Australia & New Zealand
Liver and Intestinal Transplant Registry

Report on liver and intestinal transplantation activity to 31/12/2022

34th
ANNUAL REPORT
ANZLITR

Table of Contents

1 Preface **1**

2 Executive Summary **2**

2.1 Liver Transplantation 2

2.2 Intestinal Transplantation 3

3 Australia and New Zealand Liver and Intestinal Transplant Registry Information **4**

3.1 Australia and New Zealand Liver and Intestinal Transplant Registry Overview 4

3.2 History of the Australia and New Zealand Liver and Intestinal Transplant Registry 4

3.3 Australia and New Zealand Liver and Intestinal Transplant Registry Application 5

3.4 Australia and New Zealand Liver and Intestinal Transplant Registry Website 5

3.5 Funding of the Registry 6

3.6 Registry Secretariat 6

3.7 Registry Management Committee 6

3.8 Participating Centres 6

4 Methodology **7**

4.1 Data Collection and Preparation 7

4.2 Waiting Lists 7

4.2.1 Liver Transplant Waiting List Dataset (6,807 listings) 7

4.2.2 Intestinal Transplant Waiting List Dataset (22 listings) 7

4.3 Liver Transplant Recipient Datasets 7

4.3.1 Demographics Dataset (6,989 patients) 7

4.3.2 Patient Survival and Initial Diagnosis Dataset (6,983 patients) 7

4.3.3 Graft Survival Dataset (7,580 transplants) 8

4.4 Deceased and Living Liver Donor Datasets 8

4.4.1 Deceased Liver Donor Dataset (6,884 deceased donors; 7,334 grafts) 8

4.4.2 Living Liver Donor Dataset (120 living donors) 8

4.5 Intestinal Dataset (12 transplants) 8

4.6 Patient Age Groups 8

4.7 Survival Curves 8

4.7.1 Change in Methodology to Determine Censor Date 8

4.7.2 Impact of Change in Methodology on Survival 8

4.7.3 Patient Survival 9

4.7.4 Graft Survival 9

4.8 Statistical Analysis 9

5 Liver Transplant Waiting List **10**

5.1 Waiting List Activity 10

5.2 Paediatric Waiting List Activity 11

5.3 Adult Waiting List Activity 12

5.4 Time on the Waiting List 13

5.5 Urgent Waiting List Activity 14

6 Deceased Liver Donors **16**
6.1 Deceased Donors and Grafts Transplanted Per Year 16
6.2 Machine Perfusion of Deceased Donor Livers 17
6.3 Age of Deceased Donors 18
7 Living Liver Donors **19**
8 Liver Transplantation in 2022 **20**
8.1 Demographic Data for Patients Transplanted in 2022 20
8.2 Transplants in 2022 20
9 Liver Transplantation from 1985 – 2022 **21**
9.1 Demographic Data for Patients Transplanted from 1985 - 2022 22
9.1.1 Patients Transplanted by Year of First Transplant 22
9.1.2 Recipient Age at First Transplant (1985 – 2022) 23
9.1.3 Recipient Age at First Transplant by Era of Transplant 23
9.2 Transplants (1985 – 2022) 25
9.2.1 Type of Graft – Paediatric Recipients, All Years 27
9.2.2 Type of Graft – Adult Recipients, All Years 27
10 Diagnoses at First Transplant **28**
10.1 Diagnoses in Children 28
10.2 Primary Diagnosis Trend in Children 29
10.3 All Diagnoses Trend in Children 29
10.4 Diagnoses in Adults 30
10.5 Primary Diagnosis Trend in Adults 32
10.6 All Diagnoses Trend in Adults 32
10.7 Fulminant Hepatic Failure – All Diagnoses 33
10.8 Metabolic Disorders – All Diagnoses 34
11 Incidental Liver Cancer Found at Explant **35**
11.1 Incidental Cancers Found at Explant in Children 35
11.2 Incidental Cancers Found at Explant in Adults 36
11.3 Liver Cancer Known Prior to Transplant Versus Incidental Liver Cancer by Transplant Era 37
12 Donor Derived Tumours **38**
13 De Novo Cancer Development and Liver Cancer Recurrence After Liver Transplantation **39**
13.1 De Novo Non-Skin Cancer 39
13.1.1 De Novo Non-Skin Cancer Types 39
13.1.2 Time to Diagnosis of De Novo Non-Skin Cancers by Cancer Type 40
13.1.3 Time to Diagnosis of De Novo Non-Skin Cancers by Age Category 41
13.1.4 De Novo Non-Skin Cancers by Pre-Transplant Diagnosis 41
13.1.5 De Novo Alimentary Cancers 44
13.1.6 De Novo Lymphoma 45
13.1.7 De Novo Genitourinary Cancers 46
13.1.8 De Novo Respiratory Cancers 47

13.2 Skin Cancer Development Post-Transplant 48
13.3 Cumulative Risk of Developing De Novo Skin or Non-Skin Cancer Post Liver Transplant 50
13.4 Liver Cancer Recurrence after Transplant 51
14 Patient Survival 52
14.1 All patients 52
14.2 Patient Survival by Age Group 53
14.3 Paediatric Patient Survival by Age Strata 54
14.4 Adult Patient Survival by Age Strata 55
14.5 Patient Survival by Era of Transplant 56
14.6 Paediatric Patient Survival by Era of Transplant 57
14.7 Adult Patient Survival by Era of Transplant 58
14.8 Paediatric Patient Survival by Type of Primary Graft 59
14.9 Adult Patient Survival by Type of Primary Graft 60
14.10 Paediatric Patient Survival by Weight 61
14.11 Paediatric Patient Survival by Primary Disease 62
14.12 Adult Patient Survival by Primary Disease 63
14.13 Patient Survival by Age Group with Fulminant Hepatic Failure 64
14.14 Patient Survival by Transplant Era with Hepatitis B Virus Cirrhosis 65
14.15 Patient Survival by Transplant Era with Hepatitis C Virus Cirrhosis 66
14.16 Patient Survival with Hepatocellular Carcinoma by Era of Transplant 67
14.17 Survival of Patients by Hepatocellular Carcinoma Status at Transplant 68
14.18 Paediatric Patient Survival with Diagnosis of Malignancy 69
14.19 Adult Patient Survival with a Diagnosis of Malignancy 70
14.20 Patient Survival for Adult Patients with Incidental Liver Cancer 71
14.21 Patient Survival for Adult Patients by Type of Incidental Liver Cancer 72
14.22 Patient Survival by Transplant Unit 73
15 Graft Outcome 74
15.1 All Grafts Outcome 74
15.2 Outcome of All Grafts by Age Group 75
15.3 Outcome by Graft Number 76
15.4 Paediatric Outcome by Graft Number 77
15.5 Adult Outcome by Graft Number 78
15.6 Graft Survival by Type of Graft 79
15.7 Graft Survival by Graft Type in Children 80
15.8 Graft Survival by Graft Type in Adults 81
15.9 Graft Survival by Era of Transplant 82
15.10 Graft Survival by Era of Transplant in Children 83
15.11 Graft Survival by Era of Transplant in Adults 84
15.12 Whole Graft Survival by Era of Transplant 85
15.13 Reduced Graft Survival by Era of Transplant 86
15.14 Split Graft Survival by Era of Transplant 87
15.15 Living Donor Graft Survival by Era of Transplant 88

15.16 Graft Survival by Deceased Donor Age 89
15.17 Graft Survival by Donor Type 90
15.18 Graft Survival by Donor Cause of Death 91
15.19 Graft Survival by Shipping of Organs 92
15.20 Graft Survival by Cold Ischaemia Time 93
15.21 Graft Survival by Blood Group Compatibility 94
15.22 Graft Survival by Recipient Urgency at Transplant 95
15.23 Graft Survival by Transplant Unit 96
16 Indication for Retransplantation 97
16.1 All Retransplants 97
16.2 Paediatric Retransplantation 99
16.3 Adult Retransplantation 101
17 Cause of Patient Death 103
17.1 Cause of Death – All Patients 103
17.2 Paediatric Patients - Cause of Death 104
17.3 Adult Patients – Cause of Death 104
17.4 Cause of Death Types by Age Group 105
17.5 Cause of Death by Time to Death 107
17.6 Paediatric Cause of Death by Time to Death 108
17.7 Adult Cause of Death by Time to Death 109
18 Intestinal Transplantation 110
18.1 Waiting Lis 110
18.2 Demographic Characteristics and Diagnoses 111
18.3 Organs Transplanted 112
18.4 Intestinal Patient Survival 113
18.5 Intestinal Graft Survival 114
19 Appendix I. Glossary 115
20 Appendix II. Publications utilising ANZLITR data 121
20.1 Publications in 2022 121
20.2 Publications in 2021 121
20.3 Publications in 2020 121
20.4 Publications in 2019 121
20.5 Publications in 2018 122
20.6 Publications in 2016 and earlier 122

1 Preface

We are pleased to present the 34th Annual Report of the Australia and New Zealand Liver and Intestinal Transplant Registry (ANZLITR). This report presents analyses of the cumulative liver and intestinal transplantation data since the establishment of the first liver transplant units in Australia and New Zealand in 1985 to 31st December 2022. The report can be downloaded from the ANZLITR website: https://www.anzlitr.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 or intestinal transplantation unit.

We thank the staff at all the transplantation units who contribute their data into the ANZLITR database. We are grateful to the Australian Government and the Organ and Tissue Authority (OTA) for the ongoing financial support of the Registry. We thank the Australia and New Zealand Organ Donation (ANZOD) Registry for their collaboration and provision of deceased donor data.

Thank you to Pamela Dilworth, Cancer Registry Manager for ANZLITR, for her dedication and hard work in collating, validating, analysing and reporting the cancer data for liver transplantation. Thank you to Peter Henderson, Hendos Pty Ltd for hosting the ANZLITR registry application used for data collection and for maintaining the public website. Thank you to Damian Wildie, Number 9 Management Pty Ltd, for developing and maintaining all the complex code that goes into the making sure the Registry functions properly. Finally, thank you to Debra (Debbie) Cormack, Graphic Artist, Queensland Liver Transplant Service, Princess Alexandra Hospital, for doing all the graphic layout to make the annual report look fantastic.

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, Registry Director
Ms Mandy Byrne, Registry Manager

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2 Executive Summary

2.1 Liver Transplantation

Annual waiting list mortality has decreased from a peak of 12.3% in 2007 to 5.7% in 2022. In 2022, one of 17 patients listed as category 1 and one of 13 patients listed as category 2 died waiting. There was minimal influence of the listing unit on the risk of waiting list mortality.

There has been a progressive increase in liver transplantation from deceased donors since 2007 until the impact of COVID-19 resulted in a decrease in the number of deceased donors. There have been 47 transplants using grafts that underwent normothermic machine perfusion and three using grafts that underwent hypothermic oxygenated perfusion. In 2022, 7.3% of deceased liver donors were donation after circulatory death (DCD) donors. Living donor liver transplantation accounted for 1.6% of transplants performed.

In 2022, 314 liver transplants were performed in 306 patients. The number of liver transplants increased from 307 in 2021 but has not returned to the pre-COVID peak of 369 transplants in 2018. Between 1985 and 2022, 7,580 transplants were performed in 6,983 patients, including 1,291 transplants in 1,132 children and 6,289 transplants in 5,857 adults. Paediatric age at transplant has decreased progressively and adult recipient age has increased progressively over time. Split liver transplantation is a common form of liver transplantation in children (56.8% in 2022) and whole liver transplantation is the dominant form of liver transplantation in adults (90.4% in 2022).

The commonest indication for transplantation in children is biliary atresia and in adults was hepatitis C virus cirrhosis until 2014, after which hepatocellular carcinoma (HCC) and alcohol-related cirrhosis have become the commonest indications. There has also been a recent increase in patients transplanted for non-alcoholic fatty liver disease (NAFLD). The proportion of patients transplanted primarily for hepatitis C has decreased from 33.8% in 2012 to only 4.9% in 2022.

The 1-, 3-, 5- and 10-year patient survival in recent years for paediatric patients was 99%, 96%, 95% and 88%, 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 93%, 90%, 86% and 74%, respectively. Patient survival in adults reduced progressively with increasing recipient age ($P < 0.001$) and varied significantly by primary disease ($P < 0.001$), with poorer outcomes for hepatitis C virus and alcohol-related cirrhosis. Patient survival has improved over time for hepatitis B ($P < 0.001$). There was minimal influence of the transplant unit undertaking the transplant on the risk of post-transplant mortality.

The 1-, 3-, 5- and 10-year graft survival in recent years for paediatric patients was 95%, 88%, 85% and 78%, respectively. The 1-, 3-, 5- and 10-year graft survival in recent years for adult patients was 90%, 86%, 82% and 70%, respectively. Graft survival varied significantly by era of transplant (better outcomes since 2000 – 04 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, $P < 0.001$), deceased 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 < 431 mins, $P < 0.001$) and recipient urgency category at transplant (poorer outcome for category 1 recipients to 20 years post-transplant, $P < 0.001$). There was minimal influence of the transplant unit undertaking the transplant on the risk of graft loss.

The commonest indications for retransplantation were vascular problems (27.1%), biliary complications (19.5%), rejection (17.8%), primary non-function or initial poor function (14.6%) and recurrent disease (13.4%). The commonest causes of death were malignancy (25.3%), graft-related causes (16.9%), sepsis (14.1%), cardiovascular disease (8.8%) and multi-organ failure (8.3%).

2.2 Intestinal Transplantation

Twenty-one patients have been listed for intestinal transplantation. Twelve patients were transplanted, three died waiting, four were delisted without relisting and two were still waiting at the end of 2022.

The 1- and 3-year intestinal patient survival are 91.7% and the 5- and 10-year are 76.4%. The 1- and 3-year intestinal graft survival are 83.3% and the 5- and 10-year are 69.4%.

Two patients died with a functioning graft, one from respiratory infection at 3 months and one from complications of cardiac surgery at 3.5 years post-transplant. One intestinal graft has failed with the patient supported by total parenteral nutrition (liver and pancreas grafts functioning).

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. Following formal Human Research Ethics Committee (HREC) approval for the Registry in 2019, collection of identifying data on patients that sign the new consent forms commenced. 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
- identifying data such as recipient name only if new consent form signed
- 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 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

Data have been collected on all liver transplants in Australia and New Zealand since 1985. The first liver transplant in Australia performed in New South Wales in 1968 (patient died 5 days post-transplant) is not included in the registry. Queensland performed their first liver transplant in 1985. The second transplant by NSW occurred 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, 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). In 2018, the registry name was changed to Australia and New Zealand Liver and Intestinal Transplant Registry (ANZLITR), to reflect that the Registry contains both liver and intestinal listing and transplant data.

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 Professor Sheil at Royal Prince Alfred Hospital in Sydney and Professor Russell Strong at 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 (Ms Glenda Balderson) 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 listing 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, 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 Ethics Committee approval for the Registry was obtained in 2019 under the National Mutual Acceptance scheme. Units obtained site specific ethics approval during 2020/2021 and began using the new consent forms that informed patients about identified data collection. Collection of identified patient data commenced only on patients that signed the new consent forms. Strict safeguards and security measures have been established to protect and control access to identified data. Identified data will be used to ensure integrity of data matching with external databases and will not be disclosed in research data releases or publications.

In 2021, the design of the HCC module in the Registry was updated to provide a clearer view and process for entering data and to include a more comprehensive data collection.

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 undertake the cancer reporting 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. Two factor authentication was activated in 2021.

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://www.anzlitr.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.

3.6 Registry Secretariat

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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 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 Ed Gane, 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 waiting list data are available from 1 January 2004. The waiting list dataset contains all patients who have been added to the waiting 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, waiting list mortality (patient died whilst on the waiting list 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) or listed at end of year. Waiting list mortality rate is calculated by dividing waiting list mortality by number of patients on the waiting list during the year (patients active at start of the year plus new patients listed during the year).

4.2.1 Liver Transplant Waiting List Dataset (6,807 listings)

Comprehensive waiting list data including listing and delisting date and delisting outcome are available from 1 January 2004. There are data on 6,807 active listings from this date.

A benchmarking analysis to compare 90-day and 1-year waiting list mortality between the six Australian and New Zealand liver transplant units was undertaken for patients listed from 1/1/2016 to 31/12/2020 who were ≥ 18 years old at listing, who were not listed as urgent (category 1 or 2) patients, who were listed for liver only transplantation and who had not undergone previous liver transplantation (n = 1,438 patients).

4.2.2 Intestinal Transplant Waiting List Dataset (22 listings)

Comprehensive waiting list data including listing and delisting date and delisting outcome are available from the first listing in 2007. There are 22 listings for 21 patients.

4.3 Liver Transplant Recipient Datasets

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

4.3.1 Demographics Dataset (6,989 patients)

The demographic analysis dataset is based on the first liver transplant in Australia or New Zealand for each patient. Six patients had their first liver transplant overseas prior to undergoing retransplantation in Australia and New Zealand, including one patient who had two liver transplants overseas. Their first liver transplant in Australia or New Zealand has been used for demographic data analysis.

4.3.2 Patient Survival and Initial Diagnosis Dataset (6,983 patients)

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

A benchmarking analysis to compare post-transplant mortality between the six Australian and New Zealand liver transplant units was undertaken for patients listed from 1/1/2016 to 31/12/2020 (1-year post-transplant mortality, n = 1,260 patients) and from 1/1/2012 to 31/12/2016 (5-year post-transplant mortality, n = 1,058 patients) who were ≥ 18 years old at transplantation, who were not transplanted as urgent (category 1 or 2) patients, who underwent liver only transplantation and who had not undergone previous liver transplantation.

4.3.3 Graft Survival Dataset (7,580 transplants)

All Australian and New Zealand transplants are included in this dataset. Patients who have had one or two prior transplants overseas have their first graft number in Australia or New Zealand recorded as graft two or three, respectively. Both deceased and living donor grafts are included in this analysis, unless otherwise specified.

A benchmarking analysis to compare graft loss between the six Australian and New Zealand liver transplant units was undertaken for patients listed from 1/1/2016 to 31/12/2020 (1-year graft loss, n = 1,260 grafts) and from 1/1/2012 to 31/12/2016 (5-year graft loss, n = 1,058 grafts) who were ≥ 18 years old at transplantation, who were not transplanted as urgent (category 1 or 2) patients, who underwent liver only transplantation and who had not undergone previous liver transplantation.

4.4 Deceased and Living Liver Donor Datasets

4.4.1 Deceased Liver Donor Dataset (6,884 deceased donors; 7,334 grafts)

The Australia and New Zealand Organ Donation (ANZOD) Registry provides the ANZLITR with deceased donor data for analysis. A total of 7,460 grafts were sourced from 7,010 deceased donors. Collection of deceased donor information commenced in 1989. There is no deceased donor information on 126 grafts from 1985 to 1988.

Deceased donor data are available on 6,884 donors. A total of 6,433 donated livers were allocated to a single recipient and 451 donated livers were split (one graft was not utilised as recipient found to be unsuitable at time of transplant), resulting in a total of 7,334 grafts with deceased donor data.

4.4.2 Living Liver Donor Dataset (120 living donors)

Data on 120 living liver donors (including five domino living donors) are collected in ANZLITR.

4.5 Intestinal Dataset (12 transplants)

The intestinal dataset includes data on all 21 wait-listed patients (the first listing was in 2007) and all twelve 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.

4.6 Patient Age Groups

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

4.7 Survival Curves

4.7.1 Change in Methodology to Determine Censor Date

Change in methodology in this annual report:

The censor date for Survival Curves is now based on the earlier of:

- **the date of last contact**
  or
- **31 December 2022.**

In 2022, there was a change to our survival curve analysis methodology to using the date of last contact as the censor date, rather than using 31 December 2022, for patients that had not been identified as deceased. We identified that a small proportion of patients had become lost to follow up as they had moved overseas, moved within Australia and New Zealand, had not attended any follow up or have not been able to be contacted. Where patients have moved to other liver transplant unit areas, a process was established to locate the patient and, if found, undertake documentation of date of last contact. Where patients moved overseas or could not be contacted, units documented the date of last contact, flagged them as Lost to Follow Up and made a note about reason.

4.7.2 Impact of Change in Methodology on Survival

In the 2021 Annual Report, there were 2,001 deaths identified out of 6,706 patients. An additional 60 deaths prior to 2022 have been identified during 2022 as part of our focus on updating of date of last contact of alive patients.

At analysis for this year's annual report, 4,801 (68.7%) of 6,989 transplanted patients were alive at date of last contact (censor date for survival analysis). Of these patients where death has not been reported, 4,241 (88.3%) were last confirmed alive in 2021 or 2022, 289 (6.0%) in 2020 or 2021, 180 (3.7%) between 2010 and 2019, and 91 (1.9%) before 2010.

Using the date of last contact as the censor date has resulted in a minor decrease in the survival percentage at ten years post-transplant and later compared to the previous years' methodology.

4.7.3 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 at the earlier of date of last contact or 31 December 2022) 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.

4.7.4 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 at the earlier of date of last contact or 31 December 2022) or failed (due to death, re-transplantation or for intestinal transplants, intestinal graft loss where the patient is supported by total parenteral nutrition).

4.8 Statistical Analysis

Statistical analyses were undertaken using IBM SPSS Statistics 29.

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.

For the benchmarking analysis, hierarchical regression models were generated. This method uses risk adjustment to account for variations in donor and recipient factors that might impact outcome and enables the estimation of the effect of the transplant units on outcomes. Variables to be used for risk adjustment were those that could plausibly have an effect on the outcomes of interest based on previous literature, previous analysis of the Registry data and expert opinion. Variables were recorded at the time of listing or transplantation, respectively. Risk standardised outcome rates were calculated for each unit using the estimated unit-specific parameters from the respective hierarchical models. For this analysis, the log-odds of outcomes within 90 days\1 year of listing or 1 year\5 years post-transplant were modelled as a function of patient age and clinical characteristics and a random unit specific effect. This strategy accounts for within-unit correlation of the observed outcomes and models the assumption that there are underlying differences in quality among units. These rates are obtained as the ratio of predicted to expected outcomes, multiplied by the global unadjusted rate. The ratio is the predicted outcome in each unit, given its patient mix and unit-specific effect divided by the expected outcome in that unit given the same patient mix and the average unit-specific effect. One of the results of the analysis is the intraclass coefficient (rho), which gives an estimate of the contribution of the transplant units (as opposed to donor or recipient factors) to the outcome, and is therefore an indicator of quality. These benchmarking analyses were undertaken by Prof Leonid Churilov, the University of Melbourne.

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.

The Nelson-Aalen estimator was used to estimate the cumulative expected events to determine the cumulative risk of diagnosis of skin or non-skin cancer following liver transplant.

P values < 0.05 were considered significant.

5 Liver Transplant Waiting List

5.1 Waiting List Activity

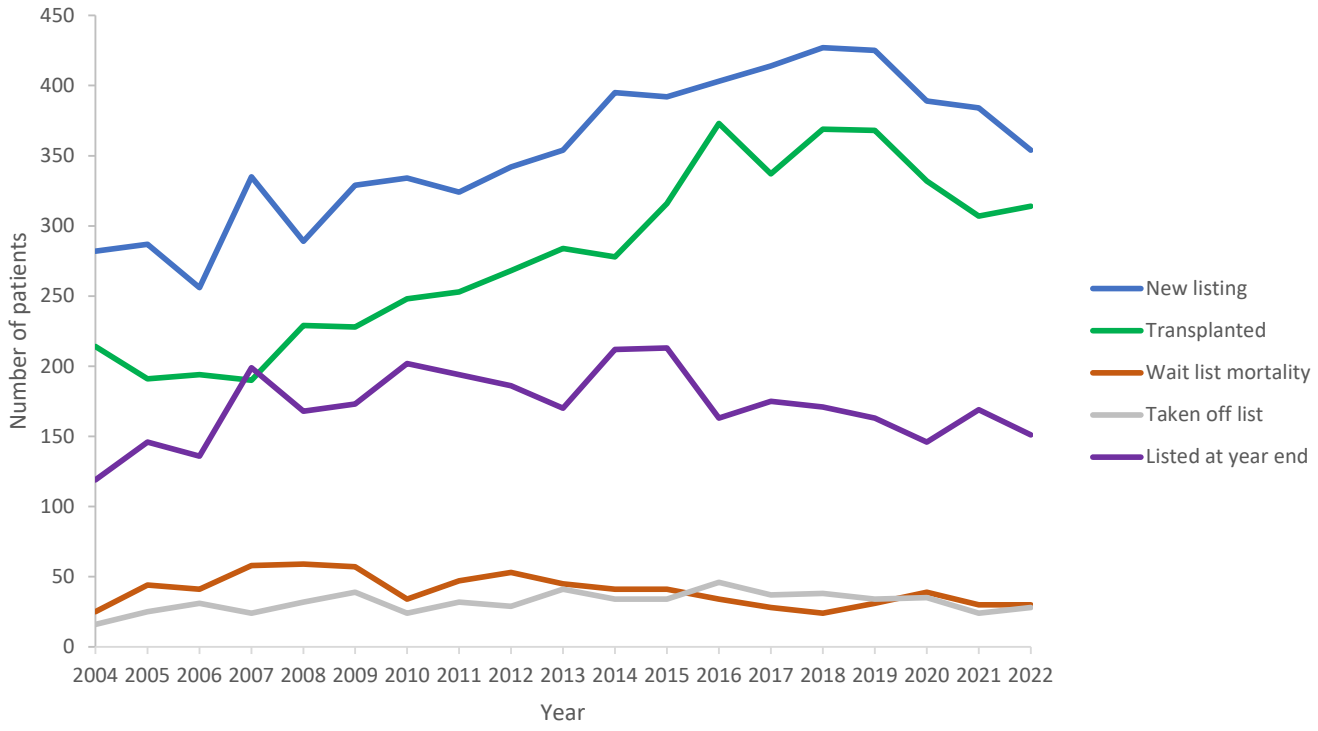
Up to 2019, there had been a steady increase in the number of new listings on the liver transplant waiting list per year, increasing 50.7% from 2004 to 2019 (282 to 425, Figure 1). However, from 2019 to 2022, the number of patients listed for liver transplantation fell by 16.7% (425 to 354).

Between 2004 and 2019, there was a 72.0% increase in the number of liver transplants performed per year (214 to 368). However, there was a 9.8% decrease (to 332) in 2020 and another 7.5% decrease in 2021 to 307 liver transplants. In 2022 there was a 2.3% increase to 314 transplants performed in Australia and New Zealand. It is likely that the reduction in transplant activity over the last few years is at least partly related to the COVID-19 pandemic.

There were 151 people on the waiting list for a liver transplant at the end of 2022.

The annual waiting list mortality rate progressively decreased from a peak of 12.3% in 2007 to 4.0% in 2018 and has remained between 5% and 7% since this time. The annual waiting list mortality was 5.7% in 2022.

Figure 1. Liver transplant waiting list activity – all patients



5.2 Paediatric Waiting List Activity

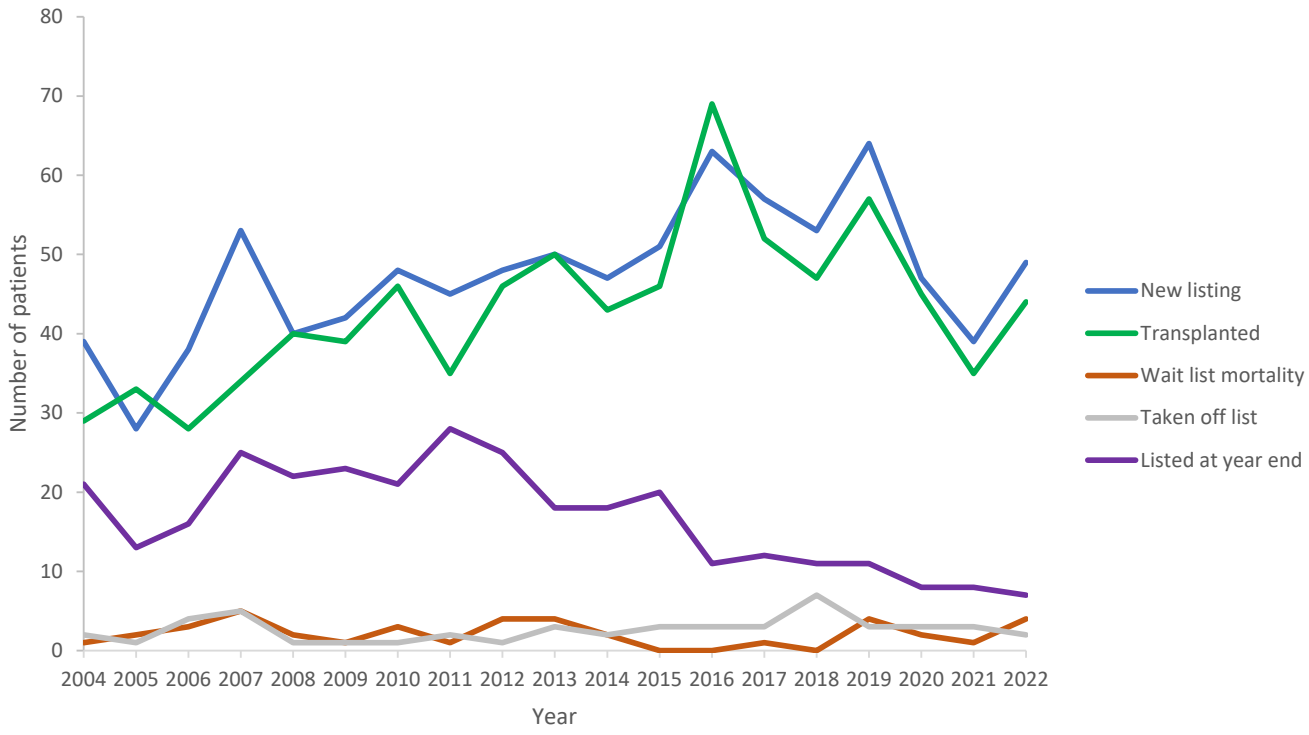
The number of new paediatric listings on the liver transplant waiting list showed a gradual increase over time, increasing 64.1% from 2004 to 2019 (39 to 64, Figure 2). However, from 2019 to 2020, the number of children listed for liver transplantation fell by 26.6% (64 to 47), then another 17.0% decrease to 39 in 2021. In 2022, there was a 25.6% increase to 49 listings.

Between 2004 and 2019, there was a 96.6% increase in the number of paediatric liver transplants performed per year (29 to 57). However, there was a 21.1% decrease (to 45) in 2020 and another 22.2% decrease (to 35) in 2021. In 2022, there was a 25.7% increase to 44 paediatric liver transplants performed in Australia and New Zealand. It is likely that the reduction in transplant activity over the last few years is at least partly related to the COVID-19 pandemic.

The number of children on the liver transplant waiting list at the end of the year peaked at 28 in 2011 and has fallen to 7 at the end of 2022.

The paediatric annual waiting list mortality rate has progressively decreased from a peak of 7.2% in 2007 to 2.1% in 2021. However, the paediatric mortality rate rose to 7.0% in 2022.

Figure 2. Paediatric liver transplant waiting list activity



5.3 Adult Waiting List Activity

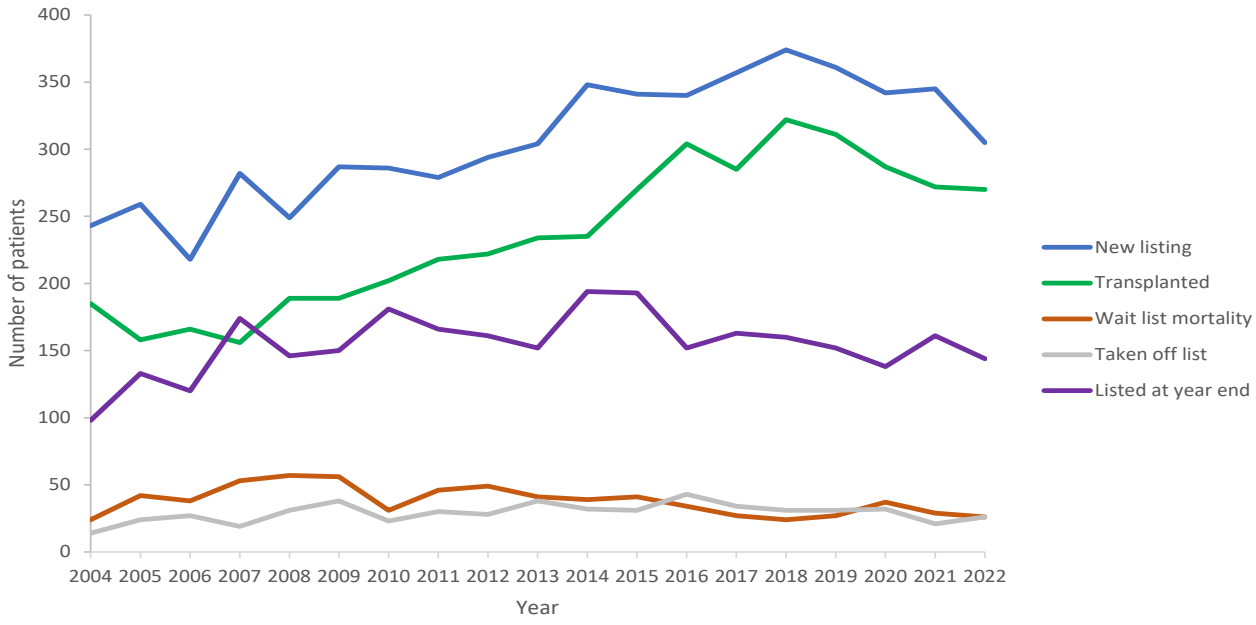
Up to 2019, there had been a steady increase in the number of new adult listings on the liver transplant waiting list per year, increasing 48.6% from 2004 to 2019 (243 to 361, Figure 3). However, from 2019 to 2020, the number of adults listed for liver transplantation fell by 5.3% (361 to 342), then there was a small 0.9% increase to 345 in 2021. In 2022, there was an 11.6% decrease to 305 listings.

Between 2004 and 2019, there was a 68.1% increase in the number of adult liver transplants performed per year (185 to 311). However, there was an 7.7% decrease (to 287) in 2020, another 5.2% decrease in 2021 to 272 and another 0.7% decrease in 2022 to 270 liver transplants performed in Australia and New Zealand. It is likely that the reduction in transplant activity over the last few years is at least partly related to the COVID-19 pandemic. It is also possible that reduction in demand for transplantation is related to a reduction in end-stage liver disease in hepatitis C virus cirrhosis related to the wide availability of direct acting antiviral therapy.

The number of adults on the waiting list for a liver transplant at the end of the year peaked at 194 in 2014 and has fallen to 144 in 2022.

The adult annual waiting list mortality rate peaked at 13.5% in 2008 and has fallen to 5.6% in 2022.

Figure 3. Adult liver transplant waiting list activity

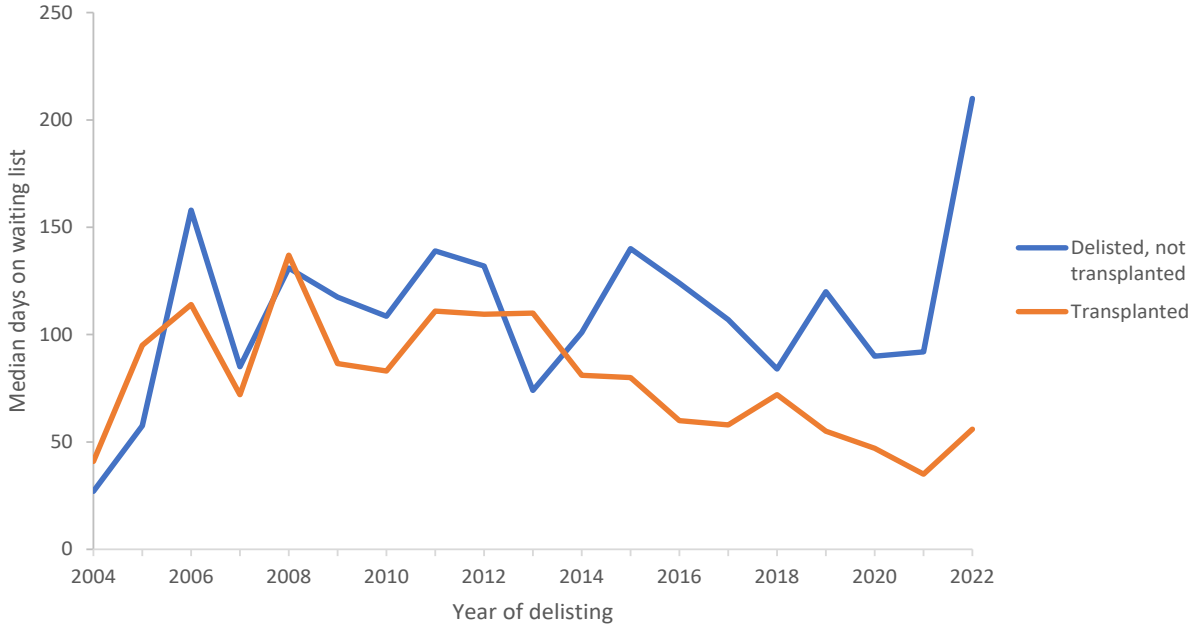


Benchmarking analysis using hierarchical regression models estimated that 4.1% of the variation in 90-day waiting list mortality and 3.0% of the variation in 1-year waiting list mortality was due to variation between liver transplant units.

5.4 Time on the Waiting List

The median time from listing to transplantation by the year of transplantation was 137 days in 2008 and has decreased to 56 days in 2022 (Figure 4). The median time from listing to delisting without transplant was 140 days in 2015 and has increased to 210 days in 2022.

Figure 4. Time on waiting list by year of delisting



5.5 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://tsanz.com.au/guidelinesethics-documents/organallocationguidelines.htm

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. It is subject to discussion between the directors (or delegates) of donor and recipient state (or New Zealand) liver transplant centres.
- 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. If a potentially suitable donor is identified, the home unit must discuss allocation of donor organs with the Victoria unit unless the home unit has a suitable liver recipient with a MELD score of 25 or greater.

Good outcomes have been achieved for patients listed as urgent category 1 and 2 (Figures 5 and 6).

The urgent category 1 waiting list mortality rate for the last five years (2018 – 2022) was 8.6% (eight deaths in 93 category 1 listings). In 2022, one of the 17 patients on the category 1 waiting list died, resulting in a waiting list mortality rate of 5.9%.

The urgent category 2 waiting list mortality rate for the last five years (2018 – 2022) was 3.9% (three deaths in 76 category 2 listings). There was one death out of 13 patients (7.7%) listed as category 2 in 2022.

Figure 5. Urgent category 1 waiting list outcomes
Data show the outcome of urgent listings for each year. The outcomes of patients still listed at the end of the year are reported in the subsequent year.

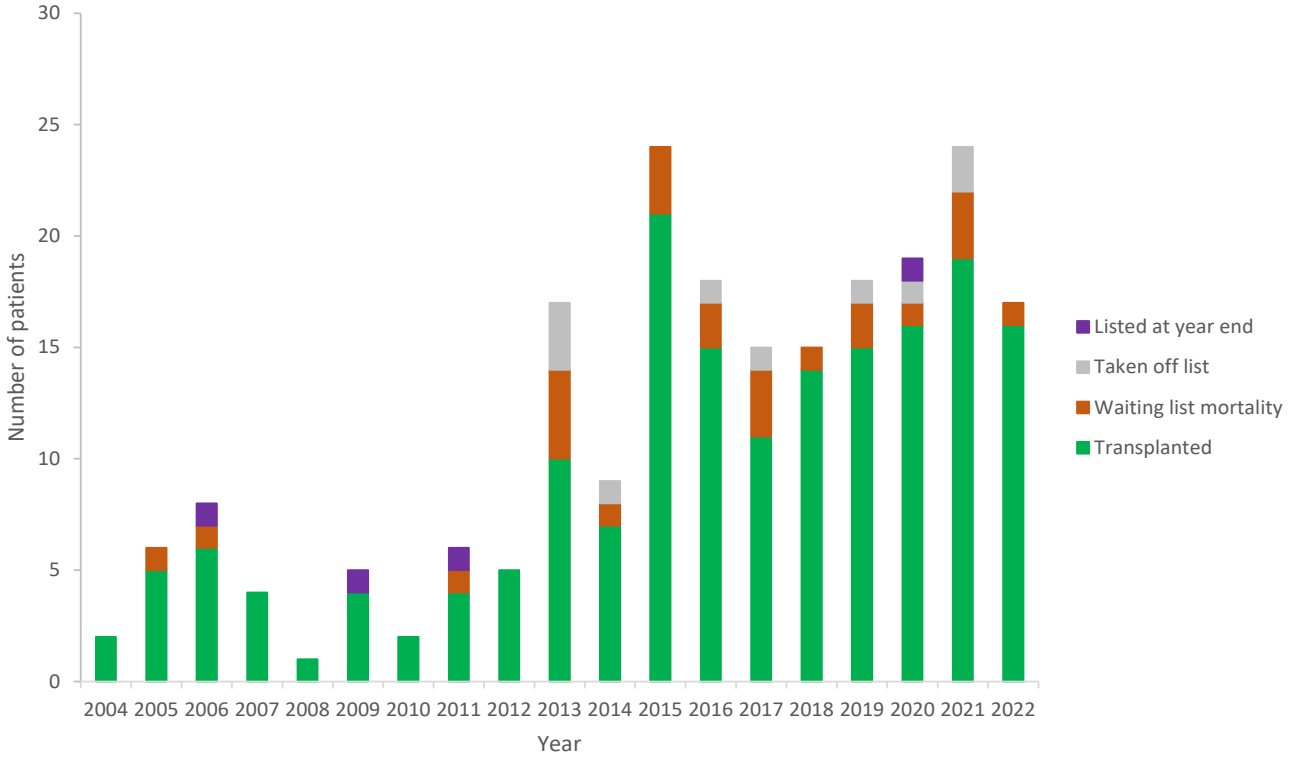
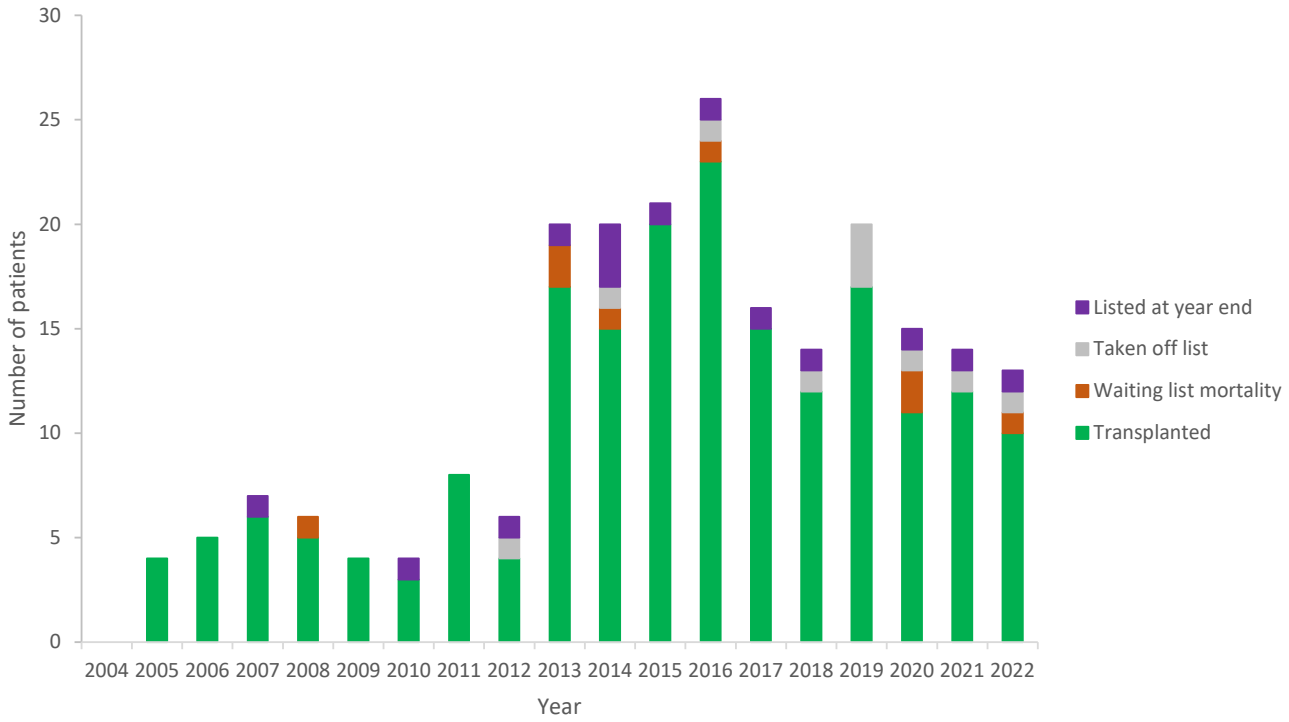


Figure 6. Urgent category 2 waiting list outcomes
Data show the outcome of urgent listings for each year. The outcomes of patients still listed at the end of the year are reported in the subsequent year.



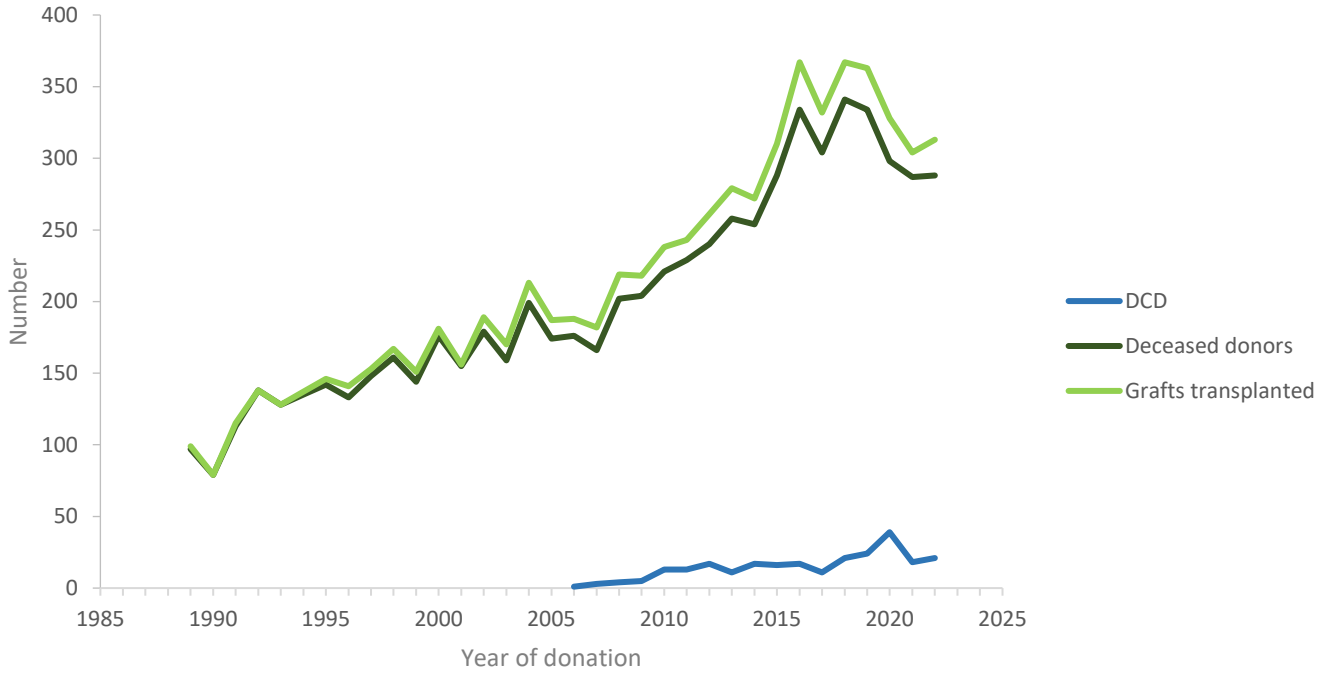
6 Deceased Liver Donors

Of 7,580 liver transplants, 7,460 (98.4%) were sourced from deceased donors, with only a small proportion from living donors (120, 1.6%). Collection of deceased donor information commenced in 1989. There is no deceased donor information on 126 transplants from 1985 to 1988. Subsequent analysis is limited to 6,884 deceased donors and 7,334 grafts from 1989 onwards with donor data.

6.1 Deceased Donors and Grafts Transplanted Per Year

Of 6,884 deceased donors with donor data, 451 donated livers were split (one graft was not utilised from one split liver, so there were 901 split grafts transplanted), resulting in a total of 7,334 grafts. The number of deceased donors has grown steadily over the years until recently (Figure 7). In 2022 there were 288 deceased donors providing 313 grafts. The number of deceased donors and grafts have not returned to the peak that occurred in 2018. Whilst there was only one more deceased donor in 2022 compared to 2021, more livers were split in 2022 compared to 2021 (25 of 288, 8.7% in 2022, 17 of 287, 5.9% in 2021) resulting in an increase in grafts utilised. Of 288 deceased donors in 2022, 21 (7.3%) were donation after circulatory death donors.

Figure 7. Deceased donors and grafts transplanted by year



Abbreviation: DCD, donation after circulatory death

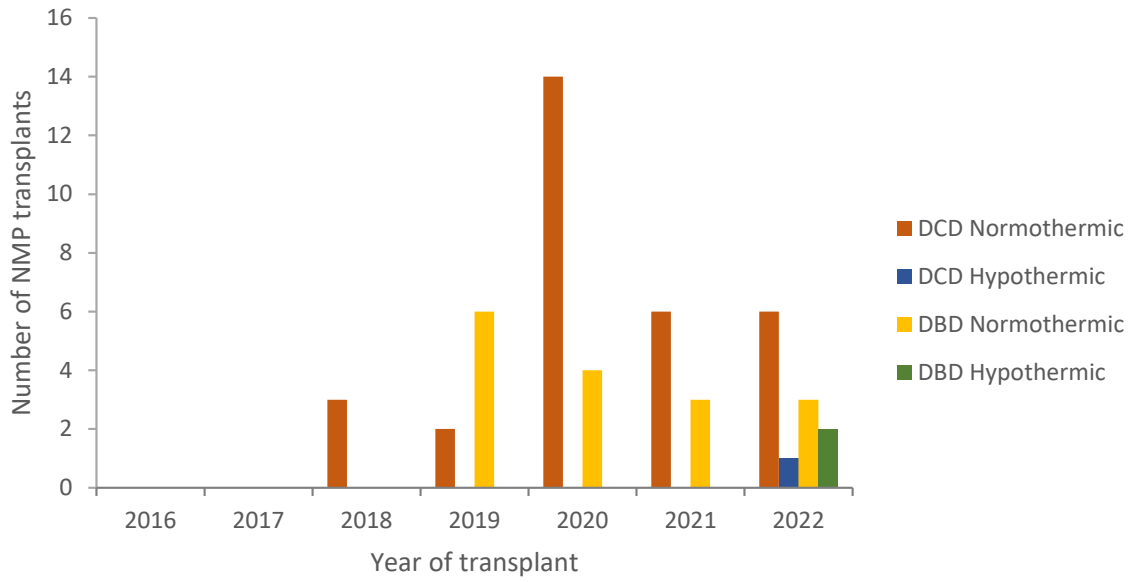
6.2 Machine Perfusion of Deceased Donor Livers

Machine perfusion has been introduced as a preservation method in liver transplantation in recent years. The availability of machine perfusion has enabled greater utilisation of donation after circulatory death donor livers as donor liver viability/functionality can be assessed whilst being perfused and increases the time the liver can be held prior to transplant.

Queensland commenced normothermic machine perfusion (NMP) in 2018 and Victoria in 2019. New Zealand commenced hypothermic oxygenated perfusion (HOPE) in 2022.

There have been 47 transplants using NMP and three using HOPE. In 2022, seven (33.3%) of the 21 transplanted livers sourced from DCD donors were supported using machine perfusion (Figure 8, Table 1).

Figure 8. Transplants utilising machine perfusion with donor source type



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

Table 1. Transplants with donor source type and use of machine perfusion

	Donation after circulatory death					Donation after Brain Death				
Transplant Year	**DCD NMP**	**DCD HOPE**	**DCD no MP**	**DCD Total**	**% DCD with MP**	**DBD NMP**	**DBD HOPE**	**DBD no MP**	**DBD Total**	**% DBD with MP**
2016	0	0	17	**17**	*0.0%*	0	0	350	**350**	*0.0%*
2017	0	0	11	**11**	*0.0%*	0	0	321	**321**	*0.0%*
2018	3	0	18	**21**	*14.3%*	0	0	346	**346**	*0.0%*
2019	2	0	22	**24**	*8.3%*	6	0	333	**339**	*1.8%*
2020	14	0	25	**39**	*35.9%*	4	0	285	**289**	*1.4%*
2021	6	0	12	**18**	*33.3%*	3	0	283	**286**	*1.0%*
2022	6	1	14	**21**	*33.3%*	3	2	287	**292**	*1.7%*

Abbreviations: DCD, donation after circulatory death; DBD, donation after brain death; NMP, normothermic machine perfusion; HOPE, hypothermic oxygenated perfusion; MP, machine perfusion

6.3 Age of Deceased Donors

There has been a progressive increase in donor age from a median of 28 years in 1990-94 to 46 years in 2010-14. The median age plateaued at 46 years over the subsequent eras (Figure 9).

Figure 9. Median age of deceased donors by transplant era
Box and whisker plot: median, interquartile range and 1.5 times interquartile range shown

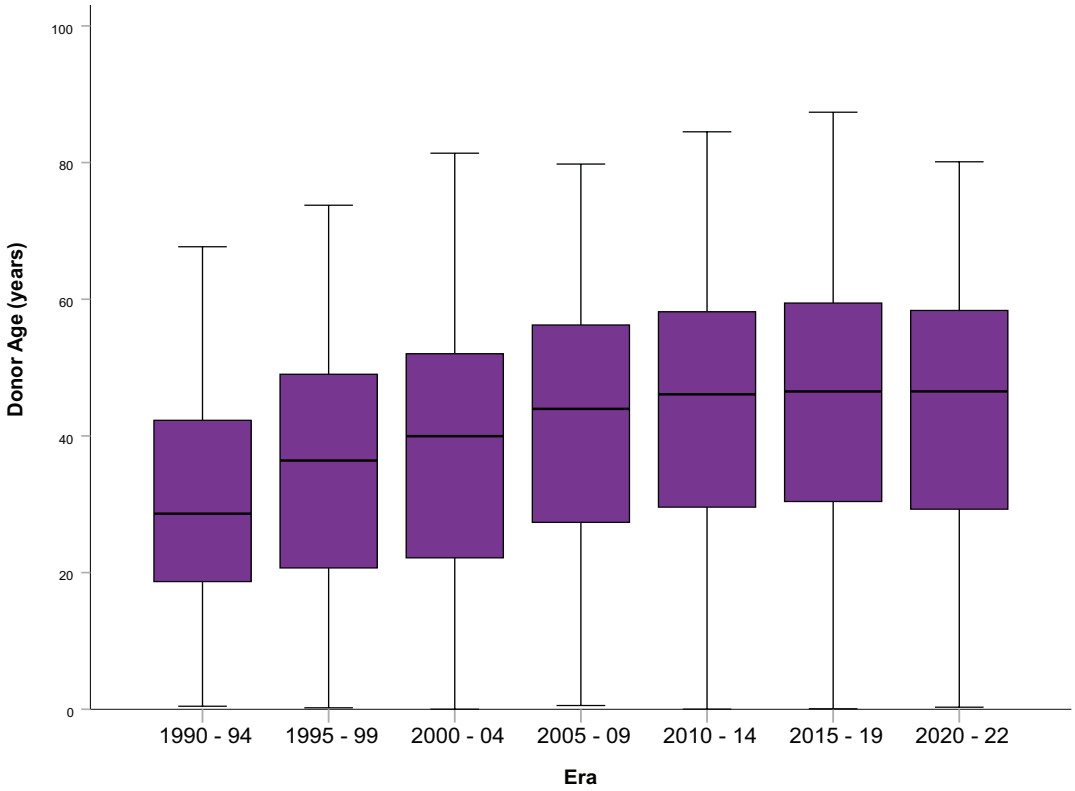
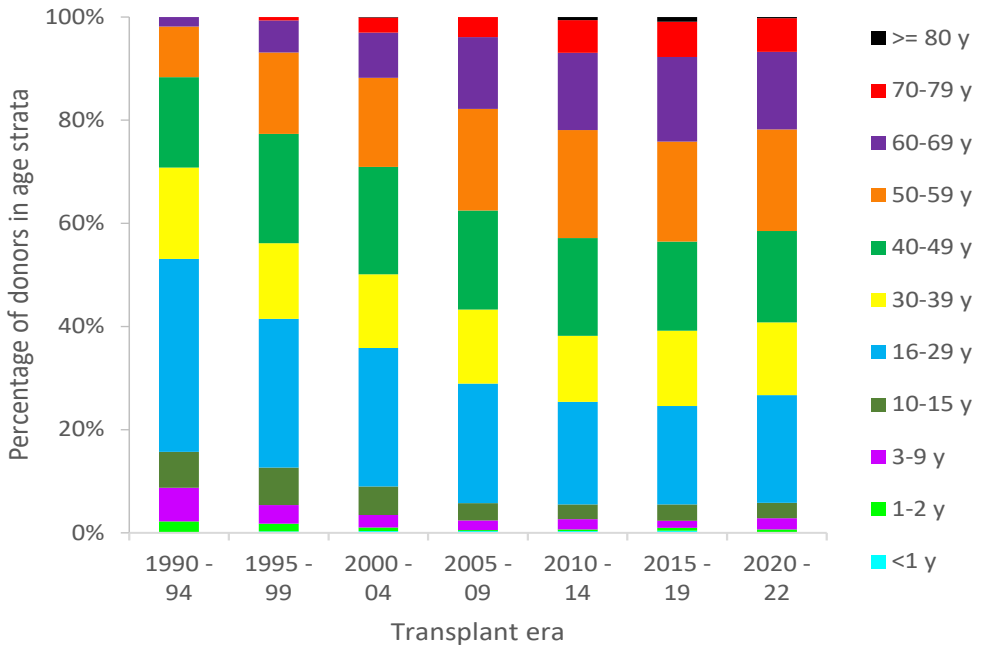


Figure 10 demonstrates the changing deceased donor age profile over the various transplant eras. There has been a progressive increase in the proportion of donors aged 50-59, 60-69, 70-79 and ≥ 80 years from 10%, 2% 0% and 0%, respectively in the 1990-94 era to 21%, 15%, 6% and 1%, respectively in the 2010-14 era but stabilisation in these proportions subsequently.

Figure 10. Deceased donor age by transplant era



7 Living Liver Donors

Of 7,580 liver transplants, 120 (1.6%) were sourced from living donors (including five domino livers). Paediatric recipients received the majority (81.7%) of living liver donations (Table 2). There have been no deaths of living liver donors.

Table 2. Living liver donor demographics

Living Donors	**Paediatric Recipient** (<16 years)	**Adult Recipient** (≥16 years)	**All Recipients**
Number of living donors	**98**	**22**	**120**
% living donors	81.7%	18.3%	
Gender of living donor			
Female *(% age category)*	46 *(46.9%)*	8 *(36.4%)*	**54 *(45.0%)***
Male *(% age category)*	52 *(53.1%)*	14 *(63.6%)*	**66 *(55.0%)***
Age of living donor (years)			
Median	34	33	**33**
Range	19 – 54	18 – 63	**18 – 63**
Living donor relationship			
Father	41	1	42
Mother	25	0	25
Aunt	11	0	11
Family friend	8	1	9
Brother	2	3	5
Domino whole liver	0	5	5
Son	0	5	5
Cousin	4	0	4
Sister	0	3	3
Uncle	3	0	3
Daughter	0	2	2
Grandmother	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 2022

There were 314 liver transplants performed on 306 recipients in 2022. The number of liver transplants increased from 307 in 2021 but has not returned to the pre-COVID peak of 369 transplants in 2018.

The liver transplant rates in 2022 for Australia and New Zealand were 9.9 and 10.5 liver transplants per million population, respectively (Australia population in 2022: 26.3 million; New Zealand population in 2022: 5.2 million, source: https://www.abs.gov.au/statistics/people/population, https://www.stats.govt.nz/topics/population).

8.1 Demographic Data for Patients Transplanted in 2022

Of the 306 patients receiving a transplant in 2022, 13.7% were children. Females represented 54.8% of paediatric patients transplanted but only 34.8% of the adult population (Table 3. Patient demographics by age group (2022).

Table 3. Patient demographics by age group (2022)

Patients Transplanted in ANZ in 2022	**Children** (<16 years)	**Adults** (≥16 years)	**Total Patients**
Number of patients *(% total patients)*	42 *(13.7%)*	264 *(86.3%)*	306
Sex			
Female *(% age category)*	23 *(54.8%)*	92 *(34.8%)*	115 *(37.6%)*
Male *(% age category)*	19 *(45.2%)*	172 *(65.2%)*	191 *(62. %)*
Age at first ANZ transplant in 2022			
Mean ± SD (years)	5 ± 5	54 ± 11	47 ± 20
Median (years)	1	57	54
Range	10 d - 15 y	18y - 75 y	10 d - 75 y
Interquartile range	8 m - 9 y	47 y - 63 y	39 y - 62 y
Status of patients at 31/12/2022			
Alive *(% age category)*	41 *(97.6%)*	250 *(94.7%)*	291 *(95.1%)*
Deceased *(% age category)*	1 *(2.4%)*	14 *(5.3%)*	15 *(4.9%)*

Abbreviations: ANZ, Australia or New Zealand; d, day; y, year

8.2 Transplants in 2022

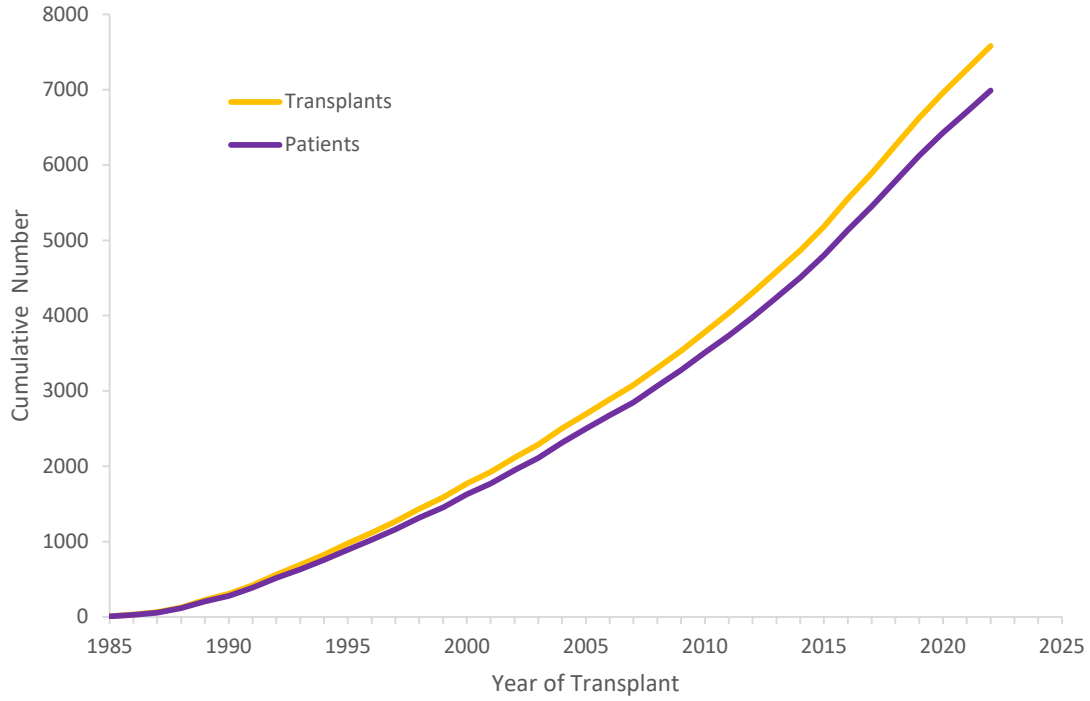
The majority of the 314 transplants were for adult patients (270, 86.0%), whilst 44 (14.0%) transplants were performed on children.

Of the 306 patients transplanted in 2022, 283 (92.5%) patients had their first transplant in 2022. Of these, six required retransplantation (i.e. two transplant operations in 2022). Twenty-two patients who had a single transplant prior to 2022 were retransplanted in 2022. Two of these went on to have another (their third) transplant in 2022. One patient who had two transplants prior to 2022 was retransplanted with their third graft in 2022.

9 Liver Transplantation from 1985 – 2022

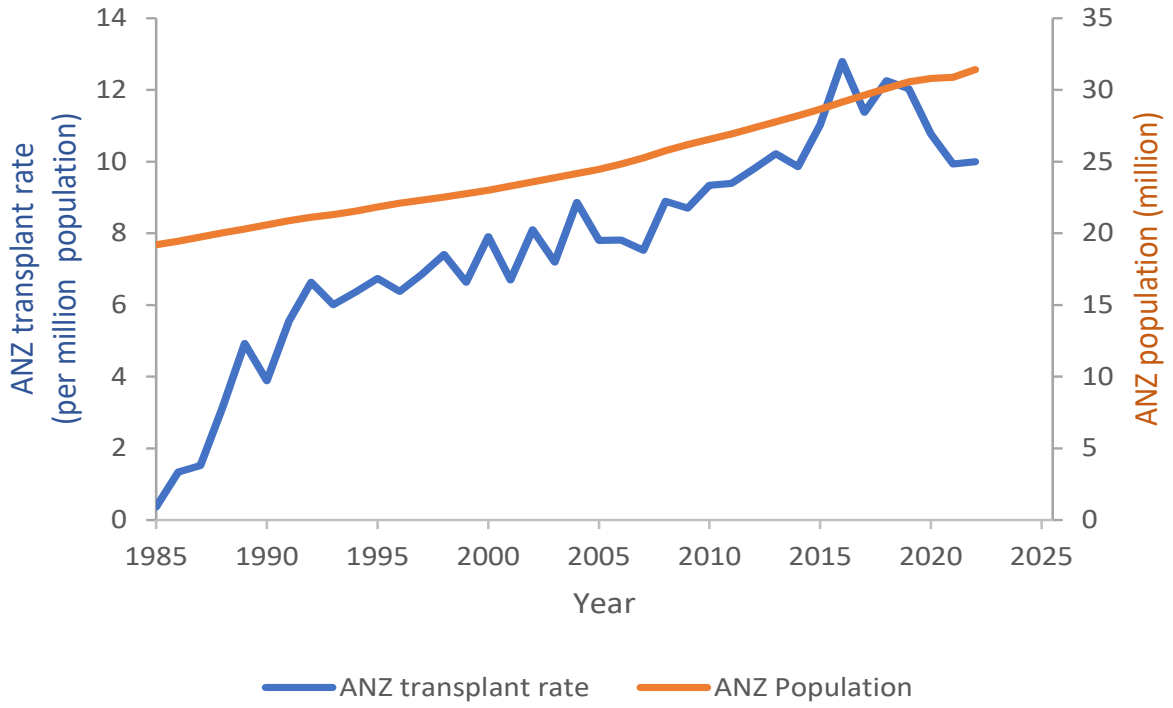
There have been 7,580 liver transplants undertaken on 6,983 patients between 1985 and 2022. Figure 11 shows the cumulative number of patients and transplants.

Figure 11. Cumulative number of liver transplants and new patients transplanted



There has been an increase over time of the number of transplants per million population from 5.6 in 1991, peaking at 12.8 in 2016 and then falling to 10.0 in 2022. (Australia and New Zealand population source: https://www.abs.gov.au/statistics/people/population, https://www.stats.govt.nz/topics/population, Figure 12).

Figure 12. Liver transplant rate and total Australia and New Zealand population



9.1 Demographic Data for Patients Transplanted from 1985 - 2022

Demographic data are based on the first liver transplant undertaken in Australia or New Zealand across all years. Six patients had their first liver transplant overseas prior to undergoing retransplantation in Australia and New Zealand, including one patient who had two liver transplants overseas. (6,989 patients, 6,983 graft 1, 5 graft 2, 1 graft 3).

Of 6,989 patients receiving a transplant from 1985 to 2022, 16.2% were children. Females comprised 51.2% of paediatric patients but only 33.7% of adult patients (Table 4).

Table 4. Patient demographics by age group (1985 – 2022)

Patients Transplanted in ANZ from 1985 to 2022	**Children** (<16 years)	**Adults** (≥16 years)	**Total Patients**
Number of patients *(% total patients)*	1,132 *(16.2%)*	5857 *(83.8%)*	6,989
Sex			
Female *(% age category)*	580 *(51.2%)*	1,973 *(33.7%)*	2,553 *(36.5%)*
Male *(% age category)*	552 *(48.8%)*	3,884 *(66.3%)*	4,436 *(63.5%)*
Age at first ANZ transplant			
Mean ± SD (years)	4 ± 4	50 ± 11	43 ± 20
Median (years)	2	53	50
Range	10 d - 15 y	16 y - 75 y	10 d - 75 y
Interquartile range	10 m - 7 y	44 y - 59 y	33 y - 58 y
Status of patient			
Alive *(% age category)*	939 *(83.0%)*	3,862 *(65.9%)*	4,801 *(68.7%)*
Deceased *(% age category)*	193 *(17.0%)*	1,995 *(34.1%)*	2,188 *(31.3%)*

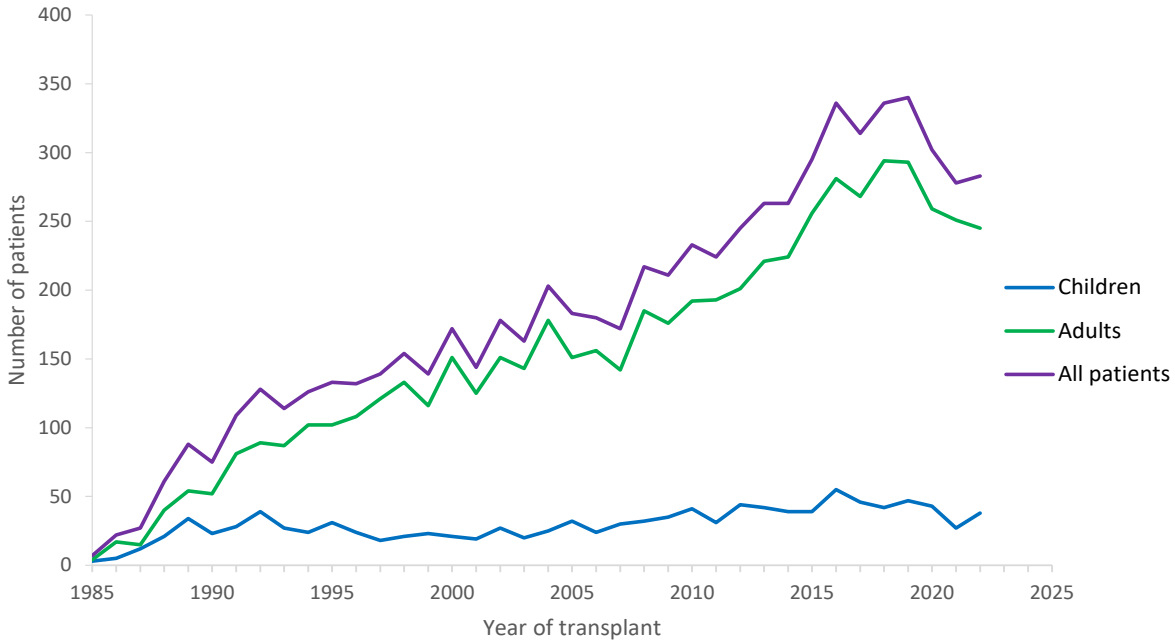
Abbreviations: ANZ, Australia or New Zealand; m, month; y, year

9.1.1 Patients Transplanted by Year of First Transplant

From 2007 to 2019, there was a 97.7% increase in the number of patients transplanted per year, based on the year of their first transplant, from 172 to 340, including a 56.7% increase in the number of children transplanted (30 to 47) and a 106.3% increase in the number of adults transplanted (142 to 293, Figure 13). From 2019 to 2021, there was a 18.2% decrease in the number of patients transplanted per year, from 340 to 278, including a 42.6% decrease in the number of children transplanted (47 to 27) and a 14.3% decrease in the number of adults transplanted (293 to 251).

From 2021 to 2022, there was a 40.7% increase in the number of children transplanted (27 to 38) with a small 2.4% decrease in the number of adults transplanted (251 to 245).

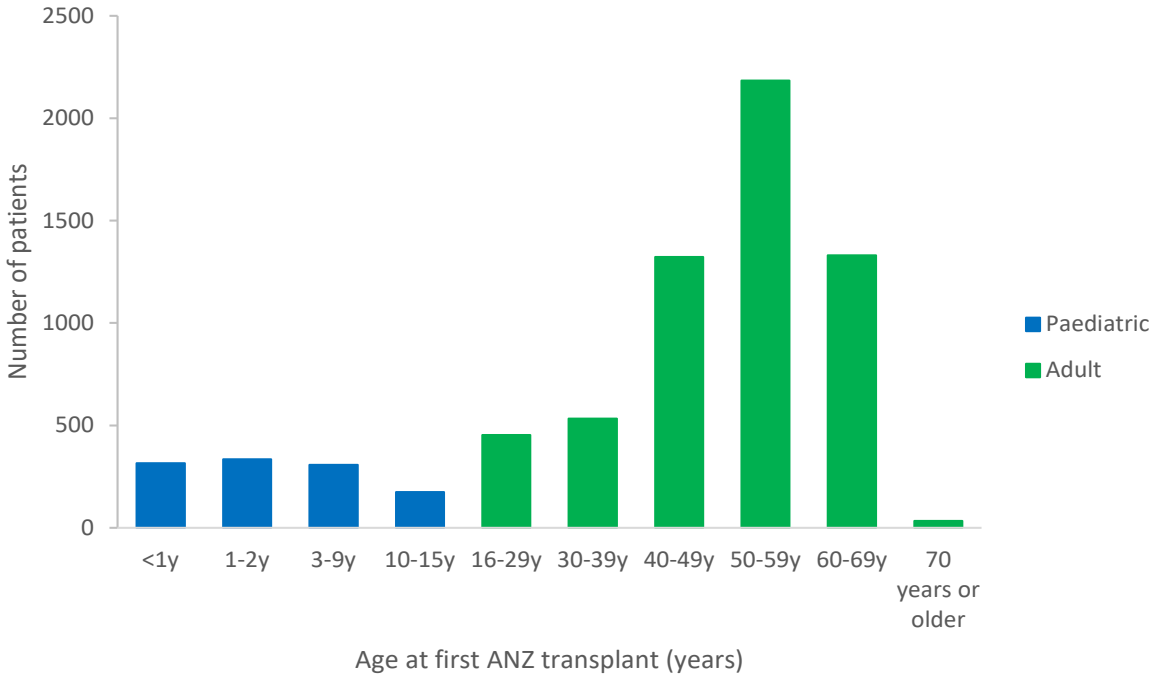
Figure 13. Number of patients transplanted by age group by year of first transplant



9.1.2 Recipient Age at First Transplant (1985 – 2022)

Of the 1,132 paediatric transplant recipients, 27.9% were infants less than one year old and 15.4% were adolescents 10 to 15 years old (Figure 14). Of the 5,857 adult recipients, 37.3% were in their 50s and only 0.6% were in their 70s.

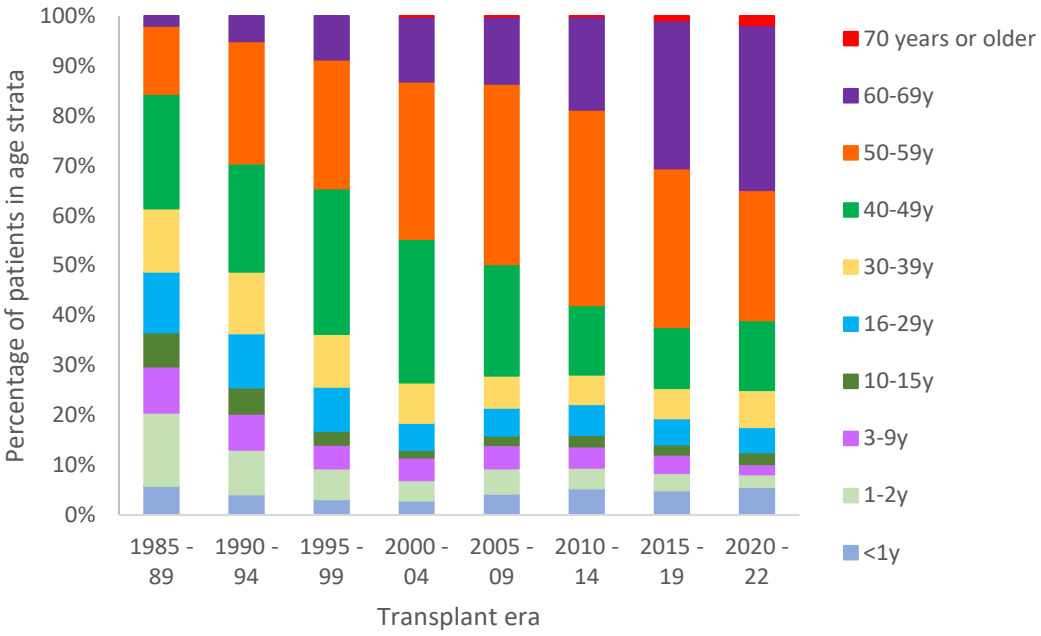
Figure 14. Recipient age strata at first Australian or New Zealand transplant (1985 – 2022)



9.1.3 Recipient Age at First Transplant by Era of Transplant

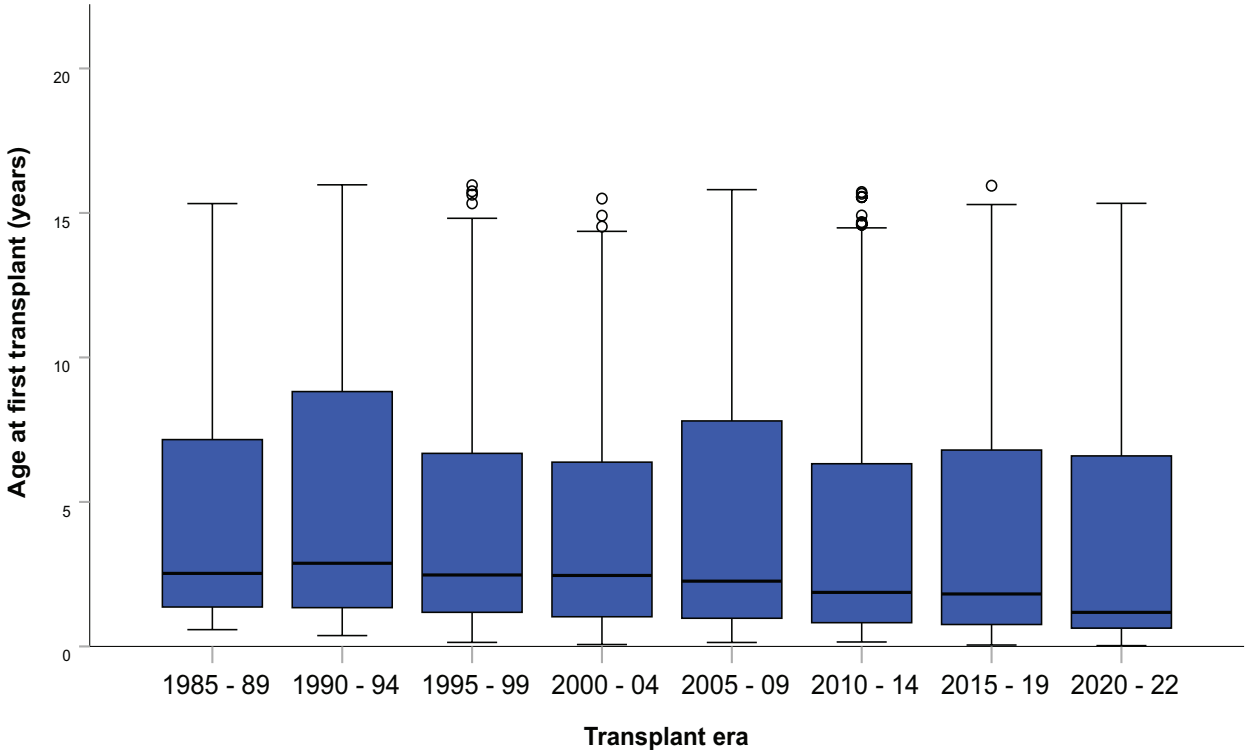
Figure 15 demonstrates the changing recipient age profile over the various transplant eras. There has been a progressive increase in the proportion of recipients aged 60-69 and ≥ 70 years from 2.0% and 0%, respectively in the 1985 - 89 era to 33.0% and 1.9%, respectively in the 2020 - 22 era. Whilst the proportion of recipients aged 50-59 years has increased over eras to peak in 2010 - 14 era at 39.2%, it has decreased to 31.8% in the 2015 - 19 era and to 26.1% in 2020 – 22 era. The proportion of recipients aged less than one year ranged between 2.9% and 5.9% in all eras.

Figure 15. Recipient age strata (percentages) by transplant era



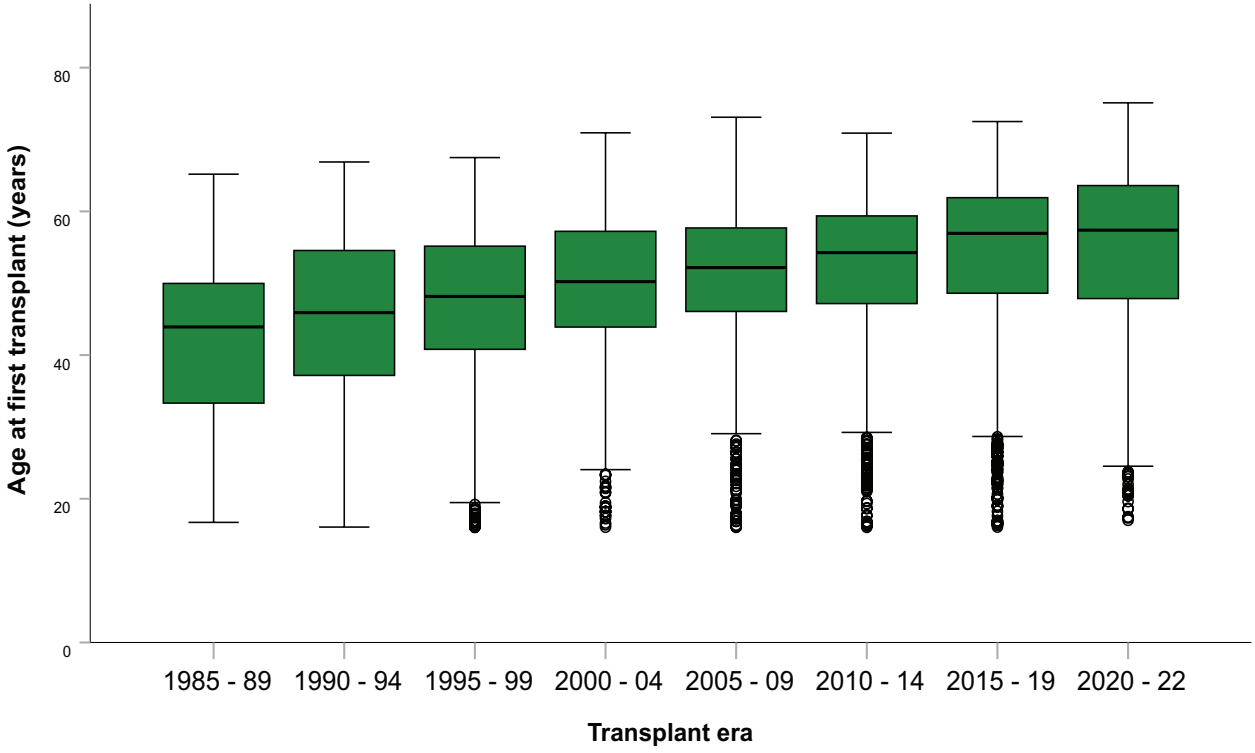
The median paediatric recipient age has been gradually decreasing over the transplant eras, from 2 years and 6 months in 1985-89 to 1 year and 2 months in 2020-22 (P=0.001, Figure 16).

Figure 16. Paediatric age at first transplant by transplant era
Box and whisker plot: median, interquartile range, 1.5 times interquartile range and outliers shown



The median adult recipient age has been gradually increasing over the transplant eras, from 43 years in 1985-89 to 57 years in 2020-22 (P<0.001, Figure 17).

Figure 17. Adult age at first transplant by transplant era
Box and whisker plot: median, interquartile range, 1.5 times interquartile range and outliers shown



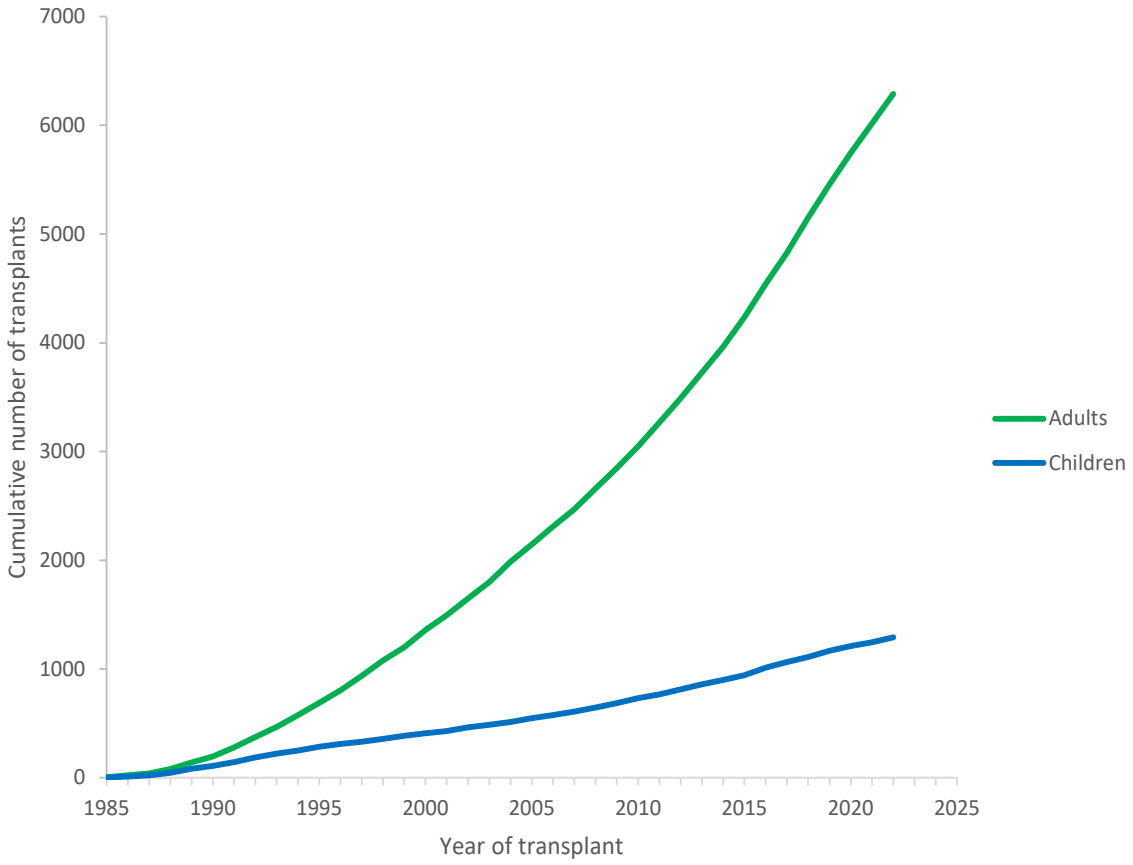
9.2 Transplants (1985 – 2022)

Of the 7,580 transplants, 6,289 (83.0%) were performed in adults and 1,291 (17.0%) in children (<16 years, Table 5, Figure 18). Since the first transplant in 1985, 522 (7.5%) recipients have undergone retransplantation in Australia or New Zealand. Of these, 467 patients had one retransplant, 59 patients have required two retransplants and two patients had three retransplants.

Table 5. Transplants by age group (1985 – 2022)

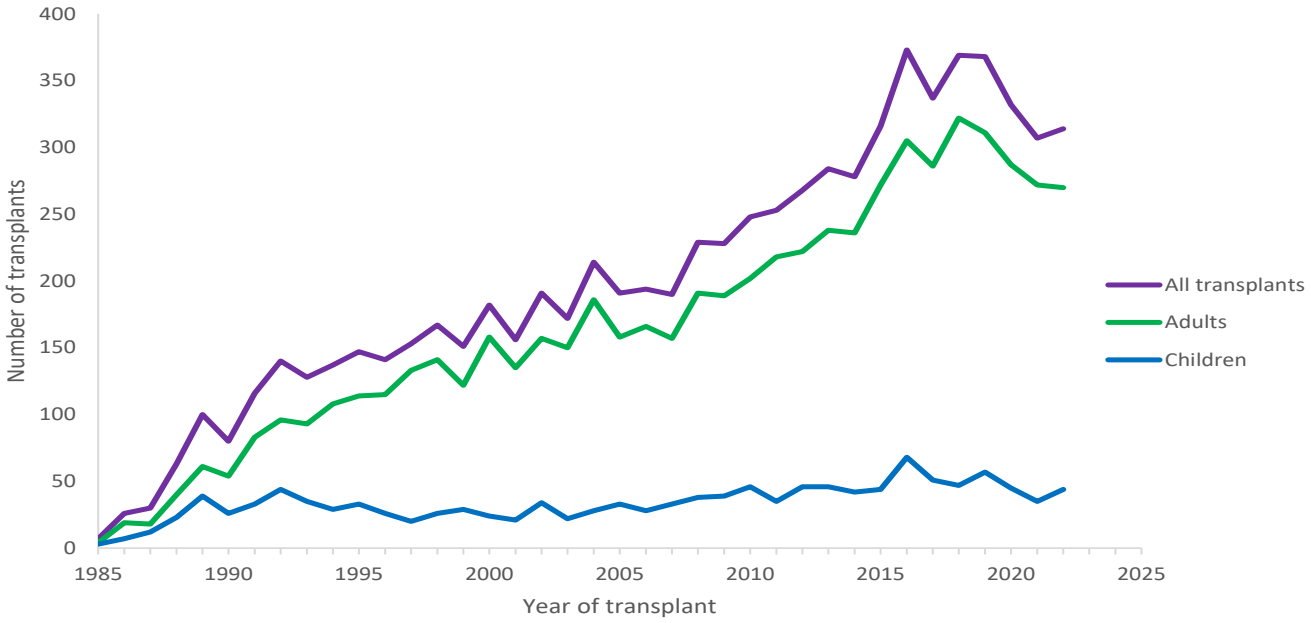
Transplants Transplanted in ANZ from 1985 to 2022	**Children** (<16 years)	**Adults** (≥ 16 years)	**Total**
Number of transplants *(% total transplants)*	1,291 *(17.0%)*	6,289 *(83.0%)*	**7,580**
Number of patients *(% total patients)*	1,132 *(16.2%)*	5,857 *(83.8%)*	**6,989**

Figure 18. Cumulative number of liver transplants per year by age category



There was a 2.3% increase in the number of transplants from 2021 to 2022, following the 7.5% reduction in liver transplants in 2020 to 2021. The number of transplants performed increased from 307 in 2021 to 314 in 2022, due to the increased number of transplants in children from 35 to 44. Adult transplants showed a very small decrease (272 in 2021, 270 in 2022 Figure 19).

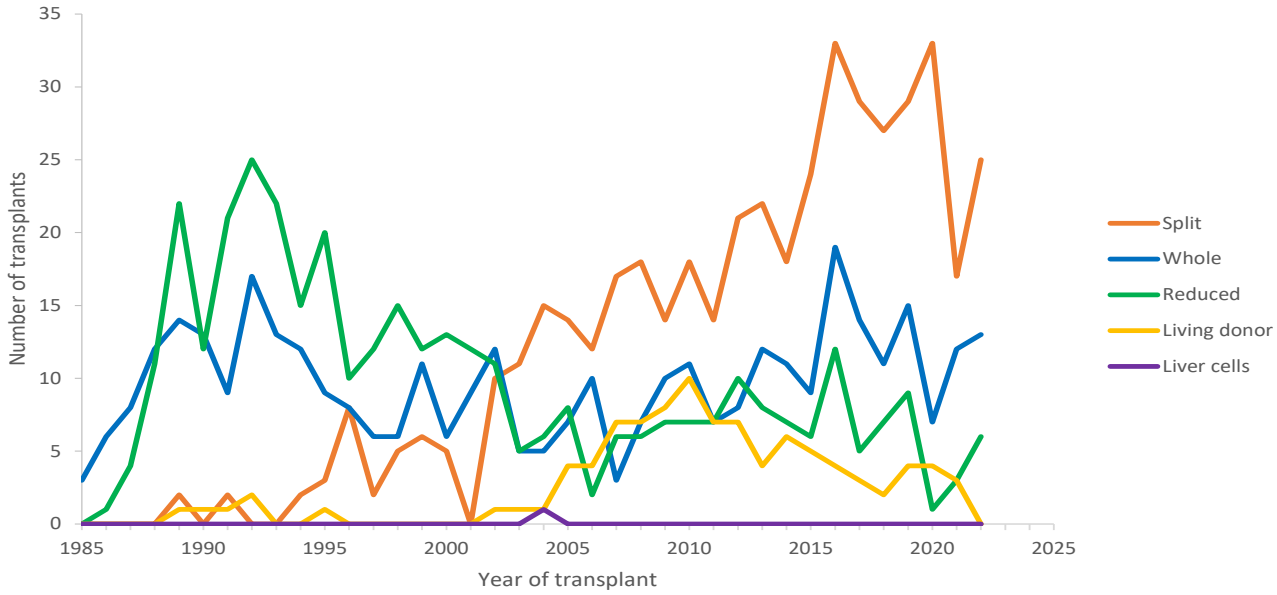
Figure 19. Number of liver transplants per year by recipient age category



9.2.1 Type of Graft – Paediatric Recipients, All Years

The first paediatric liver transplant (whole liver) 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, peaking at 73.3% in 2020, decreasing to 48.6% in 2021 and increasing to 56.8% in 2022 (Figure 20). The number of living donors peaked at 10 in 2010 and subsequently this has become an infrequent method of transplantation in children (no living donor transplants in 2022).

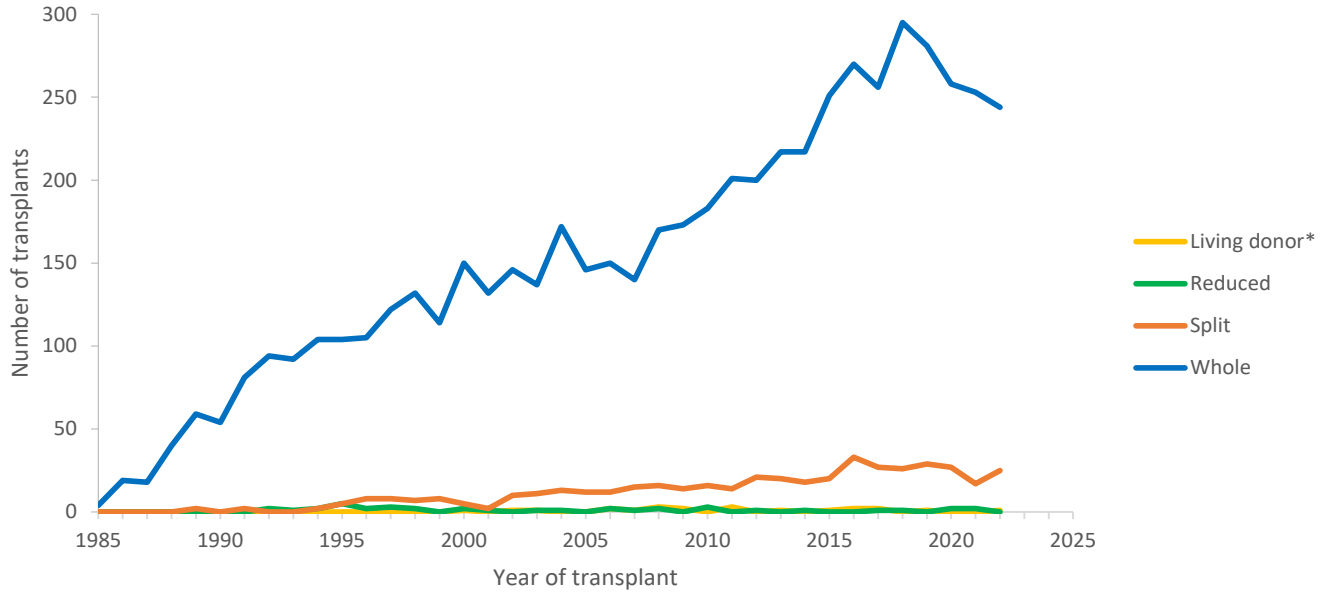
Figure 20. Type of graft for paediatric recipients – all years



9.2.2 Type of Graft – Adult Recipients, All Years

The dominant form of liver transplantation in adults is whole liver transplantation (244 of 270 transplants, 90.4% in 2022, Figure 21). The number of deceased donor split liver transplants in adults has increased from 5 of 158 transplants (3.2%) in 2000 to 25 of 270 (9.3%) in 2022. There has been a total of 22 adult-to-adult living donor liver transplants performed, including five domino liver transplants.

Figure 21. Type of graft for adult recipients – all years



* Includes domino grafts

10 Diagnoses at First Transplant

10.1 Diagnoses in Children

Of 1,130 children who underwent their first liver transplant in Australia or New Zealand, the most common primary diagnoses were biliary atresia (53.4%), metabolic disorders (14.7%) and fulminant hepatic failure (FHF, 10.6%, Table 6). The primary diagnosis and up to three additional diagnoses are collected in the ANZLITR. There were 29 secondary diagnoses and no tertiary or quaternary diagnoses recorded for children.

Table 6. Diagnosis in children

Diagnosis	Primary Diagnosis	% of Children with Primary Diagnosis	All Diagnoses	% of Children with Diagnosis
Biliary atresia	603	53.4%	**604**	53%
Metabolic disorders*	166	14.7%	**169**	15%
Fulminant hepatic failure#	120	10.6%	**122**	11%
Cancers	51	5%	**62**	5%
- Hepatoblastoma	*37*	*3%*	***38***	*3%*
- Hepatocellular carcinoma	*9*	*1%*	***15***	*1%*
- Histiocytosis X	*5*	*0.4%*	***6***	*0.5%*
- Cholangiocarcinoma	*0*	*0.0%*	***3***	*0.3%*
Alagille syndrome	43	4%	**44**	4%
PFIC	33	3%	**33**	3%
Cryptogenic cirrhosis	25	2%	**25**	2%
Cystic fibrosis	21	2%	**21**	2%
Autoimmune cirrhosis	12	1.1%	**13**	1%
Primary sclerosing cholangitis	9	0.8%	**12**	1.1%
Neonatal hepatitis	6	0.5%	**6**	0.5%
Caroli's disease	4	0.4%	**4**	0.4%
Choledochal cyst	3	0.3%	**4**	0.4%
Intestinal failure associated liver disease	4	0.4%	**4**	0.4%
Congenital intrahepatic portosystemic shunt	3	0.3%	**3**	0.3%
Ductopenia	3	0.3%	**3**	0.3%
Secondary biliary cirrhosis	3	0.3%	**3**	0.3%
Autoimmune sclerosing cholangitis	2	0.2%	**2**	0.2%
Common variable immune deficiency	2	0.2%	**2**	0.2%
Gestational alloimmune liver disease	2	0.2%	**2**	0.2%
Hepatic veno-occlusive disease	2	0.2%	**2**	0.2%
Hepatopulmonary syndrome	0	0.0%	**2**	0.2%
Polycystic liver +/- kidney disease	2	0.2%	**2**	0.2%
Arterio-venous malformation	1	0.1%	**1**	0.1%
Bile salt synthetic defect	1	0.1%	**1**	0.1%
Cornelia de Lange syndrome	1	0.1%	**1**	0.1%
Enterovirus hepatitis	1	0.1%	**1**	0.1%
Established cirrhosis with marked cholestasis	1	0.1%	**1**	0.1%
Hepatic fibrosis / polycystic kidney disease	1	0.1%	**1**	0.1%
Hepatic lymphangiomatosis	1	0.1%	**1**	0.1%
Hepatitis B virus cirrhosis	0	0.0%	**1**	0.1%
Idiopathic copper toxicosis	1	0.1%	**1**	0.1%
Ischaemic sclerosing cholangitis	1	0.1%	**1**	0.1%
Ivemark Syndrome	0	0.0%	**1**	0.1%
Nephronophthisis	0	0.0%	**1**	0.1%
Nodular regenerative hyperplasia	1	0.1%	**1**	0.1%
Parvovirus	1	0.1%	**1**	0.1%
Portopulmonary hypertension	0	0.0%	**1**	0.1%
Total	**1130**	100.0%	**1159**	102.6%

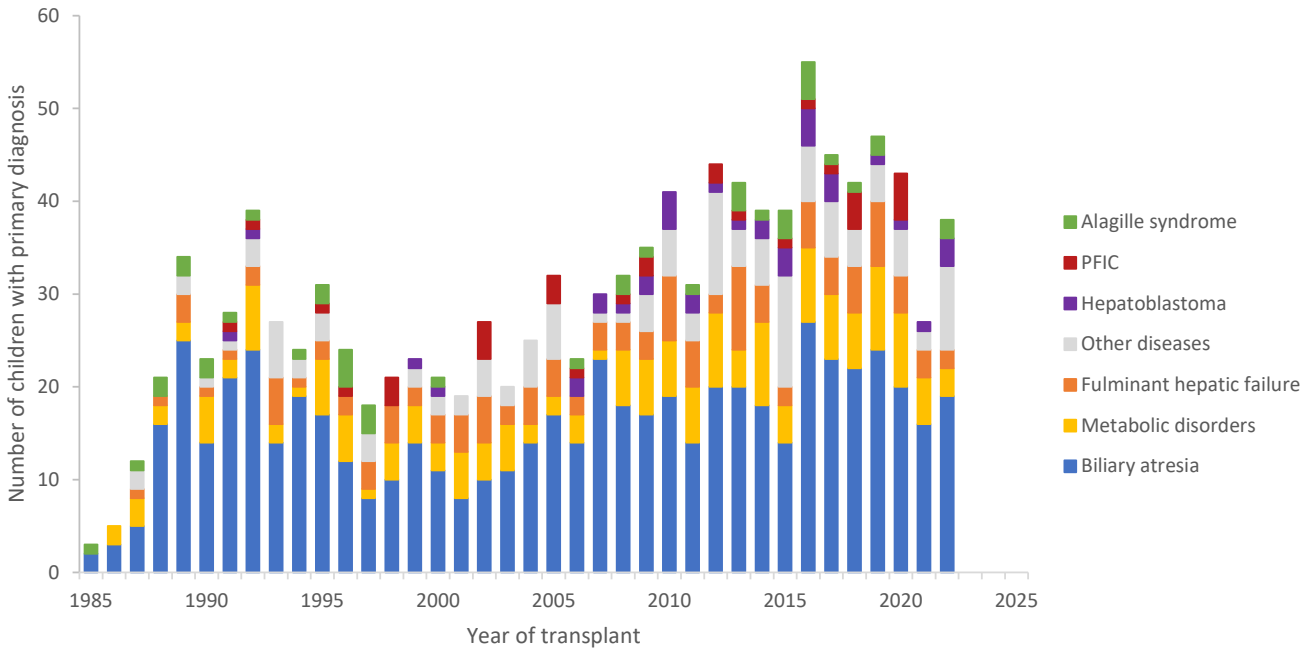
* See Table 9 for breakdown of metabolic disorders

See Table 8 for breakdown of causes of fulminant hepatic failure

10.2 Primary Diagnosis Trend in Children

The primary diagnosis indications for liver transplantation in children have remained relatively stable over time (Figure 22).

Figure 22. Primary paediatric diagnosis

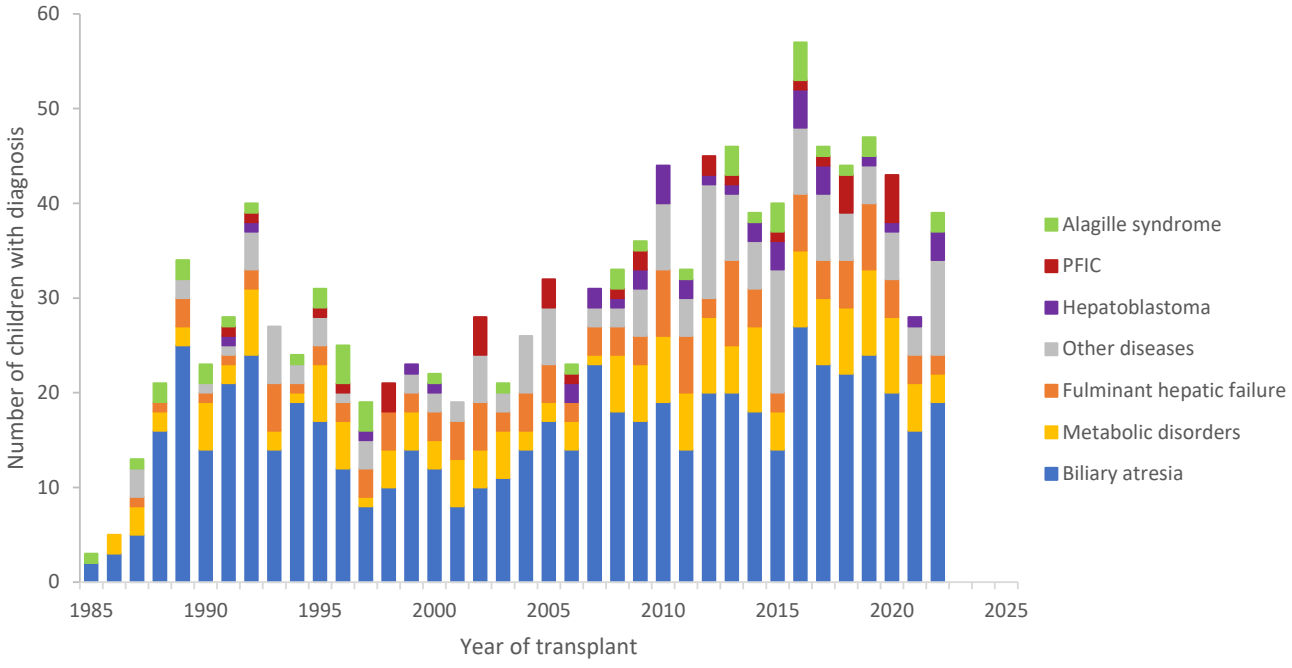


Abbreviation: PFIC, Progressive familial intrahepatic cholestasis

10.3 All Diagnoses Trend in Children

All diagnosis indications for liver transplantation in children have remained relatively stable over time (Figure 23).

Figure 23. All paediatric diagnoses



Abbreviation: PFIC, Progressive familial intrahepatic cholestasis

10.4 Diagnoses in Adults

Of 5,853 adults who underwent their first liver transplant in Australia or New Zealand, the most common primary diagnoses were hepatitis C virus cirrhosis (19.4%), alcohol-related cirrhosis (14.4%) and hepatocellular carcinoma (12.8%, Table 7).

The primary diagnosis and up to three additional diagnoses are collected in the ANZLITR. In addition to the 5,853 primary diagnoses, there were 2,527 additional diagnoses recorded for adults. The proportion of patients with hepatitis C virus cirrhosis increased from 19.4% as a primary diagnosis to 27.1% across all diagnoses. The proportion of patients with hepatocellular carcinoma as a primary diagnosis was 12.8% and increased to 26.4% across all diagnoses. The proportion of patients with alcohol-related cirrhosis as a primary diagnosis was 14.4% and increased to 24.8% across all diagnoses.

Table 7. Primary and additional diagnoses in adults

Diagnosis	Primary Diagnosis	% of Adults with Primary Diagnosis	All Diagnoses	% of Adults with Diagnosis
Hepatitis C virus cirrhosis	1137	19%	**1589**	27%
Cancers	781	13%	1616	28%
- Hepatocellular carcinoma	*749*	*13%*	***1543***	*26%*
- Cholangiocarcinoma	*12*	*0.2%*	***47***	*0.8%*
- Epithelioid haemangioendothelioma	*14*	*0.2%*	***15***	*0.3%*
- Metastatic neuroendocrine tumour	*6*	*0.1%*	***7***	*0.1%*
- Histiocytosis X	*3*	*0.05%*	***3***	*0.05%*
- Angiosarcoma	*1*	*0.02%*	***2***	*0.03%*
- Hepatoblastoma	*0*	*0%*	***1***	*0.02%*
Alcoholic cirrhosis	841	14%	**1451**	25%
NAFLD / Cryptogenic cirrhosis	562	10%	**740**	13%
Primary sclerosing cholangitis	581	10%	**605**	10%
Fulminant hepatic failure#	516	9%	**554**	9%
Hepatitis B virus cirrhosis	331	6%	**545**	9%
Metabolic disorder*	236	4%	**318**	5%
Primary biliary cirrhosis	292	5%	**296**	5%
Autoimmune cirrhosis	197	3%	**236**	4%
Polycystic liver +/- kidney disease	71	1%	**74**	1%
Biliary atresia	55	0.9%	**56**	1%
Hepatic veno-occlusive disease	44	0.8%	**47**	0.8%
Cystic fibrosis	36	0.6%	**36**	0.6%
Secondary biliary cirrhosis	22	0.4%	**25**	0.4%
Caroli's disease	20	0.3%	**20**	0.3%
Granulomatous hepatitis / sarcoidosis	15	0.3%	**17**	0.3%
Hepatopulmonary syndrome	0	0%	**13**	0.2%
Alagille syndrome	11	0.2%	**11**	0.2%
Hereditary haemorrhagic telangiectasia	10	0.2%	**11**	0.2%
Adenomatosis	5	0.1%	**9**	0.2%
Nodular regenerative hyperplasia	7	0.1%	**8**	0.1%
Cholestatic cirrhosis / Secondary cholangitis	4	0.1%	**7**	0.1%
Progressive familial intrahepatic cholestasis	7	0.1%	**7**	0.1%
Haemangioma	5	0.09%	**6**	0.1%
Portopulmonary hypertension	0	0%	**6**	0.1%
Congenital hepatic fibrosis	5	0.09%	**5**	0.09%
Drug hepatotoxicity	5	0.09%	**5**	0.09%
Haemolytic uraemic syndrome	5	0.09%	**5**	0.09%
Post hepatitic cirrhosis - Drug related	3	0.05%	**5**	0.09%
Secondary biliary cirrhosis - hepatolithiasis	4	0.07%	**5**	0.09%
Chronic cholestatic liver disease	4	0.07%	**4**	0.07%
Cirrhosis - Virus related cirrhosis - Other viruses	2	0.03%	**4**	0.07%

(table continued on next page)

Diagnosis	Primary Diagnosis	% of Adults with Primary Diagnosis	All Diagnoses	% of Adults with Diagnosis
Ductopenia	4	0.07%	**4**	0.07%
Intestinal failure associated liver disease	4	0.07%	**4**	0.07%
Non-cirrhotic portal hypertension	4	0.07%	**4**	0.07%
Recurrent cholangitis	2	0.03%	**4**	0.07%
Oriental cholangiohepatitis	3	0.05%	**3**	0.05%
Choledochal cyst	2	0.03%	**2**	0.03%
Congenital biliary fibrosis	2	0.03%	**2**	0.03%
Parasitic disease - Schistosomiasis (Bilharzia)	0	0%	**2**	0.03%
Portal biliopathy	2	0.03%	**2**	0.03%
Abernethy malformation	1	0.02%	**1**	0.02%
Acute alcohol-related hepatitis	0	0%	**1**	0.02%
Arterio-venous malformation	1	0.02%	**1**	0.02%
Biliary adenofibroma	1	0.02%	**1**	0.02%
Biliary papillomatosis	1	0.02%	**1**	0.02%
COACH syndrome	1	0.02%	**1**	0.02%
Common variable immune deficiency	1	0.02%	**1**	0.02%
Congenital heart disease	1	0.02%	**1**	0.02%
Drug induced cholestasis	1	0.02%	**1**	0.02%
Fasciola	1	0.02%	**1**	0.02%
Focal nodular hyperplasia	0	0%	**1**	0.02%
Graft vs host disease - bone marrow transplant	1	0.02%	**1**	0.02%
Liver trauma	1	0.02%	**1**	0.02%
Mesenchymal hamartoma	1	0.02%	**1**	0.02%
Parasitic disease - Infected hydatid cysts	1	0.02%	**1**	0.02%
Total	**5854**	**100%**	**8380**	**143%**

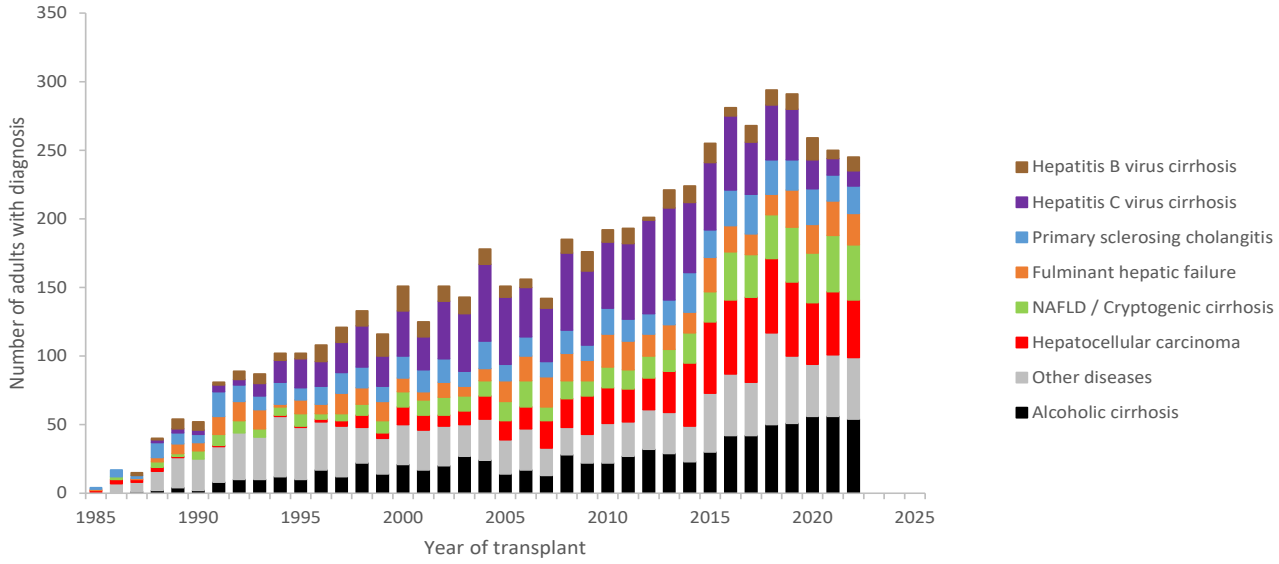
See Table 8 for breakdown of causes of fulminant hepatic failure
* See Table 9 for breakdown of metabolic disorders

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

10.5 Primary Diagnosis Trend in Adults

The commonest primary indication for transplantation in adults was hepatitis C virus cirrhosis until 2014, after which alcohol-related cirrhosis, non-alcoholic fatty liver disease and hepatocellular carcinoma have become the commonest indications. The proportion of patients transplanted primarily for hepatitis C has decreased from 33.8% in 2012 to 4.9% in 2022 (Figure 24). The proportion of patients transplanted for alcohol-related cirrhosis has increased from 15.9% in 2012 to 22.0% in 2022 and hepatocellular carcinoma has increased from 11.4% in 2012 to 16.3% in 2022. Over the same time period, the proportion of patients transplanted for non-alcoholic fatty liver disease increased from 8.0% to 16.7%.

Figure 24. Primary diagnosis trend in adults

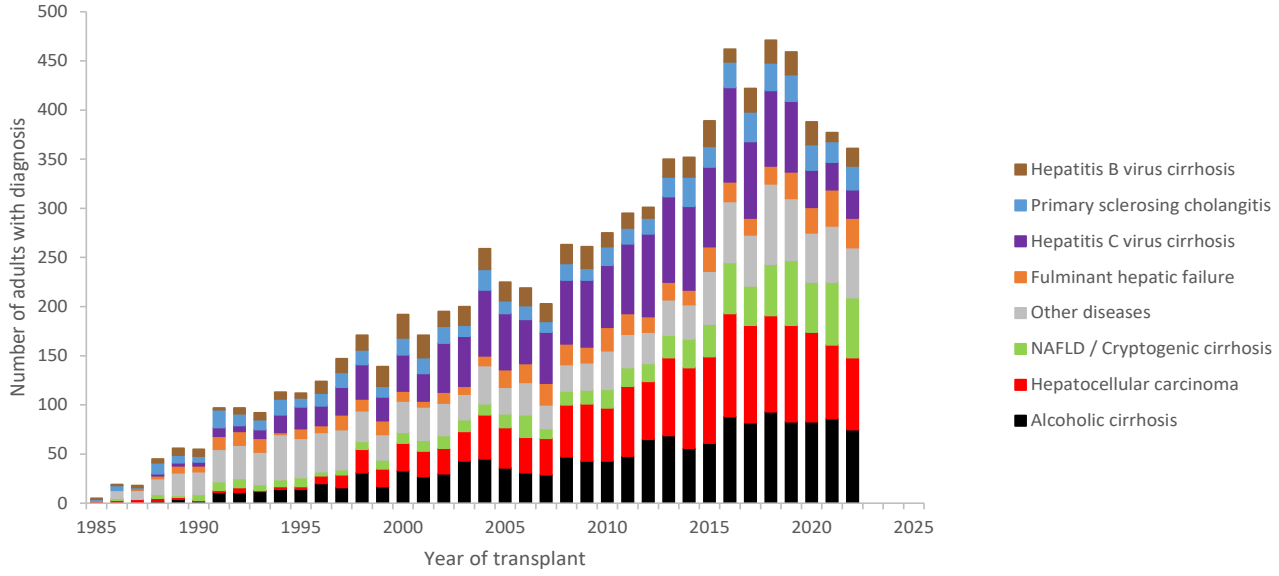


Abbreviation: NAFLD, non-alcoholic fatty liver disease

10.6 All Diagnoses Trend in Adults

Including any diagnosis recorded for each patient, alcohol-related cirrhosis has become the commonest indication for liver transplantation in adults, rising from 5.0% in 1988 to 30.6% in 2022. Hepatocellular carcinoma has increased from 1.1% in 1993 to 29.8% in 2022 and non-alcoholic fatty liver disease has increased from 3.7% in 1996 to 24.9% in 2022, commensurate with the obesity epidemic. Meanwhile, there has been a dramatic fall in hepatitis C virus cirrhosis as an indication for liver transplantation, from a high of 41.8% in 2012 to just 11.8% in 2022. This reduction corresponds to the time periods of initial compassionate availability in 2014 in Australia and subsequent wide availability of effective direct acting antiviral therapy for hepatitis C virus in 2016 in Australia and New Zealand.

Figure 25. All diagnoses trend in adults



Abbreviation: NAFLD, non-alcoholic fatty liver disease

10.7 Fulminant Hepatic Failure – All Diagnoses

Table 8 lists the detailed breakdown of the causes of fulminant hepatic failure as a primary diagnosis or any diagnosis in children and adults.

Table 8. Detailed breakdown of fulminant hepatic failure category as a primary or additional diagnosis by age group

Fulminant hepatic failure	Children	Adult	Total patients with FHF	% of all patients
Acute hepatic failure - Idiopathic	82	141	223	3.2%
Acute hepatic failure - Hepatitis B	0	103	103	1.5%
Acute hepatic failure - Other drugs	3	39	42	0.6%
Subacute hepatitis - Type unknown	5	30	35	0.5%
Acute hepatic failure - Wilson's	9	25	34	0.5%
Subacute hepatitis - Autoimmune hepatitis	2	32	34	0.5%
Acute hepatic failure - Paracetamol	4	28	32	0.5%
Subacute hepatitis - Hepatitis B	0	31	31	0.4%
Acute hepatic failure - Autoimmune hepatitis	1	24	25	0.4%
Subacute hepatitis - Hepatitis C	0	21	21	0.3%
Subacute hepatitis - Drugs	1	19	20	0.3%
Acute hepatic failure - Herbs / mushrooms	0	12	12	0.2%
Subacute hepatic failure - Wilson's	2	7	9	0.1%
Acute hepatic failure - Post-operative	2	6	8	0.1%
Acute hepatic failure - Budd Chiari	0	6	6	0.1%
Subacute hepatitis - Non A-G	0	6	6	0.09%
Acute hepatic failure - Alpha-1-antitrypsin	2	3	5	0.07%
Acute hepatic failure - Hepatitis A	1	4	5	0.07%
Acute hepatic failure - Toxic (non-drug)	1	3	4	0.06%
Subacute hepatic failure - Budd Chiari	1	2	3	0.04%
Acute hepatic failure - Other specified	1	1	2	0.03%
Subacute hepatic failure - Post surgical resection	1	1	2	0.03%
Subacute hepatitis - Hepatitis A	0	2	2	0.03%
Subacute hepatitis - Herbs	0	2	2	0.03%
Acute hepatic failure - Acute alcohol-related hepatitis	0	1	1	0.01%
Acute hepatic failure - Epstein-Barr virus hepatitis	1	0	1	0.01%
Acute hepatic failure - Hepatitis D	0	1	1	0.01%
Acute hepatic failure - Hepatitis E	0	1	1	0.01%
Acute hepatic failure - Herpes simplex hepatitis	0	1	1	0.01%
Acute hepatic failure - La foie vide	1	0	1	0.01%
Acute hepatic failure - Other virus	1	0	1	0.01%
Acute hepatic failure - Post traumatic	0	1	1	0.01%
Subacute hepatitis - Giant cell	1	0	1	0.01%
Subacute hepatitis - Ischaemic	0	1	1	0.01%
Total	**122**	**554**	**676**	9.7%
All patients	*1130*	*5853*	*6983*	

10.8 Metabolic Disorders – All Diagnoses

Alpha-1 antitrypsin deficiency, haemochromatosis and Wilson's disease were the most common primary or additional diagnoses in the metabolic disorders category (Table 9).

Table 9. Detailed breakdown of metabolic disorders category as a primary or additional diagnosis by age group

Metabolic disorders	Children	Adult	Total patients with a Metabolic Disorder	% of all patients
Alpha-1-antitrypsin deficiency	45	111	156	2%
Haemochromatosis	3	68	71	1%
Wilson's disease	8	44	52	0.7%
Familial amyloid polyneuropathy	0	47	47	0.7%
Urea cycle disorders	32	7	39	0.6%
- Ornithine transcarbamylase (OTC) deficiency	*21*	*1*	*22*	*0.3%*
- Citrullinaemia, Argininosuccinate synthetase (ASS) deficiency	*6*	*1*	*7*	*0.1%*
- Argininosuccinate lyase (ASL) deficiency	*4*	*2*	*6*	*0.09%*
- Carbamyl phosphate synthetase (CPS) 1 deficiency	*3*	*3*	*6*	*0.09%*
Primary hyperoxaluria	12	11	23	0.3%
Glycogen storage disease	5	14	19	0.3%
Crigler-Najjar	13	1	14	0.2%
Maple syrup urine disease	8	2	10	0.1%
Propionic acidaemia	10	0	10	0.1%
Homozygous hypercholesterolaemia	7	2	9	0.1%
Tyrosinaemia	8	1	9	0.1%
Protoporphyria	0	4	4	0.06%
Bile acid synthesis / transport disorder	3	0	3	0.04%
Methylmalonic acidaemia	3	0	3	0.04%
Mitochondrial disease	2	1	3	0.04%
Protein C deficiency	1	2	3	0.04%
Carnitine acylcarnitine translocase deficiency	2	0	2	0.03%
Acute intermittent porphyria	0	1	1	0.01%
Factor V Leiden deficiency	0	1	1	0.01%
Familial immunodeficiency syndrome	1	0	1	0.01%
Hereditary lysozyme amyloidosis	0	1	1	0.01%
Indian childhood cirrhosis	1	0	1	0.01%
Niemann-Pick Type C	1	0	1	0.01%
POLG mitochondrial disorder	1	0	1	0.01%
Pyridoxamine 5-phosphate oxidase deficiency	1	0	1	0.01%
Total	**169**	**318**	**487**	7%
All patients	*1130*	*5853*	*6983*	

Abbreviation: POLG, polymerase gamma

11 Incidental Liver Cancer Found at Explant

All explanted livers are examined by a pathologist to provide a pathological diagnosis. This is then compared to the listing diagnosis. An incidental liver cancer, as reported in this section, refers to a previously unknown liver cancer type being detected at pathology. It does not include the finding of additional lesions of a cancer type already identified at listing.

Incidental liver cancers were found at explant in 235 recipients (3.4% of transplanted patients).

11.1 Incidental Cancers Found at Explant in Children

Incidental liver cancers were found at explant in four children (0.4% of children transplanted). One child had both hepatocellular carcinoma (HCC) and cholangiocarcinoma found at explant, resulting a total of five new liver cancers identified (three cancer types) occurring in four children (Table 10).

Two of these children have died but their death was not because of the incidental cancer diagnosis.

Table 10. Incidental cancers found at explant in children

Incidental cancers – children	Number incidental cancers	% incidental cancers	Deaths	% deaths for this cancer type	Died of this cancer	% patients died of this cancer
Hepatocellular carcinoma	3	60%	1	33%	0	0%
Hepatoblastoma	1	20%	1	100%	0	0%
Cholangiocarcinoma	1	20%	0	0%	0	0%
Total incidental liver cancers in children	**5**					
Total children with one or more incidental liver cancers*	**4**		**2**	**50%**	**0**	**0%**
% paediatric liver transplant patients (n=1,132)		0.4%		0.2%		0%

* One child had both hepatocellular carcinoma and cholangiocarcinoma found at explant

11.2 Incidental Cancers Found at Explant in Adults

Incidental liver cancers were found at explant in 231 adults (3.9% of adults transplanted). One adult had both HCC and cholangiocarcinoma found at explant, resulting a total of 232 new liver cancers identified (Table 11).

One hundred and seven adults have died and in 37 adults, their deaths were because of their incidental cancer.

Table 11. Incidental cancers found at explant in adults

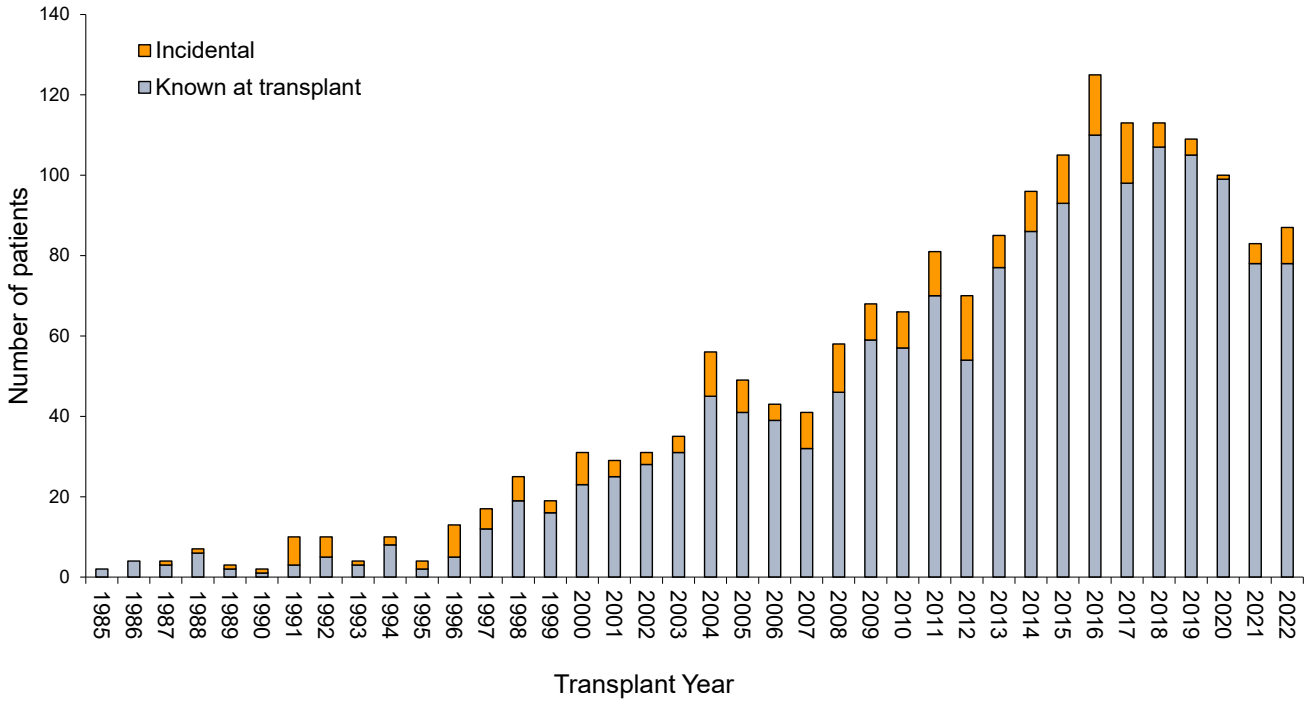
Incidental cancers – adults	Number incidental cancers	% incidental cancers	Deaths	% deaths for this cancer type	Died of this cancer	% patients died of this cancer
Hepatocellular carcinoma*	177	76.6%	68	38%	13	7%
Cholangiocarcinoma*	43	18.6%	31	72%	19	44%
Adenocarcinoma	7	3.0%	6	86%	3	43%
Angiosarcoma	2	0.4%	2	100%	2	100%
Epithelioid haemangioendothelioma	1	0.4%	0	0%	0	0%
Fibrolamellar	1	0.4%	0	0%	0	0%
Metastatic neuroendocrine tumour	1	0.4%	0	0%	0	0%
Total incidental liver cancers in adults	**232**					
Total adults with one or more incidental liver cancers*	**231**		**107**	**46%**	**37**	16%
% adult liver transplant patients (n=5,857)		3.9%		1.8%		0.6%

* One adult had both hepatocellular carcinoma and cholangiocarcinoma found at explant

11.3 Liver Cancer Known Prior to Transplant Versus Incidental Liver Cancer by Transplant Era

The number of patients found to have incidental liver cancer remains relatively stable (Figure 26).

Figure 26. Liver cancer known prior to transplant versus incidental liver cancer by transplant year



12 Donor Derived Tumours

Three recipients have died as a result of a donor derived tumour. One died of donor transmitted melanoma, one from metastatic adenocarcinoma, most likely of colorectal origin, and one from a tumour of unknown primary, with HLA (human leukocyte antigen) match with donor tissue typing.

Four recipients were retransplanted soon after a transplant due to a donor derived tumour. These patients were all alive as of 31/12/2022. One donor liver had neuroendocrine tumours, one had metastatic adenocarcinoma of unknown primary, one donor liver had lymphoma and one donor gall bladder had adenocarcinoma (liver was cancer free).

13 De Novo Cancer Development and Liver Cancer Recurrence After Liver Transplantation

One or more de novo cancers developed after transplantation in 1,226 (17.5%) patients. De novo non-skin cancer developed in 599 (8.6%) patients and de novo skin cancer developed in 1,057 patients (15.1% of all patients). Four hundred and thirty patients (6.2%) developed both a non-skin and skin cancer.

13.1 De Novo Non-Skin Cancer

13.1.1 De Novo Non-Skin Cancer Types

Five hundred and ninety-nine patients (8.6%) developed 647 de novo non-skin cancers post-transplant with 43 patients developing more than one non-skin cancer type (Table 12). Of the 599 patients, 290 (48.4%) died of their de novo non-skin cancer. Median time from first transplant to development of a non-skin cancer post-transplant ranged from 17 to 121 months.

Table 12. De novo non-skin cancer types

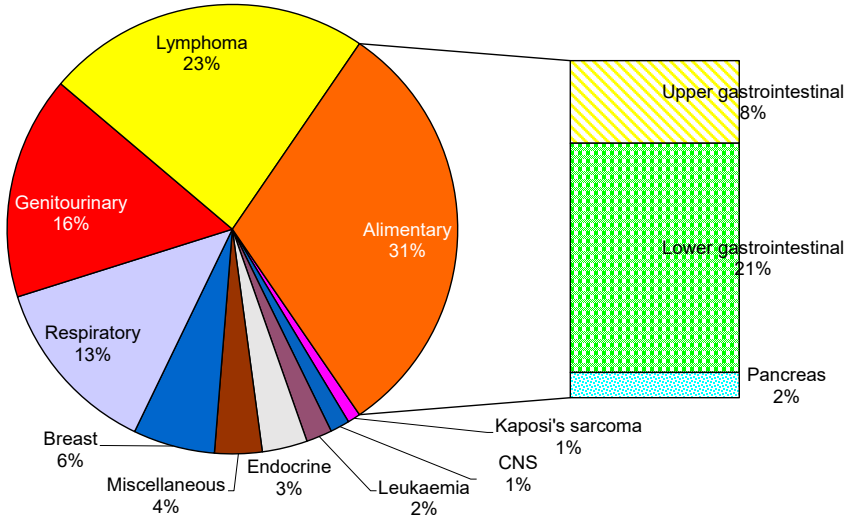
	Number of cancers	Male	Female	Age patients (years)	Median Age	Time to diagnosis (months)	Median time to diagnosis (months)	Died of this Cancer	
Alimentary*	200	146	54	5 – 84	61	1 – 376	91	106	53%
Lymphoma*	151	87	64	1– 82	51	1 – 283	64	64	42%
Genitourinary*	104	69	35	21 – 82	63	2 – 363	119	15	14%
Respiratory*	84	61	23	29 – 80	62	7 – 284	103	62	74%
Breast*	38	1	37	30 – 74	58	11 – 291	95	14	37%
Endocrine	21	12	9	28 – 77	56	6 – 346	82	5	24%
Miscellaneous*	22	13	9	49 – 82	64	6 – 301	121	12	55%
Leukaemia*	12	9	3	16 – 75	59	14– 212	30	4	33%
CNS	9	6	3	3 – 75	66	15 – 190	85	7	78%
Kaposi's	6	5	1	31 – 76	48	2 – 254	17	1	17%
Total cancers	**647**	**409**	**238**	**1 – 84**	**60**	**1 – 376**	**87**		
Total patients	**599**	**384**	**215**					**290**	**48%**

*Forty-three patients had two or more de novo non-skin malignancies

Abbreviation: CNS, Central Nervous System

The three most common types of cancers were of the alimentary tract (200, 31%), lymphoma (151, 23%) and genitourinary tract (104, 16%, Figure 27). Lower gastrointestinal cancers account for 68% of alimentary tract cancers and 21% of all de novo non-skin cancers.

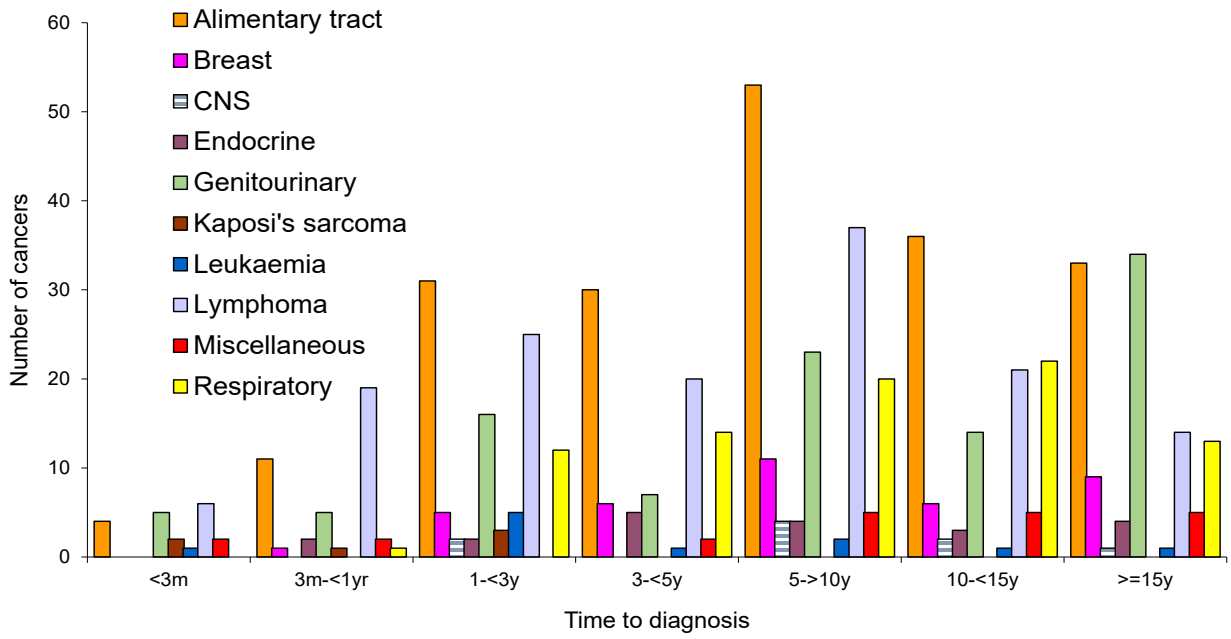
Figure 27. De novo non-skin cancer types



13.1.2 Time to Diagnosis of De Novo Non-Skin Cancers by Cancer Type

Cancers of the alimentary tract and lymphoma were predominantly diagnosed 5 to 10 years post-transplant whilst cancers of the genitourinary tract gradually increased over time (Figure 28).

Figure 28. Time to diagnosis of de novo non-skin cancer



Twenty patients developed a de novo non-skin cancer type within 90 days of their liver transplant, with lymphoma / post-transplant lymphoproliferative disorder (PTLD) occurring in six patients (Table 13).

Table 13. De novo non-skin cancer types that developed within 90 days of transplantation

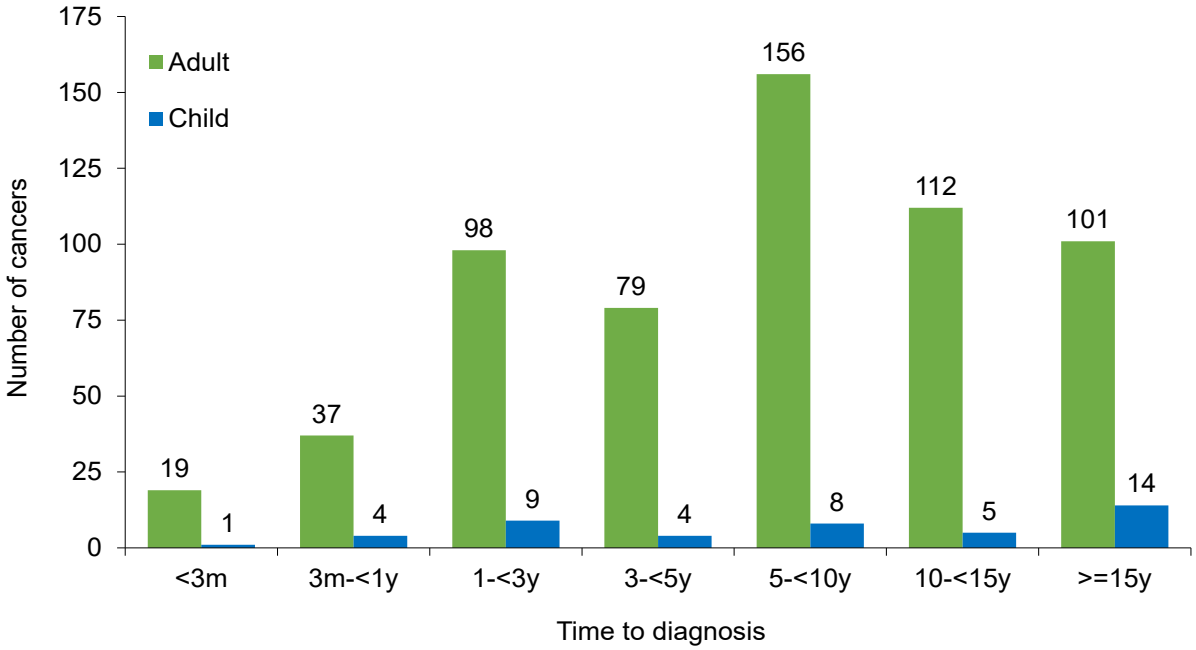
De novo non-skin cancer type	Developed within 90 days of transplantation
Lymphoma/PTLD	6
Colon	3
Kaposi's sarcoma/HHV8	2
Prostate	2
Renal cell	2
Angiosarcoma	1
Cervix	1
Gastro-intestinal stromal tumour	1
Leukaemia	1
Ovary	1
Total	**20**

Abbreviations: PTLD, Post-transplant lymphoproliferative disorder; HHV8, Human Herpes Virus-8

13.1.3 Time to Diagnosis of De Novo Non-Skin Cancers by Age Category

The largest number of de novo non-skin cancers diagnosed per 5-year period was within the first 5 years post-transplant for children (18) and adults (233, Figure 29).

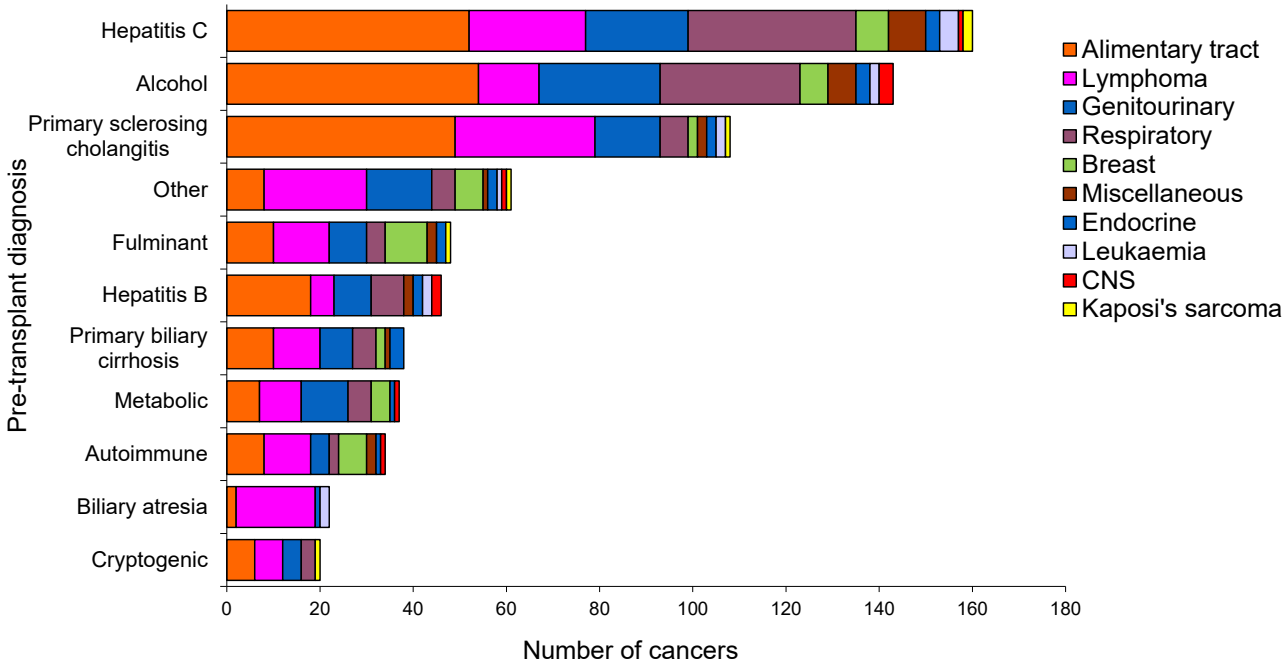
Figure 29. Time to diagnosis of any non-skin cancer by age category



13.1.4 De Novo Non-Skin Cancers by Pre-Transplant Diagnosis

The incidence of de novo non-skin cancers appears to be related to the type of pretransplant underlying disease. Most notable is the incidence of de novo non-skin cancers in patients with underlying hepatitis C virus, alcohol and primary sclerosing cholangitis, being statistically significant (p<0.001, Figure 30, Table 14).

*Figure 30. Pretransplant diagnosis and de novo non-skin cancer types**



* All listing diagnoses (1-4) included, not just primary diagnosis

Recipients with a pre-transplant diagnosis of primary sclerosing cholangitis, autoimmune cirrhosis and primary biliary cirrhosis were most likely to develop a de novo non-skin cancer (18%, 14% and 13% respectively, Table 14). Whilst more de novo cancers were observed in recipients with a pre-transplant diagnosis of alcohol-related cirrhosis or hepatitis C, there were more recipients with these diagnoses, resulting in 10% of each developing a de novo non-skin cancer.

*Table 14. Pre-transplant diagnosis and de novo non-skin cancer types**

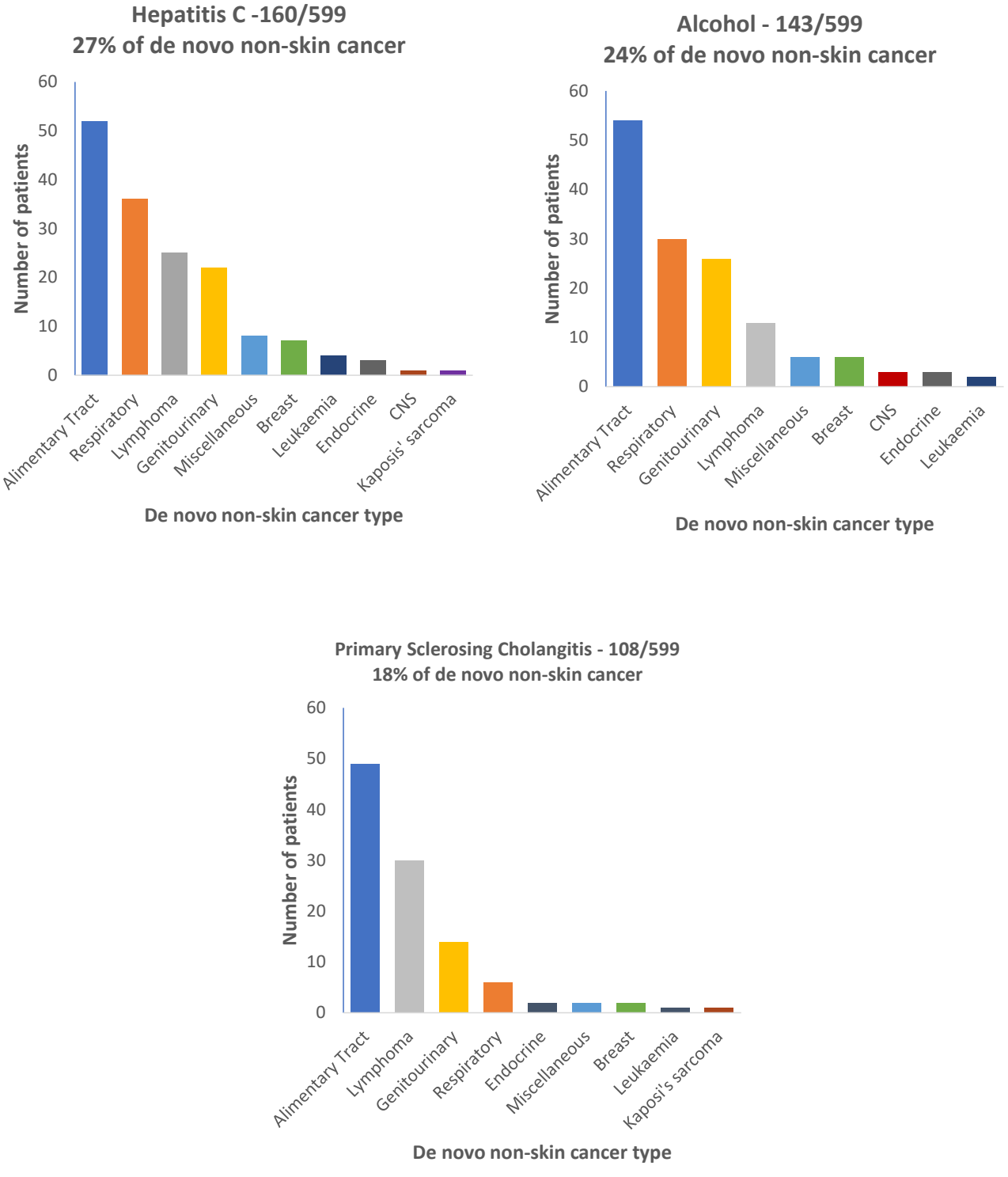
Listing diagnoses (diag 1 - 4)	Alimentary tract	Lymphoma	Genito-urinary	Respiratory	Breast	Miscellaneous	Endocrine	Leukaemia	CNS	Kaposi's sarcoma	Total de novo cancers	% of patients with diagnosis	Patients with Listing Diagnosis
PSC	49	30	14	6	2	2	2	2	0	1	**108**	18%	617
Autoimmune	8	10	4	2	6	2	1	0	1	0	**34**	14%	249
PBC	10	10	7	5	2	1	3	0	0	0	**38**	13%	299
Alcohol	54	13	26	30	6	6	3	2	3	0	**143**	10%	1,451
Hepatitis C	52	25	22	36	7	8	3	4	1	2	**160**	10%	1,589
Hepatitis B	18	5	8	7	0	2	2	2	2	0	**46**	8%	546
Metabolic	7	9	10	5	4	0	1	0	1	0	**37**	8%	487
FHF	10	12	8	4	9	2	2	0	0	1	**48**	7%	676
Cryptogenic cirrhosis	6	6	4	3	0	0	0	0	0	1	**20**	3%	765
Biliary atresia	2	17	0	0	0	0	1	2	0	0	**22**	3%	660
Other	8	22	14	5	6	1	2	1	1	1	**61**		

Abbreviations: CNS, Central nervous system; PSC, Primary sclerosing cholangitis; FHF, Fulminant hepatic failure; PBC, Primary biliary cirrhosis

* All listing diagnoses (1-4) included, not just primary diagnosis

Pretransplant hepatitis C infection, alcohol-related liver disease and primary sclerosing cholangitis were the dominant underlying disease in those patients who developed alimentary tract cancers (Figure 31). Pretransplant hepatitis C infection and alcohol-related liver disease were the dominant underlying disease for those who developed respiratory cancers.

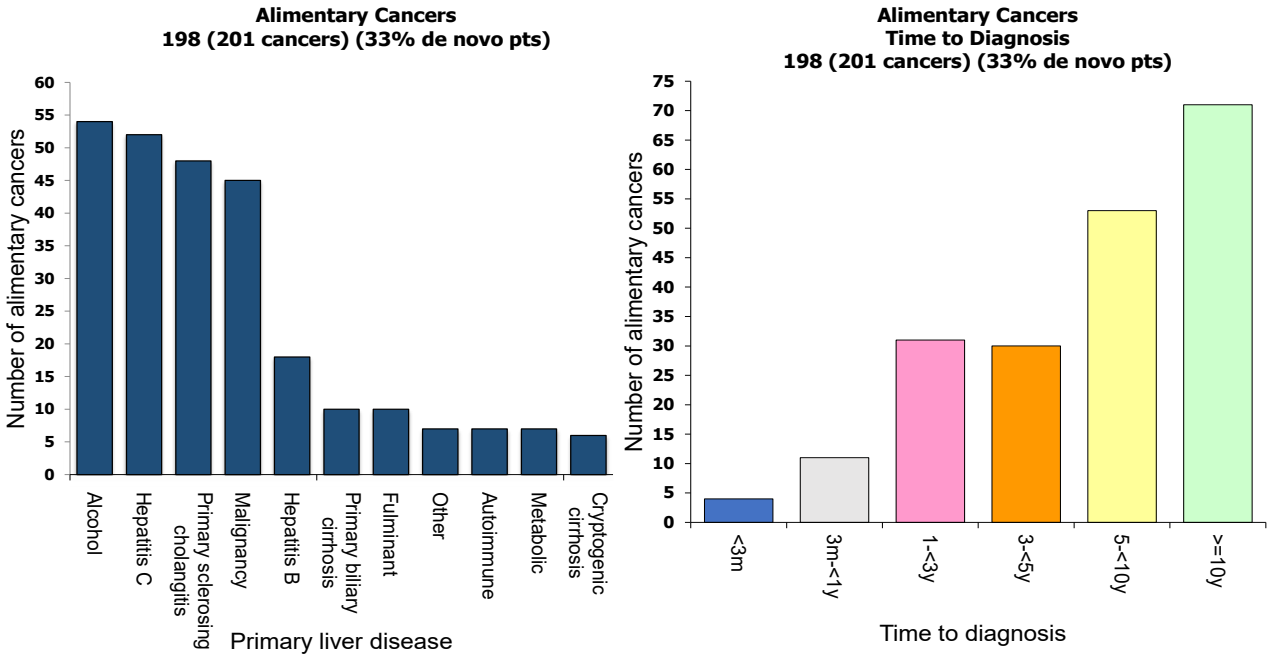
Figure 31. Hepatitis C virus, alcohol diagnosis and primary sclerosing cholangitis and types of de novo skin cancer



13.1.5 De Novo Alimentary Cancers

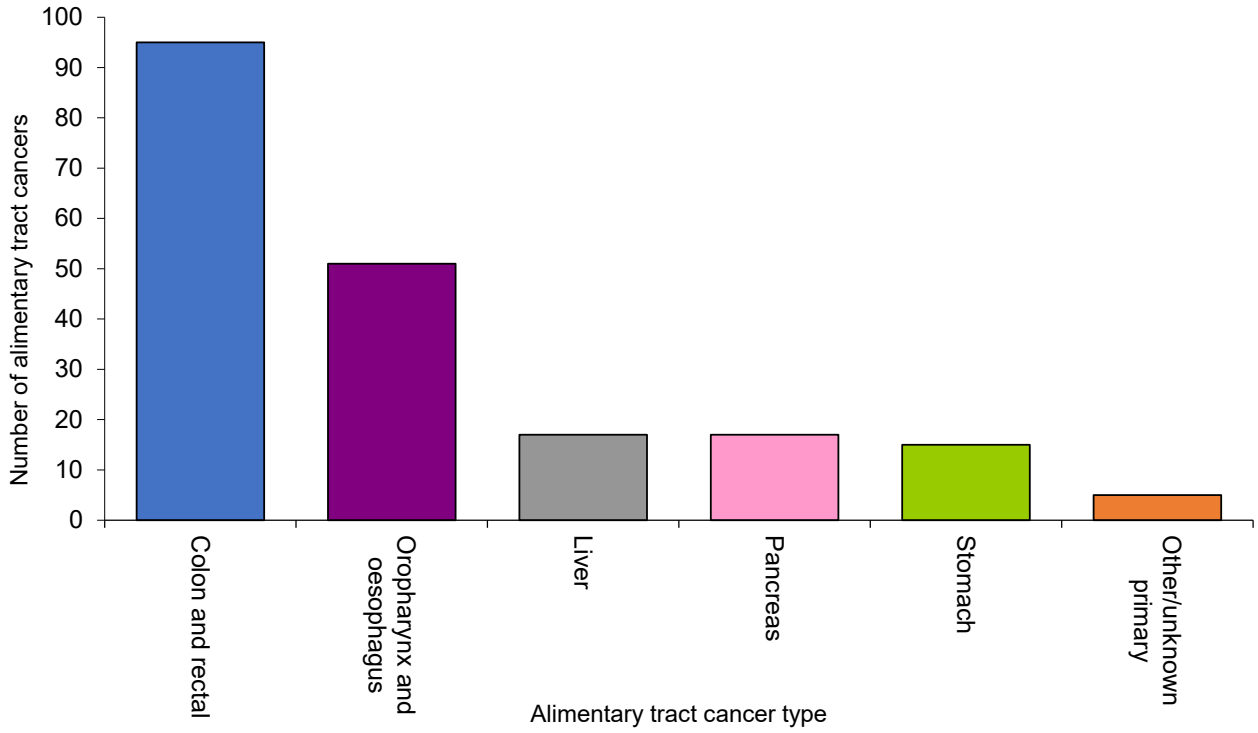
Cancer of the alimentary tract was the most prevalent non-skin cancer to develop post-transplant affecting 198 patients (201 cancers). Time to development ranged from one month to greater than 30 years with 62.9% being diagnosed after 5 years (Figure 32). Median time to diagnosis was 91 months. Pretransplant liver disease was predominantly primary sclerosing cholangitis, alcohol-related liver disease and hepatitis C infection.

Figure 32. Pretransplant diagnosis and de novo alimentary cancers



Forty-eight percent of alimentary cancers were of the colon and rectum; 26% were oropharynx and oesophagus (Figure 33).

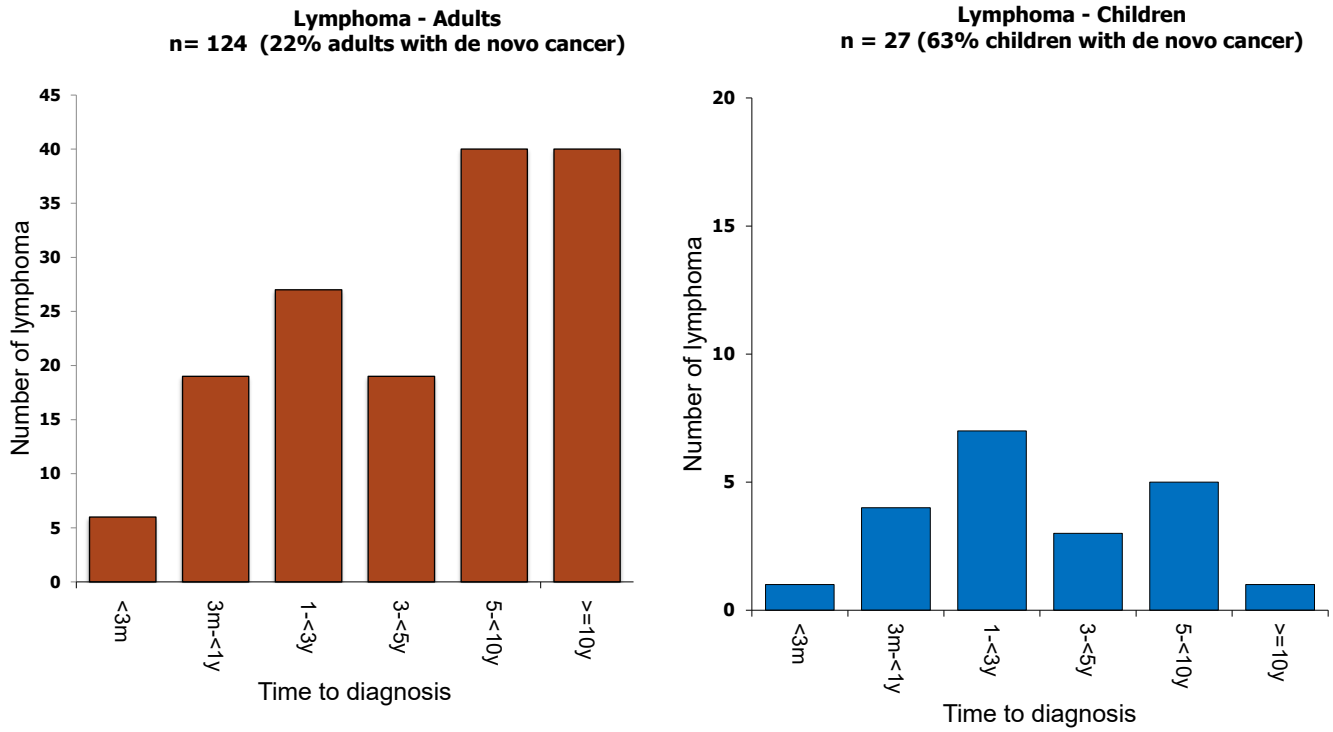
Figure 33. Incidence of de novo alimentary tract cancers by type



13.1.6 De Novo Lymphoma

Lymphoma was the second most prevalent non-skin cancer to develop post-transplant affecting 124 adults and 27 children. Time to development ranged from one month to 24 years with 56% developing after 5 years in adults and 29% after 5 years in children (Figure 34). Median time to diagnosis in adults and children was 69 and 33 months respectively.

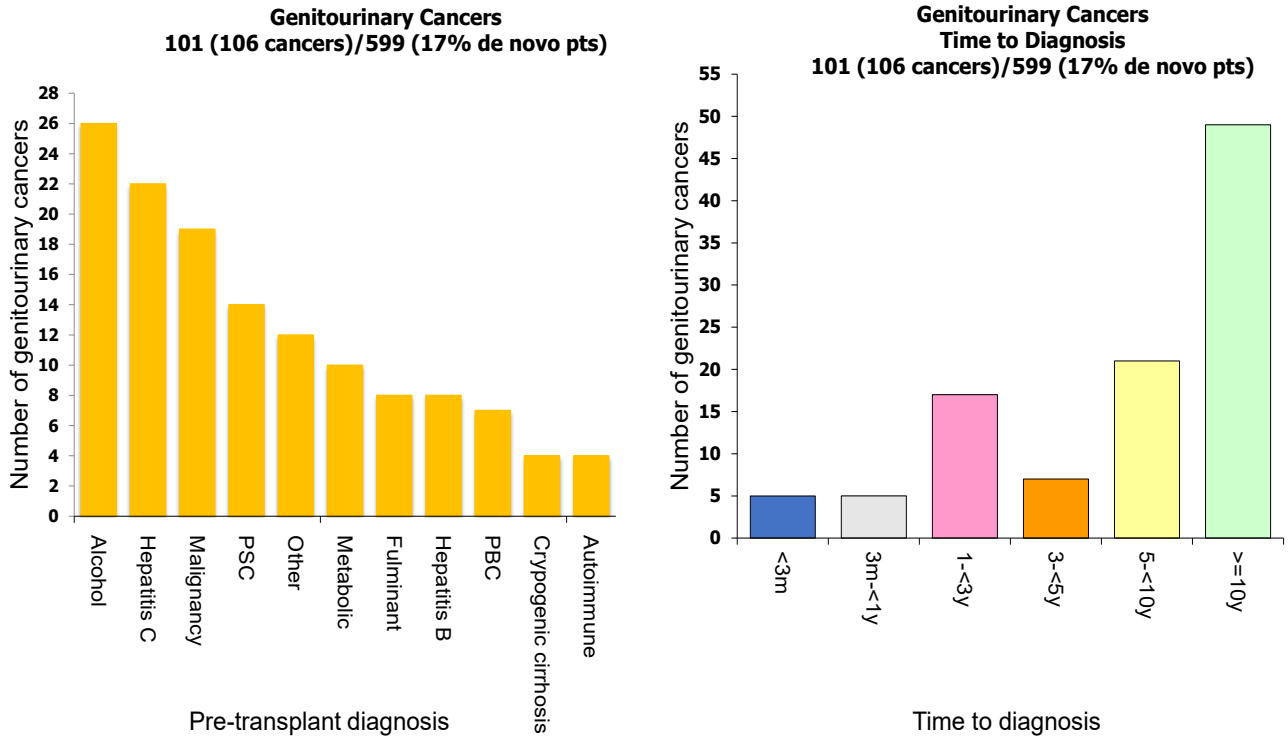
Figure 34. Time to diagnosis of de novo lymphoma by age category



13.1.7 De Novo Genitourinary Cancers

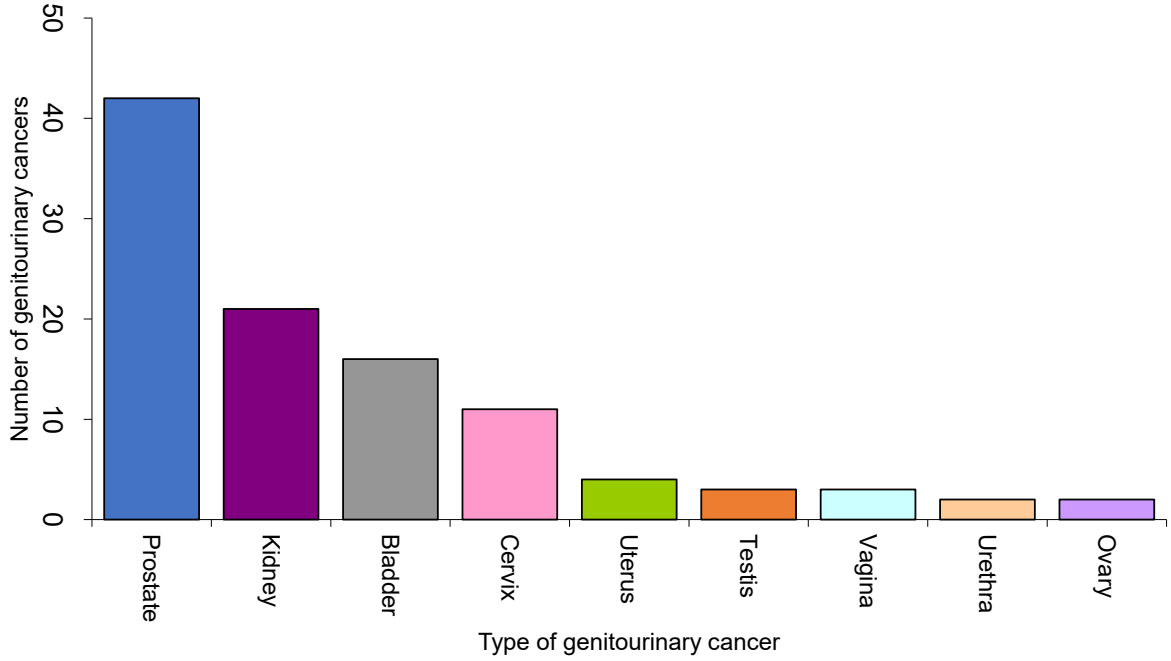
Cancers of the genitourinary tract represented 17% of all de novo non-skin cancers. Sixty-seven (66%) of these patients were transplanted for alcohol-related liver disease, hepatitis C infection or a liver cancer (Figure 35). Time to development ranged from two months to 30 years. Median time to diagnosis was 10 years.

Figure 35. Pretransplant diagnosis and de novo genitourinary cancers



Forty-two (40.4%) of genitourinary tract cancers were cancers of the prostate (Figure 36).

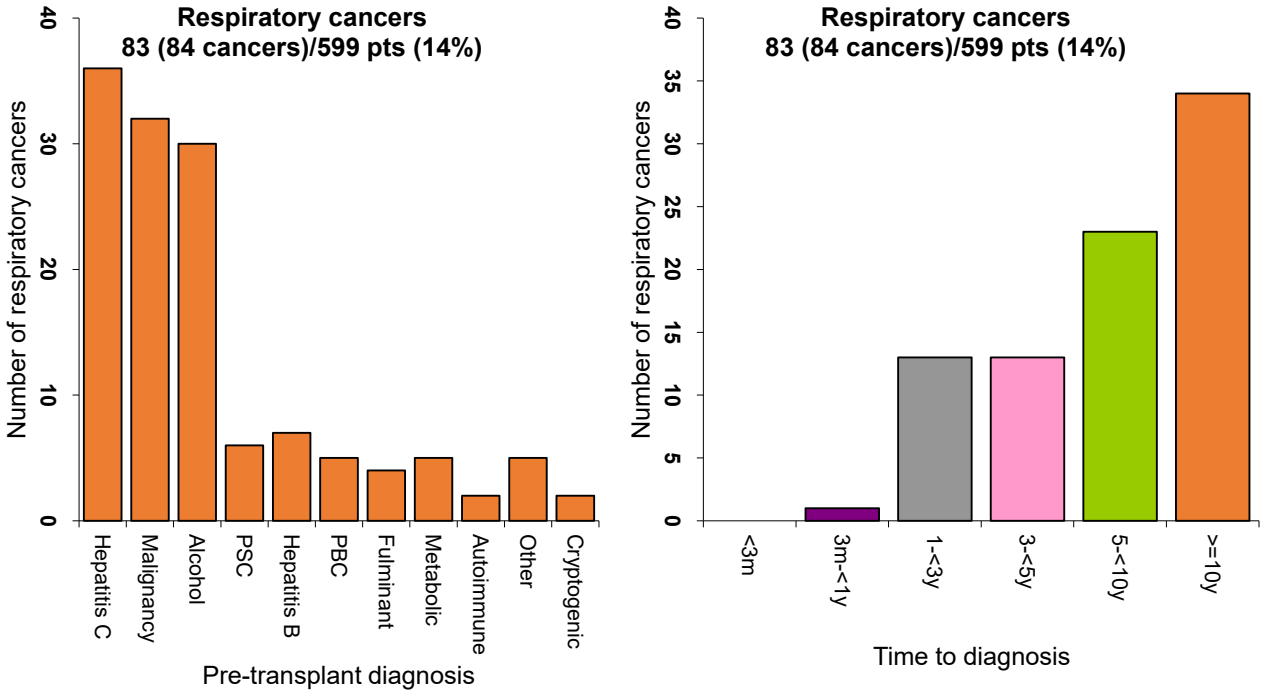
Figure 36. Incidence of de novo genitourinary tract cancers by type



13.1.8 De Novo Respiratory Cancers

Respiratory cancers represented 14% of all de novo non-skin cancers. Fifty-five (65.5%) of these patients were transplanted for hepatitis C infection, pretransplant liver cancer or alcohol-related liver disease (Figure 37). Time to development ranged from two months to 24 years with 68.7% developing after 5 years. Median time to diagnosis was 103 months. 92.9% of respiratory cancers were of the lung (Figure 38).

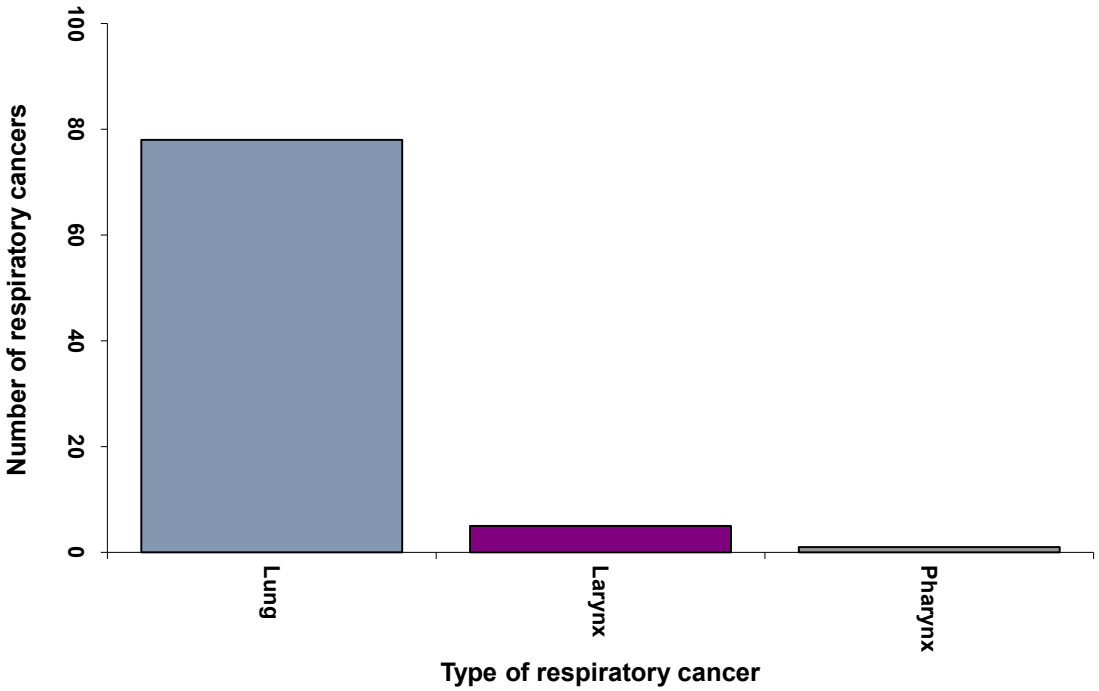
Figure 37. Pretransplant diagnosis and de novo respiratory cancers



*1 patient had 2 respiratory cancers

Abbreviations: PSC, primary sclerosing cholangitis; PBC, primary biliary cirrhosis

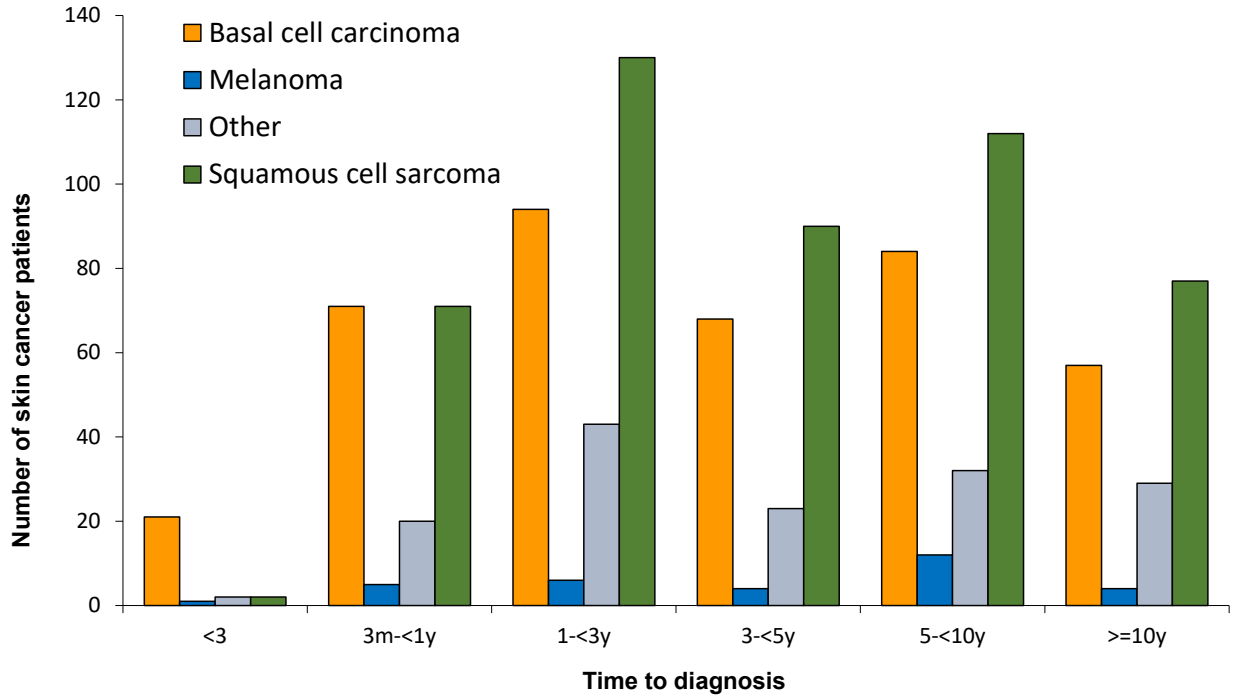
Figure 38. Incidence of de novo respiratory tract cancers by type



13.2 Skin Cancer Development Post-Transplant

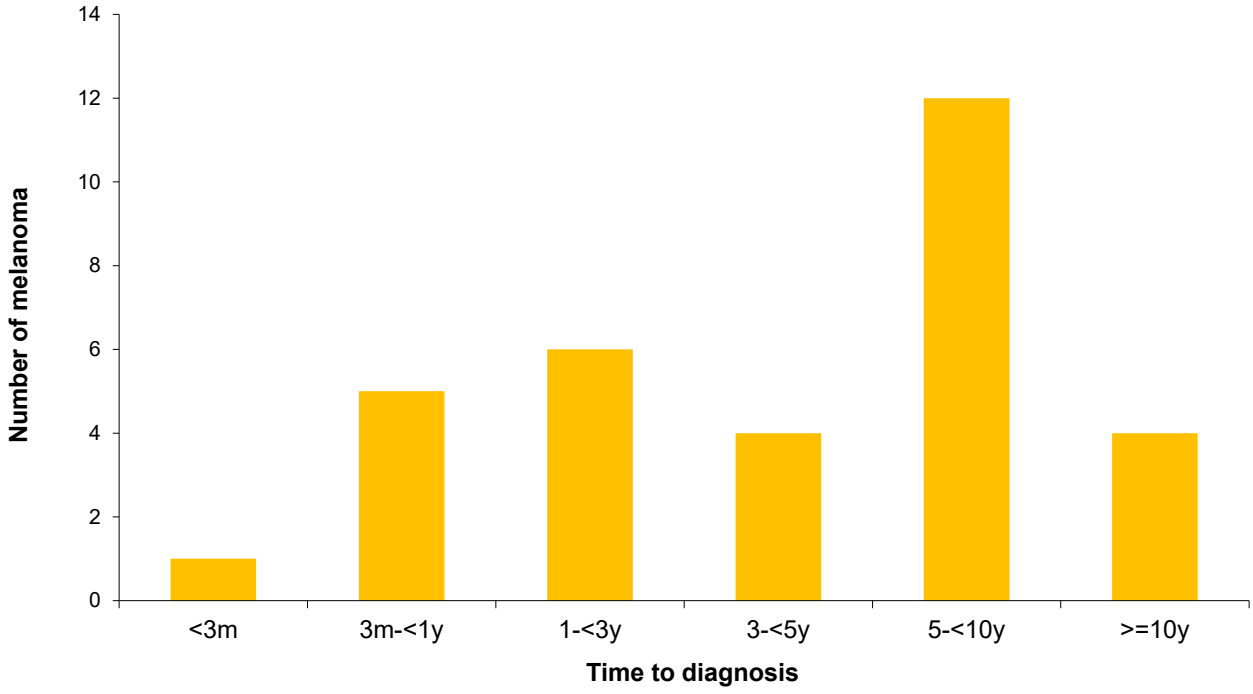
One thousand and fifty-seven patients (16%) developed a first skin cancer post-transplant with 510 going on to develop multiple skin cancer types (Figure 39).

Figure 39. Time to first skin cancer development post-transplant by type of skin cancer



Seventy-seven patients (1% of all patients) developed eighty-one melanomas (Figure 40). Thirty-six patients developed melanoma as a first skin cancer post-transplantation.

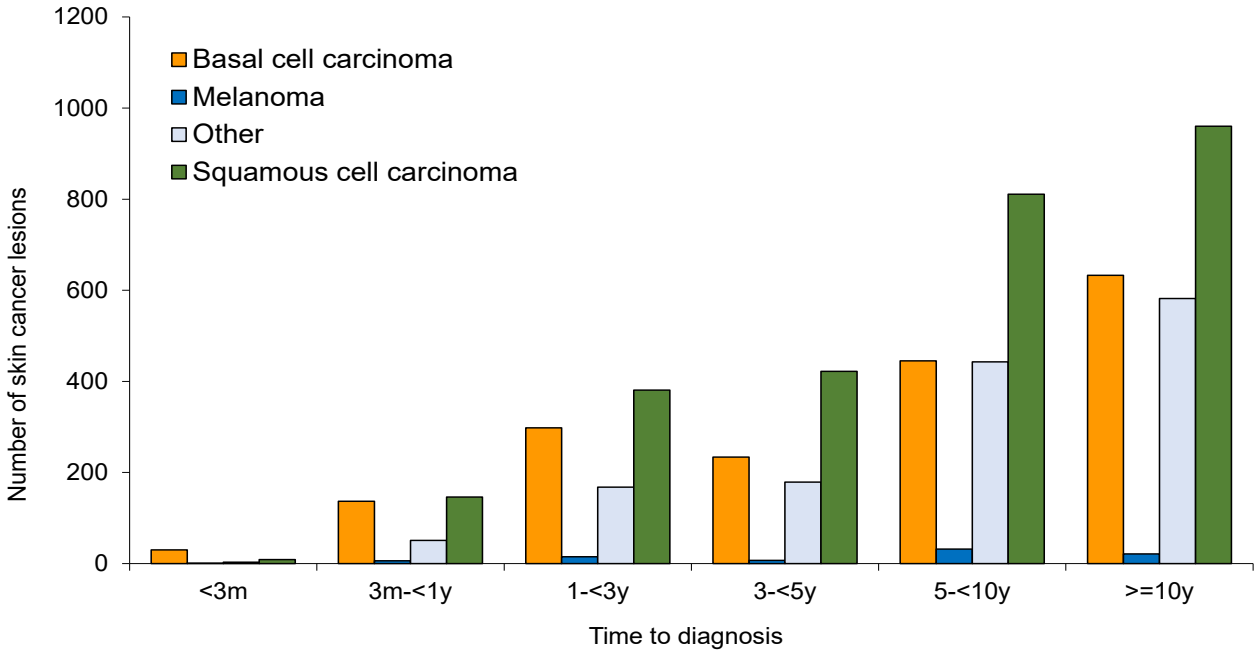
Figure 40. Time to first melanoma development post-transplant
Note: This includes patients who developed melanoma after a non-melanoma skin cancer (first skin cancer)



* 2 patients developed 2 melanomas

The number of skin cancer lesions increased over time (Figure 41).

Figure 41. Time to all skin cancer lesions development post-transplant



Males were more likely to develop skin cancer post-transplant than females (16% versus 13%, P<0.001). Males were more likely to die from squamous cell cancer but less likely than females to die of melanoma (Table 15).

Table 15. Skin Cancer Development Post-Transplant

		Male				Female			
	Number of patients that developed one or more skin cancers	**Male recipients**	% of all male transplant recipients	Died of this cancer	% males with this skin cancer type that died of this cancer	**Female recipients**	% of all female transplant recipients	Died of this cancer	% females with this skin cancer type that died of this cancer
Squamous Cell	741	521	12%	18	3%	220	9%	5	2%
Basal Cell	610	441	10%	0	0%	169	7%	0	0%
Bowen's disease	297	194	4%	0	0%	103	4%	0	0%
Miscellaneous	97	60	1%	0	0%	29	1%	0	0%
Melanoma	77	53	1%	9	17%	24	1%	7	29%
Merkel Cell	7	7	0.2%	2	29%	0	0%	0	0%
Total skin cancer patients*	**1,057**	**728**	**16%**	**29**	**4%**	**329**	**13%**	**12**	**4%**
Total transplant recipients	**6,989**	**4,461**				**2,528**			

* Note: Some patients developed more than one skin cancer type. 1,057 patients developed 6,103 skin cancers. 510 patients developed more than one skin cancer type.

13.3 Cumulative Risk of Developing De Novo Skin or Non-Skin Cancer Post Liver Transplant

The cumulative risk of developing de novo non-skin cancer post-transplant is approaching 40% by 20 years (Figure 42, Table 16). Cumulative risk of developing any cancer, skin cancer or non-skin cancer at 10 years post-transplant is 26%, 20% and 8% respectively.

Figure 42. Cumulative risk of diagnosis of skin or non-skin cancer following liver transplantation

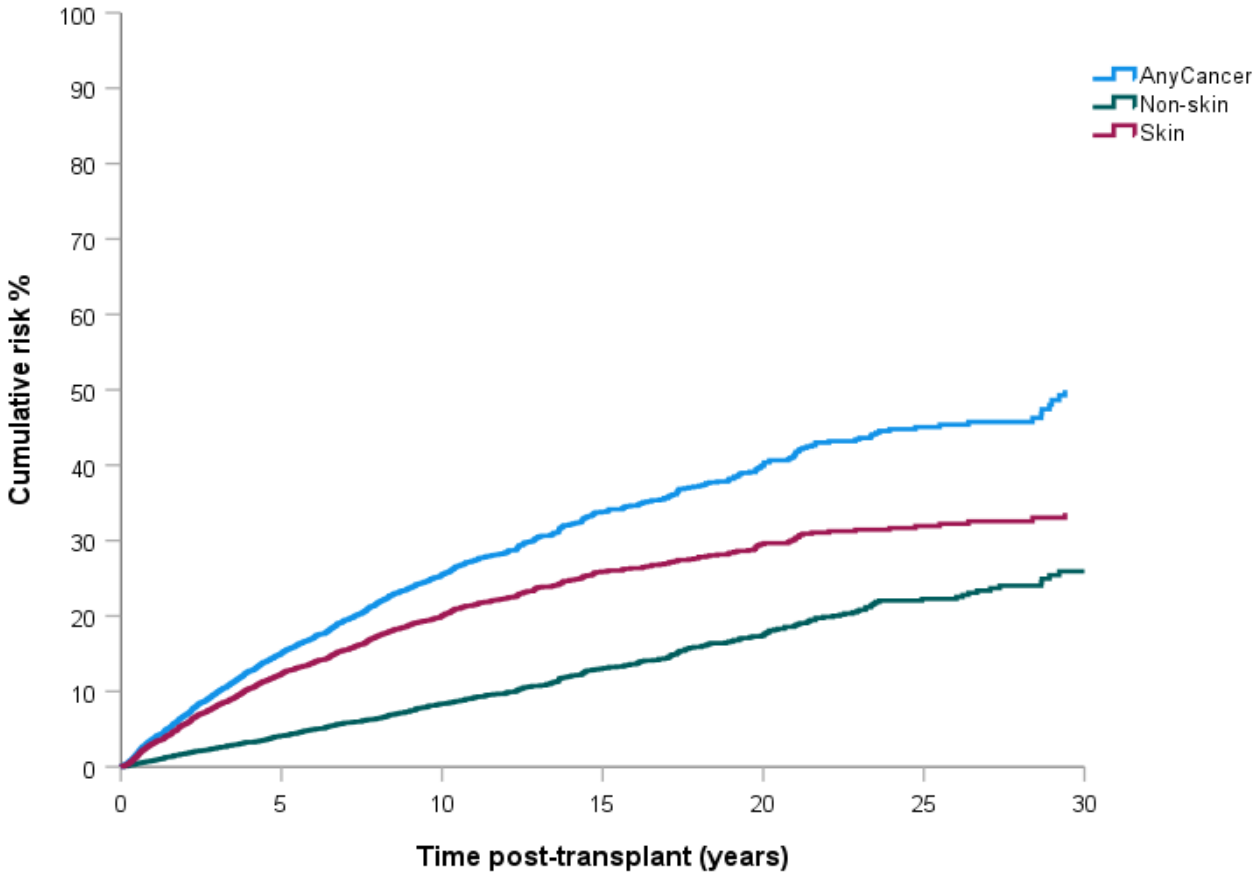


Table 16. Cumulative risk of diagnosis of cancer following liver transplantation

De novo cancer group	Time post-transplant (years)							
	0	1	5	10	15	20	25	30
Any de novo cancer	0%	3%	15%	26%	34%	40%	45%	50%
De novo skin cancer	0%	3%	12%	20%	26%	30%	32%	34%
De novo non-skin cancer	0%	1%	4%	8%	13%	17%	22%	26%

13.4 Liver Cancer Recurrence after Transplant

Recurrent liver cancer has occurred in 10.7% of patients that had either known liver cancer prior to transplant or had an incidental liver cancer found at explant (Table 17).

Table 17. Liver cancer recurrence in liver cancer patients

	Children	Adults	Total Patients	% of all liver transplant patients n = 6,989
Liver Cancer Known at Transplant	58	1,512	**1,570**	22%
Incidental Liver Cancer Found at Transplant	4	231	**235**	3%
Total Liver Cancer Patients	**62**	**1,743**	**1,805**	**26%**
Recurrent Liver Cancer	8	186	**194**	3%
% of liver cancer patients with recurrence	13%	11%	**11%**	

14 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.

14.1 All patients

6,983 patients had their first liver transplant in Australia or New Zealand (i.e. Graft 1, Figure 43 and Table 18). Six 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 74.4%. The median patient survival post-transplant was 21.6 years.

Figure 43. Patient survival curve

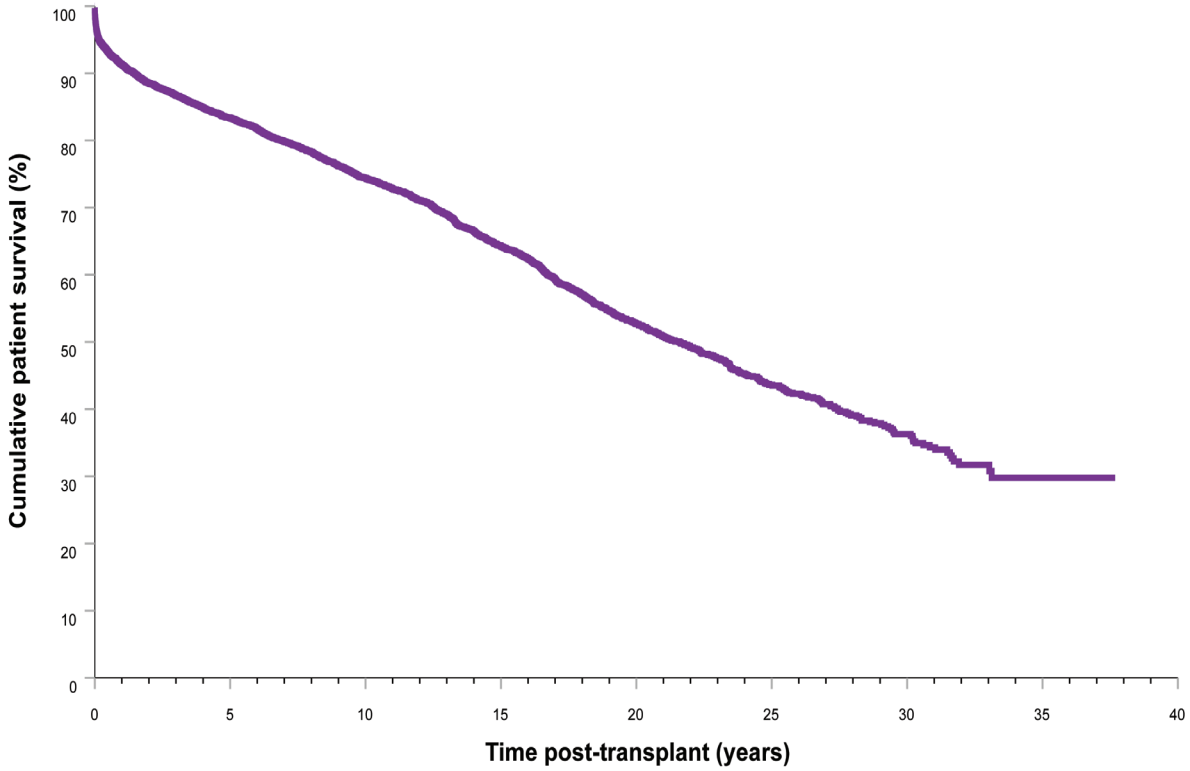


Table 18. Patient survival

Patient Survival	Time post-transplant (years)								
	0	1	3	5	10	20	30	35	40
No. at risk	6,983	6,060	5,127	4,319	2,738	853	139	6	0
Survival (%)		91%	87%	83%	74%	53%	36%	30%	

14.2 Patient Survival by Age Group

Paediatric cases are defined as less than 16 years at time of first transplant (n = 1,130). Adult cases are defined as greater than or equal to 16 years at time of first transplant (n = 5,853). Post-transplant survival was superior in the paediatric population compared to the adult population (P < 0.001, Figure 44, Table 19). Ten-year patient survival was 85.2% for children and 72.3% for adults. Median patient survival was not reached for children and was 18.8 years for adults.

Figure 44. Patient survival curve by age category

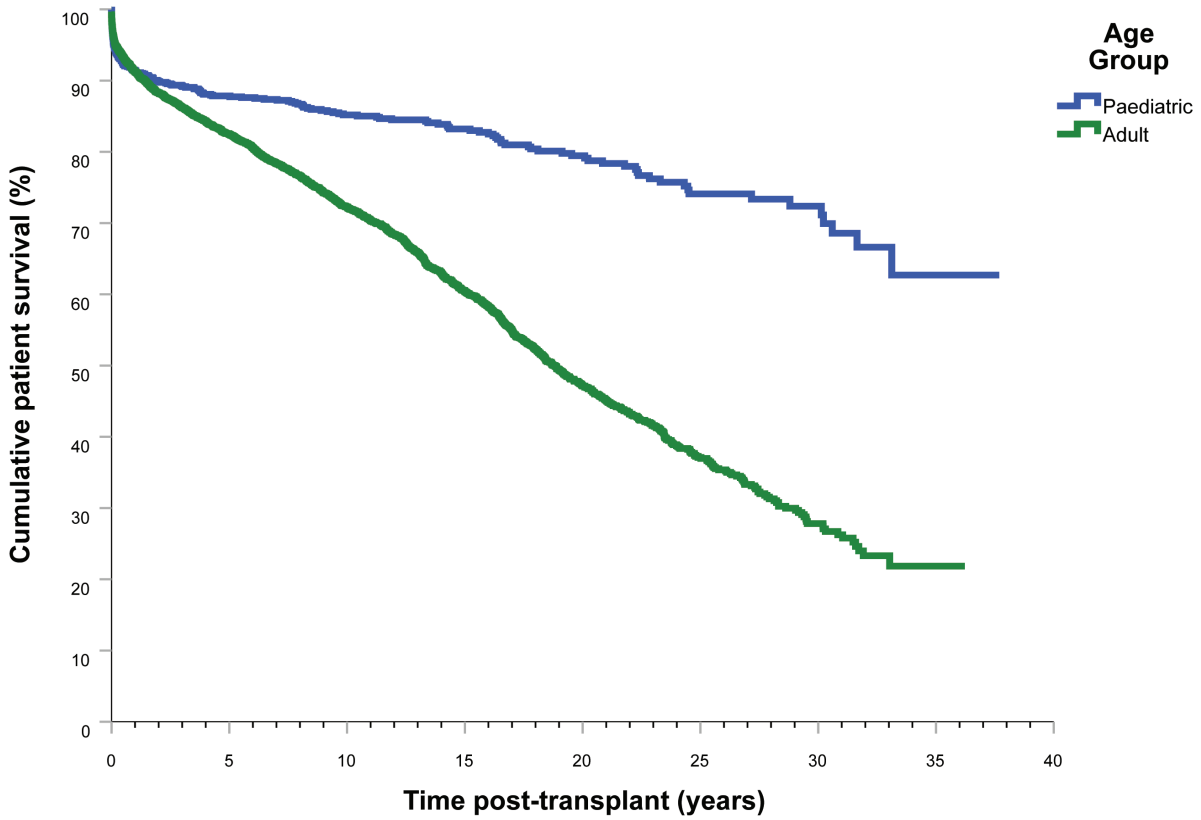


Table 19. Patient survival by age category

Age group	Patient Survival	Time post-transplant (years)								
		0	1	3	5	10	20	30	35	40
Paediatric (<16y)	No. at risk	1,130	972	854	753	530	233	60	3	0
	Survival (%)		91%	89%	88%	85%	80%	72%	63%	
Adults (≥16y)	No. at risk	5,853	5,088	4,273	3,566	2,208	620	79	3	0
	Survival (%)		91%	86%	83%	72%	47%	28%	22%	

14.3 Paediatric Patient Survival by Age Strata

There was no significant difference in patient survival by paediatric age strata (P = 0.243, Figure 45, Table 20). Ten-year patient survival was 86.4% for children less than 1 year, 81.7% for 1 – 2-year-olds, 86.9% for 3 – 9-year-olds and 87.2% for 10 – 15-year-olds. Median patient survival was not reached for all paediatric age groups.

Figure 45. Paediatric patient survival curve by age strata

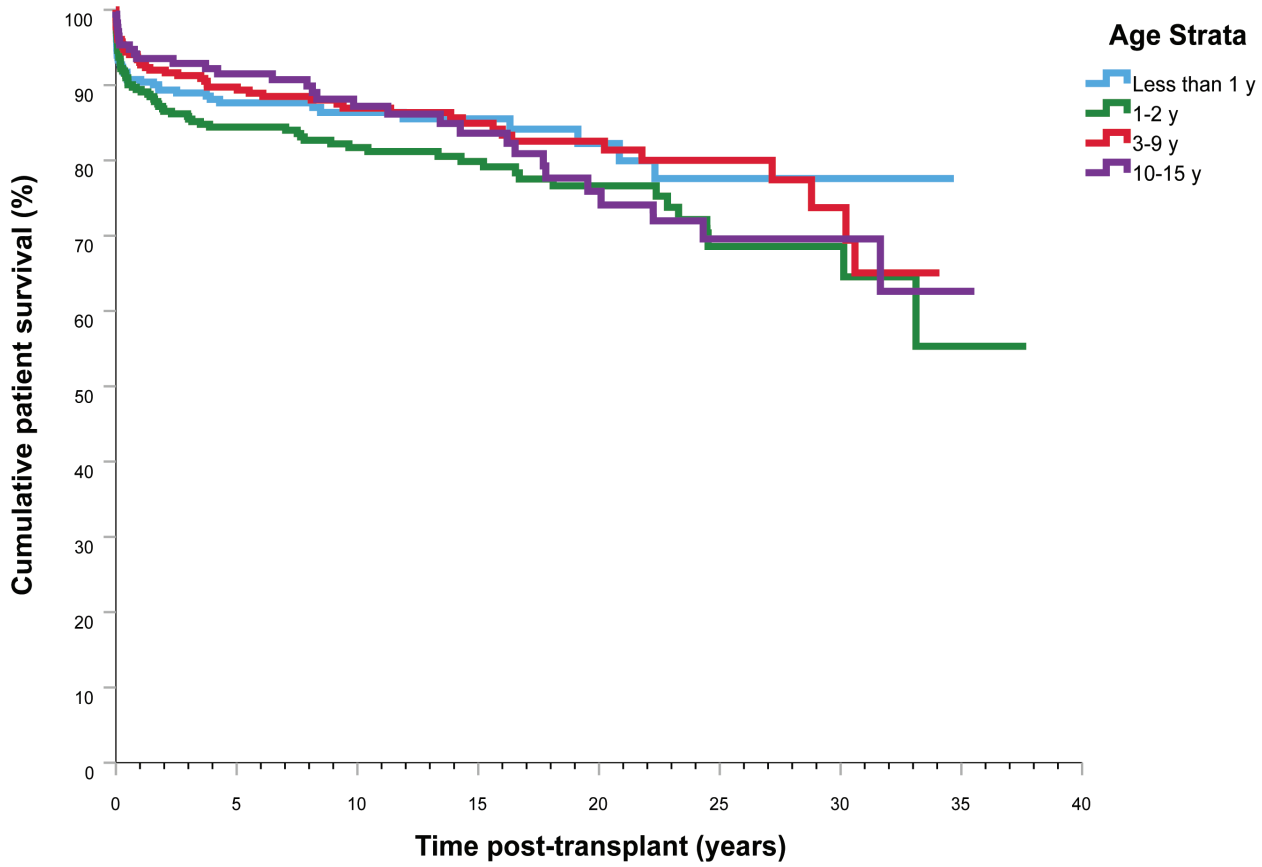


Table 20. Paediatric patient survival by age strata

Age strata	Patient Survival	Time post-transplant (years)								
		0	1	3	5	10	20	30	35	40
< 1 year	No. at risk	316	267	218	181	117	40	11	0	
	Survival (%)		91%	89%	88%	86%	82%	78%		
1 - 2 years	No. at risk	334	283	251	221	164	73	17	2	0
	Survival (%)		89%	86%	84%	82%	77%	69%	55%	
3 - 9 years	No. at risk	307	269	246	223	158	78	18	0	
	Survival (%)		93%	91%	90%	87%	83%	74%		
10 – 15 years	No. at risk	173	153	139	128	91	42	14	1	
	Survival (%)		94%	93%	92%	87%	76%	70%	63%	

14.4 Adult Patient Survival by Age Strata

Post-transplant patient survival in adults was significantly worse with increasing patient age (P < 0.001, Figure 46, Table 21). 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 78.9%, 77.2%, 74.0%, 71.7%, 64.9% and 76.3%, respectively. For patients aged 16 to 29 years, 30 to 39, 40 to 49, 50 to 59, 60 to 69 and 70 to 79 years, median patient survival was 31.9, 24.5, 22.7, 17.0, 14.5 and 11.0 years, respectively.

Figure 46. Adult patient survival curve by age strata

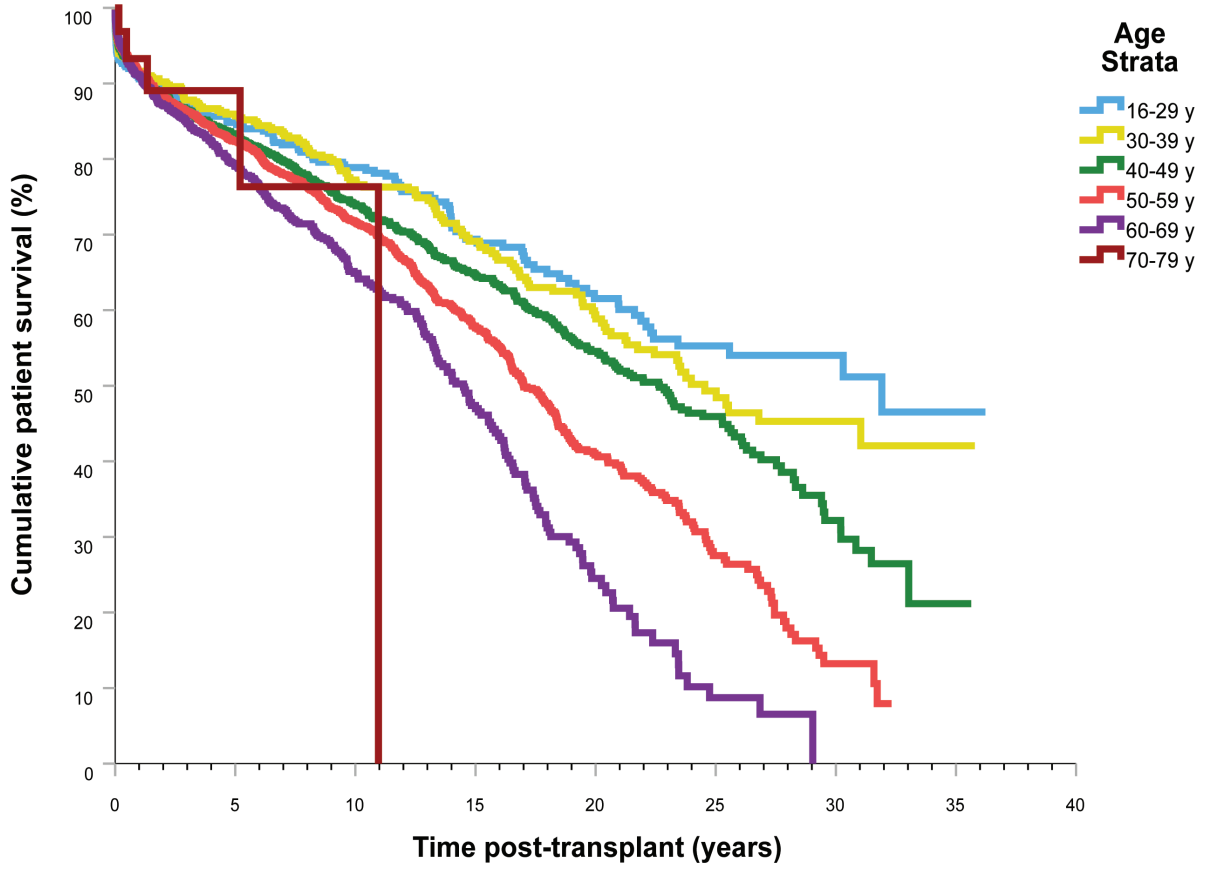


Table 21. Adult patient survival by age strata

Age strata	Patient Survival	Time post-transplant (years)								
		0	1	3	5	10	20	30	35	40
16-29 y	No. at risk	452	394	345	304	215	91	21	1	0
	Survival (%)		91%	87%	85%	79%	62%	54%	47%	
30-39 y	No. at risk	532	463	396	345	246	109	20	1	0
	Survival (%)		92%	88%	86%	77%	59%	45%	42%	
40-49 y	No. at risk	1,323	1,168	1,016	894	653	221	28	1	0
	Survival (%)		91%	86%	83%	74%	55%	32%	21%	
50-59 y	No. at risk	2,182	1,918	1,643	1,402	828	171	10	0	
	Survival (%)		91%	86%	82%	72%	41%	13%		
60-69 y	No. at risk	1,331	1,120	857	614	264	28	0		
	Survival (%)		91%	85%	79%	65%	25%			
70-79 y	No. at risk	33	25	16	7	2	0			
	Survival (%)		93%	89%	89%	76%				

14.5 Patient Survival by Era of Transplant

There has been a progressive improvement in patient survival over eras of transplantation (P < 0.001, Figure 47, Table 22). Patient survival in the most recent era was 93.9% at 1 year, 91.1% at 3 years, 87.5% at 5 years and 76.3% at 10 years. Median patient survival was not reached for recent eras since 2005 and was 20.8 years for 2000 – 2004, 19.3 years for 1995 – 99, 19.6 years for 1990 – 94 and 11.8 years for 1985 – 89.

Figure 47. Patient survival curve by era of transplant

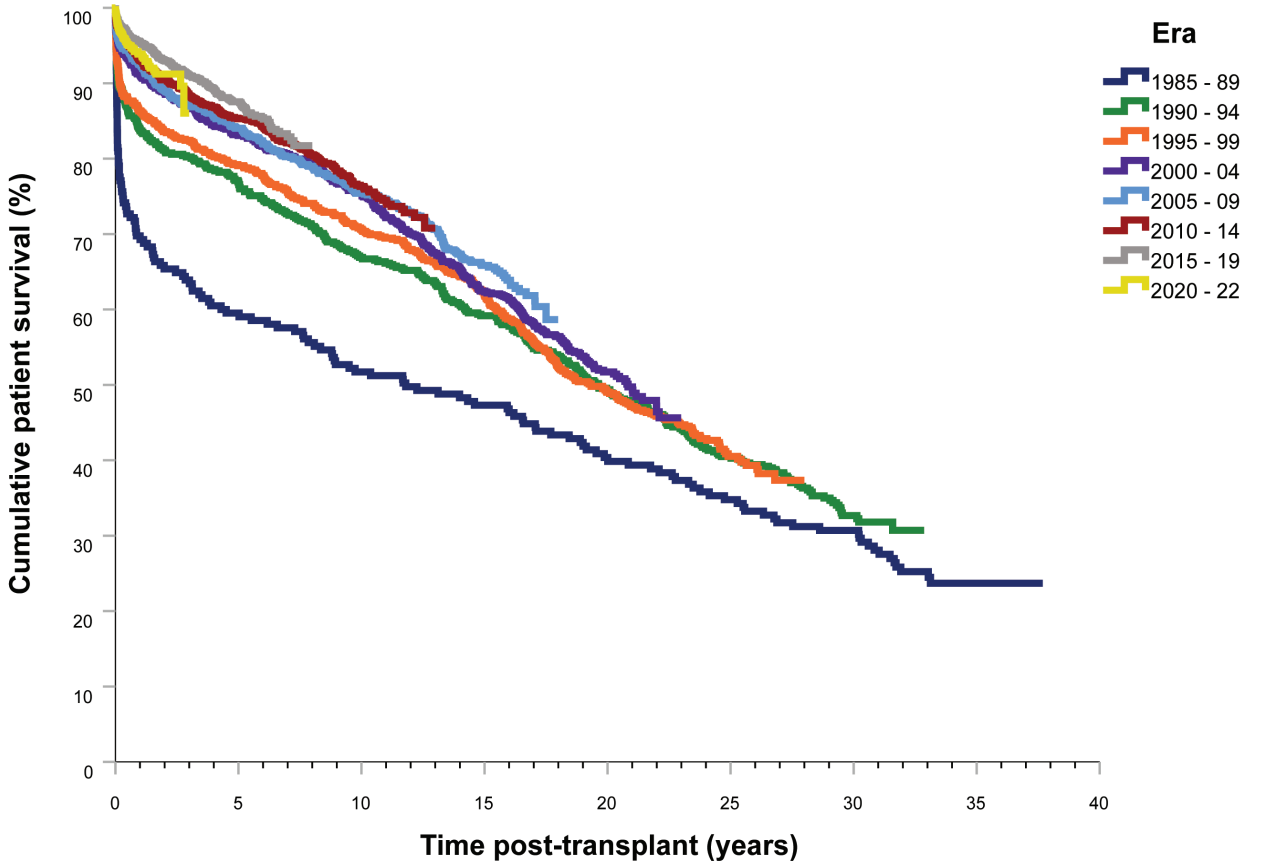


Table 22. Patient survival by transplant era

Transplant Era	Patient Survival	Time post-transplant (years)								
		0	1	3	5	10	20	30	35	40
1985 - 89	No. at risk	205	143	131	122	106	80	60	6	0
	Survival (%)		70%	64%	60%	52%	40%	31%	24%	
1990 - 94	No. at risk	552	461	438	419	355	242	79	0	
	Survival (%)		84%	80%	77%	67%	49%	33%		
1995 - 99	No. at risk	697	597	566	539	474	314	0		
	Survival (%)		86%	82%	79%	71%	49%			
2000 - 04	No. at risk	860	776	734	696	628	217	0		
	Survival (%)		91%	87%	83%	75%	52%			
2005 - 09	No. at risk	962	886	832	807	711	0			
	Survival (%)		93%	87%	85%	75%				
2010 - 14	No. at risk	1,228	1,140	1,080	1,031	464	0			
	Survival (%)		93%	88%	85%	76%				
2015 - 19	No. at risk	1,617	1,526	1,346	709	0				
	Survival (%)		96%	91%	88%					
2020 - 22	No. at risk	862	531	0						
	Survival (%)		94%							

14.6 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 48, Table 23). Paediatric patient survival in the most recent era was 98.7% at 1 year, 95.9% at 3 years, 95.3% at 5 years and 88.4% at 10 years. Median paediatric patient survival was not reached for all eras other than 1985 – 89 who had a median survival of 20.8 years.

Figure 48. Paediatric patient survival curve by era of transplant

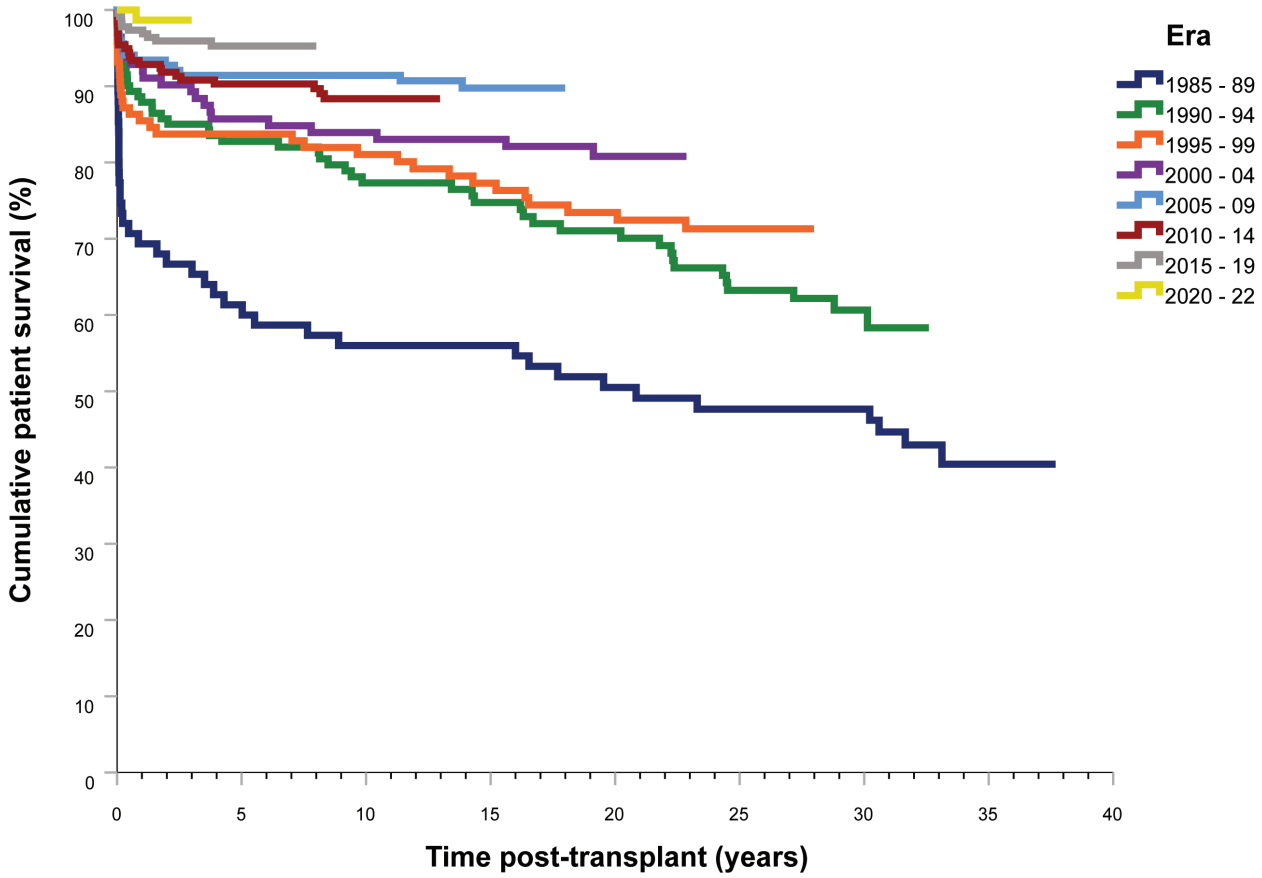


Table 23. Paediatric patient survival by transplant era

Transplant Era	Patient Survival	Time post-transplant (years)								
		0	1	3	5	10	20	30	35	40
1985 - 89	No. at risk	75	52	50	46	42	36	33	3	0
	Survival (%)		69%	67%	61%	56%	51%	48%	40%	
1990 - 94	No. at risk	141	122	115	111	96	75	27	0	
	Survival (%)		88%	85%	83%	77%	71%	61%		
1995 - 99	No. at risk	117	99	96	95	88	73	0		
	Survival (%)		86%	84%	84%	81%	73%			
2000 - 04	No. at risk	112	104	100	96	93	49	0		
	Survival (%)		93%	89%	86%	84%	81%			
2005 - 09	No. at risk	152	141	138	138	135	0			
	Survival (%)		93%	91%	91%	91%				
2010 - 14	No. at risk	197	181	177	171	76	0			
	Survival (%)		93%	91%	90%	88%				
2015 - 19	No. at risk	228	207	179	96	0				
	Survival (%)		97%	96%	95%					
2020 - 22	No. at risk	108	66	0						
	Survival (%)		99%							

14.7 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 49, Table 24). Patient survival in the most recent era was 93.2% at 1 year, 90.3% at 3 years, 86.4% at 5 years and 74.2% at 10 years. Median adult patient survival was not reached for recent eras since 2005 and was 18.8 years for 2000 – 04, 17.6 years for 1995 – 99, 16.9 years for 1990 – 94 and 9.5 years for 1985 – 89.

Figure 49. Adult patient survival curve by era of transplant

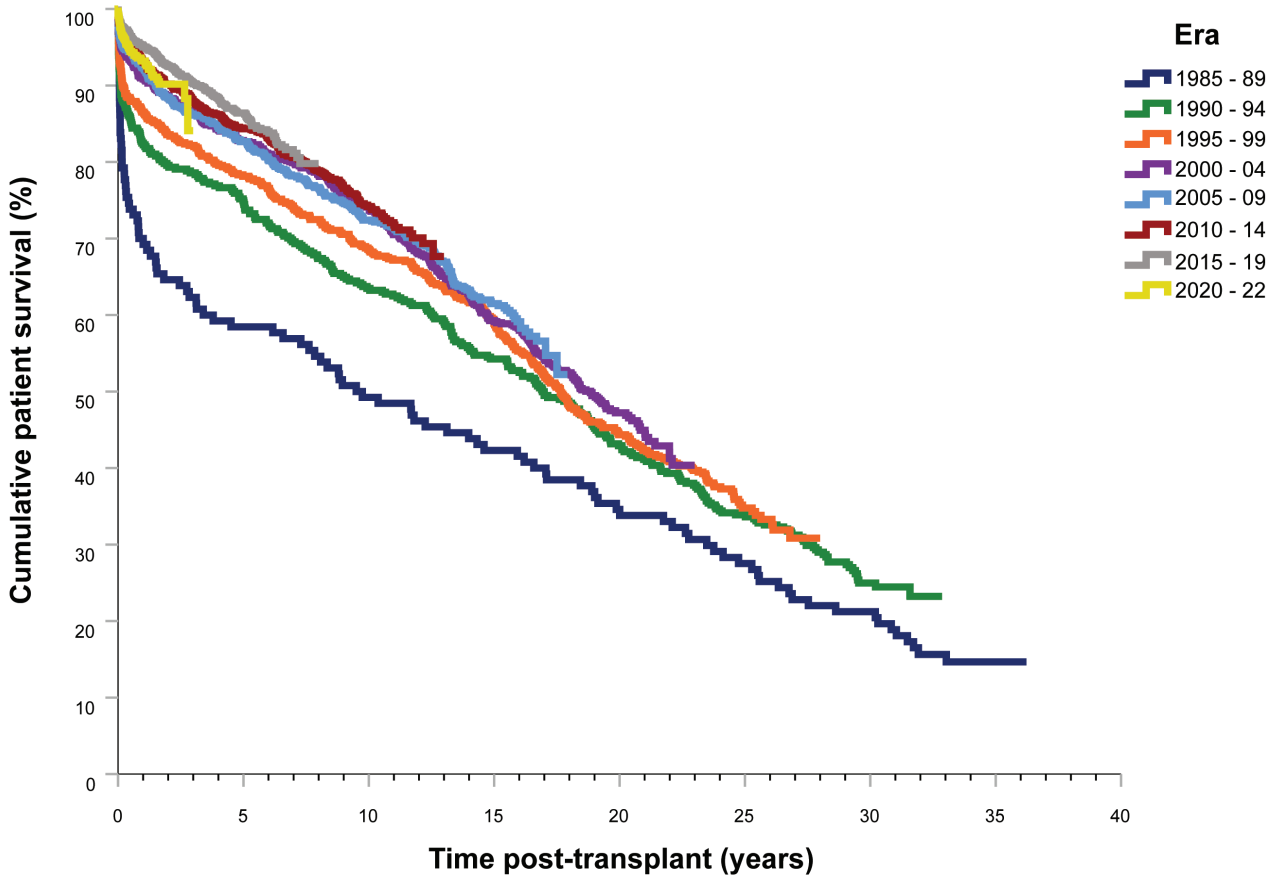


Table 24. Adult patient survival by transplant era

Transplant Era	Patient Survival	Time post-transplant (years)								
		0	1	3	5	10	20	30	35	40
1985 - 89	No. at risk	130	91	81	76	64	44	27	3	0
	Survival (%)		70%	62%	59%	49%	35%	21%	15%	
1990 - 94	No. at risk	411	339	323	308	259	167	52	0	
	Survival (%)		83%	79%	75%	64%	43%	25%		
1995 - 99	No. at risk	580	498	470	444	386	241	0		
	Survival (%)		87%	82%	78%	69%	44%			
2000 - 04	No. at risk	748	672	634	600	535	168	0		
	Survival (%)		91%	86%	83%	74%	47%			
2005 - 09	No. at risk	810	745	694	665	576	0			
	Survival (%)		92%	86%	83%	72%				
2010 - 14	No. at risk	1,031	959	903	860	388	0			
	Survival (%)		93%	88%	84%	74%				
2015 - 19	No. at risk	1,389	1,319	1,168	613	0				
	Survival (%)		95%	90%	86%					
2020 - 22	No. at risk	754	465	0						
	Survival (%)		93%							

14.8 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 50, Table 25). 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 91.8% for split liver grafts, 90.1% for living donor grafts, 85.7% for whole liver grafts and 76.8% for reduced grafts. Median paediatric patient survival was 33.1 years for reduced grafts and was not reached for other graft types.

Figure 50. Paediatric patient survival curve by type of primary graft

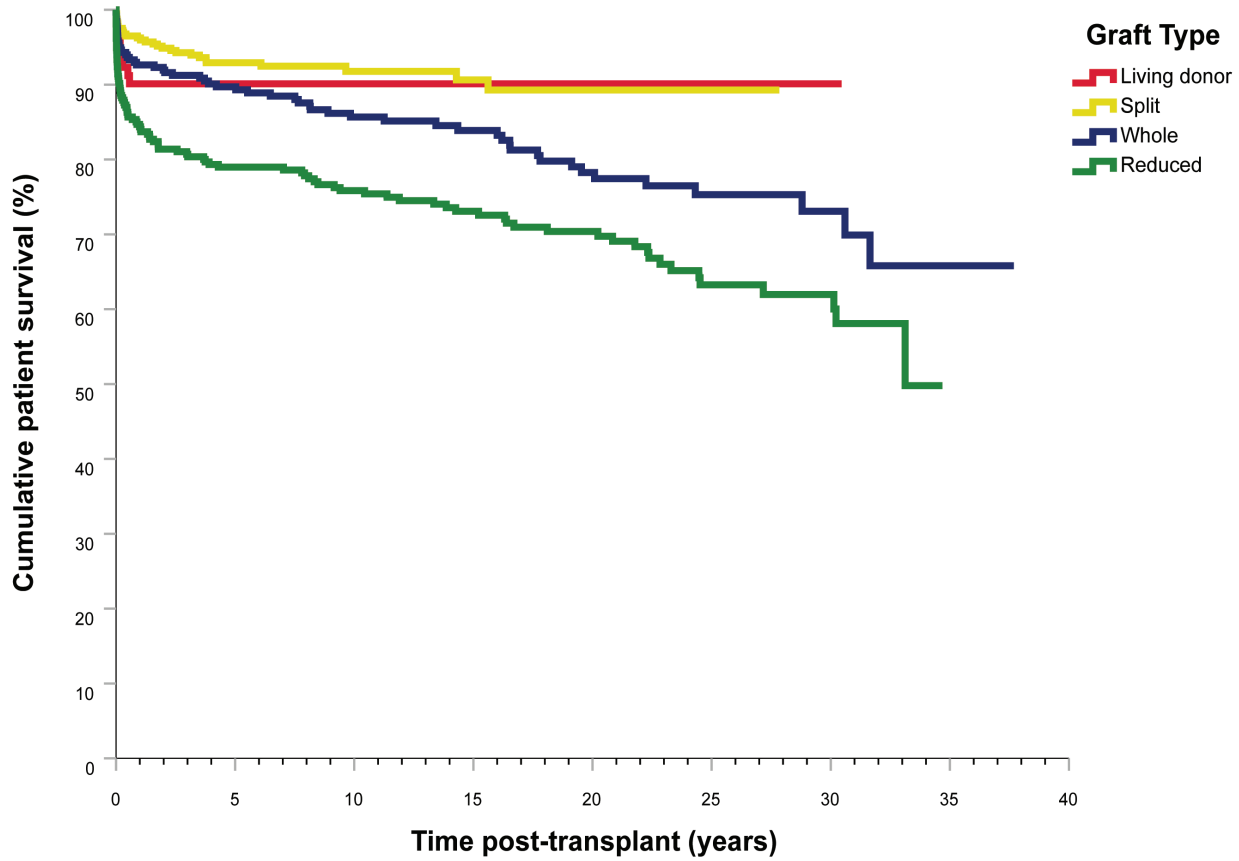


Table 25. Paediatric patient survival by type of primary graft

Graft Type Category	Patient Survival	Time post-transplant (years)								
		0	1	3	5	10	20	30	35	40
Living donor	No. at risk	91	82	74	66	49	3	1	0	
	Survival (%)		90%	90%	90%	90%	90%	90%		
Split	No. at risk	404	360	291	236	126	19	0		
	Survival (%)		96%	94%	93%	92%	89%			
Whole	No. at risk	318	273	251	226	171	99	27	3	0
	Survival (%)		93%	91%	90%	86%	78%	73%	66%	
Reduced	No. at risk	316	256	237	224	183	112	32	0	
	Survival (%)		84%	81%	79%	76%	70%	62%		

14.9 Adult Patient Survival by Type of Primary Graft

Although early survival after reduced liver transplantation appeared to be inferior to other graft types, there was no significant difference in patient survival in adults by type of primary graft (P = 0.664, Figure 51, Table 26). Ten-year patient survival was 79.8% for living donor grafts, 75.4% for split grafts, 72.1% for whole grafts and 55.3% for reduced grafts. Median adult patient survival was not reached for living and reduced donor grafts and was 23.4 years for split grafts, 18.7 years for whole grafts and 9.4 years for domino grafts.

Figure 51. Adult patient survival curve by type of primary graft

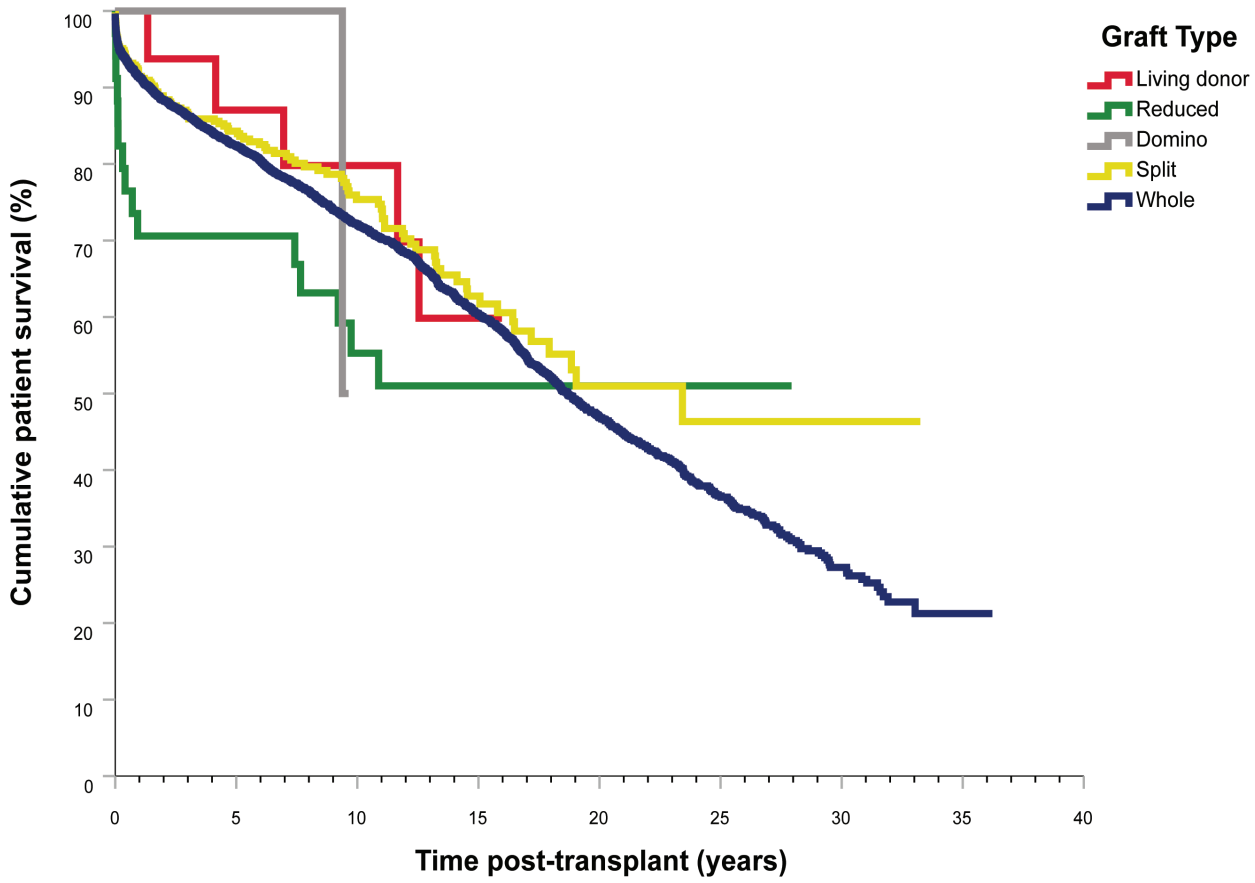


Table 26. Adult patient survival by type of primary graft

Graft Type Category	Patient Survival	Time post-transplant (years)								
		0	1	3	5	10	20	30	35	40
Living donor	No. at risk	16	16	15	13	11	0			
	Survival (%)		100%	94%	87%	80%				
Split	No. at risk	430	368	304	247	131	20	2	0	
	Survival (%)		91%	87%	84%	75%	51%	46%		
Reduced	No. at risk	34	24	21	20	14	7	0		
	Survival (%)		71%	71%	71%	55%	51%			
Whole	No. at risk	5,368	4,676	3,929	3,282	2,052	593	77	3	0
	Survival (%)		91%	86%	82%	72%	47%	27%	21%	
Domino	No. at risk	5	4	4	4	0				
	Survival (%)		100%	100%	100%					

14.10 Paediatric Patient Survival by Weight

There was no significant difference in patient survival of children of different weights (P = 0.579, Figure 52 and Table 27). Ten-year paediatric patient survival was 88.2% for children over 20 kg, 85.0% for children weighing between 8.01 and 20 kg, 82.1% for children between 5 and 8 kg and 82.6% for children under 5 kg. Median paediatric patient survival was 33.1 years for children between 5 and 8 kg and was not reached for other weight categories.

Figure 52. Paediatric patient survival curve by transplant weight

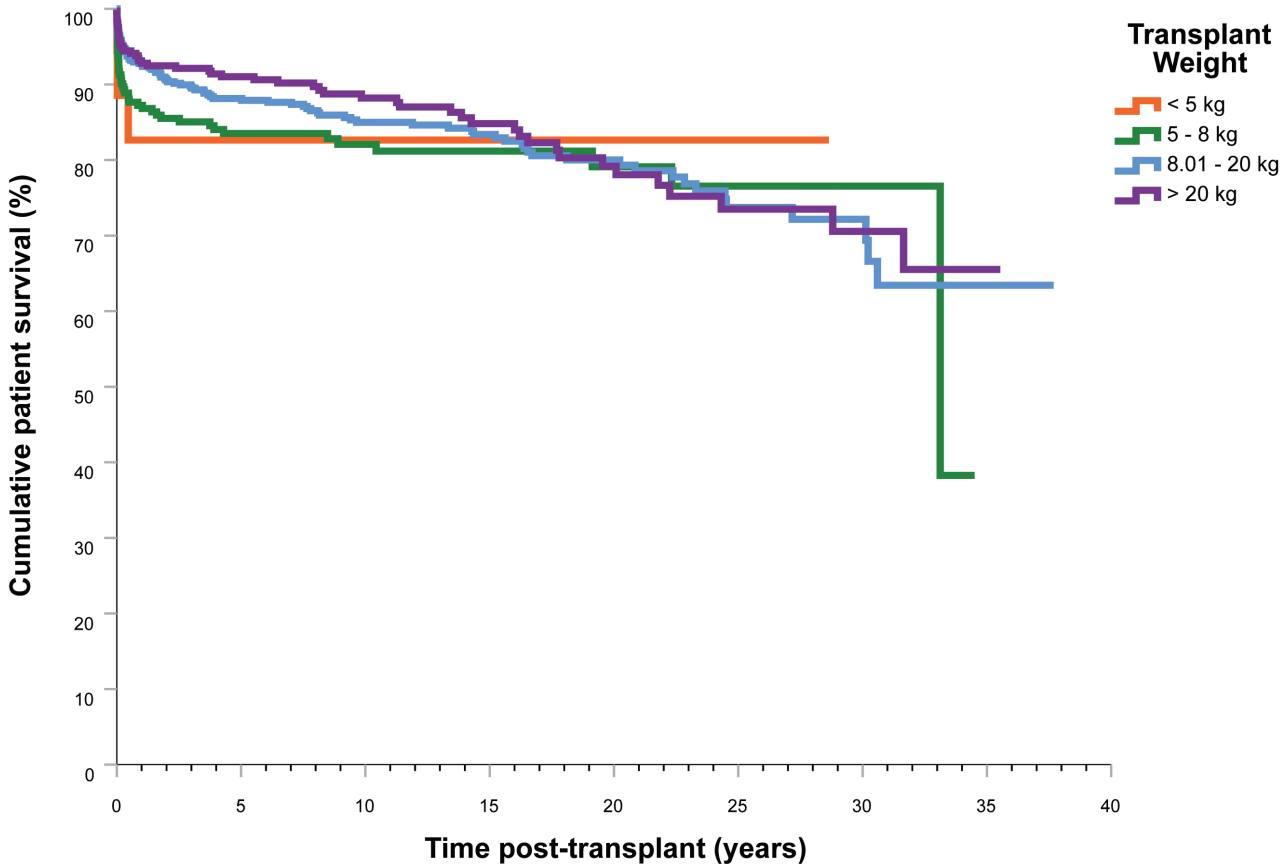


Table 27. Paediatric patient survival by transplant weight

Transplant weight	Patient Survival	Time post-transplant (years)								
		0	1	3	5	10	20	30	35	40
< 5 kg	No. at risk	18	12	11	6	5	3	0		
	Survival (%)		83%	83%	83%	83%	83%			
5 - 8 kg	No. at risk	253	207	174	152	101	37	12	0	
	Survival (%)		87%	85%	84%	82%	79%	77%		
8.01 - 20 kg	No. at risk	532	470	409	360	263	123	26	2	0
	Survival (%)		93%	90%	88%	85%	80%	72%	63%	
> 20 kg	No. at risk	326	282	259	234	161	70	22	1	0
	Survival (%)		93%	92%	91%	88%	79%	71%	66%	

14.11 Paediatric Patient Survival by Primary Disease

There was no significant difference in patient survival between different disease categories in children (P = 0.079, Figure 53, Table 28). Children with fulminant hepatic failure had the poorest ten-year survival of 77.3%. Children with hepatoblastoma had a ten-year survival of 80.9%. All other paediatric disease categories had an 83.0% or higher 10-year survival. Median patient survival was 31.6 years for children with other diseases, 27.1 years for children with progressive familial intrahepatic cholestasis and was not reached for all other disease groups.

Figure 53. Paediatric patient survival curve by primary disease

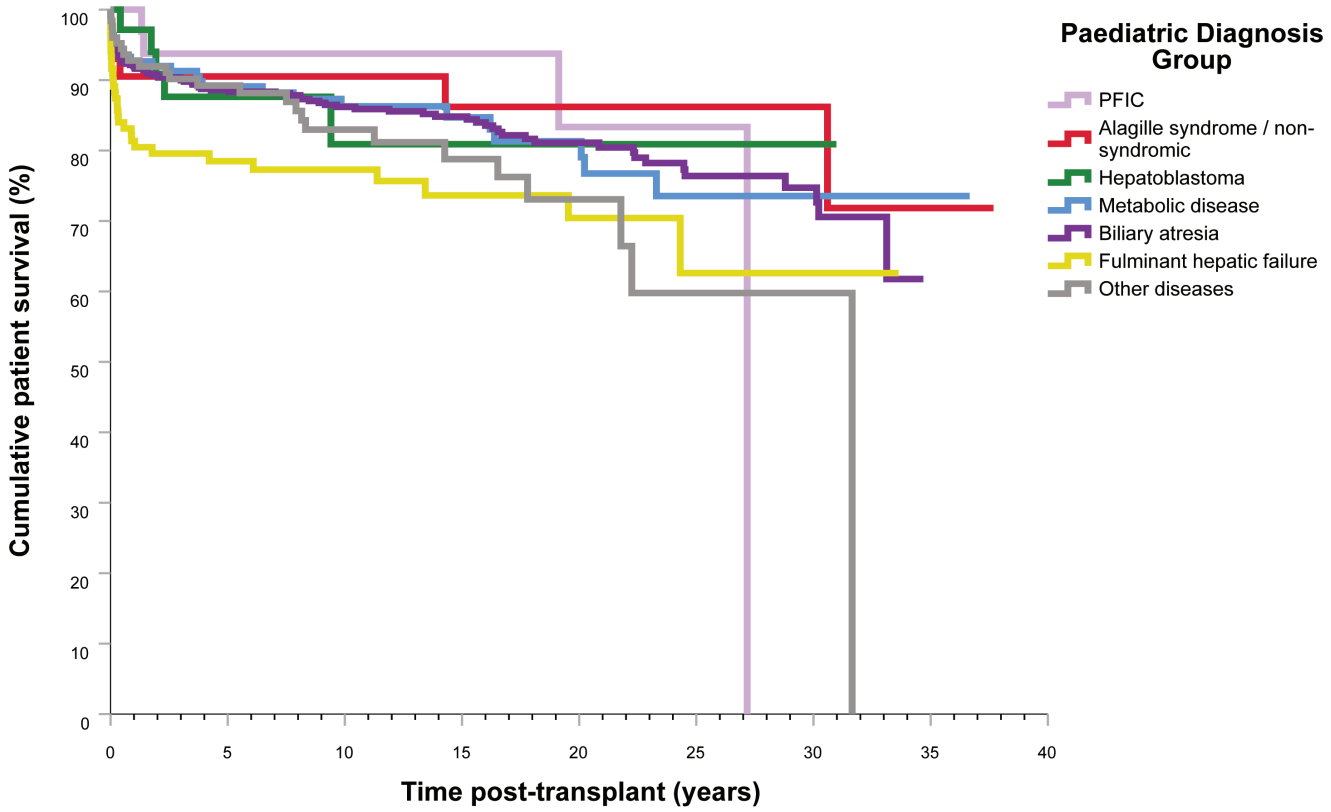


Table 28. Paediatric patient survival by primary disease

Primary Disease	Patient Survival	Time post-transplant (years)								
		0	1	3	5	10	20	30	35	40
PFIC	No. at risk	33	32	25	22	18	8	0		
	Survival (%)		100%	94%	94%	94%	83%			
Alagille syndrome / non-syndromic	No. at risk	43	36	35	34	21	16	6	1	0
	Survival (%)		91%	91%	91%	91%	86%	86%	72%	
Hepatoblastoma	No. at risk	37	32	25	20	12	2	1	0	
	Survival (%)		97%	88%	88%	81%	81%	81%		
Metabolic Diseases	No. at risk	166	145	128	114	82	37	11	2	0
	Survival (%)		93%	91%	89%	86%	81%	74%	74%	
Biliary atresia	No. at risk	603	525	461	407	293	131	36	0	
	Survival (%)		92%	90%	89%	86%	81%	75%		
Fulminant hepatic failure	No. at risk	120	92	81	67	52	22	4	0	
	Survival (%)		81%	80%	79%	77%	70%	63%		
Other Diseases	No. at risk	128	110	99	89	52	17	2	0	
	Survival (%)		93%	90%	89%	83%	73%	60%		

Abbreviation: PFIC, Progressive familial intrahepatic cholestasis

14.12 Adult Patient Survival by Primary Disease

There was a significant difference in the survival between different disease categories in adults (P < 0.001, Figure 54, Table 29). Patients with hepatocellular carcinoma, hepatitis C virus cirrhosis and non-alcoholic fatty liver disease / cryptogenic cirrhosis had the poorest 10-year patient survival (66.2%, 68.6% and 72.0%, respectively), while those with alcohol-related cirrhosis, hepatocellular carcinoma and hepatitis C virus cirrhosis had the poorest median survival (16.5 years, 16.6 years and 16.8 years, respectively). Patients with fulminant hepatic failure had poorer early survival than other diagnoses (1-year patient survival 83.3%), but long-term survival was similar to patients transplanted for other diagnoses.

Figure 54. Adult patient survival curve by primary disease

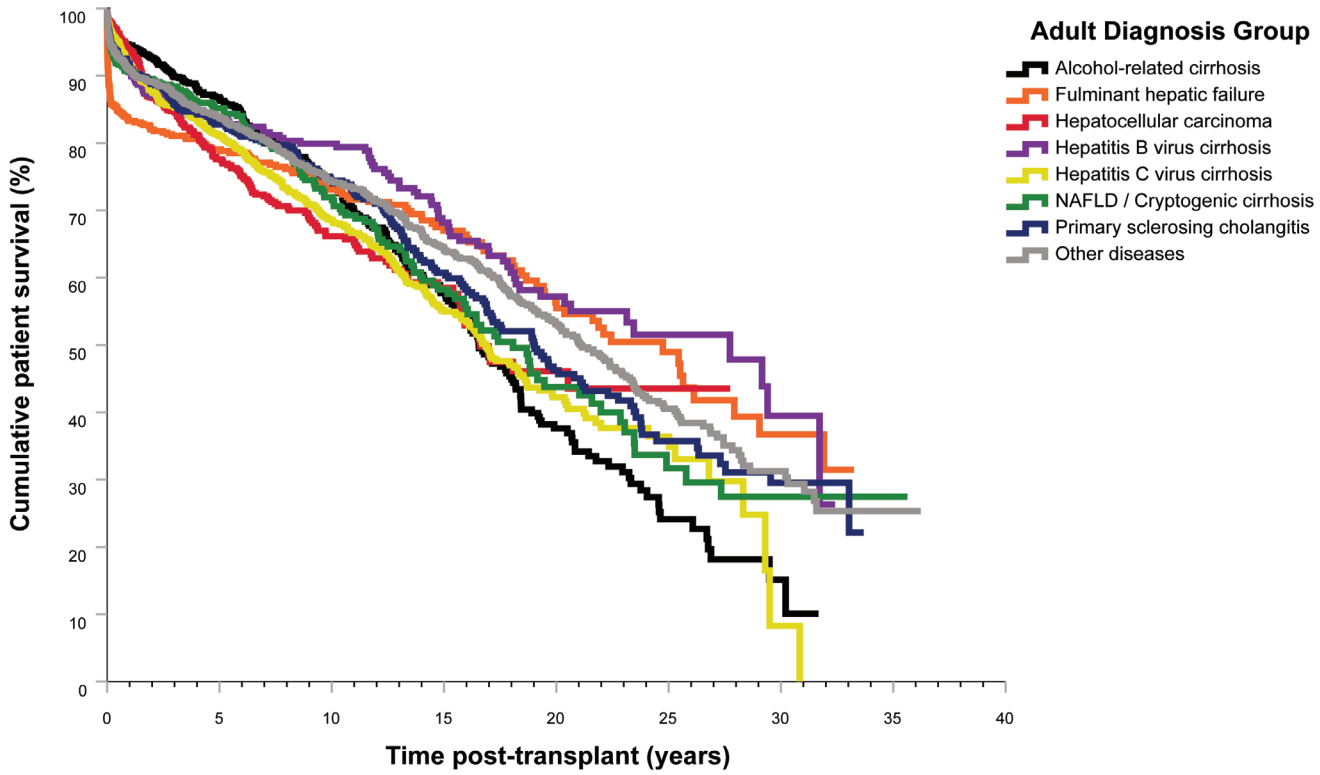


Table 29. Adult patient survival by primary disease

Primary Disease	Patient Survival	Time post-transplant (years)								
		0	1	3	5	10	20	30	35	40
Alcohol-related cirrhosis	No. at risk	841	737	582	471	284	59	3	0	
	Survival (%)		95%	90%	87%	74%	38%	15%		
Fulminant hepatic failure	No. at risk	516	406	348	297	204	66	9	0	
	Survival (%)		83%	81%	79%	73%	56%	37%		
Hepatocellular carcinoma	No. at risk	749	664	509	373	157	21	0		
	Survival (%)		94%	85%	78%	66%	46%			
Hepatitis B virus cirrhosis	No. at risk	331	288	249	223	163	58	6	0	
	Survival (%)		91%	86%	84%	80%	57%	40%		
Hepatitis C virus cirrhosis	No. at risk	1,137	1,027	916	799	481	81	1	0	
	Survival (%)		92%	85%	81%	69%	42%	8%		
NAFLD / Cryptogenic cirrhosis	No. at risk	562	469	384	310	164	40	9	1	0
	Survival (%)		91%	88%	85%	72%	44%	28%	28%	
Primary sclerosing cholangitis	No. at risk	581	513	435	376	251	82	17	0	
	Survival (%)		92%	86%	83%	74%	46%	30%		
Other diseases	No. at risk	1,136	984	850	717	504	213	34	2	0
	Survival (%)		91%	87%	84%	74%	53%	31%	25%	

Abbreviation: NAFLD, non-alcoholic fatty liver disease

14.13 Patient Survival by Age Group with Fulminant Hepatic Failure

There was no significant difference in the survival between adults and children with fulminant hepatic failure as a primary diagnosis or other diagnosis (P = 0.128, Figure 55 and Table 30). Ten-year patient survival was 77.6% for children and 73.3% for adults. Median patient survival was not reached for children and was 24.7 years for adults.

Figure 55. Patient survival curve by age group with fulminant hepatic failure – all diagnoses

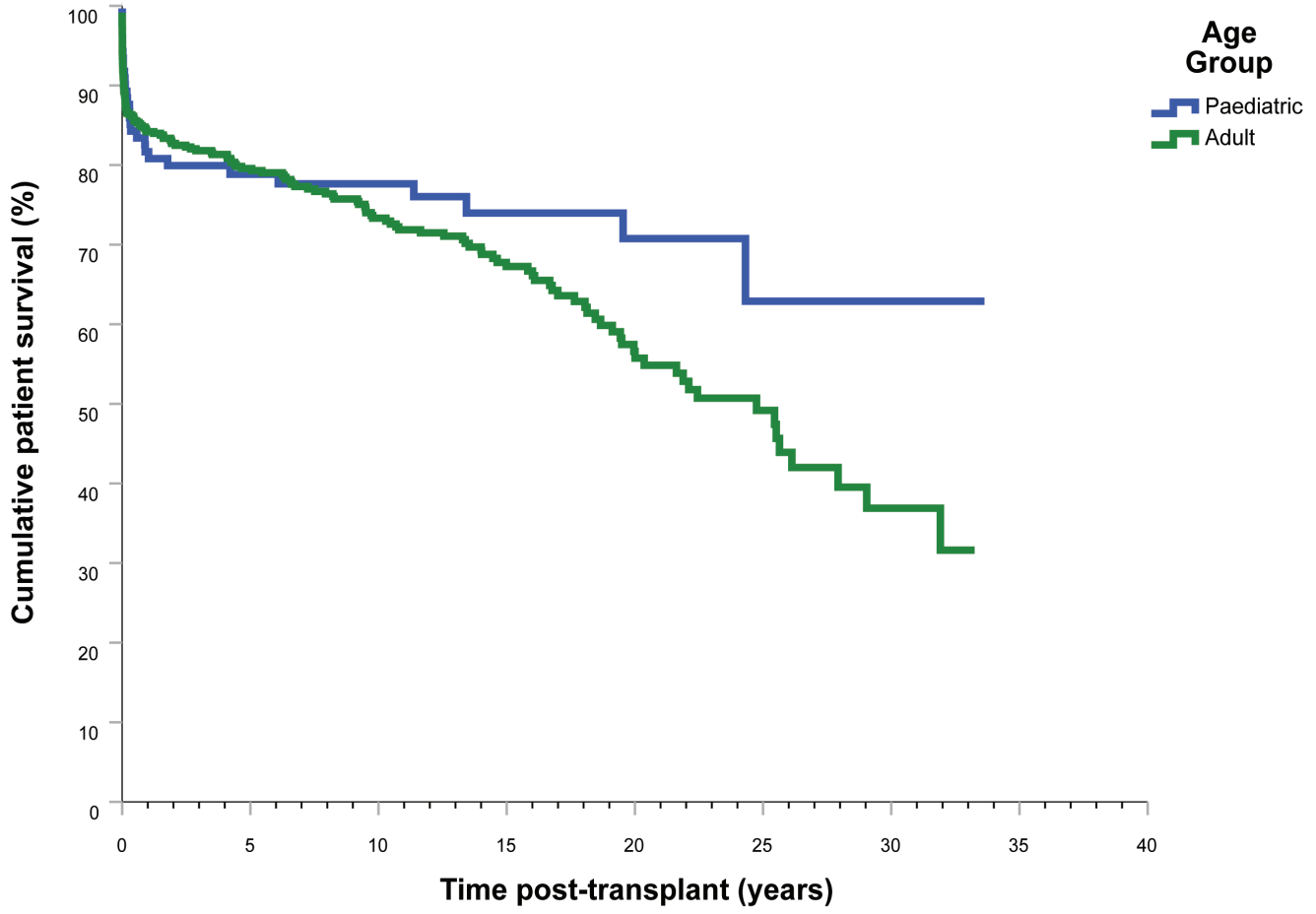


Table 30. Patient survival by age group with fulminant hepatic failure – all diagnoses

Primary Diagnosis	Patient Survival	Time post-transplant (years)								
		0	1	3	5	10	20	30	35	40
Paediatric	No. at risk	122	94	83	68	52	22	4	0	
	Survival (%)		82%	80%	79%	78%	71%	63%		
Adult	No. at risk	546	430	355	303	206	66	9	0	
	Survival (%)		84%	82%	80%	73%	57%	37%		

14.14 Patient Survival by Transplant Era with Hepatitis B Virus Cirrhosis

There has been an improvement in patient survival over the transplant eras for patients with a diagnosis of hepatitis B virus cirrhosis as a primary diagnosis or other diagnosis (P < 0.001, Figure 56, Table 31). Patient survival in the most recent era was 95.9% at 1 year, 92.4% at 3 years, 84.2% at 5 years and 81.9% at 10 years. Median patient survival was not reached for the recent eras since 2000 and was 27.7 years for 1990 – 94, 18.0 years for 1995 – 99 and 0.6 years for 1985 – 89.

Figure 56. Patient survival curve by transplant era with hepatitis B virus cirrhosis – all diagnoses

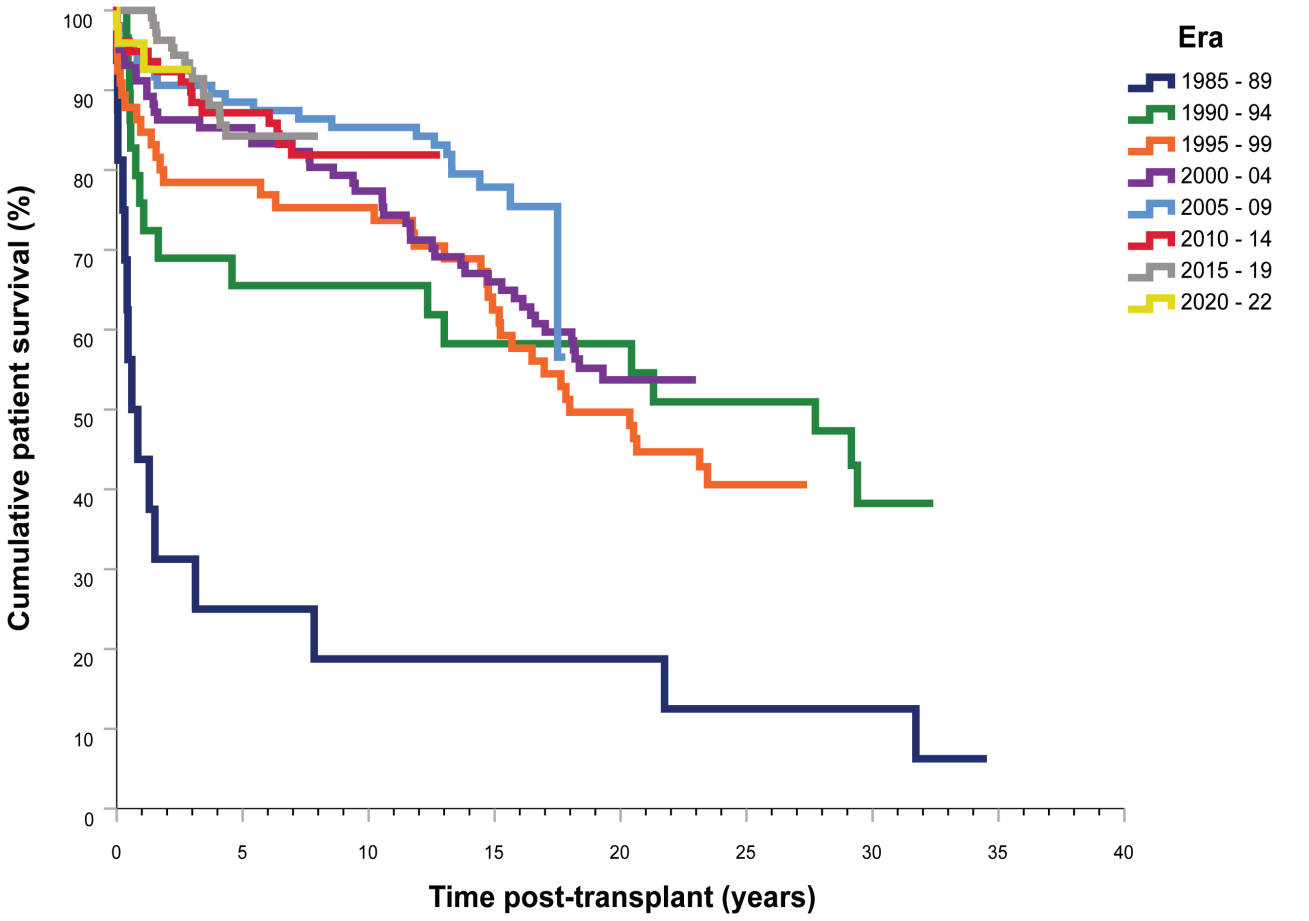


Table 31. Patient survival by transplant era with hepatitis B virus cirrhosis – all diagnoses

Transplant era	Patient Survival	Time post-transplant (years)								
		0	1	3	5	10	20	30	35	40
1985 - 89	No. at risk	16	7	5	4	3	3	2	0	
	Survival (%)		44%	31%	25%	19%	19%	13%		
1990 - 94	No. at risk	29	22	20	19	19	16	5	0	
	Survival (%)		76%	69%	66%	66%	58%	38%		
1995 - 99	No. at risk	66	54	50	50	47	30	0		
	Survival (%)		85%	79%	79%	75%	50%			
2000 - 04	No. at risk	102	93	88	86	77	33	0		
	Survival (%)		91%	86%	85%	77%	54%			
2005 - 09	No. at risk	96	90	86	84	80	0			
	Survival (%)		94%	91%	89%	85%				
2010 - 14	No. at risk	78	74	69	68	31	0			
	Survival (%)		95%	89%	87%	82%				
2015 - 19	No. at risk	109	109	95	49	0				
	Survival (%)		100%	92%	84%					
2020 - 22	No. at risk	50	30	0						
	Survival (%)		96%							

14.15 Patient Survival by Transplant Era with Hepatitis C Virus Cirrhosis

Patient survival after transplantation for hepatitis C virus cirrhosis as a primary diagnosis or other diagnosis varied over transplant eras with the best 3-year survival (100%) in 1985 - 89 and the best 5-year survival (83.9%) in 2015 - 19 (P = 0.108, Figure 57 and Table 32). Median patient survival was not reached for the recent eras since 2010 and was 17.9 years for 2000 - 04, 17.1 years for 1985 – 89, 16.7 years for 2005 – 09, 12.9 years for 1990 – 94 and 12.7 years for 1995 – 99.

Figure 57. Patient survival curve by transplant era with hepatitis C virus cirrhosis – all diagnoses

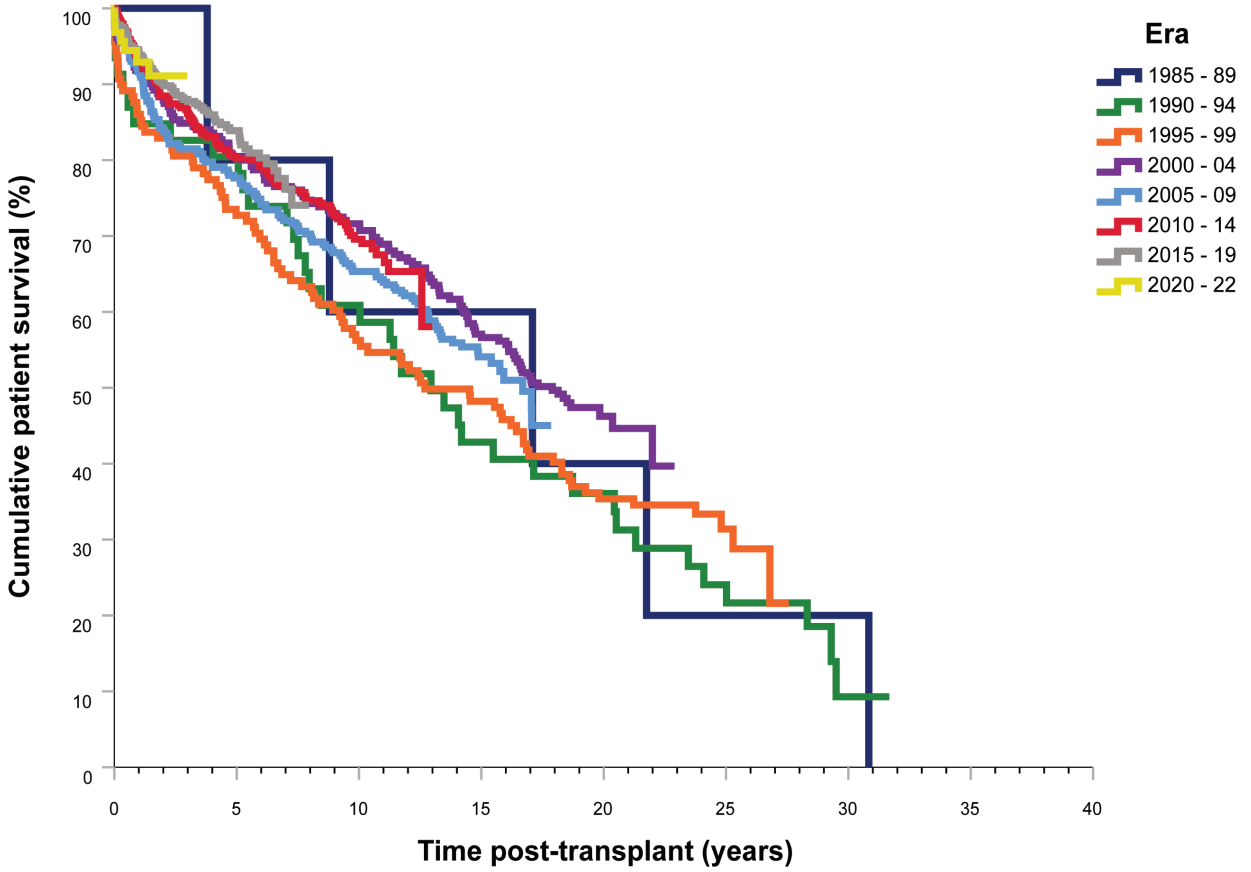


Table 32. Patient survival curve by transplant era with hepatitis C virus cirrhosis – all diagnoses

Transplant era	Patient Survival	Time post-transplant (years)								
		0	1	3	5	10	20	30	35	40
1985 - 89	No. at risk	5	5	5	4	3	2	1	0	
	Survival (%)		100%	100%	80%	60%	40%	20%		
1990 - 94	No. at risk	46	39	38	37	27	15	2	0	
	Survival (%)		85%	83%	80%	61%	36%	9%		
1995 - 99	No. at risk	129	110	103	93	71	44	0		
	Survival (%)		86%	81%	73%	56%	35%			
2000 - 04	No. at risk	233	213	195	182	160	37	0		
	Survival (%)		92%	85%	81%	72%	46%			
2005 - 09	No. at risk	287	262	233	222	185	0			
	Survival (%)		92%	82%	78%	65%				
2010 - 14	No. at risk	390	364	334	309	130	0			
	Survival (%)		93%	86%	80%	70%				
2015 - 19	No. at risk	404	380	338	186	0				
	Survival (%)		94%	88%	84%					
2020 - 22	No. at risk	95	60	0						
	Survival (%)		93%							

14.16 Patient Survival with Hepatocellular Carcinoma by Era of Transplant

There has been an improvement in patient survival over the transplant eras for patients with hepatocellular carcinoma as a primary diagnosis or other diagnosis (P<0.001, Figure 58, Table 33). Patient survival in the most recent era was 92.7% at 1 year, 88.3% at 3 years, 82.8% at 5 years and 69.2% at 10 years. Median patient survival was not reached for the recent eras since 2005 and was 16.6 years for 2000 – 04, 14.5 years for 1995 – 99, 9.9 years for 1990 – 94 and 1.5 years for 1985 – 89.

Figure 58. Patient survival curve with a diagnosis of hepatocellular carcinoma by transplant era – all diagnoses

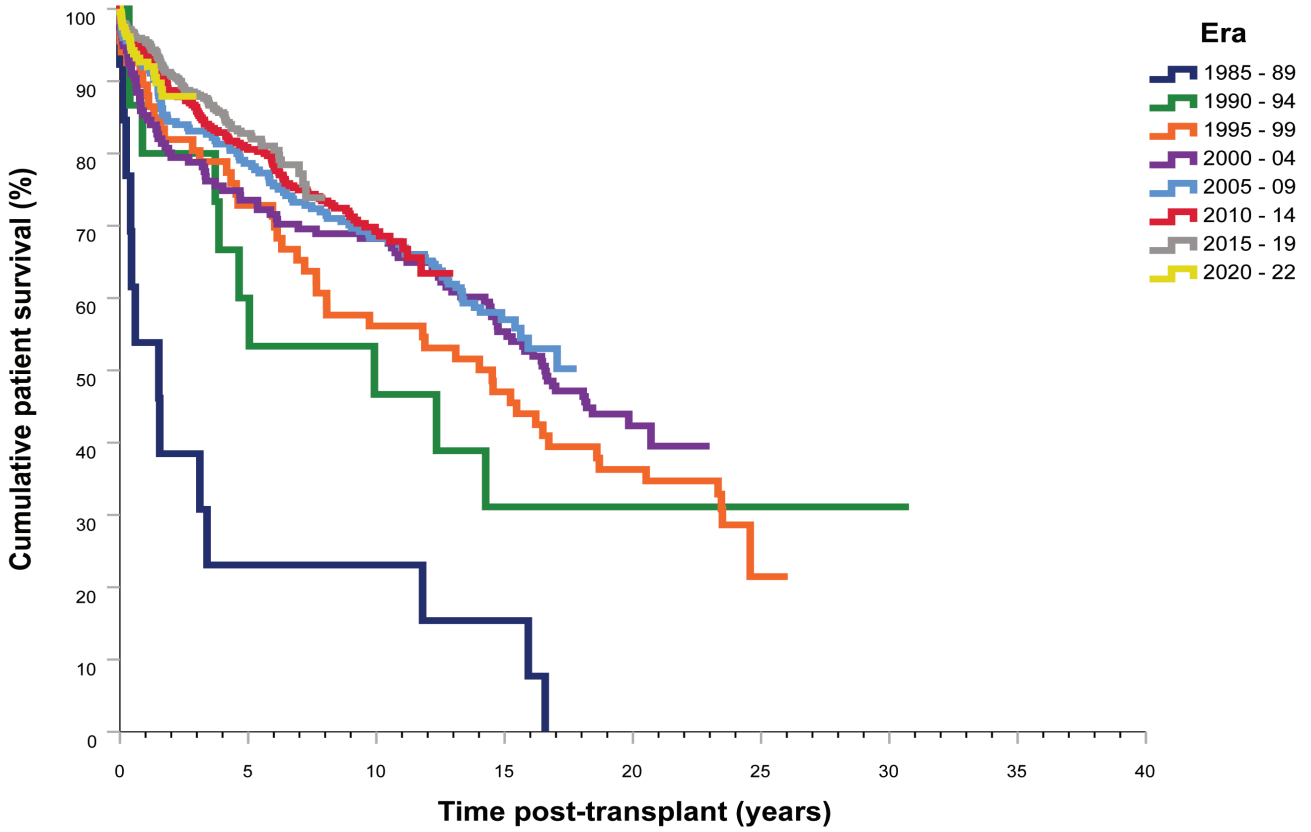


Table 33. Patient survival curve with a diagnosis of hepatocellular carcinoma by transplant era – all diagnoses

Transplant era	Patient Survival	Time post-transplant (years) 0	1	3	5	10	20	30	35	40
1985 - 89	No. at risk	13	7	5	3	3	0			
	Survival (%)		54%	39%	23%	23%				
1990 - 94	No. at risk	15	12	12	9	6	4	0		
	Survival (%)		80%	80%	60%	47%	31%			
1995 - 99	No. at risk	67	59	53	48	37	23	0		
	Survival (%)		90%	80%	73%	56%	36%			
2000 - 04	No. at risk	156	133	121	111	103	23	0		
	Survival (%)		85%	79%	74%	68%	42%			
2005 - 09	No. at risk	225	207	186	176	152	0			
	Survival (%)		92%	83%	79%	68%				
2010 - 14	No. at risk	346	324	295	276	114	0			
	Survival (%)		94%	86%	81%	69%				
2015 - 19	No. at risk	494	472	408	221	0				
	Survival (%)		96%	88%	83%					
2020 - 22	No. at risk	242	153							
	Survival (%)		93%							

14.17 Survival of Patients by Hepatocellular Carcinoma Status at Transplant

There was no significant difference in patient survival between patients with known hepatocellular carcinoma at transplant and incidental HCC detected in the explant (P=0.43, Figure 59, Table 34). Ten-year patient survival was 69% when there was known hepatocellular carcinoma and 68% when the hepatocellular carcinoma was found incidentally at explant. Median survival for both groups was 16 years.

Figure 59. Survival of patients by hepatocellular carcinoma status at transplant

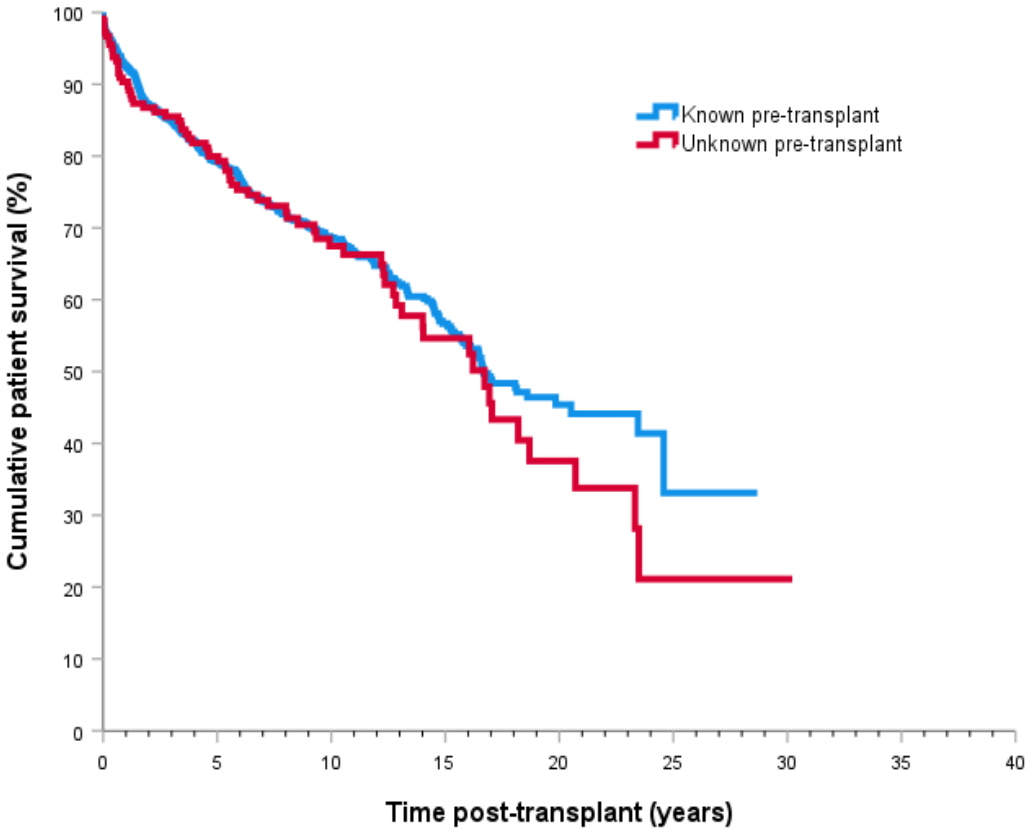


Table 34. Survival of patients by hepatocellular carcinoma status at transplant

HCC Category	Patient Survival	Time post-transplant (years)								
		0	1	5	10	15	20	25	30	35
Known pretransplant	No at risk	1,460	1,286	774	368	153	42	4	0	
	Survival %		93%	79%	69%	58%	45%	33%		
Found incidentally at explant	No at risk	180	153	126	65	30	10	2	1	0
	Survival %		90%	80%	68%	54%	38%	21%	21%	

Note: 32 patients were excluded from this analysis as they were treated HCC or suspected HCC that was not confirmed HCC on explant

14.18 Paediatric Patient Survival with Diagnosis of Malignancy

Survival of children with cholangiocarcinoma or histiocytosis X was superior to those with hepatoblastoma which was in turn superior to those with hepatocellular carcinoma (P = 0.017, Figure 60 and Table 35). Ten-year paediatric patient survival was 100% for cholangiocarcinoma and histiocytosis X, 81.7% for hepatoblastoma and 62.3% for hepatocellular carcinoma. Median paediatric patient survival was not reached for cholangiocarcinoma, histiocytosis X and hepatoblastoma and was 14.3 years for hepatocellular carcinoma.

Figure 60. Paediatric patient survival curve with a malignancy diagnosis – all diagnoses

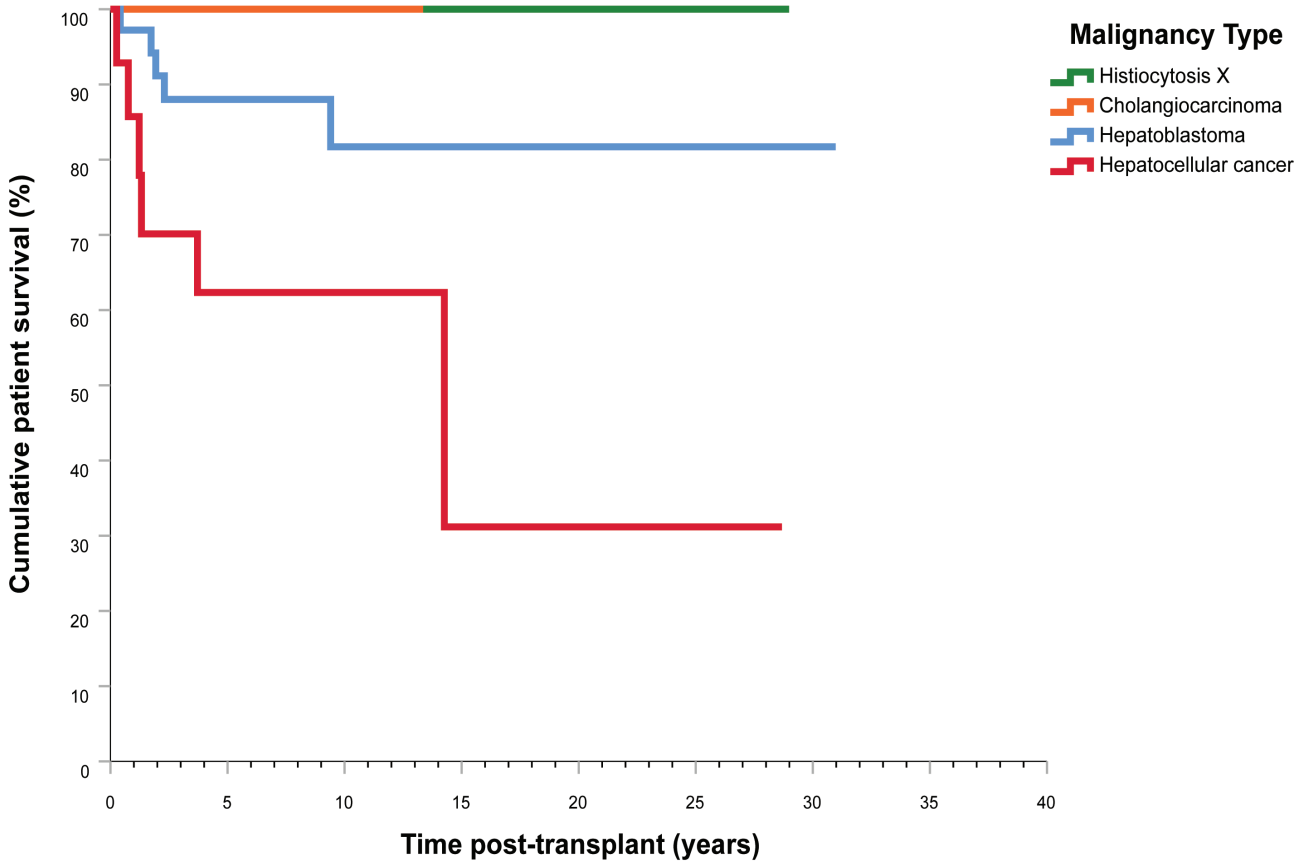


Table 35. Paediatric patient survival with malignancy diagnosis – all diagnoses

Primary Diagnosis	Patient Survival	Time post-transplant (years)								
		0	1	3	5	10	20	30	35	40
Cholangiocarcinoma	No. at risk	3	3	3	3	2	0			
	Survival (%)		100%	100%	100%	100%				
Histiocytosis X	No. at risk	6	6	6	6	4	3	0		
	Survival (%)		100%	100%	100%	100%	100%			
Hepatoblastoma	No. at risk	38	33	26	21	13	3	1	0	
	Survival (%)		97%	88%	88%	82%	82%	82%		
Hepatocellular carcinoma	No. at risk	15	12	9	6	2	1	0		
	Survival (%)		86%	70%	62%	62%	31%			

14.19 Adult Patient Survival with a Diagnosis of Malignancy

Adult patient survival after transplantation for malignancy as a primary or other diagnosis varied by diagnosis (P <0.001, Figure 61 and Table 36). Ten-year patient survival was 100% for hepatoblastoma (only one patient), 70.1% for epithelioid haemangio-endothelioma, 68.6% for hepatocellular carcinoma, 66.7% for histiocytosis X, 26.4% for cholangiocarcinoma, 0 for angiosarcoma and not reached for metastatic neuroendocrine tumours. Median adult patient survival was 16.7 years for hepatoblastoma, 16.6 years for hepatocellular carcinoma, 14.2 years for epithelioid haemangio-endothelioma, 3.2 years for cholangiocarcinoma, 3.1 years for metastatic neuroendocrine tumours and 0.8 years for angiosarcoma.

Figure 61. Adult patient survival curve with a malignancy diagnosis – all diagnoses

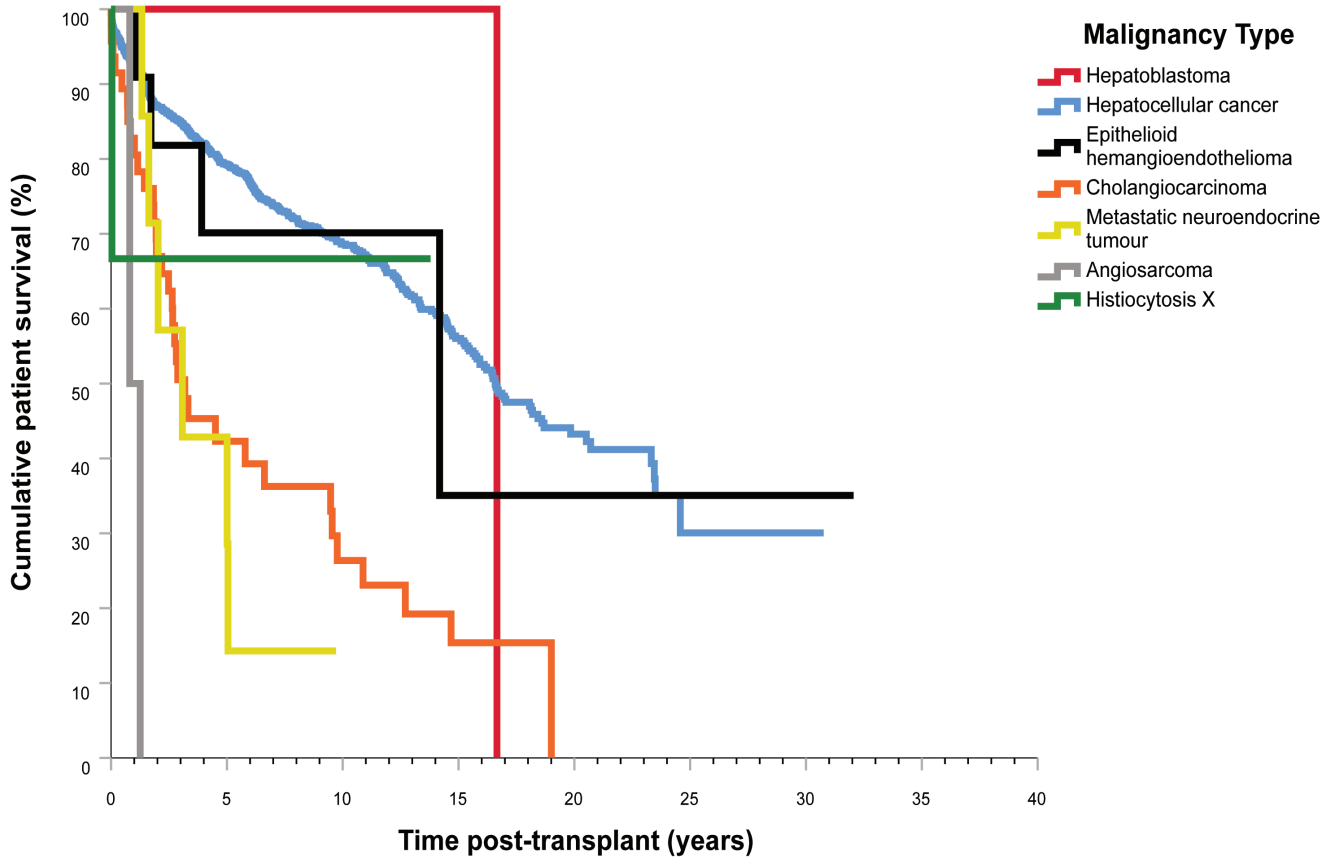


Table 36. Adult patient survival curve with a malignancy diagnosis - all diagnosis

Primary Diagnosis	Patient Survival	Time post-transplant (years)								
		0	1	3	5	10	20	30	35	40
Histiocytosis X	No. at risk	3	1	1	1	1	0			
	Survival (%)		67%	67%	67%	67%				
Hepatoblastoma	No. at risk	1	1	1	1	1	0			
	Survival (%)		100%	100%	100%	100%				
Hepatocellular carcinoma	No. at risk	1,543	1,355	1,071	838	413	49	2	0	
	Survival (%)		93%	85%	79%	69%	43%	30%		
Epithelioid haemangio-endothelioma	No. at risk	15	11	7	5	3	1	1	0	
	Survival (%)		100%	82%	70%	70%	35%	35%		
Cholangiocarcinoma	No. at risk	47	37	20	14	8	0			
	Survival (%)		83%	51%	42%	26%				
Metastatic neuroendocrine tumour	No. at risk	7	7	4	3	0				
	Survival (%)		100%	57%	43%					
Angiosarcoma	No. at risk	2	1	0						
	Survival (%)		50%							

14.20 Patient Survival for Adult Patients with Incidental Liver Cancer

Ten-year patient survival was 59% for adults with liver cancer found incidentally at explant. Median patient survival was 13 years for adults.

Figure 62. Patient Survival for Adult Patients with Incidental Liver Cancer

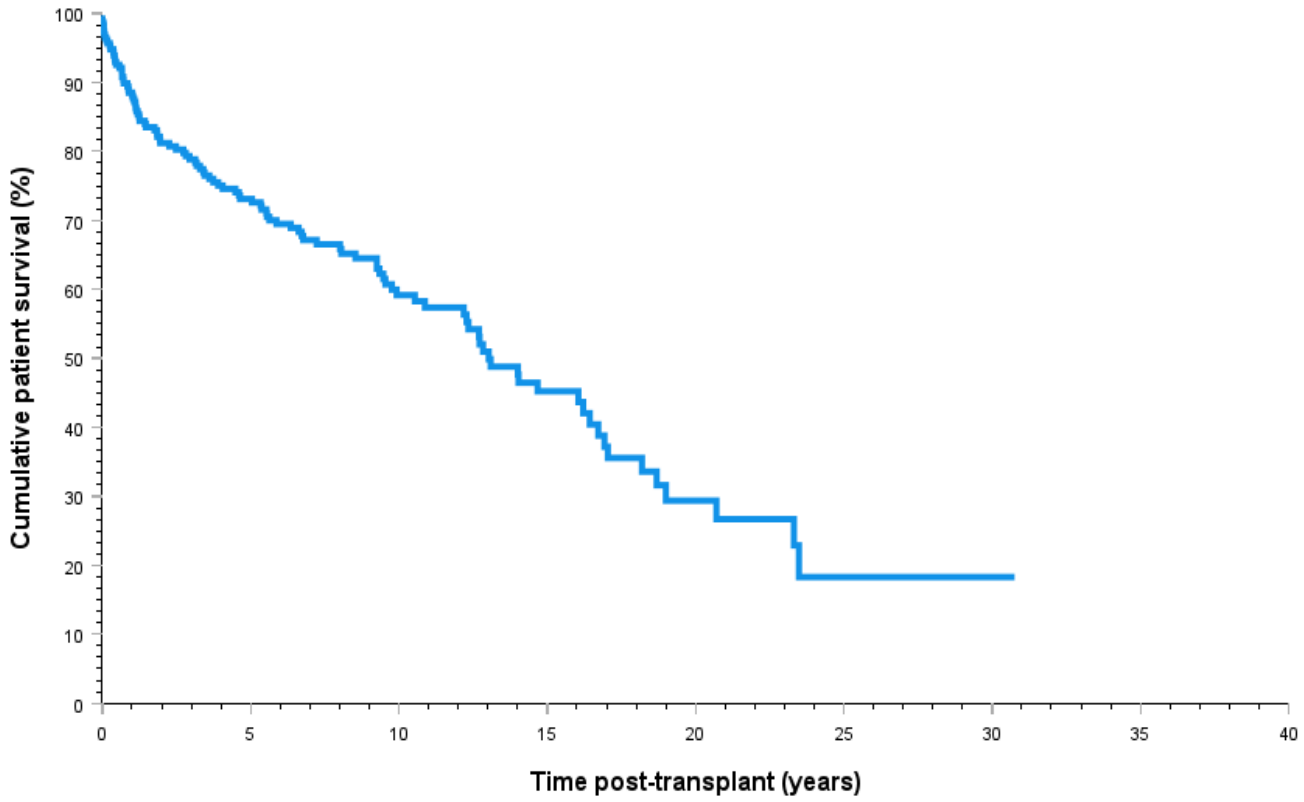


Table 37. Patient Survival for Adult Patients with Incidental Liver Cancer

Adults	Patient Survival	Time post-transplant (years)						
		0	1	5	10	20	30	35
Unknown pretransplant	No at risk	231	195	146	75	11	2	0
	Survival %		89%	73%	59%	29%	18%	

14.21 Patient Survival for Adult Patients by Type of Incidental Liver Cancer

There was a significant difference in patient survival between patients with different liver cancer types found incidentally at explant (p<0.001). Ten-year adult patient survival for those with fibrolamellar variant, hepatocellular carcinoma, cholangiocarcinoma, and other liver cancers was 100%, 67%, 34%, and 25% respectively (Figure 63, Table 38).

Figure 63. Patient Survival for Adult Patients by Type of Incidental Liver Cancer

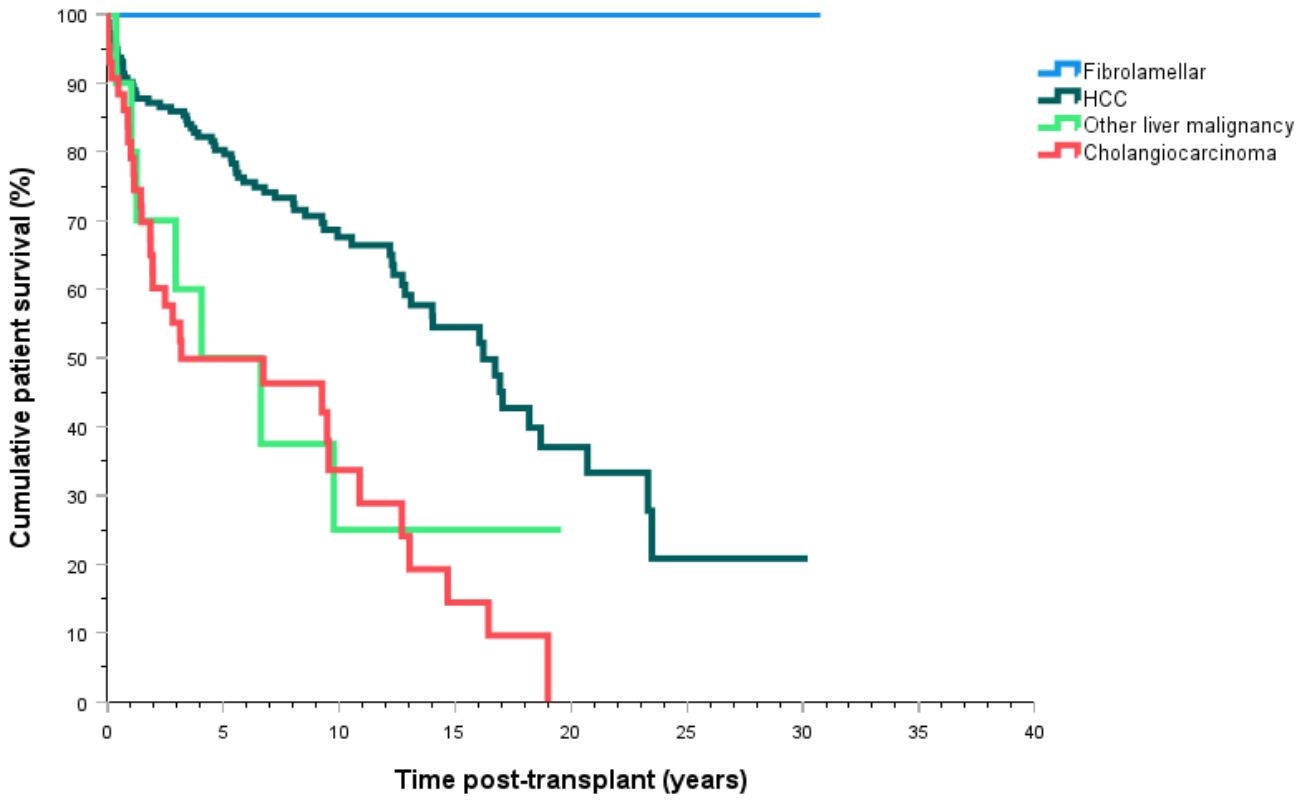


Table 38. Patient Survival for Adult Patients by Type of Incidental Liver Cancer

Transplant era	Patient Survival	Time post-transplant (years)							
		0	1	5	10	20	30	35	40
Hepatocellular carcinoma	No. at risk	177	150	125	64	10	0		
	Survival (%)		90%	80%	67%	37%			
Cholangiocarcinoma	No. at risk	43	35	15	8	0			
	Survival (%)		81%	50%	34%				
Other liver cancer	No. at risk	10	9	5	2	0			
	Survival (%)		90%	50%	25%				
Fibrolamellar	No. at risk	1	1	1	1	1	1	1	0
	Survival (%)		100%	100%	100%	100%	100%	100%	

14.22 Patient Survival by Transplant Unit

Benchmarking analysis using hierarchical regression models estimated that 4.2% of the variation in 1-year post-transplant mortality and <0.0001% of the variation in 5-year post-transplant mortality was due to variation between liver transplant units.

15 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).

15.1 All Grafts Outcome

There were 7,580 grafts in 6,989 patients (Figure 64 and Table 39). Ten-year graft survival was 68.5% across all grafts. The median graft survival was 18.3 years.

Figure 64. Graft survival curve for all grafts

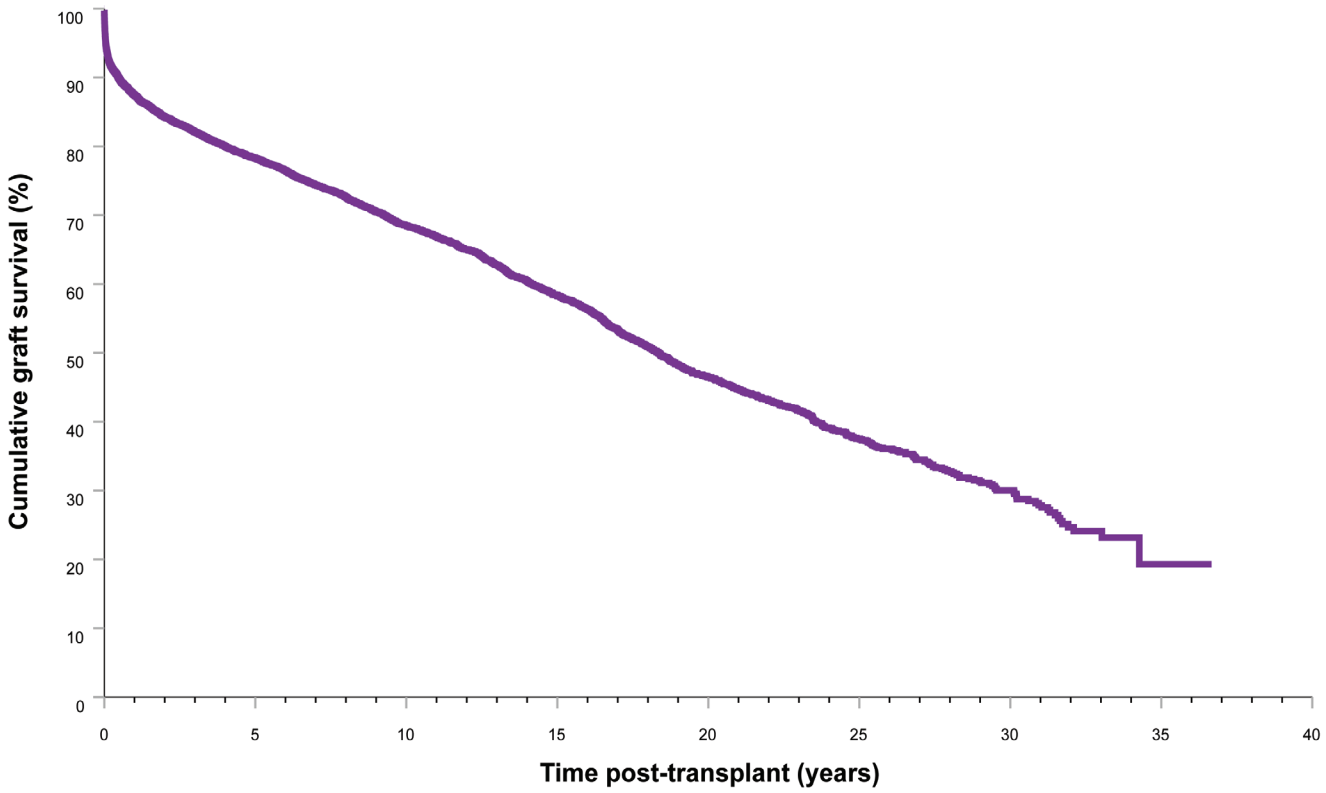


Table 39. Graft survival - all grafts

Graft Survival	Time post-transplant (years)								
	0	1	3	5	10	20	30	35	40
No. at risk	7,580	6,294	5,246	4,377	2,714	809	121	5	0
Survival (%)		87%	82%	78%	69%	47%	30%	19%	

15.2 Outcome of All Grafts by Age Group

A total of 1,291 transplants were performed in children and 6,289 in adults. Post-transplant graft survival was superior in the paediatric population (P < 0.001, Figure 65, Table 40). Ten-year graft survival was 72.8% for children and 67.6% for adults. Median graft survival was 30.2 years in children and 17.1 years in adults. Although 1-year survival was slightly worse in children (85.3% children versus 87.9% adults), the survival curve for children was subsequently flatter. However, there were several late graft losses occurring over 30 years after paediatric transplantation.

Figure 65. Graft survival curve for all grafts by age group

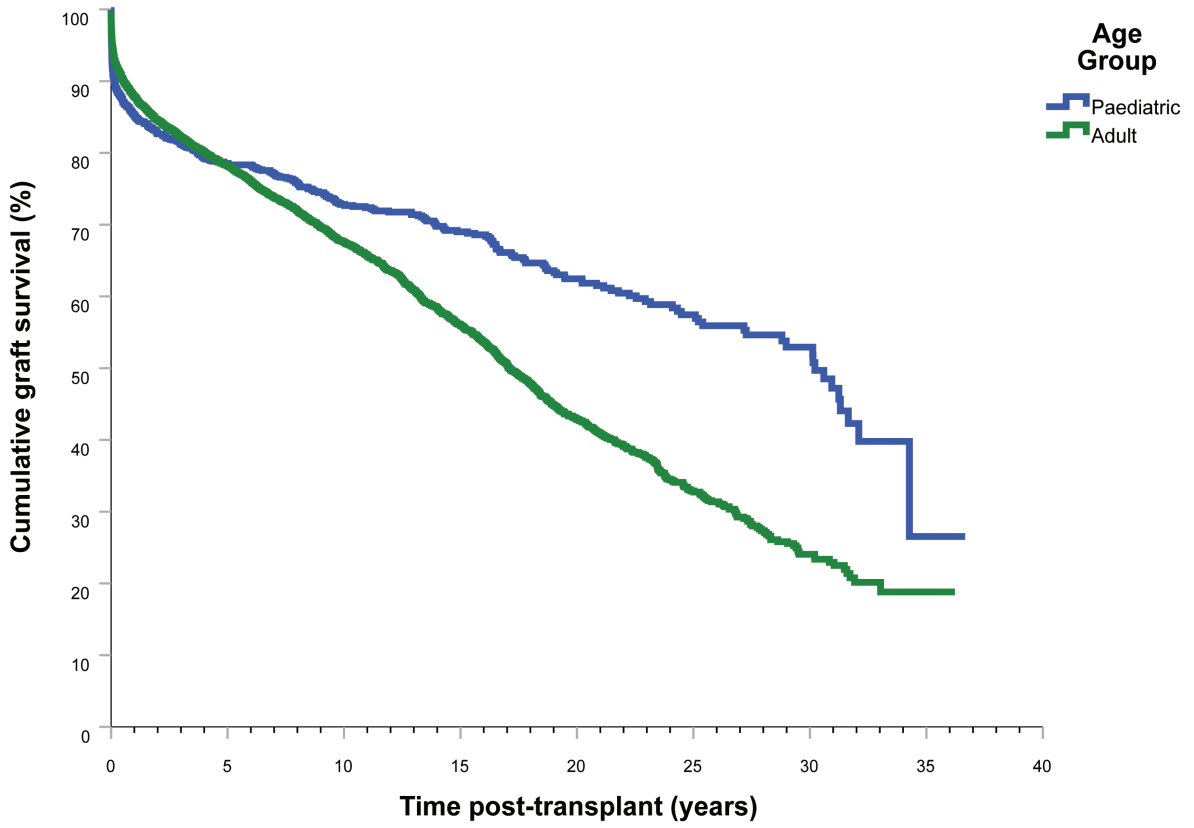


Table 40. Graft survival by age group - all grafts

Age Group	Graft Survival	Time post-transplant (years)								
		0	1	3	5	10	20	30	35	40
Paediatric <16 years	No. at risk	1,291	1,037	884	763	512	213	49	2	0
	Survival (%)		85%	81%	79%	73%	63%	53%	27%	
Adult ≥16 years	No. at risk	6,289	5,257	4,362	3,614	2,202	596	72	3	0
	Survival (%)		88%	82%	78%	68%	43%	24%	19%	

15.3 Outcome by Graft Number

There was a significant difference in graft survival by graft number (P < 0.001, Figure 66 and Table 41). Ten-year graft survival was 69.4% for the first graft, 57.9% for the second graft, 62.8% for the third graft and not reached for the fourth graft. Median graft survival was 18.5 years for the first graft, 13.2 years for the second graft, 21.1 years for the third graft and 4.3 years for the fourth graft.

Figure 66. Graft survival curve for all grafts by graft number

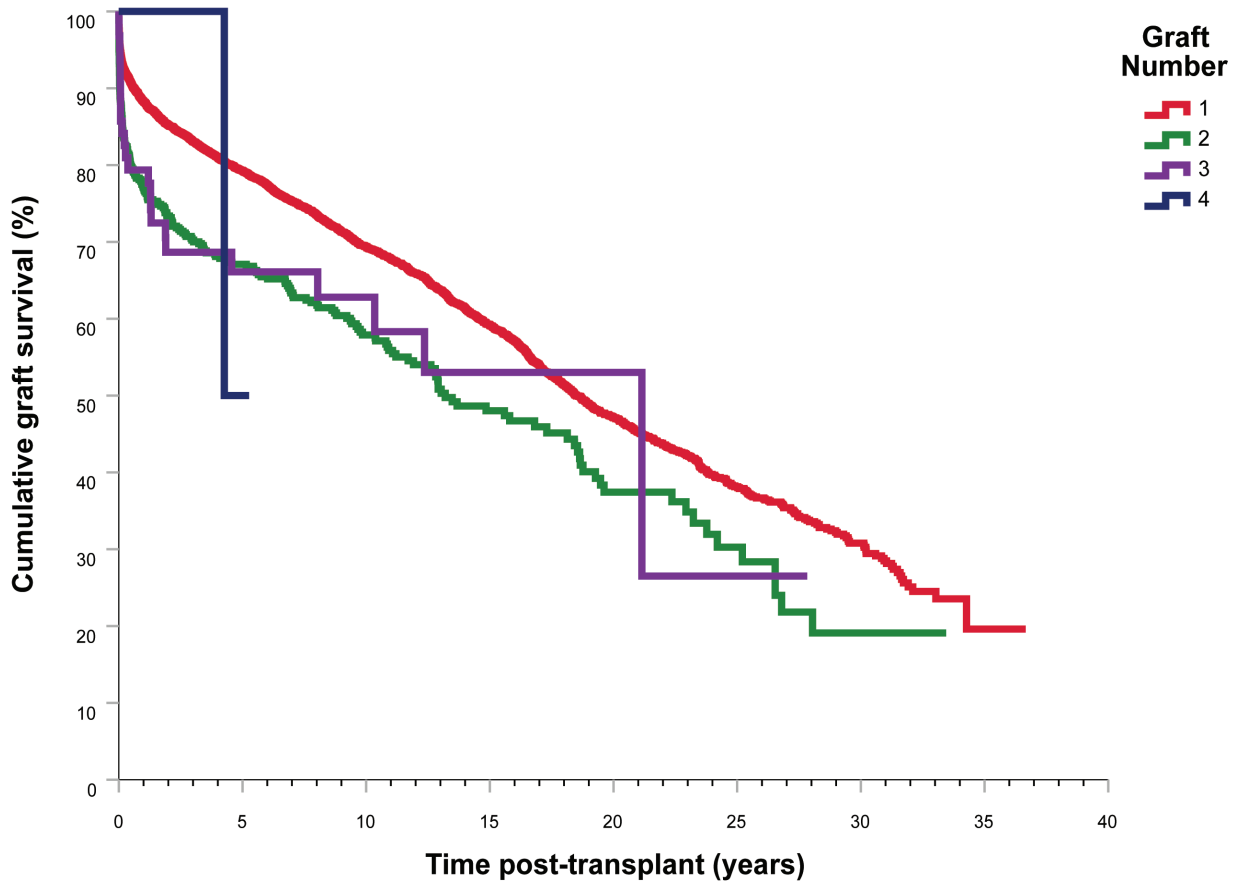


Table 41. Graft survival - all grafts

Graft Number	Graft Survival	Time post-transplant (years)								
		0	1	3	5	10	20	30	35	40
1	No. at risk	6,983	5,858	4,909	4,099	2,546	768	116	5	0
	Survival (%)		88%	83%	79%	69%	47%	31%	20%	
2	No. at risk	532	386	300	252	154	38	5	0	
	Survival (%)		77%	70%	67%	58%	37%	19%		
3	No. at risk	63	48	35	25	14	3	0		
	Survival (%)		79%	69%	66%	63%	53%			
4	No. at risk	2	2	2	1	0				
	Survival (%)		100%	100%	50%					

15.4 Paediatric Outcome by Graft Number

There was a significant difference in graft survival by graft number in children (P < 0.001, Figure 67 and Table 42). Ten-year graft survival was 75.6% for the first graft, 51.9% for the second graft and 58.3% for the third graft. Median graft survival was 31.2 years for the first graft, 10.9 years for the second graft and 21.1 years for the third graft.

Figure 67. Graft survival curve for paediatric recipients by graft number

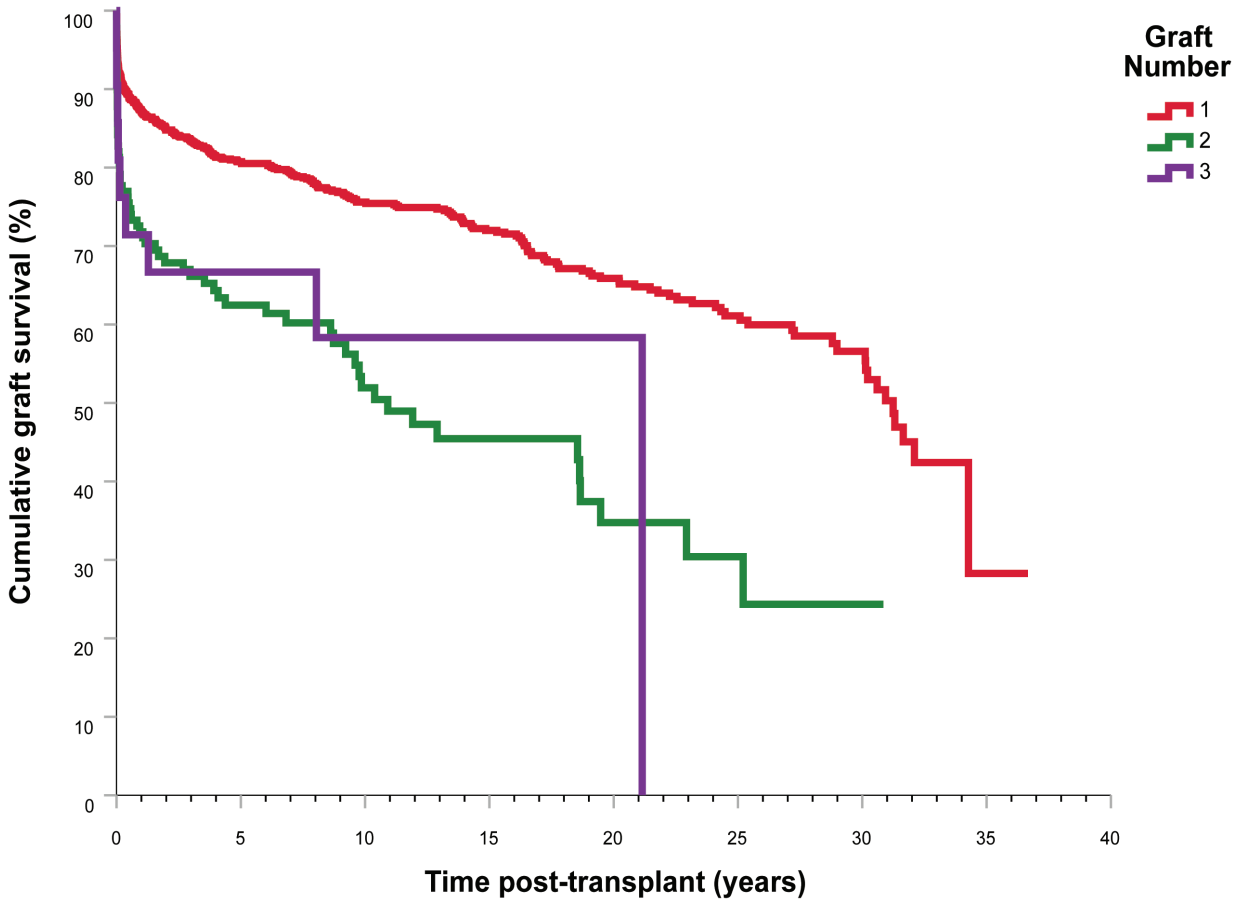


Table 42. Graft survival - paediatric by graft number

Graft Number	Graft Survival	Time post-transplant (years)								
		0	1	3	5	10	20	30	35	40
1	No. at risk	1,130	926	795	689	469	200	47	2	0
	Survival (%)		87%	83%	81%	76%	66%	57%	28%	
2	No. at risk	140	96	76	64	36	11	2	0	
	Survival (%)		72%	66%	63%	52%	35%	24%		
3	No. at risk	21	15	13	10	7	2	0		
	Survival (%)		71%	67%	67%	58%	58%			

15.5 Adult Outcome by Graft Number

There was a significant difference in graft survival by graft number in adults (P < 0.001, Figure 68 and Table 43). Ten-year graft survival was 68.2% for the first graft, 60.0% for the second graft, 65.2% for the third graft and not reached for the fourth graft. Median graft survival was 17.2 years for the first graft, 13.7 years for the second graft, 12.4 years for the third graft and 4.3 years for the fourth graft.

Figure 68. Graft survival curve for adults by graft number

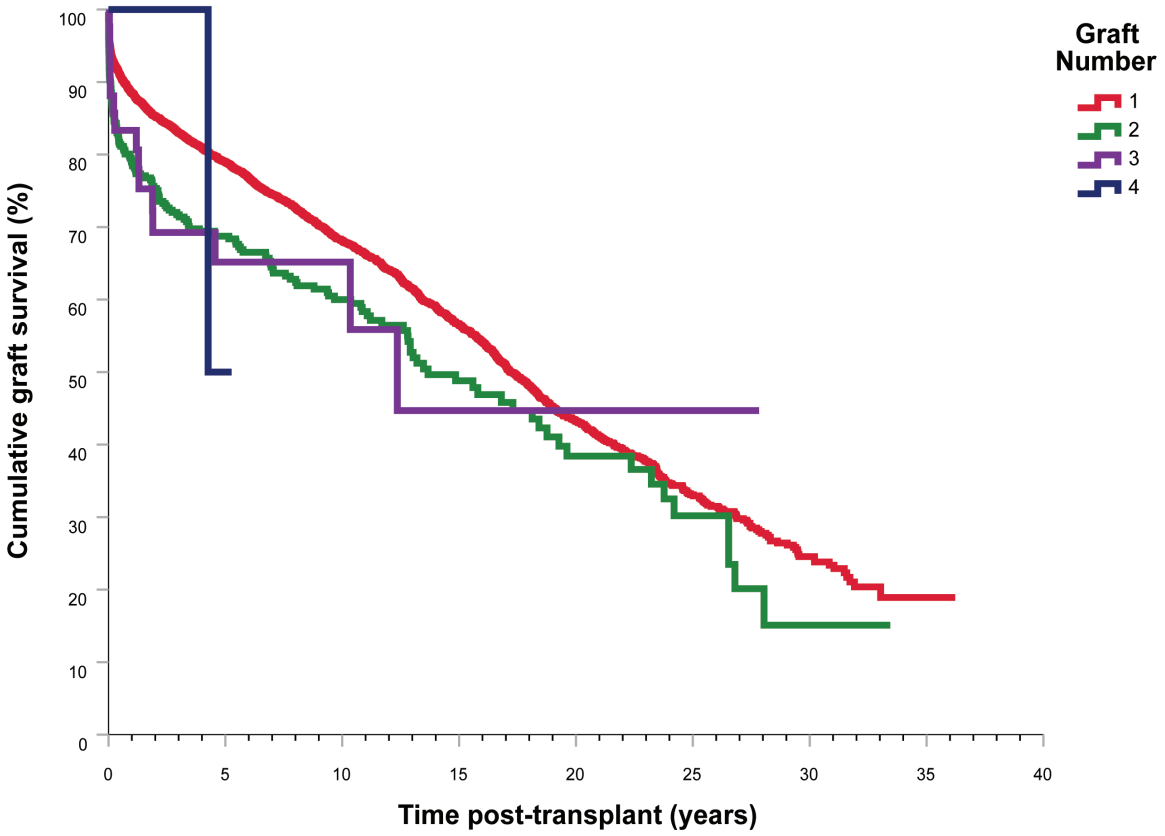


Table 43. Graft survival – adults by graft number

Graft Number	Graft Survival	Time post-transplant (years)								
		0	1	3	5	10	20	30	35	40
1	No. at risk	5,853	4,932	4,114	3,410	2,077	568	69	3	0
	Survival (%)		89%	83%	79%	68%	43%	25%	19%	
2	No. at risk	392	290	224	188	118	27	3	0	
	Survival (%)		79%	72%	69%	60%	38%	15%		
3	No. at risk	42	33	22	15	7	1	0		
	Survival (%)		83%	69%	65%	65%	45%			
4	No. at risk	2	2	2	1	0				
	Survival (%)		100%	100%	50%					

15.6 Graft Survival by Type of Graft

There was a significant difference in graft survival by graft type, with improved survival in living donor transplants after 10 years and worse survival in reduced liver transplants up to 15 years (P = 0.040, Figure 69 and Table 44). Ten-year graft survival was 79.1% for living donor grafts, 71.4% for split grafts, 68.5% for whole grafts, 59.5% for reduced grafts and not reached for domino grafts. Median graft survival was not reached for living donor grafts, 23.4 for split grafts, 21.8 years for reduced grafts, 17.8 years for whole grafts and 9.4 years for domino grafts.

Figure 69. Graft survival curve for type of graft

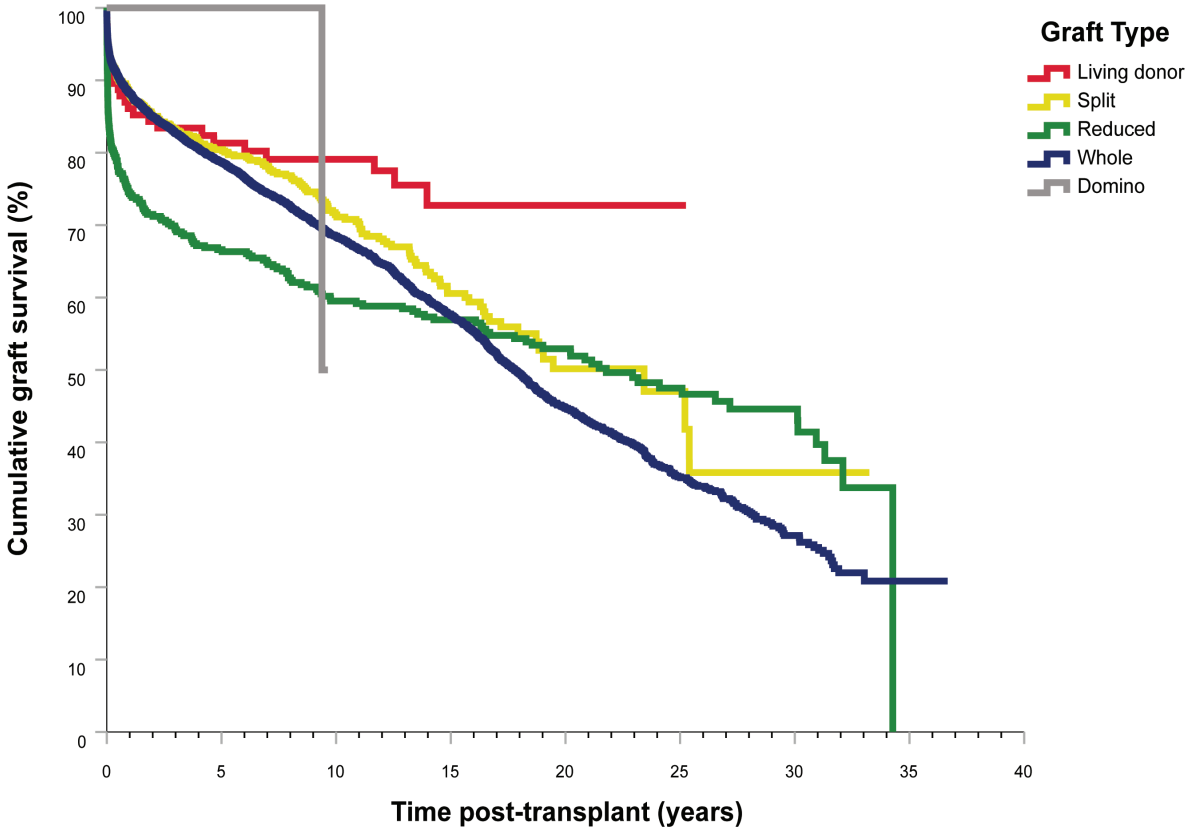


Table 44. Graft survival by type of graft - all grafts

Graft Type	Graft Survival	Time post-transplant (years)								
		0	1	3	5	10	20	30	35	40
Domino	No. at risk	5	4	4	4	0				
	Survival (%)		100%	100%	100%					
Living donor	No. at risk	115	99	87	76	58	2	0		
	Survival (%)		86%	83%	81%	79%	73%			
Split	No. at risk	901	735	589	474	234	33	2	0	
	Survival (%)		88%	83%	80%	71%	50%	36%		
Reduced	No. at risk	404	290	258	237	181	105	28	0	
	Survival (%)		74%	69%	67%	60%	53%	45%		
Whole	No. at risk	6,154	5,165	4,308	3,586	2,241	669	91	5	0
	Survival (%)		88%	83%	79%	69%	45%	27%	21%	

15.7 Graft Survival by Graft Type in Children

Graft survival in children differed significantly by graft type, with improved survival after 10 years for living donor grafts and worse survival after reduced liver transplantation (P < 0.001, Figure 70 and Table 45). Ten-year graft survival was 81.3% for living donor liver transplantation, 78.0% for whole liver transplantation, 76.7% for split liver transplantation and 60.6% for reduced liver transplantation. Median graft survival was not reached for living donor grafts and was 31.2 years for whole grafts, 25.2 for split grafts and 22.9 years for reduced grafts.

Figure 70. Paediatric graft survival curve for type of graft

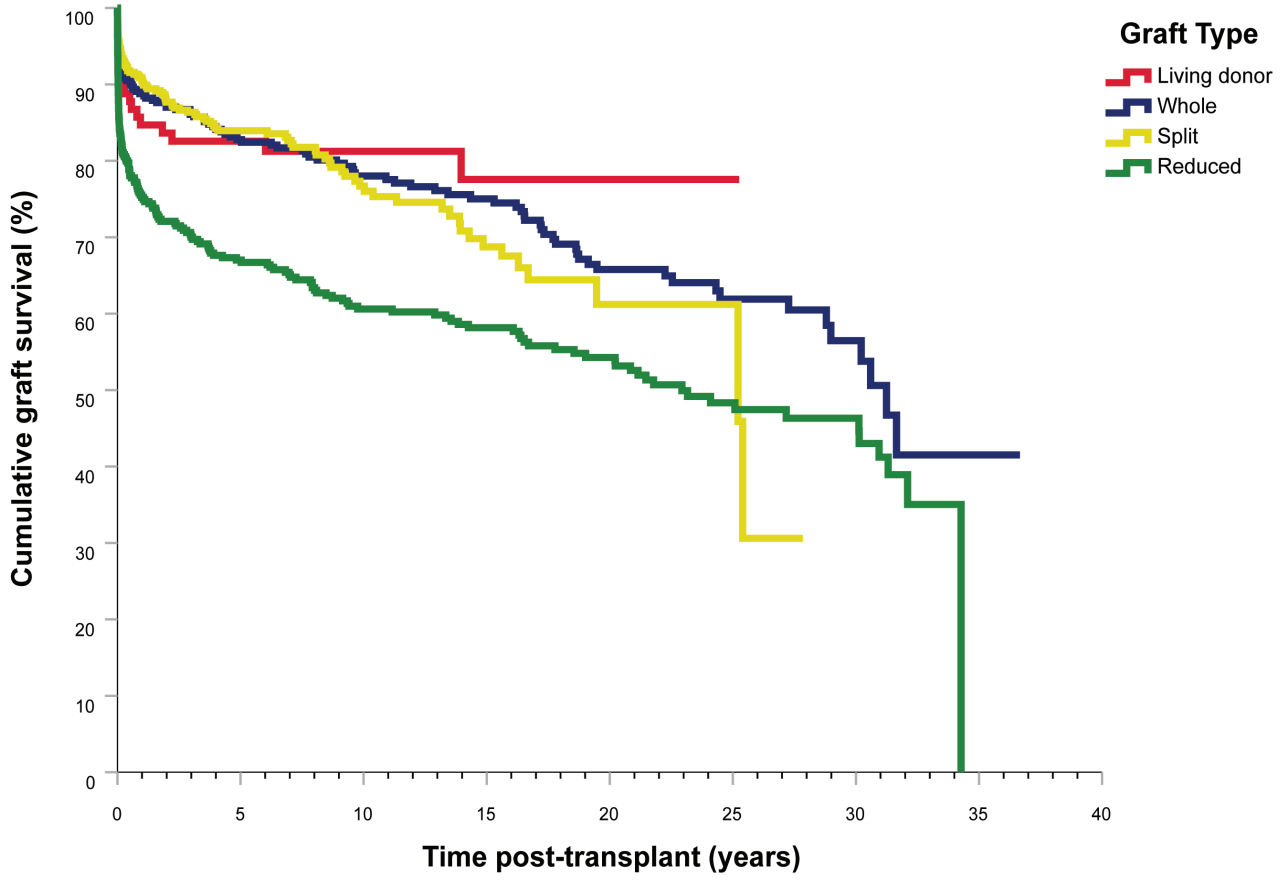


Table 45. Paediatric recipient graft survival by type of graft - all grafts

Graft Type	Graft Survival	Time post-transplant (years)								
		0	1	3	5	10	20	30	35	40
Living donor	No. at risk	98	83	72	64	48	2	0		
	Survival (%)		85%	83%	83%	81%	78%			
Whole	No. at risk	370	307	276	240	180	95	21	2	0
	Survival (%)		89%	86%	83%	78%	66%	57%	42%	
Split	No. at risk	456	381	299	241	116	17	0		
	Survival (%)		91%	86%	84%	77%	61%			
Reduced	No. at risk	366	265	237	218	168	99	28	0	
	Survival (%)		75%	70%	67%	61%	54%	46%		

15.8 Graft Survival by Graft Type in Adults

Although there appeared to be worse graft survival after reduced liver transplantation, there was no significant difference in graft survival in adults by graft type (P = 0.542, Figure 71 and Table 46). Ten-year graft survival was 68.8% for living donor liver transplantation, 67.8% for whole liver transplantation, 66.4% for split liver transplantation, 48.5% for reduced liver transplantation and not reached for domino liver transplantation. Median graft survival was 17.1 years for whole liver transplantation, 16.5 years for split transplantation, 9.7 years for reduced liver transplantation, 9.4 years for domino liver transplantation and was not reached for living donor transplantation.

Figure 71. Adult graft survival curve for type of graft, all grafts

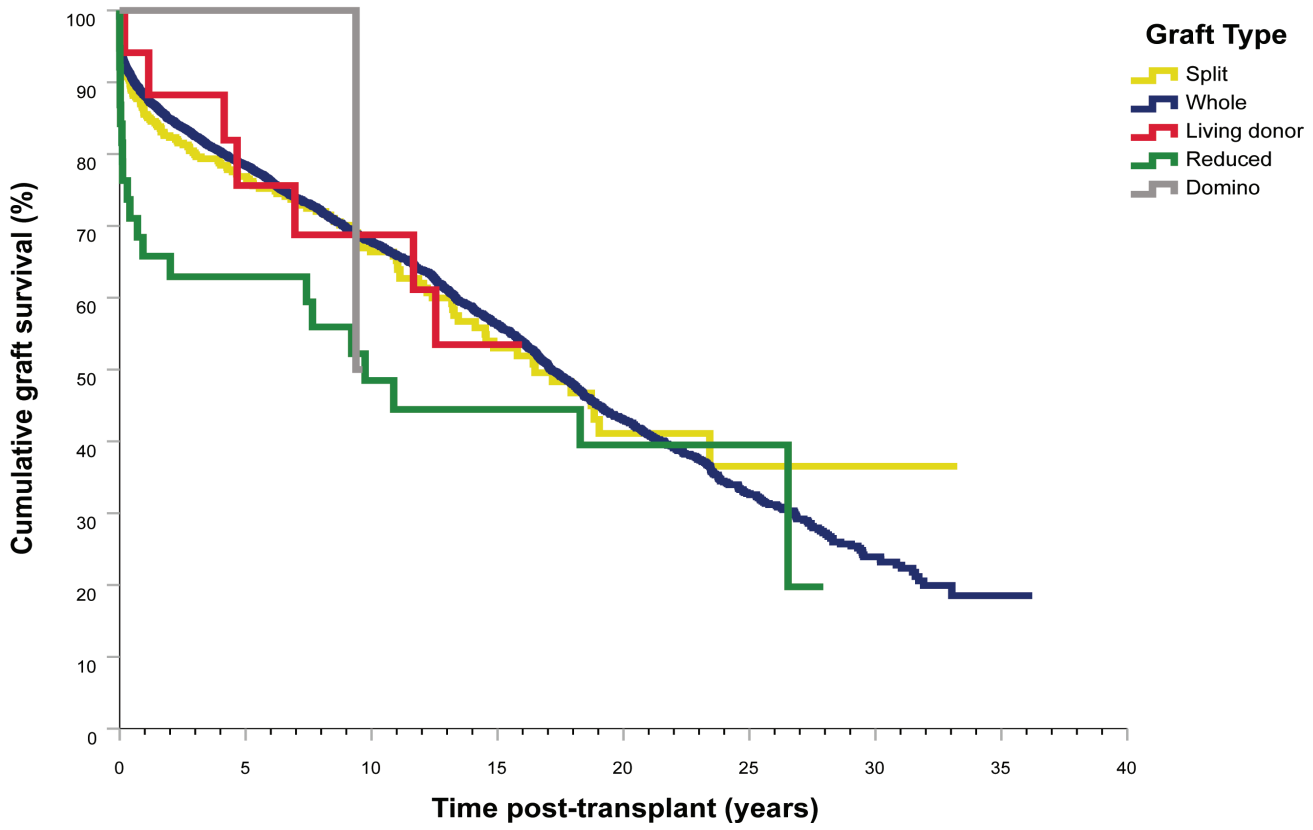


Table 46. Adult graft survival for type of graft, all grafts

Graft Type	Graft Survival	Time post-transplant (years)								
		0	1	3	5	10	20	30	35	40
Split	No. at risk	445	354	290	233	118	16	2	0	
	Survival (%)		86%	80%	77%	66%	41%	37%		
Whole	No. at risk	5,784	4,858	4,032	3,346	2,061	574	70	3	0
	Survival (%)		88%	83%	78%	68%	43%	24%	19%	
Living donor	No. at risk	17	16	15	12	10	0			
	Survival (%)		94%	88%	76%	69%				
Reduced	No. at risk	38	25	21	19	13	6	0		
	Survival (%)		66%	63%	63%	49%	40%			
Domino	No. at risk	5	4	4	4	0				
	Survival (%)		100%	100%	100%					

15.9 Graft Survival by Era of Transplant

There has been an improvement in graft survival over eras of transplantation, with better outcomes since 2000 – 04 (P < 0.001, Figure 72, Table 47). Graft survival in the most recent era was 90.4% at 1 year, 86.6% at 3 years, 82.5% at 5 years and 71.2% at 10 years. Median graft survival was not reached for recent eras since 2005 and was 18.2 years for 2000 – 04, 16.5 years for 1995 – 99, 16.6 years for 1990 – 94 and 7.7 years for 1985 – 89.

Figure 72. Graft (deceased and living donors) survival curve by era of transplant

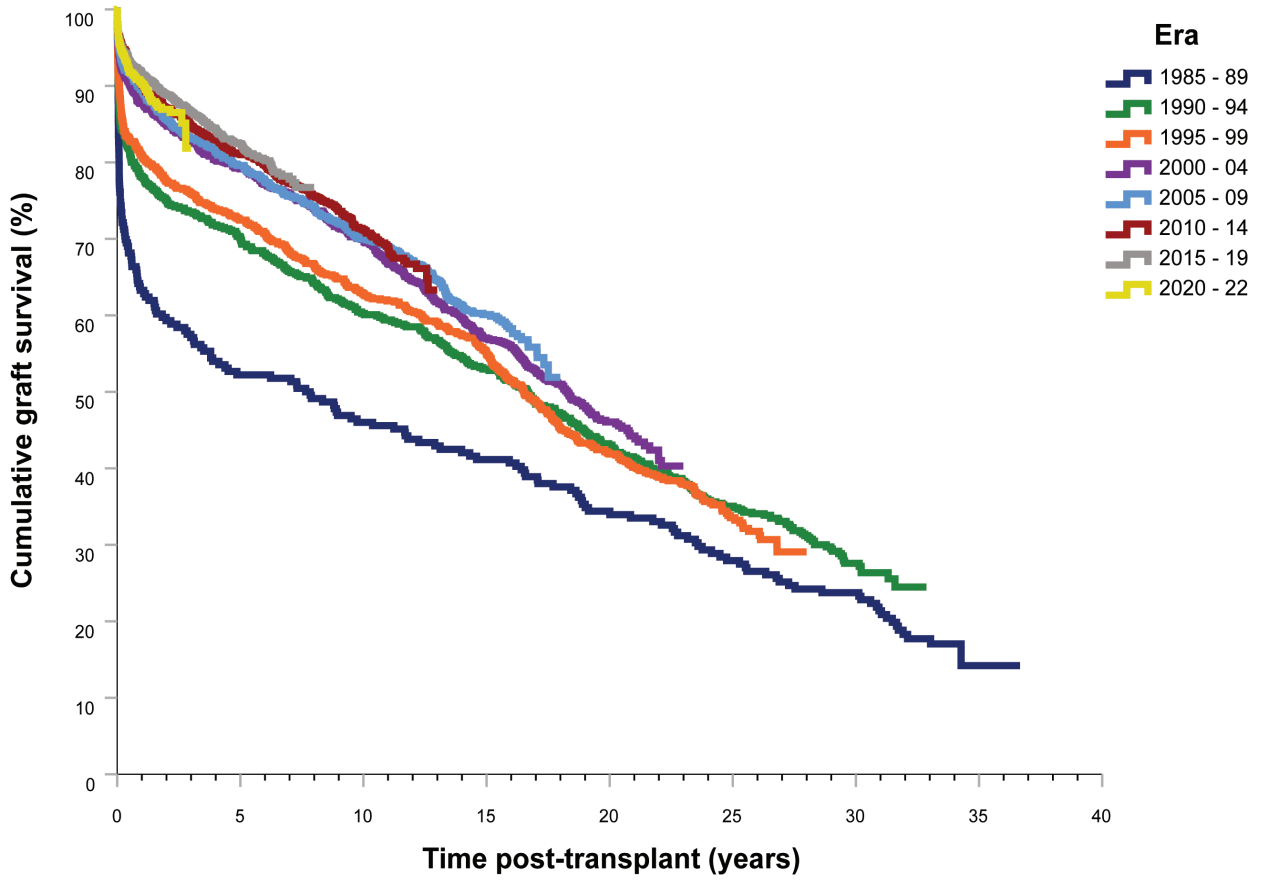


Table 47. Graft (deceased and living donors) survival by era of transplant

Transplant Era	Graft Survival	Time post-transplant (years)								
		0	1	3	5	10	20	30	35	40
1985 - 89	No. at risk	226	143	129	118	104	75	51	5	0
	Survival (%)		63%	57%	52%	46%	34%	24%	14%	
1990 - 94	No. at risk	601	468	437	416	348	229	70	0	
	Survival (%)		78%	74%	70%	60%	43%	28%		
1995 - 99	No. at risk	759	609	568	538	460	293	0		
	Survival (%)		81%	76%	73%	63%	42%			
2000 - 04	No. at risk	915	794	744	706	619	212	0		
	Survival (%)		88%	83%	79%	70%	46%			
2005 - 09	No. at risk	1,032	920	853	816	708	0			
	Survival (%)		90%	83%	80%	70%				
2010 - 14	No. at risk	1,331	1,198	1,123	1,063	475	0			
	Survival (%)		90%	85%	81%	71%				
2015 - 19	No. at risk	1,763	1,597	1,392	720	0				
	Survival (%)		92%	87%	83%					
2020 - 22	No. at risk	953	565	0						
	Survival (%)		90%							

15.10 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 73, Table 48). Graft survival in the most recent era was 95.4% at 1 year, 88.0% at 3 years, 84.9% at 5 years and 77.6% at 10 years. Median paediatric graft survival was not reached for transplant eras since 2000 and was 25.1 years for 1995 – 99, 25.2 years for 1990 – 94 and 7.7 years for 1985 – 89.

Figure 73. Paediatric graft (deceased and living donors) survival curve by era of transplant

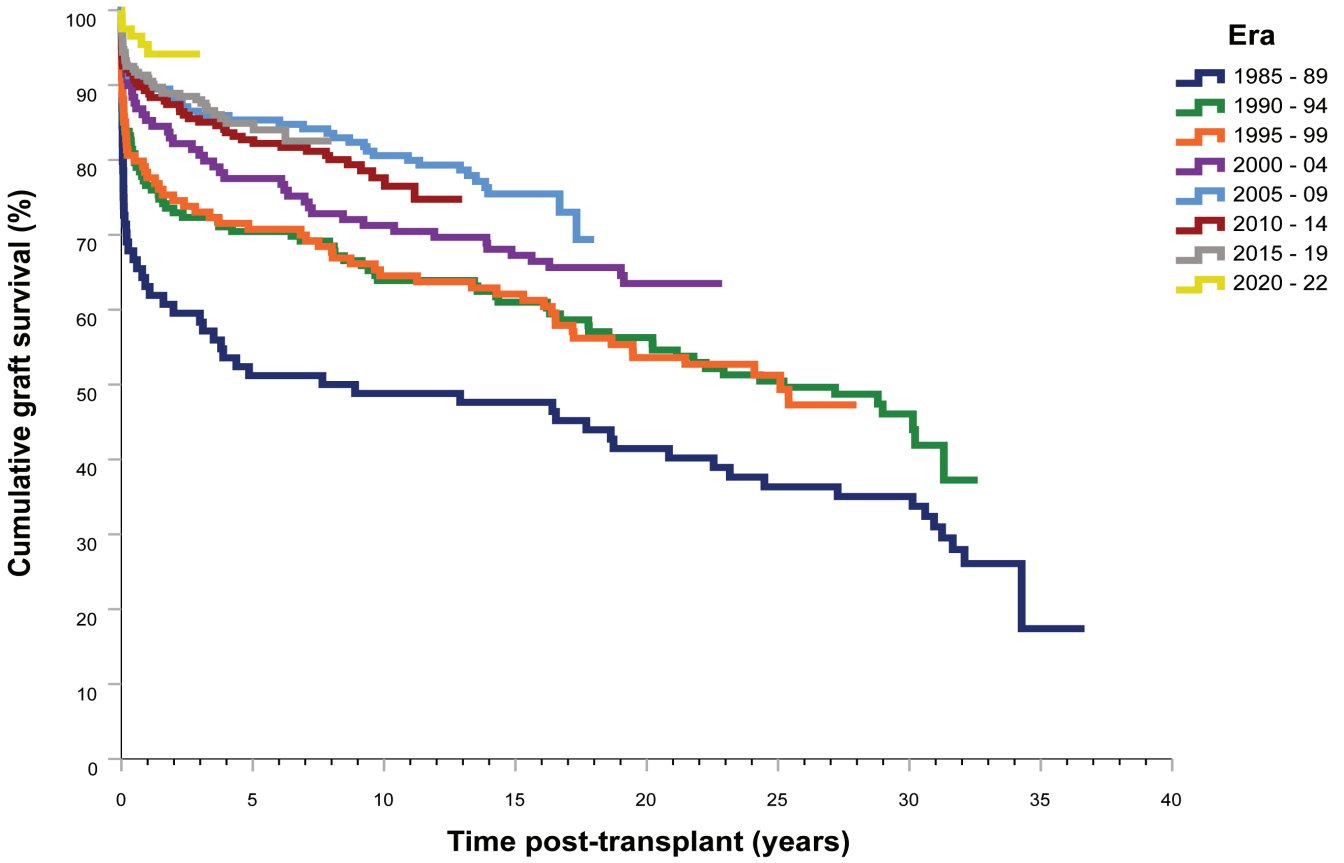


Table 48. Paediatric graft (deceased and living donors) survival by era of transplant

Transplant Era	Graft Survival	Time post-transplant (years)								
		0	1	3	5	10	20	30	35	40
1985 - 89	No. at risk	84	53	49	43	41	33	27	2	0
	Survival (%)		63%	58%	51%	49%	41%	35%	17%	
1990 - 94	No. at risk	167	126	116	112	94	70	22	0	
	Survival (%)		77%	72%	70%	64%	56%	46%		
1995 - 99	No. at risk	134	103	96	92	81	62	0		
	Survival (%)		78%	73%	71%	65%	54%			
2000 - 04	No. at risk	129	110	104	100	90	48	0		
	Survival (%)		85%	81%	78%	71%	64%			
2005 - 09	No. at risk	171	153	146	145	134	0			
	Survival (%)		90%	86%	85%	81%				
2010 - 14	No. at risk	215	190	181	171	72	0			
	Survival (%)		89%	85%	83%	78%				
2015 - 19	No. at risk	267	227	192	100	0				
	Survival (%)		91%	88%	85%					
2020 - 22	No. at risk	124	75	0						
	Survival (%)		95%							

15.11 Graft Survival by Era of Transplant in Adults

There has been a progressive improvement in graft survival in adults over eras of transplantation, albeit relatively modest since 2000 (P < 0.001, Figure 74, Table 49). Graft survival in the most recent era was 89.6% at 1 year, 86.4% at 3 years, 82.1% at 5 years and 70.1% at 10 years. Median adult graft survival was not reached for transplant eras since 2010 and was 17.5 years for 2005 – 09, 17.2 years for 2000 – 04, 15.8 years for 1995 – 99, 15.1 years for 1990 – 94 and 7.3 years for 1985 – 89.

Figure 74. Adult graft (deceased and living donors) survival curve by era of transplant

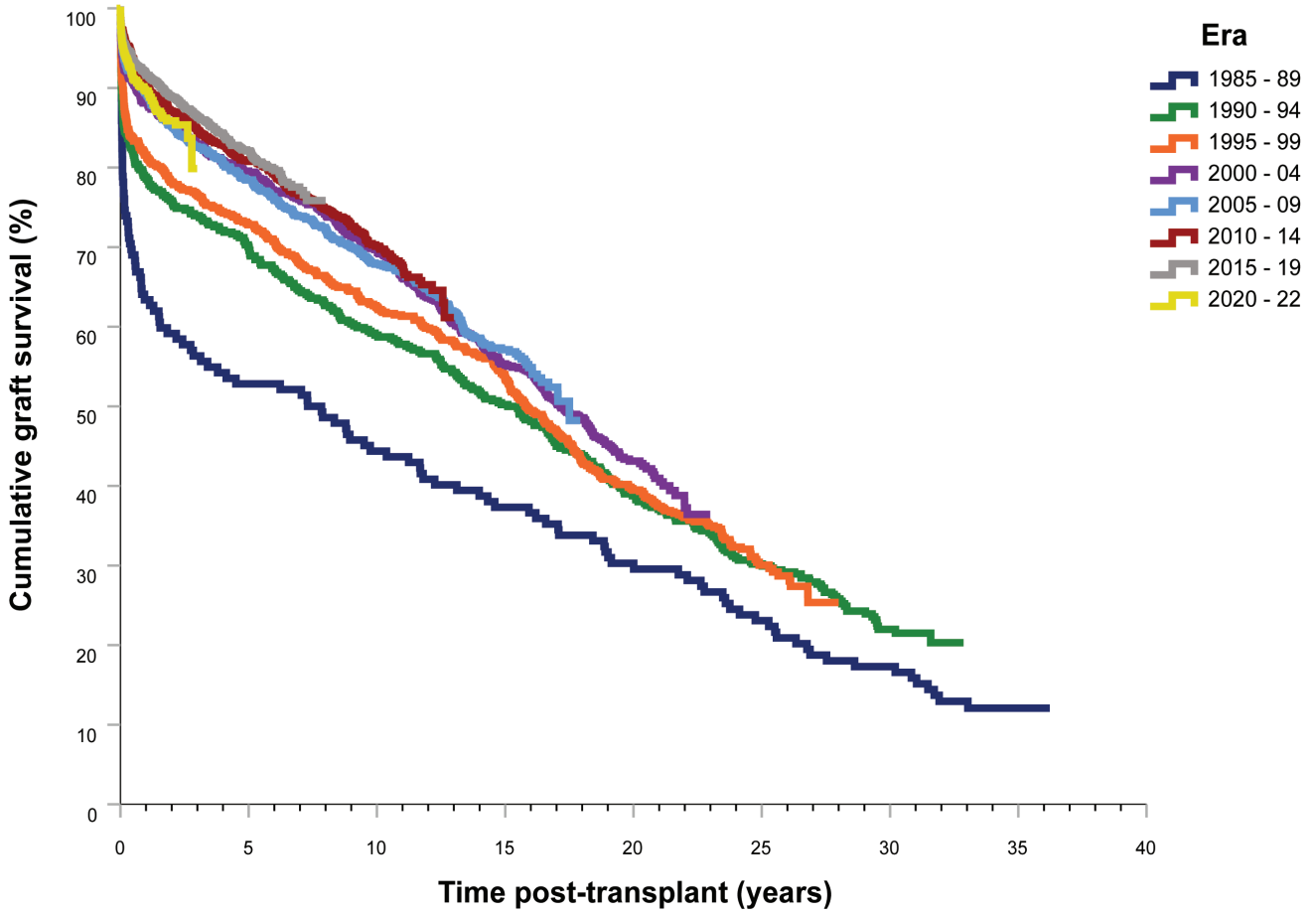


Table 49. Adult graft (deceased and living donors) survival by era of transplant

Transplant Era	Graft Survival	Time post-transplant (years)								
		0	1	3	5	10	20	30	35	40
1985 - 89	No. at risk	142	90	80	75	63	42	24	3	0
	Survival (%)		63%	56%	53%	44%	30%	17%	12%	
1990 - 94	No. at risk	434	342	321	304	254	159	48	0	
	Survival (%)		79%	74%	70%	59%	39%	22%		
1995 - 99	No. at risk	625	506	472	446	379	231	0		
	Survival (%)		82%	77%	73%	63%	40%			
2000 - 04	No. at risk	786	684	640	606	529	164	0		
	Survival (%)		88%	83%	79%	70%	43%			
2005 - 09	No. at risk	861	767	707	671	574	0			
	Survival (%)		89%	83%	78%	68%				
2010 - 14	No. at risk	1,116	1,008	942	892	403	0			
	Survival (%)		90%	85%	81%	70%				
2015 - 19	No. at risk	1,496	1,370	1,200	620	0				
	Survival (%)		92%	86%	82%					
2020 - 22	No. at risk	829	490	0						
	Survival (%)		90%							

15.12 Whole Graft Survival by Era of Transplant

There has been an improvement in graft survival after whole liver transplantation over eras of transplantation up to 2000, after which graft survival has been similar over progressive eras (P < 0.001, Figure 75,Table 50). Graft survival in the most recent era was 89.6% at 1 year, 87.1% at 3 years, 82.6% at 5 years and 71.1% at 10 years. Median graft survival was not reached for eras since 2010 and was 18.1 years for 2000 – 04, 17.5 years for 2005 – 09, 16.8 years for 1995 – 99, 16.4 years for 1990 – 94 and 8.3 years for 1985 – 89.

Figure 75. Whole graft survival curve by era of transplant

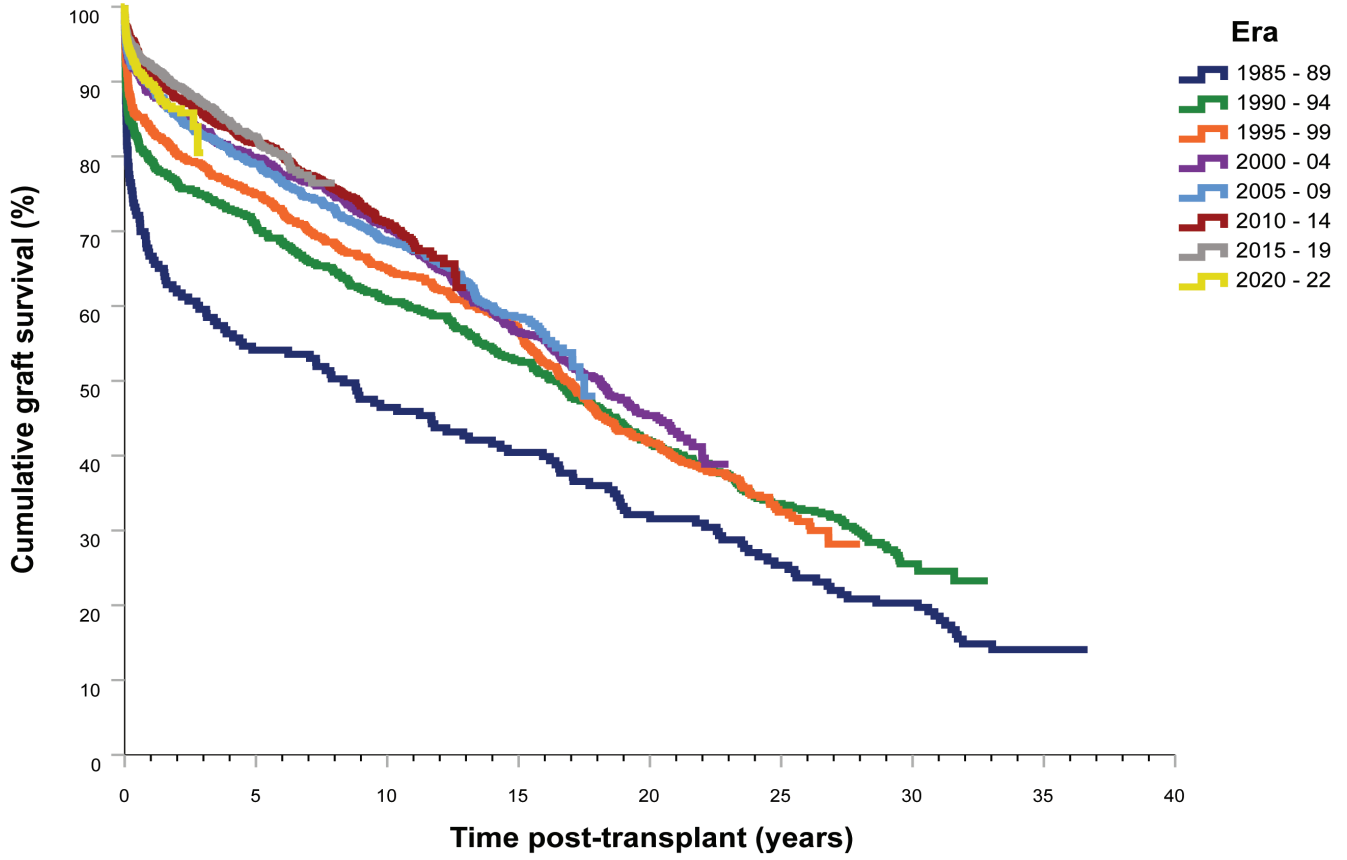


Table 50. Whole graft survival by era of transplant

Transplant Era	Graft Survival	Time post-transplant (years)								
		0	1	3	5	10	20	30	35	40
1985 - 89	No. at risk	183	122	109	99	85	57	36	5	0
	Survival (%)		67%	60%	54%	46%	32%	20%	14%	
1990 - 94	No. at risk	489	388	365	345	289	189	55	0	
	Survival (%)		80%	75%	71%	61%	42%	26%		
1995 - 99	No. at risk	617	512	478	452	389	243	0		
	Survival (%)		84%	79%	75%	65%	42%			
2000 - 04	No. at risk	774	678	634	602	531	180	0		
	Survival (%)		89%	83%	80%	71%	45%			
2005 - 09	No. at risk	816	729	671	640	552	0			
	Survival (%)		90%	83%	79%	69%				
2010 - 14	No. at risk	1,067	968	909	861	395	0			
	Survival (%)		91%	86%	82%	71%				
2015 - 19	No. at risk	1,421	1,303	1,142	587	0				
	Survival (%)		92%	87%	83%					
2020 - 22	No. at risk	787	465	0						
	Survival (%)		90%							

15.13 Reduced Graft Survival by Era of Transplant

Graft survival after reduced liver transplantation varied over transplant eras without a clear trend (P = 0.033, Figure 76, Table 51). Graft survival in the most recent era was 85.7% at 1 year, 84.9% at 3 years, 78.4% at 5 years and 57.6% at 10 years. Median graft survival was not reached for eras since 2015 and between 2000 and 2009. It was 20.2 years for 1990 – 94, 11.2 years for 2010 – 14, 9.2 years for 1995 – 99 and 3.0 years for 1985 – 89.

Figure 76. Reduced graft survival curve by era of transplant

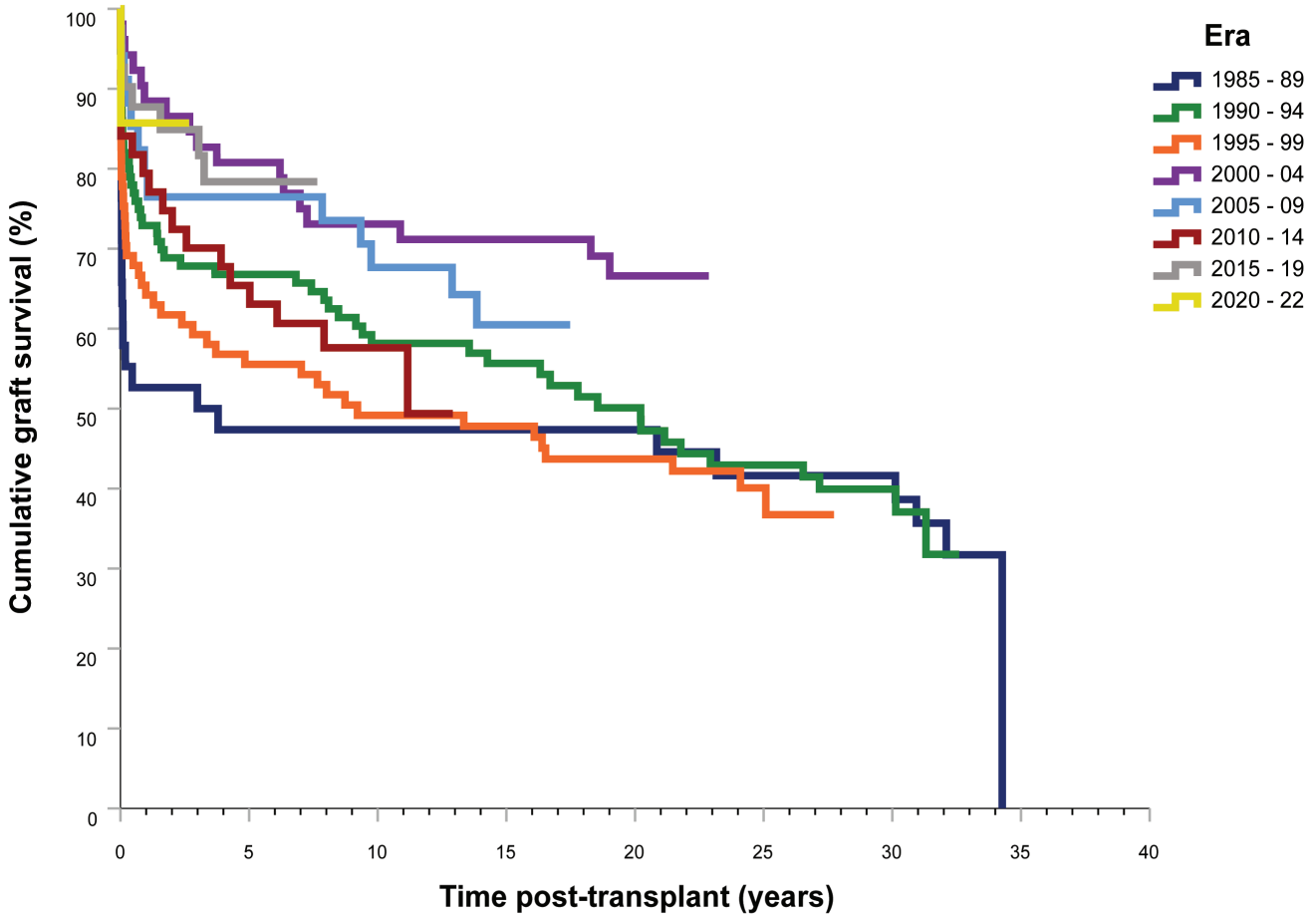


Table 51. Reduced graft (deceased donor) survival by era of transplant

Transplant Era	Graft Survival	Time post-transplant (years)								
		0	1	3	5	10	20	30	35	40
1985 - 89	No. at risk	38	20	19	18	18	17	14	0	
	Survival (%)		53%	50%	47%	47%	47%	42%		
1990 - 94	No. at risk	100	72	65	64	53	36	14	0	
	Survival (%)		73%	68%	67%	58%	50%	40%		
1995 - 99	No. at risk	81	52	48	44	37	30	0		
	Survival (%)		64%	59%	56%	49%	44%			
2000 - 04	No. at risk	52	46	43	42	38	22	0		
	Survival (%)		89%	83%	81%	73%	67%			
2005 - 09	No. at risk	34	27	26	26	23	0			
	Survival (%)		79%	77%	77%	68%				
2010 - 14	No. at risk	44	34	30	28	12	0			
	Survival (%)		79%	70%	65%	58%				
2015 - 19	No. at risk	41	32	27	15	0				
	Survival (%)		88%	85%	78%					
2020 - 22	No. at risk	14	7	0						
	Survival (%)		86%							

15.14 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 = 0.006, Figure 77, Table 52). Graft survival in the most recent era was 94.6% at 1 year, 85.2% at 3 years, 83.1% at 5 years and 73.3% at 10 years. Median graft survival was not reached for transplant eras since 2005 and was 16.3 years for 2000 – 04, 14.5 years for 1995 – 99 and 5.0 years for 1985 – 94.

Figure 77. Split graft (deceased donor) survival curve by era of transplant

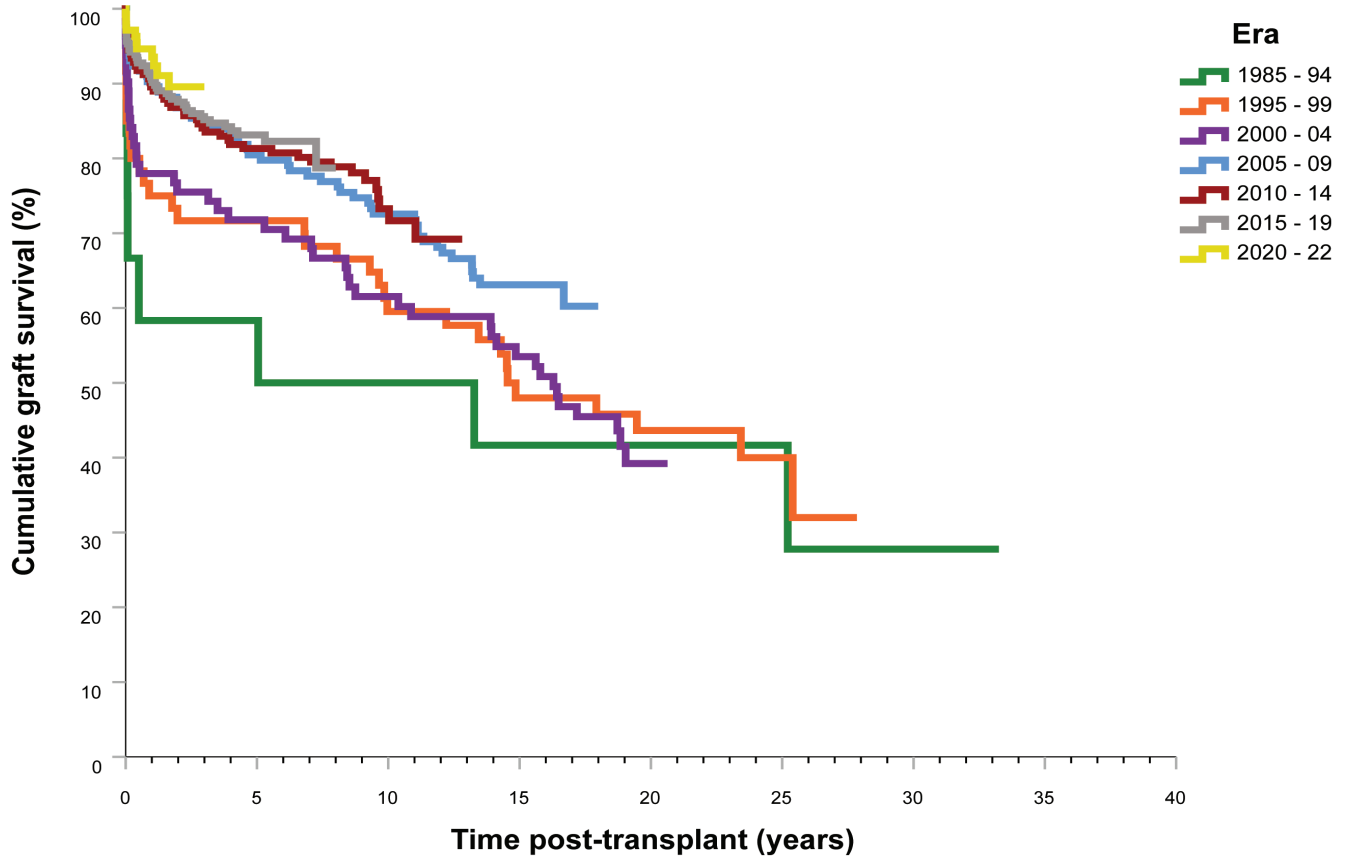


Table 52. Split graft (deceased donor) survival by era of transplant

Transplant Era	Graft Survival	Time post-transplant (years)								
		0	1	3	5	10	20	30	35	40
1985 - 94	No. at risk	12	7	7	7	6	4	2	0	
	Survival (%)		58%	58%	58%	50%	42%	28%		
1995 - 99	No. at risk	60	45	42	42	34	20	0		
	Survival (%)		75%	72%	72%	60%	44%			
2000 - 04	No. at risk	82	63	61	56	46	9	0		
	Survival (%)		78%	76%	72%	62%	39%			
2005 - 09	No. at risk	144	128	121	115	100	0			
	Survival (%)		90%	85%	81%	73%				
2010 - 14	No. at risk	182	163	153	144	48	0			
	Survival (%)		90%	84%	81%	73%				
2015 - 19	No. at risk	277	243	205	110	0				
	Survival (%)		91%	85%	83%					
2020 - 22	No. at risk	144	86	0						
	Survival (%)		95%							

15.15 Living Donor Graft Survival by Era of Transplant

There were 115 living donor grafts (excluding domino grafts). There had been a progressive deterioration in graft survival after living donor transplantation over eras of transplantation after 2000 until 2019, although there have been no graft losses to date in living donor liver transplants performed in 2020 - 22 (P = 0.006, Figure 78 and Table 53). Graft survival in the most recent era was 100% at 1 year, 77.3% at 3 years, 69.5% at 5 years and 78.4% at 10 years. Median graft survival was not reached for transplant eras since 2000 and was 0.8 years for 1985 – 99.

Figure 78. Living donor (excluding domino) graft survival curve by era of transplant

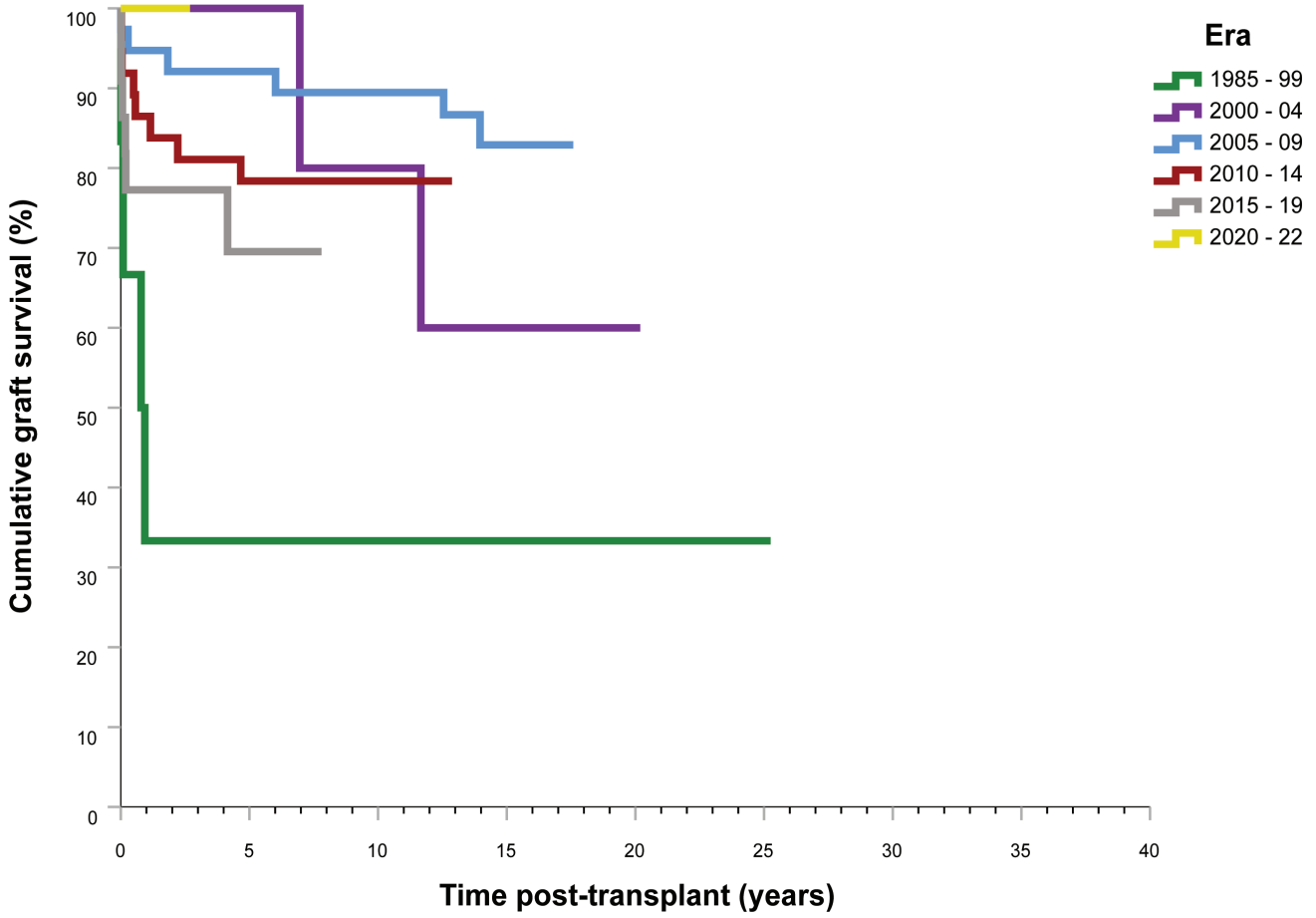


Table 53. Living donor (excluding domino) graft survival by era of transplant

Transplant Era	Graft Survival	Time post-transplant (years)								
		0	1	3	5	10	20	30	35	40
1985 - 99	No. at risk	6	2	1	1	1	1	0		
	Survival (%)		33%	33%	33%	33%	33%			
2000 - 04	No. at risk	5	5	5	5	4	1	0		
	Survival (%)		100%	100%	100%	80%	60%			
2005 - 09	No. at risk	38	36	35	35	33	0			
	Survival (%)		95%	92%	92%	90%				
2010 - 14	No. at risk	37	32	30	29	20	0			
	Survival (%)		87%	81%	78%	78%				
2015 - 19	No. at risk	22	17	16	6	0				
	Survival (%)		77%	77%	70%					
2020 - 22	No. at risk	7	7	0						
	Survival (%)		100%							

15.16 Graft Survival by Deceased Donor Age

A total of 7,460 grafts were sourced from 7,010 deceased donors, however there is no deceased donor information on 126 grafts from 1985 to 1988. This survival analysis is limited to 7,334 grafts (from 6,884 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 79 and Table 54). Ten-year graft survival was 79.8% for donors aged 10 – 15 years, 76.9% for donors aged 0 – 9 years, 71.4% for donors aged 16 – 29 years, 66.8% for donors aged 60 – 69 years, 66.7% for donors aged 30 – 39 years, 66.0% for donors aged 70 years and older, and 64.9% for donors aged 50 – 59 years. Median graft survival was not reached for donors aged 0 – 9 years and was 26.8 years for donors aged 10 – 15 years, 20.3 years for donors aged 16 – 29 years, 17.0 years for donors aged 30 – 39 years, 16.8 years for donors aged 40 – 49 years, 16.4 years for donors aged 60 – 69 years, 16.1 years for donors aged 50 – 59 years and 16.1 years for donors aged 70 years and older.

Figure 79. Graft survival curve by deceased donor age

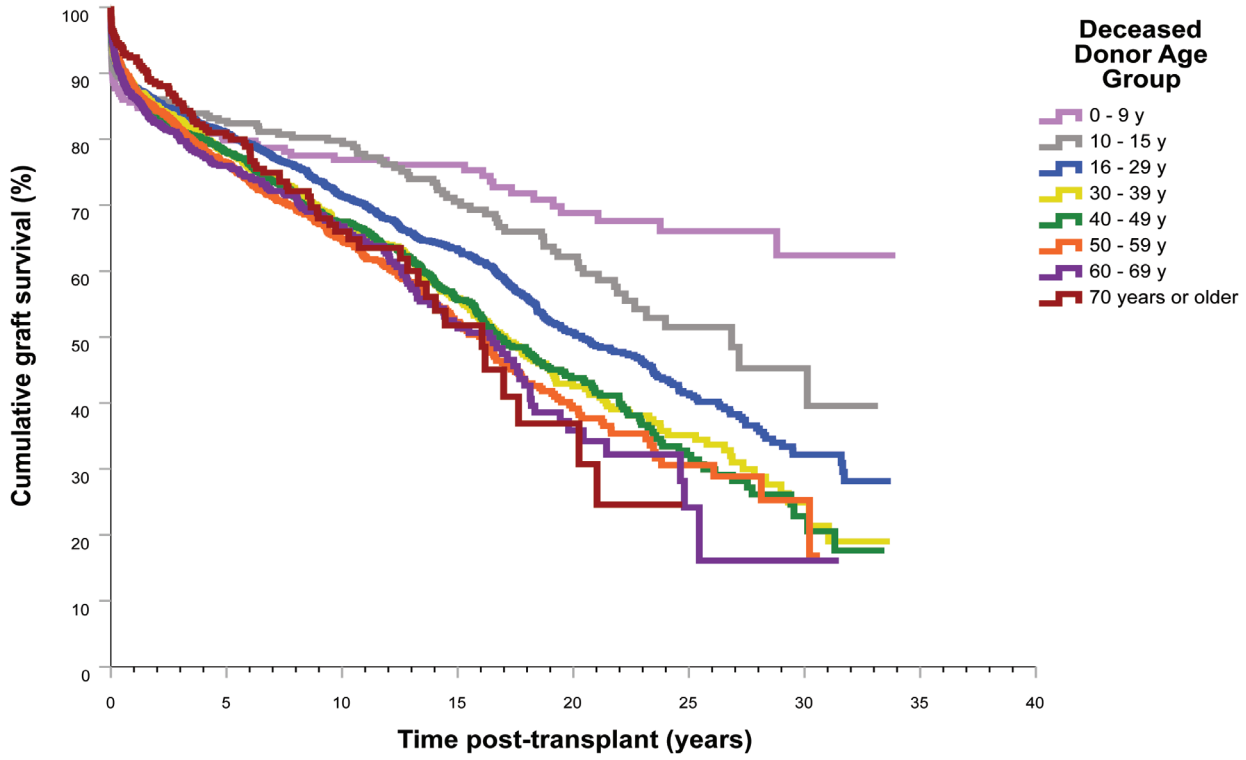


Table 54. Graft survival by deceased donor age

Donor Age	Graft Survival	Time post-transplant (years)								
		0	1	3	5	10	20	30	35	40
0 – 9 y	No. at risk	246	196	172	153	117	66	10	0	
	Survival (%)		86%	83%	80%	77%	69%	62%		
10 – 15 y	No. at risk	325	270	240	212	163	75	8	0	
	Survival (%)		87%	85%	83%	80%	62%	45%		
16 – 29 y	No. at risk	1,865	1,562	1,334	1,144	762	279	50	0	
	Survival (%)		88%	84%	81%	71%	51%	32%		
30 – 39 y	No. at risk	1,085	909	759	625	380	105	15	0	
	Survival (%)		88%	83%	78%	67%	43%	25%		
40 – 49 y	No. at risk	1,376	1,145	940	797	500	133	10	0	
	Survival (%)		88%	81%	78%	68%	44%	23%		
50 – 59 y	No. at risk	1,266	1,047	859	702	400	82	3	0	
	Survival (%)		88%	82%	76%	65%	39%	25%		
60 – 69 y	No. at risk	837	687	553	440	217	24	1	0	
	Survival (%)		86%	80%	76%	67%	36%	16%		
70 years and older	No. at risk	334	292	226	158	61	6	0		
	Survival (%)		92%	85%	81%	66%	37%			

All grafts from deceased donors since 1989 (n=7,334)

15.17 Graft Survival by Donor Type

Graft survival was superior for transplantation from living donors and slightly inferior for transplantation from donation after circulatory death donors in comparison to transplantation from donation after brain death donors (P = 0.016, Figure 80 and Table 55). Ten-year graft survival was 78.5% for transplantation from living donors, 68.5% for transplantation from donation after brain death donors and 64.3% for transplantation from donation after circulatory death donors. Median survival was not reached for transplantation from living donors and donation after circulatory death donors. Median survival was 18.3 years for transplantation from donation after brain death donors.

Figure 80. Graft survival curve by donor type – all grafts

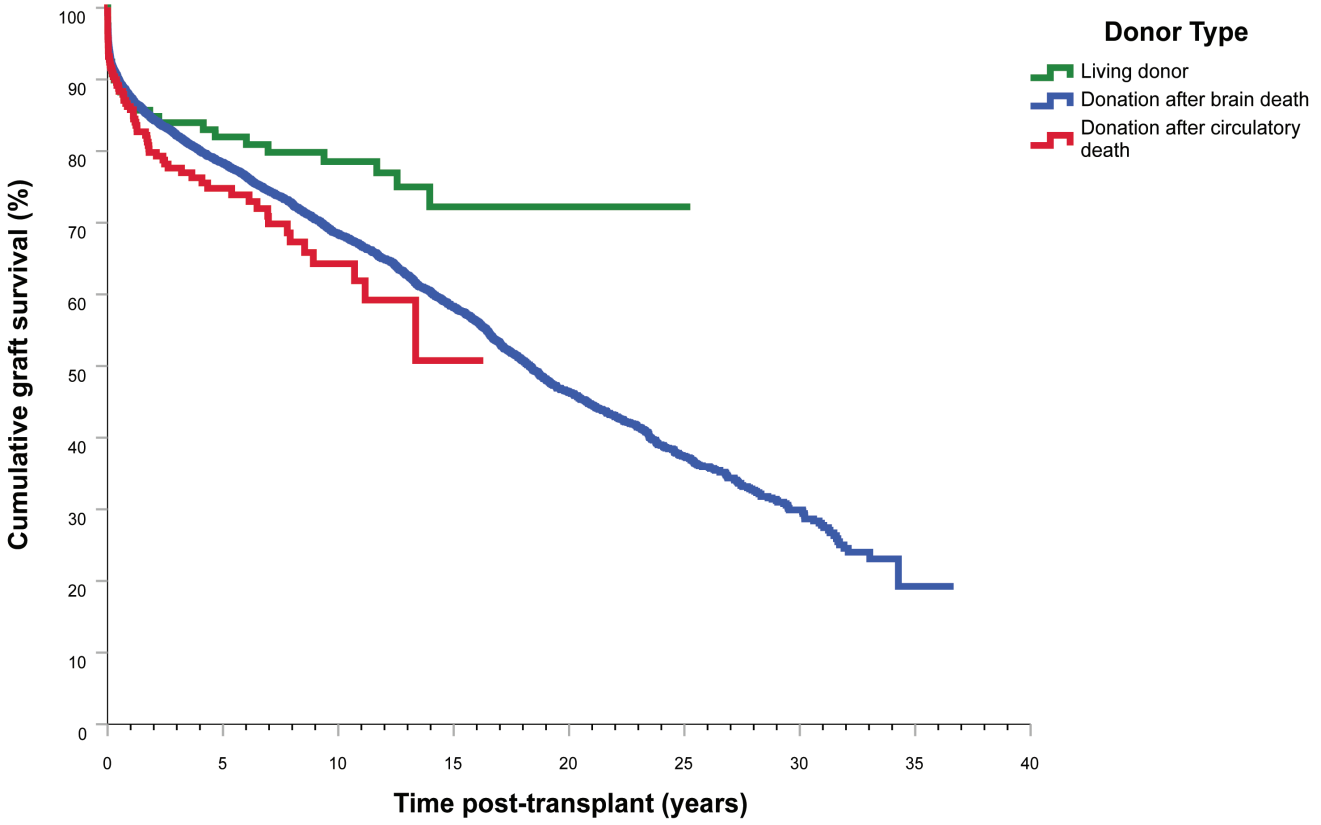


Table 55. Graft survival by donor type – all grafts

Donor Type	Graft Survival	Time post-transplant (years)								
		0	1	3	5	10	20	30	35	40
Living donor	No. at risk	120	103	91	80	58	2	0		
	Survival (%)		87%	84%	82%	79%	72%			
DBD	No. at risk	7,209	5,993	5,029	4,210	2,624	807	121	5	0
	Survival (%)		88%	82%	78%	69%	46%	30%	19%	
DCD	No. at risk	251	198	126	87	32	0			
	Survival (%)		86%	78%	75%	64%				

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

All grafts (n=7,580)

15.18 Graft Survival by Donor Cause of Death

Graft survival varied significantly by donor cause of death (P < 0.001, Figure 81, Table 56). Ten-year graft survival was 73.9% for other cause, 70.9% for anoxia, 69.8% for trauma and 66.5% for stroke. Median survival was 23.3 years for other cause, 19.4 years for trauma, 18.7 years for anoxia and 16.9 years for stroke.

Figure 81. Graft survival curve by donor cause of death

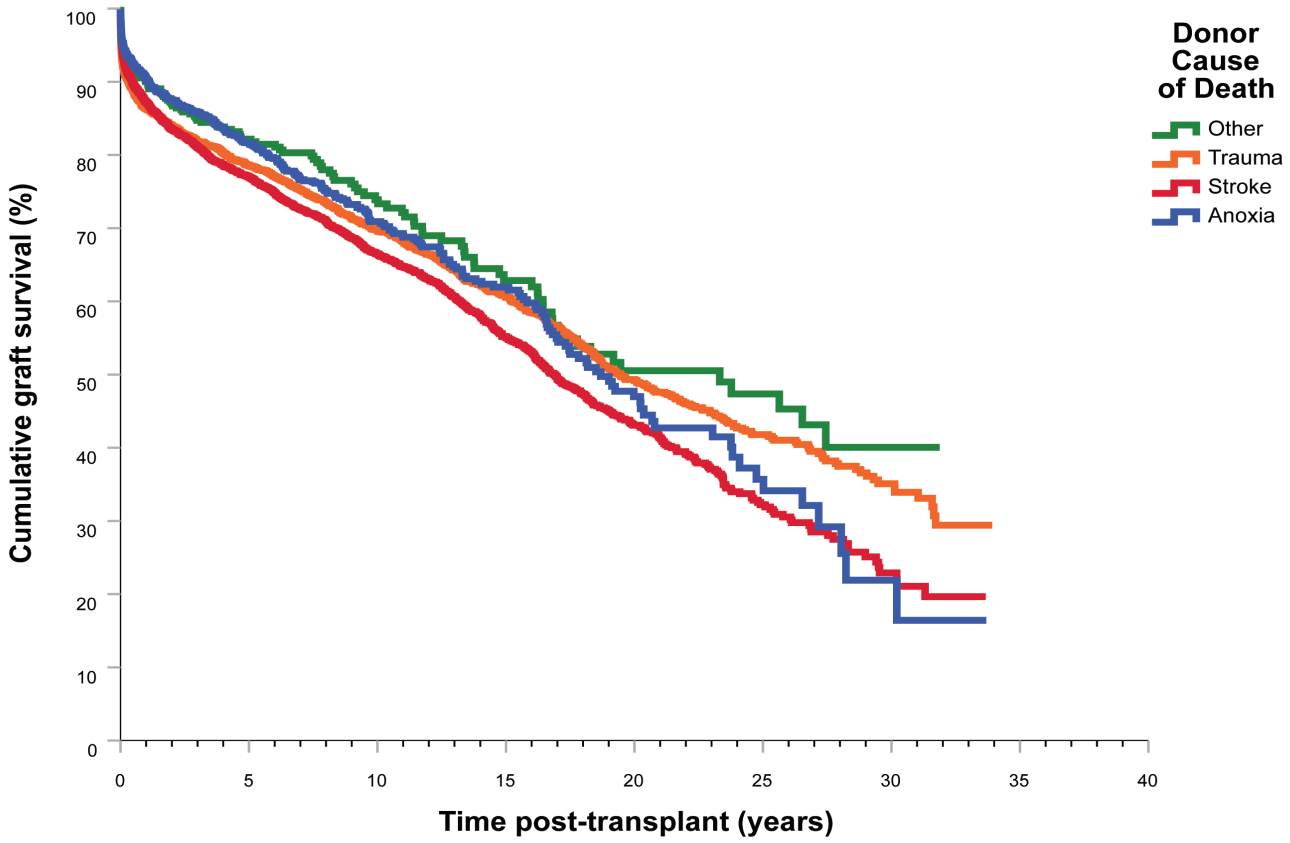


Table 56. Graft survival by donor cause of death

Donor cause of death	Graft Survival	Time post-transplant (years)								
		0	1	3	5	10	20	30	35	40
Other	No. at risk	429	363	296	233	132	42	6	0	
	Survival (%)		90%	85%	82%	74%	51%	40%		
Trauma	No. at risk	2,063	1,712	1,493	1,323	954	363	61	0	
	Survival (%)		86%	82%	79%	70%	49%	35%		
Stroke	No. at risk	3,348	2,797	2,325	1,951	1,194	301	25	0	
	Survival (%)		87%	81%	77%	67%	43%	23%		
Anoxia	No. at risk	1,494	1,236	969	724	320	64	5	0	
	Survival (%)		90%	86%	82%	71%	47%	22%		

All grafts from deceased donors since 1989 (n=7,334)

15.19 Graft Survival by Shipping of Organs

Graft survival was better for transplants performed with a liver from the unit's donor region than shipped grafts (P < 0.001, Figure 82, Table 57). Ten-year graft survival was 70.1% for transplants performed with a non-shipped liver and 64.9% for a liver shipped from another unit. Median graft survival was 18.3 years for transplants performed with a donor liver from the unit's donor region and 17.8 years for a liver shipped from another unit.

Figure 82. Graft survival curve by organ shipping

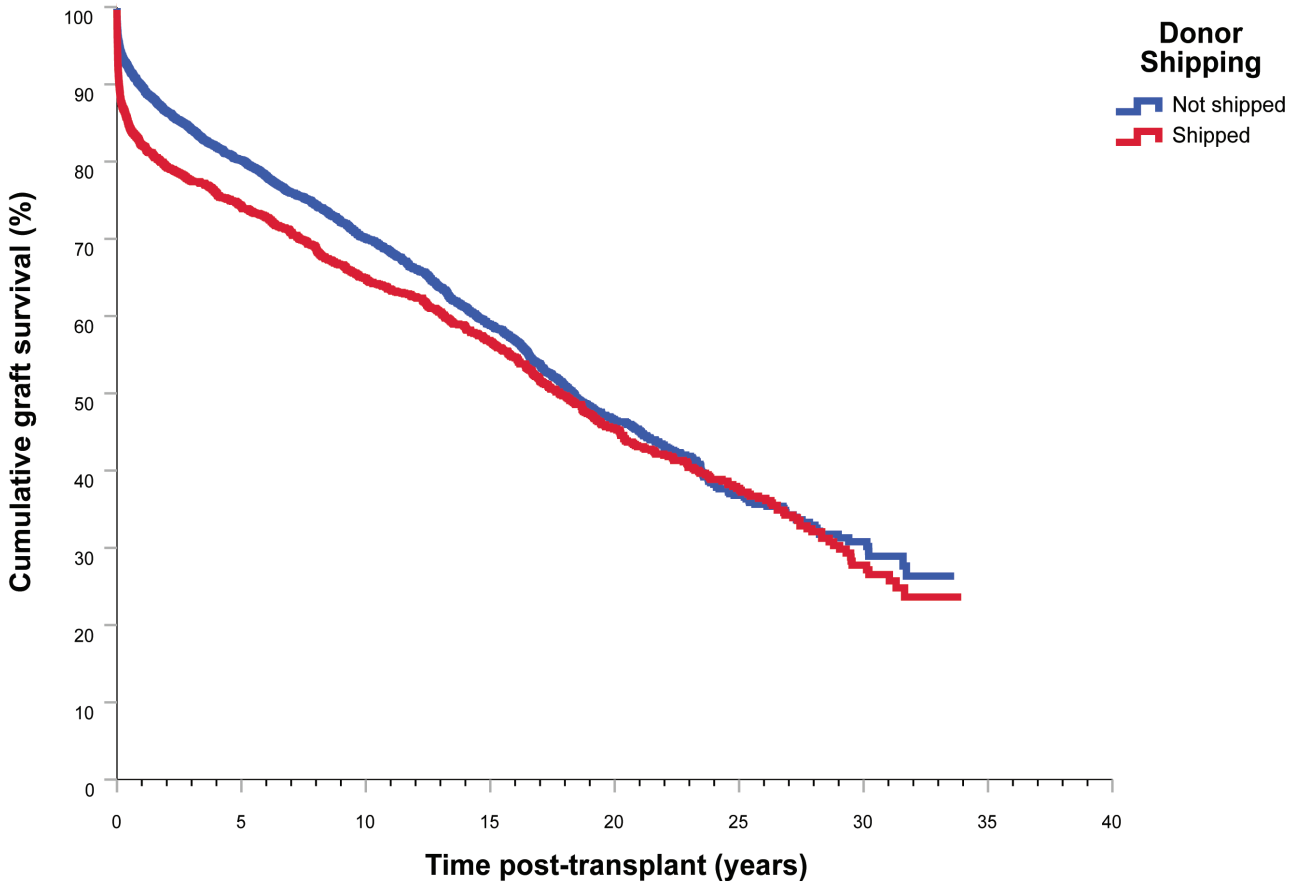


Table 57. Graft survival by organ shipping

Organ Shipping	Graft Survival	Time post-transplant (years)								
		0	1	3	5	10	20	30	35	40
Not shipped	No. at risk	5,491	4,663	3,837	3,139	1,838	437	51	0	
	Survival (%)		90%	84%	80%	70%	47%	31%		
Shipped	No. at risk	1,843	1,445	1,246	1,092	762	333	46	0	
	Survival (%)		82%	78%	74%	65%	45%	28%		

All grafts from deceased donors since 1989 (n=7,334)

15.20 Graft Survival by Cold Ischaemia Time

Graft survival was significantly better for transplants performed with a cold ischaemia time less than 431 minutes compared to transplants performed with a cold ischaemia time 431 minutes or greater (P < 0.001, see Figure 83 and Table 58). Ten-year graft survival was 73.2% for transplants with a cold ischaemia time less than 431 minutes and 66.4% for transplants with a cold ischaemia time greater than or equal to 431 minutes. Median survival was 19.2 years for transplants with a cold ischaemia time less than 431 minutes and 16.5 years for transplants with a cold ischaemia time greater than or equal to 431 minutes.

Figure 83. Graft survival curve by cold ischaemia time

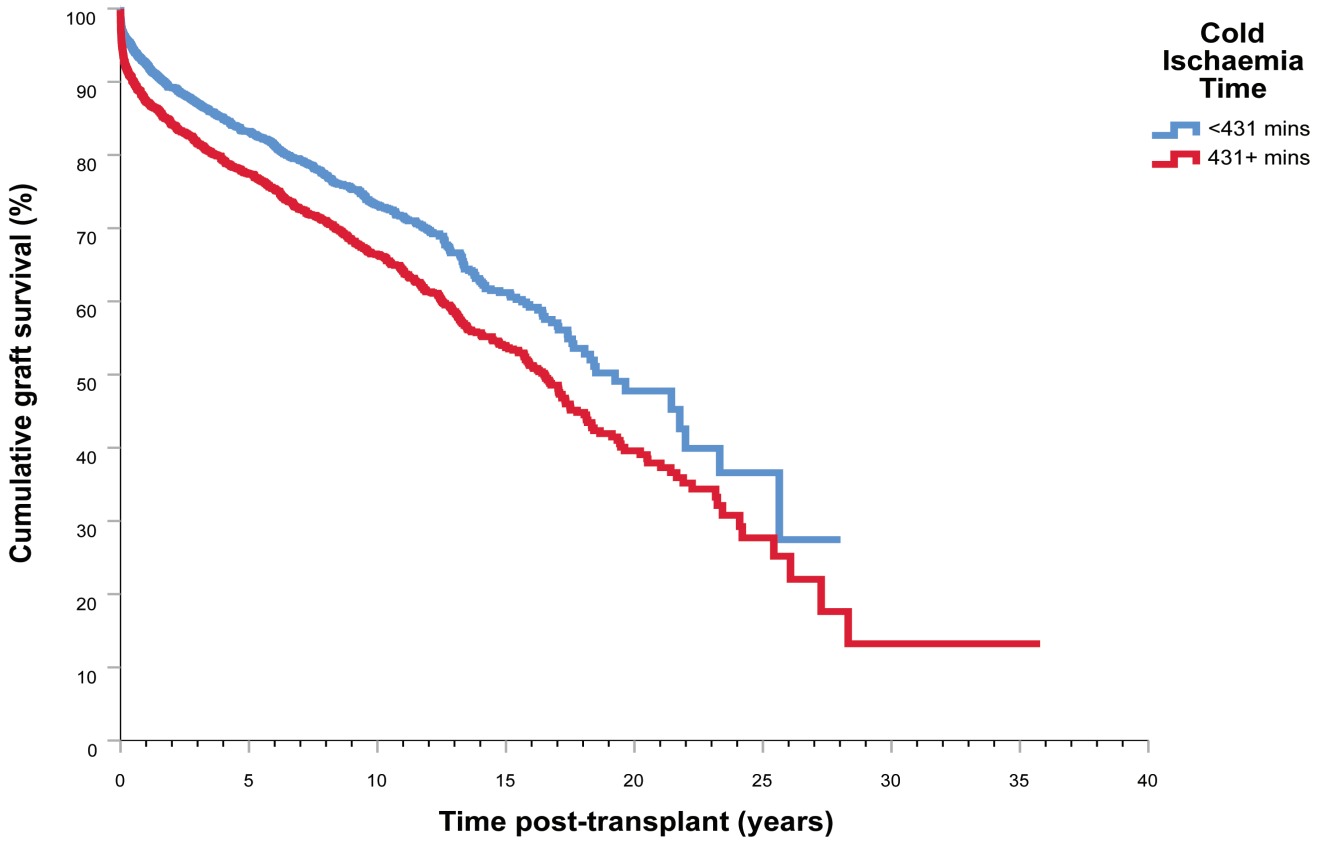


Table 58. Graft survival by cold ischaemia time

Cold Ischaemia Time	Graft Survival	Time post-transplant (years)								
		0	1	3	5	10	20	30	35	40
<431 min	No. at risk	3,362	2,859	2,177	1,629	682	32	0		
	Survival (%)		93%	87%	83%	73%	48%			
431+ min	No. at risk	2,137	1,800	1,552	1,312	791	80	2	0	
	Survival (%)		87%	82%	77%	66%	40%	13%		

2,081 cases missing

15.21 Graft Survival by Blood Group Compatibility

Recording of A blood subtypes was only done for a small number of cases prior to 2015 in the Registry. Any blood type A without subtyping is classified as A.

There was no difference in graft survival by deceased donor/recipient blood group compatibility (P=0.994, Figure 84 and Table 59). Ten-year graft survival was 71.7% 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), 70.5% for blood group incompatible transplants (excluding A2 donors), 69.2% for blood group-compatible transplants and 68.7% for blood group-identical transplants. Median graft survival was not reached for blood group incompatible transplants, 20.9 years for incompatible "A2" transplants, 19.1 years for transplants in which the donor and recipient blood groups were compatible and 18.2 years for transplants between identical blood groups.

Figure 84. Graft survival curve by blood group compatibility

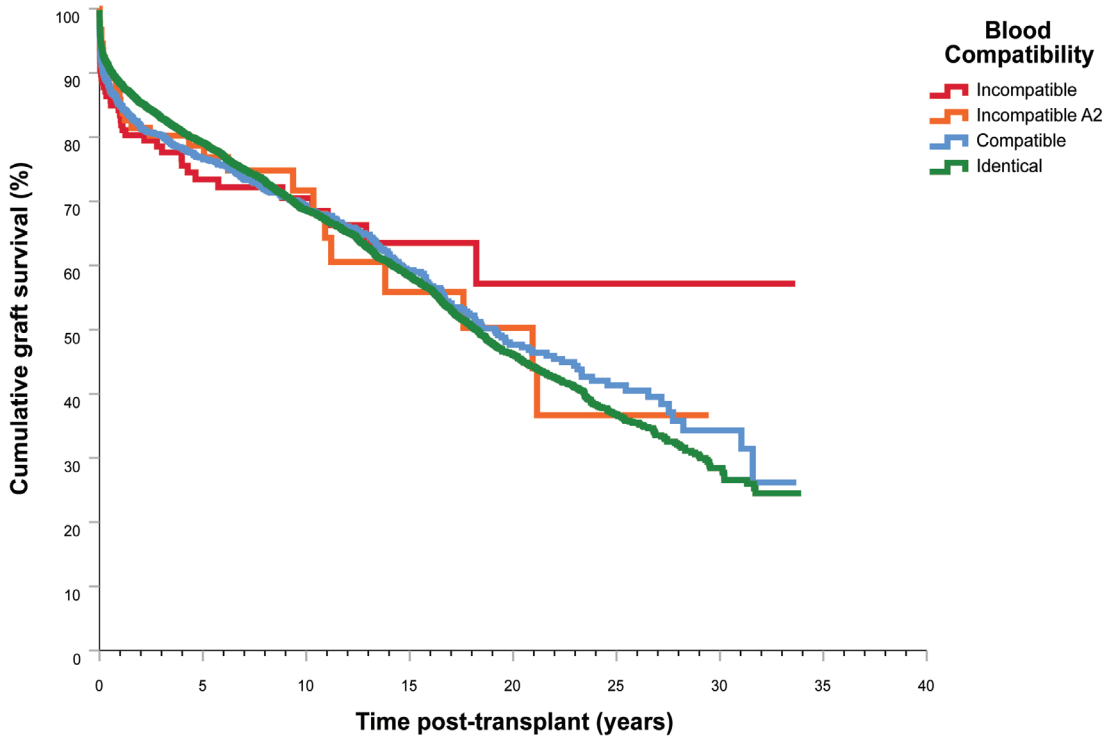


Table 59. Graft survival by blood group compatibility

Compatibility	Graft Survival	Time post-transplant (years)								
		0	1	3	5	10	20	30	35	40
Incompatible	No. at risk	149	109	85	65	39	9	3	0	
	Survival (%)		83%	79%	73%	71%	57%	57%		
Incompatible A2	No. at risk	92	79	64	44	20	8	0		
	Survival (%)		86%	80%	79%	72%	50%			
Compatible	No. at risk	1,009	816	680	578	371	126	15	0	
	Survival (%)		85%	80%	77%	69%	48%	34%		
Identical	No. at risk	6,068	5,093	4,254	3,544	2,170	627	79	0	
	Survival (%)		88%	83%	79%	69%	46%	28%		

All grafts from deceased donors since 1989, 16 deceased donor blood types missing from 1989 onwards (n = 7,318)

15.22 Graft Survival by Recipient Urgency at Transplant

Graft survival varied significantly by recipient urgency at transplant with poorer outcomes for category 1 to up 20 years post-transplant (P < 0.001, Figure 85 and Table 60). Ten-year graft survival was 76.2% for category 2, 68.7% for non-urgent and 57.0% for category 1 patients. Median graft survival was 25.6 years for category 2, 18.3 years for non-urgent patients and 13.9 years for category 1.

Figure 85. Graft survival curve by recipient urgency at transplant

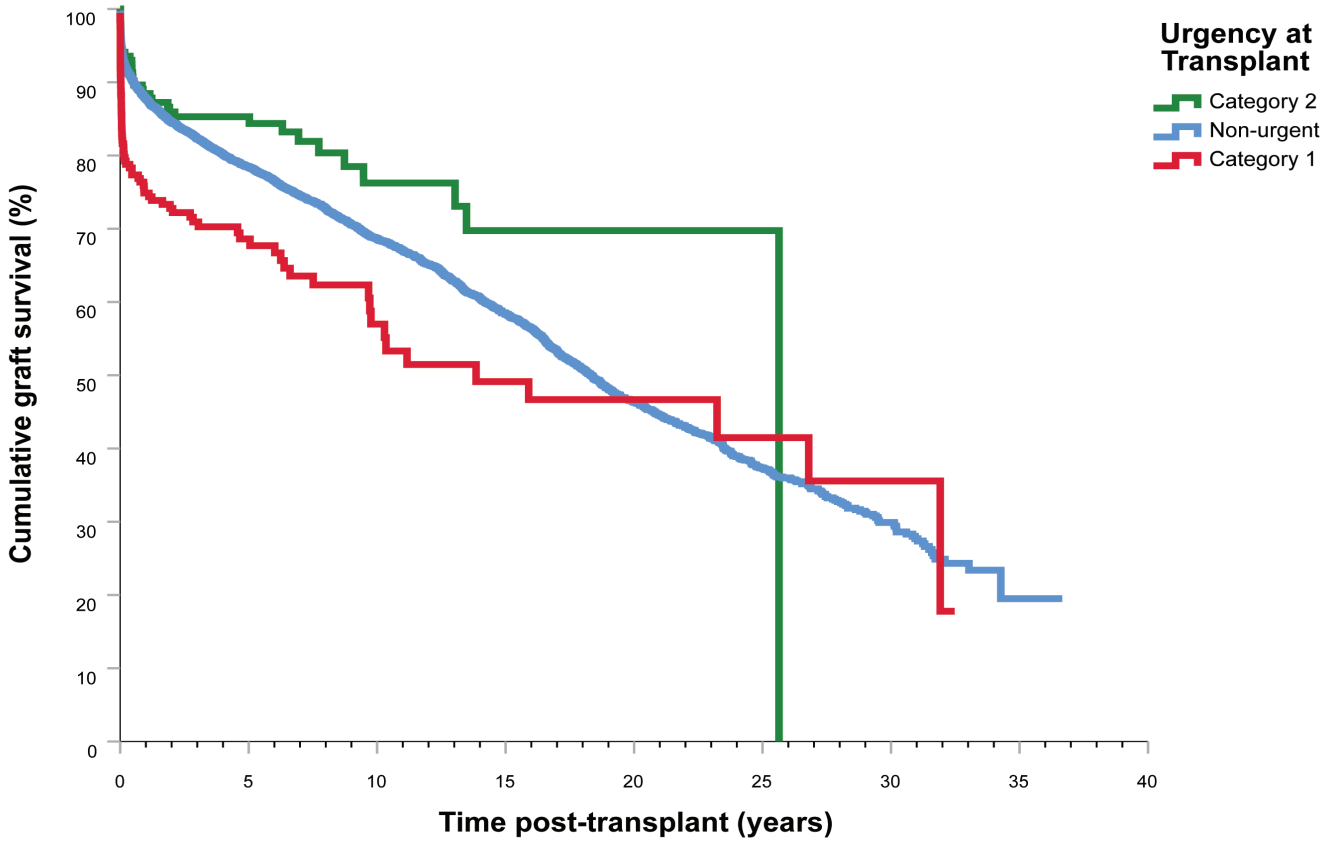


Table 60. Graft survival by recipient urgency at transplant

Urgency at Transplant	Graft Survival	Time post-transplant (years)								
		0	1	3	5	10	20	30	35	40
Category 2	No. at risk	187	151	115	92	30	3	0		
	Survival (%)		89%	85%	85%	76%	70%			
Non-urgent	No. at risk	7,179	5,993	5,022	4,209	2,653	794	117	5	0
	Survival (%)		88%	82%	78%	69%	46%	30%	20%	
Category 1	No. at risk	214	150	109	76	31	12	4	0	
	Survival (%)		75%	71%	69%	57%	47%	36%		

15.23 Graft Survival by Transplant Unit

Benchmarking analysis using hierarchical regression models estimated that 1.2% of the variation in 1-year graft loss and <0.000001% of the variation in 5-year graft loss was due to variation between liver transplant units.

16 Indication for Retransplantation

16.1 All Retransplants

There were 591 retransplants after the previous graft failed. There have been 527 second grafts, 62 third grafts and two fourth grafts. The commonest indications for retransplantation were vascular complications (27.1%), biliary complications (19.5%), rejection (17.8%), primary non-function or initial poor function (14.6%) and recurrent disease (13.4%, Table 61).

Table 61. Reason for retransplantation

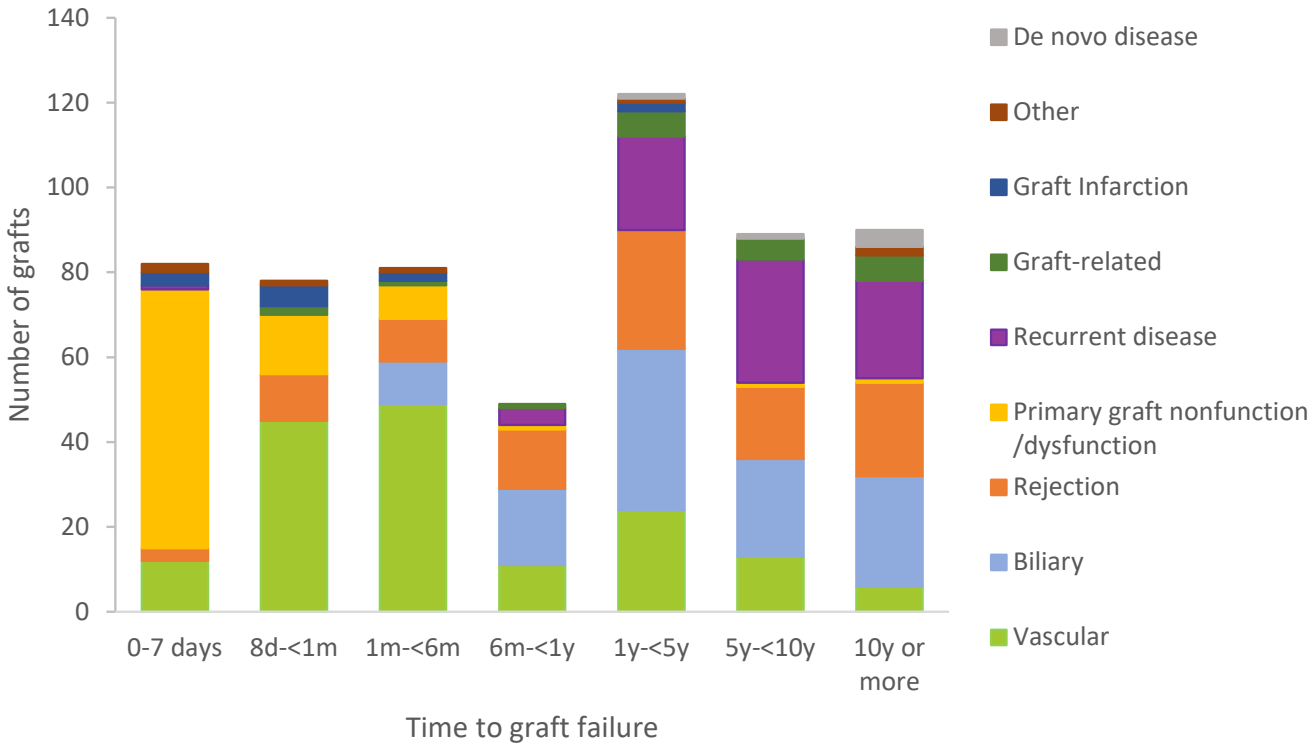
Reason for retransplantation	Graft 2	Graft 3	Graft 4	Total grafts	% Total
Vascular	**143**	**17**	**0**	**160**	**27%**
Hepatic artery thrombosis	*111*	*12*	*0*	*123*	*21%*
Portal vein thrombosis	*11*	*0*	*0*	*11*	*2%*
Hepatic vein thrombosis /Budd Chiari	*8*	*1*	*0*	*9*	*2%*
Haemorrhage (hepatic artery)	*4*	*0*	*0*	*4*	*0.7%*
Hepatic artery stenosis	*3*	*0*	*0*	*3*	*0.5%*
Hepatic vein stenosis	*1*	*2*	*0*	*3*	*0.5%*
Hepatic artery pseudoaneurysm	*2*	*0*	*0*	*2*	*0.3%*
Arterio-portal vein fistula	*1*	*0*	*0*	*1*	*0.2%*
Hepatic artery dissection	*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%*
Biliary	**108**	**7**	**0**	**115**	**19%**
Cholangiopathy	*74*	*3*	*0*	*77*	*13%*
Cholangitis	*11*	*2*	*0*	*13*	*2%*
Biliary cirrhosis / fibrosis	*10*	*0*	*0*	*10*	*2%*
Anastomotic	*6*	*0*	*0*	*6*	*1%*
Cholestatic disease	*4*	*0*	*0*	*4*	*0.7%*
Biliary necrosis	*0*	*2*	*0*	*2*	*0.3%*
Ductopenia	*2*	*0*	*0*	*2*	*0.3%*
Biliopathy caused by ABO incompatible transplant	*1*	*0*	*0*	*1*	*0.2%*
Rejection	**91**	**13**	**1**	**105**	**18%**
Chronic rejection	*67*	*11*	*0*	*78*	*13%*
Acute rejection	*16*	*1*	*1*	*18*	*3%*
ABO incompatible	*4*	*1*	*0*	*5*	*1%*
Donor antibody mediated	*2*	*0*	*0*	*2*	*0.3%*
Hyperacute rejection	*2*	*0*	*0*	*2*	*0.3%*
Primary graft nonfunction /dysfunction	**73**	**13**	**0**	**86**	**15%**
Primary nonfunction (ReTx <= 7 days)	*56*	*11*	*0*	*67*	*11%*
Primary dysfunction (ReTx > 7 days)	*17*	*2*	*0*	*19*	*3%*
Recurrent disease	**72**	**7**	**0**	**79**	**13%**
Primary sclerosing cholangitis	*29*	*5*	*0*	*34*	*6%*
Hepatitis C	*22*	*0*	*0*	*22*	*4%*
Autoimmune hepatitis	*9*	*1*	*0*	*10*	*2%*
Primary biliary cirrhosis	*6*	*1*	*0*	*7*	*1%*
Hepatitis B	*4*	*0*	*0*	*4*	*0.7%*
Crigler-Najjar	*1*	*0*	*0*	*1*	*0.2%*
Erythropoietic protoporphyria	*1*	*0*	*0*	*1*	*0.2%*
Graft-related	**15**	**3**	**0**	**18**	**3%**
Post necrotic cirrhosis	*5*	*3*	*0*	*8*	*1%*
Cryptogenic cirrhosis	*3*	*1*	*0*	*4*	*0.7%*
Graft infection	*4*	*0*	*0*	*4*	*0.7%*
Nodular regenerative hyperplasia	*3*	*0*	*0*	*3*	*0.5%*
Immune/nonviral hepatitis	*2*	*0*	*0*	*2*	*0.3%*

(table continued on next page)

Reason for retransplantation	Graft 2	Graft 3	Graft 4	Total grafts	% Total
Graft Infarction	**11**	**0**	**1**	**12**	**2%**
Non thrombotic	*5*	*0*	*1*	*6*	*1%*
Thrombotic	*6*	*0*	*0*	*6*	*1%*
Other	**8**	**2**	**0**	**10**	**2%**
Donor derived malignancy	*3*	*1*	*0*	*4*	*0.7%*
Unspecified	*2*	*0*	*0*	*2*	*0.3%*
Acute hepatic failure - Drug related: interferon	*1*	*0*	*0*	*1*	*0.2%*
De novo disease	**6**	**0**	**0**	**6**	**1%**
Hepatitis C	*2*	*0*	*0*	*2*	*0.3%*
Hepatocellular cancer	*2*	*0*	*0*	*2*	*0.3%*
Hepatitis B	*1*	*0*	*0*	*1*	*0.2%*
Hepatitis D	*1*	*0*	*0*	*1*	*0.2%*
Total	**527**	**62**	**2**	**591**	

Forty-one percent of graft failures occurred within the first six months post-transplant (13.9% 0 – 7 days, 13.2% day 8 to less than 1 month, 13.7% 1 month to less than 6 months). Primary graft non-function (74.4%) was the main reason for retransplantation in the first 7 days post-transplant whilst vascular causes were the main indication for 8 days to less than 1 month (57.7%) and 1 month to less than 6 months (60.5% Figure 86). Recurrent disease and biliary causes were the leading causes of graft failure after five years post-transplant.

Figure 86. Time to graft failure by reason for retransplantation



16.2 Paediatric Retransplantation

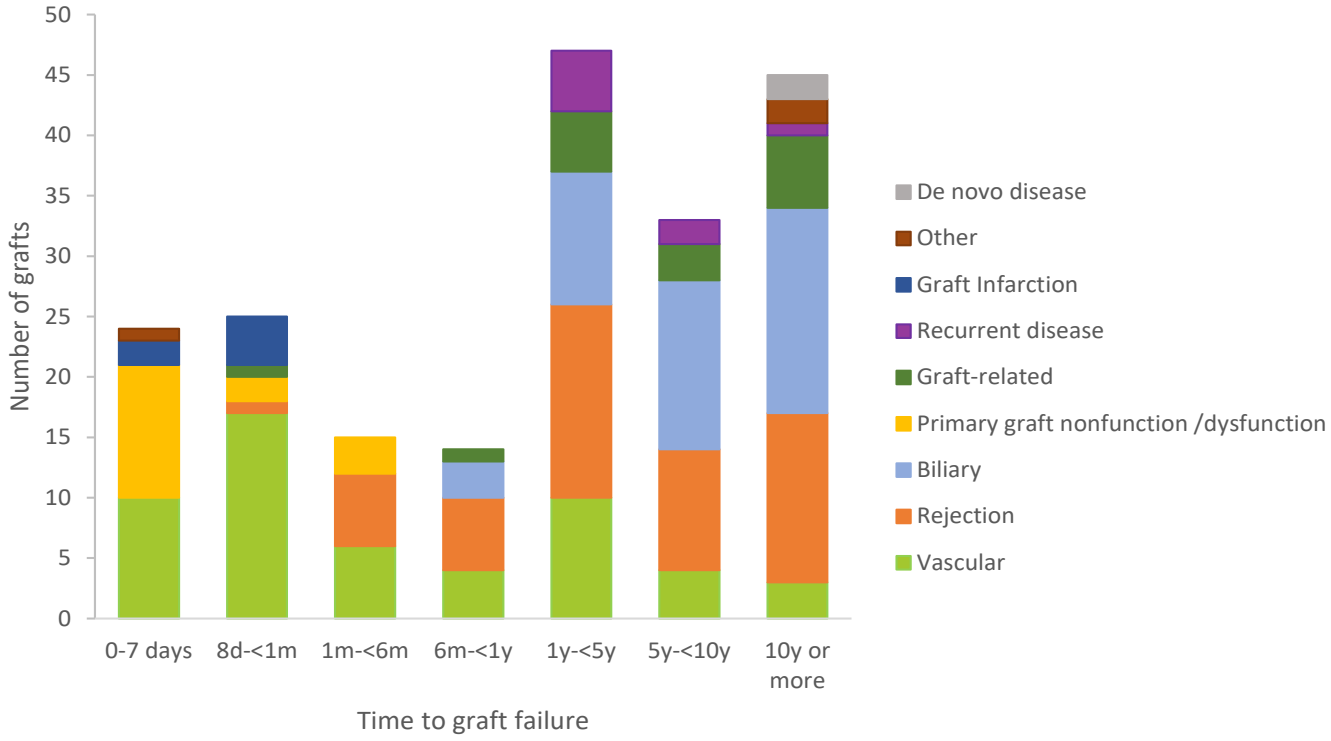
There were 203 retransplants following paediatric graft failure. There have been 174 second grafts and 29 third grafts. The commonest indications for retransplantation were vascular complications (26.6%), rejection (26.1%) and biliary complications (22.2%, Table 62).

Table 62. Reason for retransplantation following paediatric graft failure

Reason for retransplantation	Graft 2	Graft 3	Total grafts	% Total
Vascular	**45**	**9**	**54**	**27%**
Hepatic artery thrombosis	*30*	*6*	*36*	*18%*
Portal vein thrombosis	*8*	*0*	*8*	*4%*
Hepatic vein thrombosis /Budd Chiari	*4*	*1*	*5*	*2%*
Hepatic vein stenosis	*1*	*1*	*2*	*1%*
Arterio-portal vein fistula	*1*	*0*	*1*	*0.5%*
Hepatic artery stenosis	*1*	*0*	*1*	*0.5%*
Recurrent bleeds	*0*	*1*	*1*	*0.5%*
Rejection	***43***	***10***	***53***	***26%***
Chronic rejection	*42*	*9*	*51*	*25%*
Acute rejection	*1*	*1*	*2*	*1%*
Biliary	***43***	***2***	***45***	***22%***
Cholangiopathy	*21*	*1*	*22*	*11%*
Biliary cirrhosis / fibrosis	*7*	*0*	*7*	*3%*
Cholangitis	*7*	*0*	*7*	*3%*
Anastomotic	*4*	*0*	*4*	*2%*
Ductopenia	*2*	*0*	*2*	*1%*
Biliary necrosis	*0*	*1*	*1*	*0.5%*
Biliopathy caused by ABO incompatible transplant	*1*	*0*	*1*	*0.5%*
Cholestatic disease	*1*	*0*	*1*	*0.5%*
Primary graft nonfunction /dysfunction	***12***	***4***	***16***	***8%***
Primary nonfunction (ReTx <= 7 days)	*7*	*4*	*11*	*5%*
Primary dysfunction (ReTx > 7 days)	*5*	*0*	*5*	*2%*
Graft-related	***14***	***2***	***16***	***8%***
Post necrotic cirrhosis	*5*	*1*	*6*	*3%*
Cryptogenic cirrhosis	*3*	*1*	*4*	*2%*
Graft infection	*2*	*0*	*2*	*1%*
Immune/nonviral hepatitis	*2*	*0*	*2*	*1%*
Nodular regenerative hyperplasia	*2*	*0*	*2*	*1%*
Recurrent disease	***7***	***1***	***8***	***4%***
Autoimmune hepatitis	*2*	*1*	*3*	*1%*
Primary biliary cirrhosis	*2*	*0*	*2*	*1%*
Primary sclerosing cholangitis	*2*	*0*	*2*	*1%*
Crigler-Najjar	*1*	*0*	*1*	*0.5%*
Graft Infarction	***6***	***0***	***6***	***3%***
Thrombotic	*4*	*0*	*4*	*2%*
Non thrombotic	*2*	*0*	*2*	*1%*
Other	***2***	***1***	***3***	***1%***
Unspecified	*2*	*0*	*2*	*1%*
Donor derived malignancy	*0*	*1*	*1*	*0.5%*
De novo disease	**2**	**0**	**2**	**1%**
Hepatitis C	*1*	*0*	*1*	*0.5%*
Hepatocellular cancer	*1*	*0*	*1*	*0.5%*
Total	**174**	**29**	**203**	

Thirty-two percent of graft failures occurred within the first six months post-transplant (11.8% 0 – 7 days, 12.3% day 8 to less than 1 month, 7.4% 1 month to less than 6 months). Vascular causes were the main reason for retransplantation in the first month post-transplant (Figure 87). Rejection, biliary and vascular causes were the leading causes of graft failure after one-year post-transplant.

Figure 87. Paediatric time to graft failure by reason for retransplantation



16.3 Adult Retransplantation

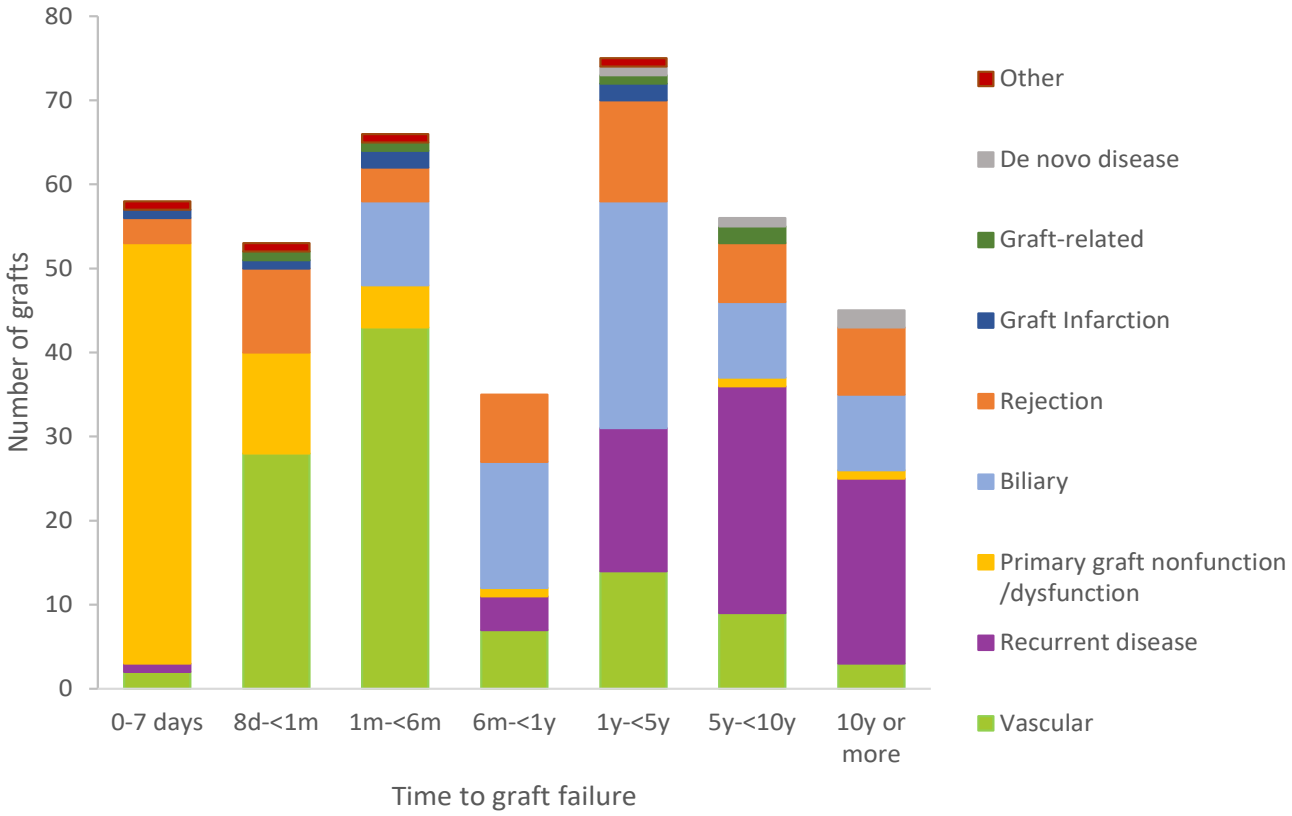
There were 388 retransplants following adult graft failure. There have been 353 second grafts, 33 third grafts and two fourth grafts. The commonest indications for retransplantation were vascular (27.3%), disease recurrence (18.3%) and primary non-function or initial poor function (18.0%, Table 63).

Table 63. Reason for retransplantation following adult graft failure

Reason for retransplantation	Graft 2	Graft 3	Graft 4	Total grafts	% Total
Vascular	**98**	**8**	**0**	**106**	**27%**
Hepatic artery thrombosis	*81*	*6*	*0*	*87*	*22%*
Haemorrhage (hepatic artery)	*4*	*0*	*0*	*4*	*1%*
Hepatic vein thrombosis /Budd Chiari	*4*	*0*	*0*	*4*	*1%*
Portal vein thrombosis	*3*	*0*	*0*	*3*	*1%*
Hepatic artery pseudoaneurysm	*2*	*0*	*0*	*2*	*0.5%*
Hepatic artery stenosis	*2*	*0*	*0*	*2*	*0.5%*
Hepatic artery dissection	*1*	*0*	*0*	*1*	*0.3%*
Hepatic artery injury	*1*	*0*	*0*	*1*	*0.3%*
Hepatic vein stenosis	*0*	*1*	*0*	*1*	*0.3%*
Ruptured hepatic artery anastomosis	*0*	*1*	*0*	*1*	*0.3%*
Recurrent disease	**65**	**6**	**0**	**71**	**18%**
Primary sclerosing cholangitis	*27*	*5*	*0*	*32*	*8%*
Hepatitis C	*22*	*0*	*0*	*22*	*6%*
Autoimmune hepatitis	*7*	*0*	*0*	*7*	*2%*
Primary biliary cirrhosis	*4*	*1*	*0*	*5*	*1%*
Hepatitis B	*4*	*0*	*0*	*4*	*1%*
Erythropoietic protoporphyria	*1*	*0*	*0*	*1*	*0.3%*
Primary graft nonfunction /dysfunction	**61**	**9**	**0**	**70**	**18%**
Primary nonfunction (ReTx <= 7 days)	*49*	*7*	*0*	*56*	*14%*
Primary dysfunction (ReTx > 7 days)	*12*	*2*	*0*	*14*	*4%*
Biliary	**65**	**5**	**0**	**70**	**18%**
Cholangiopathy	*53*	*2*	*0*	*55*	*14%*
Cholangitis	*4*	*2*	*0*	*6*	*2%*
Biliary cirrhosis / fibrosis	*3*	*0*	*0*	*3*	*0.8%*
Cholestatic disease	*3*	*0*	*0*	*3*	*0.8%*
Anastomotic	*2*	*0*	*0*	*2*	*0.5%*
Biliary necrosis	*0*	*1*	*0*	*1*	*0.3%*
Rejection	**48**	**3**	**1**	**52**	**13%**
Chronic rejection	*25*	*2*	*0*	*27*	*7%*
Acute rejection	*15*	*0*	*1*	*16*	*4%*
ABO incompatible	*4*	*1*	*0*	*5*	*1%*
Donor antibody mediated	*2*	*0*	*0*	*2*	*0.5%*
Hyperacute rejection	*2*	*0*	*0*	*2*	*0.5%*
Graft Infarction	**5**	**0**	**1**	**6**	**2%**
Non thrombotic	*3*	*0*	*1*	*4*	*1%*
Thrombotic	*2*	*0*	*0*	*2*	*0.5%*
Graft-related	**3**	**2**	**0**	**5**	**1%**
Graft infection	*2*	*0*	*0*	*2*	*0.5%*
Post necrotic cirrhosis	*0*	*2*	*0*	*2*	*0.5%*
Nodular regenerative hyperplasia	*1*	*0*	*0*	*1*	*0.3%*
De novo disease	**4**	**0**	**0**	**4**	**1%**
Hepatitis B	*1*	*0*	*0*	*1*	*0.3%*
Hepatitis C	*1*	*0*	*0*	*1*	*0.3%*
Hepatitis D	*1*	*0*	*0*	*1*	*0.3%*
Hepatocellular cancer	*1*	*0*	*0*	*1*	*0.3%*
Other	**4**	**0**	**0**	**4**	**1%**
Donor derived malignancy	*3*	*0*	*0*	*3*	*0.8%*
Acute hepatic failure - Drug related: interferon	*1*	*0*	*0*	*1*	*0.3%*
Total	**353**	**33**	**2**	**388**	**100%**

Forty-six percent of graft failures occurred within the first six months' post-transplant (14.9% 0 – 7 days, 13.7% day 8 to less than 1 month, 17.0% 1 month to less than 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 less than 6 months (Figure 88). Recurrent disease was the leading cause of graft failure after five years post-transplant.

Figure 88. Adult time to graft failure by reason for retransplantation

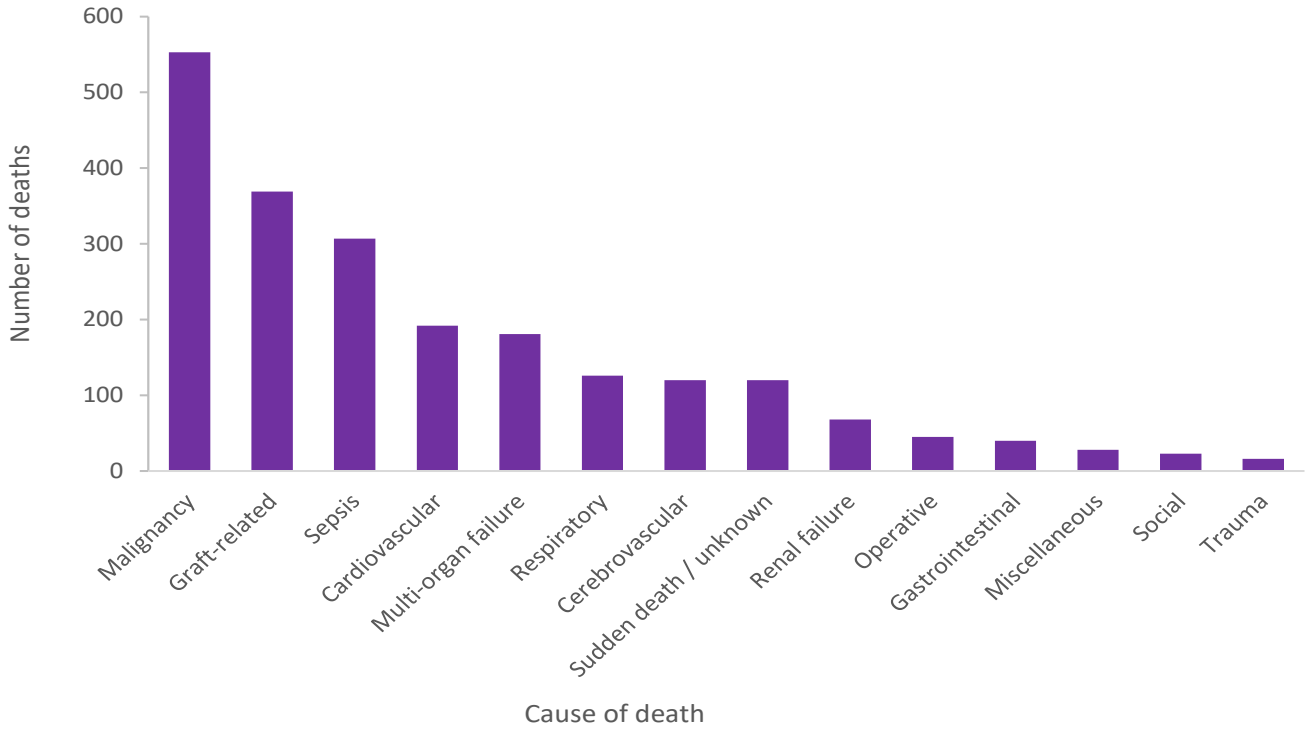


17 Cause of Patient Death

17.1 Cause of Death – All Patients

2,188 liver transplant patients (193 children and 1,995 adults based on age group at first transplant) have died. The commonest causes of death were malignancy (25.3%), graft-related causes (16.9%), sepsis (14.0%), cardiovascular disease (8.8%) and multi-organ failure (8.3%, Figure 89, Table 64).

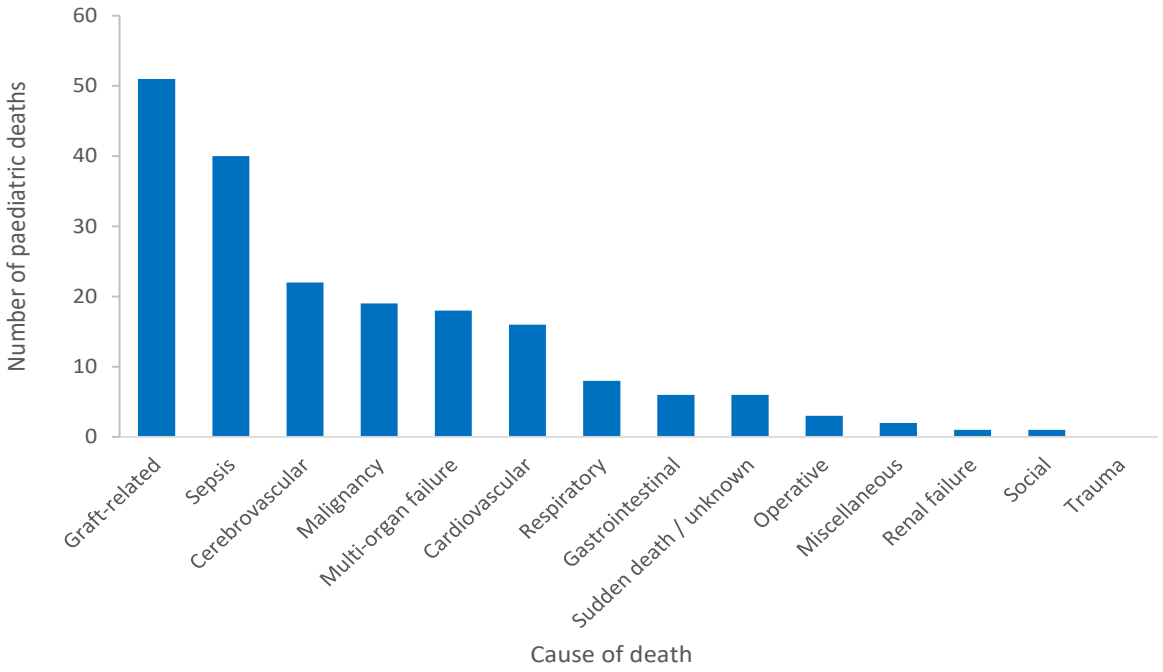
Figure 89. Cause of death by categories



17.2 Paediatric Patients - Cause of Death

Graft-related causes (26.4%) are the leading cause of death in children, with sepsis being the cause of death in a further 20.7% of paediatric patients (Figure 90, Table 64).

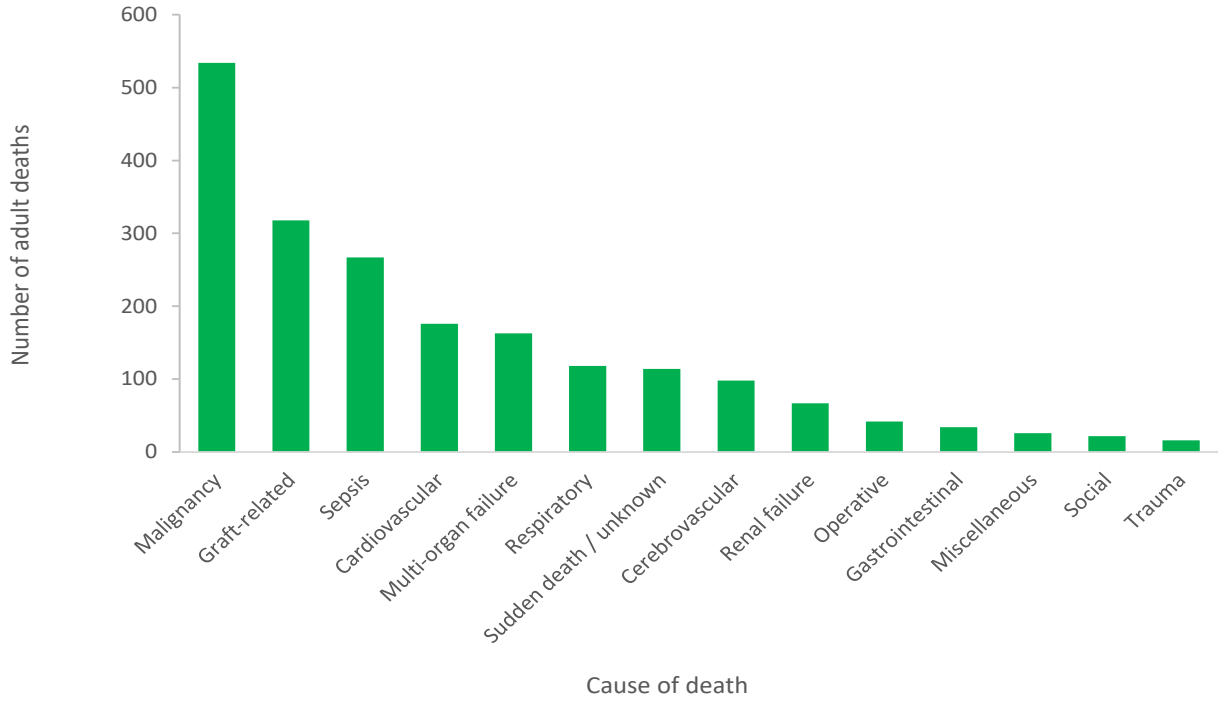
Figure 90. Paediatric cause of death



17.3 Adult Patients – Cause of Death

Malignancy (26.8% total: de novo malignancy 14.6%; recurrent malignancy 12.0%; donor transmitted malignancy 0.2%) is the most frequent cause of death in adult patients. Graft-related causes (15.9%) and sepsis (13.4%) are the next largest categories of adult deaths (Figure 91, Table 64).

Figure 91. Adult cause of death



17.4 Cause of Death Types by Age Group

Table 64. Cause of death by age group

Cause of death	Children	Adults	Total deaths	% of all deaths
Malignancy	**19**	**534**	**553**	**25%**
De novo malignancy	11	293	304	14%
Recurrent malignancy	8	238	246	11%
Donor transmitted malignancy	0	3	3	0.1%
Graft-related	**51**	**318**	**369**	**17%**
Other graft related	41	148	189	9%
- Rejection	*18*	*80*	*98*	*4%*
- Primary non-function / dysfunction	*6*	*22*	*28*	*1%*
- Biliary complications	*3*	*18*	*21*	*1.0%*
- Graft vs host disease	*0*	*10*	*10*	*0.5%*
- Late graft failure	*0*	*10*	*10*	*0.5%*
- Unspecified	*2*	*3*	*5*	*0.2%*
- Hepatitis	*4*	*0*	*4*	*0.2%*
- Massive haemorrhagic necrosis	*4*	*0*	*4*	*0.2%*
- Non-thrombotic infarction	*3*	*1*	*4*	*0.2%*
- De novo hepatitis C	*0*	*2*	*2*	*0.09%*
- Hepato-renal syndrome	*0*	*1*	*1*	*0.05%*
- Portopulmonary hypertension	*0*	*1*	*1*	*0.05%*
- Post necrotic cirrhosis	*1*	*0*	*1*	*0.05%*
Disease recurrence	0	151	151	7%
- Hepatitis C	*0*	*96*	*96*	*4%*
- Hepatitis B	*0*	*19*	*19*	*0.9%*
- Alcohol-related cirrhosis	*0*	*12*	*12*	*0.5%*
- Primary sclerosing cholangitis	*0*	*10*	*10*	*0.5%*
- Autoimmune hepatitis	*0*	*4*	*4*	*0.2%*
- Primary biliary cirrhosis	*0*	*4*	*4*	*0.2%*
- NASH	*0*	*3*	*3*	*0.1%*
- Progressive familial amyloid polyneuropathy	*0*	*2*	*2*	*0.09%*
- Erythropoietic protoporphyria	*0*	*1*	*1*	*0.05%*
Vascular complications	10	19	29	1%
- Hepatic artery thrombosis	*6*	*9*	*15*	*0.7%*
- Portal vein thrombosis	*2*	*10*	*12*	*0.5%*
- Hepatic vein thrombosis	*1*	*0*	*1*	*0.05%*
- Inferior vena cava thrombosis	*1*	*0*	*1*	*0.05%*
Sepsis	**40**	**267**	**307**	**14%**
Bacterial	16	109	125	6%
Fungal	7	48	55	3%
Unspecified infection	6	48	54	2%
Viral	6	33	39	2%
Mixed	5	29	34	2%
Cardiovascular	**16**	**176**	**192**	**9%**
Multi-organ failure	**18**	**163**	**181**	**8%**
Respiratory	**8**	**118**	**126**	**6%**
Cerebrovascular	**22**	**98**	**120**	**5%**
Sudden death / unknown	**6**	**114**	**120**	**5%**
Renal failure	**1**	**67**	**68**	**3%**
Operative	**3**	**42**	**45**	**2%**
Gastrointestinal	**6**	**34**	**40**	**2%**
Miscellaneous	**2**	**26**	**28**	**1%**

(table continued on next page)

Cause of death	Children	Adults	Total deaths	% of all deaths
Neurological	0	7	7	0.3%
Haematological	1	4	5	0.2%
Dementia	0	5	5	0.2%
Old age	0	5	5	0.2%
Metabolic	1	2	3	0.1%
Allergy	0	1	1	0.05%
Donor transferred OTC deficiency	0	1	1	0.05%
Veno-occlusive disease	0	1	1	0.05%
Social	**1**	**22**	**23**	**1%**
Treatment withdrawal	0	9	9	0.4%
Suicide	0	7	7	0.3%
Non-compliance immunosupportive therapy	1	3	4	0.2%
Overdose / Substance abuse	0	3	3	0.1%
Trauma	**0**	**16**	**16**	**1%**
Motor vehicle accident	0	8	8	0.4%
Other accident excluding MVA	0	6	6	0.3%
Homicide	0	2	2	0.09%
Total	**193**	**1995**	**2188**	

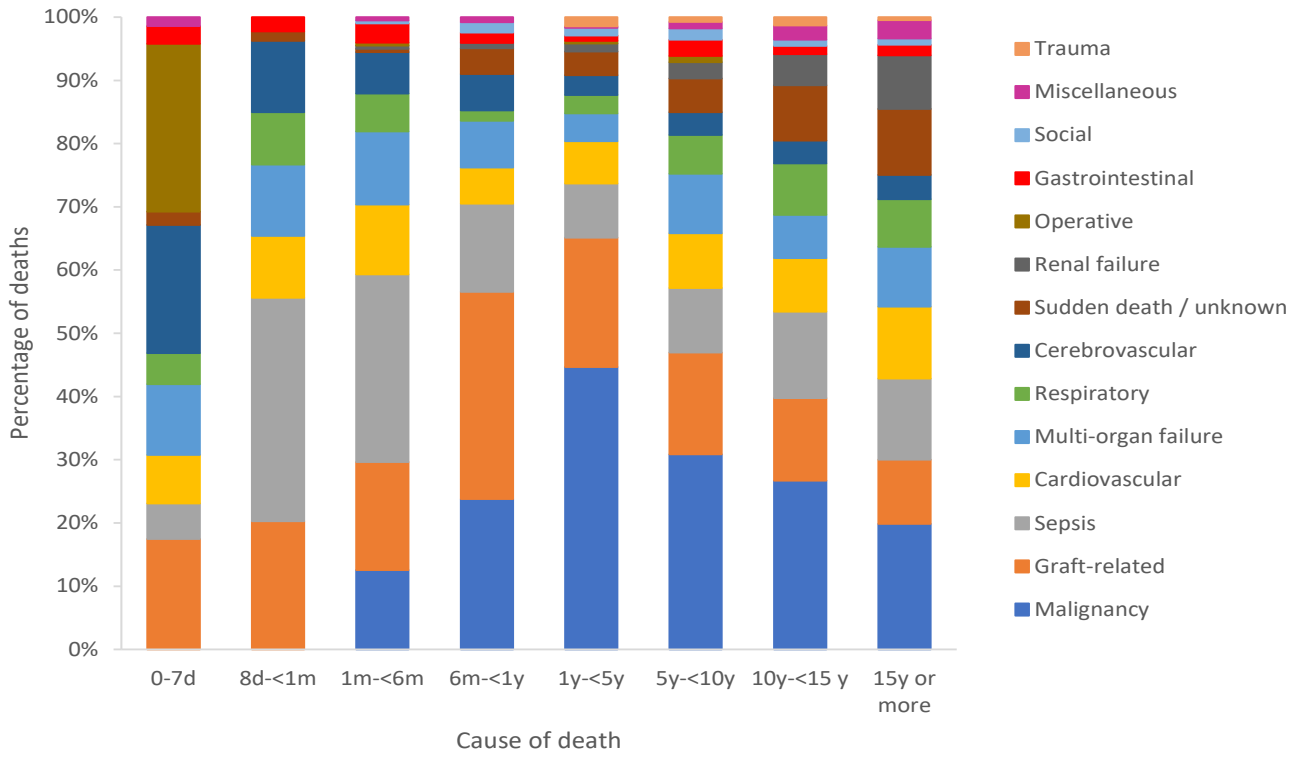
Abbreviations: MVA, motor vehicle accident; NASH, non-alcoholic steatohepatitis; OTC, Ornithine transcarbamylase

17.5 Cause of Death by Time to Death

Just under one third of post-transplant deaths occurred within the first year of transplant (6.5% in the first 7 days, 6.1% from day 8 to the end of the first month and 14.7% after the first month and before the end of the first year), nearly 40% between 1 and 10 years (21.9% between years 1 and 5 and 17.9% between years 5 and 10) and just under one third (32.9%) after 10 years.

The cause of death profile changes over the different post-transplant time periods (Figure 92). 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 92. Cause of death by time to death post-transplant – all patients

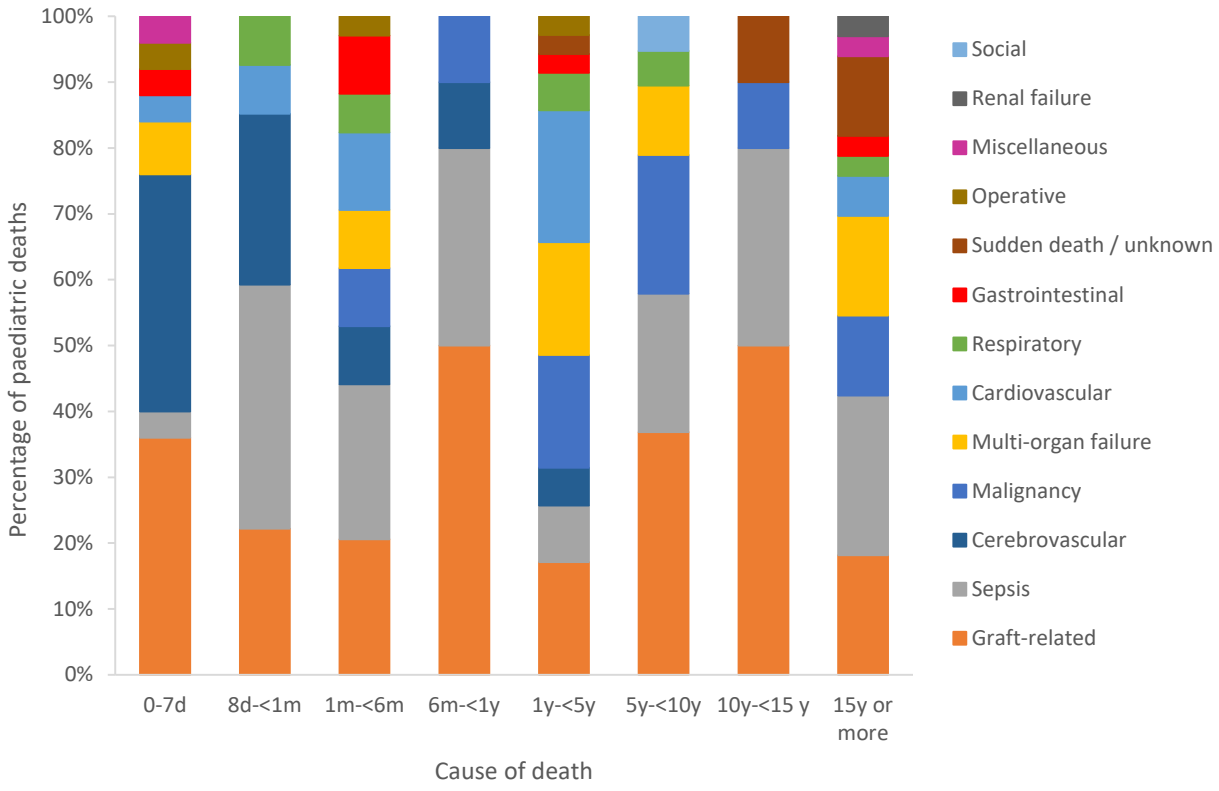


17.6 Paediatric Cause of Death by Time to Death

In children, 49.7% of deaths occurred within the first year of transplant (13.0% in the first 7 days, 14.0% from day 8 to the end of the first month and 22.8% after the first month and before the end of the first year), 18.1% between years 1 and 5, 9.8% between years 5 and 10 and 22.3% after 10 years.

Cerebrovascular and graft-related causes of death predominated in the first week post-transplant (Figure 93). 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 93. Paediatric cause of death by time to death post-transplant

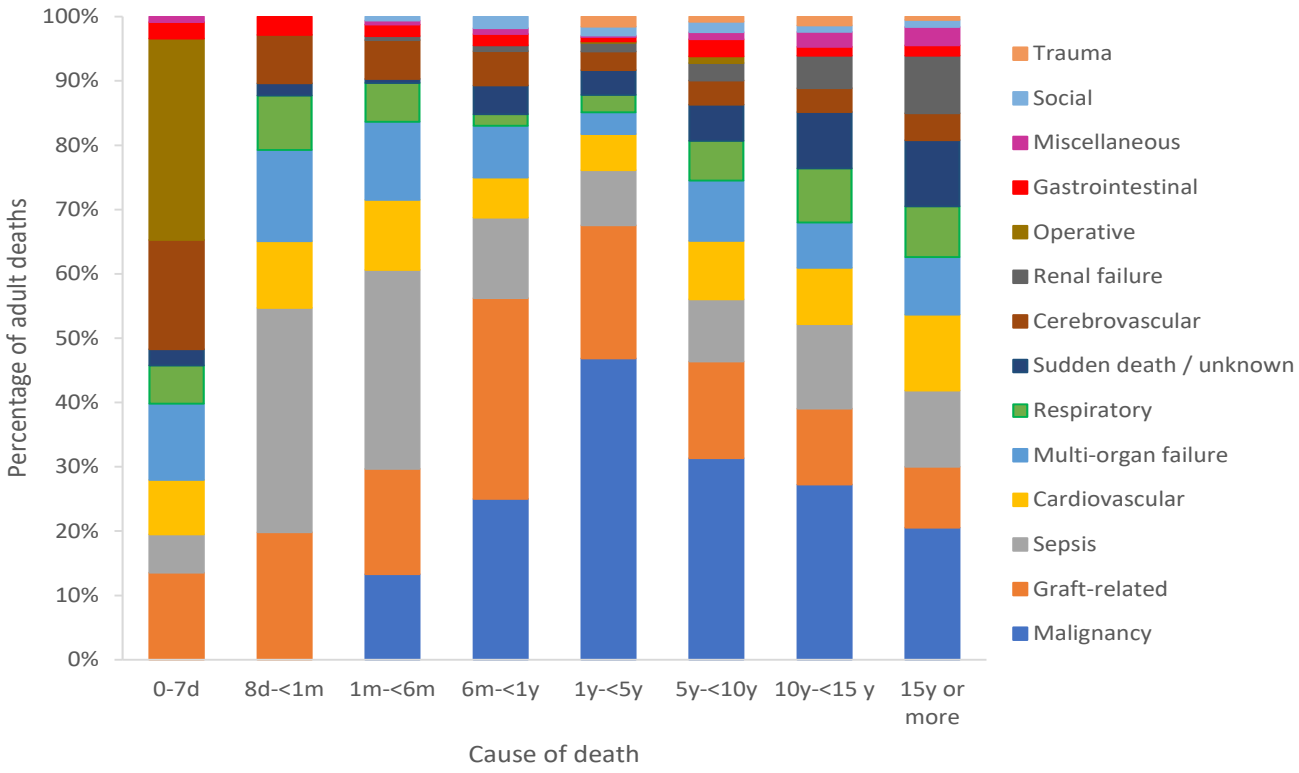


17.7 Adult Cause of Death by Time to Death

In adults, 25.1% of deaths occurred within the first year of transplant (5.9% in the first 7 days, 5.3% from day 8 to the end of the first month and 13.9% after the first month and before the end of the first year), 22.3% between years 1 and 5, 18.7% between years 5 and 10 and 33.9% after 10 years.

Operative, cerebrovascular and graft-related causes and multi-organ failure were prominent in the first week post-transplant (Figure 94). Sepsis was the predominant cause from 8 days to 6 months and malignancy and graft-related causes from 6 months.

Figure 94. Adult cause of death by time to death post-transplant



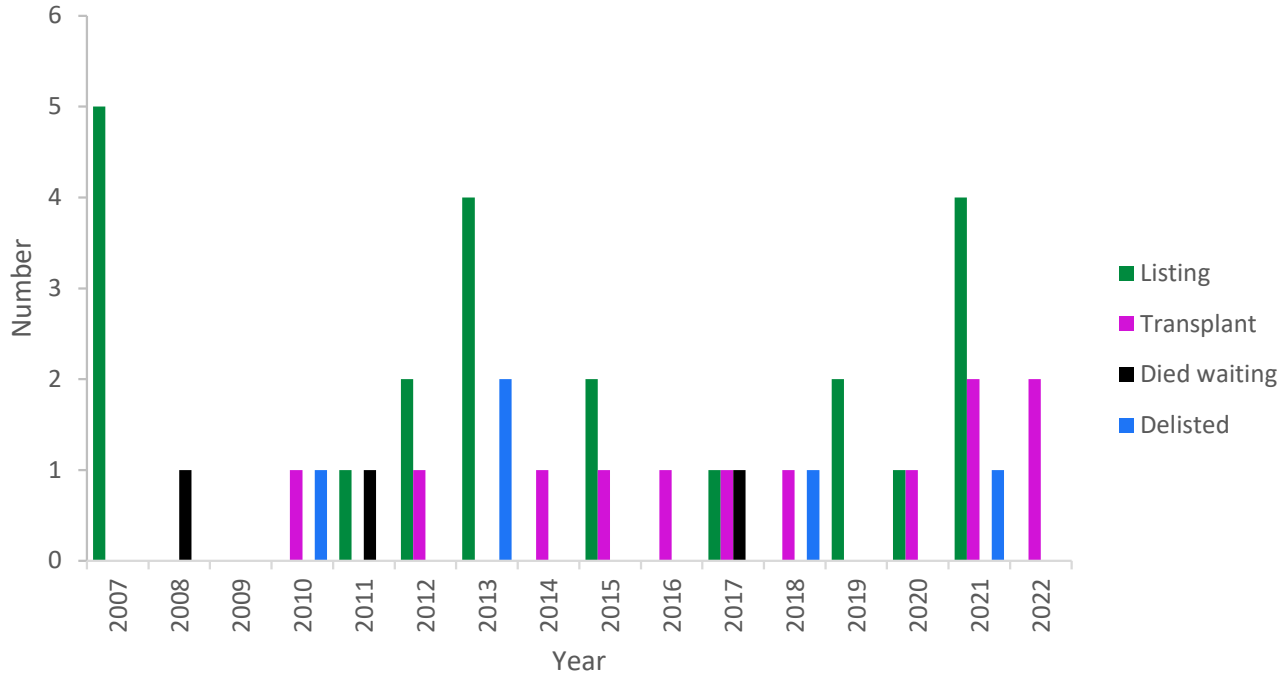
18 Intestinal Transplantation

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

18.1 Waiting List

Twenty-one patients have been listed for intestinal transplantation, with one patient relisted in 2019, six years after initial delisting without transplant (22 listings, see Figure 95). Twelve patients were transplanted, three died waiting, four were delisted without relisting and two were still waiting at the end of 2022.

Figure 95. Waiting list trends over time for intestinal transplantation



18.2 Demographic Characteristics and Diagnoses

The demographic characteristics and diagnoses of patients listed for intestinal transplantation and for those transplanted are shown in Table 65. The majority of the eight children listed had short bowel syndrome due to gastroschisis, whilst the 13 adults were listed for short bowel syndrome after intestinal resection for a variety of causes, motor disorders and liver failure with porto-mesenteric thrombosis. Five children have been transplanted, three for short bowel syndrome, one for chronic idiopathic intestinal pseudo-obstruction and one for Hirschsprung's disease. Seven adults have been transplanted, three for short bowel syndrome, one for chronic idiopathic intestinal pseudo-obstruction, one for Hirschsprung's disease, one for hollow visceral myopathy and one for liver failure with porto-mesenteric thrombosis.

Table 65. 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	8	13	5	7
Age	8 (4-15)	43 (22-60)	10 (5-13)	32 (24-54)
Gender				
Male	4	10	3	5
Female	4	3	2	2
Diagnosis				
Short bowel syndrome				
- Gastroschisis	5	0	3	0
- Intra-abdominal desmoid tumour	0	2	0	2
- Small intestine leiomyoma	0	1	0	0
- Small intestine adenocarcinoma	0	1	0	0
- Volvulus	0	1	0	1
Motor disorder				
- Chronic idiopathic intestinal pseudo-obstruction	2	2	1	1
- Hirschsprung's disease and variants	1	1	1	1
- Hollow visceral myopathy	0	1	0	1
Other				
- Liver failure with porto-mesenteric thrombosis	0	4	0	1

18.3 Organs Transplanted

Nine of the twelve recipients receiving a small intestine transplant also received a liver graft.

Table 66. Organs transplanted with intestinal transplants

Transplanted Organ	Children	Adults	Total transplants
Small intestine, stomach, pancreas, colon	0	1	1
Small intestine, liver, stomach, pancreas	1	1	2
Small intestine, liver, pancreas	2	3	5
Small intestine, liver, pancreas, colon	1	0	1
Small intestine, liver, pancreas, kidney	0	1	1
Small intestine, colon	1	0	1
Small intestine, kidney	0	1	1
Total	**5**	**7**	**12**

18.4 Intestinal Patient Survival

Nine of the twelve intestinal transplant recipients are alive with a functioning graft and full enteral autonomy. The intestinal graft has failed for one patient who is alive and supported by total parenteral nutrition (liver and pancreas grafts functioning). Two patients died with a functioning graft, one from respiratory infection at 3 months and one from complications of cardiac surgery at 3.5 years post-transplant. The 1- and 3-year patient survival are 91.7% and the 5- and 10-year patient survival are 76.4% (Figure 96, Table 67).

Figure 96. Patient survival after intestinal transplantation

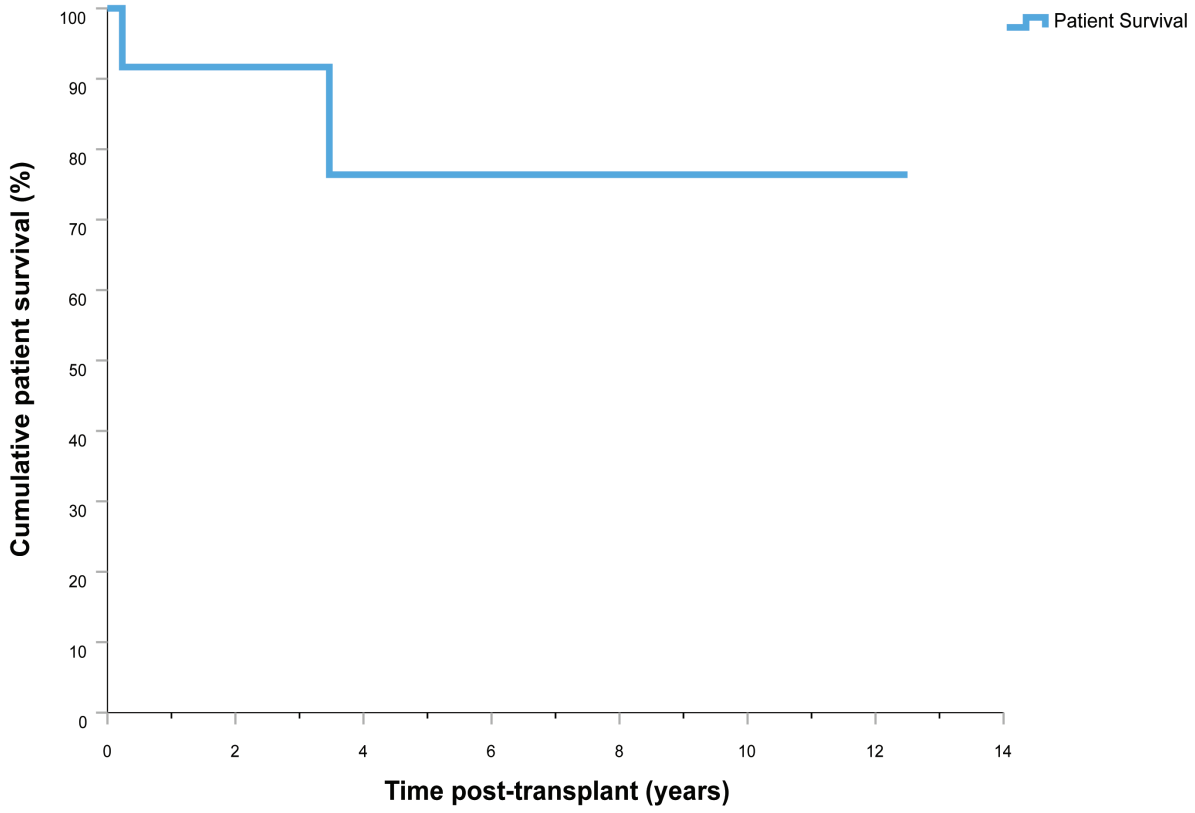


Table 67. Intestinal patient survival

Patient Survival	Time post-transplant (years)					
	0	1	3	5	10	15
No. at risk	12	9	6	4	2	0
Survival (%)		92%	92%	76%	76%	

18.5 Intestinal Graft Survival

The 1- and 3-year graft survival are 83.3% and the 5- and 10-year graft survival are 69.4% (Figure 97, Table 68).

Figure 97. Graft survival after intestinal transplantation

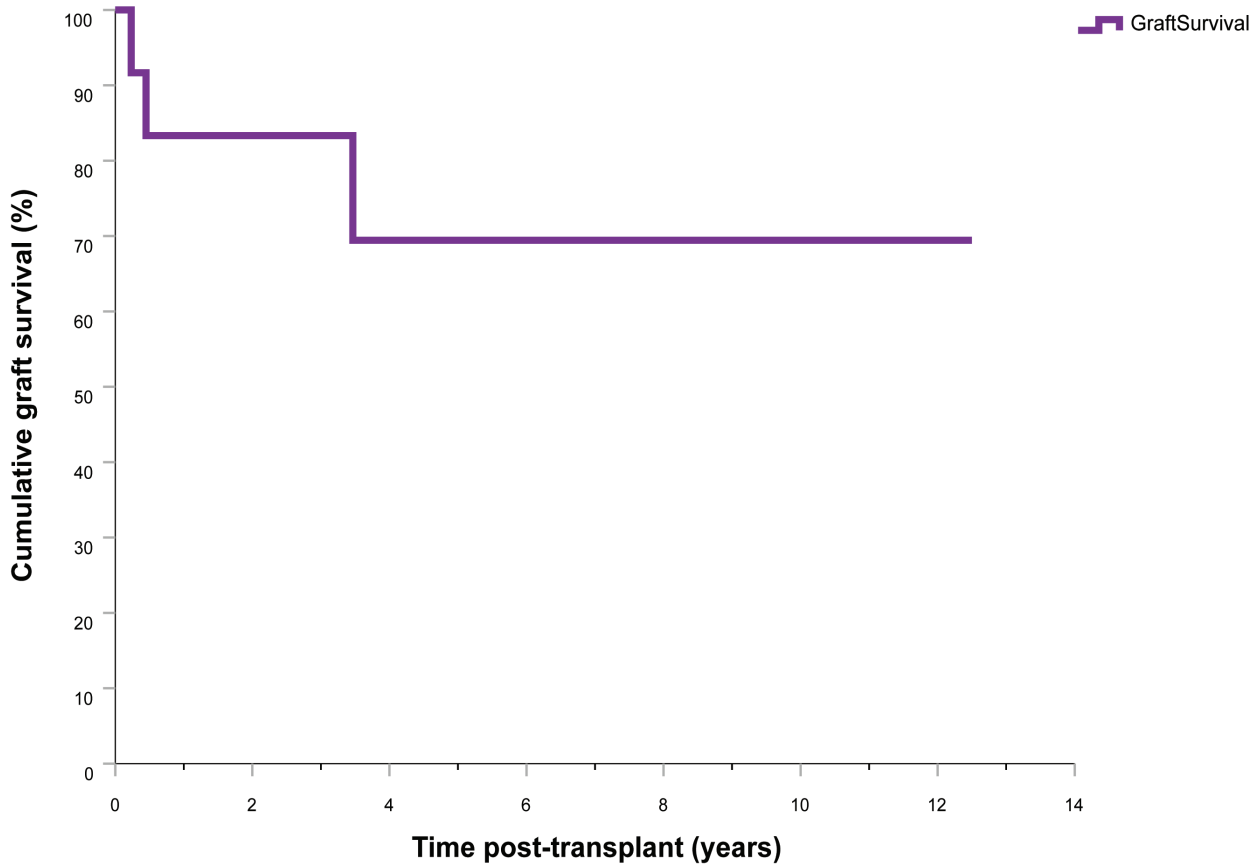


Table 68. Intestinal graft survival

Graft Survival	Time post-transplant (years)					
	0	1	3	5	10	15
No. at risk	12	9	6	4	2	0
Survival (%)		83%	83%	69%	69%	

19 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 attached to a ventilator. They have a very high risk of dying without a liver transplant. Because of this, any available 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 the removal of the organ from the ice bath prior to implantation
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 organ/s (liver or part of their liver and/or intestine) 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 transplantation (liver transplantation in this case) 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 date of last contact or end of the reporting year (31 December, 2022 for this report), whichever occurred first, for patients who have not been retransplanted or died by that date.

Graft number	The number of liver transplants the patient has previously undergone plus one. 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 (scarring of the liver) and liver cancer. There are now very effective drugs that can cure the virus but some patients still have cirrhosis 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. This can lead to intestinal failure and require intestinal transplantation.
Hollow visceral myopathy	A rare condition affecting the muscles in the wall of the bowel and sometimes the urinary tract. This can lead to intestinal failure and require intestinal transplantation.
Hypothermic Oxygenated Perfusion (HOPE)	A process of supporting a liver on a machine that perfuses the organ with oxygenated blood at low temperature. This can enable assessment of liver function prior to transplantation, might improve early liver function after transplantation and can enable delay of transplantation for logistical reasons, such as when there are simultaneous donors.
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. A quarter of cases will be below the lower end of the interquartile range and a quarter of cases will be above the upper end of the interquartile range.
Kaplan-Meier survival curve	The survival rate (for example, patient or graft survival) of a group of patients over time (for example, after transplantation) can be displayed in a graph that has the proportion or percentage surviving on the Y (vertical) axis and time on the X (horizontal) 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 or intestinal 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 places with a reasonable deceased donor rate, such as 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.
Normothermic Machine Perfusion (NMP)	A process of supporting a liver on a machine that perfuses the organ with oxygenated blood at body temperature. This can enable assessment of liver function prior to transplantation, might improve early liver function after transplantation and can enable delay of transplantation for logistical reasons, such as when there are simultaneous donors.
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 < 0.05 (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 date of last contact or end of the reporting year (31 December 2022 for this report), whichever occurred first, 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 and/or intestine 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 and/or intestinal 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 transplantation to delisting (in the case of liver waiting time to transplantation, this the time from listing for liver transplantation to the liver 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.

20 Appendix II. Publications utilising ANZLITR data

20.1 Publications in 2022

Expansion of Liver Transplantation Criteria for Hepatocellular Carcinoma from Milan to UCSF in Australia and New Zealand and Justification for Metroticket 2.0

Barreto SG, Strasser SI, McCaughan GW, Fink MA, Jones R, McCall J, Munn S, Macdonald GA, Hodgkinson P, Jeffrey GP, Jaques B, Crawford M, Brooke-Smith ME and Chen JW. Cancers (Basel) 2022 Jun 3;14(11):2777. doi: 10.3390/cancers14112777.

Turning the Tide on Hepatitis C Virus-Related Liver Transplantation: The Return on Investment in Hepatitis C Virus Treatment in Australia and New Zealand.

Howell J, Majumdar A, Fink MA, Byrne M, McCaughan G, Strasser SI, Crawford M, Hodgkinson P, Stuart KA, Tallis C, Chen J, Wigg A, Jones R, Jaques B, Jeffrey G, Adams L, Wallace MC, Munn S, Gane E, Thompson AJ, Gow P. Liver Transpl. 2022 Feb;28(2):236-246. doi: 10.1002/lt.26329. Epub 2021 Nov 10.

20.2 Publications in 2021

Predicting recurrence of hepatocellular carcinoma after liver transplantation using a novel model that incorporates tumor and donor-related factors.

Orci LA, Combescure C, Fink M, Oldani G, Compagnon P, Andres A, Berney T, Toso C. Transpl Int 2021; 34: 2875–2886.

Trends and Outcomes in Simultaneous Liver and Kidney Transplantation in Australia and New Zealand.

Drak D, Tangirala N, Fink M, Adams LA, Fawcett J, Jeffrey GP, Byrne M, McCaughan G, Chadban S, Wyburn K, Wong G, Lim WH, Gracey DM. Transplant Proc. Jan-Feb 2021;53(1):136-140.

20.3 Publications in 2020

Outcomes for children after second liver transplantations are similar to those after first transplantations: a binational registry analysis.

Jeffrey AW, Jeffrey GP, Stormon M, Thomas G, O'Loughlin E, Shun A, Hardikar W, Jones R, McCall J, Evans H, Starkey G, Hodgkinson P, Ee LC, Moore D, Mews C, McCaughan GW, Angus PW, Wigg AJ, Crawford M, Fawcett J. Med J Aust 2020; 213 (10): 464-470.

Paediatric liver transplantation in Australia and New Zealand: 1985-2018.

Stormon MO, Hardikar W, Evans HM, Hodgkinson P. 1985-2018. Journal Paediatrics and Child Health 2020 Nov;56(11):1739-1746.

20.4 Publications in 2019

Increasing incidence of nonalcoholic steatohepatitis as an indication for liver transplantation in Australia and New Zealand.

Calzadilla-Bertot L, Jeffrey GP, 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 LA. 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.

Jeffrey AW, Delriviere L, McCaughan G, Crawford M, Angus P, Jones R, Macdonald GA, Fawcett J, Wigg A, Chen J, Gane E, Munn S and Jeffrey GP. 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.

20.5 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, Allen RDM, Hawthorne WJ, Pleass HC. Liver Transplantation. 24(11):1536-1544, 2018 11.

20.6 Publications in 2016 and earlier

Additive impact of pre-liver transplant metabolic factors on survival post-liver transplant.
Adams LA, Arauz O, Angus PW, Sinclair M, MacDonald GA, Chelvaratnam U, Wigg AJ, Yeap S, Shackel N, Lin L, Raftopoulos S, McCaughan GW, Jeffrey GP, 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.
Lau SY, Woodman RJ, Silva MF, Muller K, Libby L, Chen JW, Padbury R, Wigg AJ. 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.

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.

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.

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 AE, Meagher NS, McCaughan GW, Keogh AM, Vajdic CM, 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.

Minimal but significant improvement in survival for non-hepatitis C-related adult liver transplant patients beyond the one-year posttransplant mark.
McCaughan GW, Shackel NA, Strasser SI, Dilworth P, Tang P for Australian and New Zealand Liver Transplant Study Group. Liver Transplantation 16: 130-137, 2010.

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.
Chen JWC, Know L, Verran DJ, McCall JL, Munn S, Balderson GA, Fawcett JW, Gow PJ, Jones RM, Jeffrey GP, House AK, Strasser SI. HPB 2009, 11, 81–89.

The epidemiology of hepatitis C in Australia: Notifications, treatment uptake and liver transplantations, 1997–2006.
Gidding HF, Topp L, Middleton M, Robinson K, Hellard M, McCaughan G, Maher L, Kaldor JM, Dore GJ and Law MG. 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.

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