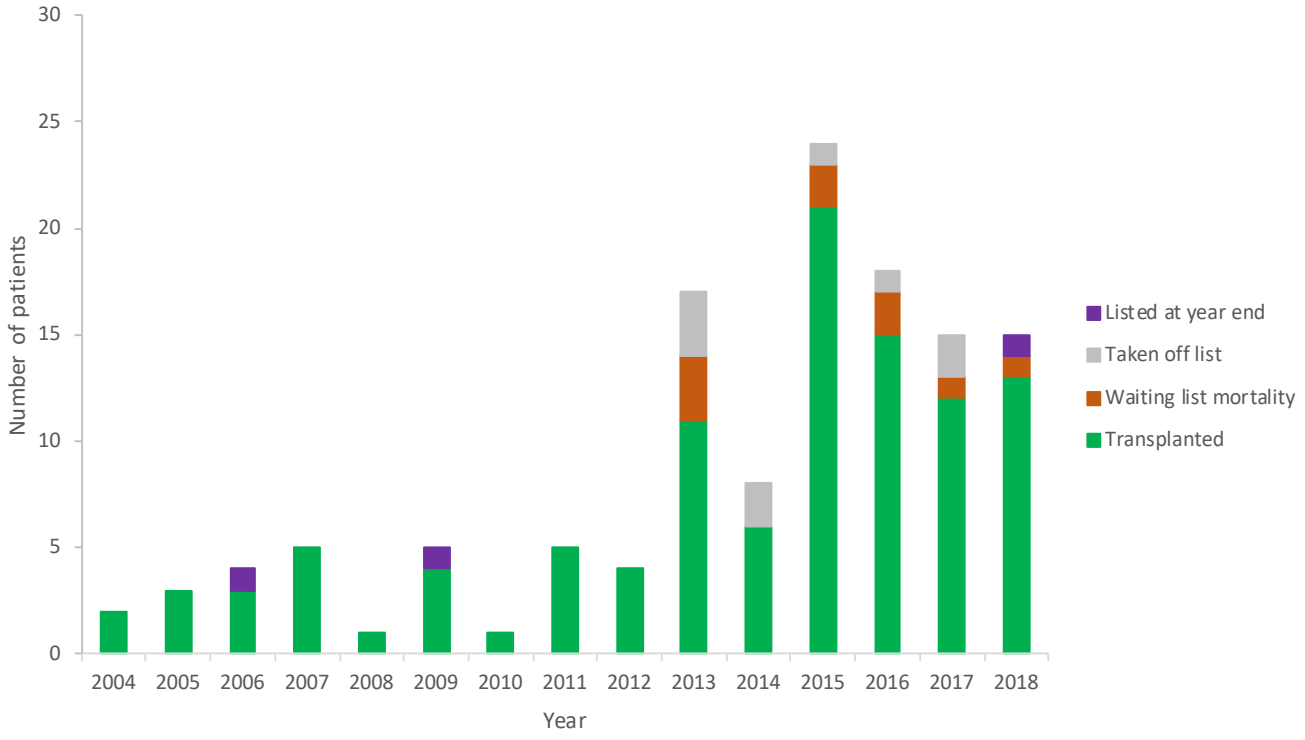
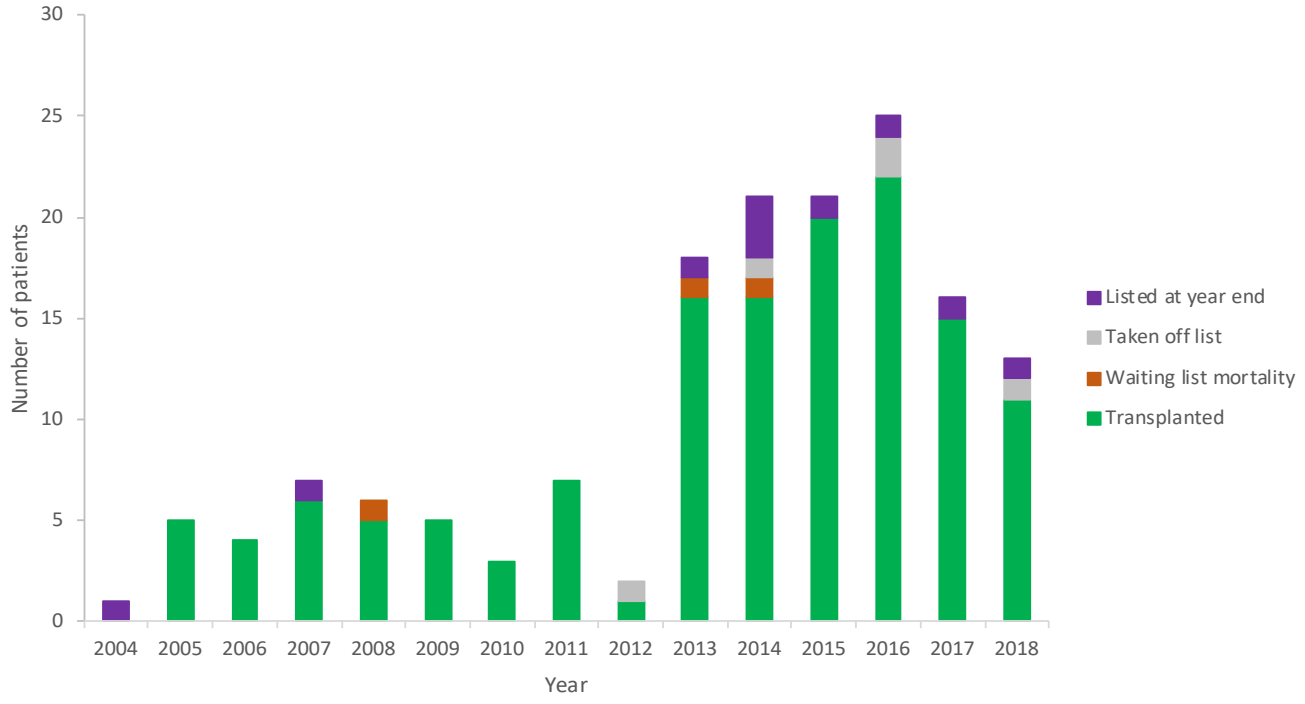


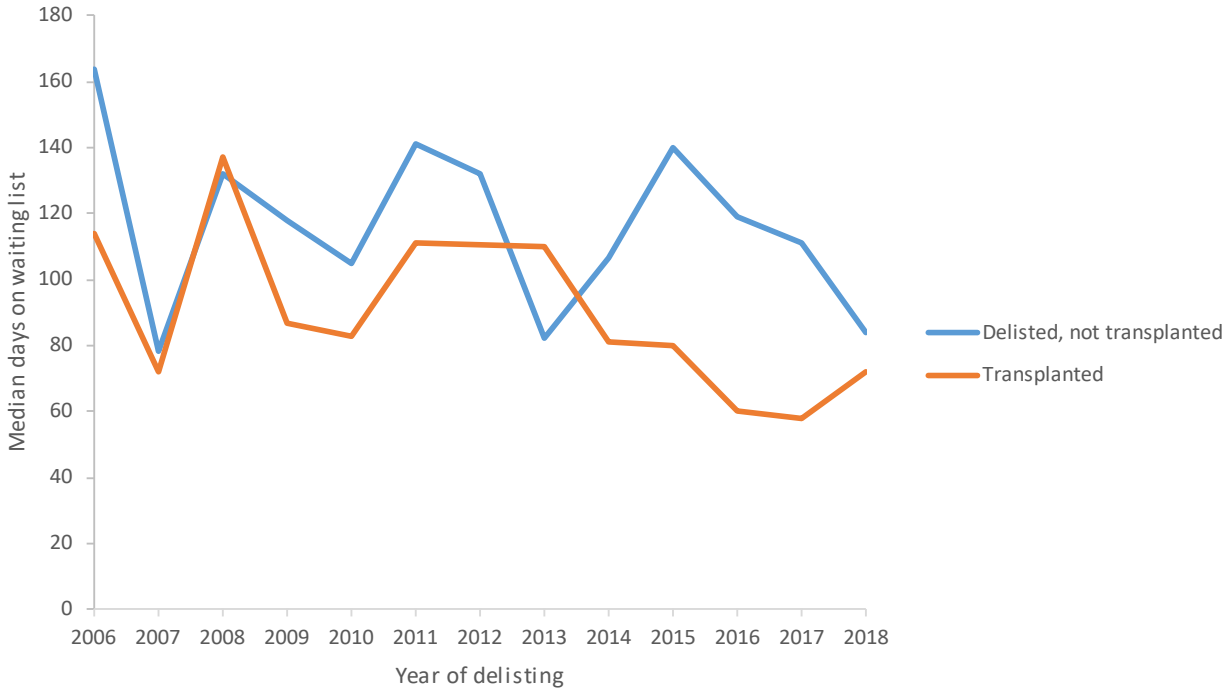
Figure 5. Urgent category 2 waiting list outcomes



5.5 Time on the waiting list

The median time from listing to transplantation by the year of transplantation was 111 days in 2012 and has decreased to 72 days in 2018 (Figure 6). The median time from listing to delisting without transplant was 132 days in 2012 and has decreased to 84 days in 2018.

Figure 6. Time on waiting list by year of delisting

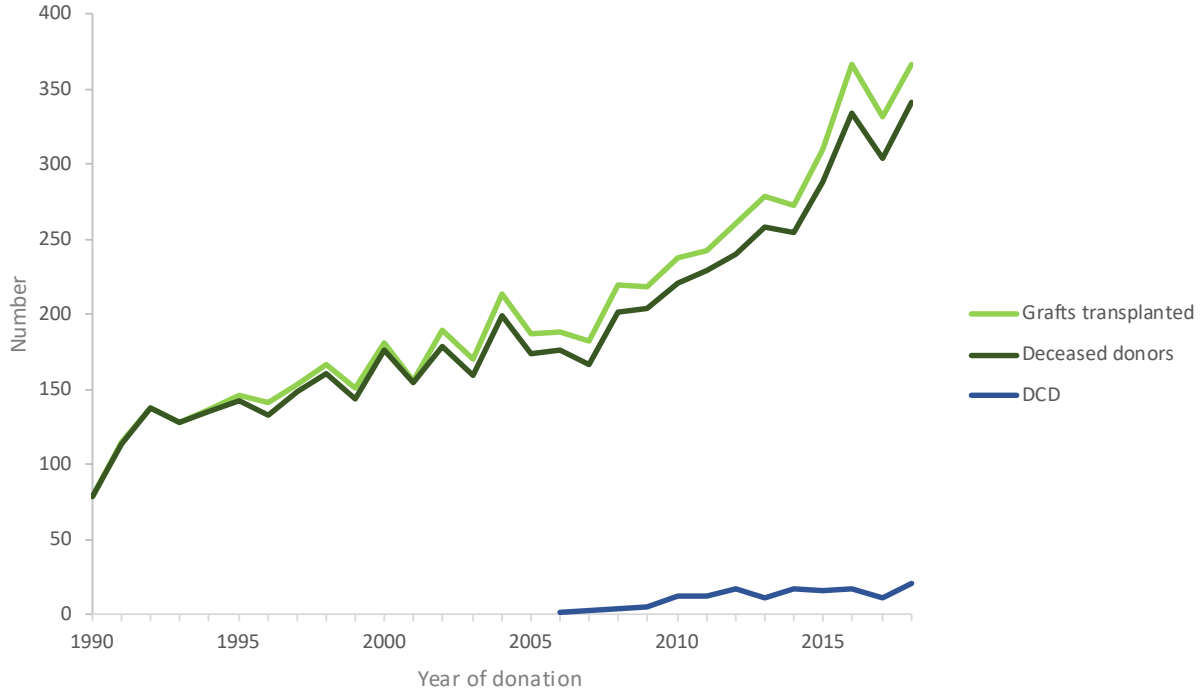


6 Deceased Liver Donors

Of 6,259 liver transplants, 6,152 (98.3%) were sourced from deceased donors, with only a small proportion from living donors (107, 1.7%). Collection of deceased donor information commenced during 1989. There is no deceased donor information on 127 transplants from 1985 to 1989.

Subsequent analysis is limited to 5,676 deceased donors that have donor information recorded. Of these, 349 of donated livers were split resulting in a total of 6,025 grafts. The number of deceased donors has grown steadily over the years (Figure 7). Of 362 deceased donors in 2018, 21 (5.8%) were donation after circulatory death donors.

Figure 7. Deceased donors and grafts transplanted by year

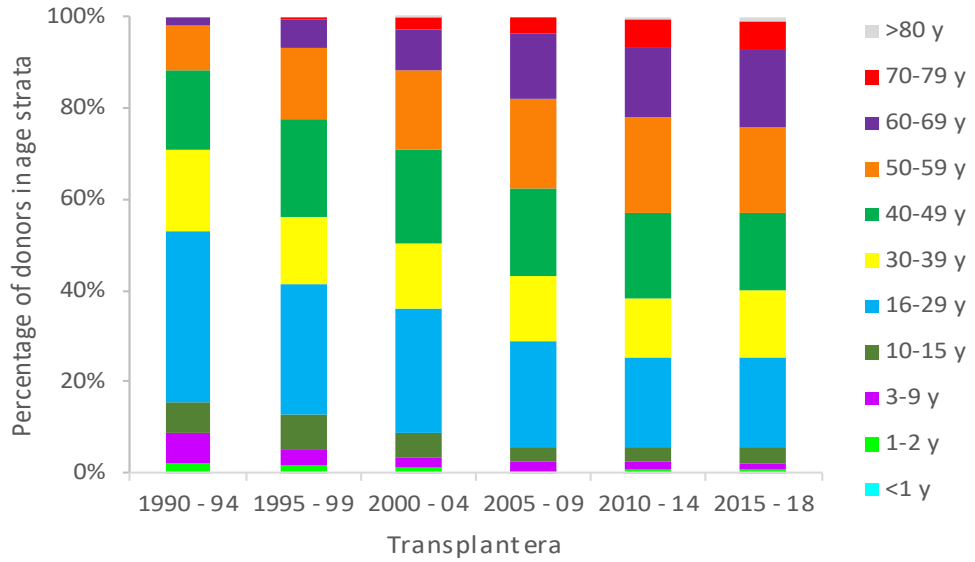


Abbreviation: DCD, donation after circulatory death

There has been a progressive increase in donor age from a median of 29 years in 1990-94 to 46 years in 2015-18.

Figure 8 demonstrates the changing deceased donor age profile over the various transplant eras. There has been a progressive increase in the proportion of donors aged 50-59, 60-69, 70-79 and ≥ 80 years from 10%, 2% 0% and 0%, respectively in the 1990-94 era to 19%, 17%, 7% and 1%, respectively in the 2015-18 era.

Figure 8. Deceased donor age by transplant era



7 Living Liver Donors

Of 6,259 liver transplants, 107 (1.7%) were sourced from living donors (including four domino livers). Paediatric recipients received the majority (81.3%) of living liver donations (Table 1). There have been no deaths of living liver donors.

Table 1. Living liver donor demographics

Living Donors	**Paediatric Recipient** (<16 years)	**Adult Recipient** (≥16 years)	**All Recipients**
Number of living donors	**87**	**20**	**107**
% living donors	81.3%	18.7%	
Gender of living donor			
Female *(% age category)*	42 *(48.3%)*	7 *(35%)*	**49** *(45.8%)*
Male *(% age category)*	45 *(51.7%)*	13 *(65%)*	**58** *(54.2%)*
Age of living donor (years)			
Median	34	31	**33**
Range	19 – 54	18 – 54	**18 – 54**
Living donor relationship			
Father	35	1	**36**
Mother	23	0	**23**
Aunt	10	0	**10**
Friend	8	1	**9**
Brother	2	3	**5**
Son	0	5	**5**
Domino whole liver	0	4	**4**
Cousin	3	0	**3**
Daughter	0	2	**2**
Grandmother	2	0	**2**
Sister	0	2	**2**
Uncle	2	0	**2**
Grandfather	1	0	**1**
Half sister	0	1	**1**
Husband	0	1	**1**
Second cousin	1	0	**1**

8 Liver Transplantation in 2018

There were 369 liver transplants performed on 356 recipients in 2018. This equates to 12.5 liver transplant recipients per million population (Australia and New Zealand combined population in 2018: 29.6 million).

8.1 Demographic Data for Patients Transplanted in 2018

Demographic data are based on the first Australia or New Zealand liver transplant per patient undertaken in 2018. (356 patients, 336 graft 1; 16 graft 2; four graft 3).

Of patients receiving a transplant in 2018, 12.9% were children. Females represented 58.7% of paediatric patients but only 34.2% of the adult population (Table 2).

Table 2. Patient demographics by age group (2018)

Patients Transplanted in ANZ in 2018	**Children** (<16 years)	**Adults** (≥16 years)	**Total Patients**
Number of patients *(% total pts)*	46 *(12.9%)*	310 *(87.1%)*	356
Gender			
Female *(% age category)*	27 *(58.7%)*	106 *(34.2%)*	133 *(37.4%)*
Male *(% age category)*	19 *(41.3%)*	204 *(65.8%)*	223 *(62.6%)*
Age at first ANZ transplant			
Mean ± SD (years)	4 ± 4	54 ± 12	48 ± 20
Median (years)	1	56	54
Range	18 d - 14 y	17 y - 72 y	18 d - 72 y
Interquartile range	7 m - 6 y	48 y - 63 y	42 y - 62 y
Status of patient at 31/12/2018			
Alive *(% age category)*	46 *(100%)*	301 *(97.1%)*	347 *(97.5%)*
Deceased *(% age category)*	0	9 *(2.9%)*	9 *(2.5%)*

Abbreviation: ANZ: Australia or New Zealand

8.2 Transplants in 2018

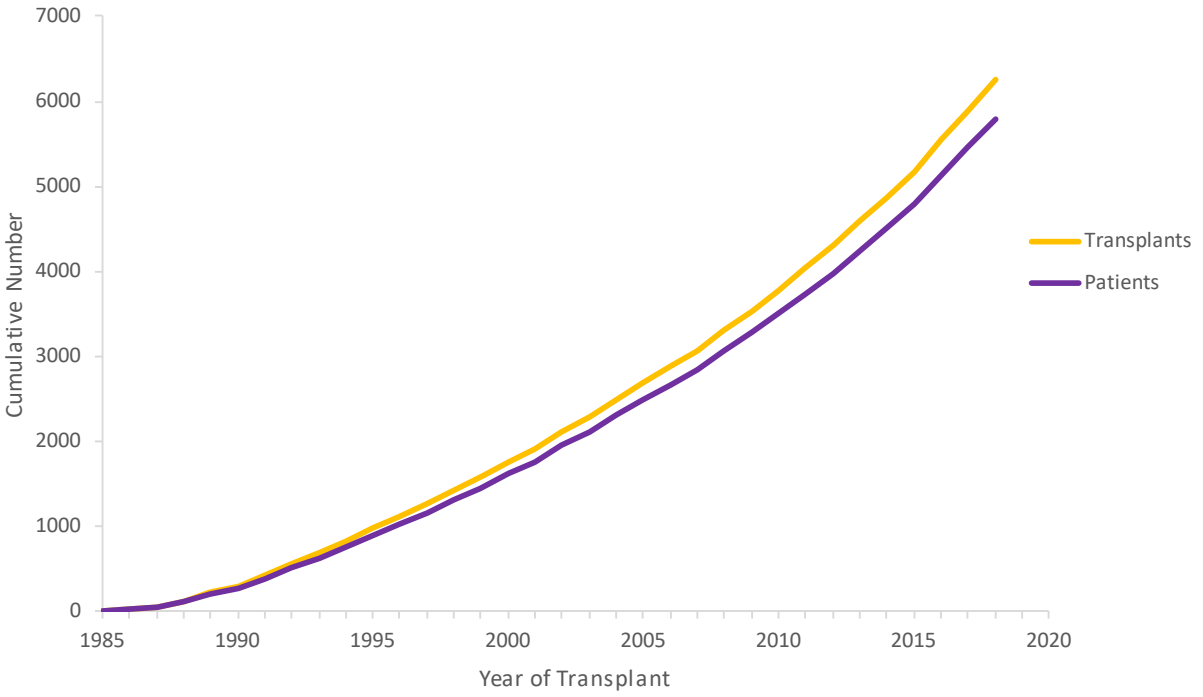
The majority of the 369 transplants were for adult patients (322, 87.3%), whilst 47 (12.7%) transplants were performed on paediatric patients (<16 years).

Of the 356 patients, 336 (94.3%) patients had their first transplant in 2018. Of these, 10 required retransplantation and one of these was retransplanted again (i.e. three transplant operations in 2018). Sixteen patients who had a single transplant prior to 2018 were retransplanted in 2018. Two of these went on to have their third transplant in 2018. Four patients who had two transplants prior to 2018 were retransplanted with their third graft in 2018.

9 Liver Transplantation from 1985 – 2018

There have been 6,259 liver transplants undertaken on 5,786 patients between 1985 and 2018. Figure 9 shows the cumulative number of patients and transplants.

Figure 9. Cumulative number of liver transplants and new patients transplanted



9.1 Demographic Data for Patients Transplanted from 1985 - 2018

Demographic data are based on the first liver transplant undertaken in Australia or New Zealand across all years. In three cases, this is actually the patient's second liver transplant as their first transplant was done outside Australia or New Zealand. (5,786 patients, 5,783 graft 1; 3 graft 2)

Of patients receiving a transplant from 1985 to 2018, 16.9% were children. Females comprised 51.8% of paediatric patients but only 33.7% of adult patients (Table 3).

Table 3. Patient demographics by age group (1985 – 2018)

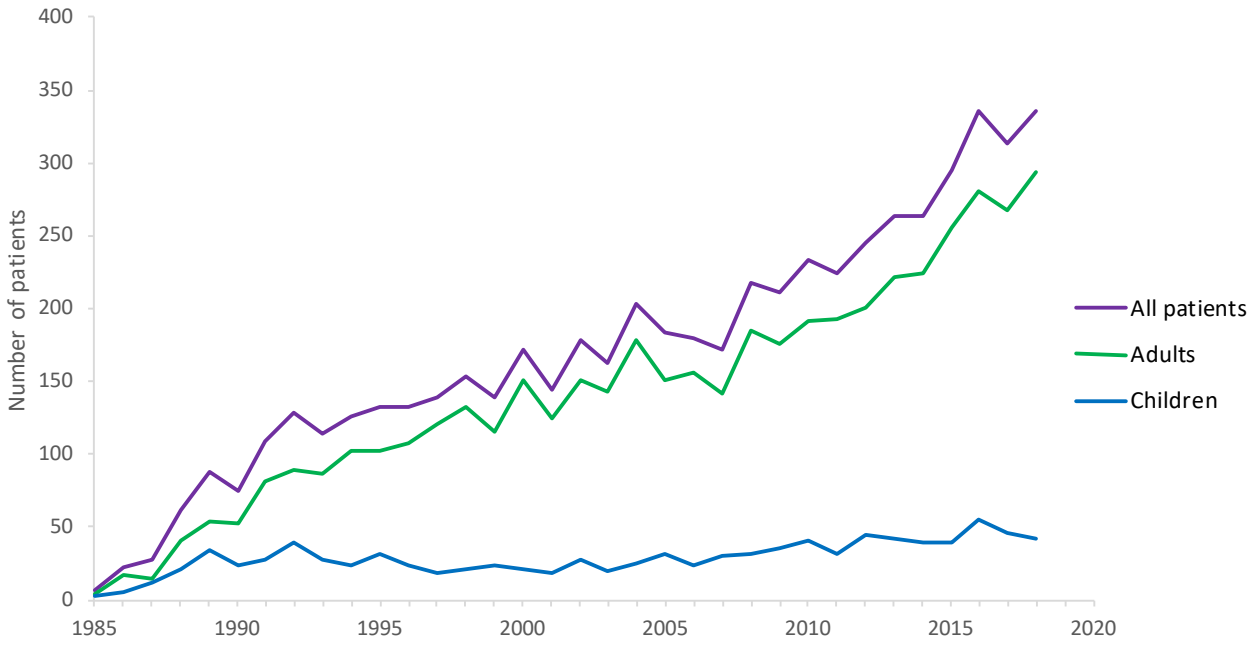
Patients Transplanted in ANZ from 1985 to 2018	**Children** (<16 years)	**Adults** (≥16 years)	**Total Patients**
Number of patients *(% total pts)*	977 *(16.9%)*	4,809 *(83.1%)*	5,786
Gender			
Female *(% age category)*	506 *(51.8%)*	1,619 *(33.7%)*	2,125 *(36.7%)*
Male *(% age category)*	471 *(48.2%)*	3,190 *(66.3)*	3,661 *(63.3%)*
Age at first ANZ transplant (years)			
Mean ± SD (years)	4 ± 4	50 ± 12	42 ± 20
Median (years)	2	52	49
Range	18 d - 15 y	16 y - 73 y	18 d - 73 y
Interquartile range	1 y - 7 y	44 y - 59 y	32 y - 57 y
Status of patient at 31/12/2018			
Alive *(% age category)*	808 *(82.7%)*	3,338 *(69.4%)*	4,146 *(71.7%)*
Deceased *(% age category)*	169 *(17.3%)*	1,471 *(30.6%)*	1,640 *(28.3%)*

Abbreviation: ANZ: Australia or New Zealand

9.1.1 Patients transplanted by year of first transplant

From 2007 to 2018, there was a 95% increase in the number of patients transplanted per year, based on the year of their first transplant, from 172 to 336, including a 40% increase in the number of children transplanted (30 to 42) and a 107% increase in the number of adults transplanted (142 to 294, Figure 10).

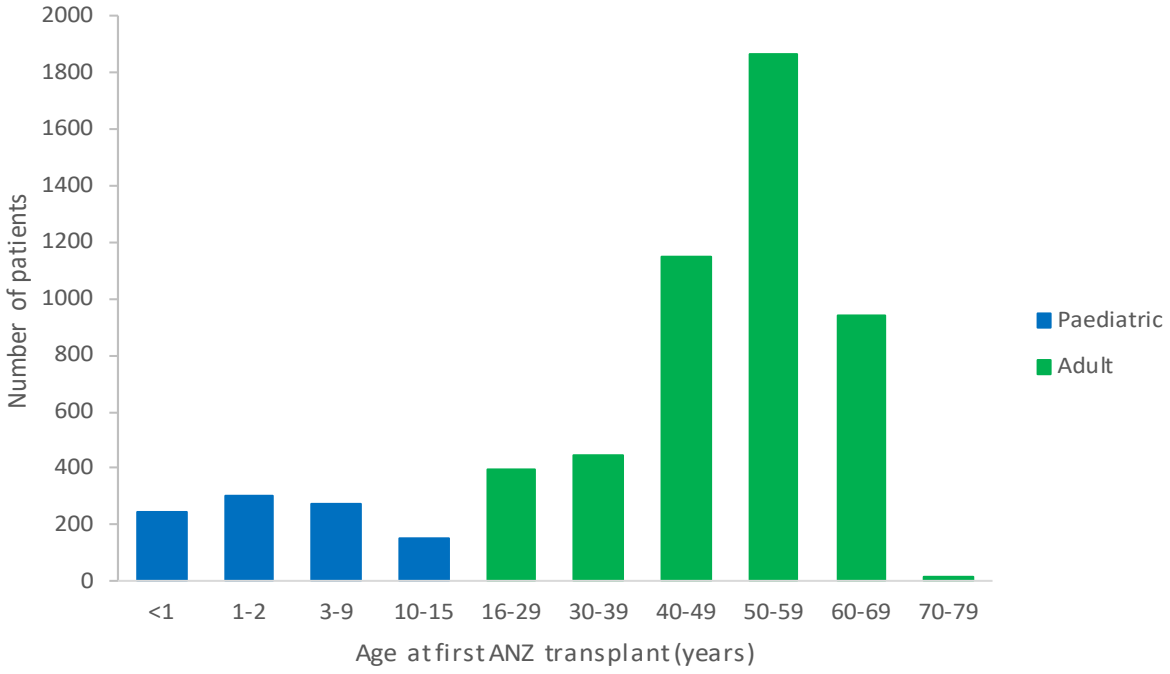
Figure 10. Number of patients transplanted by age group by year of first transplant



9.1.2 Recipient age at first transplant (1985 – 2018)

Of the 977 paediatric transplant recipients, 25% were infants less than one year old and 15% were adolescents 10 to 15 years old (Figure 11). Of the 4,809 adult recipients, 39% were in their 50s and only 0.3% were in their 70s.

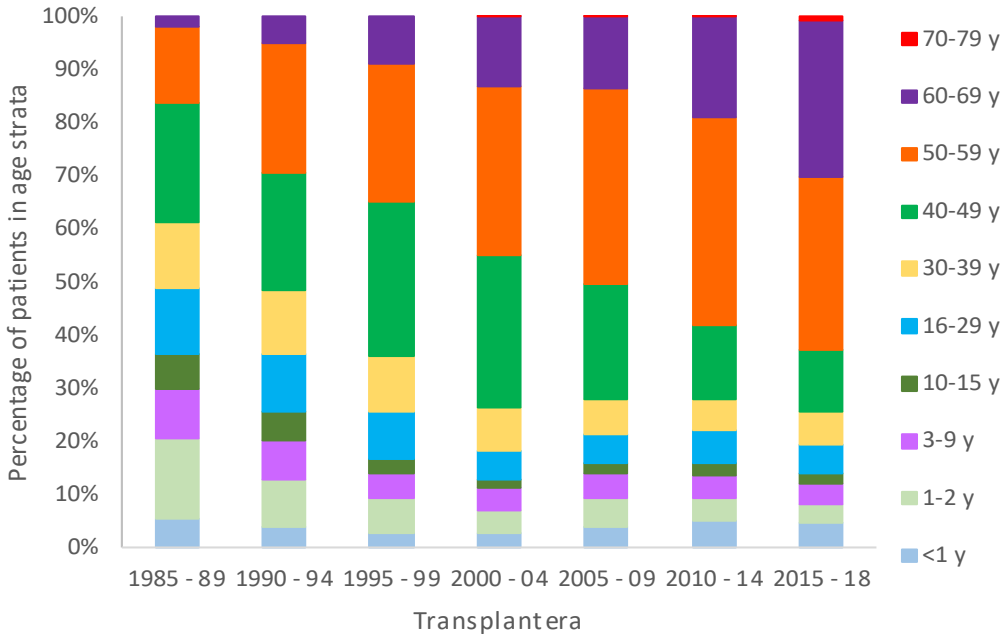
Figure 11. Recipient age strata at first Australian or New Zealand transplant (1985 – 2018)



9.1.3 Recipient age at first transplant by era of transplant

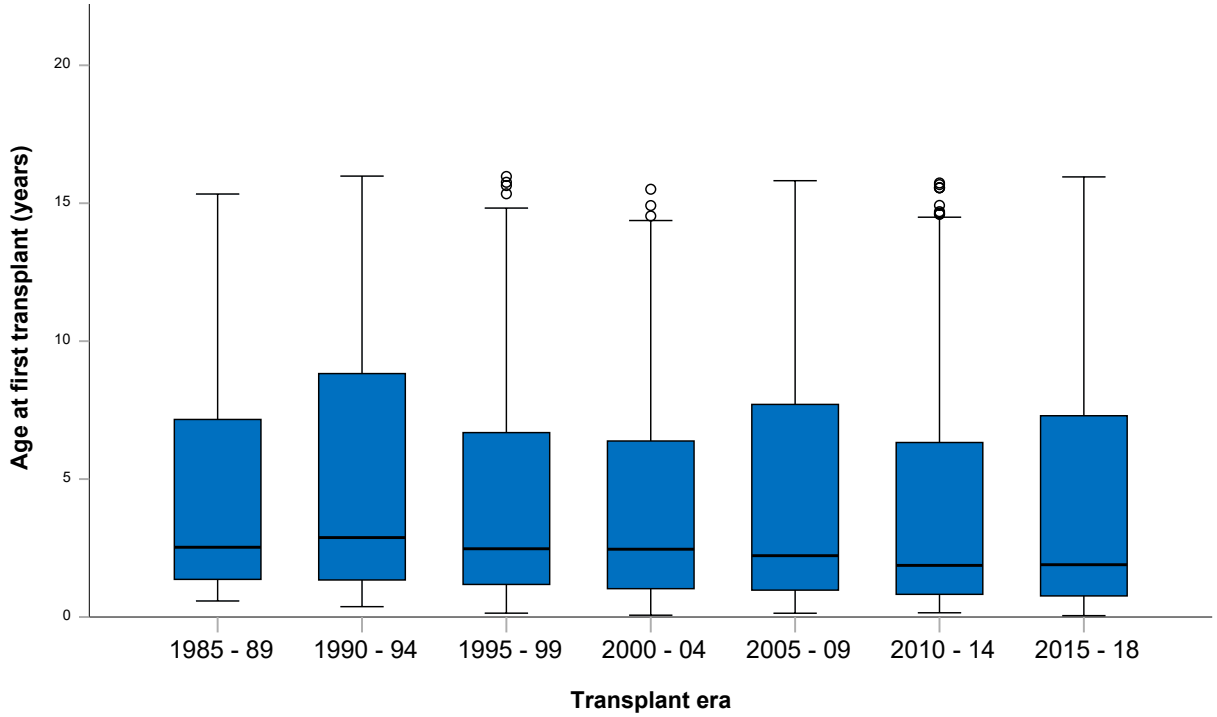
Figure 12 demonstrates the changing recipient age profile over the various transplant eras. There has been a progressive increase in the proportion of recipients aged 50-59, 60-69 and ≥ 70 years from 14%, 2% and 0%, respectively in the 1985-1989 era to 33%, 29% and 1%, respectively in the 2015-2018 era.

Figure 12. Recipient age strata (percentages) by transplant era



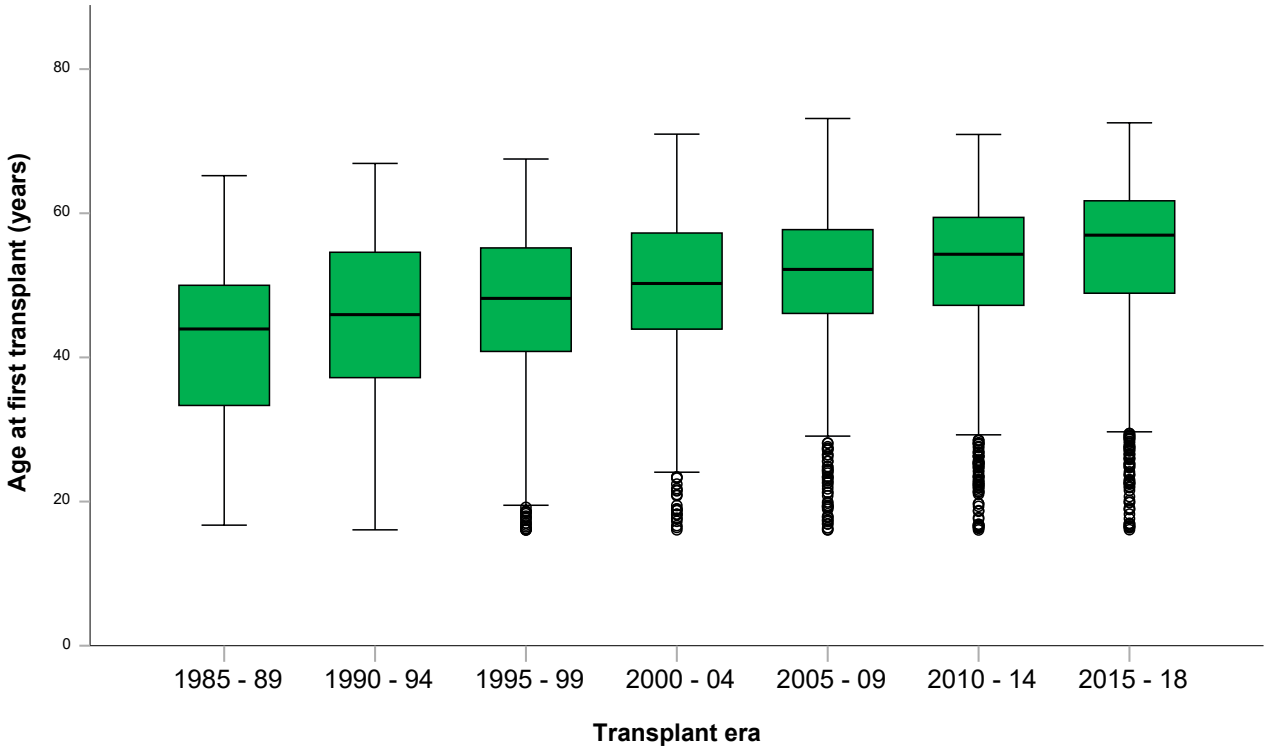
The median paediatric recipient age has been gradually decreasing over the transplant eras, from 2 years and 6 months in 1985-89 to 1 year and 10 months in 2015-18 (P=0.045, Figure 13. Box and whisker plot: median, interquartile range, 1.5 times interquartile range and outliers shown).

Figure 13. Paediatric age at first transplant by transplant era



The median adult recipient age has been gradually increasing over the transplant eras, from 43 years in 1985-89 to 56 years in 2015-18 (P<0.001, Figure 14. Box and whisker plot: median, interquartile range, 1.5 times interquartile range and outliers shown).

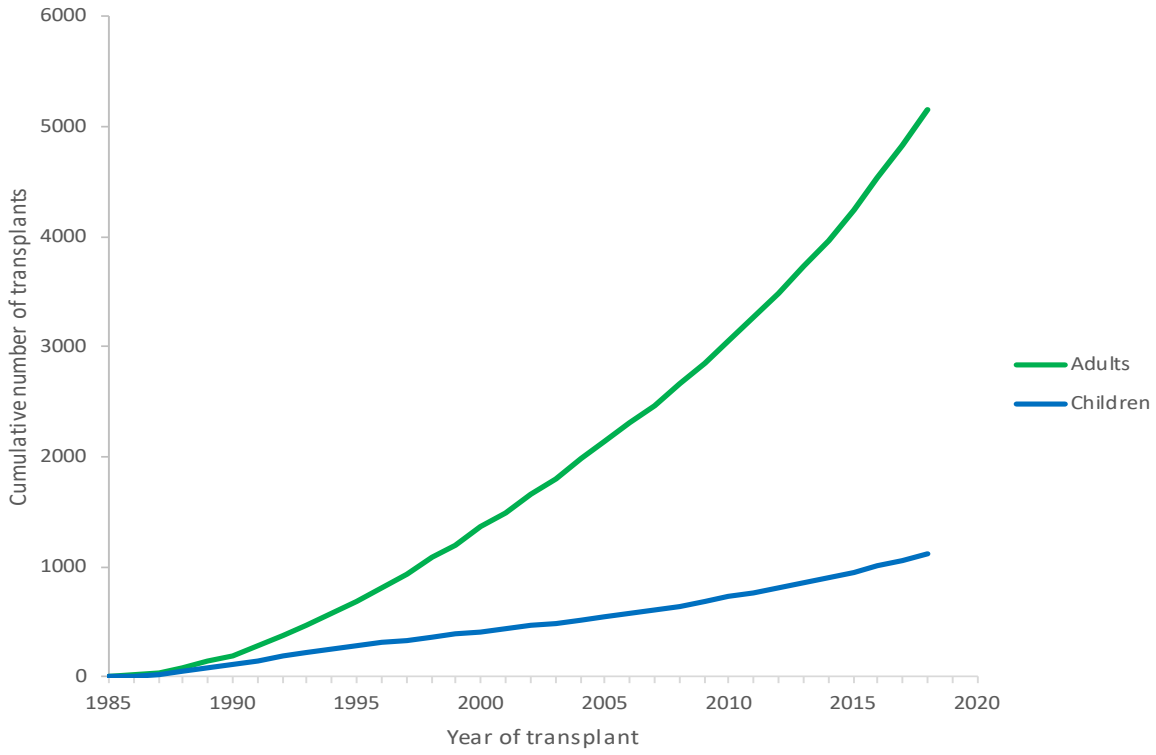
Figure 14. Adult age at first transplant by transplant era



9.2 Transplants (1985 – 2018)

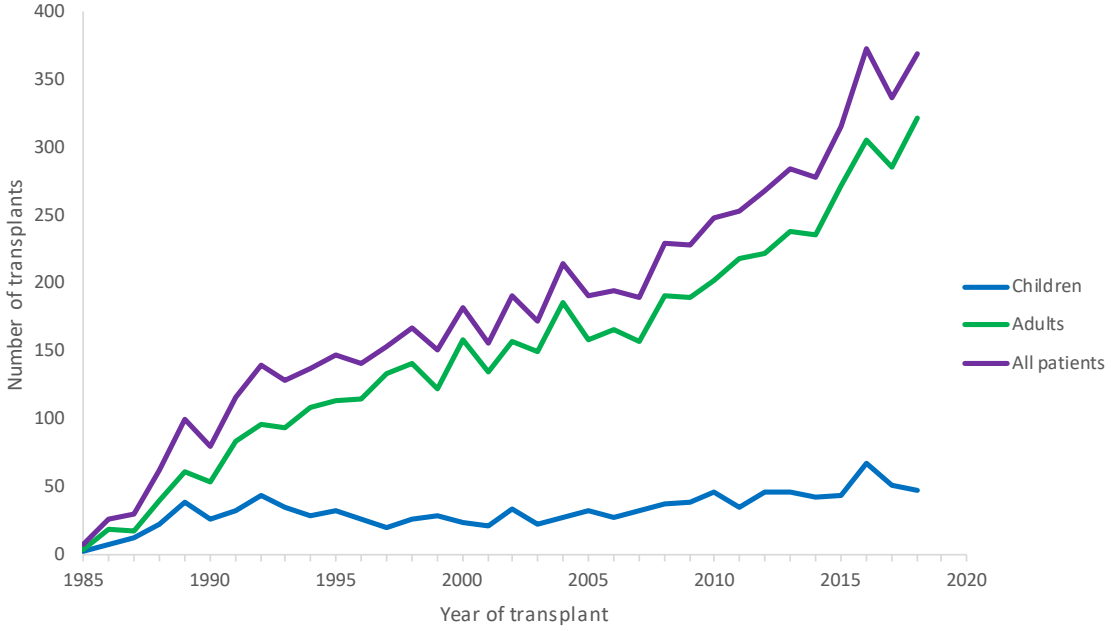
Of the 6,259 transplants, 5,149 (82.3%) were performed in adults and 1,110 (17.7%) in children (<16 years, Figure 15).

Figure 15. Cumulative number of liver transplants per year by age category



From 2007 to 2018, there was a 94% increase in the number of transplants performed per year, from 190 to 369, including a 42% increase in the number of transplants in children (33 to 47) and a 105% increase in the number of transplants in adults (157 to 322, Figure 16).

Figure 16. Number of liver transplants per year by recipient age category

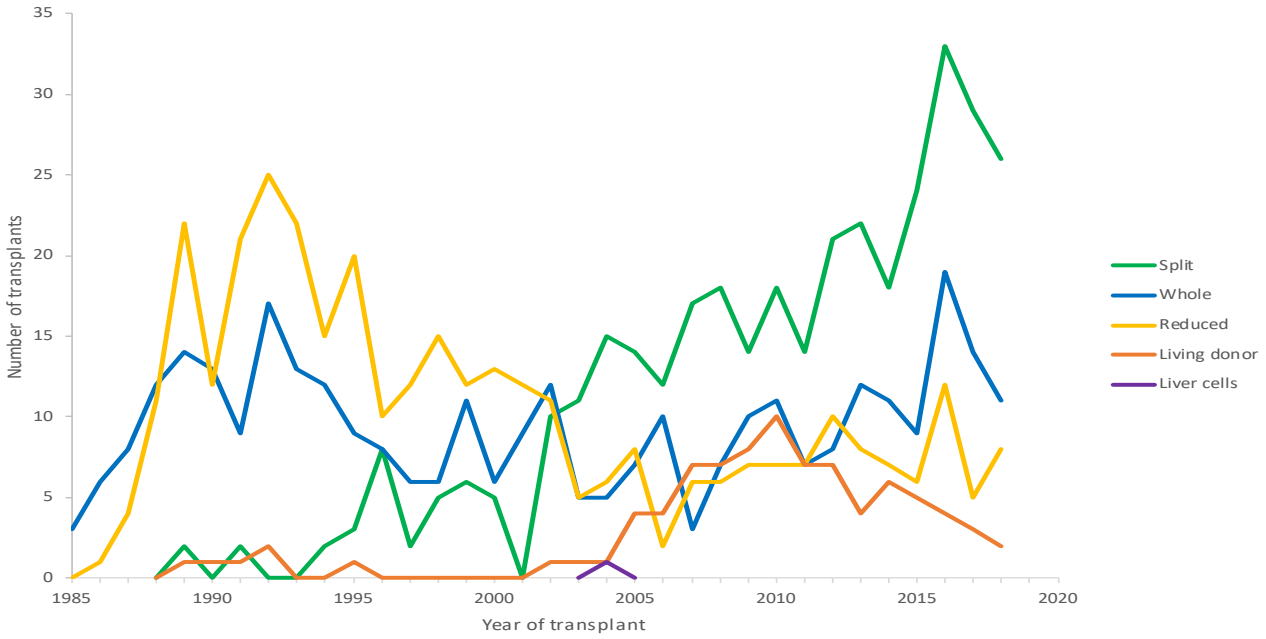


Since the first transplant in 1985, 7.3% of recipients (425) have undergone retransplantation. Of these, 379 patients had one retransplantation, 44 patients have required two retransplantations and two patients had three retransplantations.

9.2.1 Type of Graft – paediatric recipients, all years

The first paediatric liver transplant was performed in 1985, the first reduced size liver transplant in 1986, the first split liver transplant in 1989 and the first successful living donor liver transplant in the world was performed by Professor Strong in Brisbane in July 1989. In the 1990s, the majority of partial grafts were reduced grafts. However, since 2000, the proportion of split grafts has increased to become the dominant method of transplantation in children (55% in 2018, Figure 17). The number of living donors peaked at 10 in 2010 and subsequently this has become an infrequent method of transplantation in children (two transplants in 2018).

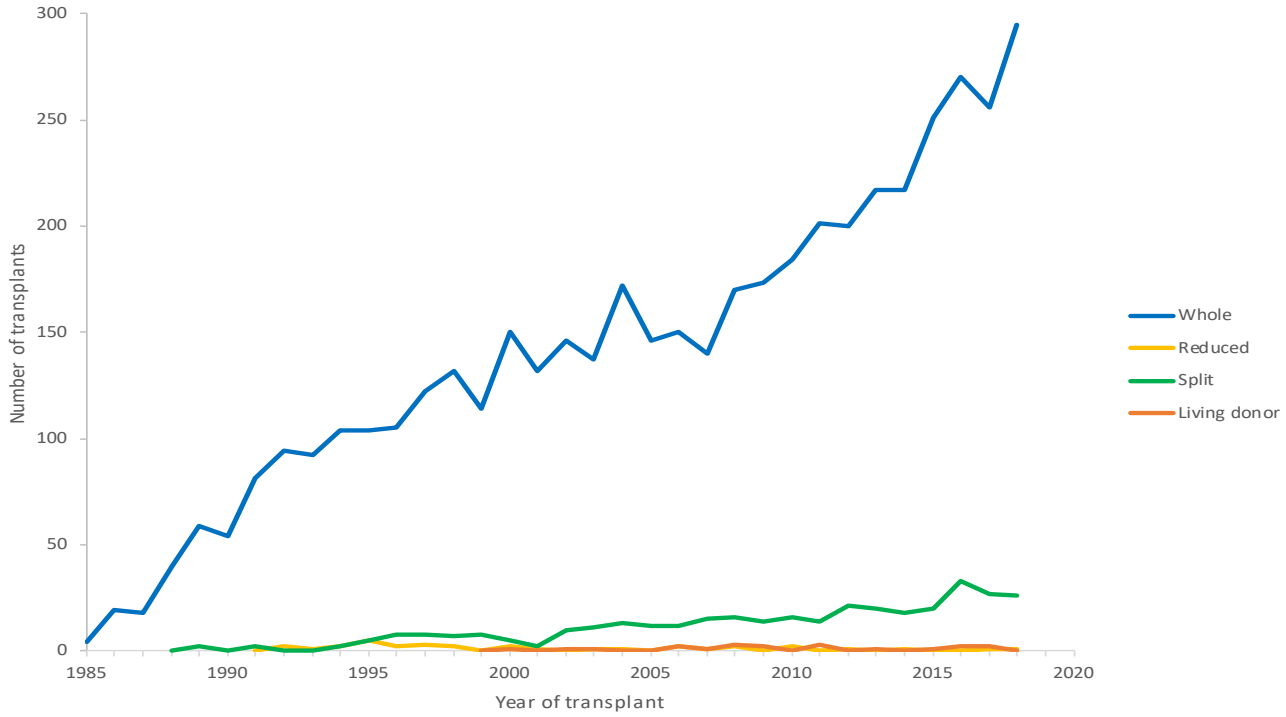
Figure 17. Type of graft for paediatric recipients – all years



9.2.2 Type of Graft – adult recipients, all years

The dominant form of liver transplantation in adults is whole liver transplantation (295 of 322 transplants, 92% in 2018, Figure 18). The number of deceased donor split liver transplants in adults has increased from 5 of 158 transplants (3%) in 2000 to 26 of 322 (8%) in 2018. There has been a total of 20 adult-to-adult living donor liver transplants performed, including four domino liver transplants.

Figure 18. Type of graft for adult recipients – all years



10 Diagnoses at First Transplant

Diagnosis at First Transplant Analysis Population: n = 5,783 patients - first liver transplant in Australia or New Zealand (ie. Graft 1). Excludes three patients who had first graft overseas.

10.1 Primary Diagnosis in Children

Of 975 children who underwent their first liver transplant in Australia or New Zealand, the most common primary diagnoses were biliary atresia (54%), metabolic disease (14%) and fulminant hepatic failure, (11%, Table 4).

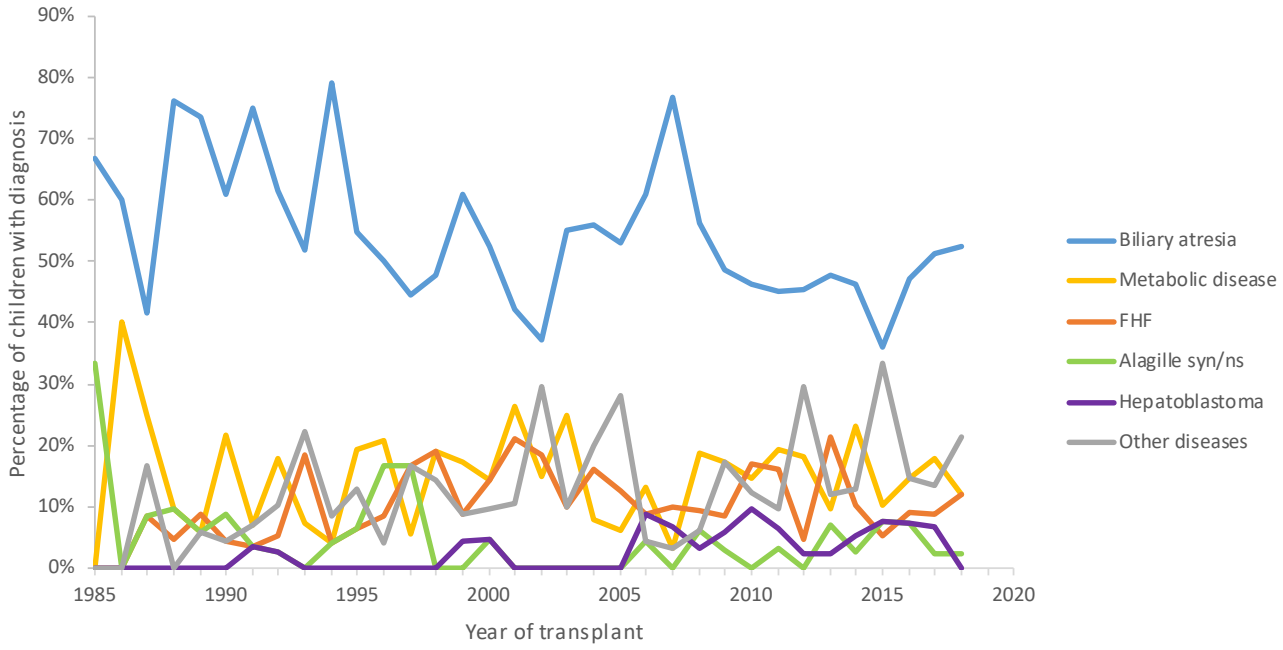
Table 4. Primary diagnosis in children

Primary diagnosis	N (%)
Biliary atresia	524 (54%)
Metabolic disease	142 (15%)
Fulminant hepatic failure	104 (11%)
Alagille syndrome	39 (4%)
Hepatoblastoma	31 (3%)
Progressive familial intrahepatic cholestasis	28 (3%)
Cryptogenic cirrhosis	22 (2%)
Cystic fibrosis	15 (2%)
Autoimmune cirrhosis	10 (1%)
Primary sclerosing cholangitis	8 (1%)
Neonatal hepatitis	6 (1%)
Histiocytosis X	5 (1%)
Caroli's disease	4 (0.4%)
Hepatocellular carcinoma	4 (0.4%)
Choledocal cyst	3 (0.3%)
Ductopenia	3 (0.3%)
Intestinal failure associated liver disease	3 (0.3%)
Secondary biliary cirrhosis	3 (0.3%)
Chronic Budd Chiari	2 (0.2%)
Common variable immune deficiency	2 (0.2%)
Liver cancer, not otherwise specified	2 (0.2%)
Polycystic liver and kidney disease	2 (0.2%)
Autoimmune sclerosing cholangitis	1 (0.1%)
Bile salt synthetic defect	1 (0.1%)
Congenital Intrahepatic portosystemic shunt	1 (0.1%)
Cornelia de Lange syndrome	1 (0.1%)
Enterovirus hepatitis	1 (0.1%)
Established cirrhosis with marked cholestasis	1 (0.1%)
Gestational alloimmune liver disease	1 (0.1%)
Hepatic cholangiocellular carcinoma	1 (0.1%)
Hepatic fibrosis/polycystic kidney disease	1 (0.1%)
Hepatic lymphangiomatosis	1 (0.1%)
Idiopathic copper toxicosis	1 (0.1%)
Ischaemic sclerosing cholangitis	1 (0.1%)
Parvovirus	1 (0.1%)
Total	**975**

10.2 Primary Diagnosis Trend in Children

The indications for liver transplantation in children have remained relatively stable over time (Figure 19).

Figure 19. Paediatric (< 16 years) primary diagnosis percentages (based on graft 1) all years



Abbreviations: FHF, fulminant hepatic failure; Alagille syn/ns, Alagille syndrome / non-syndromic

10.3 Primary Diagnosis in Adults

Of 4,808 adults who underwent their first liver transplant in Australia or New Zealand, the most common primary diagnoses were hepatitis C virus cirrhosis (22%), alcoholic cirrhosis (13%) and hepatocellular carcinoma (12%, Table 5).

Table 5. Primary diagnosis in adults

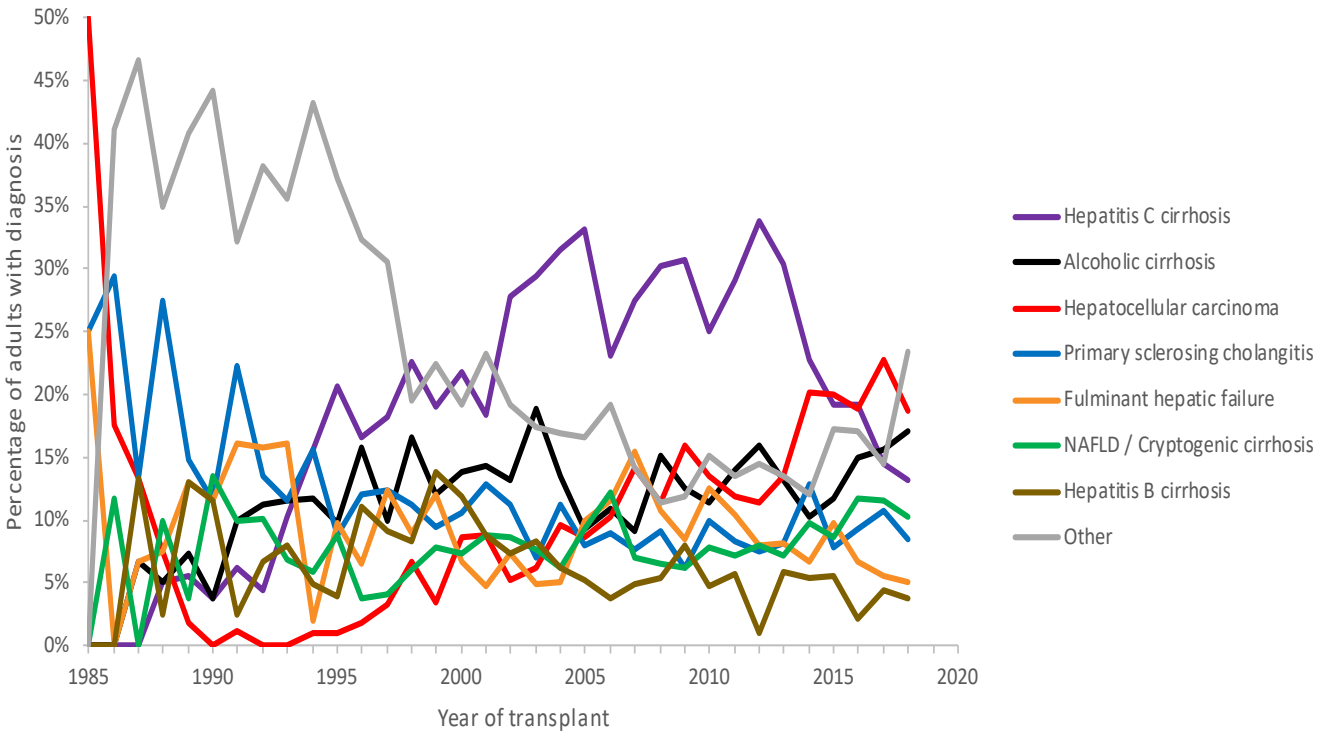
Primary diagnosis	N (%)
Hepatitis C virus cirrhosis	1056 (22%)
Alcoholic cirrhosis	625 (13%)
Hepatocellular carcinoma	556 (12%)
Primary sclerosing cholangitis	494 (10%)
Fulminant hepatic failure	419 (9%)
NAFLD / Cryptogenic cirrhosis	405 (8%)
Hepatitis B virus cirrhosis	288 (6%)
Primary biliary cirrhosis	262 (5%)
Metabolic disease	206 (4%)
Autoimmune cirrhosis	172 (4%)
Polycystic liver +/- kidney disease	52 (1%)
Biliary atresia	47 (1%)
Chronic Budd Chiari	37 (1%)
Cystic fibrosis	27 (1%)
Secondary biliary cirrhosis	20 (0.4%)
Caroli's disease	19 (0.4%)
Hepatic cholangiocellular carcinoma	11 (0.2%)
Alagille syndrome	10 (0.2%)
Granulomatous hepatitis / sarcoidosis	9 (0.2%)
Hereditary haemorrhagic telangiectasia	8 (0.2%)
Epithelioid hemangioendothelioma	7 (0.1%)
Nodular regenerative hyperplasia	7 (0.1%)
Progressive familial intrahepatic cholestasis	6 (0.1%)
Congenital hepatic fibrosis	5 (0.1%)
Haemangioma	5 (0.1%)
Metastatic neuroendocrine tumour	5 (0.1%)
Secondary biliary cirrhosis - Hepatolithiasis	4 (0.1%)
Drug hepatotoxicity	3 (0.1%)
Ductopenia	3 (0.1%)
Haemolytic uraemic syndrome	3 (0.1%)
Oriental cholangiohepatitis	3 (0.1%)
Post hepatitic cirrhosis - Drug related	3 (0.1%)
Adenomatosis	2 (0.04%)
Common variable immune disorder	2 (0.04%)
Choledocal cyst	2 (0.04%)
Congenital biliary fibrosis	2 (0.04%)
Intestinal failure associated liver disease	2 (0.04%)
Angiosarcoma	1 (0.02%)
Arterio-venous malformation	1 (0.02%)
Biliary papillomatosis	1 (0.02%)
Cholestatic cirrhosis	1 (0.02%)
Chronic cholestatic liver disease	1 (0.02%)
COACH syndrome	1 (0.02%)
Congenital heart disease	1 (0.02%)
Drug induced cholestasis	1 (0.02%)
Fasciola	1 (0.02%)
Flucloxacillin-associated liver injury	1 (0.02%)
Graft vs host disease – bone marrow transplant	1 (0.02%)
Histiocytosis X	1 (0.02%)
Infected hydatid cysts	1 (0.02%)
Liver trauma	1 (0.02%)
Non-cirrhotic portal hypertension	1 (0.02%)
Portal biliopathy	1 (0.02%)
Portal vein thrombosis	1 (0.02%)
Recurrent cholangitis	1 (0.02%)
Secondary cholangitis	1 (0.02%)
Secondary liver tumours - Gastrinoma	1 (0.02%)
Secondary sclerosing cholangitis	1 (0.02%)
Total	**4808**

Abbreviation: COACH, cerebellar vermis aplasia, oligophrenia, congenital ataxia, coloboma and hepatic fibrosis; NAFLD, Non-alcoholic fatty liver disease

10.4 Primary Diagnosis Trend in Adults

The commonest indication for transplantation in adults was hepatitis C virus cirrhosis until 2014, after which hepatocellular carcinoma has become the commonest indication. The proportion of patients transplanted primarily for hepatitis C has decreased from 33.8% in 2012 to 13.3% in 2018 (Figure 20). Including cases with hepatitis C virus cirrhosis recorded as any of up to four diagnoses, the proportion of patients transplanted primarily for hepatitis C has decreased from 42% in 2012 to 26% in 2018. The proportion of patients transplanted for hepatocellular carcinoma has increased from 11.4% in 2012 to 18.7% in 2018. Over the same time period, the proportion of patients transplanted for non-alcoholic fatty liver disease increased from 8.0% to 10.2%.

Figure 20. Adult primary diagnosis percentages (based on graft 1) all years



Abbreviations: NAFLD, non-alcoholic fatty liver disease

10.5 Fulminant Hepatic Failure

Table 6 lists the detailed breakdown of the causes of fulminant hepatic failure primary diagnoses for adults and children.

Table 6. Detailed breakdown of fulminant hepatic failure category by age group

Fulminant hepatic failure	Paediatric	Adult	All patients
Acute - Unknown / unspecified	56	105	**161**
Acute - Hepatitis B	0	77	**77**
Acute - Hepatitis non A-G	15	21	**36**
Acute - Other drugs	3	31	**34**
Subacute - Hepatitis unknown	4	29	**33**
Acute - Wilson's	8	20	**28**
Acute - Paracetamol	4	24	**28**
Subacute - Autoimmune hepatitis	2	22	**24**
Subacute - Hepatitis B	0	21	**21**
Subacute - Drugs	1	15	**16**
Acute - Autoimmune hepatitis	1	11	**12**
Subacute - Wilson's	2	7	**9**
Acute - Herbs / mushrooms	0	8	**8**
Subacute - Hepatitis non A-G	0	6	**6**
Acute - Post-operative	1	4	**5**
Acute - Hepatitis A	1	3	**4**
Acute - Toxic (non-drug)	1	3	**4**
Subacute - Budd Chiari	1	2	**3**
Acute - alpha-1-antitrypsin	2	0	**2**
Acute - Budd Chiari	0	2	**2**
Acute - Other virus	1	1	**2**
Subacute - Hepatitis A	0	2	**2**
Acute - Hepatitis E	0	1	**1**
Acute - Post traumatic	0	1	**1**
Subacute - Herbs	0	1	**1**
Subacute - Hepatitis C	0	1	**1**
Subacute - Hepatitis - giant cell	1	0	**1**
Subacute - Hepatitis - ischaemic	0	1	**1**
Total	**104**	**419**	**523**

10.6 Metabolic disorders

Alpha-1 antitrypsin deficiency, familial amyloid polyneuropathy and Wilson's disease were the most common primary diagnoses in the metabolic disorders category (Table 7).

Table 7. Detailed breakdown of metabolic disorders category by age group

Metabolic Disorders	Paediatric	Adult	All patients
Alpha-1 antitrypsin deficiency	40	60	**100**
Familial amyloid polyneuropathy	0	45	**45**
Wilson's disease	8	35	**43**
Haemochromatosis	3	33	**36**
Urea cycle disorder	26	4	**30**
Ornithine transcarbamylase deficiency	*14*	*1*	***15***
Argininosuccinate lyase deficiency	*4*	*1*	***5***
Citrullinaemia [argininosuccinate synthetase deficiency]	*4*	*1*	***5***
Carbamyl phosphate synthetase 1 deficiency	*2*	*1*	***3***
Unspecified	*1*	*0*	***1***
Primary hyperoxaluria	10	9	**19**
Glycogen storage disease	4	10	**14**
Crigler-Najjar	12	1	**13**
Homozygous hypercholesterolaemia	7	2	**9**
Maple syrup urine disease	8	1	**9**
Propionic acidaemia	7	0	**7**
Tyrosinaemia	6	0	**6**
Protoporphyria	0	3	**3**
Methyl malonic acidaemia	2	0	**2**
Bile acid synthesis / transport disorder	3	0	**3**
Protein C Deficiency	1	2	**3**
Cirrhosis secondary to Niemann-Pick Type C	1	0	**1**
Familial immunodeficiency syndrome	1	0	**1**
Indian childhood cirrhosis	1	0	**1**
Methylmalonic acidaemia	1	0	**1**
Mitochondrial disease	1	0	**1**
Other porphyria	0	1	**1**
Pyridoxamine 5 - phosphate oxidase deficiency	1	0	**1**
Total	**142**	**206**	**348**

11 Patient Survival

Patient survival (alive/deceased) is based on patients who had their initial liver transplant in Australia or New Zealand (i.e. Graft 1). Both deceased and living donor grafts are included in this analysis.

11.1 All patients

5,783 patients had their first liver transplant in Australia or New Zealand (i.e. Graft 1, Figure 21 and Table 8). Three patients who had their first liver transplant overseas and subsequently had a liver transplant in Australia or New Zealand have been excluded from this patient survival analysis. Ten-year patient survival was 74.7%. The median patient survival post-transplant was 23.9 years.

Figure 21. Patient survival curve

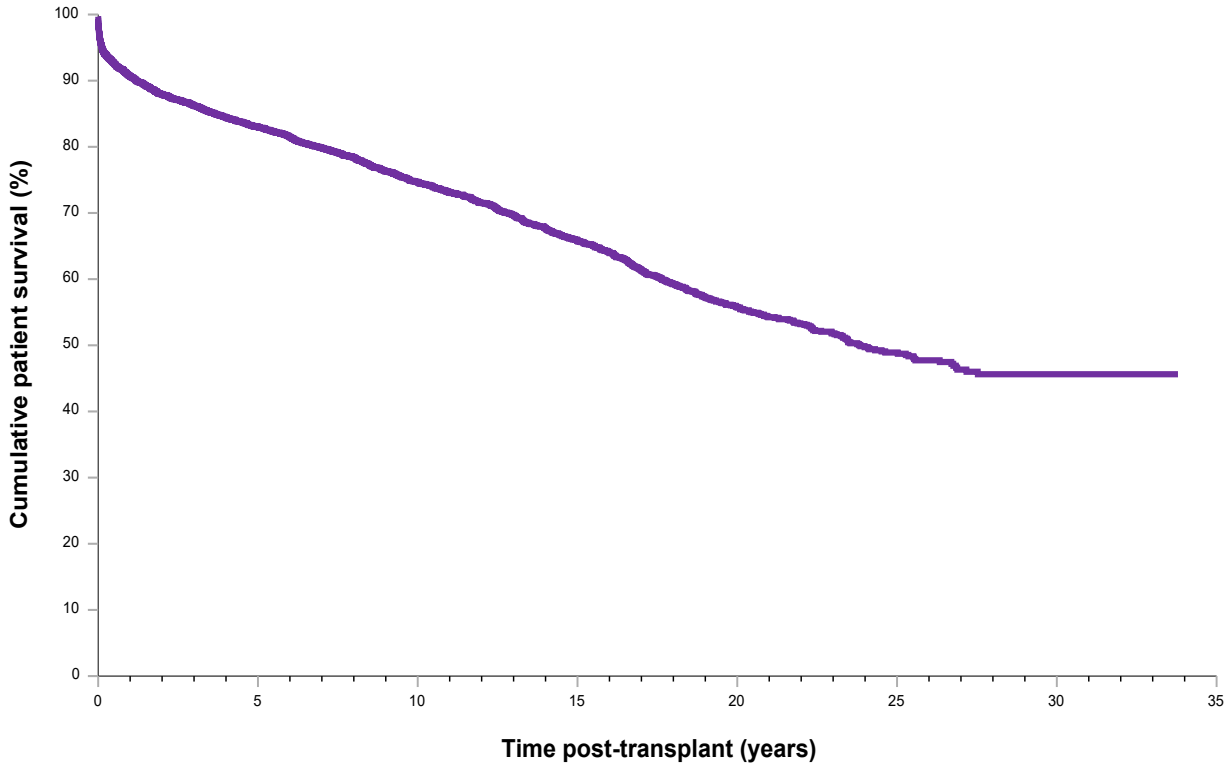


Table 8. Patient survival

Patient Survival	Time post-transplant (years)								
	0	1	3	5	10	15	20	25	30
No. at risk	5,783	4,921	4,090	3,459	2,190	1,293	658	265	34
Survival (%)		91%	86%	83%	75%	66%	56%	49%	46%

11.2 Patient Survival by Age Group

Paediatric cases are defined as less than 16 years at time of first transplant (n = 975). Adult cases are defined as greater than or equal to 16 years at time of first transplant (n = 4,808). Post-transplant survival was superior in the paediatric population compared to the adult population (P < 0.001, Figure 22, Table 9). Ten-year patient survival was 84.3% for children and 72.6% for adults. Median patient survival was not reached for children and was 20.1 years for adults.

Figure 22. Patient survival curve by age category

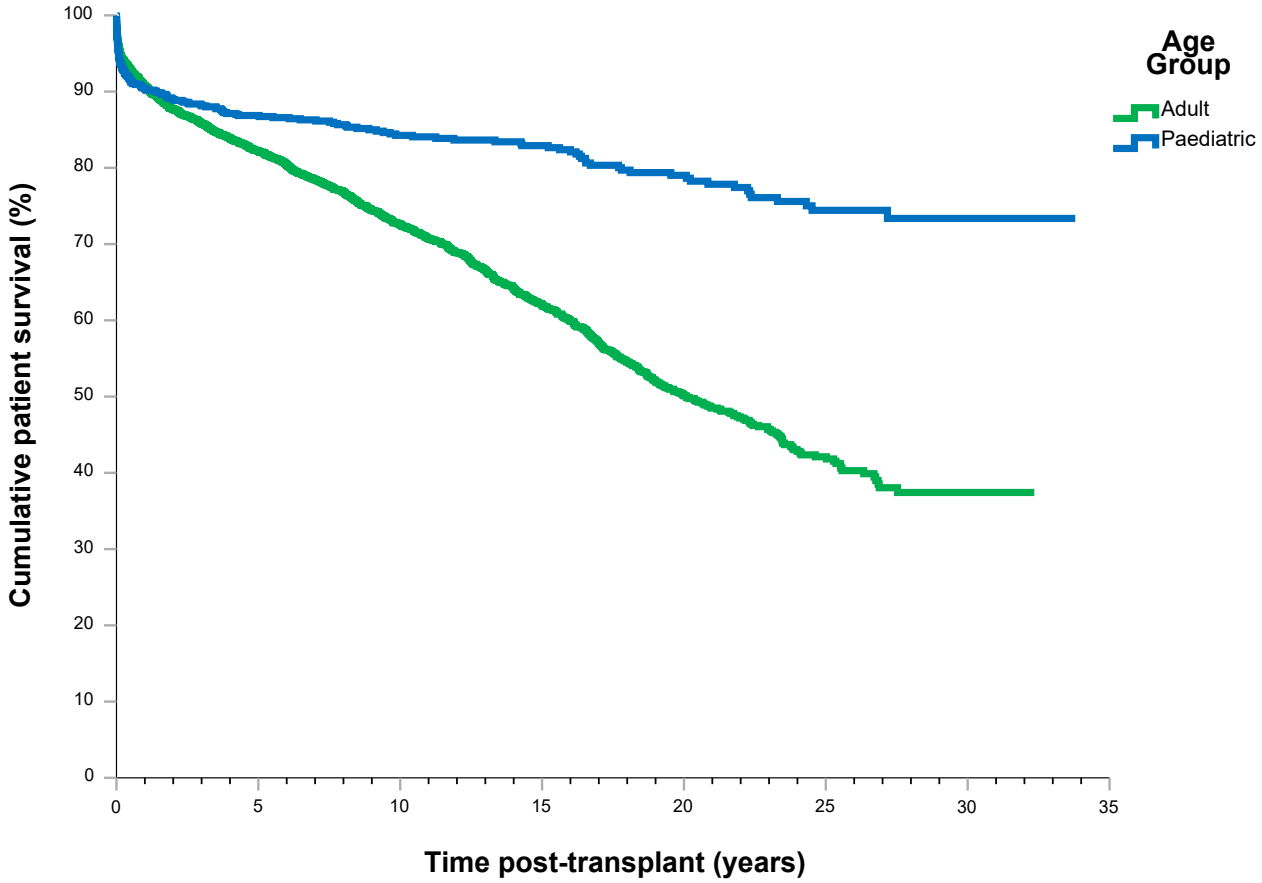


Table 9. Patient survival by age category

Age group	Patient Survival	Time post-transplant (years)								
		0	1	3	5	10	15	20	25	30
Adults (≥16y)	No. at risk	4,808	4,082	3,365	2,819	1,741	979	448	150	13
	Survival (%)		91%	86%	82%	73%	62%	50%	42%	37%
Paediatric (<16y)	No. at risk	975	839	725	640	449	314	210	115	21
	Survival (%)		90%	88%	87%	84%	83%	79%	74%	73%

11.3 Paediatric Patient Survival by Age Strata

There was no significant difference in patient survival by paediatric age strata (P = 0.205, Figure 23, Table 10). Ten-year patient survival was 85.5% for children less than 1 year, 80.1% for children aged between 1 – 2-year-olds, 86.6% for 3 – 9-year-olds and 87.8% for 10 – 15-year-olds. Median patient survival was not reached for any paediatric age group.

Figure 23. Paediatric patient survival curve by age strata

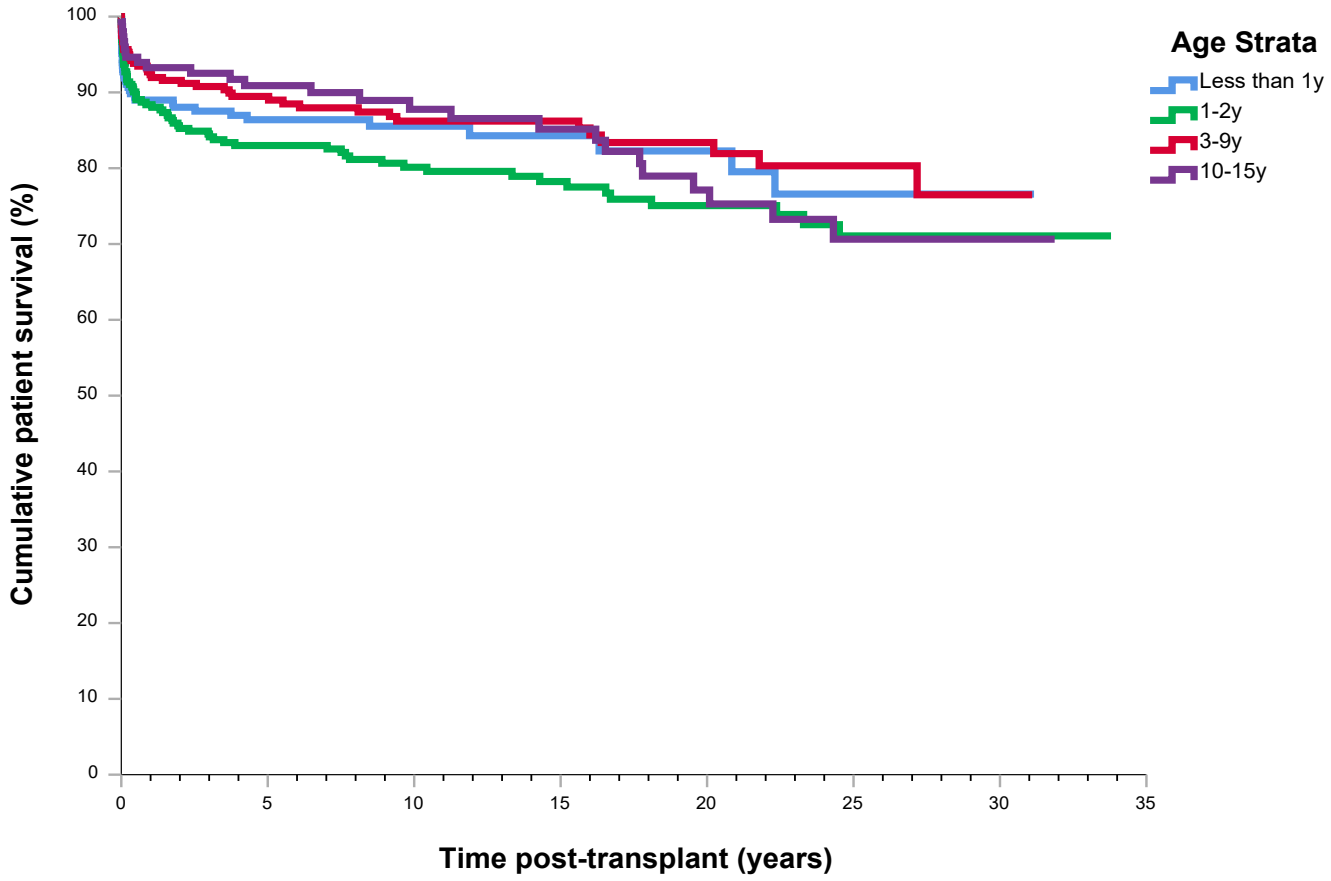


Table 10. Paediatric patient survival by age strata

Age strata	Patient Survival	Time post-transplant (years)								
		0	1	3	5	10	15	20	25	30
< 1 year	No. at risk	247	198	166	143	89	48	32	17	3
	Survival (%)		89%	88%	86%	86%	84%	82%	77%	77%
1 - 2 years	No. at risk	302	260	225	203	150	109	74	43	7
	Survival (%)		88%	85%	83%	80%	78%	75%	71%	71%
3 - 9 years	No. at risk	276	246	215	187	135	97	62	31	5
	Survival (%)		92%	91%	90%	87%	86%	83%	80%	77%
10 – 15 years	No. at risk	150	135	119	107	75	60	42	25	6
	Survival (%)		93%	93%	91%	88%	85%	77%	71%	71%

11.4 Adult Patient Survival by Age Strata

Post-transplant patient survival in adults was significantly worse with increasing patient age (P < 0.001, Figure 24, Table 11). For patients aged 16 to 29, 30 to 39, 40 to 49, 50 to 59, 60 to 69 and 70 to 79 years, 10-year patient survival was 79.2%, 78.4%, 73.3%, 71.9%, 64.6% and 66.7%, respectively. Median patient survival was not reached for patients aged 16 to 29 years. For patients aged 30 to 39, 40 to 49, 50 to 59, 60 to 69 and 70 to 79 years, median patient survival was 24.0, 23.0, 17.8, 14.7 and 11.0 years, respectively.

Figure 24. Adult patient survival curve by age strata

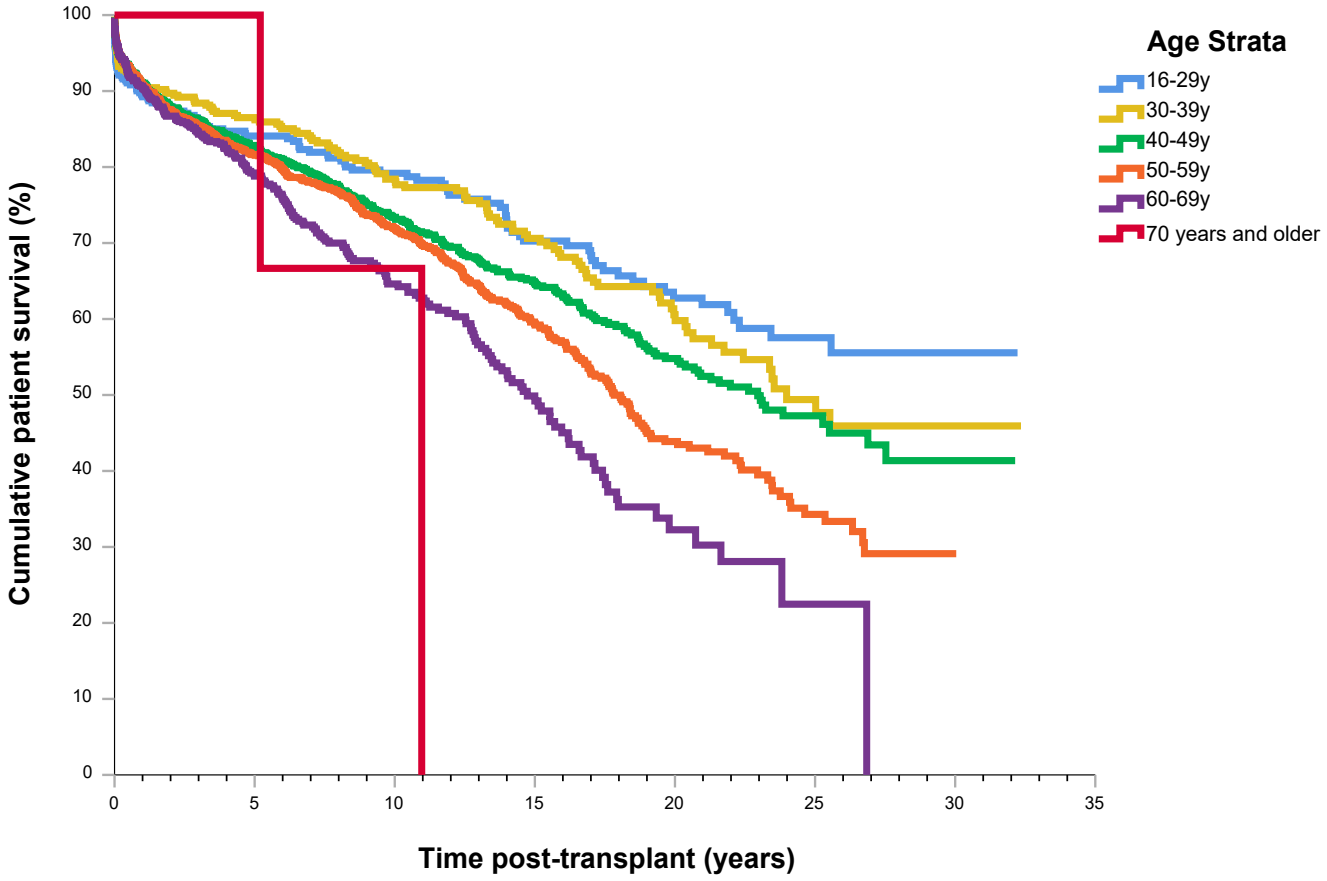


Table 11. Adult patient survival by age strata

Age strata	Patient Survival	Time post-transplant (years)								
		0	1	3	5	10	15	20	25	30
16-29 y	No. at risk	393	340	295	258	179	119	81	36	5
	Survival (%)		90%	86%	84%	79%	70%	63%	58%	56%
30-39 y	No. at risk	444	385	334	305	213	148	78	29	2
	Survival (%)		91%	88%	87%	78%	71%	61%	49%	46%
40-49 y	No. at risk	1,149	1,001	883	783	560	330	155	44	5
	Survival (%)		91%	86%	83%	73%	65%	55%	47%	41%
50-59 y	No. at risk	1,865	1,598	1,311	1,082	605	306	113	38	1
	Survival (%)		91%	85%	82%	72%	59%	44%	34%	29%
60-69 y	No. at risk	944	751	537	388	183	76	21	3	0
	Survival (%)		91%	84%	79%	65%	9%	32%	23%	
70-79 y	No. at risk	13	7	5	3	1	0			
	Survival (%)		100%	100%	100%	67%				

11.5 Patient Survival by Era of Transplant

There has been a progressive improvement in patient survival over eras of transplantation (P < 0.001, Figure 25, Table 12). Patient survival in the most recent era was 95.5% at 1 year, 91.8% at 3 years, 85.7% at 5 years and 76.2% at 10 years. Median patient survival was 22.0 years for 1995 – 99 era, 20.7 years for 1990 – 99 era and 11.8 years for 1985 – 89 era. Median patient survival was not reached for recent eras from 2000 - 04 onwards.

Figure 25. Patient survival curve by era of transplant

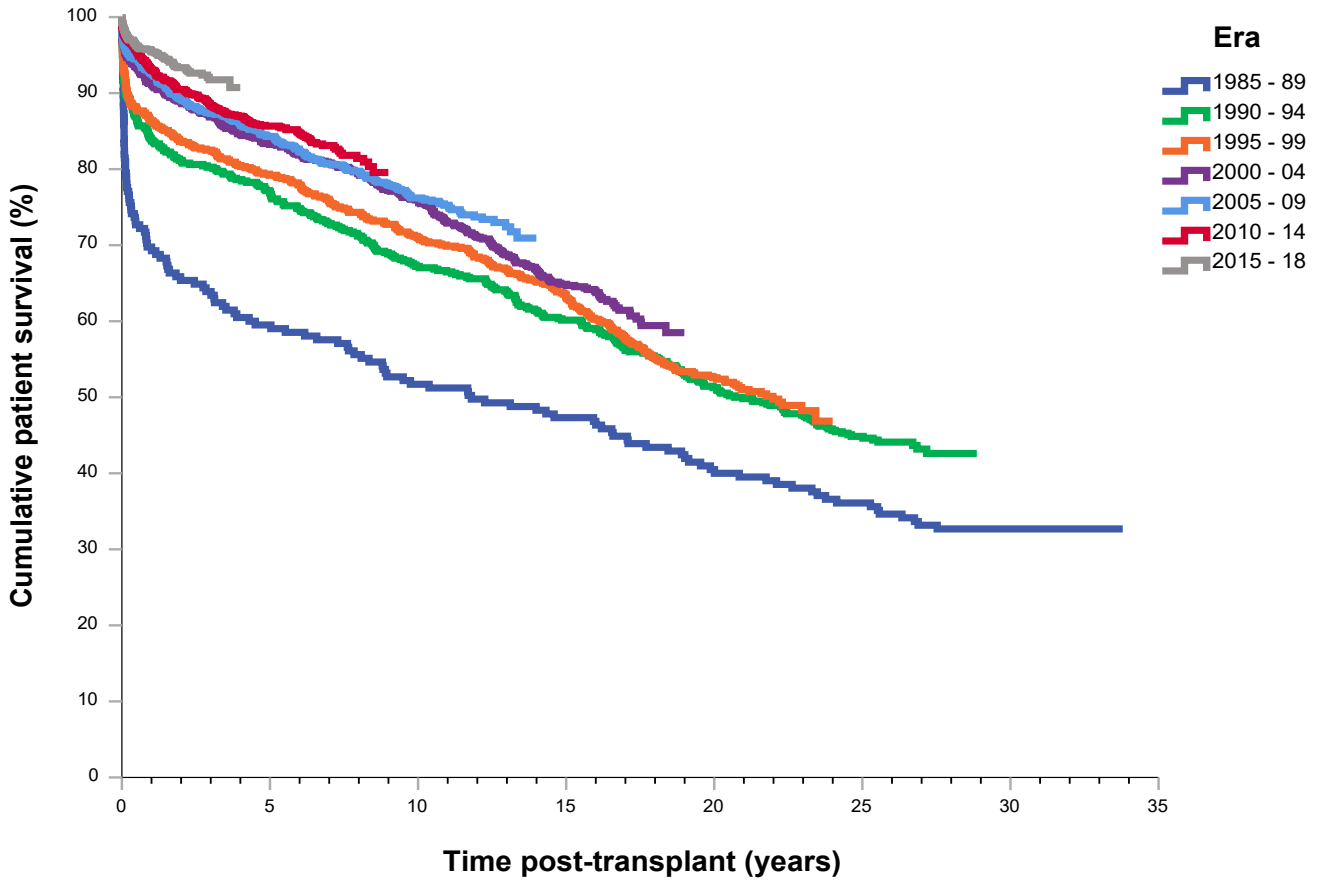


Table 12. Patient survival by transplant era

Transplant Era	Patient Survival	Time post-transplant (years) 0	1	3	5	10	15	20	25	30
1985 - 89	No. at risk	205	143	131	122	106	97	83	74	34
	Survival (%)		70%	64%	60%	52%	47%	41%	36%	33%
1990 - 94	No. at risk	552	463	443	425	371	332	283	191	0
	Survival (%)		84%	80%	77%	67%	60%	51%	45%	
1995 - 99	No. at risk	697	602	575	552	495	440	292	0	
	Survival (%)		86%	83%	79%	71%	63%	53%		
2000 - 04	No. at risk	860	785	747	716	653	424	0		
	Survival (%)		91%	87%	83%	76%	65%			
2005 - 09	No. at risk	962	891	840	811	565	0			
	Survival (%)		93%	87%	84%	76%				
2010 - 14	No. at risk	1,228	1,143	1,085	833	0				
	Survival (%)		93%	88%	86%					
2015 - 18	No. at risk	1,279	894	269	0					
	Survival (%)		96%	92%						

11.6 Paediatric Patient Survival by Era of Transplant

There has been a progressive improvement in paediatric patient survival over eras of transplantation (P < 0.001, Figure 26, Table 13). Paediatric patient survival in the most recent era was 97.2% at 1 year, 97.2% at 3 years, 90.9% at 5 years and 92.1% at 10 years. Median paediatric patient survival was 20.8 years for 1985 – 89 era and was not reached for all other eras.

Figure 26. Paediatric patient survival curve by era of transplant

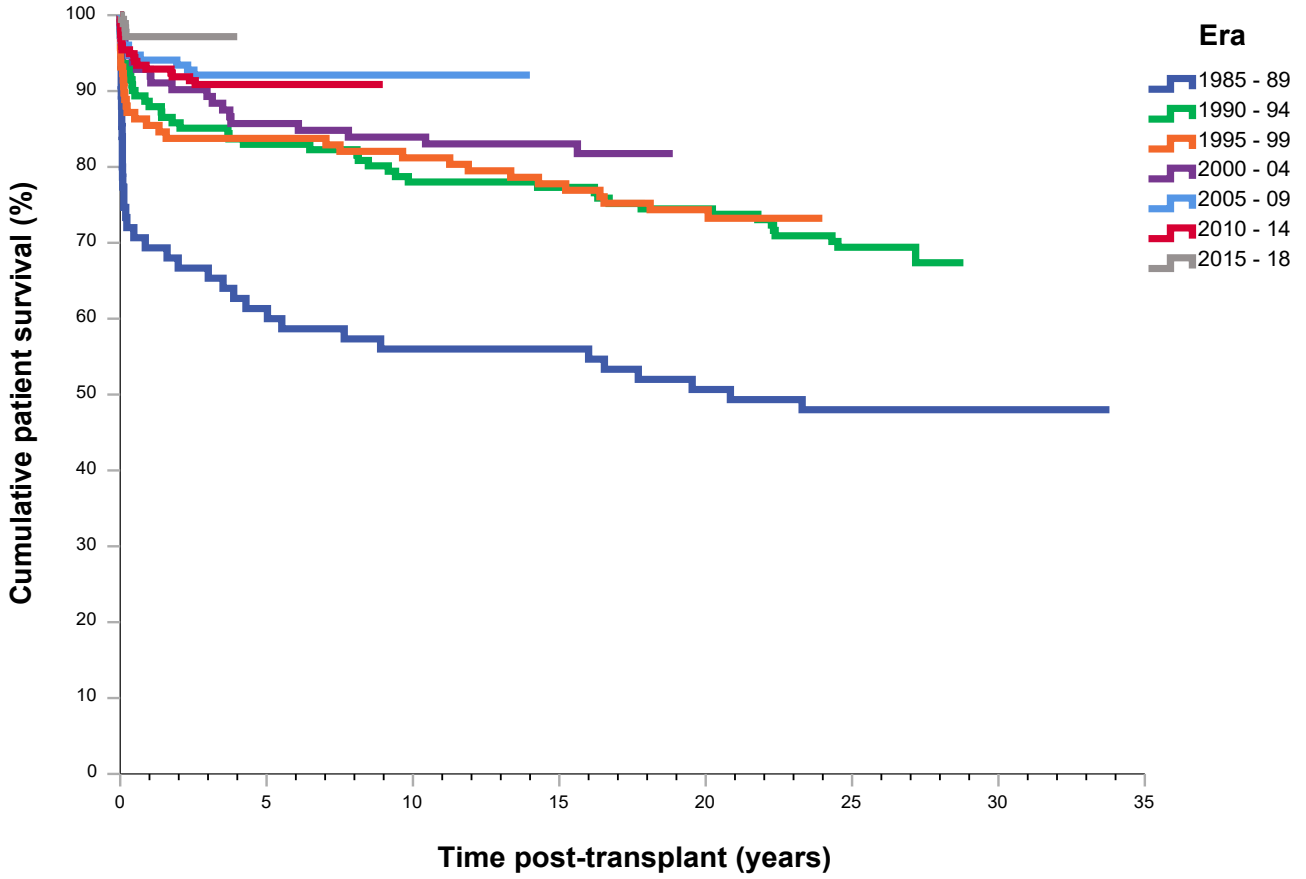


Table 13. Paediatric patient survival by transplant era

Transplant Era	Patient Survival	Time post-transplant (years)								
		0	1	3	5	10	15	20	25	30
1985 - 89	No. at risk	75	52	50	46	42	42	38	36	21
	Survival (%)		69%	67%	61%	56%	56%	51%	48%	48%
1990 - 94	No. at risk	141	124	120	117	110	109	105	79	0
	Survival (%)		88%	85%	83%	78%	77%	75%	69%	
1995 - 99	No. at risk	117	100	98	98	95	91	67	0	
	Survival (%)		86%	84%	84%	81%	78%	74%		
2000 - 04	No. at risk	112	104	100	96	94	72	0		
	Survival (%)		93%	89%	86%	84%	83%			
2005 - 09	No. at risk	152	143	140	140	108	0			
	Survival (%)		94%	92%	92%	92%				
2010 - 14	No. at risk	197	183	179	143	0				
	Survival (%)		93%	91%	91%					
2015 - 18	No. at risk	181	133	38	0					
	Survival (%)		97%	97%						

11.7 Adult Patient Survival by Era of Transplant

There has been a progressive improvement in adult patient survival over eras of transplantation (P < 0.001, Figure 27, Table 14). Patient survival in the most recent era was 95.2% at 1 year, 90.9% at 3 years, 84.7% at 5 years and 73.2% at 10 years. Median adult patient survival was 18.5 years for 1995 – 99 era, 17.0 years for 1990 – 99 era and 9.5 years for 1985 – 89 era. Median adult patient survival was not reached for recent eras from 2000 - 04 onwards.

Figure 27. Adult patient survival curve by era of transplant

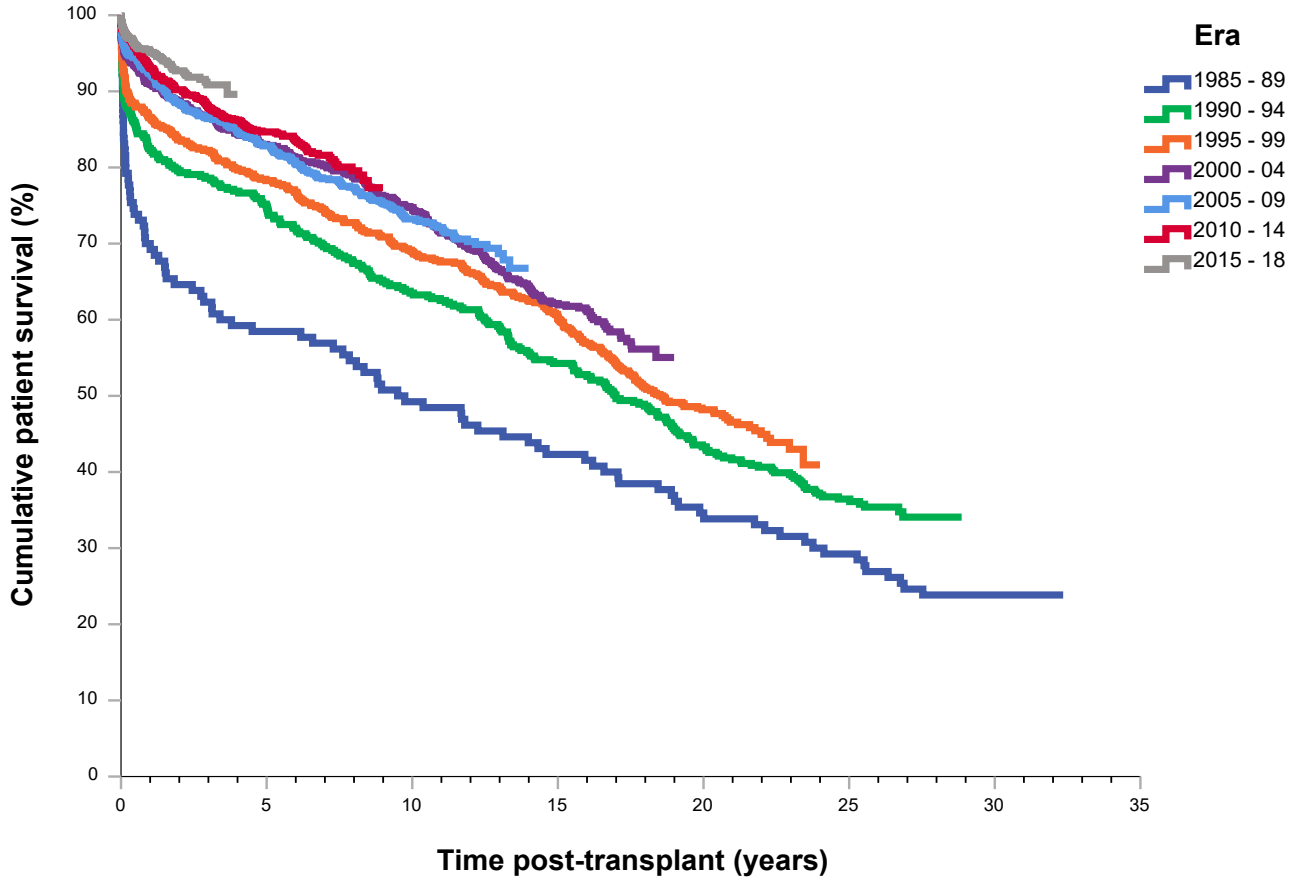


Table 14. Adult patient survival by transplant era

Transplant Era	Patient Survival	Time post-transplant (years)								
		0	1	3	5	10	15	20	25	30
1985 - 89	No. at risk	130	91	81	76	64	55	45	38	13
	Survival (%)		70%	62%	59%	49%	42%	35%	29%	24%
1990 - 94	No. at risk	411	339	323	308	261	223	178	112	0
	Survival (%)		83%	79%	75%	64%	54%	43%	36%	
1995 - 99	No. at risk	580	502	477	454	400	349	225	0	
	Survival (%)		87%	82%	78%	69%	60%	48%		
2000 - 04	No. at risk	748	681	647	620	559	352	0		
	Survival (%)		91%	87%	83%	75%	62%			
2005 - 09	No. at risk	810	748	700	671	457	0			
	Survival (%)		92%	86%	83%	73%				
2010 - 14	No. at risk	1,031	960	906	690	0				
	Survival (%)		93%	88%	85%					
2015 - 18	No. at risk	1,098	761	231	0					
	Survival (%)		95%	91%						

11.8 Paediatric Patient Survival by Type of Primary Graft

Children transplanted with a living donor graft or split liver graft had survival that was slightly superior to those transplanted with a whole graft and survival after reduced liver transplantation was inferior to other forms of transplantation (P < 0.001, Figure 28, Table 15). However, this may be partly due to era effect, since more reduced liver transplantation was performed in the earlier eras. One case of hepatocyte transplantation was excluded from this analysis. Ten-year patient survival was 90.7% for split liver grafts, 88.8% for living donor grafts, 84.8% for whole liver grafts and 76.6% for reduced grafts. Median paediatric patient survival was not reached for all graft types.

Figure 28. Paediatric patient survival curve by type of primary graft

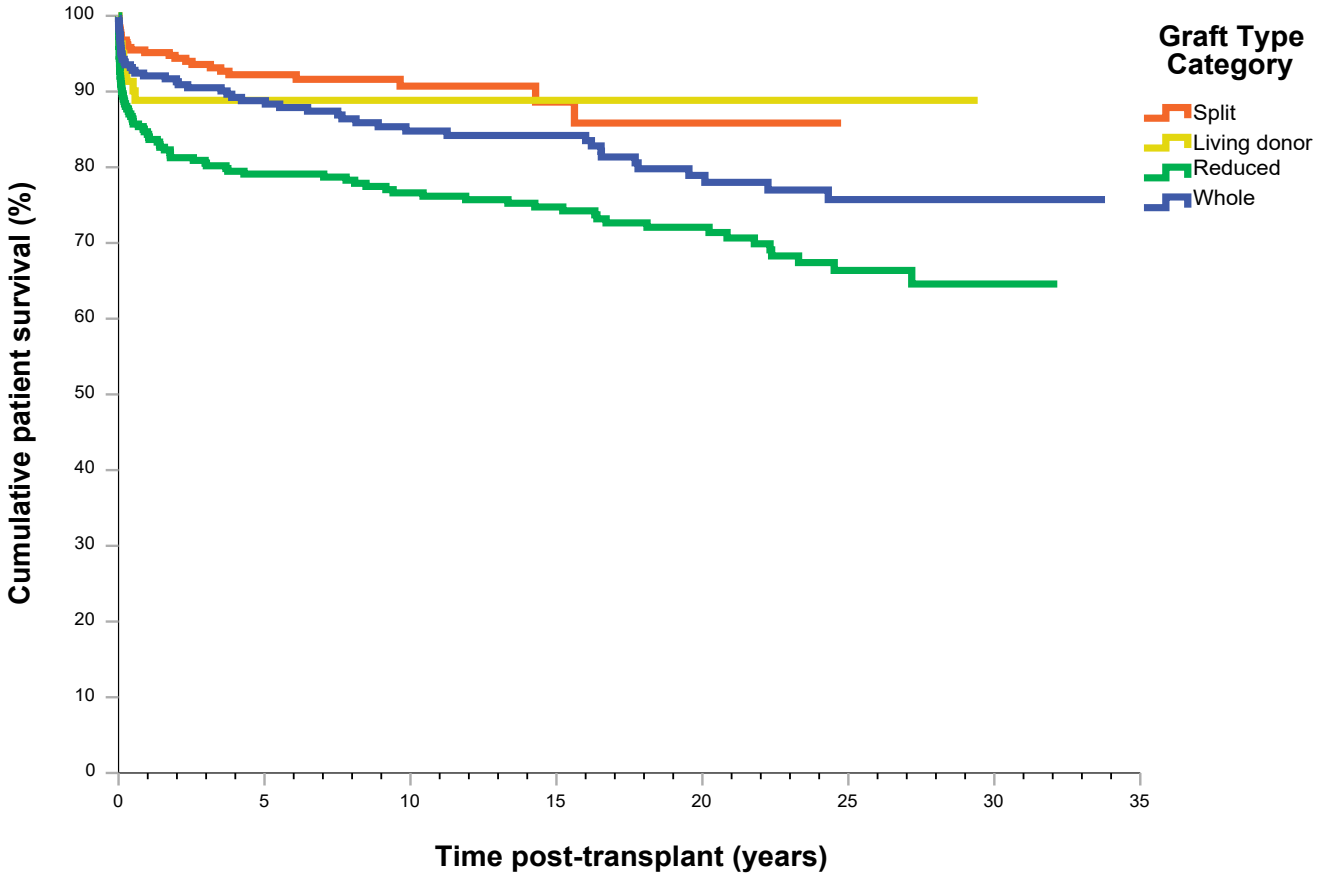


Table 15. Paediatric patient survival by type of primary graft

Graft Type Category	Patient Survival	Time post-transplant (years)								
		0	1	3	5	10	15	20	25	30
Whole	No. at risk	279	249	219	199	149	128	87	52	13
	Survival (%)		92%	91%	89%	85%	84%	79%	76%	76%
Reduced	No. at risk	301	248	226	212	176	148	108	60	8
	Survival (%)		84%	81%	79%	77%	75%	72%	66%	64%
Split	No. at risk	313	271	214	173	96	33	12	0	
	Survival (%)		95%	94%	92%	91%	89%	86%		
Living donor	No. at risk	81	70	65	55	27	5	3	3	0
	Survival (%)		89%	89%	89%	89%	89%	89%	89%	

11.9 Adult Patient Survival by Type of Primary Graft

There was no significant difference in patient survival in adults by type of primary graft, although there was a trend to worse survival after reduced liver transplantation (P = 0.268, Figure 29, Table 16). Ten-year patient survival was 85.6% for living donor grafts, 75.7% for split grafts, 72.5% for whole grafts and 0 for domino grafts. Median adult patient survival was not reached for split and living donor grafts, and was 19.8 years for whole grafts, 10.9 years for reduced grafts and 9.4 years for domino grafts.

Figure 29. Adult patient survival curve by type of primary graft

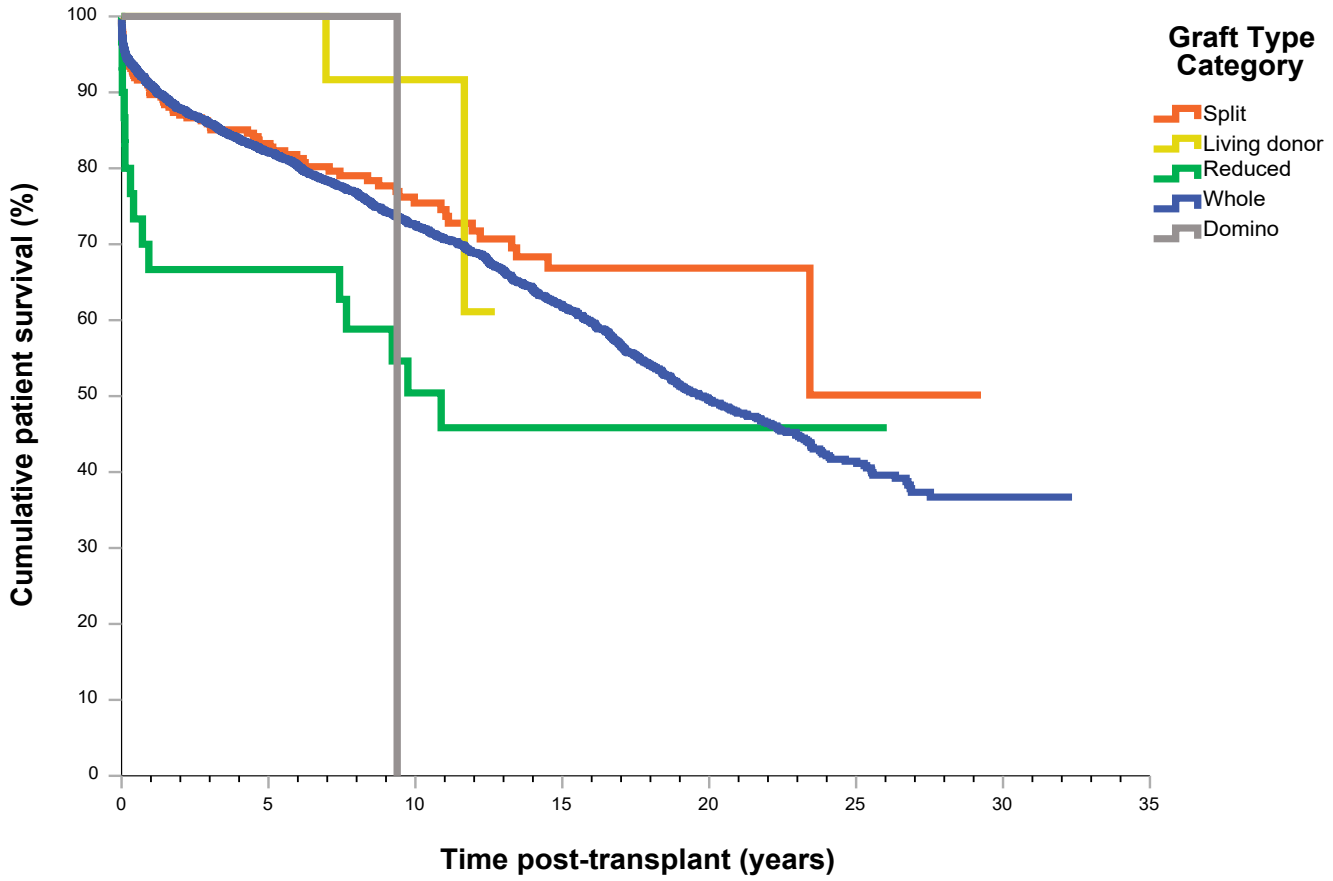


Table 16. Adult patient survival by type of primary graft

Graft Type Category	Patient Survival	Time post-transplant (years)								
		0	1	3	5	10	15	20	25	30
Whole	No. at risk	4,423	3,765	3,116	2,610	1,627	931	423	146	13
	Survival (%)	100%	91%	86%	82%	73%	62%	50%	41%	37%
Reduced	No. at risk	30	20	19	18	12	10	7	2	0
	Survival (%)	100%	67%	67%	67%	50%	46%	46%	46%	
Split	No. at risk	336	278	215	177	96	38	18	2	0
	Survival (%)	100%	90%	86%	84%	76%	67%	67%	50%	
Domino	No. at risk	4	4	3	2	0				
	Survival (%)	100%	100%	100%	100%					
Living donor	No. at risk	15	14	12	12	6	0			
	Survival (%)	100%	93%	93%	93%	86%				

11.10 Paediatric Patient Survival by Weight

There was no significant difference in patient survival of children of different weights (P = 0.385, Figure 30 and Table 17). The analysis excludes three cases with missing transplant weight (n = 972). Ten-year paediatric patient survival was 88.5% for children over 20 kg, 84.6% for children under 5 kg, 83.6% for children weighing between 8.01 and 20kg and 80.4% for children between 5 and 8 kg. Median paediatric patient survival was not reached for all weight categories.

Figure 30. Paediatric patient survival curve by transplant weight

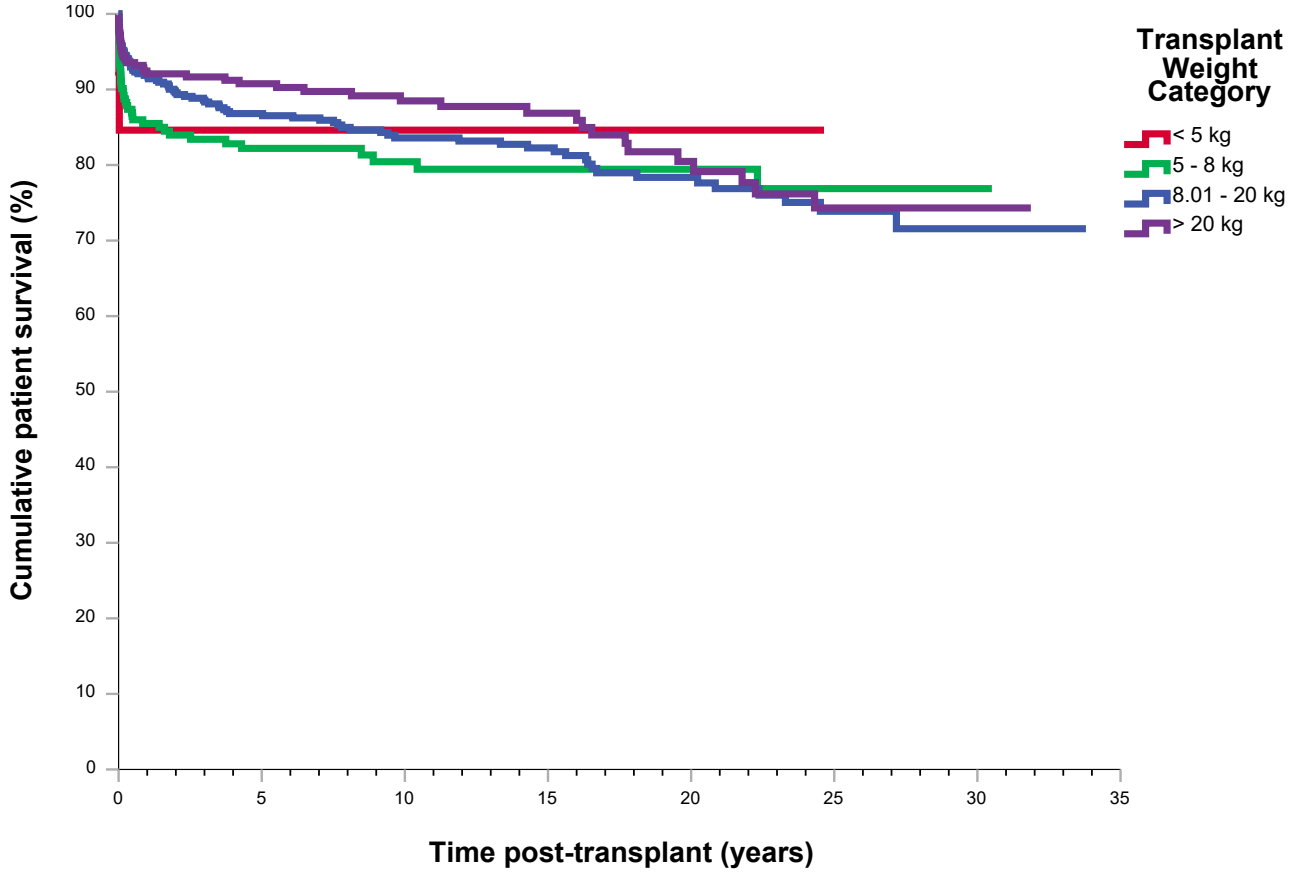


Table 17. Paediatric patient survival by transplant weight

Transplant weight	Patient Survival	Time post-transplant (years) 0	1	3	5	10	15	20	25	30
< 5 kg	No. at risk	13	7	7	6	4	3	1	0	
	Survival (%)		85%	85%	85%	85%	85%	85%		
5 - 8 kg	No. at risk	223	173	145	133	84	49	36	22	3
	Survival (%)		86%	83%	82%	80%	79%	79%	77%	77%
8.01 - 20 kg	No. at risk	456	409	355	310	228	165	110	57	10
	Survival (%)		92%	89%	87%	84%	82%	78%	74%	72%
> 20 kg	No. at risk	280	247	215	188	130	95	61	35	7
	Survival (%)		92%	92%	91%	89%	87%	81%	74%	74%

11.11 Paediatric Patient Survival by Primary Disease

There was a trend to difference in patient survival between different disease categories in children (P = 0.051, Figure 31, Table 18). Children with hepatoblastoma had the poorest ten-year survival of 71.7%. Children with fulminant hepatic failure had a ten-year survival of 74.1%. All other paediatric disease categories had an 85% or higher 10-year survival. Median patient survival was not reached for all disease groups.

Figure 31. Paediatric patient survival curve by primary disease

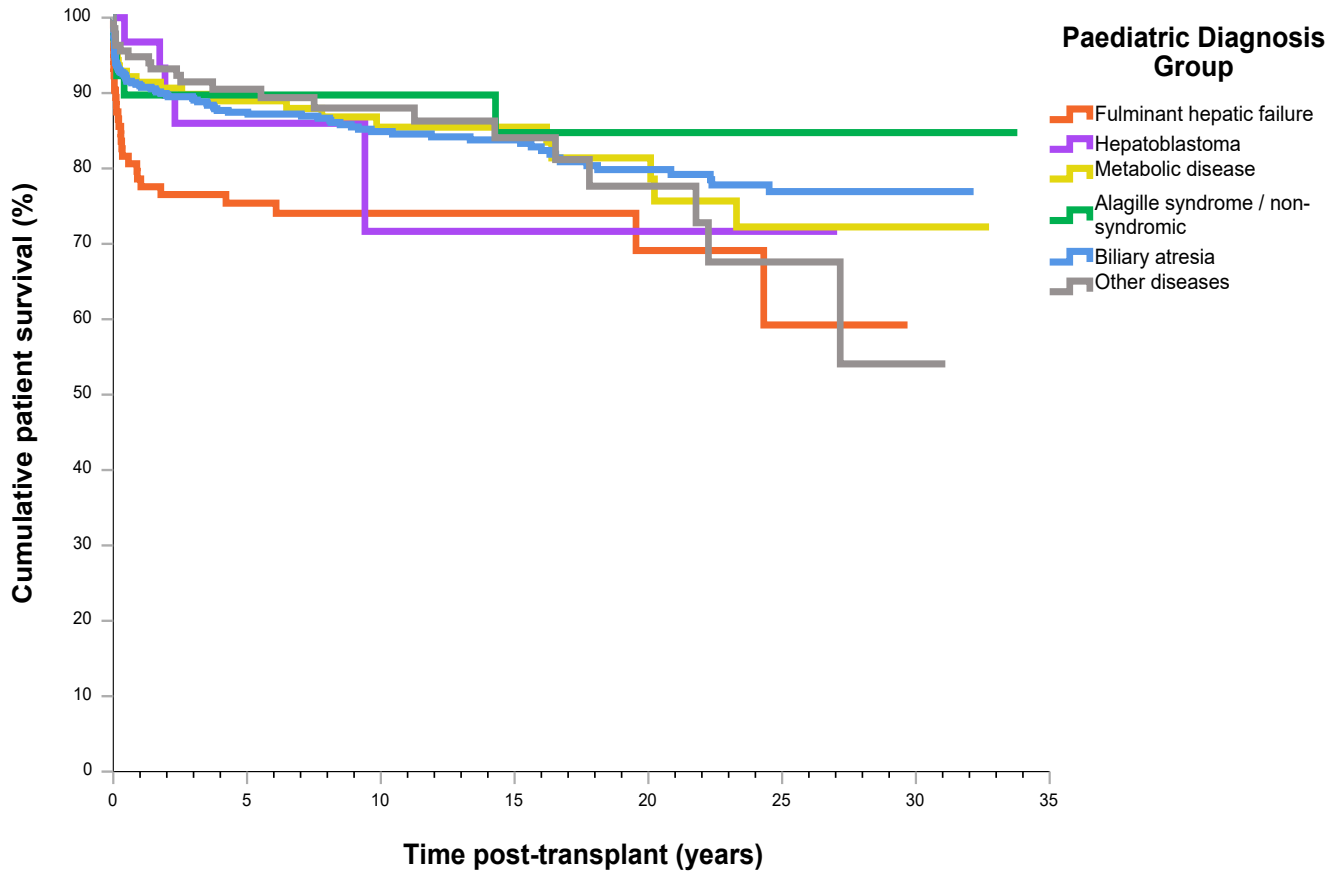


Table 18. Paediatric patient survival by primary disease

Primary Diagnosis	Patient Survival	Time post-transplant (years)								
		0	1	3	5	10	15	20	25	30
Alagille syndrome / non-syndromic	No. at risk	39	34	29	25	21	17	16	7	3
	Survival (%)		90%	90%	90%	90%	85%	85%	85%	85%
Biliary atresia	No. at risk	523	453	398	359	267	183	131	77	12
	Survival (%)		91%	89%	88%	85%	84%	80%	77%	77%
Hepatoblastoma	No. at risk	31	30	20	15	5	2	1	1	0
	Survival (%)		97%	86%	86%	72%	72%	72%	72%	
Fulminant hepatic failure	No. at risk	104	77	68	63	41	28	14	5	0
	Survival (%)		79%	77%	75%	74%	74%	69%	59%	
Metabolic diseases	No. at risk	141	124	107	94	63	49	29	15	5
	Survival (%)		91%	90%	89%	86%	86%	81%	72%	72%
Other diseases	No. at risk	137	121	103	84	52	35	19	10	1
	Survival (%)		95%	92%	91%	88%	84%	78%	68%	54%

11.12 Adult Patient Survival by Primary Disease

There was a significant difference in the survival between different disease categories in adults (P = 0.038, Figure 32, Table 19). Patients with hepatocellular carcinoma, hepatitis C virus cirrhosis and non-alcoholic fatty liver disease (NAFLD) / cryptogenic cirrhosis had the poorest 10-year patient survival (67.0%, 68.9% and 70.7%, respectively), while those with hepatitis C virus cirrhosis, alcoholic cirrhosis and NAFLD / cryptogenic cirrhosis had the poorest median survival (17.1 years, 17.1 years and 18.8 years, respectively).

Figure 32. Adult patient survival curve by primary disease

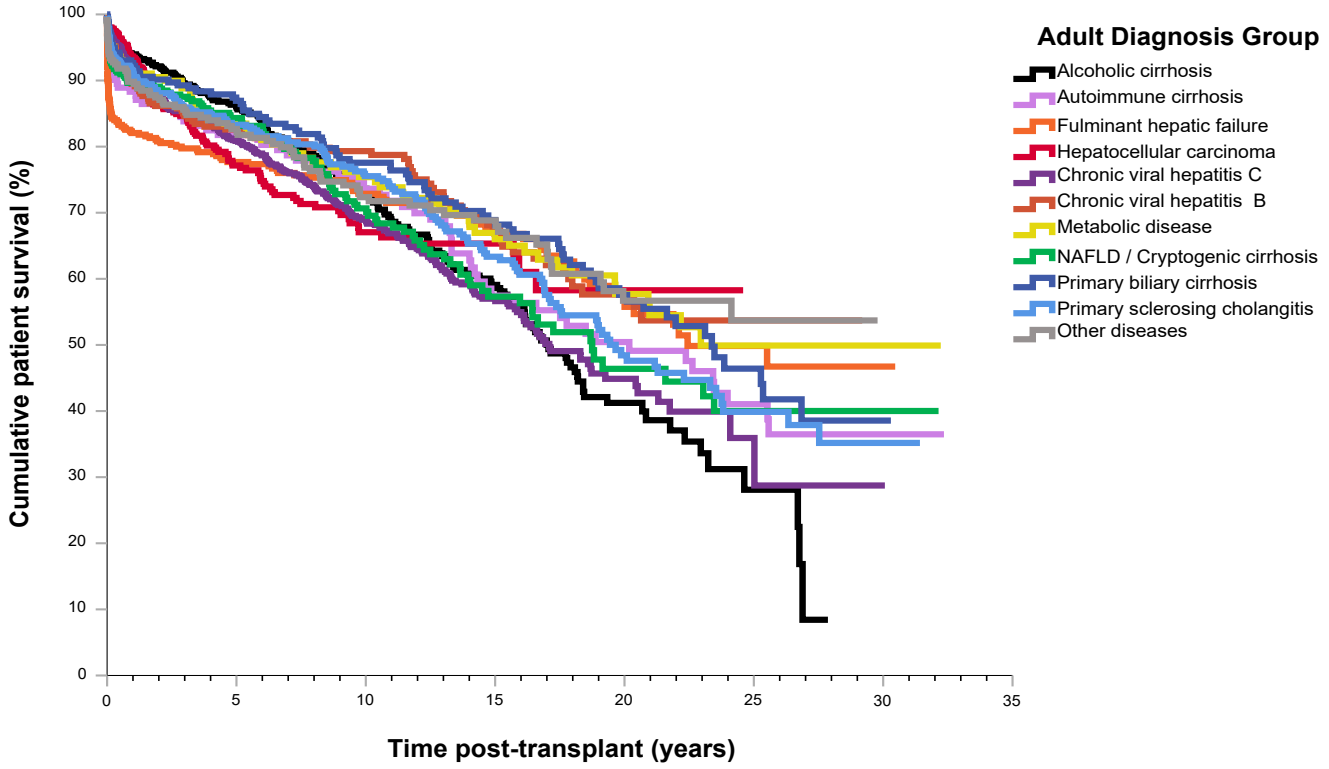


Table 19. Adult patient survival by primary disease

Primary Diagnosis	Patient Survival	Time post-transplant (years)								
		0	1	3	5	10	15	20	25	30
Alcoholic cirrhosis	No. at risk	625	538	436	370	214	122	42	9	0
	Survival (%)		94%	89%	86%	74%	59%	41%	28%	
Autoimmune cirrhosis	No. at risk	172	144	127	116	83	54	39	19	1
	Survival (%)		88%	84%	82%	74%	58%	50%	41%	37%
Fulminant hepatic failure	No. at risk	419	332	292	252	171	94	53	21	1
	Survival (%)		82%	80%	78%	73%	67%	57%	50%	47%
Hepatitis B virus cirrhosis	No. at risk	288	247	217	190	139	84	33	13	0
	Survival (%)		90%	85%	83%	79%	67%	58%	54%	
Hepatitis C virus cirrhosis	No. at risk	1,056	929	783	660	350	156	48	5	1
	Survival (%)		92%	85%	81%	69%	57%	45%	36%	29%
Hepatocellular carcinoma	No. at risk	556	466	322	217	94	36	8	0	
	Survival (%)		94%	85%	77%	67%	65%	58%		
Metabolic diseases	No. at risk	204	175	153	135	99	69	39	8	2
	Survival (%)		91%	89%	84%	75%	66%	58%	50%	50%
NAFLD / Cryptogenic cirrhosis	No. at risk	401	331	263	214	127	65	30	12	1
	Survival (%)		90%	88%	84%	71%	57%	46%	40%	40%
Primary biliary cirrhosis	No. at risk	262	227	200	179	136	98	57	22	2
	Survival (%)		93%	89%	87%	78%	68%	58%	46%	39%
Primary sclerosing cholangitis	No. at risk	493	426	351	299	208	121	60	28	5
	Survival (%)		91%	86%	83%	76%	63%	48%	40%	35%
Other diseases	No. at risk	332	268	221	187	120	80	39	13	0
	Survival (%)		90%	86%	83%	72%	69%	57%	54%	

Abbreviations: NAFLD, non-alcoholic fatty liver disease

11.13 Patient Survival by Age Group with Primary Diagnosis of Fulminant Hepatic Failure

There was no significant difference in the survival between adults and children with a primary diagnosis of fulminant hepatic failure (FHF) (P = 0.412, Figure 33 and Table 20). Ten-year patient survival was 74.1% for children and 72.9% for adults. Median patient survival was not reached for children and was 22.4 years for adults.

Figure 33. Patient survival curve by age group with primary diagnosis of fulminant hepatic failure

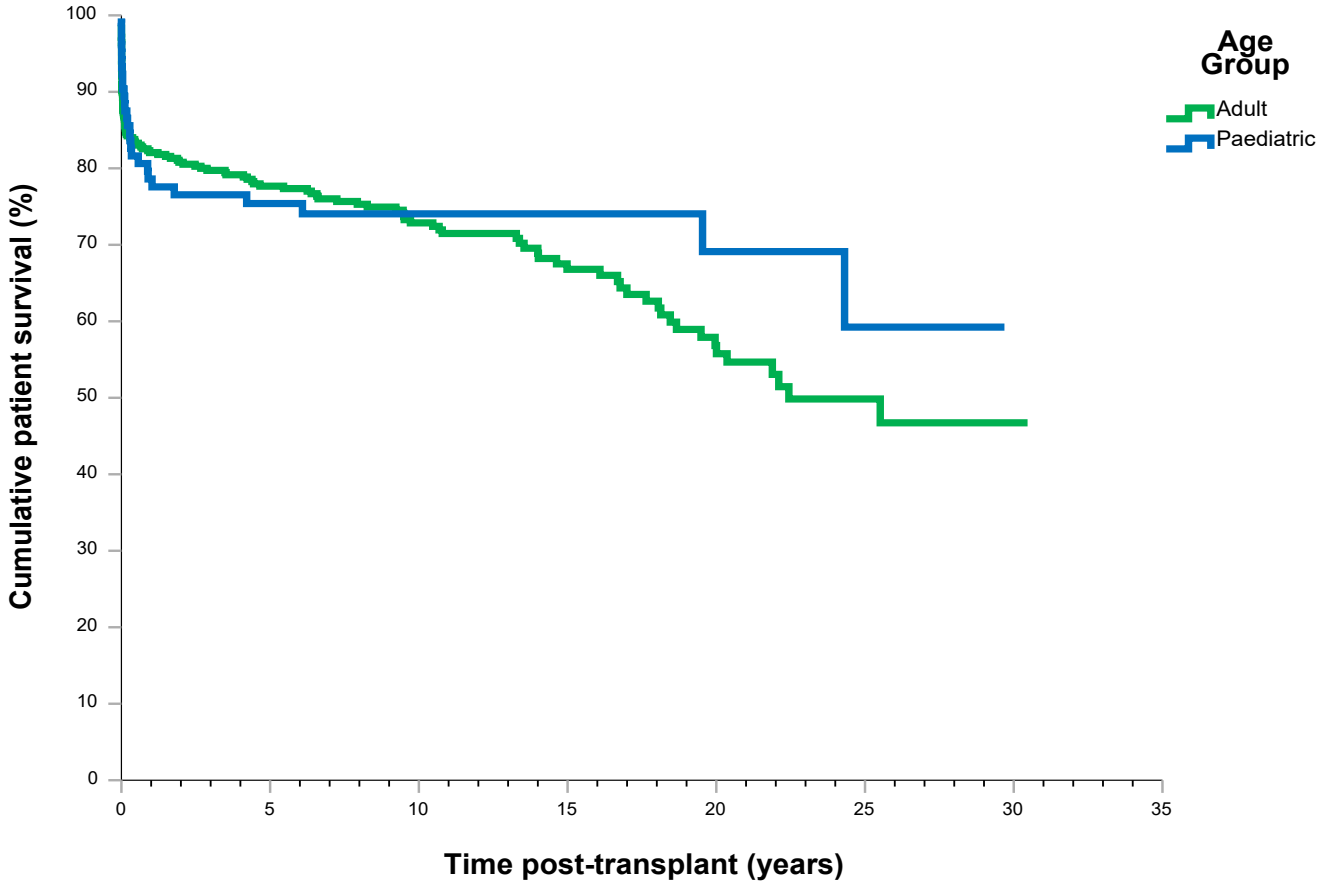


Table 20. Patient survival by age group with primary diagnosis of fulminant hepatic failure

Primary Diagnosis	Patient Survival	Time post-transplant (years)								
		0	1	3	5	10	15	20	25	30
Paediatric FHF	No. at risk	104	77	68	63	41	28	14	5	0
	Survival (%)		79%	77%	75%	74%	74%	69%	59%	
Adult FHF	No. at risk	419	332	292	252	171	94	53	21	1
	Survival (%)		82%	80%	78%	73%	67%	57%	50%	47%
All FHF	No. at risk	523	409	360	315	212	122	67	26	1
	Survival (%)		81%	79%	77%	73%	68%	59%	52%	49%

11.14 Adult Patient Survival by Transplant Era with Chronic Viral Hepatitis B

There has been an improvement in patient survival over the transplant eras for patients with a primary diagnosis of hepatitis B (P<0.001, Figure 34, Table 21). Median adult patient survival was 0.6 years for the 1985 – 89 era, 13.3 years for the 1990 – 94 era, 20.4 years for the 1995 – 99 era and was not reached for the recent eras.

Figure 34. Adult patient survival curve by transplant era with primary diagnosis of Chronic Viral Hepatitis B

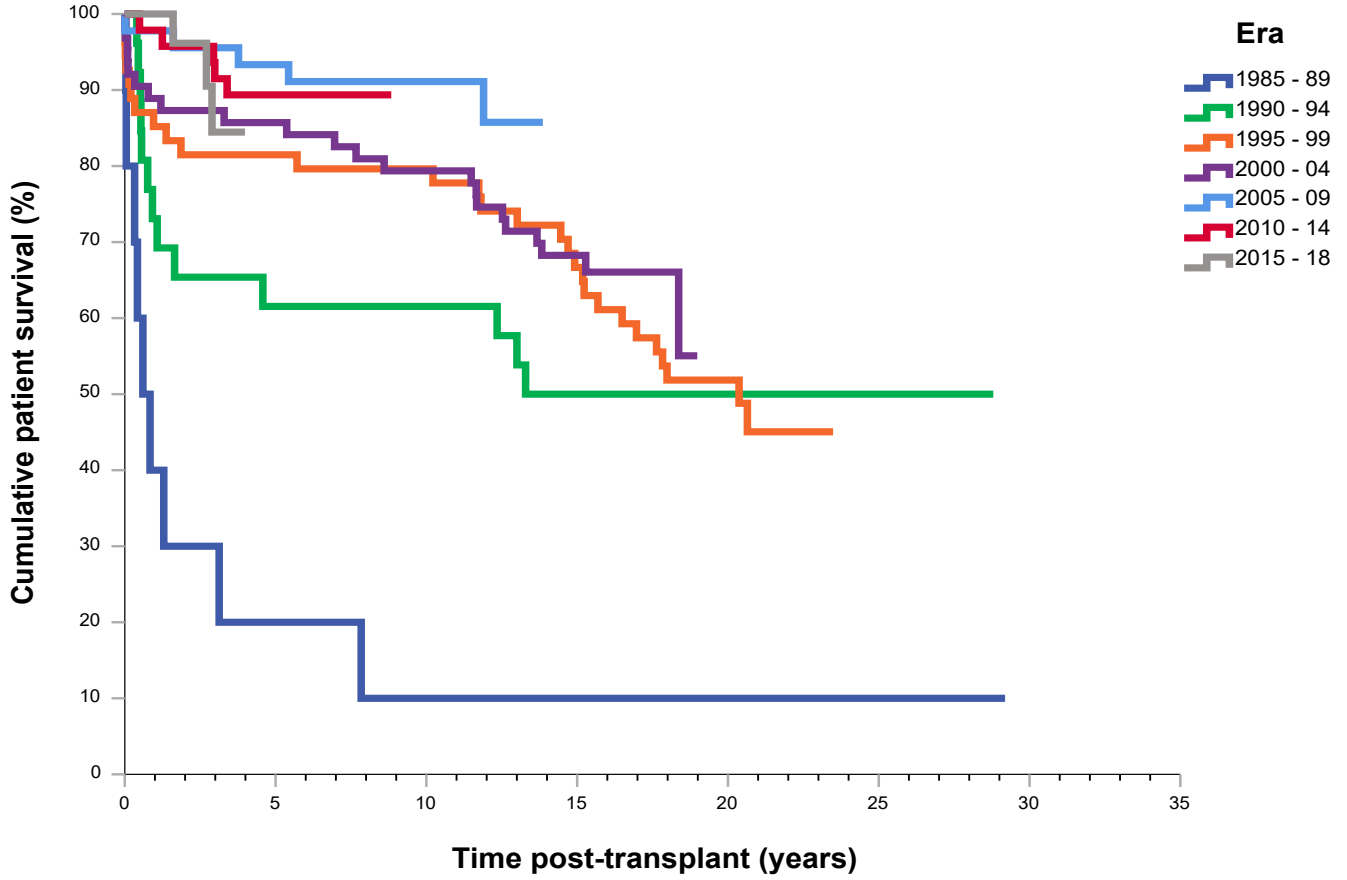


Table 21. Patient survival by transplant era with primary diagnosis of Chronic Viral Hepatitis B

Transplant era	Patient Survival	Time post-transplant (years)							
		0	1	3	5	10	15	20	25
1985 - 89	No. at risk	10	4	3	2	1	1	1	1
	Survival (%)		40%	30%	20%	10%	10%	10%	10%
1990 - 94	No. at risk	26	19	17	16	16	13	13	12
	Survival (%)		73%	65%	61%	61%	50%	50%	50%
1995 - 99	No. at risk	54	46	44	44	43	36	19	0
	Survival (%)		85%	81%	81%	80%	67%	52%	
2000 - 04	No. at risk	63	56	55	54	50	34	0	
	Survival (%)		90%	87%	86%	79%	68%		
2005 - 09	No. at risk	45	44	43	42	29	0		
	Survival (%)		98%	96%	93%	91%			
2010 - 14	No. at risk	47	46	43	32	0			
	Survival (%)		98%	91%	89%				
2015 - 18	No. at risk	43	32	12	0				
	Survival (%)		100%	84%					

11.15 Adult Patient Survival by Transplant Era with Hepatitis C Virus Cirrhosis

Patient survival after transplantation for hepatitis C virus cirrhosis varied over transplant eras without a clear trend, although the best 3-year survival (91.3%) occurred in the period 2015-2018 (P=0.016, Figure 35 and Table 22). Median adult patient survival was 17.1 years for the 1985 – 89 era, 12.9 years for the 1990 – 94 era, 12.7 years for the 1995 – 99 era and was not reached for the recent eras.

Figure 35. Adult patient survival curve by transplant era with primary diagnosis of Chronic Viral Hepatitis C

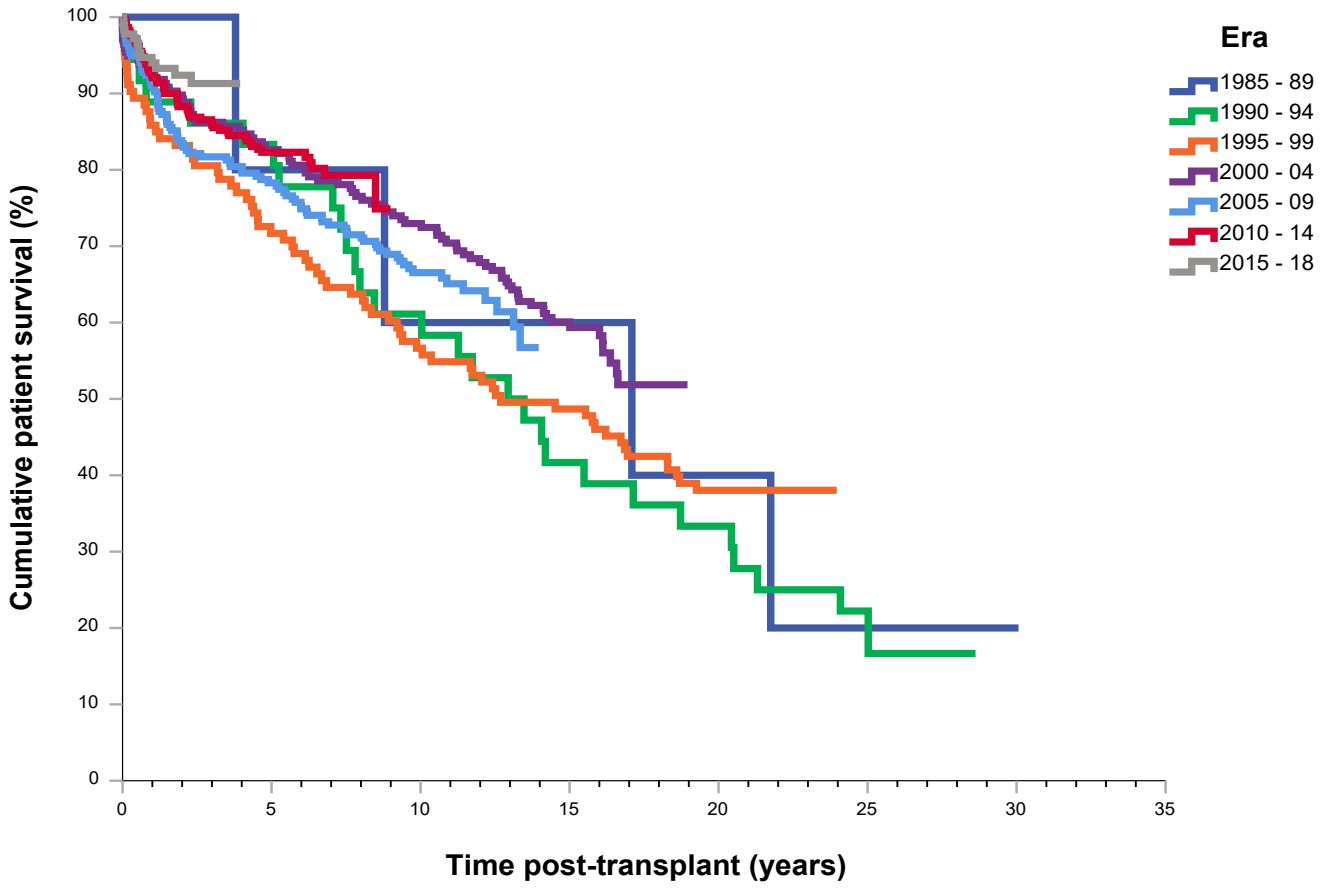


Table 22. Adult patient survival curve by transplant era with primary diagnosis of Chronic Viral Hepatitis C

Transplant era	Patient Survival	Time post-transplant (years)								
		0	1	3	5	10	15	20	25	30
1985 - 89	No. at risk	5	5	4	4	3	3	2	1	1
	Survival (%)		100%	100%	80%	60%	60%	40%	20%	20%
1990 - 94	No. at risk	36	32	31	30	22	15	12	4	0
	Survival (%)		89%	86%	83%	61%	42%	33%	22%	
1995 - 99	No. at risk	113	97	91	81	64	55	34	0	
	Survival (%)		86%	80%	72%	57%	49%	38%		
2000 - 04	No. at risk	196	181	169	162	143	83	0		
	Survival (%)		92%	86%	83%	73%	60%			
2005 - 09	No. at risk	235	214	192	184	118	0			
	Survival (%)		91%	82%	78%	66%				
2010 - 14	No. at risk	290	268	249	199	0				
	Survival (%)		92%	86%	82%					
2015 - 18	No. at risk	181	132	46						
	Survival (%)		94%	91%						

11.16 Paediatric Patient Survival with Primary Diagnosis of Malignancy

There was a trend for better paediatric patient survival after transplantation for hepatoblastoma and other malignancies than for hepatocellular carcinoma (P = 0.052, Figure 36 and Table 23). Ten-year paediatric patient survival was 71.7% for hepatoblastoma and 37.5% for hepatocellular carcinoma. Median paediatric patient survival for hepatocellular carcinoma was 3.7 years and was not reached for hepatoblastoma and other malignancies.

Figure 36. Paediatric patient survival curve with primary diagnosis of malignancy

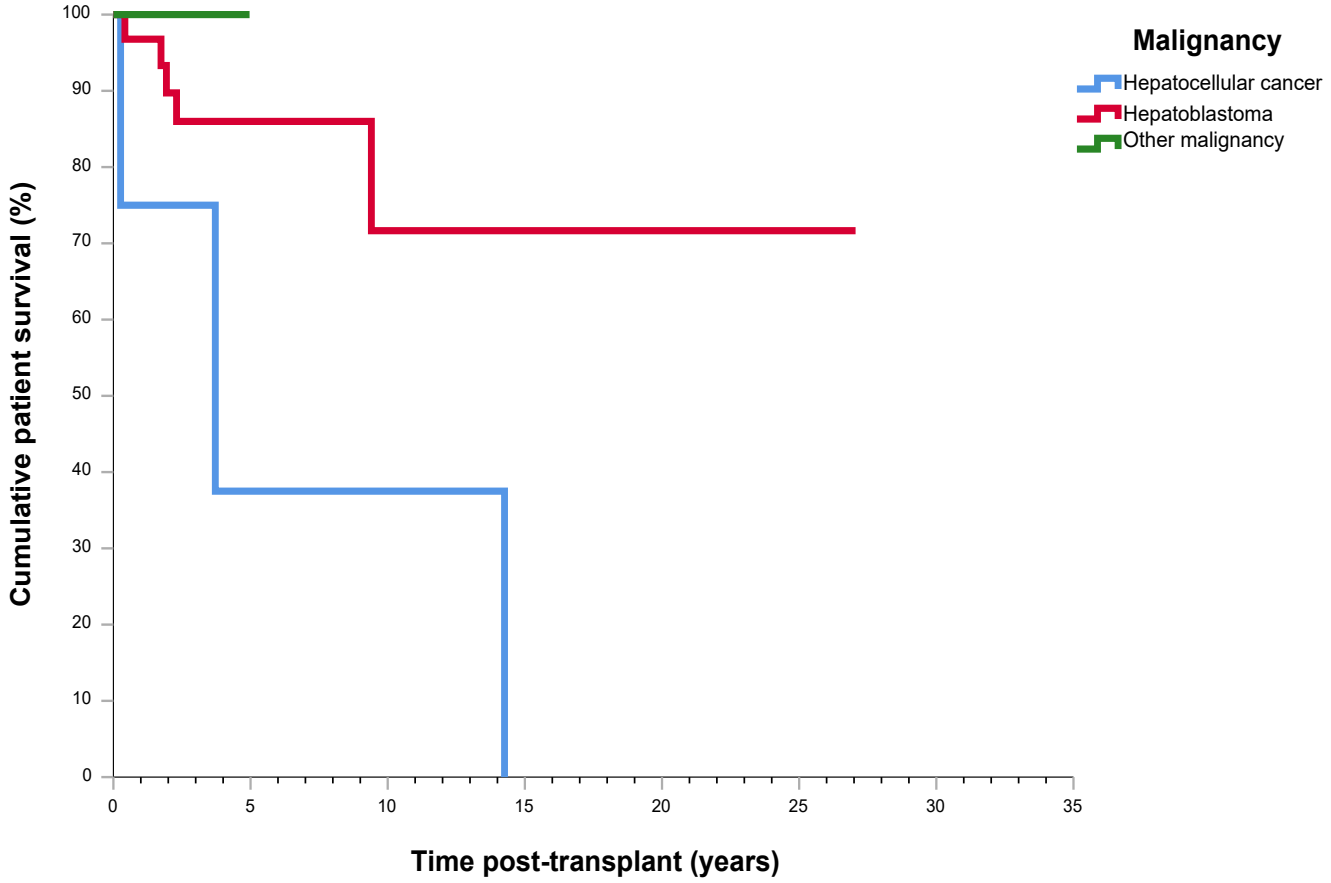


Table 23. Paediatric patient survival with primary diagnosis of malignancy

Primary Diagnosis	Patient Survival	Time post-transplant (years)							
		0	1	3	5	10	15	20	25
Hepatoblastoma	No. at risk	31	30	20	15	5	2	1	1
	Survival (%)		97%	86%	86%	72%	72%	72%	72%
Hepatocellular carcinoma	No. at risk	4	2	2	1	1	0		
	Survival (%)		75%	75%	38%	38%			
Other malignancy	No. at risk	3	3	2	0				
	Survival (%)		100%	100%					

11.17 Adult Patient Survival with Primary Diagnosis of Malignancy

Adult patient survival after transplantation for malignancy was better for hepatocellular carcinoma than for other malignancies (P = 0.048, Figure 37 and Table 24). Ten-year patient survival was 67.0% for hepatocellular carcinoma and 46.5% for other malignancies. Median adult patient survival was not reached for hepatocellular carcinoma and was 5.0 years for other malignancies.

Figure 37. Adult patient survival curve with primary diagnosis of malignancy

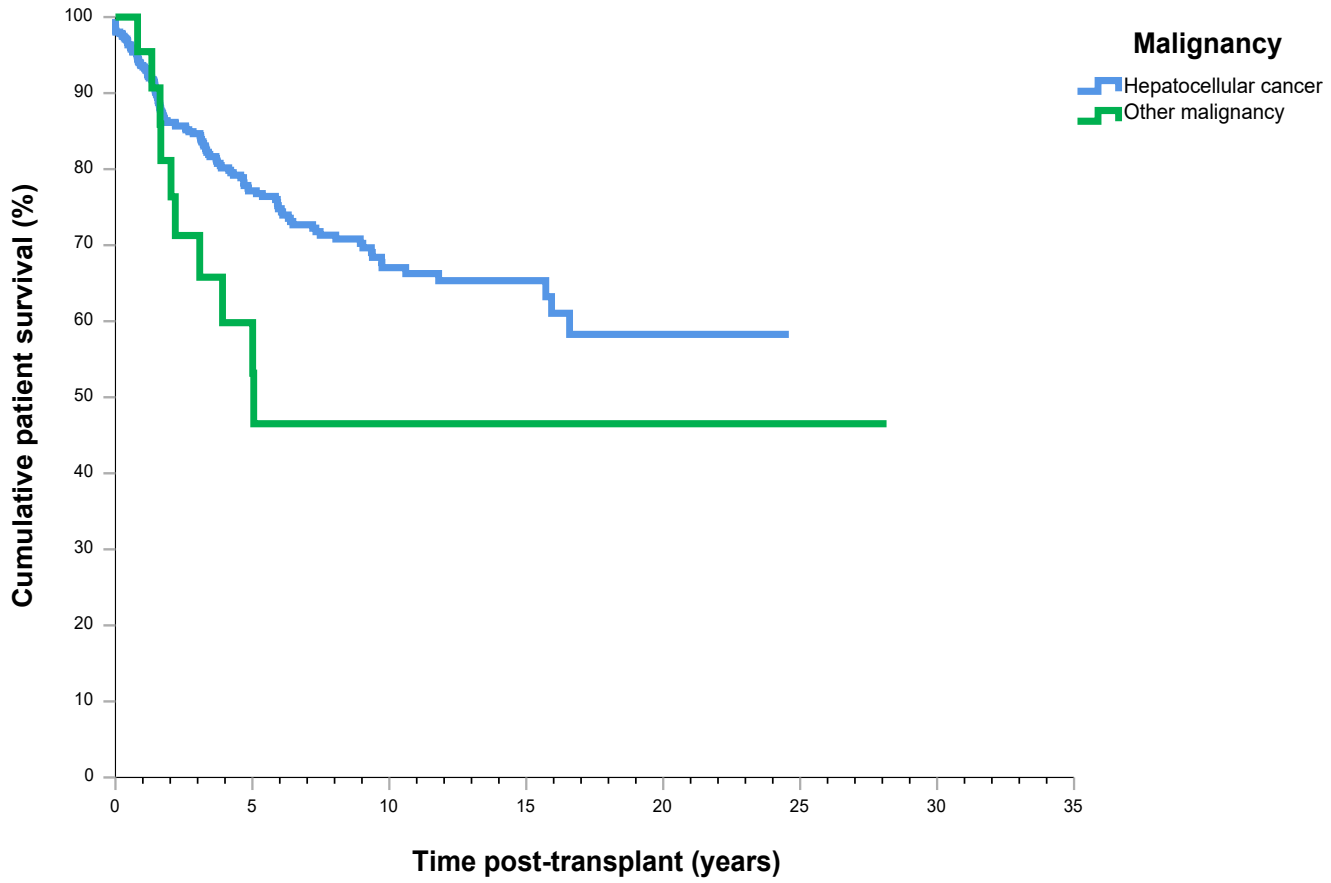


Table 24. Adult patient survival curve with primary diagnosis of malignancy

Primary Diagnosis	Patient Survival	Time post-transplant (years)							
		0	1	3	5	10	15	20	25
Hepato-cellular carcinoma	No. at risk	556	466	322	217	94	36	8	0
	Survival (%)		94%	85%	77%	67%	65%	58%	
Other malignancy	No. at risk	26	20	13	9	3	2	1	1
	Survival (%)		96%	71%	60%	47%	47%	47%	47%

12 Graft Outcome

Graft survival analysis is based on all Australian and New Zealand liver transplants. This includes both initial transplantation and retransplantation. Both deceased and living donor grafts are included in this analysis. Grafts are classified as functioning or failed (death or retransplantation).

12.1 All Grafts Outcome

There were 6,259 grafts in 5,786 patients (Figure 38 and Table 25). Ten-year graft survival was 68.6% across all grafts. The median graft survival was 19.5 years.

Figure 38. Graft survival curve for all grafts

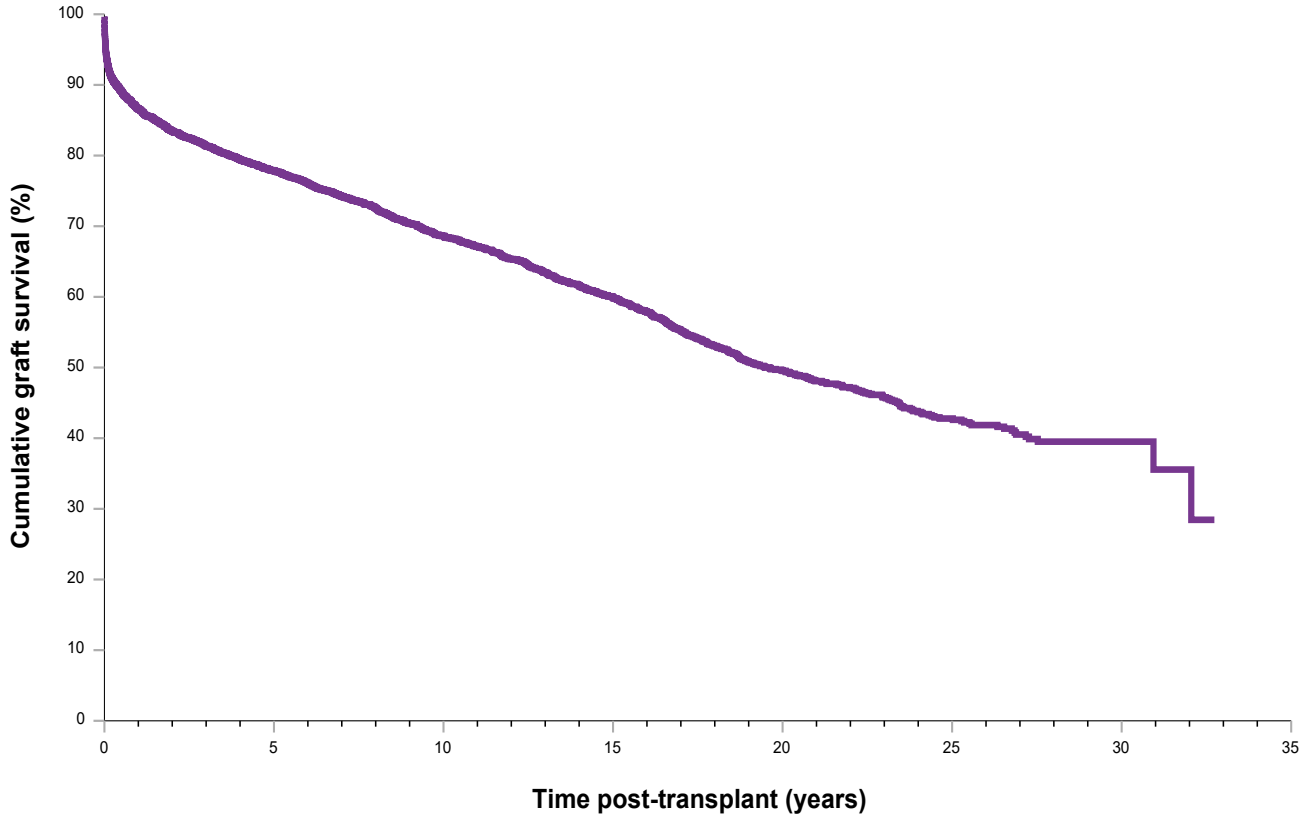


Table 25. Graft survival- all grafts

Graft Survival	Time post-transplant (years)								
	0	1	3	5	10	15	20	25	30
No. at risk	6,259	5,082	4,168	3,500	2,158	1,263	623	245	28
Survival (%)	100%	87%	81%	78%	69%	60%	50%	43%	40%

12.2 Outcome of all Grafts by Age Group

A total of 1,110 transplants were performed in children and 5,149 in adults. Post-transplant graft survival was superior in the paediatric population (P < 0.001, Figure 39, Table 26). 10-year graft survival was 72.1% for children and 67.8% for adults. Median graft survival was 30.9 years in children and 18.0 years in adults.

Figure 39. Graft survival curve for all grafts by age group

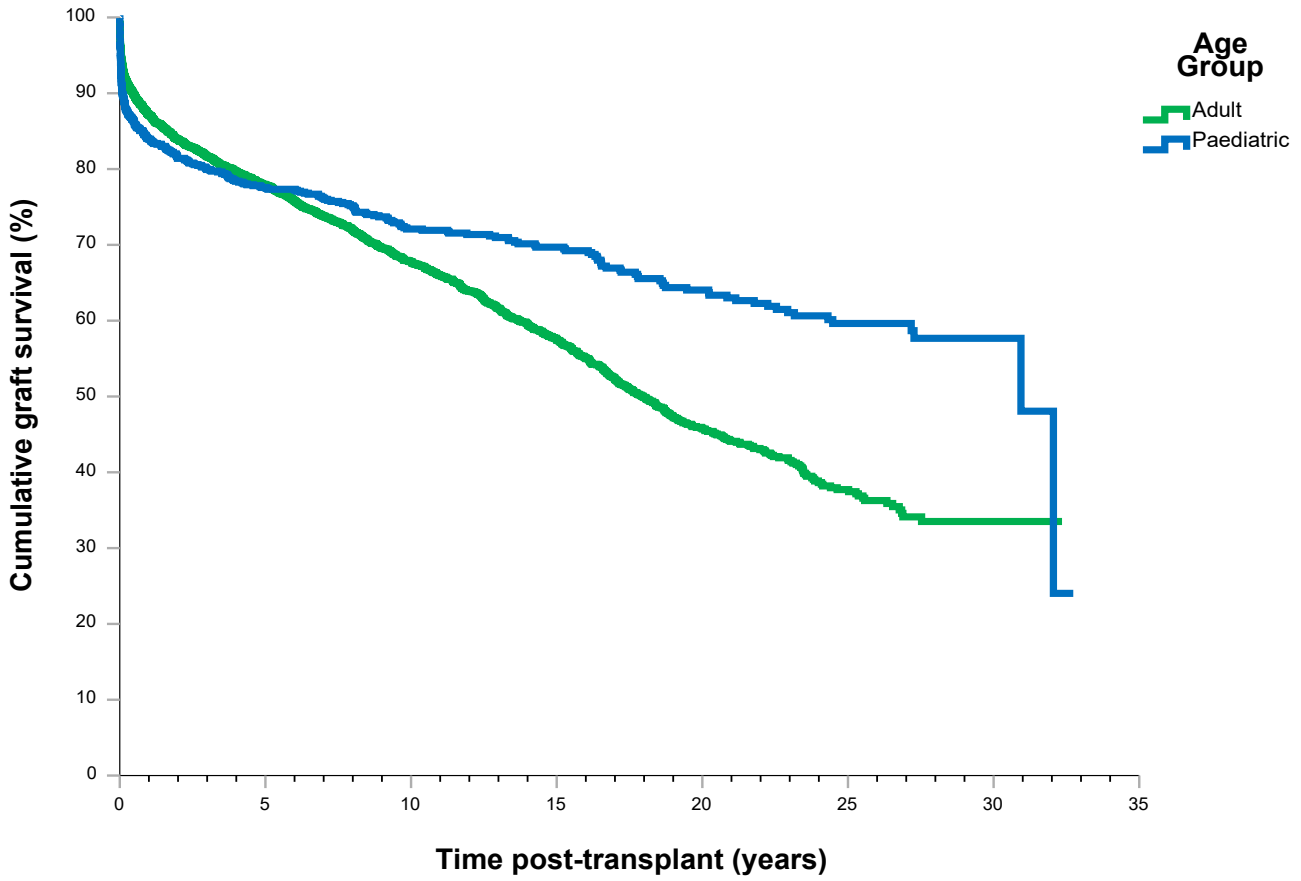


Table 26. Graft survival by age group - all grafts

Age Group	Graft Survival	Time post-transplant (years)								
		0	1	3	5	10	15	20	25	30
Adult ≥16 years	No. at risk	5,149	4,196	3,426	2,855	1,721	960	432	140	11
	Survival (%)		87%	82%	78%	68%	58%	46%	38%	34%
Paediatric <16 years	No. at risk	1,110	886	742	645	437	303	191	105	17
	Survival (%)		84%	80%	78%	72%	70%	64%	60%	58%

12.3 Outcome by Graft Number

There was a significant difference in graft survival by graft number (P < 0.001, Figure 40 and Table 27). Ten-year graft survival was 69.7% for the first graft, 55.1% for the second graft, 60.3% for the third graft and not reached for the fourth graft. Median graft survival was 20.2 years for the first graft, 12.9 years for the second graft, 21.1 years for the third graft and not reached for the fourth graft.

Figure 40. Graft survival curve for all grafts by graft number

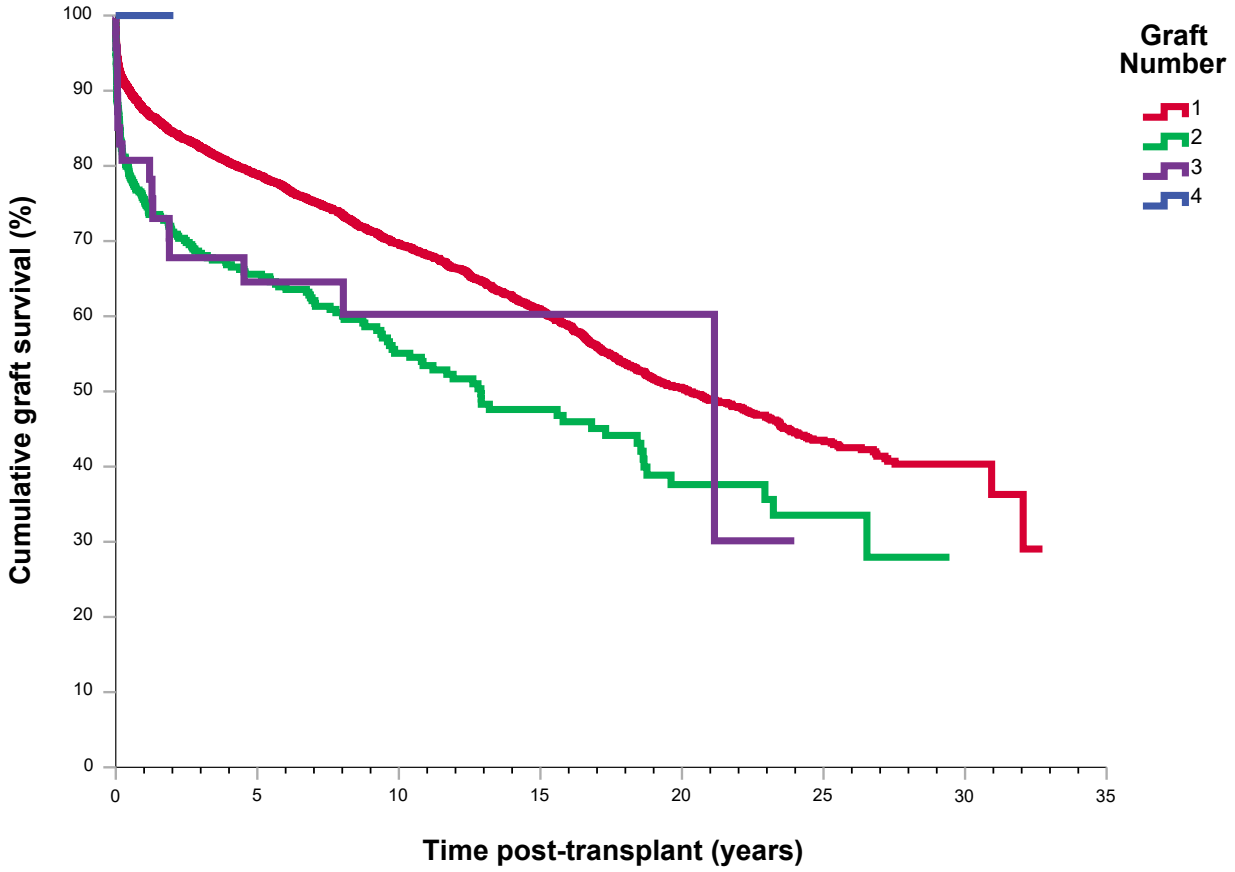


Table 27. Graft survival - all grafts

Graft Number	Graft Survival	Time post-transplant (years) 0	1	3	5	10	15	20	25	30
1	No. at risk	5,783	4,746	3,913	3,280	2,042	1,196	593	233	28
	Survival (%)		88%	82%	79%	70%	61%	51%	44%	40%
2	No. at risk	427	302	232	202	106	63	28	12	0
	Survival (%)		76%	68%	66%	55%	48%	38%	34%	
3	No. at risk	47	32	23	18	10	4	2	0	
	Survival (%)		81%	68%	65%	60%	60%	60%		
4	No. at risk	2	2	0						
	Survival (%)		100%							

12.4 Paediatric Outcome by Graft Number

There was a significant difference in graft survival by graft number in children (P < 0.001, Figure 41 and Table 28). Ten-year graft survival was 75.0% for the first graft, 49.2% for the second graft and 57.4% for the third graft. Median graft survival was 32.1 years for the first graft, 9.8 years for the second graft and 21.1 years for the third graft.

Figure 41. Graft survival curve for paediatric recipients by graft number

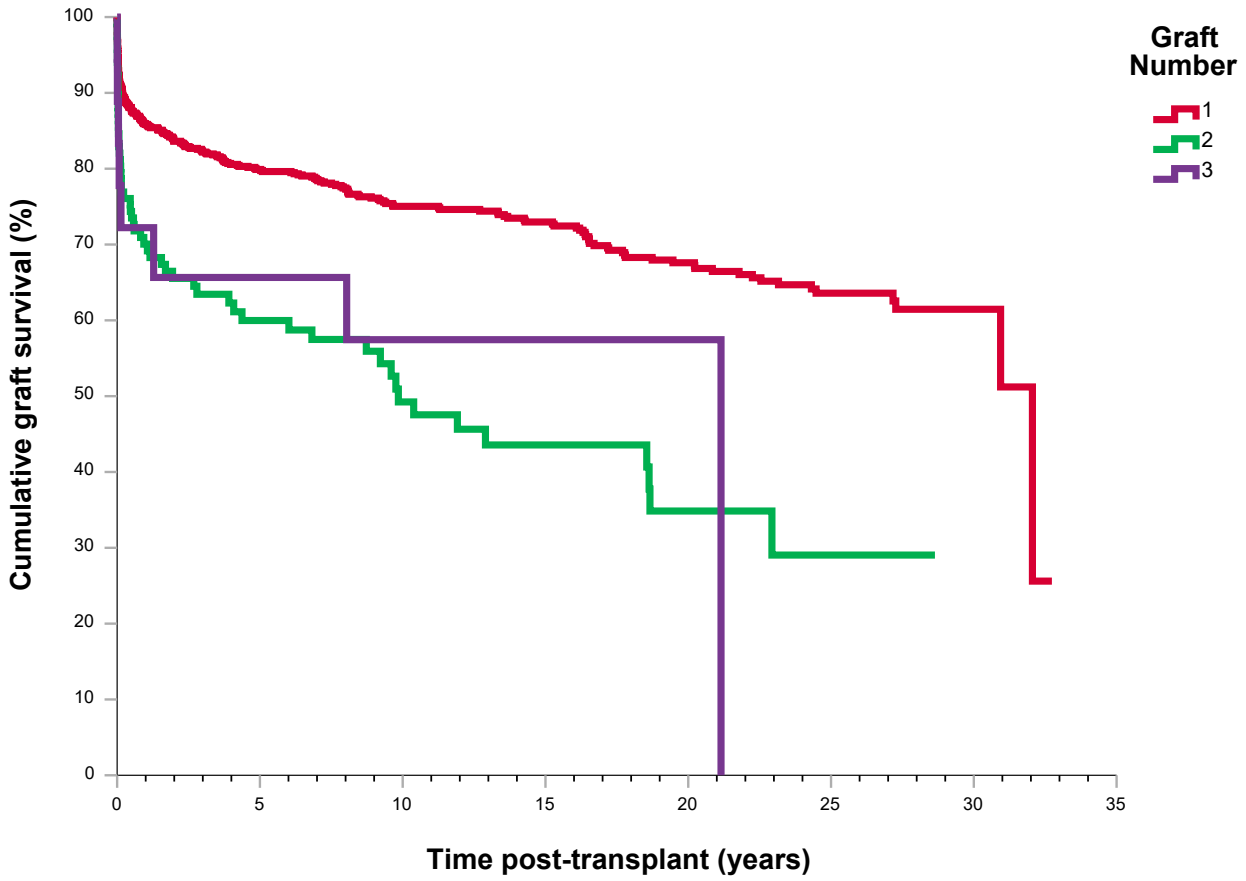


Table 28. Graft survival - paediatric by graft number

Graft Number	Graft Survival	Time post-transplant (years)								
		0	1	3	5	10	15	20	25	30
1	No. at risk	975	795	675	586	401	280	182	101	17
	Survival (%)		86%	82%	80%	75%	73%	68%	64%	62%
2	No. at risk	117	80	58	51	29	20	8	4	0
	Survival (%)		70%	63%	60%	49%	44%	35%	29%	
3	No. at risk	18	11	9	8	7	3	1	0	
	Survival (%)		72%	66%	66%	57%	57%	57%		

12.5 Adult Outcome by Graft Number

There was a significant difference in graft survival by graft number in adults (P < 0.001, Figure 42 and Table 29). Ten-year graft survival 68.5% for the first graft, 57.3% for the second graft, 63.7% for the third graft and not reached for the fourth graft. Median graft survival was 18.1 years for the first graft, 13.2 years for the second graft and not reached for the third and fourth grafts.

Figure 42. Graft survival curve for adults by graft number

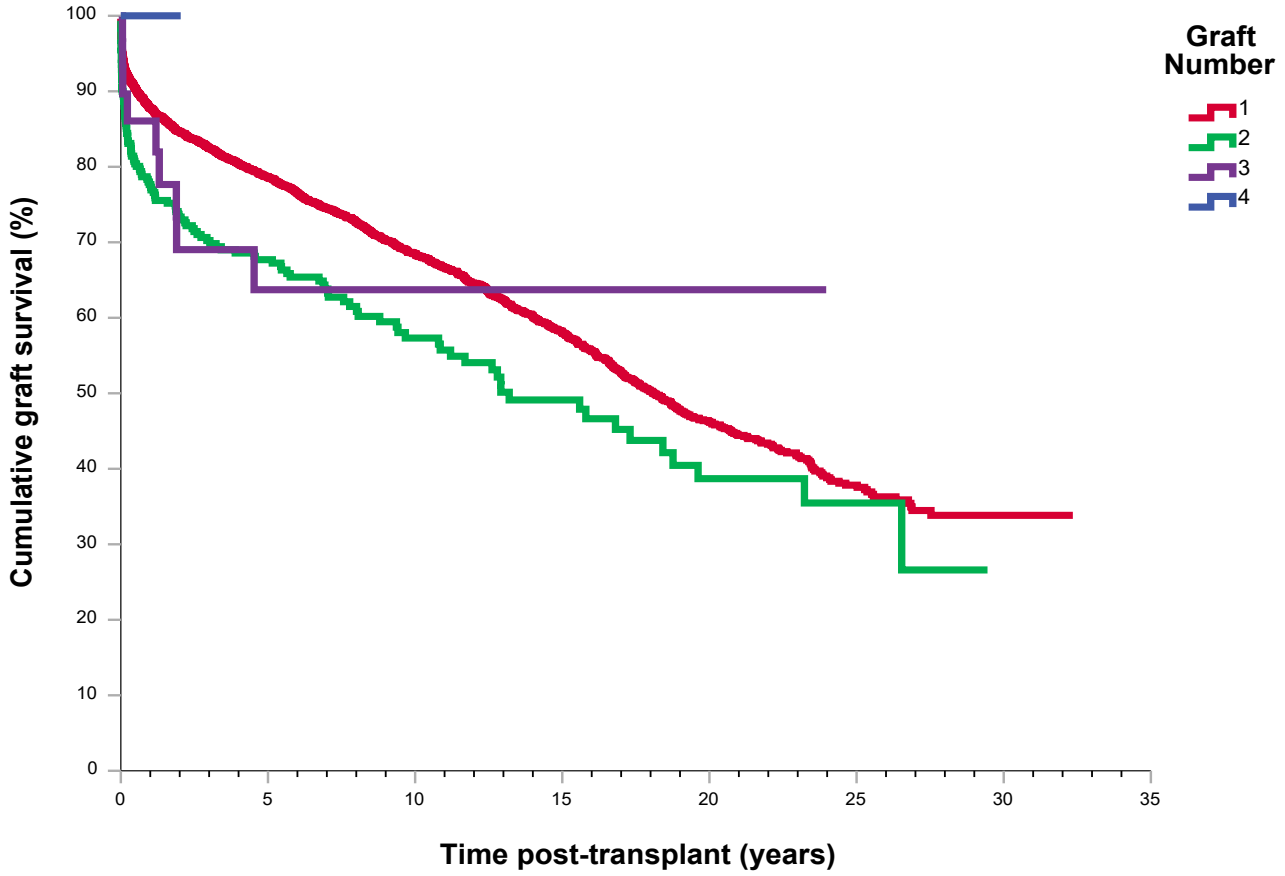


Table 29. Graft survival – adults by graft number

Graft Number	Graft Survival	Time post-transplant (years)								
		0	1	3	5	10	15	20	25	30
1	No. at risk	4,808	3,951	3,238	2,694	1,641	916	411	132	11
	Survival (%)		88%	82%	79%	69%	58%	46%	38%	34%
2	No. at risk	310	222	174	151	77	43	20	8	0
	Survival (%)		78%	70%	68%	57%	49%	39%	36%	
3	No. at risk	29	21	15	10	3	1	1	0	
	Survival (%)		86%	69%	64%	64%	64%	64%		
4	No. at risk	2	2	0						
	Survival (%)		100%							

12.6 Graft Survival by Type of Graft

There was no significant difference in graft survival by graft type, although there was a trend to improved survival in living donor transplants after 10 years and worse survival in reduced liver transplants up to 15 years (P = 0.210, Figure 43 and Table 30). Ten-year graft survival was 77.5% for living donor grafts, 70.9% for split grafts, 68.8% for whole grafts, 59.7% for reduced grafts and 0 for domino grafts. Median graft survival was 27.1 years for reduced grafts, 18.7 years for whole grafts, 9.4 years for domino grafts and not reached for split and living donor grafts.

Figure 43. Graft survival curve for type of graft, all grafts

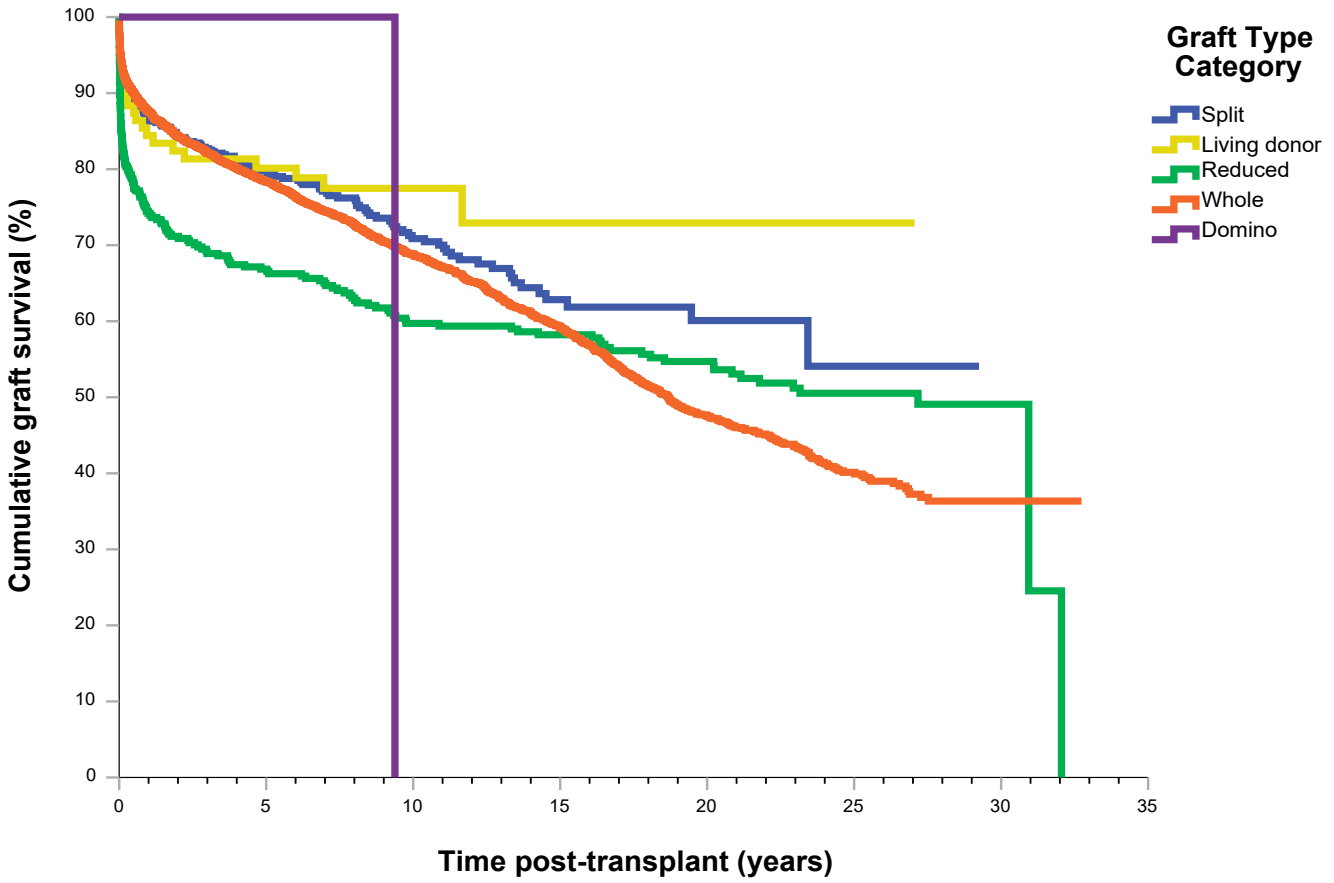


Table 30. Graft survival by type of graft - all grafts

Graft Type	Graft Survival	Time post-transplant (years)								
		0	1	3	5	10	15	20	25	30
Whole	No. at risk	5,072	4,162	3,422	2,869	1,776	1,045	490	185	20
	Survival (%)		88%	82%	78%	69%	59%	48%	40%	36%
Split	No. at risk	698	556	428	341	175	67	30	2	0
	Survival (%)		87%	83%	80%	71%	63%	60%	54%	
Reduced	No. at risk	381	274	240	223	174	147	101	56	8
	Survival (%)		74%	69%	67%	60%	58%	55%	51%	49%
Living donor	No. at risk	103	85	75	65	33	4	2	2	0
	Survival (%)		84%	81%	80%	78%	73%	73%	73%	
Domino	No. at risk	4	4	3	2	0				
	Survival (%)		100%	100%	100%	0				

12.7 Graft Survival by Graft Type in Children

Graft survival in children differed significantly by graft type, with worse survival after reduced liver transplantation (P < 0.001, Figure 44 and Table 31). Ten-year graft survival was 78.7% for living donor liver transplantation, 78.2% for whole liver transplantation, 75.8% for split liver transplantation and 61.1% for reduced liver transplantation. Median graft survival was 30.9 years for reduced grafts and not reached for the other graft types.

Figure 44. Paediatric graft survival curve for type of graft, all grafts

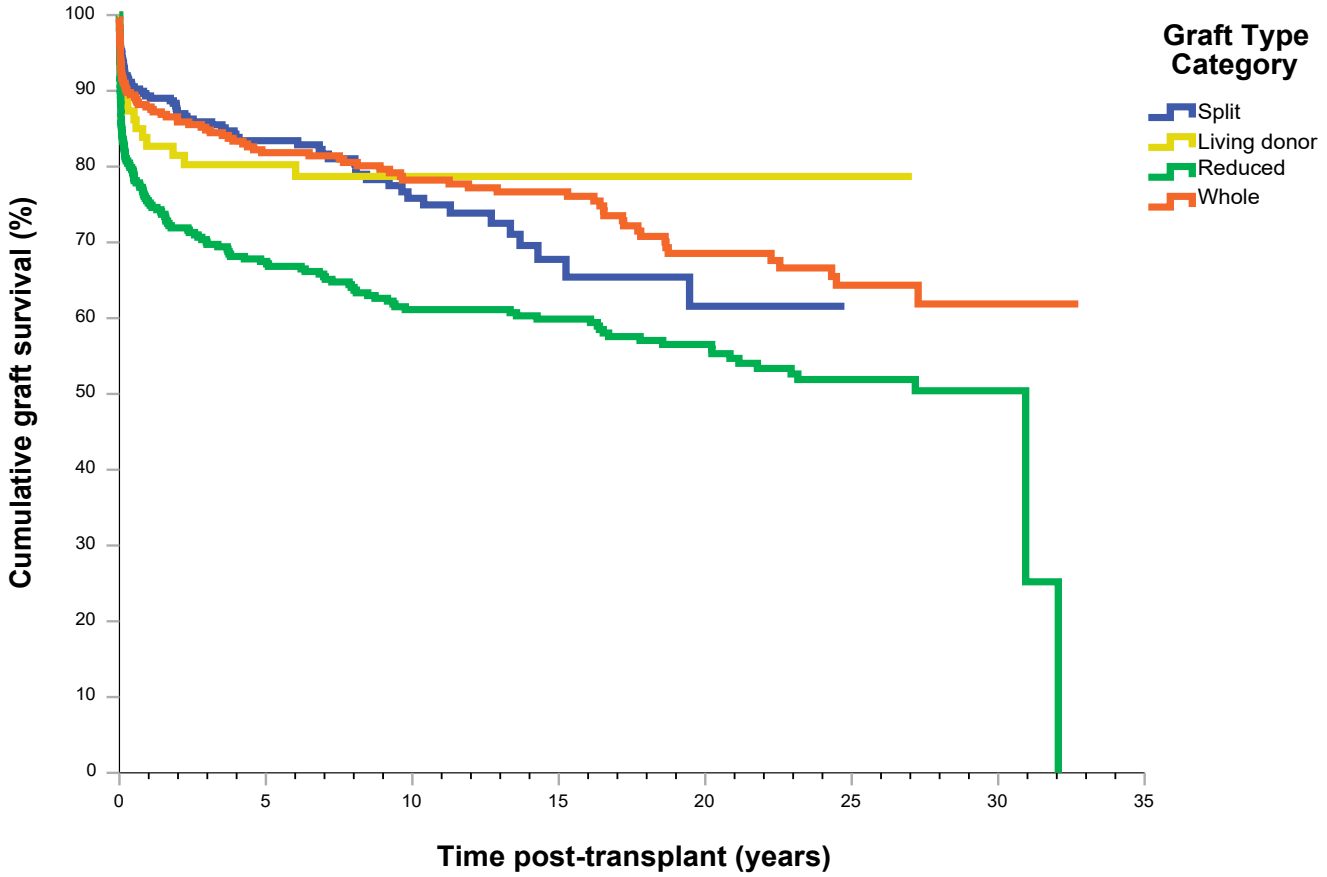


Table 31. Paediatric Recipient Graft survival by type of graft - all grafts

Graft Type	Graft Survival	Time post-transplant (years)								
		0	1	3	5	10	15	20	25	30
Whole	No. at risk	323	274	236	210	161	132	82	49	9
	Survival (%)		88%	85%	82%	78%	77%	69%	64%	62%
Split	No. at risk	351	287	221	175	88	30	13	0	
	Survival (%)		89%	86%	83%	76%	68%	62%		
Reduced	No. at risk	348	254	222	206	162	137	94	54	8
	Survival (%)		75%	70%	68%	61%	60%	57%	52%	50%
Living donor	No. at risk	87	70	63	54	26	4	2	2	0
	Survival (%)		83%	80%	80%	79%	79%	79%	79%	

12.8 Graft Survival by Graft Type in Adults

There was no significant difference in graft survival in adults by graft type, although there was a trend to worse graft survival after reduced liver transplantation (P = 0.476, Figure 45 and Table 32). Ten-year graft survival was 72.9% for living donor liver transplantation, 68.1% for whole liver transplantation, 66.0% for split liver transplantation, 45.0% for reduced liver transplantation and 0 for domino liver transplantation. Median graft survival was 23.4 years for split liver transplantation, 17.9 years for whole liver transplantation, 11.7 years for living donor liver transplantation, 9.4 years for domino liver transplantation and 9.2 years for reduced liver transplantation.

Figure 45. Adult graft survival curve for type of graft, all grafts

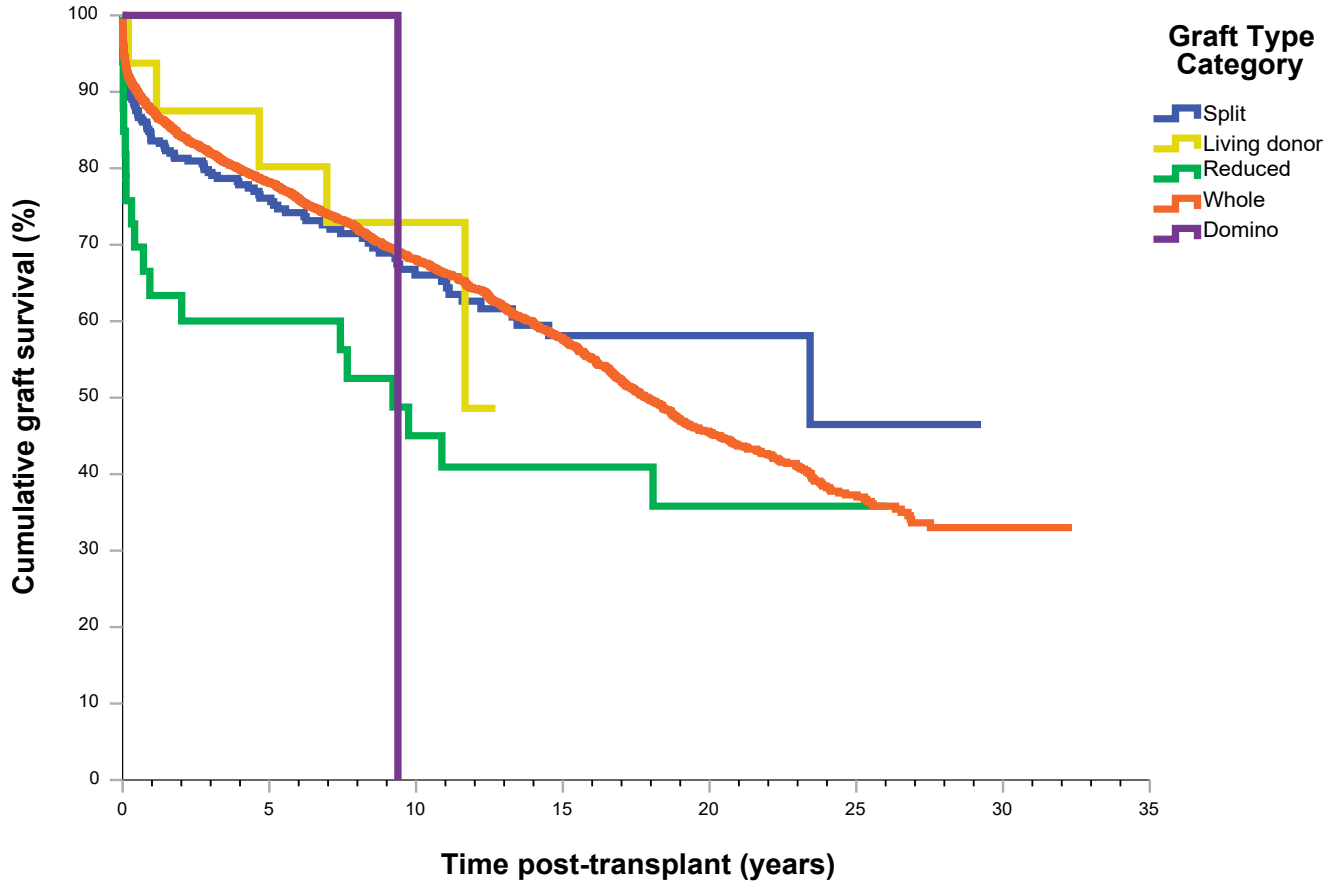


Table 32. Adult graft survival for type of graft, all grafts

Graft Type	Graft Survival	Time post-transplant (years)								
		0	1	3	5	10	15	20	25	30
Whole	No. at risk	4,749	3,888	3,186	2,659	1,615	913	408	136	11
	Survival (%)		88%	82%	78%	68%	58%	46%	37%	33%
Split	No. at risk	347	269	207	166	87	37	17	2	0
	Survival (%)		84%	79%	76%	66%	58%	58%	47%	
Reduced	No. at risk	33	20	18	17	12	10	7	2	0
	Survival (%)		63%	60%	60%	45%	41%	36%	36%	
Domino	No. at risk	4	4	3	2	0				
	Survival (%)		100%	100%	100%	0				
Living donor	No. at risk	16	14	12	11	7	0			
	Survival (%)		94%	88%	80%	73%				

12.9 Graft Survival by Era of Transplant

There has been a progressive improvement in graft survival over eras of transplantation (P < 0.001, Figure 46, Table 33). Graft survival in the most recent era was 91% at 1 year, 87% at 3 years, 81% at 5 years and 71% at 10 years. Median graft survival was 17.2 years for 1995 – 99 era, 17.0 years for 1990 – 94 era, 7.7 years for 1985 – 89 era and was not reached for recent eras.

Figure 46. Graft (deceased and living donors) survival curve by era of transplant

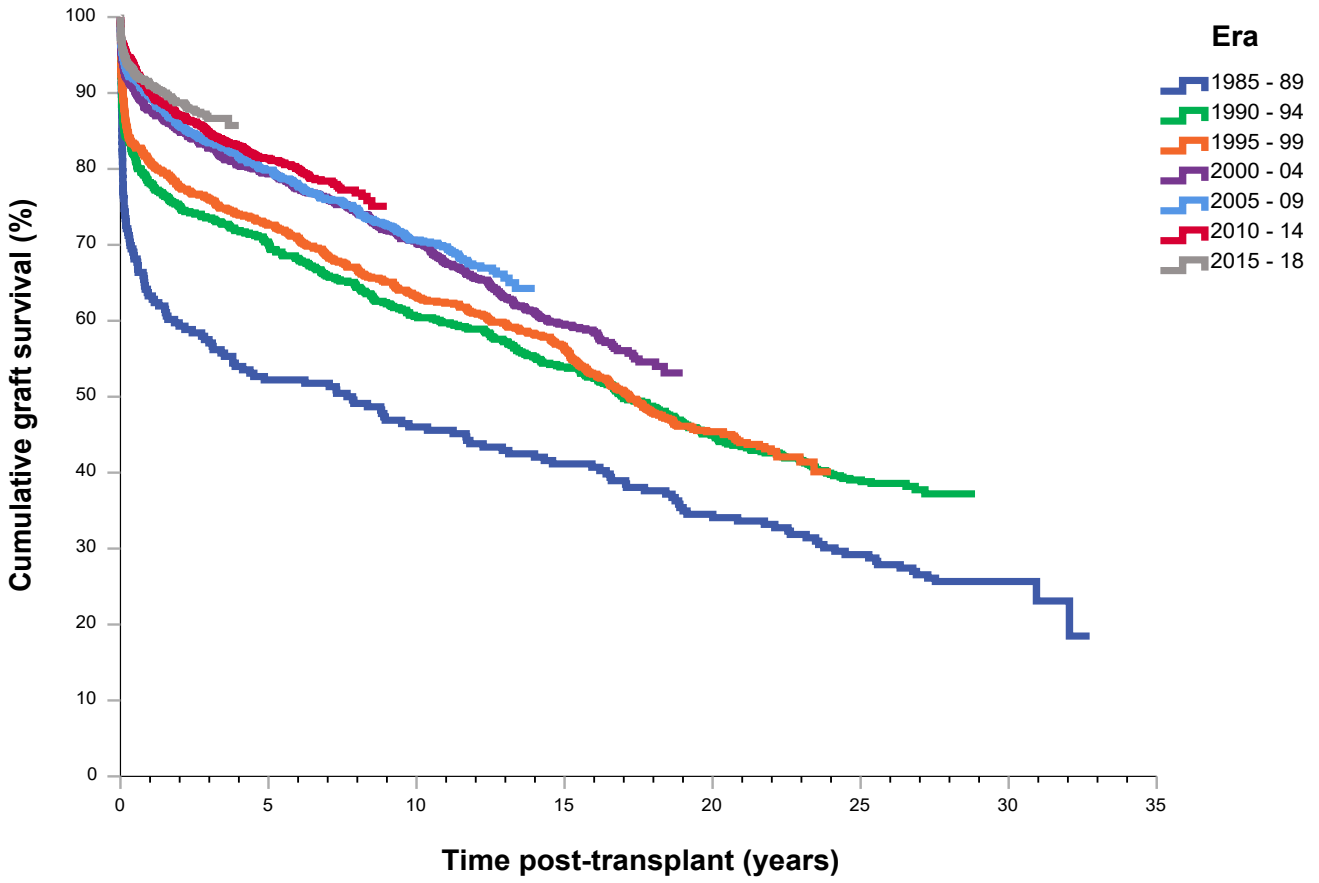


Table 33. Graft (deceased and living donors) survival by era of transplant

Transplant Era	Graft Survival	Time post-transplant (years)								
		0	1	3	5	10	15	20	25	30
1985 - 89	No. at risk	226	143	129	118	104	93	78	66	28
	Survival (%)		63%	57%	52%	46%	41%	34%	29%	26%
1990 - 94	No. at risk	601	470	442	422	364	324	270	179	0
	Survival (%)		78%	73%	70%	61%	54%	45%	39%	
1995 - 99	No. at risk	759	614	577	551	480	427	275	0	
	Survival (%)		81%	76%	73%	63%	56%	45%		
2000 - 04	No. at risk	915	803	757	726	645	419	0		
	Survival (%)		88%	83%	79%	70%	60%			
2005 - 09	No. at risk	1,032	925	861	824	565	0			
	Survival (%)		90%	83%	80%	71%				
2010 - 14	No. at risk	1,331	1,200	1,127	859	0				
	Survival (%)		90%	85%	81%					
2015 - 18	No. at risk	1,395	927	275	0					
	Survival (%)		91%	87%						

12.10 Graft Survival by Era of Transplant in Children

There has been a progressive improvement in graft survival in children over eras of transplantation (P < 0.001, Figure 47, Table 34). Graft survival in the most recent era was 91% at 1 year, 90% at 3 years, 83% at 5 years and 81% at 10 years. Median paediatric graft survival was 7.7 years for 1985 – 89 era and was not reached for all other transplant eras.

Figure 47. Paediatric graft (deceased and living donors) survival curve by era of transplant

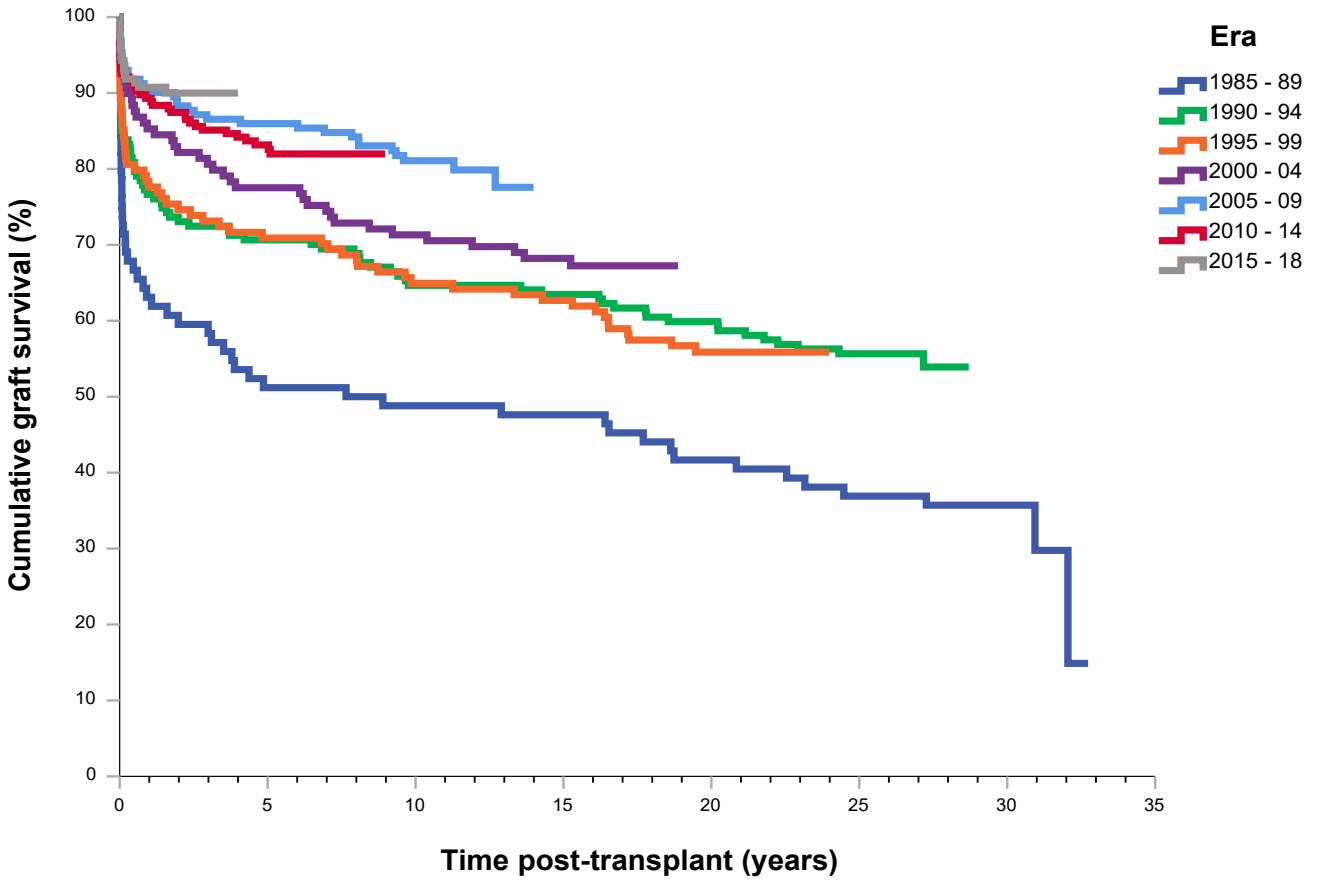


Table 34. Paediatric graft (deceased and living donors) survival by era of transplant

Transplant Era	Graft Survival	Time post-transplant (years) 0	1	3	5	10	15	20	25	30
1985 - 89	No. at risk	84	53	49	43	41	40	35	31	17
	Survival (%)		63%	58%	51%	49%	48%	42%	37%	36%
1990 - 94	No. at risk	167	128	121	118	108	106	100	74	0
	Survival (%)		77%	72%	71%	65%	63%	60%	56%	
1995 - 99	No. at risk	134	104	98	95	87	84	56	0	
	Survival (%)		78%	73%	71%	65%	63%	56%		
2000 - 04	No. at risk	129	110	104	100	92	73	0		
	Survival (%)		85%	81%	77%	71%	68%			
2005 - 09	No. at risk	171	155	148	147	109	0			
	Survival (%)		91%	86%	86%	81%				
2010 - 14	No. at risk	215	192	183	142	0				
	Survival (%)		89%	85%	83%					
2015 - 18	No. at risk	210	144	39	0					
	Survival (%)		91%	90%						

12.11 Graft Survival by Era of Transplant in Adults

There has been a progressive improvement in graft survival in adults over eras of transplantation (P < 0.001, Figure 48, Table 35). Graft survival in the most recent era was 91% at 1 year, 86% at 3 years, 81% at 5 years and 69% at 10 years. Median adult graft survival was 16.6 years for 1995 – 99 era, 15.1 years for 1990 – 94 era, 7.3 years for 1985 – 89 era and not reached for other transplant eras.

Figure 48. Adult graft (deceased and living donors) survival curve by era of transplant

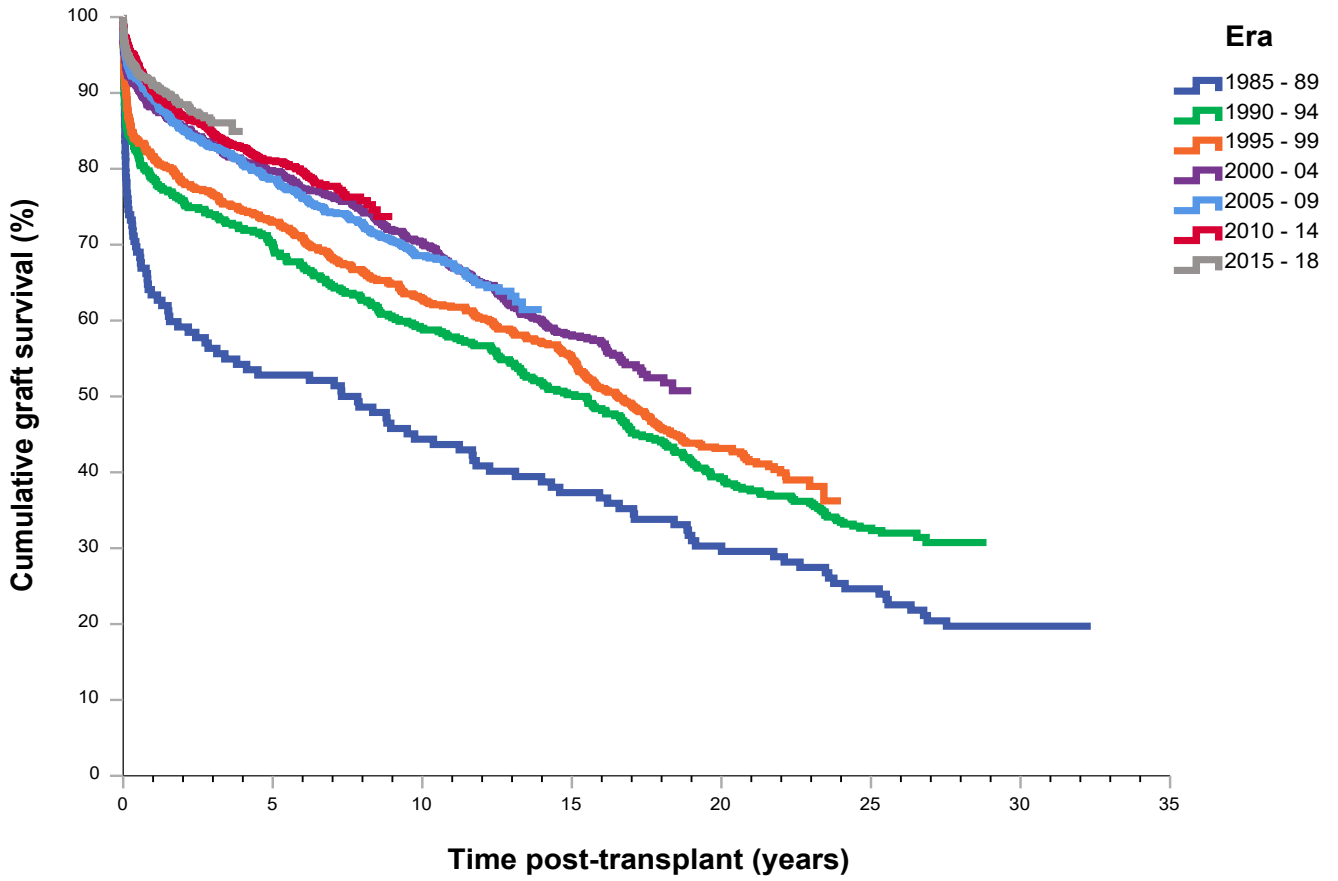


Table 35. Adult graft (deceased and living donors) survival by era of transplant

Transplant Era	Graft Survival	Time post-transplant (years)								
		0	1	3	5	10	15	20	25	30
1985 - 89	No. at risk	142	90	80	75	63	53	43	35	11
	Survival (%)		63%	56%	53%	44%	37%	30%	25%	20%
1990 - 94	No. at risk	434	342	321	304	256	218	170	104	
	Survival (%)		79%	74%	70%	59%	50%	39%	33%	
1995 - 99	No. at risk	625	510	479	456	393	343	219	0	
	Survival (%)		82%	77%	73%	63%	55%	43%		
2000 - 04	No. at risk	786	693	653	626	553	346	0		
	Survival (%)		88%	83%	80%	70%	58%			
2005 - 09	No. at risk	861	770	713	677	456	0			
	Survival (%)		89%	83%	79%	69%				
2010 - 14	No. at risk	1,116	1,008	944	717	0				
	Survival (%)		90%	85%	81%					
2015 - 18	No. at risk	1,185	783	236	0					
	Survival (%)		91%	86%						

12.12 Whole Graft Survival by Era of Transplant

There has been a progressive improvement in graft survival after whole liver transplantation over eras of transplantation (P < 0.001, Figure 49,Table 36). Graft survival in the most recent era was 92% at 1 year, 86% at 3 years, 82% at 5 years and 69% at 10 years. Median graft survival was 17.4 years for 1995 – 99 era, 16.7 years for 1990 – 94 era, 8.3 years for 1985 – 89 era and not reached for other eras.

Figure 49. Whole graft survival curve by era of transplant

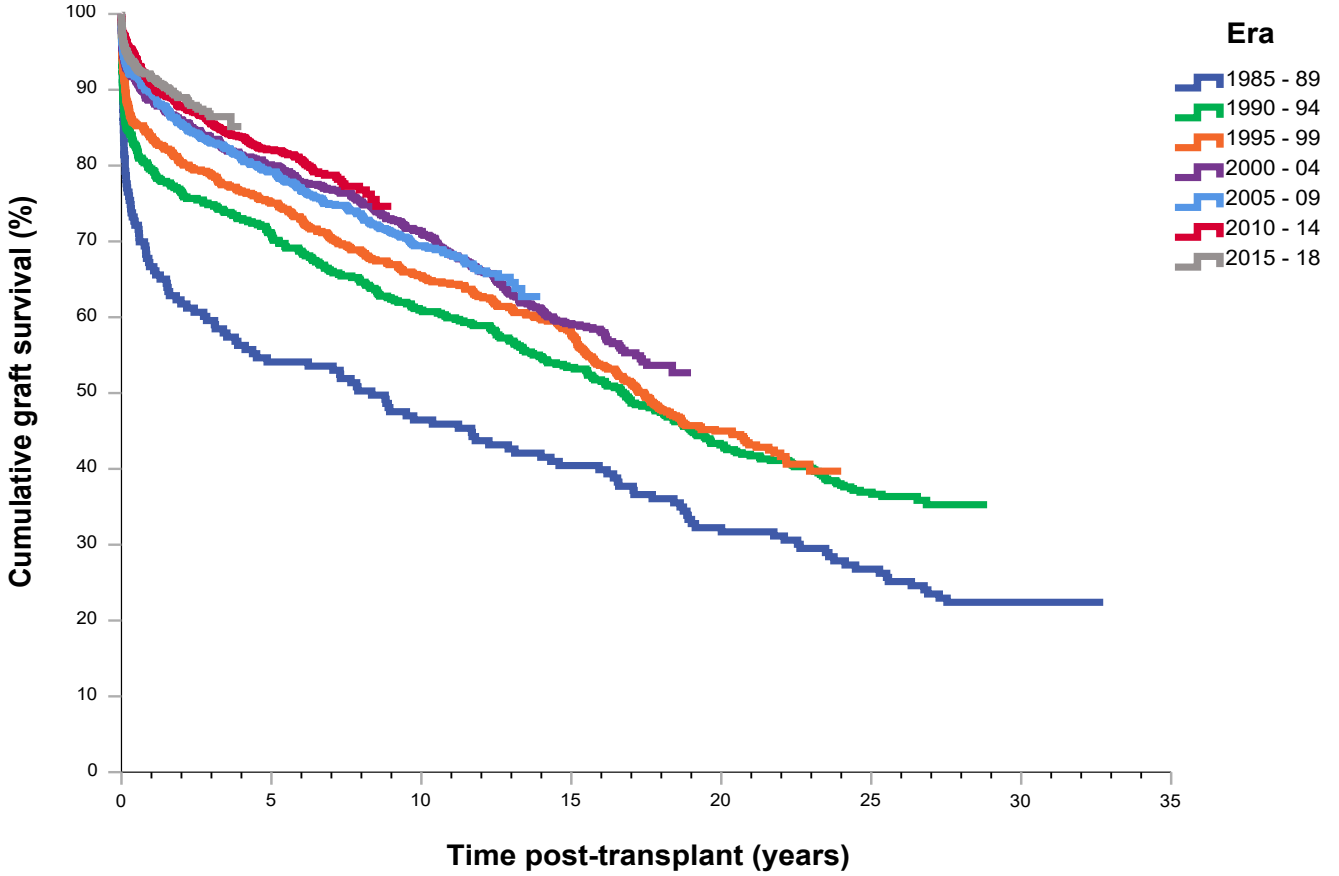


Table 36. Whole graft survival by era of transplant

Transplant Era	Graft Survival	Time post-transplant (years)								
		0	1	3	5	10	15	20	25	30
1985 - 89	No. at risk	183	122	109	99	85	74	59	49	20
	Survival (%)		68%	60%	54%	46%	40%	32%	27%	22%
1990 - 94	No. at risk	489	389	366	347	298	261	211	136	0
	Survival (%)		80%	75%	71%	61%	53%	43%	37%	
1995 - 99	No. at risk	617	517	486	463	404	356	220	0	
	Survival (%)		84%	79%	75%	65%	58%	45%		
2000 - 04	No. at risk	774	686	646	619	552	354	0		
	Survival (%)		89%	83%	80%	71%	59%			
2005 - 09	No. at risk	816	732	677	646	437	0			
	Survival (%)		90%	83%	79%	69%				
2010 - 14	No. at risk	1,068	970	913	695	0				
	Survival (%)		91%	85%	82%					
2015 - 18	No. at risk	1,125	746	225	0					
	Survival (%)		92%	86%						

12.13 Reduced Graft Survival by Era of Transplant

Graft survival after reduced liver transplantation varied over transplant eras without a clear trend (P = 0.012, Figure 50, Table 37). Graft survival in the most recent era was 91% at 1 year, 86% at 3 years, 67% at 5 years and 70% at 10 years. Median graft survival was 21.1 years for 1990 – 94 era, 9.2 years for 1995 – 99 era, 3.0 years for 1985 – 89 era and not reached for other eras.

Figure 50. Reduced graft survival curve by era of transplant

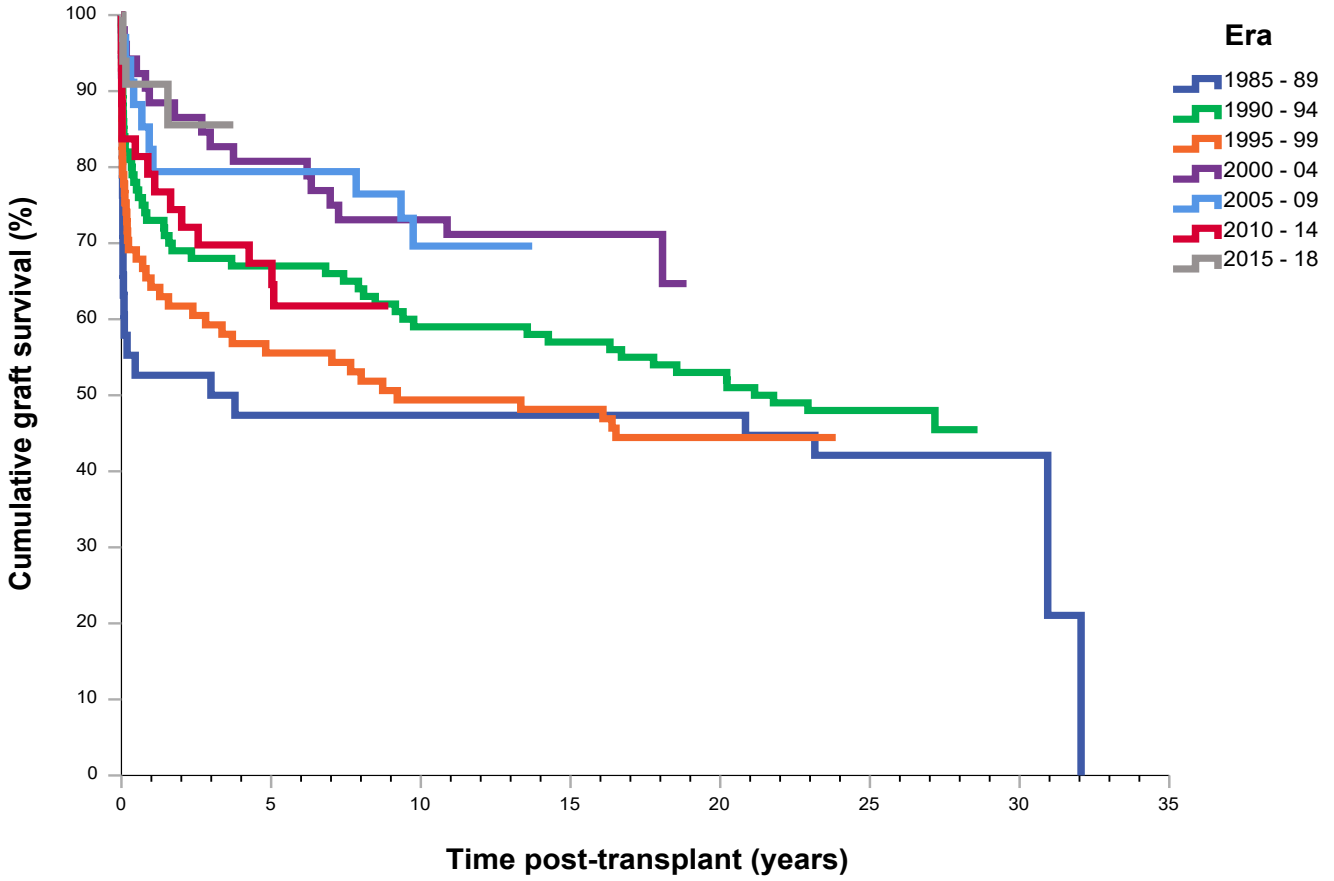


Table 37. Reduced graft (deceased donor) survival by era of transplant

Transplant Era	Graft Survival	Time post-transplant (years)								
		0	1	3	5	10	15	20	25	30
1985 - 89	No. at risk	38	20	19	18	18	18	18	16	8
	Survival (%)		53%	50%	47%	47%	47%	47%	42%	42%
1990 - 94	No. at risk	100	73	68	67	59	57	53	40	0
	Survival (%)		73%	68%	67%	59%	57%	53%	48%	
1995 - 99	No. at risk	81	52	48	45	40	39	30	0	
	Survival (%)		64%	59%	56%	49%	48%	44%		
2000 - 04	No. at risk	52	46	43	42	38	33	0		
	Survival (%)		88%	83%	81%	73%	71%			
2005 - 09	No. at risk	34	28	27	27	19	0			
	Survival (%)		82%	79%	79%	70%				
2010 - 14	No. at risk	43	34	30	24	0				
	Survival (%)		79%	70%	67%					
2015 - 18	No. at risk	33	21	5	0					
	Survival (%)		91%	86%						

12.14 Split Graft Survival by Era of Transplant

There has been a progressive improvement in graft survival after split liver transplantation over eras of transplantation, particularly with regard to early graft survival after 2004 (P = 0.003, Figure 51, Table 38). Graft survival in the most recent era was 90% at 1 year, 89% at 3 years, 81% at 5 years and 73% at 10 years. Median graft survival was 23.4 years for 1995 – 99 era, 5.0 years for 1985 – 94 era and not reached for other transplant eras.

Figure 51. Split graft (deceased donor) survival curve by era of transplant

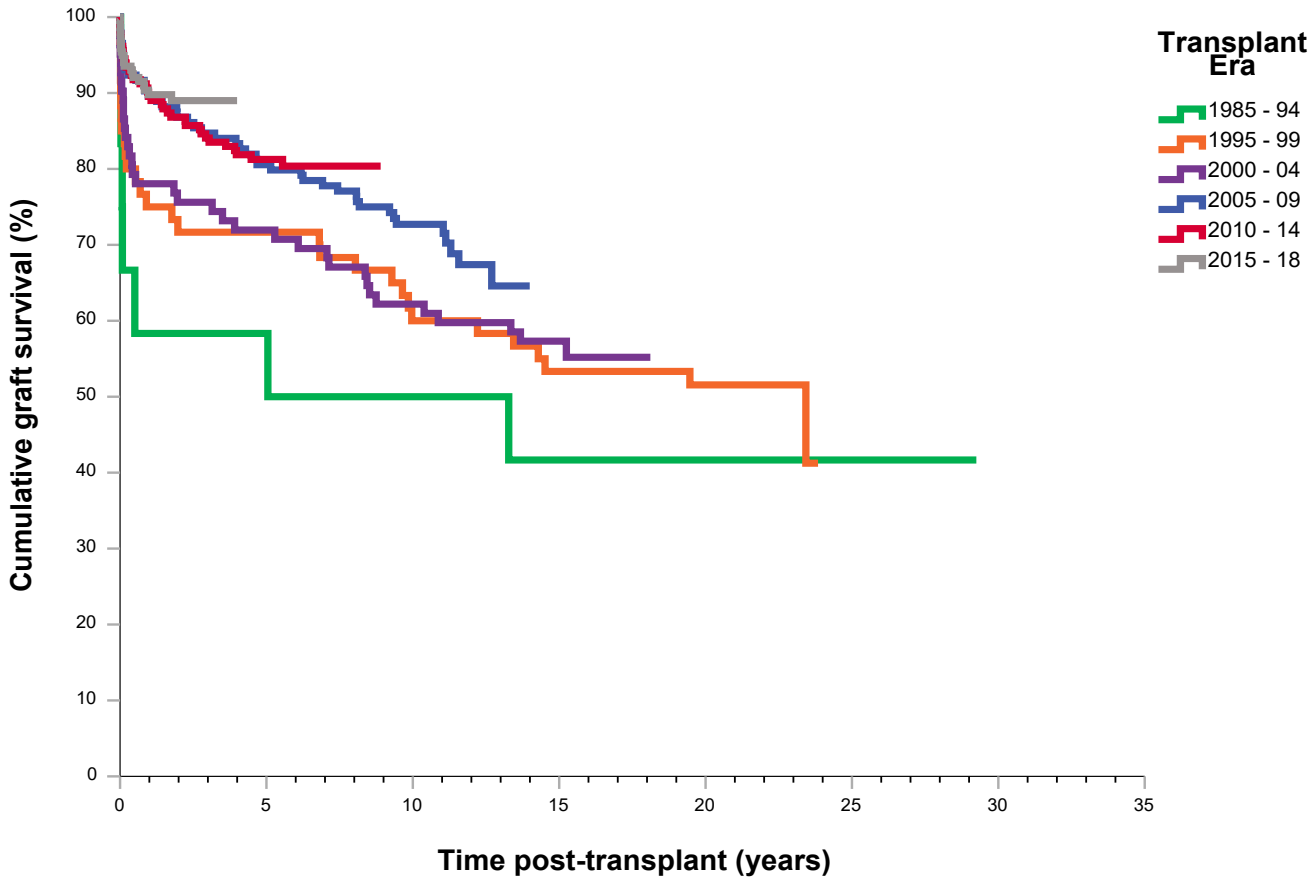


Table 38. Split graft (deceased donor) survival by era of transplant

Transplant Era	Graft Survival	Time post-transplant (years)							
		0	1	3	5	10	15	20	25
1985 - 94	No. at risk	12	7	7	7	6	5	5	2
	Survival (%)		58%	58%	58%	50%	42%	42%	42%
1995 - 99	No. at risk	60	45	43	43	36	32	25	0
	Survival (%)		75%	72%	72%	60%	53%	52%	
2000 - 04	No. at risk	82	64	62	59	51	30	0	
	Survival (%)		78%	76%	72%	62%	57%		
2005 - 09	No. at risk	144	129	122	116	82	0		
	Survival (%)		90%	85%	81%	73%			
2010 - 14	No. at risk	182	167	153	116	0			
	Survival (%)		90%	84%	81%				
2015 - 18	No. at risk	218	148	41	0				
	Survival (%)		90%	89%					

12.15 Living Donor Graft Survival by Era of Transplant

There has been a progressive deterioration in graft survival after living donor transplantation over eras of transplantation after 2000 (P = 0.001, Figure 52 and Table 39). Graft survival in the most recent era was 71% at 1 year (2015-2018 era), 71% at 3 years (2015-2018 era), 78% at 5 years (2010-2014 era) and 90% at 10 years (2005-2009 era). Median graft survival was 0.8 years for 1985 – 99 era and not reached for other transplant eras. Multivariate analysis determined that transplant era was not independently associated with graft survival.

Figure 52. Living donor graft survival curve by era of transplant

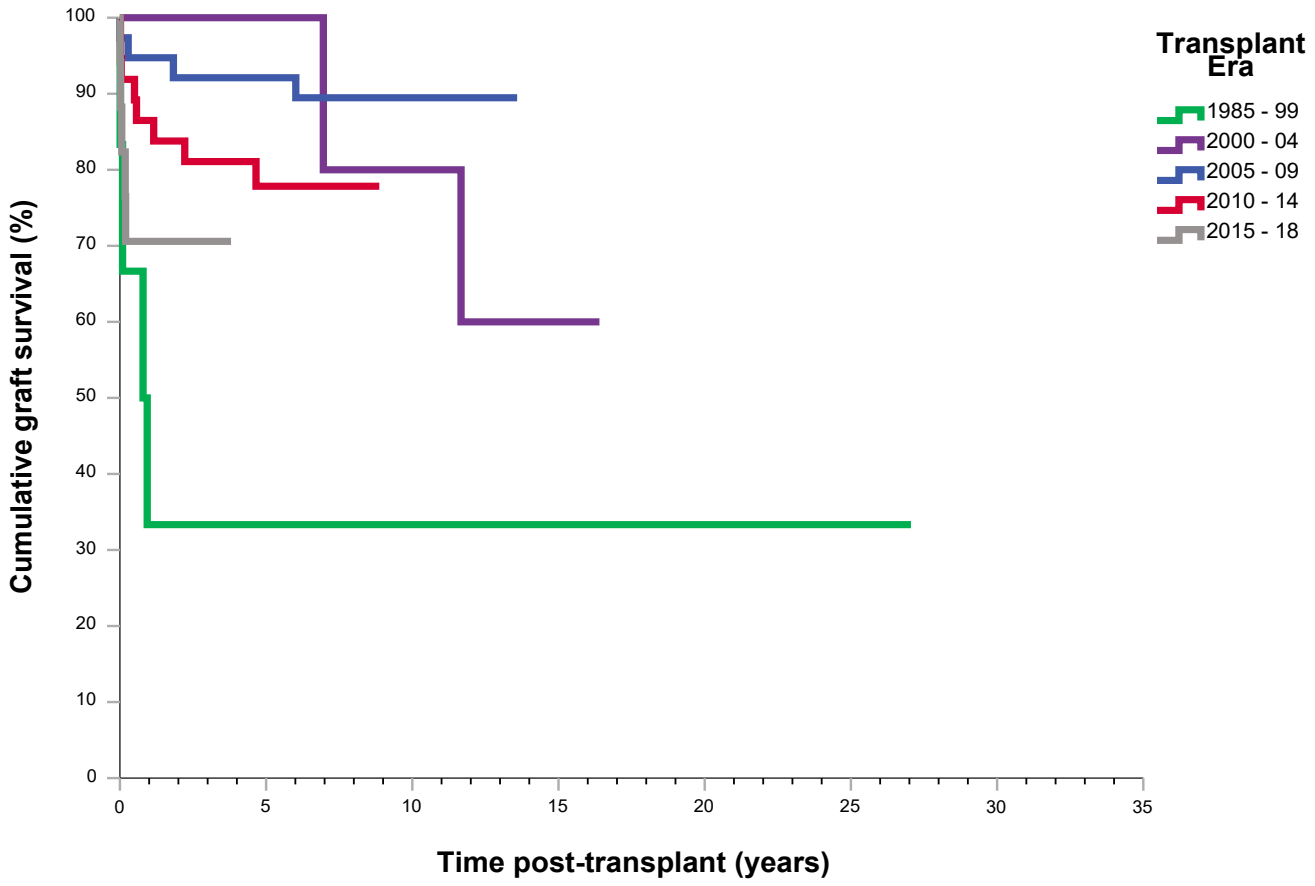


Table 39. Living donor graft survival by era of transplant

Transplant Era	Graft Survival	Time post-transplant (years)							
		0	1	3	5	10	15	20	25
1985 - 99	No. at risk	6	2	2	2	2	2	2	2
	Survival (%)		33%	33%	33%	33%	33%	33%	33%
2000 - 04	No. at risk	5	4	4	4	3	2	0	
	Survival (%)		100%	100%	100%	80%	60%		
2005 - 09	No. at risk	38	36	35	35	27	0		
	Survival (%)		95%	92%	92%	90%			
2010 - 14	No. at risk	37	32	30	23	0			
	Survival (%)		86%	81%	78%				
2015 - 18	No. at risk	17	10	3	0				
	Survival (%)		71%	71%					

12.16 Graft Survival by Deceased Donor Age

There is no deceased donor information on 127 transplants from 1985 to 1988 and a few from 1989. This survival analysis is limited to 6,025 grafts (from 5,676 deceased donors) that have donor information recorded. There is a significant difference in the graft survival outcome based on the age of the deceased donor, with grafts from younger donors having better survival rates (P<0.001, Figure 53 and Table 40). Ten-year graft survival was 80.1% for donors aged 10 – 15 years, 77.3% for donors aged 0 – 9 years, 71.9% for donors aged 16 – 29 years, 68.3% for donors aged 30 – 39 years, 67.4% for donors aged 40 – 49 years, 67.0% for donors aged 70 years and older, 65.2% for donors aged 60 – 69 years and 63.2% for donors aged 50 – 59 years. Median graft survival was 26.8 years for donors aged 10 – 15 years, 22.2 years for donors aged 16 – 29 years, 18.1 years for donors aged 30 – 39 years, 17.4 years for donors aged 40 – 49 years, 16.1 years for donors aged 50 - 59 years, 16.4 years for donors aged 60 – 69 years and was not reached for donors aged 0 – 9 years and 70 years and older.

Figure 53. Graft survival curve by deceased donor age

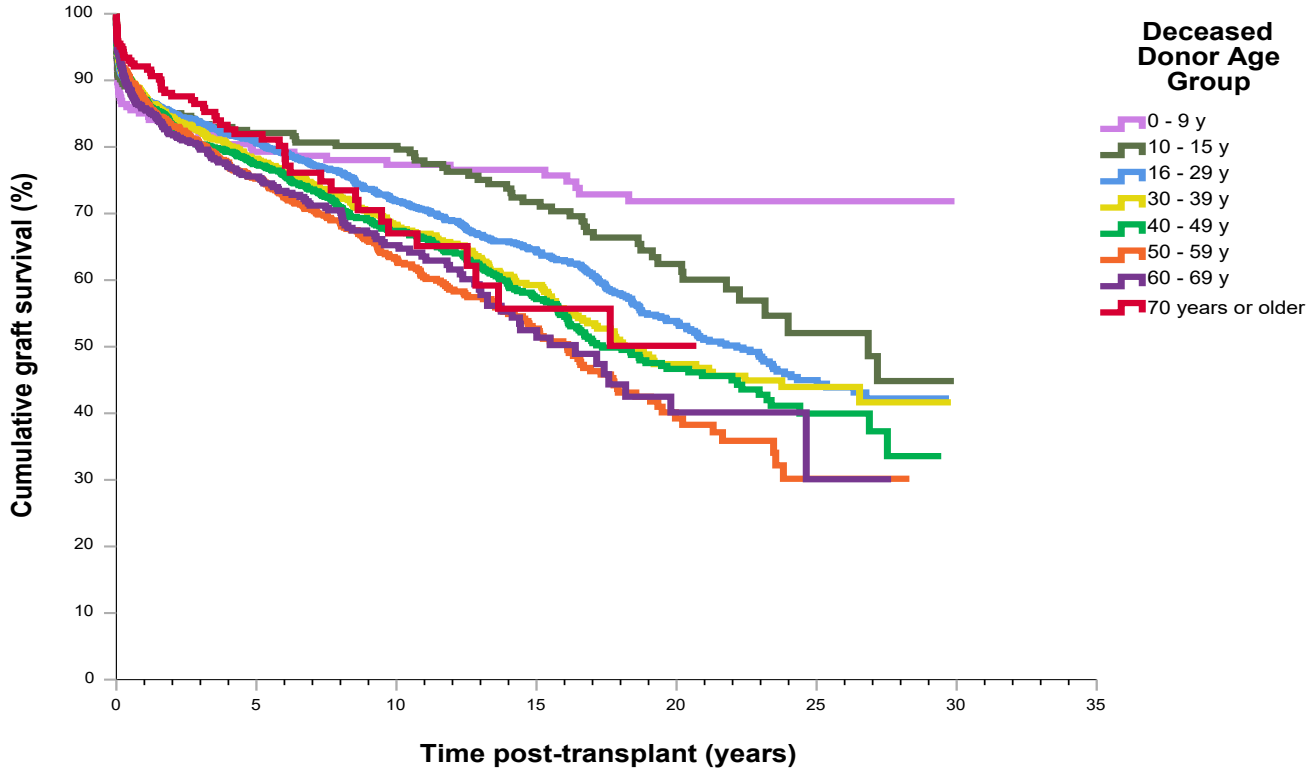


Table 40. Graft survival by deceased donor age

	Graft Survival	Time post-transplant (years)							
		0	1	3	5	10	15	20	25
0 – 9 y	No. at risk	214	177	156	139	109	92	56	32
	Survival (%)		85%	82%	79%	77%	77%	72%	72%
10 – 15 y	No. at risk	285	232	198	181	149	104	54	18
	Survival (%)		86%	83%	82%	80%	72%	62%	52%
16 – 29 y	No. at risk	1,570	1,294	1,110	964	644	406	221	85
	Survival (%)		87%	84%	81%	72%	64%	54%	45%
30 – 39 y	No. at risk	892	731	592	499	309	175	89	35
	Survival (%)		88%	82%	78%	68%	59%	47%	44%
40 – 49 y	No. at risk	1,143	940	761	649	404	235	103	26
	Survival (%)		87%	80%	77%	67%	57%	47%	40%
50 – 59 y	No. at risk	1,022	836	660	530	289	139	43	12
	Survival (%)		87%	80%	75%	63%	53%	39%	30%
60 – 69 y	No. at risk	654	509	394	303	128	47	15	3
	Survival (%)		86%	80%	76%	65%	53%	40%	30%
70 years and older	No. at risk	245	191	147	102	37	15	1	0
	Survival (%)		92%	87%	82%	67%	56%	50%	

12.17 Graft Survival by Donor Type

There was a trend to better graft survival for transplantation from living donors and worse graft survival for transplantation from donation after circulatory death donors in comparison to transplantation from donation after brain death donors (P = 0.110, Figure 54 and Table 41). Ten-year graft survival was 75.9% for transplantation from living donors, 68.6% for transplantation from donation after brain death donors and 64.2% for transplantation from donation after circulatory death donors. Median survival for transplantation from donation after brain death donors was 19.5 years and was not reached for transplantation from living donors and donation after circulatory death donors.

Figure 54. Graft survival curve by donor type – all grafts

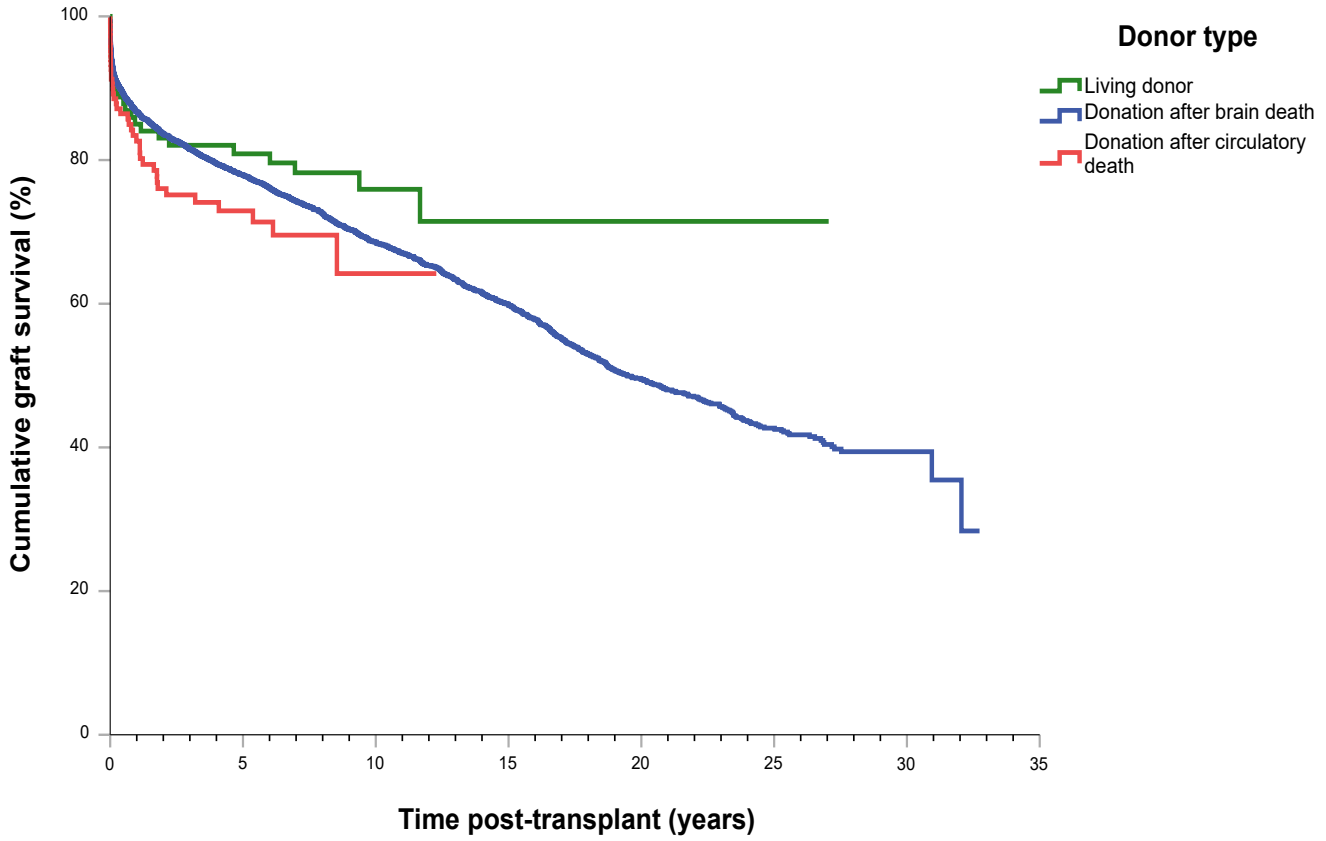


Table 41. Graft survival by donor type – all grafts

Donor Type	Graft Survival	Time post-transplant (years)								
		0	1	3	5	10	15	20	25	30
Living donor	No. at risk	107	89	78	67	33	4	2	2	0
	Survival (%)		85%	82%	81%	76%	72%	72%	72%	
DBD	No. at risk	6,003	4,888	4,017	3,385	2,120	1,259	621	243	28
	Survival (%)		87%	82%	78%	69%	60%	50%	43%	39%
DCD	No. at risk	149	105	73	48	5	0			
	Survival (%)		83%	75%	73%	64%				

Abbreviations: DBD, donation after brain death; DCD, donation after circulatory death

12.18 Graft Survival by Donor Cause of Death

Graft survival varied significantly by donor cause of death (P < 0.001, Figure 55, Table 42). Ten-year graft survival was 74.5% for other cause, 71.1% for anoxia, 70.2% for trauma and 66.7% for stroke. Median survival was not reached for other cause, 21.8 years for trauma, 20.2 years for anoxia and 17.7 years for stroke.

Figure 55. Graft survival curve by donor cause of death

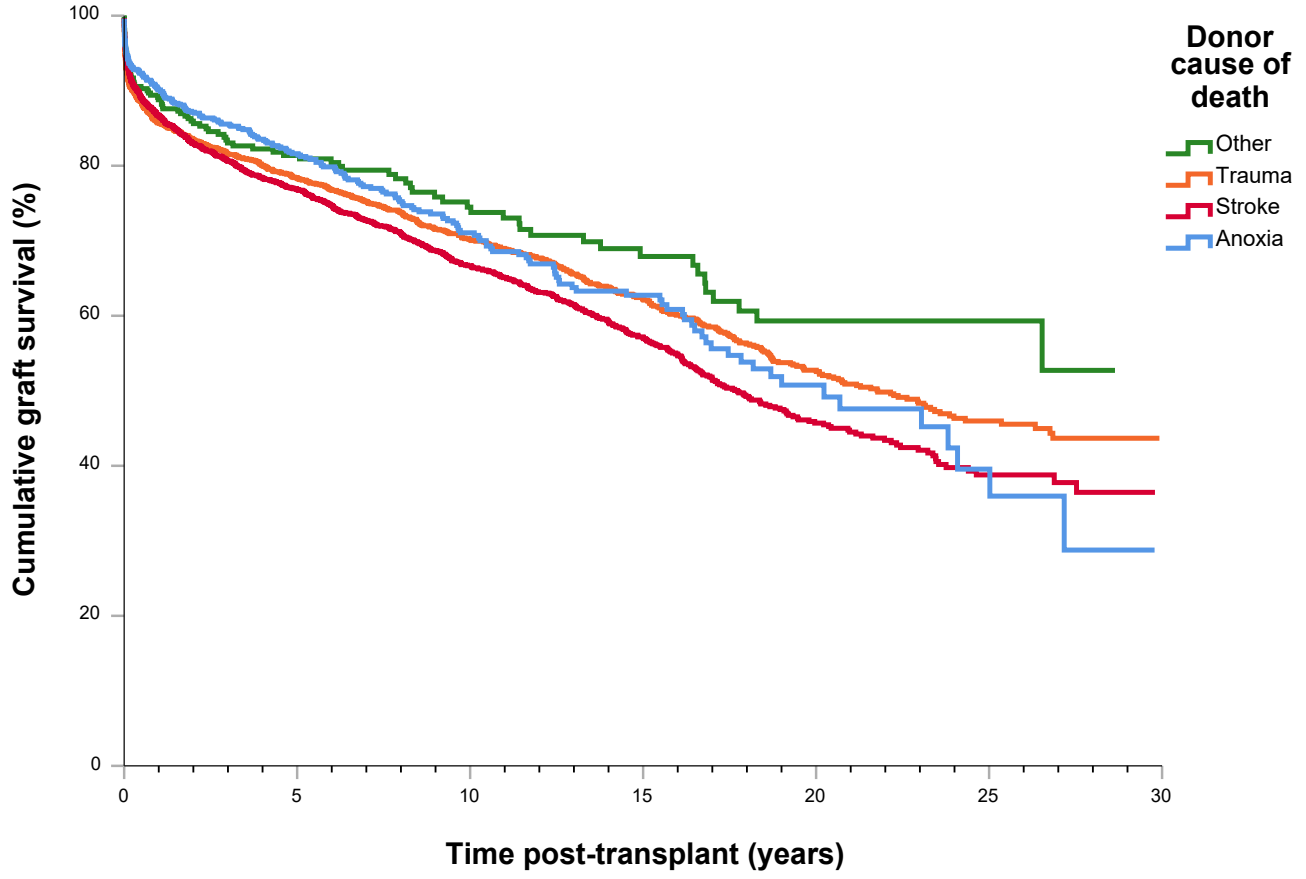


Table 42. Graft survival by donor cause of death

Donor cause of death	Graft Survival	Time post-transplant (years)							
		0	1	3	5	10	15	20	25
Other	No. at risk	362	295	214	180	106	65	37	15
	Survival (%)		89%	83%	81%	75%	68%	59%	59%
Trauma	No. at risk	1,827	1,508	1,328	1,179	831	547	299	114
	Survival (%)		86%	82%	78%	70%	62%	53%	46%
Stroke	No. at risk	2,811	2,282	1,872	1,572	921	496	211	70
	Survival (%)		87%	81%	77%	67%	57%	46%	39%
Anoxia	No. at risk	1,025	824	604	436	211	105	35	12
	Survival (%)		90%	86%	82%	71%	63%	51%	40%

All deceased donors since 1989

12.19 Graft Survival by Shipping of Organs

Graft survival was better for transplants performed with a local donor liver (P < 0.001, Figure 56, Table 43). Ten-year graft survival was 70.5% for transplants performed with a local donor liver and 65.0% for a liver shipped from another unit. Median graft survival was 20.6 years for transplants performed with a local donor liver and 18.7 years for a liver shipped from another unit.

Figure 56. Graft survival curve by organ shipping

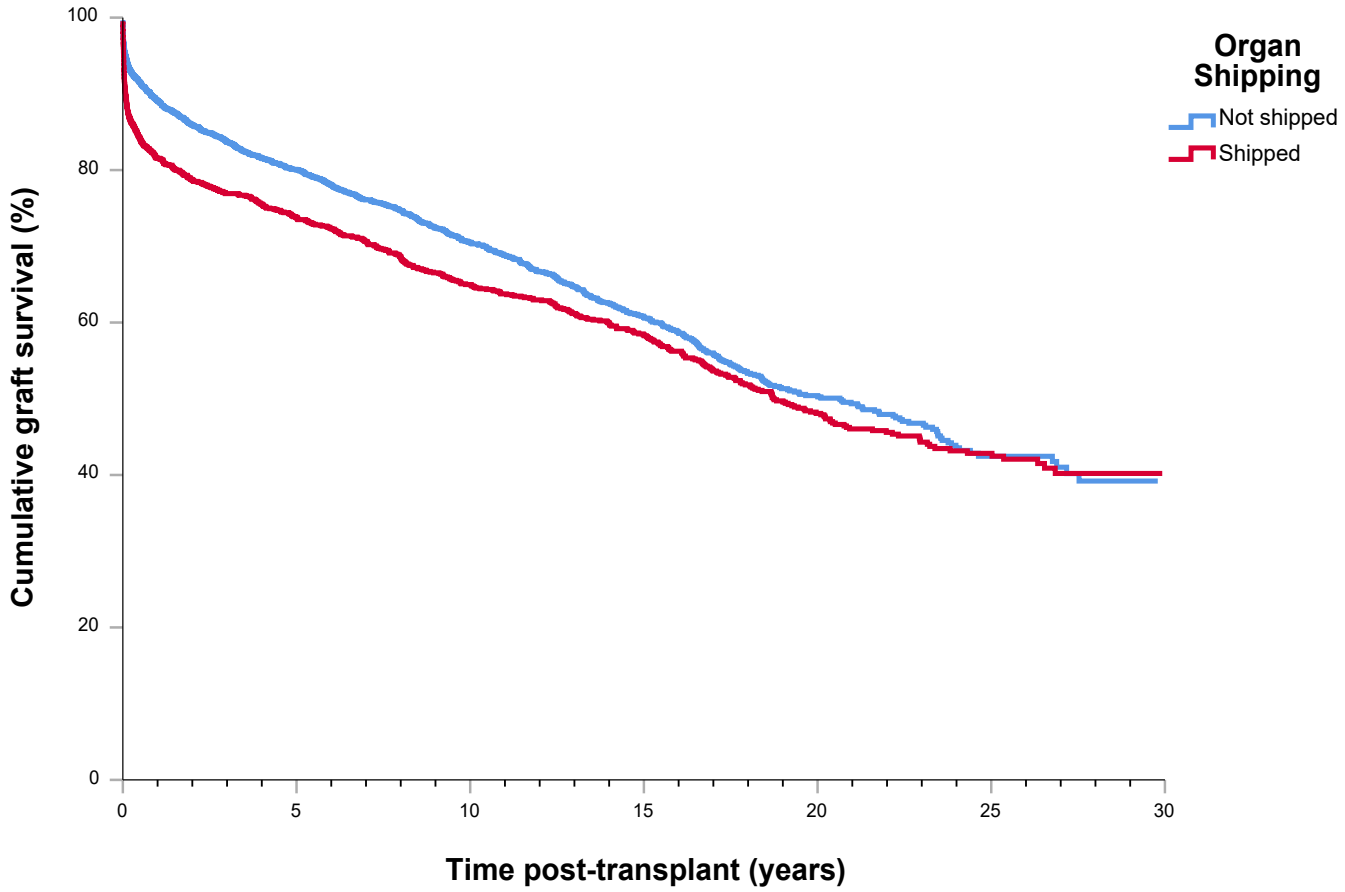


Table 43. Graft survival by organ shipping

Organ Shipping	Graft Survival	Time post-transplant (years)							
		0	1	3	5	10	15	20	25
Not shipped	No. at risk	4,422	3,646	2,933	2,399	1,363	715	306	97
	Survival (%)		89%	84%	80%	71%	61%	50%	43%
Shipped	No. at risk	1,603	1,264	1,085	968	706	498	276	114
	Survival (%)		82%	77%	74%	65%	58%	48%	43%

All deceased donors since 1989

12.20 Graft Survival by Cold Ischaemia Time

Graft survival was significantly better for transplants performed with a cold ischaemia time less than 442 minutes compared to transplants performed with a cold ischaemia time 442 minutes or greater (P < 0.001, see Figure 57 and Table 44). Ten-year graft survival was 74.8% for transplants with a cold ischaemia time less than 442 minutes and 66.3% for transplants with a cold ischaemia time greater than or equal to 442 minutes. Median survival was 19.7 years for transplants with a cold ischaemia time less than 442 minutes and 15.5 years for transplants with a cold ischaemia time greater than or equal to 442 minutes.

Figure 57. Graft survival curve by cold ischaemia time

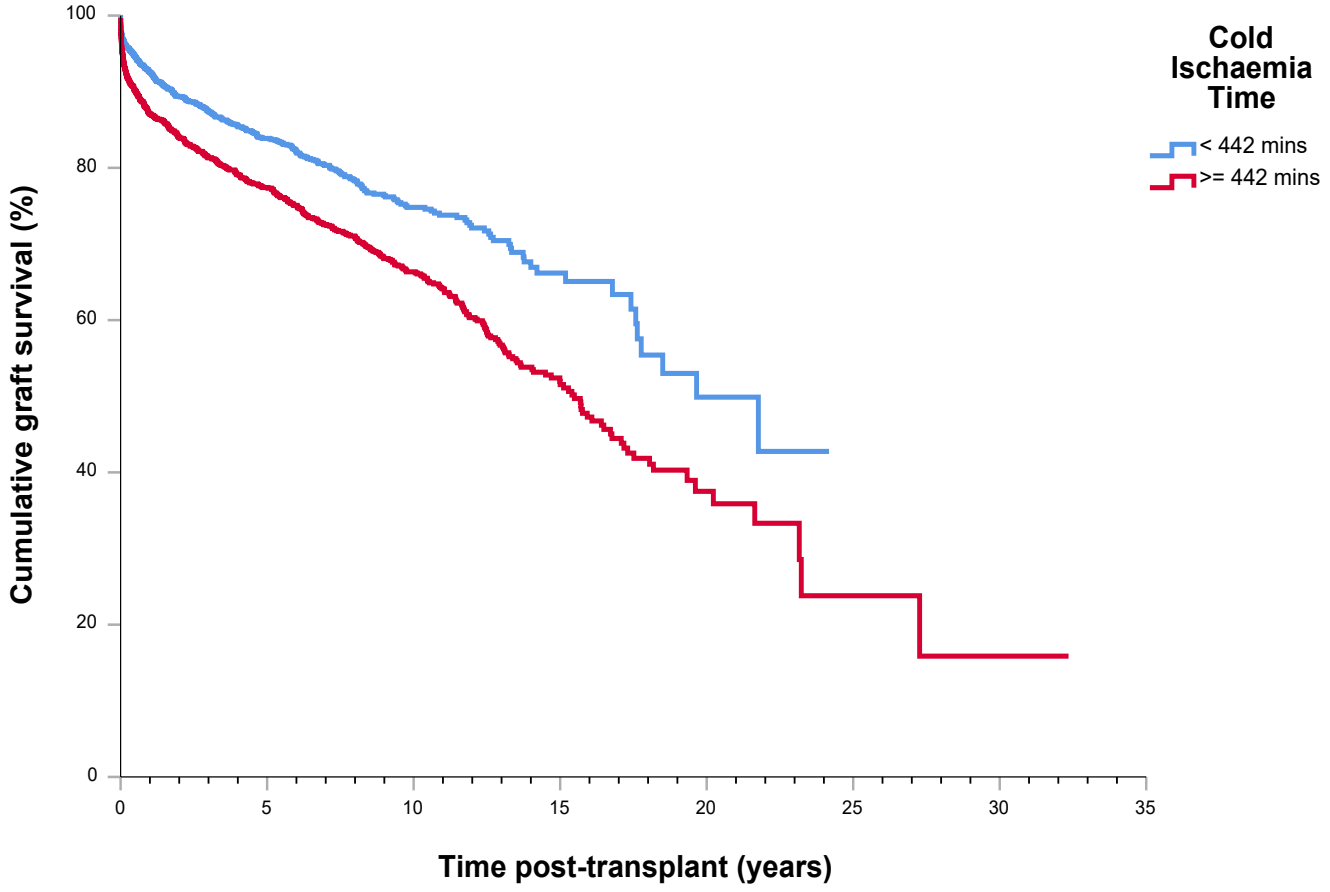


Table 44. Graft survival by cold ischaemia time

Cold Ischaemia Time	Graft Survival	Time post-transplant (years)								
		0	1	3	5	10	15	20	25	30
< 442 mins	No. at risk	2,400	1,968	1,424	1,020	341	61	14	0	
	Survival (%)		93%	87%	84%	75%	66%	50%		
≥ 442 mins	No. at risk	1,684	1,399	1,150	962	491	119	25	4	2
	Survival (%)		87%	81%	77%	66%	52%	38%	24%	16%

2,175 cases missing

12.21 Graft Survival by Blood Group Compatibility

There was no difference in graft survival by donor/recipient blood group compatibility (P=0.954, Figure 58 and Table 45). Ten-year graft survival was 73.8% for blood group-incompatible "A2" transplants (i.e. blood group A, non-A1 donor to O or B recipient or blood group AB, non-A1B to B recipient), 72.1% for blood group-incompatible transplants (excluding A2 donors), 70.1% for blood group-compatible transplants and 68.8% for blood group-identical transplants. Median graft survival was not reached for blood group-incompatible transplants and incompatible "A2" transplants, 20.8 years for transplants in which the donor and recipient blood groups were compatible and 19.5 years for transplants between identical blood groups.

Figure 58. Graft survival curve by blood group compatibility

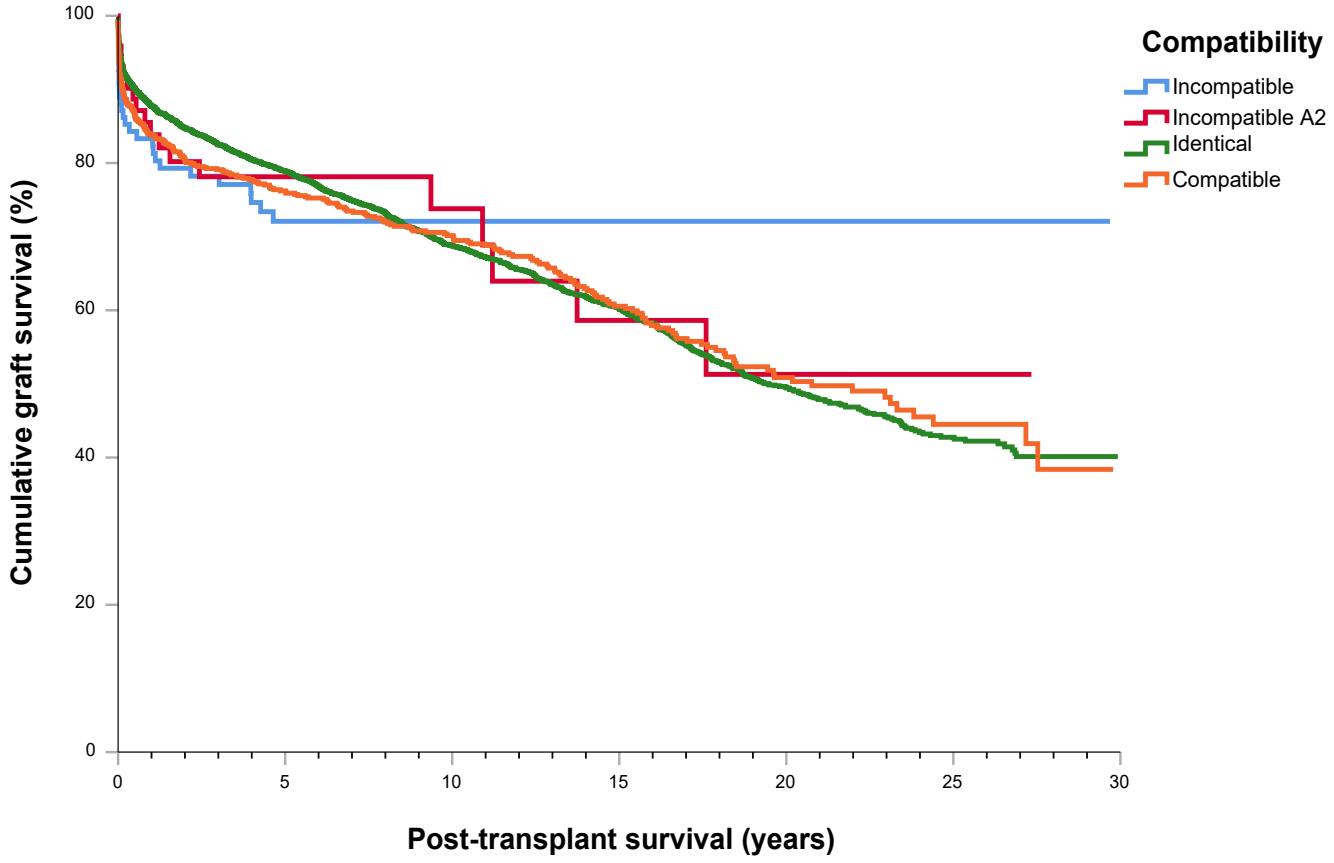


Table 45. Graft survival by blood group compatibility

Compatibility	Graft Survival	Time post-transplant (years)							
		0	1	3	5	10	15	20	25
Incompatible	No. at risk	109	84	70	54	26	11	4	3
	Survival (%)		83%	78%	72%	72%	72%	72%	72%
Incompatible A2	No. at risk	73	50	31	23	16	11	3	2
	Survival (%)		84%	78%	78%	74%	59%	51%	51%
Identical	No. at risk	4,978	4,098	3,363	2,814	1,710	999	477	168
	Survival (%)		88%	83%	79%	69%	60%	50%	43%
Compatible	No. at risk	867	679	555	477	317	192	98	38
	Survival (%)		84%	79%	76%	70%	61%	51%	45%

232 cases missing

12.22 Graft Survival by Recipient Urgency

Graft survival varied significantly by recipient urgency (P = 0.001, Figure 59 and Table 46). Ten-year graft survival was 76.5% for category 2, 68.7% for non-urgent and 57.9% for category 1 patients. Median graft survival was not reached for category 2, 19.5 years for non-urgent and 15.4 years for category 1 patients.

Figure 59. Graft survival curve by recipient urgency

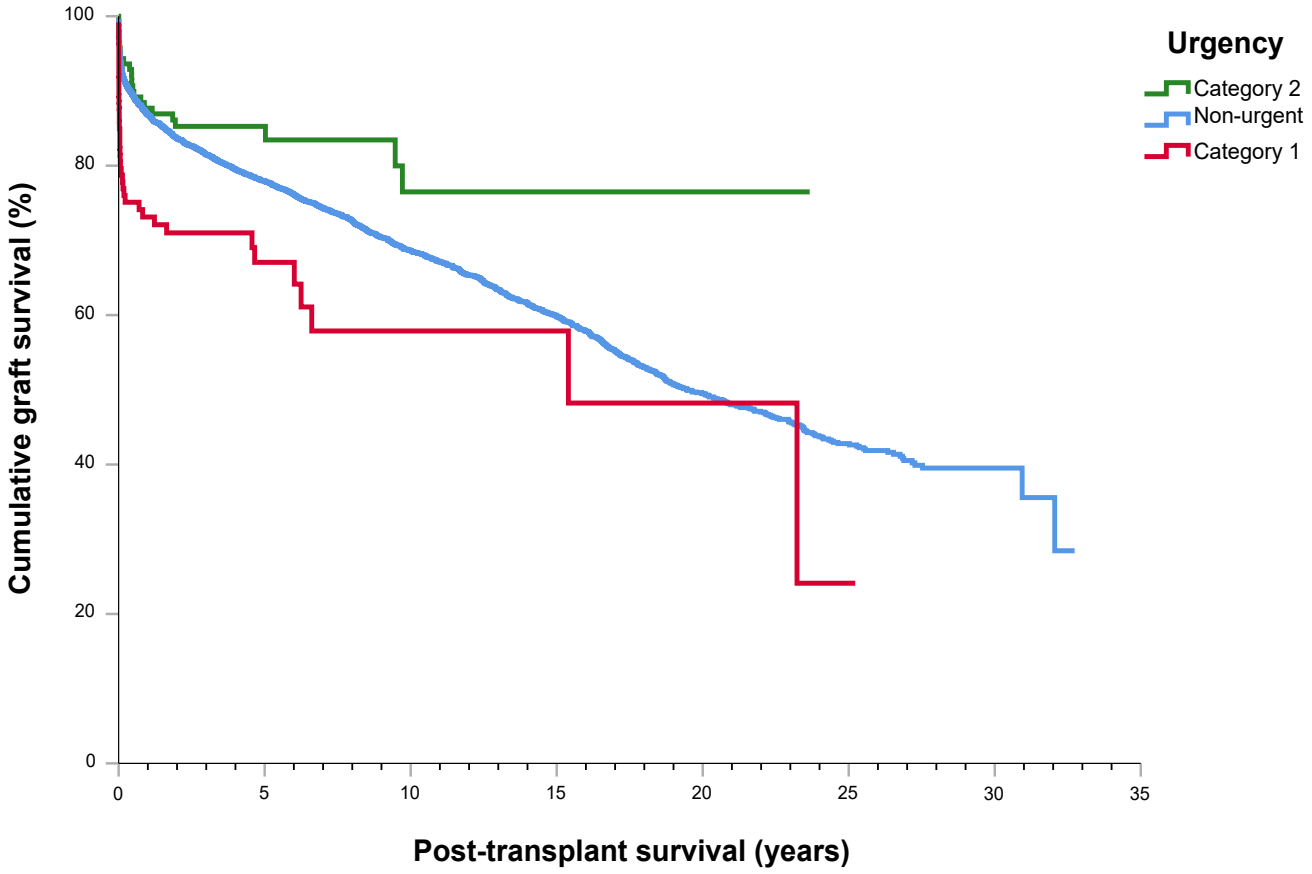


Table 46. Graft survival by recipient urgency

Urgency	Graft Survival	Time post-transplant (years)								
		0	1	3	5	10	15	20	25	30
Category 2	No. at risk	141	116	80	48	21	3	1	0	
	Survival (%)		88%	85%	85%	77%	77%	77%		
Non-urgent	No. at risk	6,005	4,894	4,037	3,420	2,125	1,254	618	244	28
	Survival (%)		87%	82%	78%	69%	60%	50%	43%	40%
Category 1	No. at risk	113	72	51	32	12	6	4	1	0
	Survival (%)		73%	71%	67%	58%	58%	48%	24%	

13 Indication for Retransplantation

13.1 All Retransplants

There were 473 retransplants after the previous graft failed. There have been 424 second grafts, 47 third grafts and two fourth grafts. The commonest indications for retransplantation were vascular problems (31%), rejection (18%), biliary (14%), primary non-function or initial poor function (14%) and recurrent disease (14%, Table 47).

Table 47. Reason for retransplantation

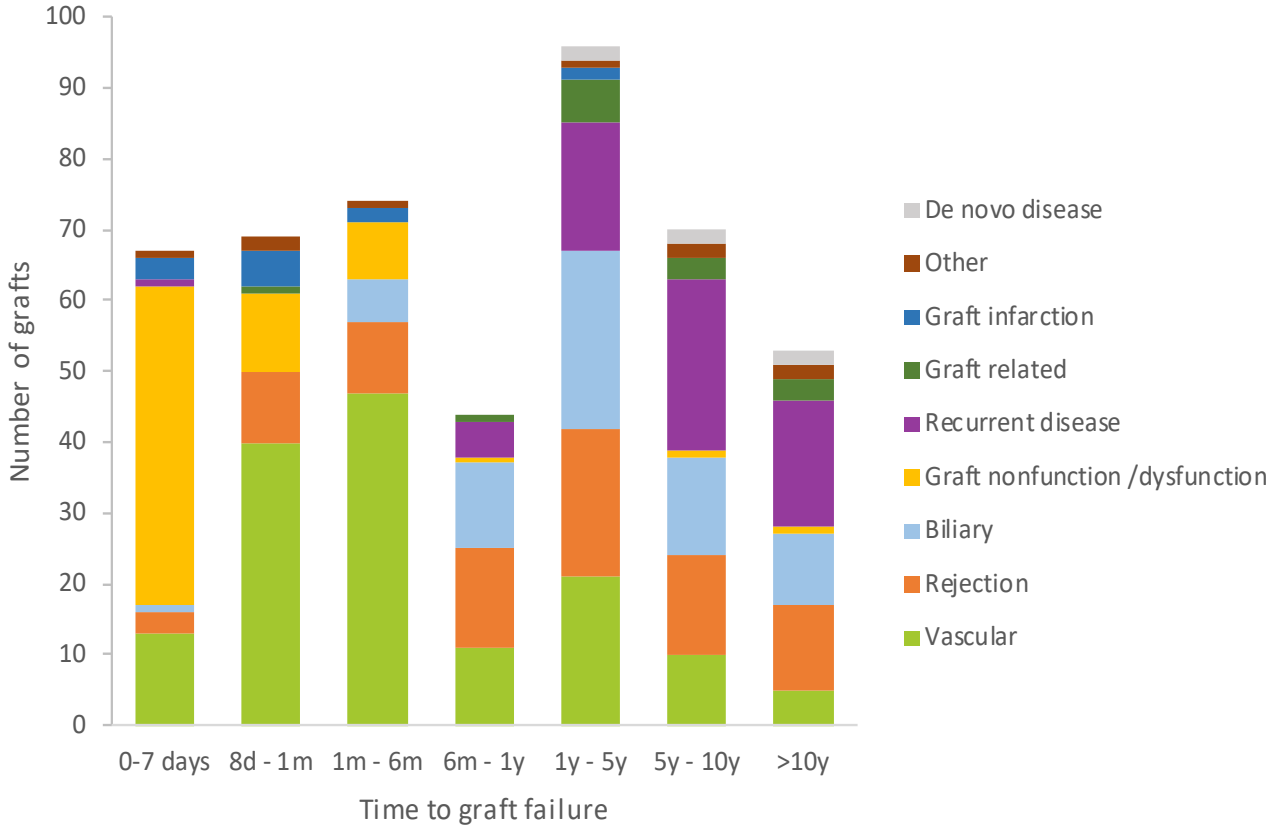
Reason for retransplantation	Graft 2	Graft 3	Graft 4	Total grafts	% total
Vascular	**132**	**15**	**0**	**147**	**31%**
- Hepatic artery thrombosis	*100*	*10*	*0*	*110*	*23%*
- Portal vein thrombosis	*10*	*0*	*0*	*10*	*2%*
- Hepatic vein thrombosis	*5*	*1*	*0*	*6*	*1%*
- Unspecified	*5*	*0*	*0*	*5*	*1%*
- Haemorrhage (Hepatic artery)	*4*	*0*	*0*	*4*	*1%*
- Hepatic artery stenosis	*3*	*0*	*0*	*3*	*1%*
- Hepatic artery pseudoaneurysm	*2*	*0*	*0*	*2*	*0.4%*
- Hepatic vein stenosis	*0*	*2*	*0*	*2*	*0.4%*
- Arterio-portal vein fistula	*1*	*0*	*0*	*1*	*0.2%*
- Budd Chiari	*1*	*0*	*0*	*1*	*0.2%*
- Hepatic artery injury	*1*	*0*	*0*	*1*	*0.2%*
- Recurrent bleeds	*0*	*1*	*0*	*1*	*0.2%*
- Ruptured hepatic artery anastomosis	*0*	*1*	*0*	*1*	*0.2%*
Rejection	**74**	**9**	**1**	**84**	**18%**
- Chronic rejection	*51*	*9*	*0*	*60*	*13%*
- Acute rejection	*16*	*0*	*1*	*17*	*4%*
- ABO incompatible	*4*	*0*	*0*	*4*	*1%*
- Hyperacute rejection	*2*	*0*	*0*	*2*	*0.4%*
- Donor mediated antibody	*1*	*0*	*0*	*1*	*0.2%*
Biliary	**65**	**3**	*0*	**68**	**14%**
- Unspecified	*25*	*2*	*0*	*27*	*6%*
- Biliary strictures type unspecified	*12*	*0*	*0*	*12*	*3%*
- Non anastomotic	*9*	*0*	*0*	*9*	*2%*
- Anastomotic	*5*	*0*	*0*	*5*	*1%*
- Cholangiopathy	*5*	*0*	*0*	*5*	*1%*
- Biliary cirrhosis / fibrosis	*4*	*0*	*0*	*4*	*1%*
- Cholestatic disease	*2*	*0*	*0*	*2*	*0.4%*
- Ductopenia	*2*	*0*	*0*	*2*	*0.4%*
- Biliary necrosis	*0*	*1*	*0*	*1*	*0.2%*
- Cholangitis	*1*	*0*	*0*	*1*	*0.2%*
Primary graft nonfunction /dysfunction	**58**	**9**	*0*	**67**	**14%**
- Primary graft nonfunction (Retransplant <= 7 days)	*43*	*7*	*0*	*50*	*11%*
- Primary graft dysfunction (Retransplant > 7 days)	*15*	*2*	*0*	*17*	*4%*
Recurrent disease	**61**	**6**	*0*	**67**	**14%**
- Primary sclerosing cholangitis	*22*	*4*	*0*	*26*	*5%*
- Hepatitis C	*22*	*0*	*0*	*22*	*5%*
- Autoimmune hepatitis	*6*	*1*	*0*	*7*	*1%*
- Primary biliary cirrhosis	*5*	*1*	*0*	*6*	*1%*
- Hepatitis B	*4*	*0*	*0*	*4*	*1%*
- Crigler-Najjar	*1*	*0*	*0*	*1*	*0.2%*
- Erythropoietic protoporphyria	*1*	*0*	*0*	*1*	*0.2%*
Graft related	**10**	**3**	*0*	**13**	**3%**
- Post necrotic cirrhosis	*5*	*3*	*0*	*8*	*2%*
- Nodular regenerative hyperplasia	*3*	*0*	*0*	*3*	*1%*
- Immune/non-viral hepatitis	*2*	*0*	*0*	*2*	*0.4%*
Graft Infarction	**11**	*0*	**1**	**12**	**3%**
- Thrombotic	*6*	*0*	*0*	*6*	*1%*
- Non thrombotic	*5*	*0*	*1*	*6*	*1%*

(table continued on next page)

Reason for retransplantation	Graft 2	Graft 3	Graft 4	Total grafts	% total
De novo disease	**6**	*0*	*0*	**6**	**1%**
- Hepatitis C	*2*	*0*	*0*	*2*	*0.4%*
- Unspecified	*2*	*0*	*0*	*2*	*0.4%*
- Hepatitis B	*1*	*0*	*0*	*1*	*0.2%*
- Hepatitis D	*1*	*0*	*0*	*1*	*0.2%*
Other	**7**	**2**	*0*	**9**	**2%**
- Unspecified	*3*	*1*	*0*	*4*	*1%*
- Cryptogenic cirrhosis	*1*	*1*	*0*	*2*	*0.4%*
- Donor derived malignancy	*2*	*0*	*0*	*2*	*0.4%*
- Acute hepatic failure - Drug related: interferon	*1*	*0*	*0*	*1*	*0.2%*
Total	**424**	**47**	**2**	**473**	

Forty-four percent of graft failures occurred within the first six months' post-transplant (14.2% 0 – 7 days, 14.6% day 8 to 1 month, 15.6% 1 month to 6 months). Primary graft non-function was the main reason for retransplantation in the first 7 days post-transplant whilst vascular causes was the main type between 8 days and 6 months (Figure 60). Recurrent disease was the leading cause of graft failure after five years post-transplant.

Figure 60. Time to graft failure by reason for retransplantation



13.2 Paediatric Retransplantation

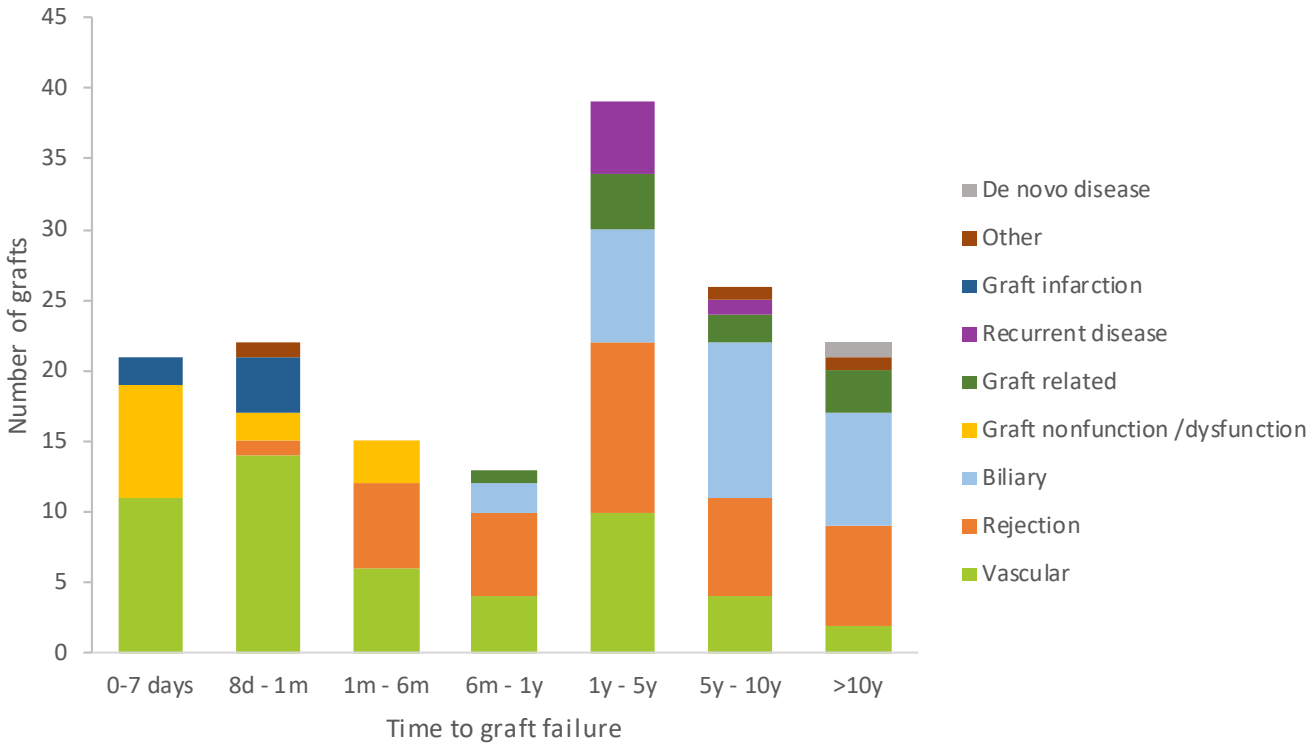
There were 158 retransplantations following paediatric graft failure. There have been 134 second grafts and 24 third grafts. The commonest indications for retransplantation were vascular complications (32%), rejection (25%) and biliary complications (18%, Table 48).

Table 48. Reason for retransplantation following paediatric graft failure

Reason for retransplantation	Total grafts	% total
Vascular	**51**	**32%**
- Hepatic artery thrombosis	*33*	*21%*
- Portal vein thrombosis	*7*	*4%*
- Hepatic vein thrombosis	*4*	*3%*
- Unspecified	*3*	*2%*
- Arterio-portal vein fistula	*1*	*1%*
- Hepatic artery stenosis	*1*	*1%*
- Hepatic vein stenosis	*1*	*1%*
- Recurrent bleeds	*1*	*1%*
Rejection	**39**	**25%**
- Chronic rejection	*38*	*24%*
- Acute rejection	*1*	*1%*
Biliary	**29**	**18%**
- Unspecified	*8*	*5%*
- Biliary strictures type unspecified	*5*	*3%*
- Anastomotic stricture	*4*	*3%*
- Non-anastomotic strictures	*4*	*3%*
- Biliary cirrhosis / fibrosis	*3*	*2%*
- Ductopenia	*2*	*1%*
- Biliary necrosis	*1*	*1%*
- Cholangitis	*1*	*1%*
- Cholestatic disease	*1*	*1%*
Graft nonfunction /dysfunction	**13**	**8%**
- Primary nonfunction (ReTx or death <= 7 days)	*8*	*5%*
- Primary dysfunction (ReTx or death > 7 days)	*5*	*3%*
Graft related	**10**	**6%**
- Post necrotic cirrhosis	*6*	*4%*
- Immune/nonviral hepatitis	*2*	*1%*
- Nodular regenerative hyperplasia	*2*	*1%*
Recurrent disease	**6**	**4%**
- Autoimmune hepatitis	*3*	*2%*
- Crigler-Najjar	*1*	*1%*
- Primary biliary cirrhosis	*1*	*1%*
- Primary sclerosing cholangitis	*1*	*1%*
Graft infarction	**6**	**4%**
- Thrombotic	*4*	*3%*
- Non-thrombotic	*2*	*1%*
Other	**3**	**2%**
- Cryptogenic cirrhosis	*2*	*1%*
- Unspecified	*1*	*1%*
De novo disease	**1**	**1%**
- De novo disease - hepatitis C	*1*	*1%*
Total	**158**	

Thirty-seven percent of graft failures occurred within the first six months' post-transplant (13.3% 0 – 7 days, 13.9% day 8 to 1 month, 9.5% 1 month to 6 months). Vascular causes were the main reason for retransplantation in the first month post-transplant (Figure 61). Rejection, biliary and vascular causes were the leading causes of graft failure after one-year post-transplant.

Figure 61. Paediatric time to graft failure by reason for retransplantation



13.3 Adult Retransplantation

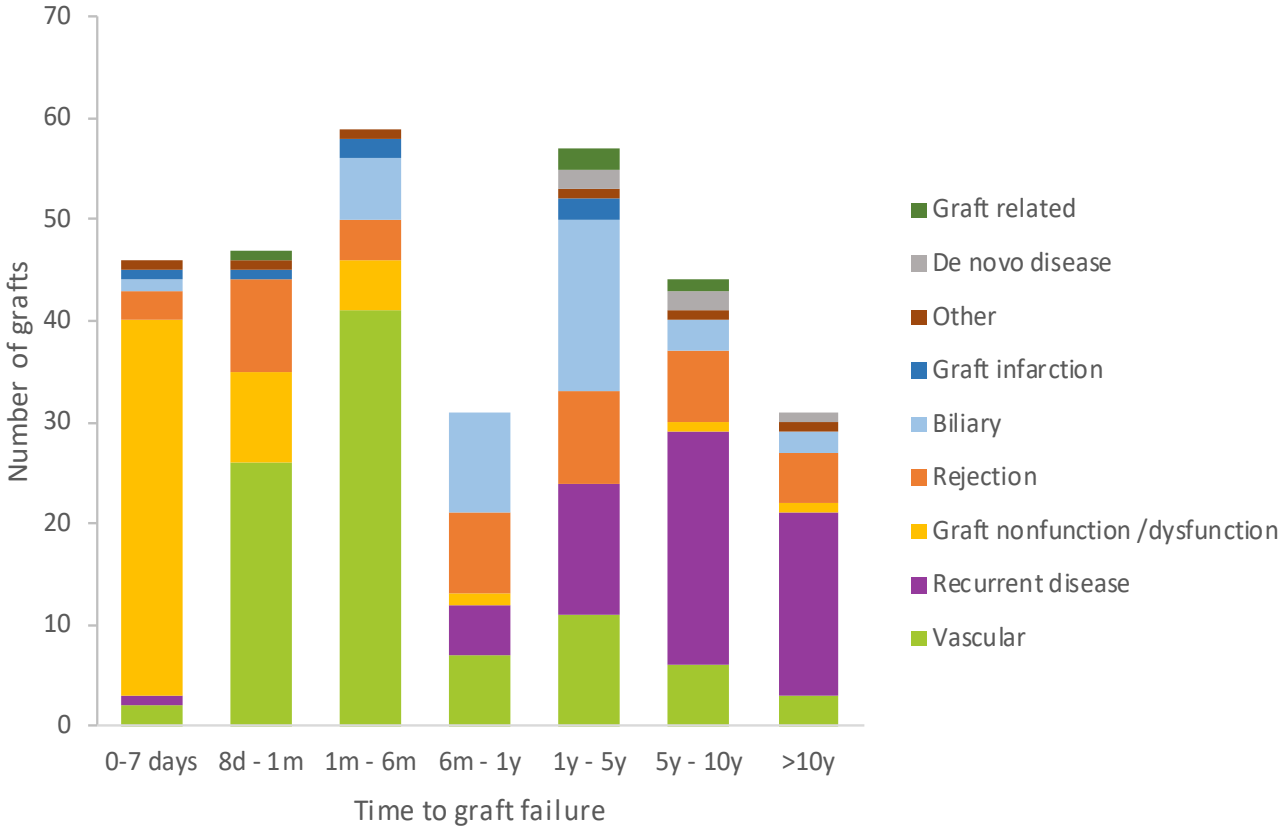
There were 315 retransplantations following adult graft failure. There have been 290 second grafts, 23 third grafts and two fourth grafts. The commonest indications for retransplantation were vascular (30%), disease recurrence (19%) and primary non-function or initial poor function (17%, Table 49).

Table 49. Reason for retransplantation following adult graft failure

Reason for retransplantation	Total grafts	% total
Vascular	**96**	**30%**
- Hepatic artery thrombosis	*77*	*24%*
- Haemorrhage	*4*	*1%*
- Hepatic vein thrombosis	*3*	*1%*
- Portal vein thrombosis	*3*	*1%*
- Hepatic artery pseudoaneurysm	*2*	*1%*
- Hepatic artery stenosis	*2*	*1%*
- Unspecified	*2*	*1%*
- Hepatic artery injury	*1*	*0.3%*
- Hepatic vein stenosis	*1*	*0.3%*
- Ruptured hepatic artery anastomosis	*1*	*0.3%*
Recurrent disease	**61**	**19%**
- Primary sclerosing cholangitis	*25*	*8%*
- Hepatitis C	*22*	*7%*
- Primary biliary cirrhosis	*5*	*2%*
- Autoimmune hepatitis	*4*	*1%*
- Hepatitis B	*4*	*1%*
- Erythropoietic protoporphyria	*1*	*0.3%*
Graft nonfunction /dysfunction	**54**	**17%**
- Primary nonfunction (ReTx or death <= 7 days)	*42*	*13%*
- Primary dysfunction (ReTx or death > 7 days)	*12*	*4%*
Rejection	**45**	**14%**
- Chronic rejection	*22*	*7%*
- Acute rejection	*16*	*5%*
- ABO incompatible	*4*	*1%*
- Hyperacute rejection	*2*	*1%*
- Donor mediated antibody	*1*	*0.3%*
Biliary	**39**	**12%**
- Unspecified	*19*	*6%*
- Non-anastomotic strictures	*10*	*3%*
- Biliary strictures type unspecified	*7*	*2%*
- Anastomotic stricture	*1*	*0.3%*
- Biliary cirrhosis / fibrosis	*1*	*0.3%*
- Cholestatic disease	*1*	*0.3%*
De novo disease	**5**	**2%**
- Unspecified	*2*	*1%*
- Hepatitis B	*1*	*0.3%*
- Hepatitis C	*1*	*0.3%*
- Hepatitis D	*1*	*0.3%*
Graft infarction	**6**	**2%**
- Non thrombotic	*4*	*1%*
- Thrombotic	*2*	*1%*
Other	**6**	**2%**
- Unspecified	*3*	*1%*
- Donor derived malignancy	*2*	*1%*
- Acute hepatic failure drug related - interferon	*1*	*0.3%*
Graft related	**3**	**1%**
- Post necrotic cirrhosis	*2*	*1%*
- Nodular regenerative hyperplasia	*1*	*0.3%*
Total	**315**	

Forty-eight percent of graft failures occurred within the first six months' post-transplant (14.6% 0 – 7 days, 14.9% day 8 to 1 month, 18.7% 1 month to 6 months). Primary graft non-function was the main reason for retransplantation in the first 7 days post-transplant whilst vascular causes were the main type between 8 days and 6 months (Figure 62). Recurrent disease was the leading cause of graft failure after five years post-transplant.

Figure 62. Adult time to graft failure by reason for retransplantation



14 Cause of Patient Death

14.1 Cause of death – all patients

1,640 liver transplant patients (169 children and 1,471 adults) have died. The commonest causes of death were malignancy (23%), graft-related causes (20%), sepsis (14%), cardiovascular disease (8%) and multi-organ failure (8%, Figure 63, Table 50).

Figure 63. Cause of death by categories

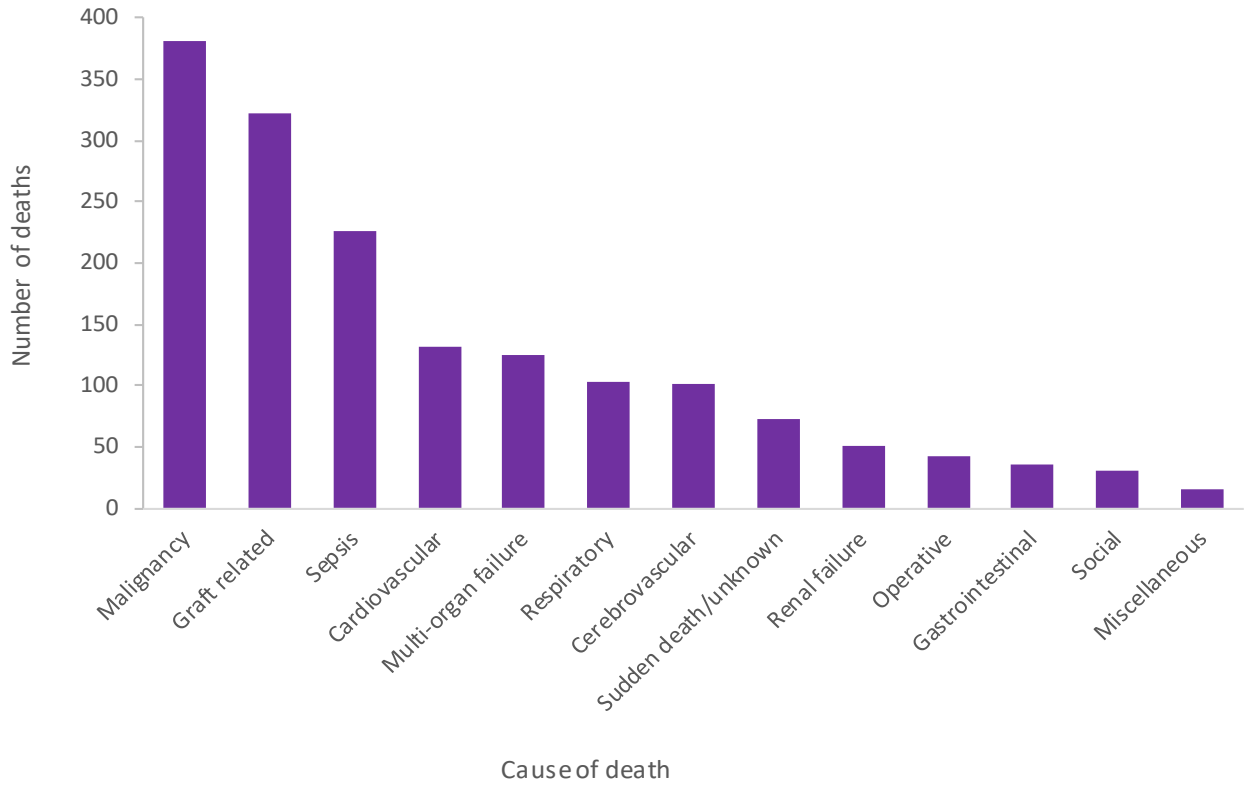


Table 50. Cause of death by age group

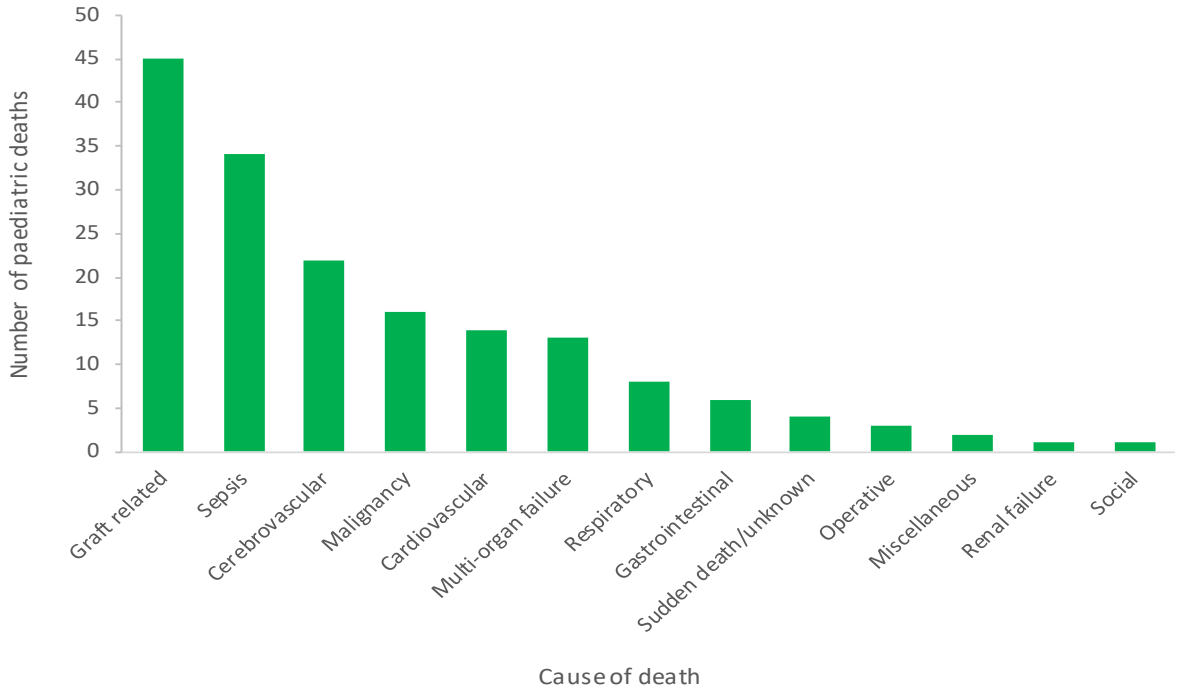
Cause of death	Paediatric	Adult	Total deaths	% all deaths
Malignancy	**16**	**366**	**382**	**23%**
- De novo malignancy	*10*	*193*	*203*	*12%*
- Recurrent malignancy	*6*	*171*	*177*	*11%*
- Donor transmitted malignancy	*0*	*2*	*2*	*0.1%*
Graft related	**45**	**278**	**323**	**20%**
Other graft related	37	119	156	10%
- Rejection	*15*	*69*	*84*	*5%*
- Primary non-function / dysfunction	*4*	*20*	*24*	*1%*
- Biliary complications	*3*	*15*	*18*	*1%*
- Graft versus host disease	*0*	*6*	*6*	*0.4%*
- Massive haemorrhagic necrosis	*4*	*0*	*4*	*0.2%*
- Non-thrombotic infarction	*3*	*1*	*4*	*0.2%*
- Unspecified	*2*	*2*	*4*	*0.2%*
- Hepatitis	*4*	*0*	*4*	*0.2%*
- Late graft failure	*0*	*3*	*3*	*0.2%*
- De novo hepatitis C	*0*	*2*	*2*	*0.1%*
- Hepato-renal syndrome	*0*	*1*	*1*	*0.1%*
- Outflow obstruction	*1*	*0*	*1*	*0.1%*
- Post necrotic cirrhosis	*1*	*0*	*1*	*0.1%*
Disease recurrence	0	141	141	9%
- Hepatitis C	*0*	*93*	*93*	*6%*
- Hepatitis B	*0*	*18*	*18*	*1%*
- Alcoholic cirrhosis	*0*	*11*	*11*	*1%*
- Primary sclerosing cholangitis	*0*	*7*	*7*	*0.4%*
- Autoimmune hepatitis	*0*	*4*	*4*	*0.2%*
- NASH	*0*	*2*	*2*	*0.1%*
- Primary biliary cirrhosis	*0*	*2*	*2*	*0.1%*
- Progressive familial amyloid polyneuropathy	*0*	*2*	*2*	*0.1%*
- Erythropoietic protoporphyria	*0*	*1*	*1*	*0.1%*
- Type not specified	*0*	*1*	*1*	*0.1%*
Vascular complications	8	18	26	2%
- Hepatic artery thrombosis	*4*	*9*	*13*	*1%*
- Portal vein thrombosis	*2*	*9*	*11*	*1%*
- Hepatic vein thrombosis	*2*	*0*	*2*	*0.1%*
Sepsis	**34**	**192**	**226**	**14%**
- Bacterial	*12*	*76*	*88*	*5%*
- Unspecified infection	*6*	*41*	*47*	*3%*
- Fungal	*6*	*38*	*44*	*3%*
- Mixed	*4*	*22*	*26*	*2%*
- Viral	*6*	*15*	*21*	*1%*
Cardiovascular	**14**	**117**	**131**	**8%**
Multi-organ failure	**13**	**112**	**125**	**8%**
Respiratory	**8**	**96**	**104**	**6%**
Cerebrovascular	**22**	**80**	**102**	**6%**
Sudden death / unknown	**4**	**68**	**72**	**4%**
Renal failure	**1**	**50**	**51**	**3%**
Operative	**3**	**40**	**43**	**3%**
Gastrointestinal	**6**	**29**	**35**	**2%**
Social (accident, suicide, non-compliance, treatment withdrawal)	**1**	**29**	**30**	**2%**
Miscellaneous	**2**	**14**	**16**	**1%**
- Neurological	*0*	*6*	*6*	*0.4%*
- Haematological	*1*	*3*	*4*	*0.2%*
- Metabolic	*1*	*2*	*3*	*0.2%*
- Allergy	*0*	*1*	*1*	*0.1%*
- Donor transferred OTC deficiency	*0*	*1*	*1*	*0.1%*
- Veno-occlusive disease	*0*	*1*	*1*	*0.1%*
Total	**169**	**1471**	**1640**	

Abbreviations: NASH, non-alcoholic steatohepatitis

14.2 Paediatric Patients - Cause of Death

Graft-related causes (27%) are the leading cause of death in children, with sepsis being the cause of death in a further 20% of paediatric patients (Figure 64).

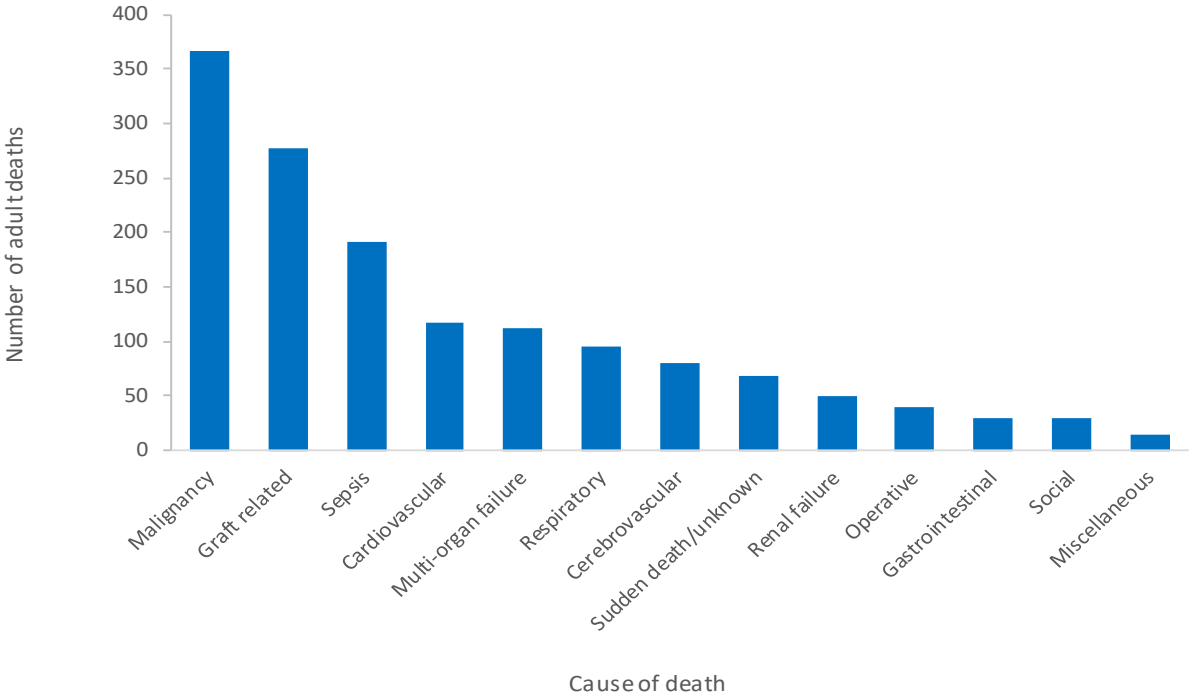
Figure 64. Paediatric cause of death



14.3 Adult Patients – Cause of Death

Malignancy (25% total: de novo malignancy 13%; recurrent malignancy 12%; donor transmitted malignancy 0.1%) is the most frequent cause of death in adult patients. Graft-related causes (19%) and sepsis (13%) are the next largest categories of adult deaths (Figure 65).

Figure 65. Adult cause of death

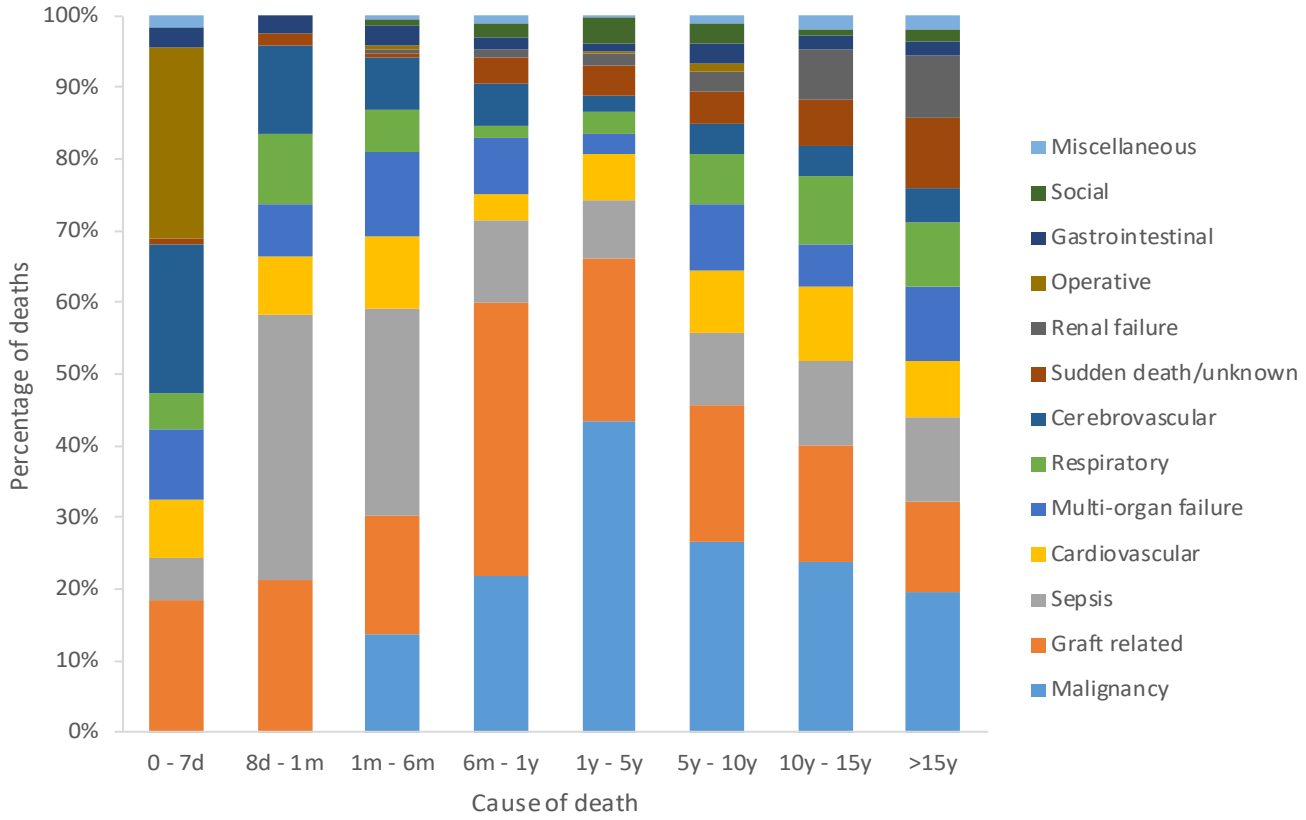


14.4 Cause of Death by Time to Death

Just under a third of all deaths occurred within the first year of transplant. In the first 7 days post-transplant, 8% deaths occurred, a further 7% from day 8 to the end of the first month and 16% after the first month and before the end of the first year. 23% of patients died between years 1 and 5, 18% between years 5 and 10 and 27% after 10 years.

The cause of death profile changes over the different time post-transplant time periods (Figure 66). Operative, cerebrovascular and graft-related causes of death predominate in the first week, sepsis is commonest from 8 days to 6 months, malignancy and graft-related commonest from 6 months to 5 years and malignancy, graft related and sepsis causes are dominant causes of death after 5 years.

Figure 66. Cause of death by time to death post-transplant – all patients

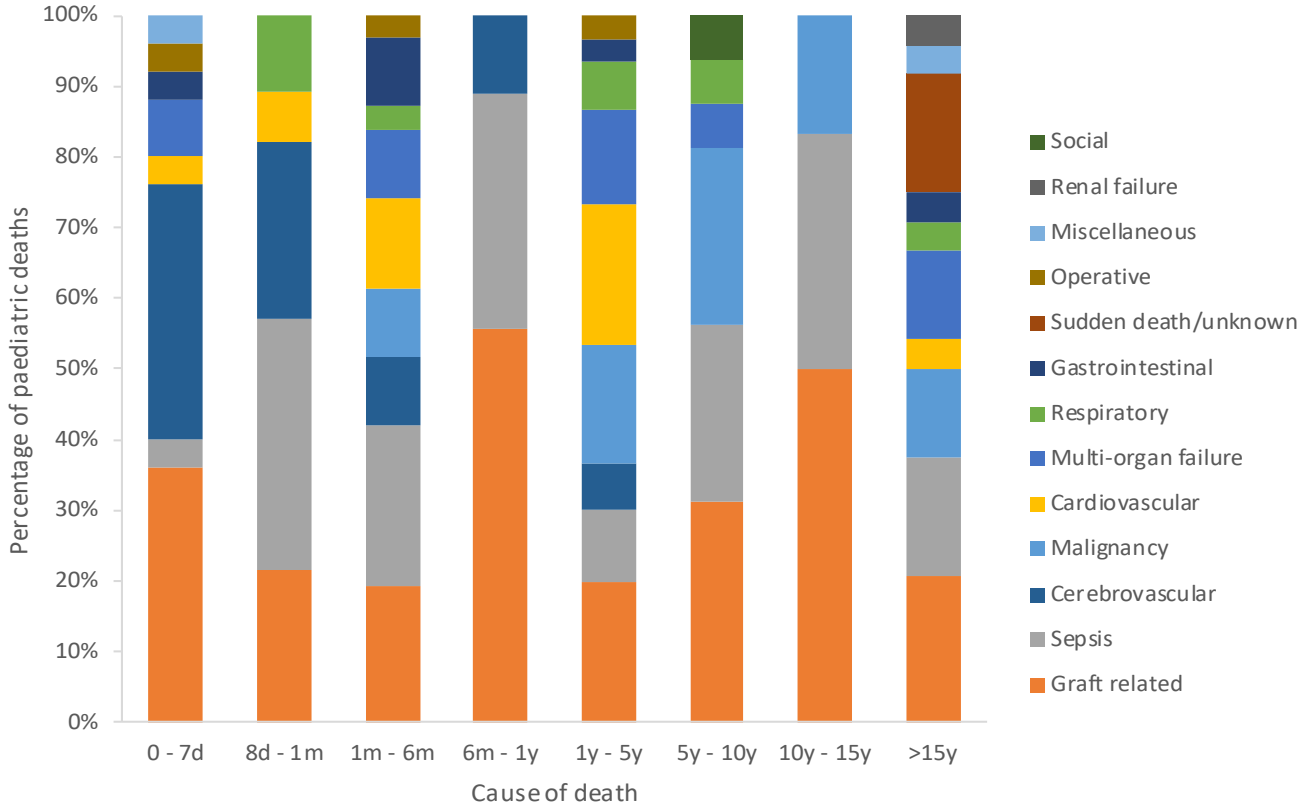


14.5 Paediatric Cause of Death by Time to Death

In children, 55% all deaths occurred within the first year of transplant. In the first 7 days post-transplant, 15% deaths occurred, a further 17% from day 8 to the end of the first month, 23% after the first month and before the end of the first year, 18% between years 1 and 5, 9% between years 5 and 10 and 18% after 10 years.

Cerebrovascular and graft-related causes of death predominated in the first week post-transplant (Figure 67). Rejection was the main type of graft-related deaths after one month. Sepsis and graft-related causes were important causes of death in all time periods after the first week and malignancy became an important cause of death after 5 years.

Figure 67. Paediatric cause of death by time to death post-transplant

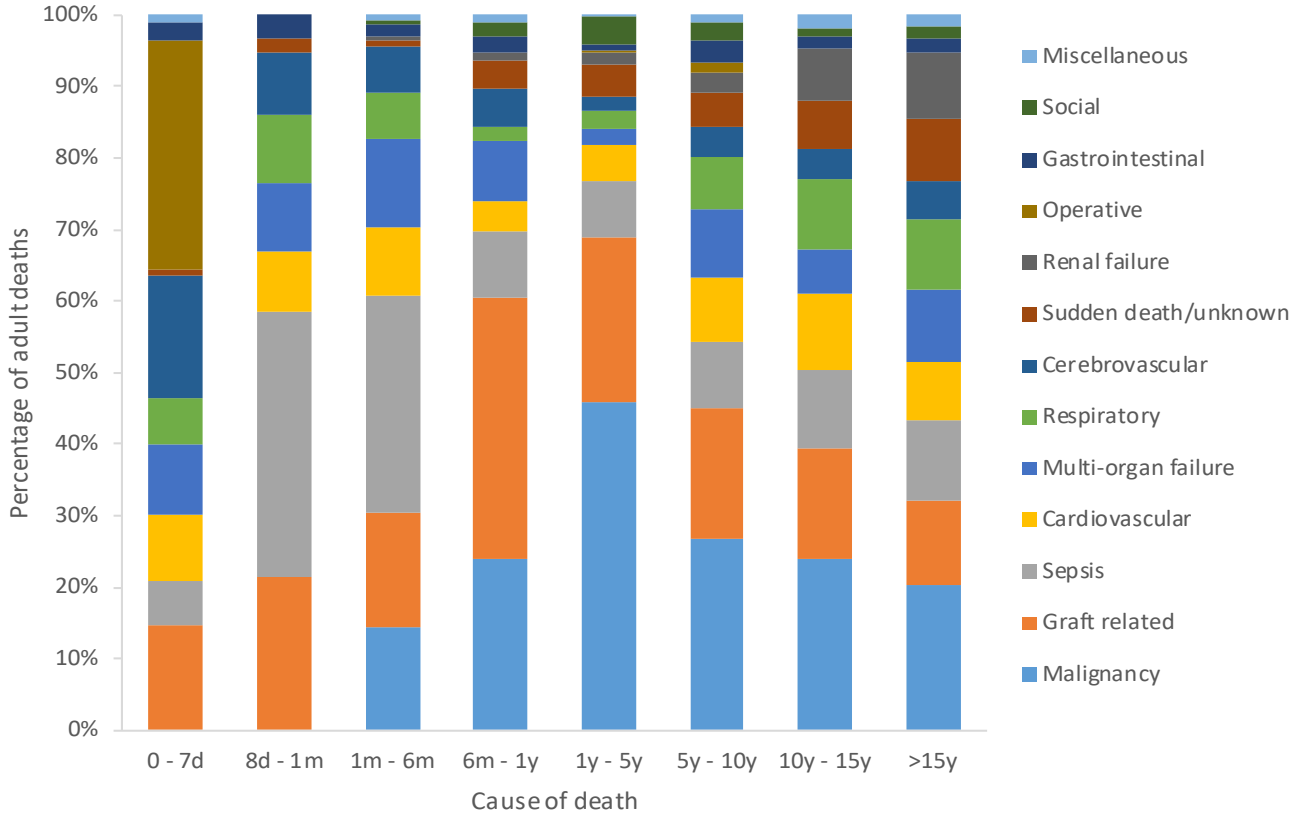


14.6 Adult Cause of Death by Time to Death

In adults, 30% all deaths occurred within the first year of transplant. In the first 7 days post-transplant, 7% deaths occurred, a further 6% from day 8 to the end of the first month, 16% after the first month and before the end of the first year, 23% between years 1 and 5, 19% between years 5 and 10 and 28% after 10 years.

Operative, cerebrovascular and graft-related causes and multi-organ failure were prominent in the first week post-transplant (Figure 68). Sepsis was the predominant cause from 8 days to 6 months, graft-related causes from 6 months to 1 year and malignancy and graft related causes from 1 year.

Figure 68. Adult cause of death by time to death post-transplant



15 Liver Transplantation and Cancer

The Liver Transplantation and Cancer Report is produced by Pamela Dilworth, Liver Cancer Registry, Royal Prince Alfred Hospital, Sydney.

15.1 Cancer in Liver Transplant Recipients

Total number patients transplanted = 5786

At Transplant	Number of patients	
Liver cancer as indication for transplant	557	(10%)
Liver cancer as a secondary diagnosis	869	(15%) 873 cancers
Total*	1423	(25%)
Post Transplant		
Recurrent liver cancer	169	(12% pts with cancer at transplant)
De novo cancer	453	(7%) 484 cancers
Skin cancer	898	(15%)
Total	1448	(27%)
Multiple cancer types (non skin and skin)	343	(6% of all patients)
Multiple non skin cancers	124	(2% of all patients)
Developed non skin cancer < 90days	10	

* 3 pts had a primary & secondary liver cancer, 4 patients had 2 secondary/incidental liver cancers

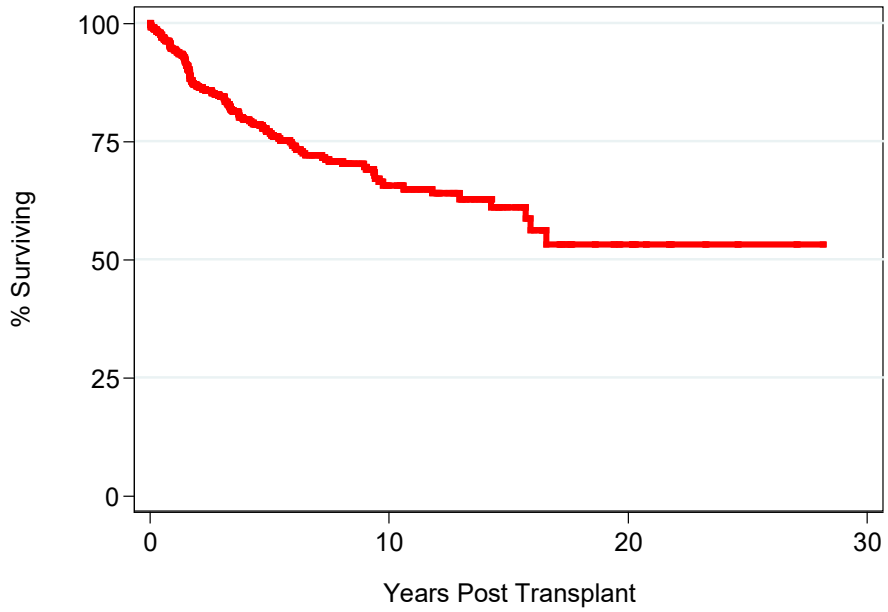
15.2 Liver Cancer as Primary Diagnosis

n = 557/5786 (10%)

Type of cancer	Number of patients	Died	Died of this cancer	
Hepatocellular cancer	499	108	54	(11%)
Hepatoblastoma	32	5	4	(13%)
Fibrolamellar	6	5	2	(33%)
Cholangiocarcinoma	6	1	1	(17%)
Epitheloid haemangioendothelioma	5	0	0	
Carcinoid	4	4	4	(100%)
Hepatocellular malignant neoplasm	1	0	0	
Angiosarcoma	1	1	1	(100%)
Erythyoid leukaemia	1	1	1	(100%)
Gastrinoma	1	1	1	(100%)
Pancreatic islet cell	1	1	1	(100%)
Total	**557**	**127**	**69**	
	10% (of all pts)	23% (of primary liver cancer pts)	12% (of primary liver cancer pts)	

15.3 Overall Survival - Primary Liver Cancer

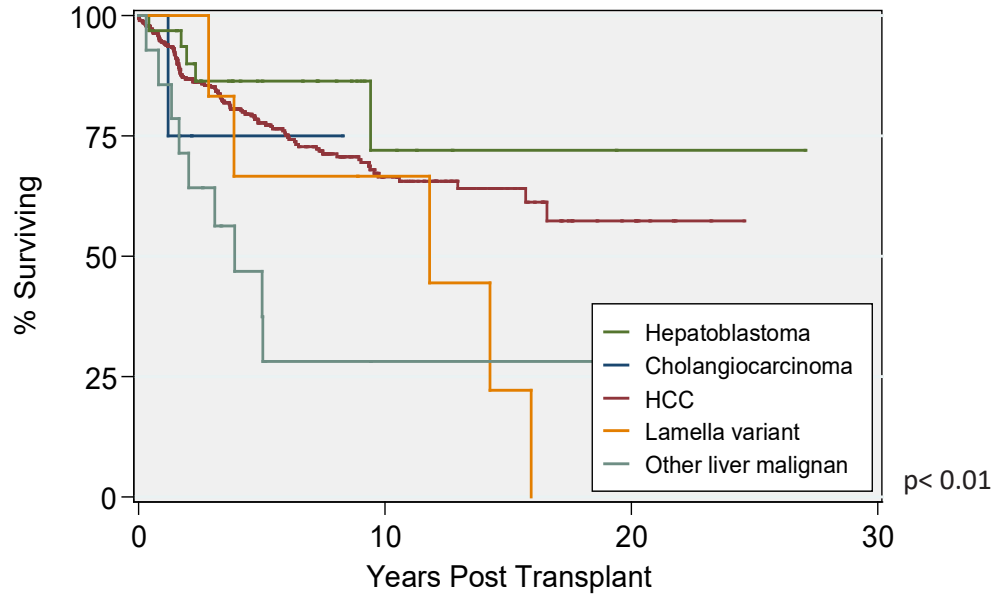
n =557/5786 (10% of pts transplanted)



Number at risk				
	553	90	10	0

15.4 Overall Survival – Primary Liver Cancer by Type

n =557/5786 (10% of pts transplanted)

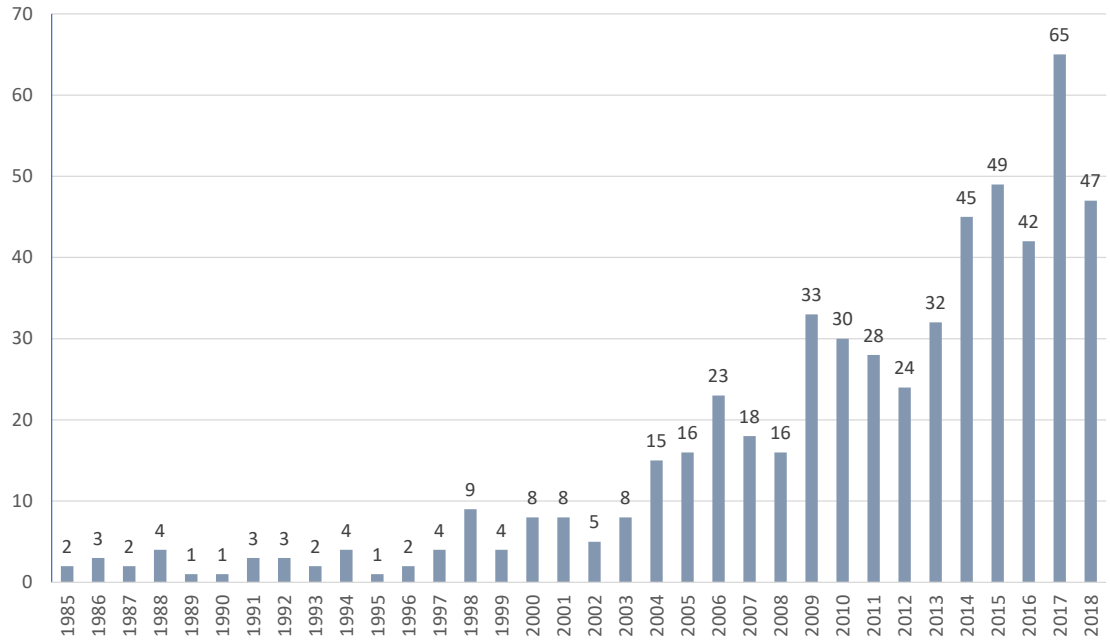


Number at risk				
Cholangiocarcinoma	6	0	0	0
HCC	495	81	8	0
Hepatoblastoma	32	5	1	0
Lamella variant	6	3	0	0
Other liver malignan	14	1	1	0

* 3 pts had two primary liver cancers

15.5 Primary Liver Cancer Incidence

n=557/5786 (10%)



15.6 Liver Cancer as a Secondary Diagnosis

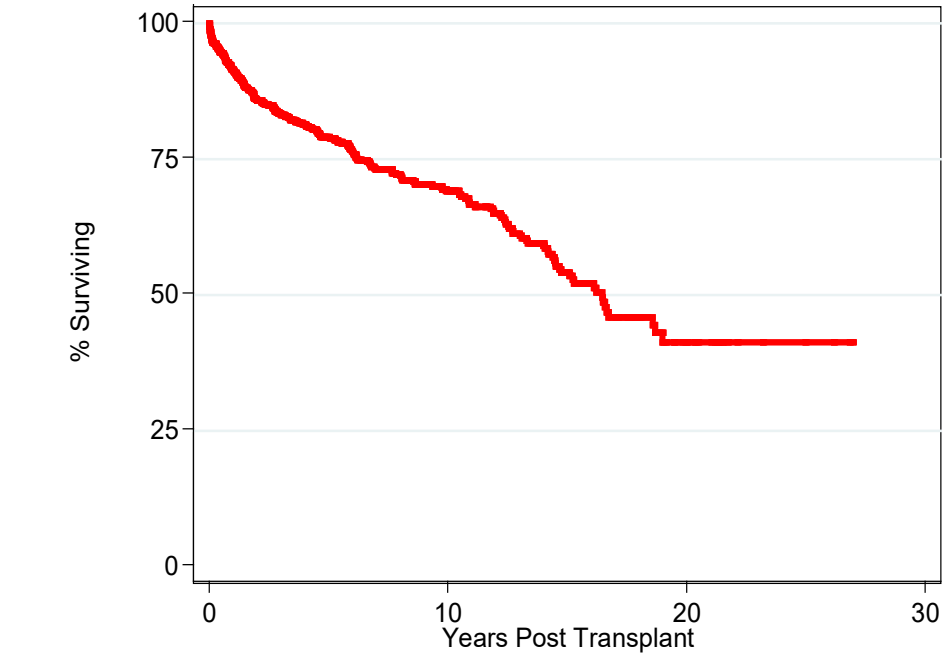
n = 869/5786 (15% pts)

	Number of patients	Died	Died of This Cancer	
Hepatocellular cancer*	812	206	61	(7%)
Cholangio cancer*	46	33	21	(46%)
Adenocarcinoma	5	4	1	(20%)
Fibrolamellar	4	0	0	
Hepatoblastoma*	3	2	0	
Epitheloid haemangioendothelioma	2	1	1	(50%)
Angiosarcoma	1	1	1	(100%)
	873	**247**	**85**	
Total	*Cancer in 869 pts	31% (of secondary liver cancer pts)	12% (of secondary liver cancer pts)	

* 4 patients had 2 secondary liver cancers

15.7 Overall Survival - Liver Cancer as a Secondary Diagnosis by Type

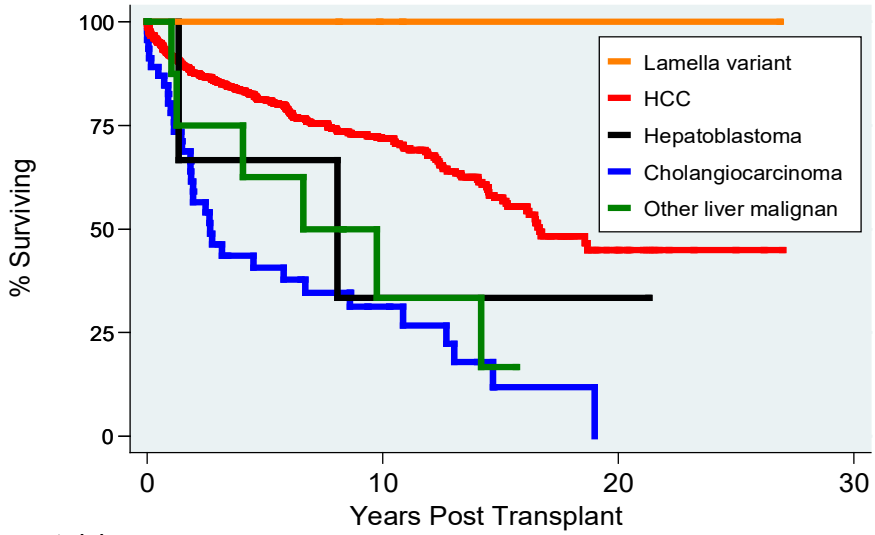
n = 869/5786 (15% pts)



Number at risk				
	868	213	18	0

15.8 Liver Cancer as a Secondary Diagnosis by Type

n = 869/5786 (15% pts)



Number at risk				
Cholangiocarcinoma	46	8	0	0
HCC	807	200	16	0
Hepatoblastoma	3	1	1	0
Lamella variant	4	2	1	0
Other liver malignan	8	2	0	0

15.9 Liver Cancer - (Primary or Secondary Diagnosis)

n = 1423/5786 (25%)

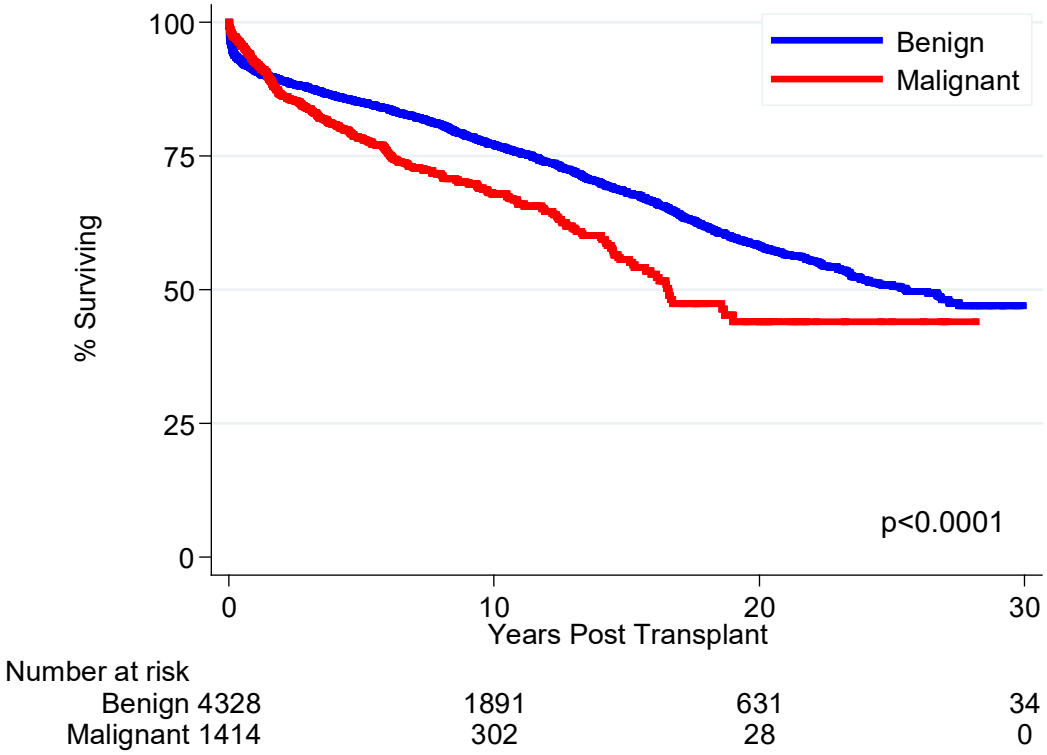
Type of cancer	Number of cancers	Died	Died of this cancer	
Hepatocellular cancer*	1311	314	115	(9%)
Cholangiocarcinoma*	52	34	22	(47%)
Hepatoblastoma*	35	7	4	(11%)
Fibrolamellar	10	5	2	(20%)
Epitheloid haemangioendothelioma	7	1	1	(14%)
Adenocarcinoma	5	4	1	
Carcinoid	4	4	4	(100%)
Angiosarcoma	2	2	2	(100%)
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	
Total	**1430**	**374**	**154**	
	* Cancer in 1423 pts	26% (of liver cancer pts)	11% (of liver cancer pts)	

* 3 patients had primary & secondary liver cancers, 4 patients had 2 secondary liver cancers

15.10 Patient Actuarial Survival

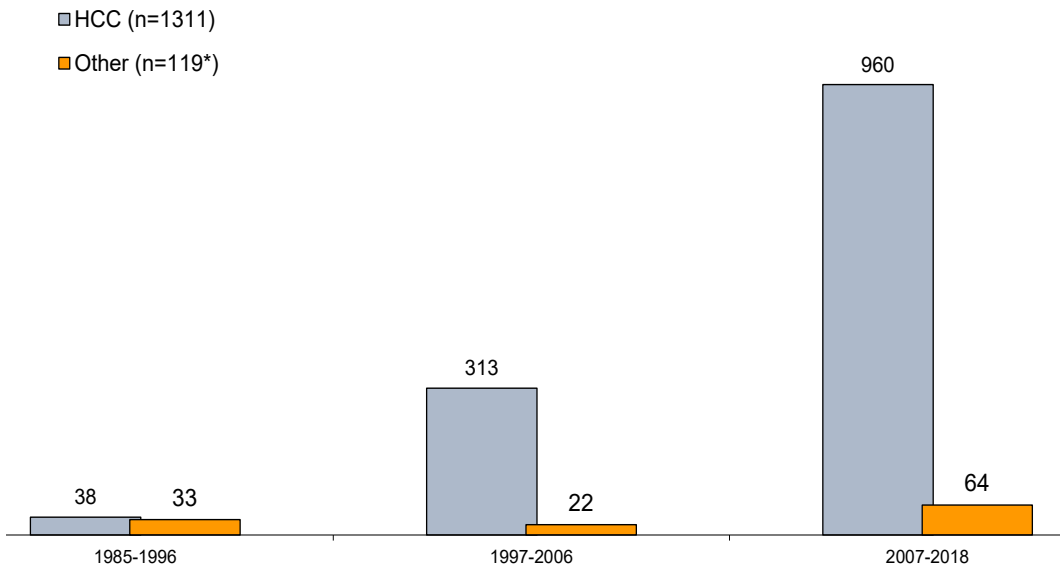
Benign Disease vs Pre Transplant Liver Malignancy

n =5786



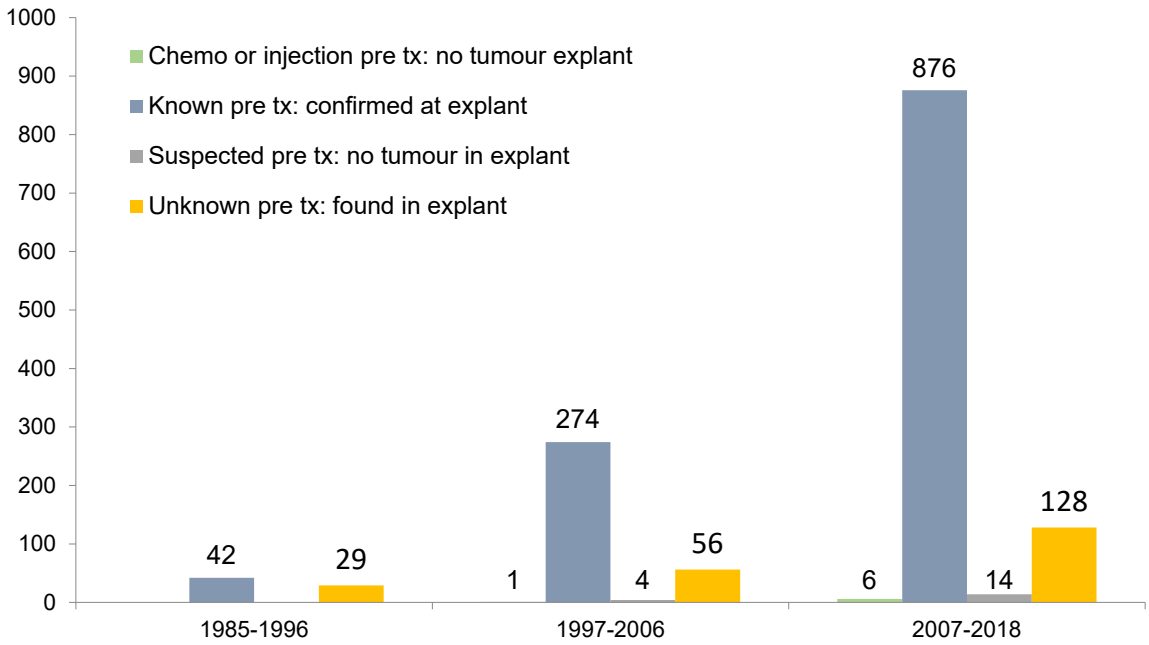
15.11 Liver Cancer at Transplantation

n = 1423/5786 (25%)

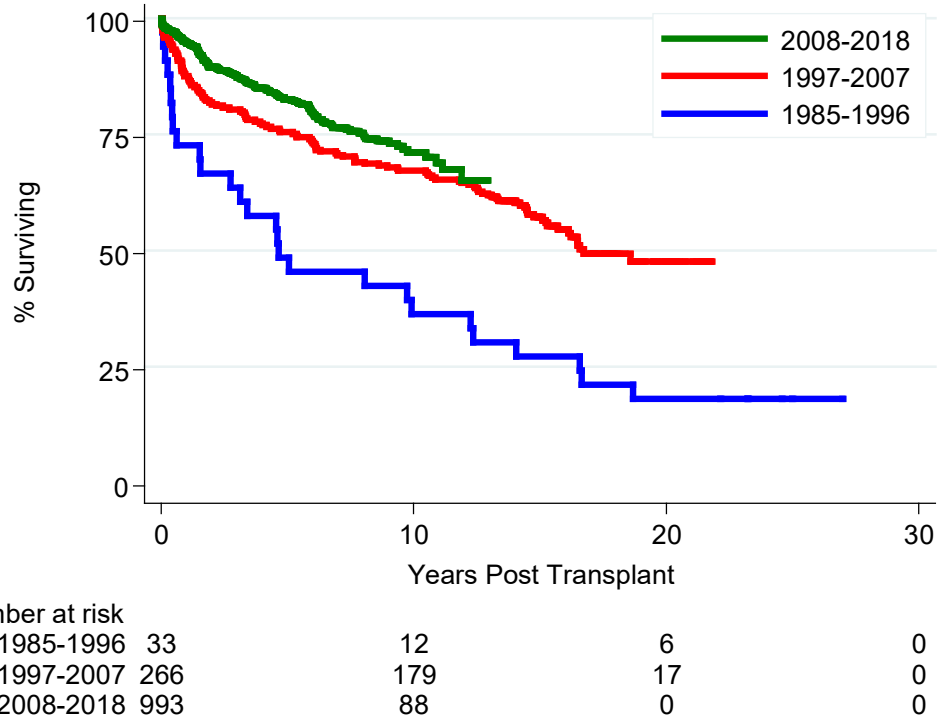


* 4 patients had 2 secondary cancers; 3 patients had a primary and secondary cancer

15.12 HCC at Transplantation



15.13 HCC vs Era (Primary and Secondary Indication)



15.14 De Novo Non Skin Cancer

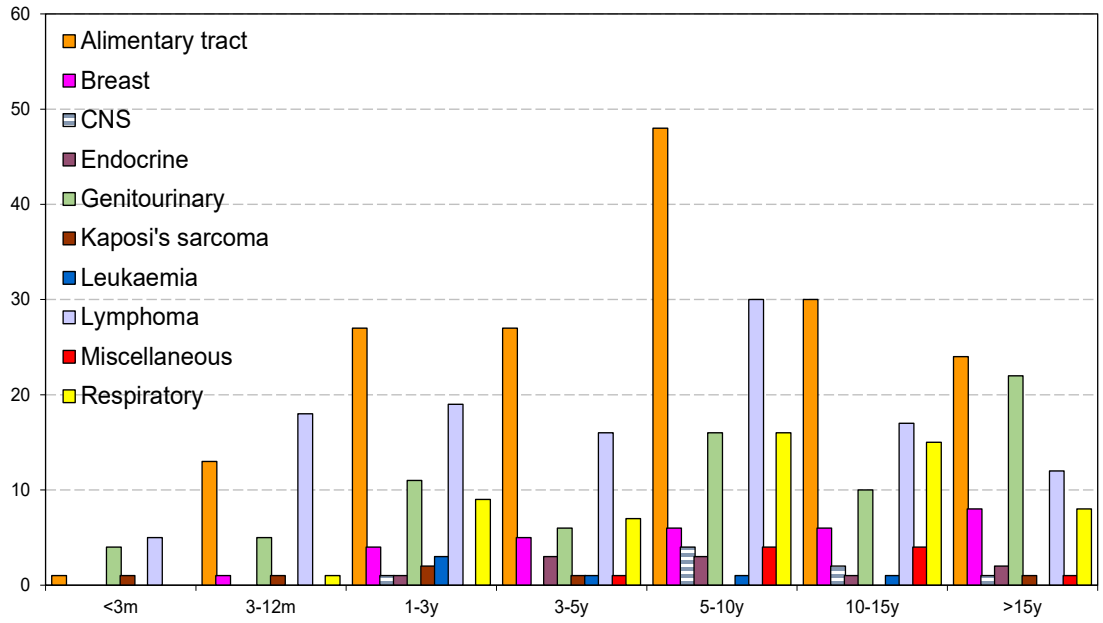
n = 453/5786 (8%)

	Number of patients	Male	Female	Age of pts (years)	Median age	Time to diagnosis (months)	Median time to diagnosis	Died of This Cancer	
Alimentary*	166	121	45	5 – 84	60	3 – 316	83	77	46%
Lymphoma*	121	70	51	1 – 79	50	1 – 283	66	48	39%
Genitourinary*	72	45	27	21 – 82	61	1 – 350	100	8	11%
Respiratory*	55	41	14	29 – 80	61	7 – 278	103	42	75%
Breast*	31	1	30	30 – 74	56	11 – 291	101	12	37%
Endocrine	10	4	6	36 – 70	53	35 – 346	82	2	20%
Miscellaneous*	9	6	3	57 – 73	65	41 – 191	110	6	70%
CNS*	8	5	3	16 – 75	65	14 – 212	89	6	75%
Leukaemia*	6	4	2	3 – 66	54	16 – 157	37	2	33%
Kaposi's	6	4	2	32 – 76	56	2 – 254	26	0	
Total	**484**	**301**	**183**	**1 – 84**	**59**	**1 – 350**	**58**	**203**	**45%**
*Cancer in 453 pts									(of pts with cancer)

* 28 patients had 2 de novo cancers, 3 patients had 3 de novo cancers

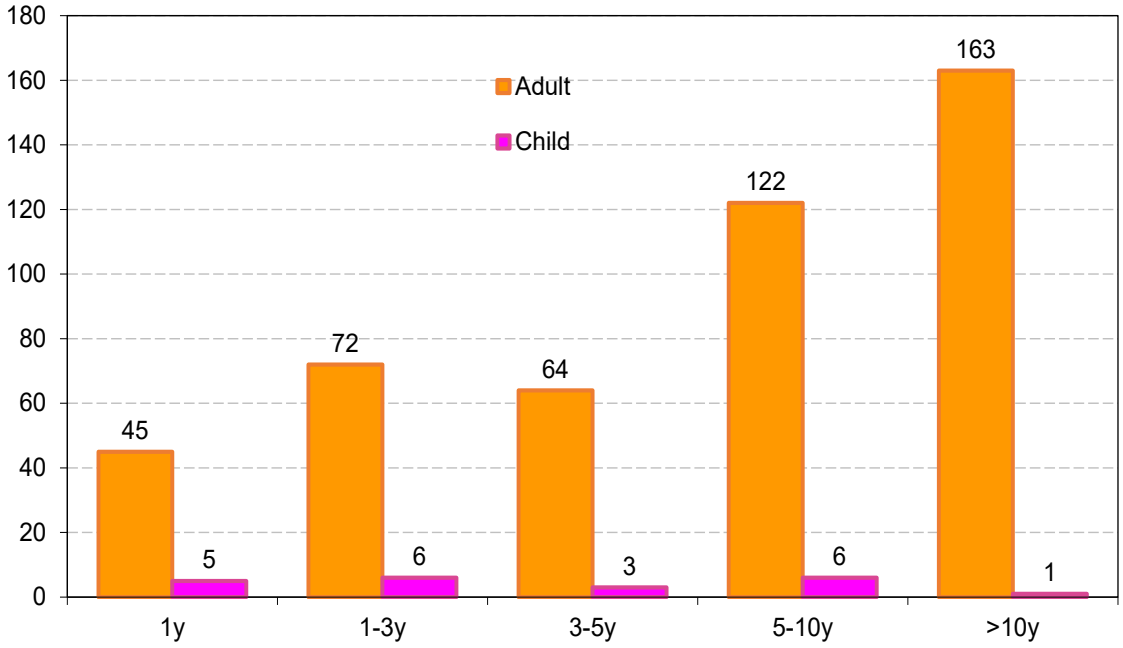
15.15 Time to Diagnosis of De Novo Non Skin Cancer (3m - >15y)

484 cancers in 453 pts (8% of all pts)
n = 5786



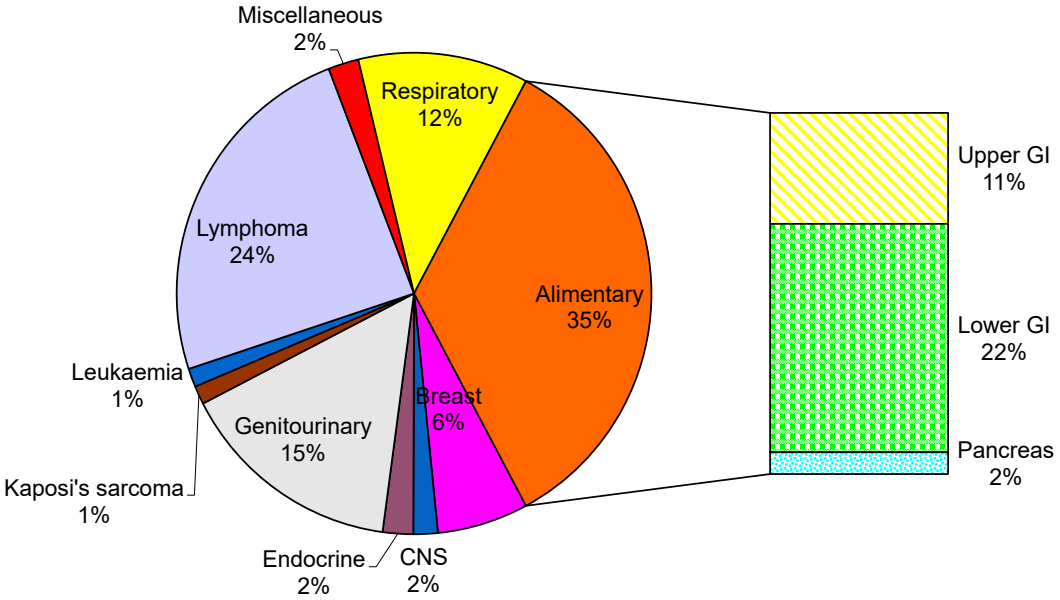
15.16 Time to Diagnosis of Any Non Skin Cancer

484 cancers in 453 pts (8% of all pts)
n = 5786



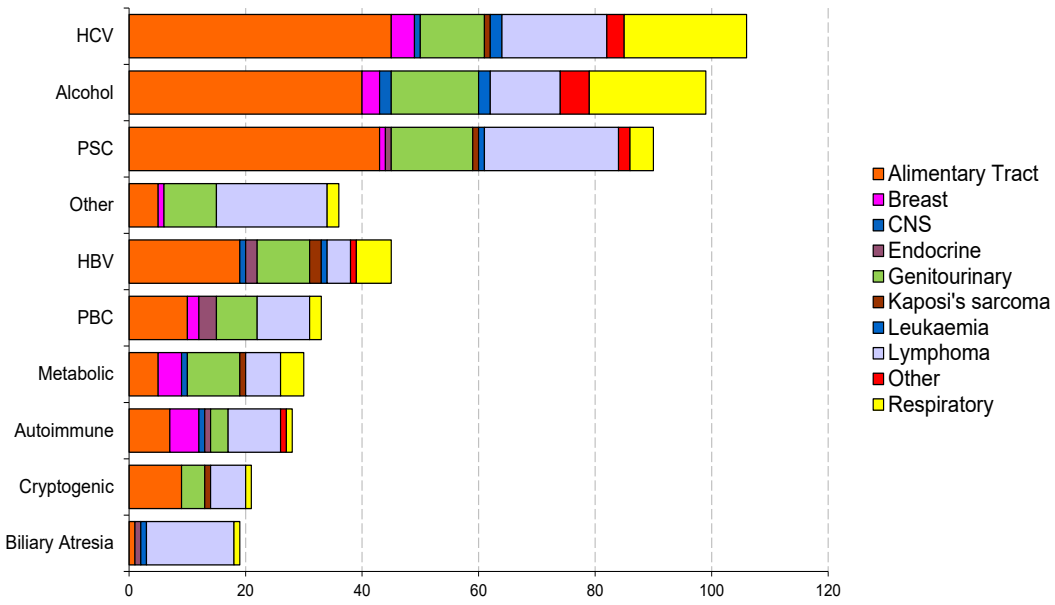
15.17 De Novo Non Skin Cancer

n = 453/5786 (8%)



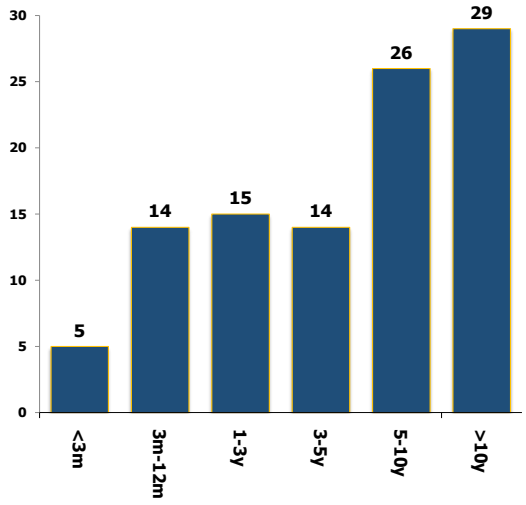
15.18 Pre Transplant Disease and De Novo Non Skin Cancer

n = 453/5786 pts (8%)

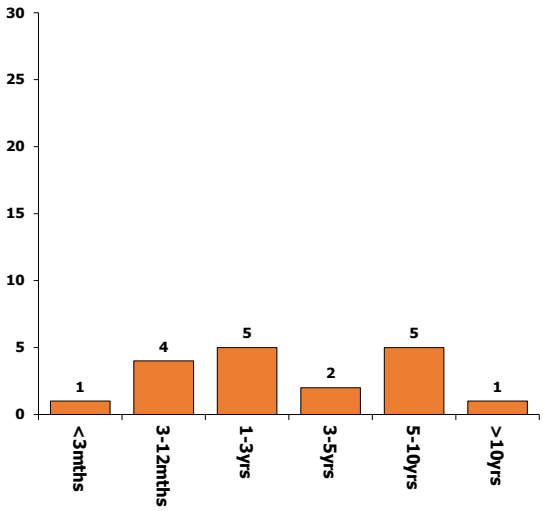


15.19 Time to Diagnosis of Lymphoma

Lymphoma - Adults
n= 103 (21% adults with de novo cancer)



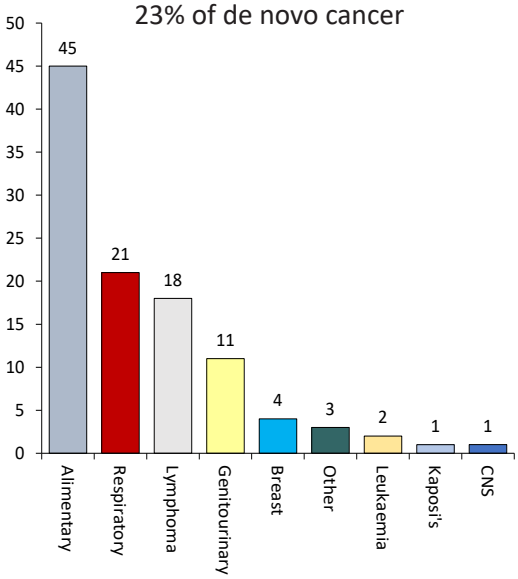
Lymphoma - Children
n = 18 (86% children with de novo cancer)



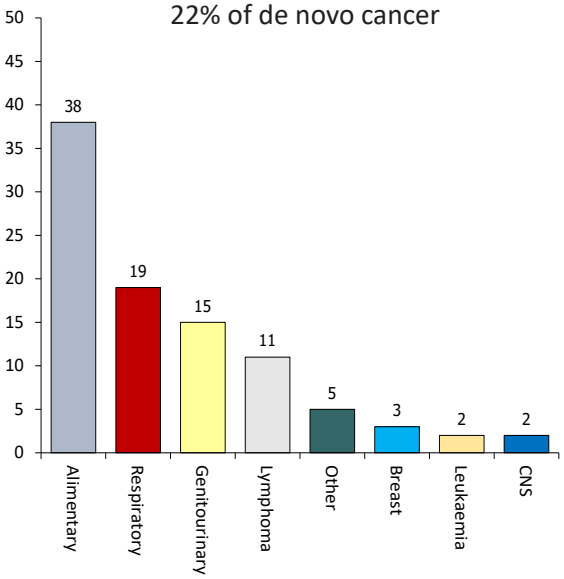
15.20 Pre Transplant Disease and De Novo Non Skin Cancer

n = 453 (484 cancer)/5786 pt (8%)

HCV - 106/454
23% of de novo cancer

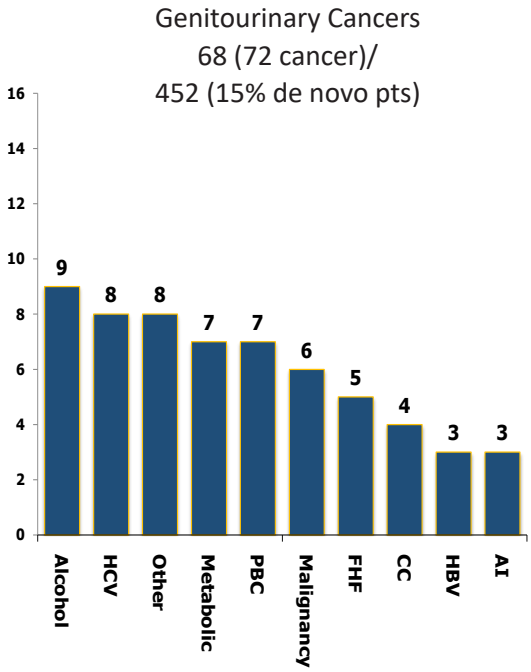


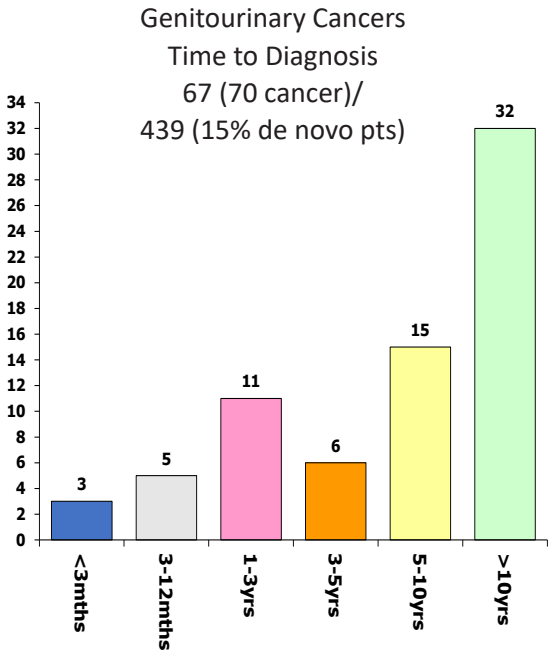
Alcohol - 95/454
22% of de novo cancer



15.21 Pre Transplant Primary Liver Disease and De Novo Non Skin Cancer

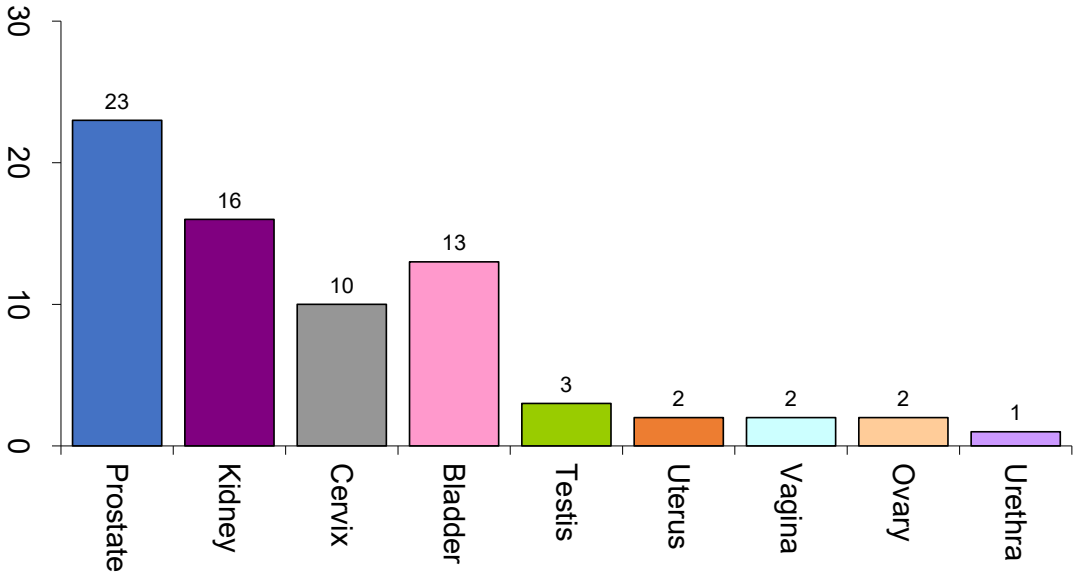
n = 453 (484 cancer)/5786 pts (8%)





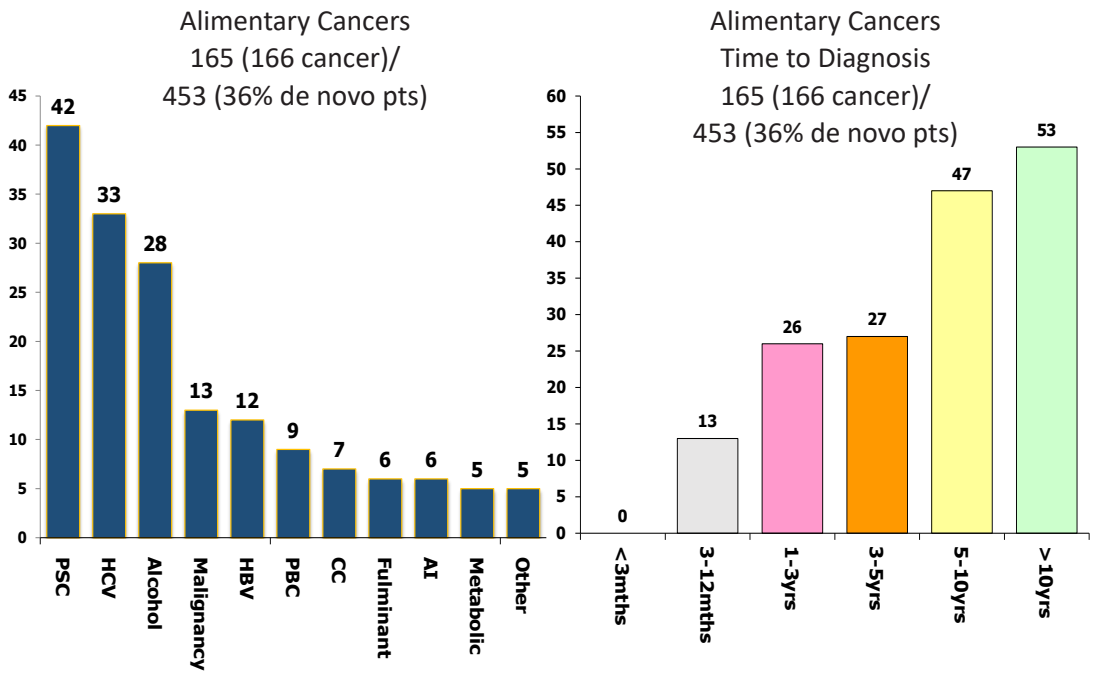
15.22 De Novo Non Skin Cancer - Genitourinary Tract Incidence

n = 72/484 cancers (15%)



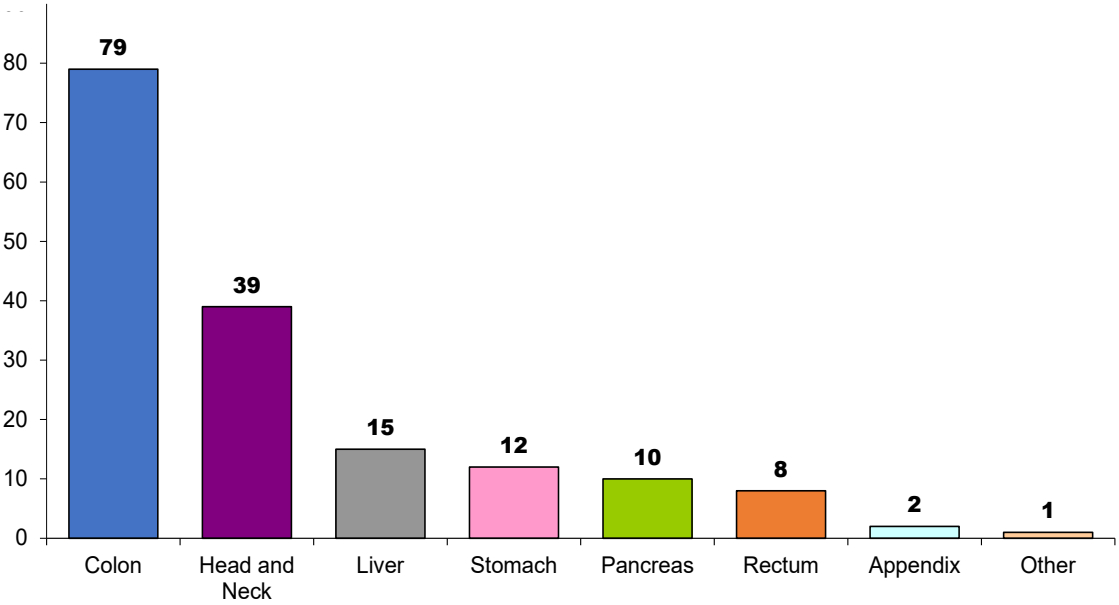
15.23 Pre Transplant Primary Disease and Alimentary Cancer

n = 453 (484 cancer)/5786 pts (8%)

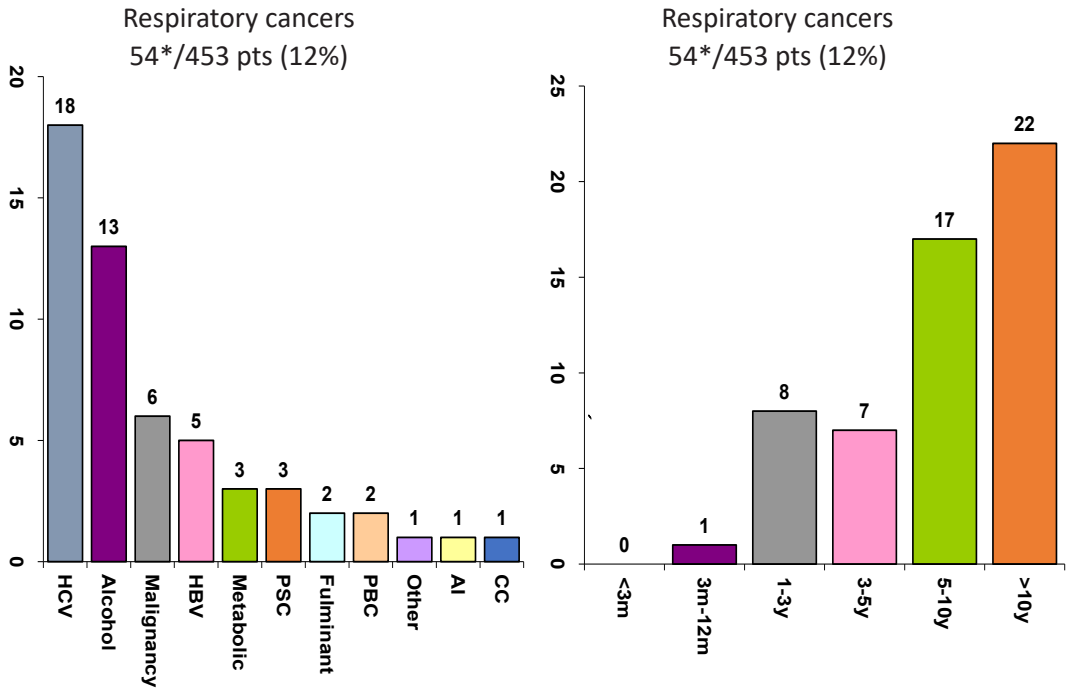


15.24 De Novo Non Skin Cancer - Alimentary Tract Incidence

n = 165 (166 cancer) /453 pts (38%)



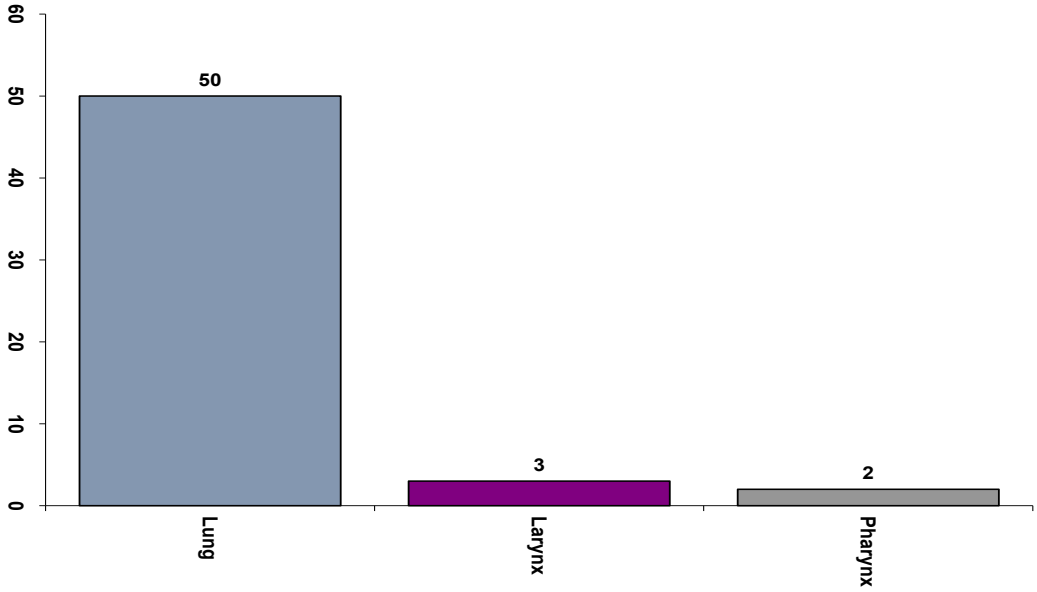
15.25 De Novo Non Skin Cancer - Respiratory Cancer Incidence



* 1 patient had 2 respiratory cancers

15.26 De Novo Non Skin Cancer - Respiratory Cancer Incidence

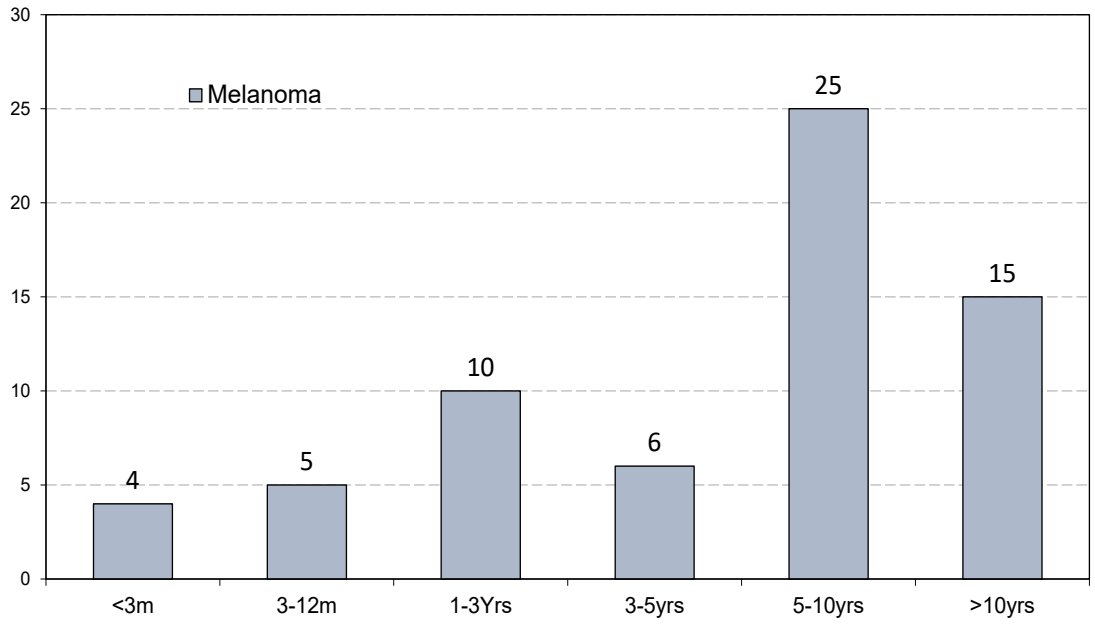
Respiratory cancers
54*/453 pts (12%)



1 patient had 2 respiratory cancers

15.27 Time to Melanoma Skin Cancer Development Post Transplant

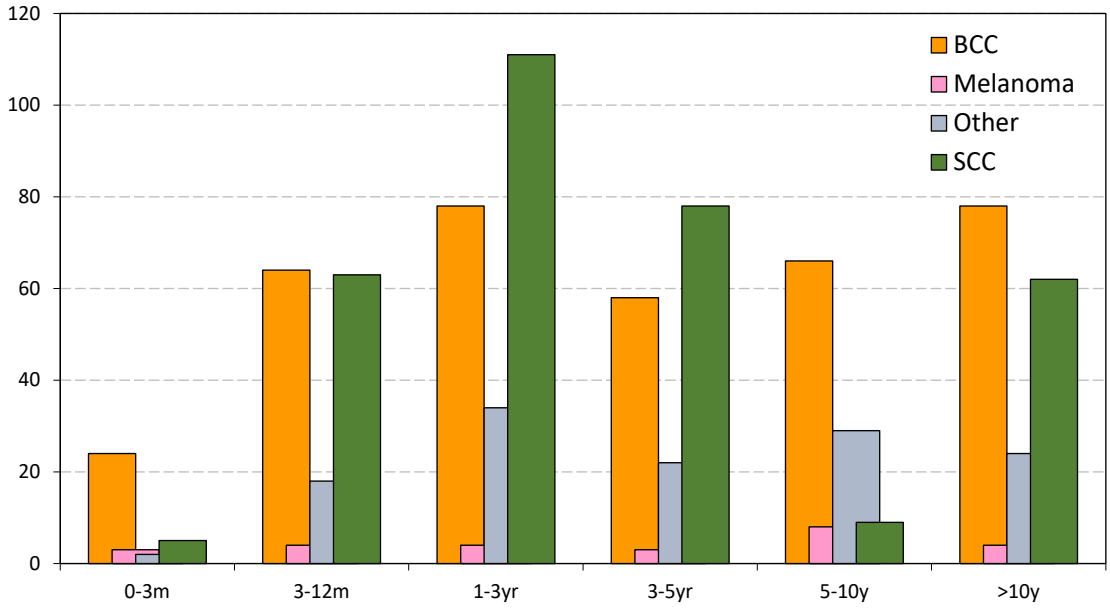
63* (1% of all pts)
n =5786



* 2 patients developed 2 melanoma

15.28 Time to 1st Skin Cancer Development

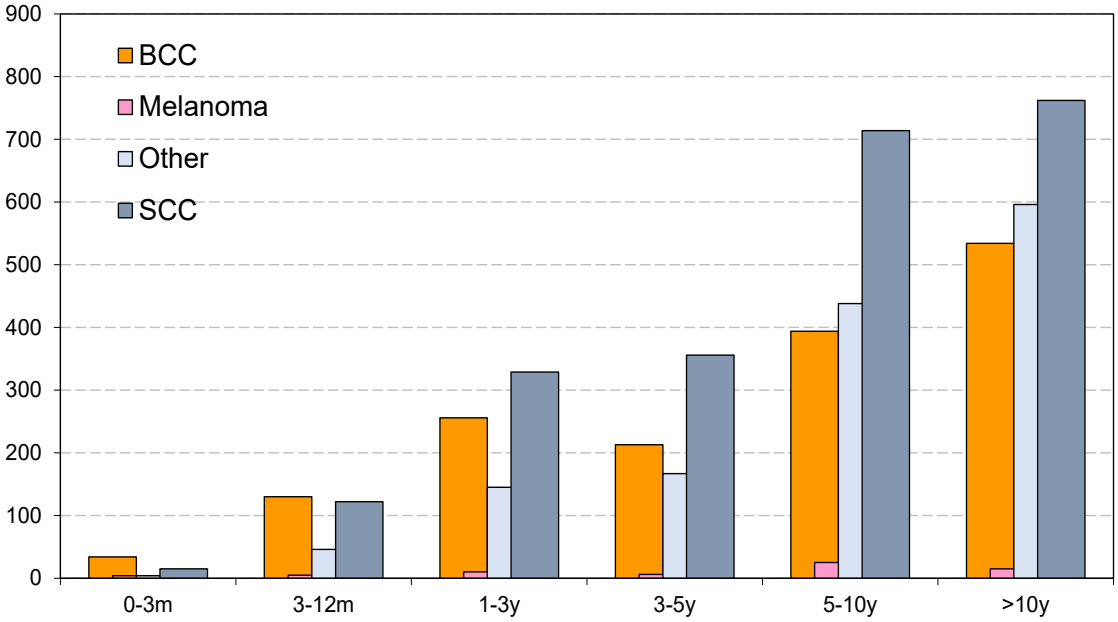
898*/5786 (15% of all pts)



* 426 Patients developed multiple skin cancer types

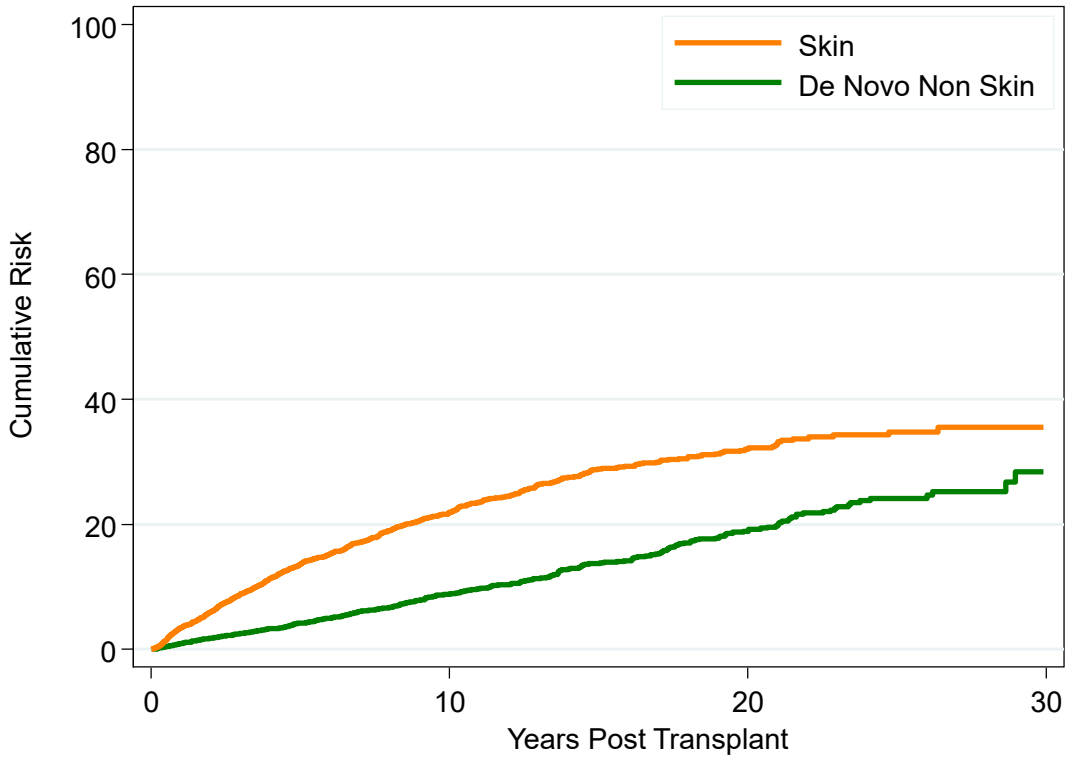
15.29 Time to Any Skin Cancer Development

898/5786 (15% of all pts)



898 (15%) pts developed skin cancer post transplant 426 (47%) pts have multiple skin cancer types

15.30 Cumulative Risk of Diagnosis of Skin or Non Skin Cancer Following Liver Transplant 1985-2017



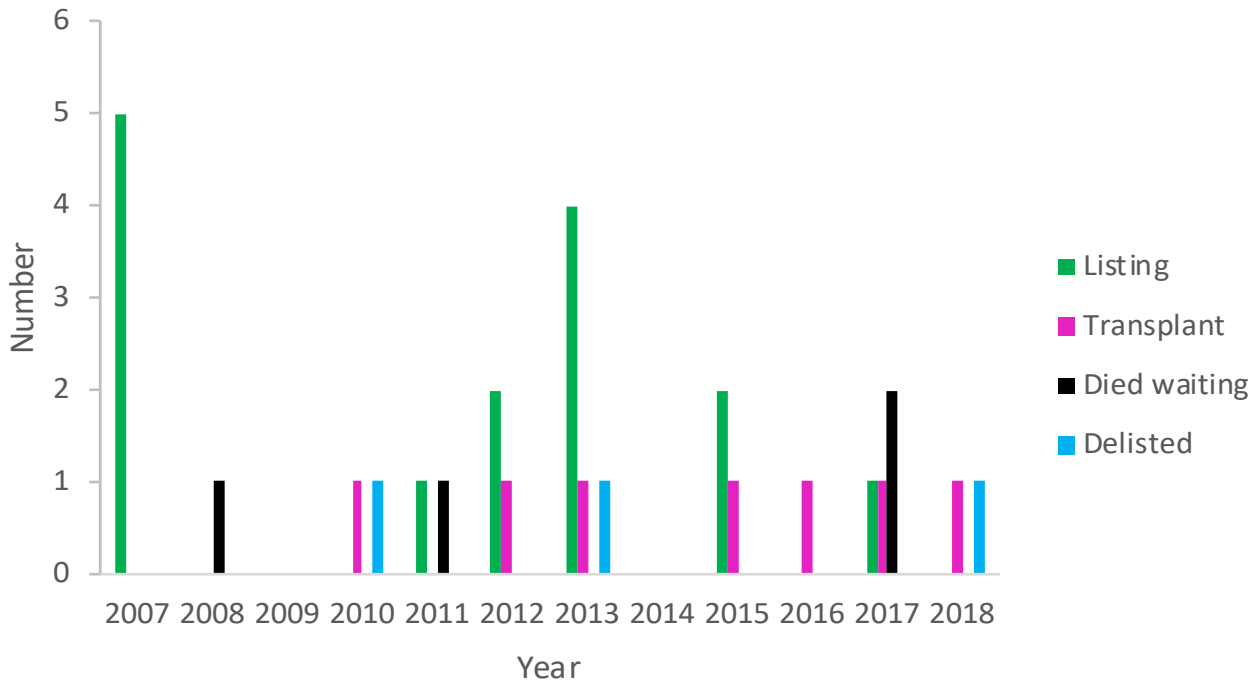
16 Intestinal Transplantation

The Australian Intestinal Transplant Service, co-located with the Victorian Liver Transplant Unit, offers an intestinal transplant service to Australian and New Zealand paediatric and adult patients. The first intestinal transplant was performed by the unit in 2010.

16.1 Waiting list

Fifteen patients have been listed for intestinal transplantation (see Figure 69). Seven patients were transplanted, three were delisted, four died waiting and one was still waiting at the end of 2018.

Figure 69. Waiting list trends over time for intestinal transplantation



16.2 Demographic Characteristics and Diagnoses

The demographic characteristics and diagnoses of patients listed for intestinal transplantation and for those transplanted is shown in Table 51. The majority of the five children listed had short bowel syndrome due to gastroschisis, whilst the 10 adults were listed for short bowel syndrome after intestinal resection for a variety of causes, motor disorders and liver failure with porto-mesenteric thrombosis. Three children have been transplanted, two for short bowel syndrome and one for Hirschsprung's disease. Four adults have been transplanted, one for short bowel syndrome, two for Hirschsprung's disease and one for liver failure with porto-mesenteric thrombosis.

Table 51. Demographic characteristics and diagnoses of children and adults listed and transplanted for intestinal transplantation. Data are shown as number or median (range).

Characteristic	Listed		Transplanted	
	Children	Adults	Children	Adults
N	5	10	3	4
Age	7 (4-9)	36 (22-60)	10 (5-13)	29 (24-47)
Gender				
Male	4	7	3	3
Female	1	3	0	1
Diagnosis				
Short bowel syndrome				
Gastroschisis	4	0	2	0
Small intestine leiomyoma	0	1	0	0
Small intestine adenocarcinoma	0	1	0	0
Volvulus	0	1	0	1
Motor disorder				
Hirschsprung's disease and variants	1	3	1	2
Hollow visceral myopathy	0	1	0	0
Other				
Liver failure with porto-mesenteric thrombosis	0	3	0	1

16.3 Organs Transplanted

Four patients underwent liver, pancreas and small intestine transplantation, one underwent multivisceral (liver, stomach, pancreas and small intestine) transplantation, one underwent liver, pancreas, small intestine and kidney transplantation and one patient underwent intestine and kidney transplantation.

16.4 Survival

Six of the seven intestinal transplant recipients are alive with a functioning graft and full enteral autonomy. One patient died of respiratory infections with a functioning graft at 3 months. The 1-, 3- and 5-year patient and graft survival is 86% (Figure 70, Figure 71).

Figure 70. Patient survival after intestinal transplantation

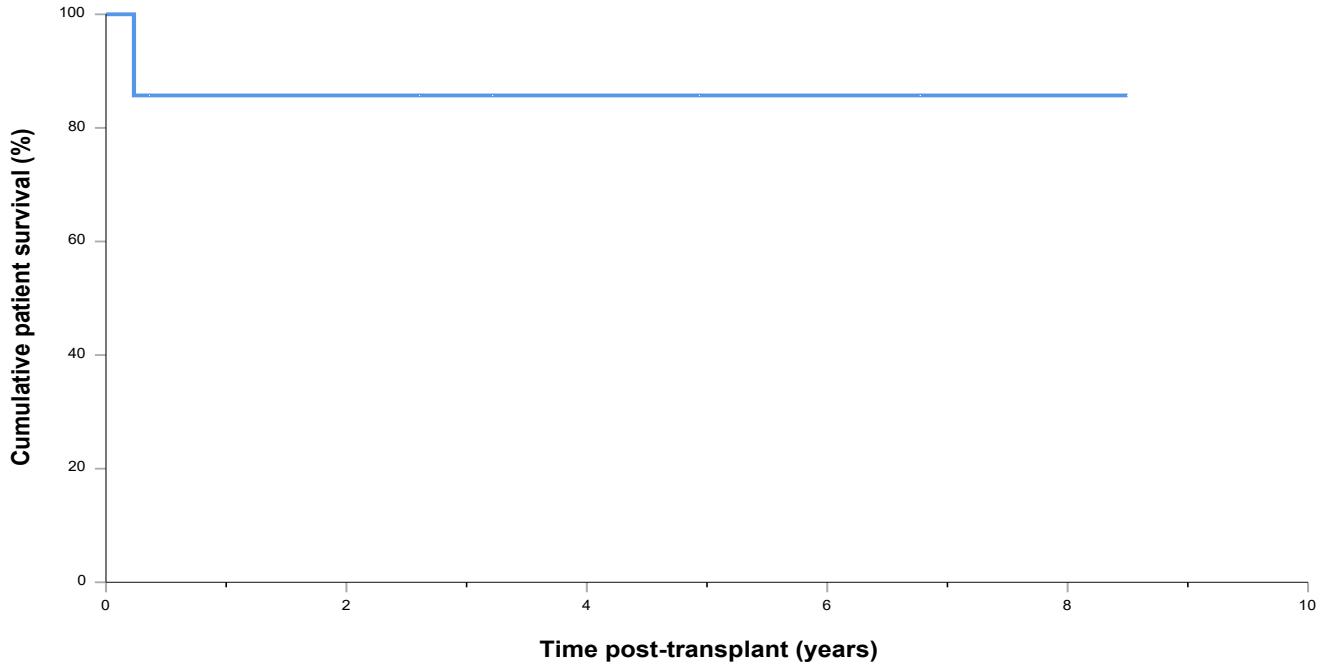
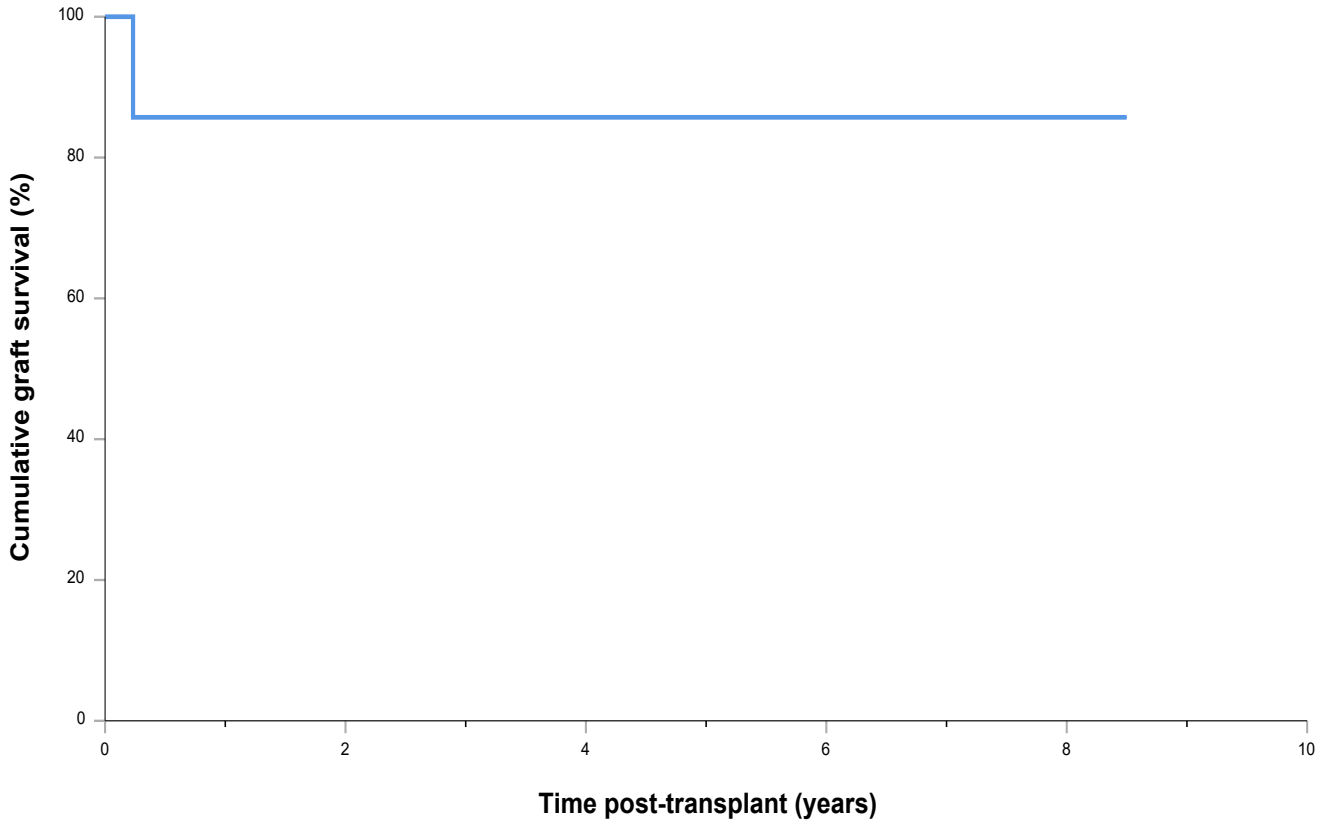


Figure 71. Graft survival after intestinal transplantation



17 Appendix I. Glossary

Adenocarcinoma	A cancer that arises from tissues that form glands.
Anoxia	Inadequate delivery of oxygen to the brain that can lead to brain death. Examples include drowning and severe asthma.
Biliary atresia	A rare condition that babies can be born with in which the bile ducts do not form properly. Sometimes this can be fixed by doing an operation to join the bile ducts in the liver to the bowel but sometimes a liver transplant is required.
Blood group compatibility	The relationship between the donor and recipient blood groups. These can be identical (A to A, AB to AB, B to B or O to O), compatible (O to A, AB or B, or A or B to AB) or incompatible (A, AB or B to O, AB to A or O, A to B or B to A). Some blood group A patients have a low level of A antigen (a protein on the surface of the cells) that means they are less likely to be rejected when transplanted into a patient who is technically incompatible. This is called blood group A, non-A1 or sometimes A2.
Category 1	These are patients who have acute liver failure and have become extremely unwell, requiring admission to the Intensive Care Unit and have a breathing tube. They have a very high risk of dying without a liver transplant. Because of this, any available, suitable donor liver in Australia and New Zealand is offered to the liver transplant unit looking after the patient to try to save their life.
Category 2	These are patients who are usually not as sick as category 1 patients but who have a high risk of dying without transplantation and who are likely to get worse while they are waiting for transplantation. This includes certain patients with acute liver failure who do not yet require a breathing tube, children with chronic (longstanding) liver disease who have been admitted to an Intensive Care Unit, children with a severe metabolic disorder (disturbance of function of cells) or a rare form of liver cancer that occurs in children and patients who need a combined liver-intestine transplant. The liver transplant units in Australia and New Zealand are notified when these sorts of patients are waiting for a liver transplant so that if a suitable donor liver becomes available, the liver could be offered to the liver transplant unit looking that patient.
Cholestatic disease	A collection of diseases that affect the bile ducts in the liver that can lead to liver failure.
Cirrhosis	Scarring of the liver accompanied by liver regeneration (regrowth). It can arise from many different disease processes and can lead to liver failure or hepatocellular carcinoma. Some patients with cirrhosis need liver transplantation.
Cold ischaemia time	The time between perfusing the liver with cold preservation solution in the donor to restoration of blood flow in the recipient.
Cryptogenic cirrhosis	Cirrhosis with no known underlying cause (sometimes called idiopathic).
Cumulative number	The progressive number of cases occurring over time.
Data validation and cleaning	Processes undertaken in managing the database to ensure completeness and accuracy of data.

De novo malignancy	Cancer that occurs after transplantation that was not present before transplantation.
Delisting	Taking a patient off the waiting list. This can occur because of transplantation, death, progression of liver disease or tumour or other reasons (such as the patient's condition improving, psychosocial issues or non-compliance).
Donor	A person who donates their liver or part of their liver to another person. Donors can be deceased (dead – see glossary entry on donation after brain death and donation after circulatory death) or living (see glossary entry on living donor liver transplantation).
Domino liver transplantation	In some metabolic diseases that progress slowly, it is possible to use the liver that is removed at the time of transplant and use that liver to transplant another (usually older) patient.
Donation after brain death	Death can occur in patients who have no brain function but who still have a beating heart. To determine that the patient is brain dead, two experienced doctors must confirm that the brain is no longer functioning and that the lack of brain function is permanent. This can be done by testing for reflexes that are controlled by the brain stem, the most primitive part of the brain, to make sure that all of the reflexes are absent and by making sure that there is no reversible cause for the lack of brain stem reflexes. Sometimes a scan of the brain showing no blood flow to the brain is performed instead. If the patient has been declared brain dead and the family of the deceased (dead person) has consented to organ donation, donation after brain death can occur. This is also known as DBD and has also been called heart-beating donation in the past.
Donation after circulatory death	Some patients with a severe brain injury (and occasionally in some other circumstances such as a high spinal cord injury) but who are not initially brain dead can become deceased (dead) donors if the breathing tube is removed and the heart stops. Once the heart has stopped beating and the doctor determines that it is not going to start again, the patient can be declared dead. If consent for organ donation has been obtained, the person who has been declared dead can then donate their organs. This is also known as DCD and has also been called donation after cardiac death and non-heart-beating donation in the past.
Fulminant hepatic failure	Acute liver failure (usually occurring in a person who was not known to have pre-existing liver disease). This can be due to viruses, drugs or the cause may be unknown.
Gastroschisis	A condition in which babies are born with most of their bowel outside the abdomen.
Graft survival	The proportion (often expressed as a percentage) of patients undergoing liver transplantation who are still alive with the same graft (transplanted organ) at different time periods after the transplant. In this report, graft survival time is calculated from the date of transplantation to the date the patient has another liver transplant if this has occurred or until death for patients who die without being retransplanted or until the end of the reporting year (31 December, 2018 for this report) for patients who have not been retransplanted or died by that date.

Graft number	The number of liver transplants the patient previously undergone plus 1. Thus, a patient's first liver transplant will be performed using graft 1, the second, with graft 2 and so on.
Hepatitis B virus	A blood-borne virus that can damage the liver and lead to cirrhosis and liver cancer or can occasionally cause acute liver failure. There is a vaccine available to prevent transmission of hepatitis B virus and drugs are available that slow down the multiplication of the virus. However, some patients still have cirrhosis (scarring of the liver) or liver cancer or they may present with acute liver failure. These conditions may require liver transplantation.
Hepatitis C virus	A blood-borne virus that can damage the liver and lead to cirrhosis and liver cancer. There are now very effective drugs that can cure the virus but some patients still have cirrhosis (scarring of the liver) or liver cancer which may require liver transplantation.
Hepatoblastoma	A rare liver cancer that occurs in childhood.
Hepatocellular carcinoma	A type of primary (not spread from another organ) liver cancer. It often occurs in a patient with cirrhosis (scarring of the liver) and sometimes requires liver transplantation.
Hirschsprung's disease	A condition in which the nervous system of the bowel is partly or completely absent resulting in the bowel not moving properly.
Hollow visceral myopathy	A rare condition affecting the muscles in the wall of the bowel and sometimes the urinary tract.
Initial poor function	Sometimes the new liver does not work well which results in metabolic problems that the liver normally takes care of. This can require retransplantation.
Interquartile range	The central half of data points.
Kaplan-Meier survival curve	The survival rate (patient or graft survival) of a group of patients over time after transplantation can be displayed in a graph that has the percentage surviving on the Y axis and time on the X axis. Each curve is a line that runs horizontally if there are no events (deaths for patient survival and deaths or retransplants for graft survival) and drops down vertically whenever an event occurs. Several curves representing different patient groups can be displayed on the same graph.
Kruskal-Wallis test	A statistical test that can determine whether it is likely that two or more groups of continuous data (data that can be represented as numbers) are significantly different.
Leiomyoma	A tumour affecting the muscle in the wall of the bowel.
Listing	Placing a patient on a liver transplant waiting list while they wait for a suitable organ donor. This is also known as activation.
Liver transplantation	The process of replacing the liver of a patient who has end-stage liver disease, some forms of liver cancer or some forms of metabolic disease caused at least in part by the liver with a liver or part of a liver from a deceased or living donor.

Living donor liver transplantation	This is where a piece of liver from a healthy person is carefully removed for transplantation into a patient who needs liver transplantation. This is a common form of liver transplantation in some parts of the world, notably Asia, but is a relatively uncommon form of transplantation in Australia and New Zealand. This form of transplantation can be performed in a child or an adult.
Log-rank test	A statistical test that can determine whether it is likely that there is a significant difference in survival between two or more groups of patients.
Mean	Average (the sum of the data points divided by the number of data points).
Median	The middle data point.
Metabolic disease	A disease where the biochemical processes in the liver are deranged.
Multiorgan failure	Failure of multiple organ systems. Because the liver is involved in many metabolic processes, if it functions poorly or not at all, this can lead to failure of other organ systems, such as the lungs, heart, circulation and kidneys.
Non-alcoholic fatty liver disease (NAFLD)	A condition in which fat accumulates in the liver in the absence of significant alcohol intake. This can lead to cirrhosis and liver failure.
P-value	The likelihood that a difference between sets of data occurred by chance. The lower the P-value, the less likely the difference occurred by chance alone and the more likely the difference is significant. P-values < 0.5 (that is 1 in 20) are generally considered to be statistically significant.
Patient survival	The proportion (often expressed as a percentage) of patients undergoing a particular treatment (liver transplantation in this case) who are alive at different time periods after the treatment. In this report, patient survival time is calculated from the date of first transplantation (that is, if the patient has another liver transplant, this is ignored for the purpose of calculation of patient survival) until the date of death for patients who die or until the end of the reporting year (31 December, 2018 for this report) for patient who were still alive at that time.
Porto-mesenteric thrombosis	Clotting of blood in the blood vessels leading from the bowel to the liver.
Primary biliary cirrhosis	Scarring in the liver associated with abnormalities in the small bile ducts inside the liver.
Primary non-function	This describes the fact that occasionally the liver fails to work after transplantation. This requires emergency retransplantation to prevent death.
Primary sclerosing cholangitis	A disease that results in narrowing of bile ducts inside and/or outside the liver.
Range	The lowest data point to the highest data point.
Recipient	A patient who undergoes a (liver in this case) transplant.
Recurrent malignancy	Cancer that was present before transplantation that comes back after transplantation.

Reduced liver transplantation	A transplant performed by cutting down a deceased donor liver to the appropriate size to fit inside a recipient. Usually the donor is an adult and the recipient is a child. The other part of the liver is not transplanted in this case (unlike split liver transplantation).
Registry	A database that stores information on patients with a similar disease process or method of treatment; in this case, liver transplantation. Patients give permission for their data to be stored on the database and for subsequent use in generating reports and research.
Rejection	When a transplant is performed, the patient's immune system sees the new organ as a foreign invader and tries to destroy it, just like it would try to destroy an infection or cancer. Patients are given medications to reduce this effect of the immune system. However, sometimes the immune system can still injure the organ. This is called rejection. It can be suspected because the blood tests become abnormal and confirmed with a biopsy (small piece of tissue obtained with a needle). Rejection can be treated by giving more powerful medications but occasionally the liver can be so damaged that it needs to be replaced by performing another transplant.
Sepsis	Severe infection.
Split liver transplantation	In some good quality liver donors (relatively young with good liver function and suitable anatomy), it is possible to divide the liver into two parts so that it can be transplanted into two patients. Usually the left part of the liver is transplanted into a child and right part of the liver is transplanted into an adult.
Stroke	A sudden vascular event (bleed or blockage to blood supply) in the brain.
Trauma	Injury (to the brain in this case, which can lead to brain death).
Vascular complications	When a liver transplant is performed, the donor's and recipient's (patient receiving the transplant) artery and veins that supply blood to and drain blood from the liver are joined together. Sometimes there can be problems after the transplant related to these blood vessels. Often these problems can be fixed but sometimes another transplant is required to fix the problem, for example, if the main artery to the liver is blocked.
Volvulus	A condition in which the bowel twists.
Waiting list mortality rate	The rate of patients dying waiting for a liver transplant. Unfortunately, some patients' condition can deteriorate (for example, progression of liver failure or cancer) while they are waiting for a liver transplant. This includes patients who are taken off the waiting list and who subsequently die within 1 year. The waiting list mortality rate is the number of these patients divided by the number of patients on the waiting list (the number active at the start of the period under evaluation plus the number added to the waiting list during that period), usually expressed as a percentage.
Waiting time	Time from listing for liver transplantation to delisting (in the case of waiting time to transplantation, this the time from listing for liver transplantation to the transplant date.
Whole liver transplantation	Transplantation of the whole liver from a deceased (dead) donor to replace the liver of a patient who has been waiting for liver transplantation. This is the commonest form of liver transplantation in Australia and New Zealand.

18 Appendix II. Publications utilising ANZLITR data

18.1 Publications in 2019

Increasing incidence of nonalcoholic steatohepatitis as an indication for liver transplantation in Australia and New Zealand.
Calzadilla-Bertot L., Jeffrey, G.P., Jacques, B., McCaughan, G., Crawford, M., Angus, P., Jones, R., Gane, E., Munn, S., Macdonald, G., Fawcett, J., Wigg, A. Chen, J., Fink, M., Adams, L.A.
Liver Transplantation, 25 (1):25-34, 2019.

Characteristics and outcomes of patients with acute liver failure admitted to Australian and New Zealand intensive care units.
Warrillow S; Bailey M; Pilcher D; Kazemi A; McArthur C; Young P; Bellomo R.
Internal Medicine Journal. 49(7):874-885, 2019 07.

Excellent Contemporary Graft Survival for Adult Liver Retransplantation: An Australian and New Zealand Registry Analysis from 1986 to 2017.
Angus W. Jeffrey, Luc Delriviere, Geoff McCaughan, Michael Crawford, Peter Angus, Robert Jones, Graeme A. Macdonald, Jonathan Fawcett, Alan Wigg, John Chen, Ed Gane, Stephen Munn, and Gary P. Jeffrey.
Transplantation Direct 2019;5: e472; doi: 10.1097/TXD.0000000000000920

Longitudinal immunosuppression data can minimize misclassification bias in solid organ transplantation cohorts.
Laaksonen MA, Webster AC, McCaughan GW, Keogh AM, Grulich AE, Vajdic CM. Clin Transplant. 2019 Feb;33(2):e13470

18.2 Publications in 2018

Aortic Versus Dual Perfusion for Retrieval of the Liver After Brain Death: A National Registry Analysis.
Hameed AM; Pang T; Yoon P; Balderson G; De Roo R; Yuen L; Lam V; Laurence J; Crawford M; D M Allen R; Hawthorne WJ; Pleass HC.
Liver Transplantation. 24(11):1536-1544, 2018 11.

18.3 Publications in 2016

Additive impact of pre-liver transplant metabolic factors on survival post-liver transplant.
Leon A Adams, Oscar Arauz, Peter W Angus, Marie Sinclair, Graeme A MacDonald, Utti Chelvaratnam, Alan J Wigg, Sze Yeap, Nicholas Shackel, Linda Lin, Spiro Raftopoulos, Geoffrey W McCaughan, Gary P Jeffrey, on behalf of the Australian New Zealand Liver Transplant Study Group.
Journal of Gastroenterology and Hepatology. 31(2016) 1016–1024

Good outcomes of liver transplantation for hepatitis C at a low volume centre.
Su Yin Lau, Richard J. Woodman, Mauricio F. Silva, Kate Muller, John Libby, John W. Chen, Robert Padbury, Alan J. Wigg.
Annals of Hepatology 2016; 15(2): 207-214

The increasing burden of potentially preventable liver disease among adult liver transplant recipients: A comparative analysis of liver transplant indication by era in Australia and New Zealand.
Howell J; Balderson G; Hellard M; Gow P; Strasser S; Stuart K; Wigg A; Jeffrey G; Gane E; Angus PW.
Journal of Gastroenterology & Hepatology. 31(2):434-41, 2016 Feb.

Liver transplantation in Australia and New Zealand.
McCaughan GW; Munn SR.
Liver Transplantation. 22(6):830-8, 2016 06.

High azathioprine dose and lip cancer risk in liver, heart, and lung transplant recipients: A population-based cohort study.
Na R, Laaksonen MA, Grulich AE, Meagher NS, McCaughan GW, Keogh AM, Vajdic CM, J Am Acad Dermatol. 2016 Jun;74(6):1144-1152.e6.

Iatrogenic immunosuppression and risk of non-Hodgkin lymphoma in solid organ transplantation: A population-based cohort study in Australia.
Na R, Laaksonen MA, Grulich AE, Meagher NS, McCaughan GW, Keogh AM, Vajdic CM, Br J Haematol. 2016 Aug;174(4):550-62

18.4 Publications in 2015

Longitudinal dose and type of immunosuppression in a national cohort of Australian liver, heart, and lung transplant recipients
Na R, Laaksonen MA, Grulich AE, Webster AC, Meagher NS, McCaughan GW, Keogh AM, Vajdic CM, , 1984-2006. Clin Transplant. 2015 Nov;29(11):978-90.

18.5 Publications in 2014

Liver transplantation outcomes for Australian Aboriginal and Torres Strait Islanders.
Chinnaratha MA; Chelvaratnam U; Stuart KA; Strasser SI; McCaughan GW; Gow P; Adams LA; Wigg AJ; Australia and New Zealand Liver Transplant Clinical Study Group.
Liver Transplantation. 20(7):798-806, 2014 Jul.

18.6 Publications in 2013

Nature and outcomes of the increased incidence of colorectal malignancy after liver transplantation in Australasia.
Verran DJ; Mulhearn MH; Dilworth PJ; Balderson GA; Munn S; Chen JW; Fink MA; Crawford MD; McCaughan GW.
Medical Journal of Australia. 199(9):610-2, 2013 Nov 04

Comparison of De Novo Cancer Incidence in Australian Liver, Heart and Lung Transplant Recipients.
Na, R., Grulich, A.E., Meagher, N.S., McCaughan, G.W., Keogh, A.M., Vajdic, C.M., Am J Transplant. 2013 Jan;13(1):174-83

De Novo cancer- related death in Australian Liver and cardiothoracic transplant recipients.
Na R, Grulich AE, Meagher NS, McCaughan GW, Keogh AM, Vajdic CM. American Journal of Transplantation. 2013; 13:1293-1304

Combination of lamivudine and adefovir without hepatitis B immune globulin is safe and effective prophylaxis against hepatitis B virus recurrence in hepatitis B surface antigen-positive liver transplant candidates
Gane EJ, Patterson S, Strasser SI, McCaughan GW, Angus PW.. Liver Transplantation. 2013;3: 268-274

18.7 Publications in 2012 and earlier

Poorer survival in patients whose explanted hepatocellular carcinoma (HCC) exceeds Milan or UCSF Criteria. An analysis of liver transplantation in HCC in Australia and New Zealand.
John W.C. Chen, Lilian Kow, Deborah J. Verran, John L. McCall, Stephen Munn, Glenda A. Balderson,
Jonathan W. Fawcett, Paul J. Gow, Robert M. Jones, Gary P. Jeffrey, Anthony K. House & Simone I. Strasser. HPB 2009, 11, 81–89.

Minimal but significant improvement in survival for non-hepatitis C-related adult liver transplant patients beyond the one-year posttransplant mark.
McCaughan, Geoffrey W; Shackel, Nicholas A; Strasser, Simone I; Dilworth, Pamela; Tang, Patrick for Australian and New Zealand Liver Transplant Study Group. Liver Transplantation 16: 130-137, 2010

The epidemiology of hepatitis C in Australia: Notifications, treatment uptake and liver transplantations, 1997–2006.
Heather F Gidding, Libby Topp, Melanie Middleton, Kate Robinson, Margaret Hellard, Geoffrey McCaughan, Lisa Maher, John M Kaldor, Gregory J Dore and Matthew G Law. Journal of Gastroenterology and Hepatology 24 (2009) 1648–1654

A randomised study of Adefovir dipivoxil in place of HBIG in combination with lamivudine as post-liver transplantation hepatitis B prophylaxis.
Angus PW, Patterson SJ, Strasser SI, McCaughan GW, Gane E. Hepatology. 2009;48:1460-6

Lamivudine plus Low-Dose Hepatitis B Immunoglobulin to Prevent Recurrent Hepatitis B Following Liver Transplantation.
Gane EJ, Angus PW, Strasser SI, Crawford DHG, Ring J, Jeffrey GP, McCaughan GW. Gastroenterology 2007;132:931-937

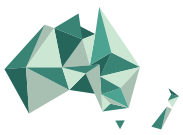
Patient and graft survival after liver transplantation for hereditary hemochromatosis: Implications for pathogenesis.
Crawford DH, Fletcher LM, Hubscher SG, Stuart KA, Gane E, Angus PW, Jeffrey GP, McCaughan GW, Kerlin P, Powell LW, Elias EE. Hepatology 2004;39:1655-662

Liver transplantation for HCV-associated liver cirrhosis: predictors of outcomes in a population with significant genotype 3 and 4 distribution.
Zekry A, Whiting P, Crawford DH, Angus PW, Jeffrey GP, Padbury RT, Gane EJ and McCaughan GW. Liver Transplantation 2003;9:339-347

Combination low-dose hepatitis B immune globulin and lamivudine therapy provides effective prophylaxis against posttransplantation hepatitis B
Angus PW, McCaughan GW, Gane EJ, Crawford DHG, Harley H.. Liver Transplantation 2000;6(4)429-433

Australia & New Zealand
Liver and Intestinal Transplant Registry

ANZLITR



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