1984-2017

Catalan Liver Transplant Registry

Statistical Report

Generalitat de Catalunya
Departament de Salut

OCATT
Organització Catalana de Trasplantaments

Catalan Liver Transplant Registry

Statistical Report 1984-2017

Notifying centers

Hospital Universitari de Bellvitge
Hospital Clínic de Barcelona
Hospital Universitari General Vall d'Hebron
Hospital Universitari Maternoinfantil Valld'Hebron

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Introduction

In 1984, the first liver transplant in Catalonia and Spain was performed in Bellvitge University hospital, in 1985, Vall d'Hebron Children's Hospital began work in this field and Vall d'Hebron General Hospital and Hospital Clínic were authorized in 1988.

The Catalan Liver Transplant Registry (RTHC) began operation in 1994 and contains data on the transplants carried out in Catalonia since 1984, the data on transplants performed between 1984 and 1993 were collected retrospectively. The registry has collected data periodically and systematically since 1994.

In accordance with its objectives, the registry responds to the information requirements of the Catalan Health Service (Servei Català de la Salut) and of the Catalan Department of Health for planning and managing resources and purchasing services, the registry is also a source of information that can be accessed by professionals working in the field of health care and also serves demand from other areas, in all cases, release of data from RTHC is subject to the current legislation on the treatment and use of personal data.

Obtaining this body of information is proof of the results that can be achieved from collaboration between health care professionals and the authorities in order to develop and consolidate instruments that allow health care and service policies to be made effective.

The main objective of this document is to publicise the activity, characteristics and results of the liver transplants carried out in Catalonia between 1984 and 2017, both for the professionals directly involved in this treatment and for the health care authorities.

Methodological Aspects and Definitions

The report is divided into three sections: the first section provides a brief descriptive analysis of the evolution of liver transplants in Catalonia using global data from the registry; the second and third sections provide specific data for adults and children.

The last two sections analyse the characteristics of the recipients, donors, transplants and results obtained, recipient characteristics include patient data at the time of the first transplant, thereby excluding patients who received their first transplant outside Catalonia (also excluded are adults who received their first transplant as children) and who received a retransplant in Catalonia.

The same classification of indication and causes of failure and death have been used as in previous reports, the 2002-2003 report, available from the OCATT website, describes in detail the codes for disease and failure included in each of the categories.

Patient survival (time until death) and graft survival (time until graft failure or patient death), were calculated using the Kaplan- Meier method and the level of statistical significance between the different curves was determined using the Log-rank test, survival curves were interrupted when the number of cases was below 10 and patients who, previously or subsequently, underwent a transplant in another hospital were excluded.

The probability of receiving a transplant was calculated taking into account a model of competitive risks with three events of interest: transplant, death and removal from the waiting list.

Description of indicators:

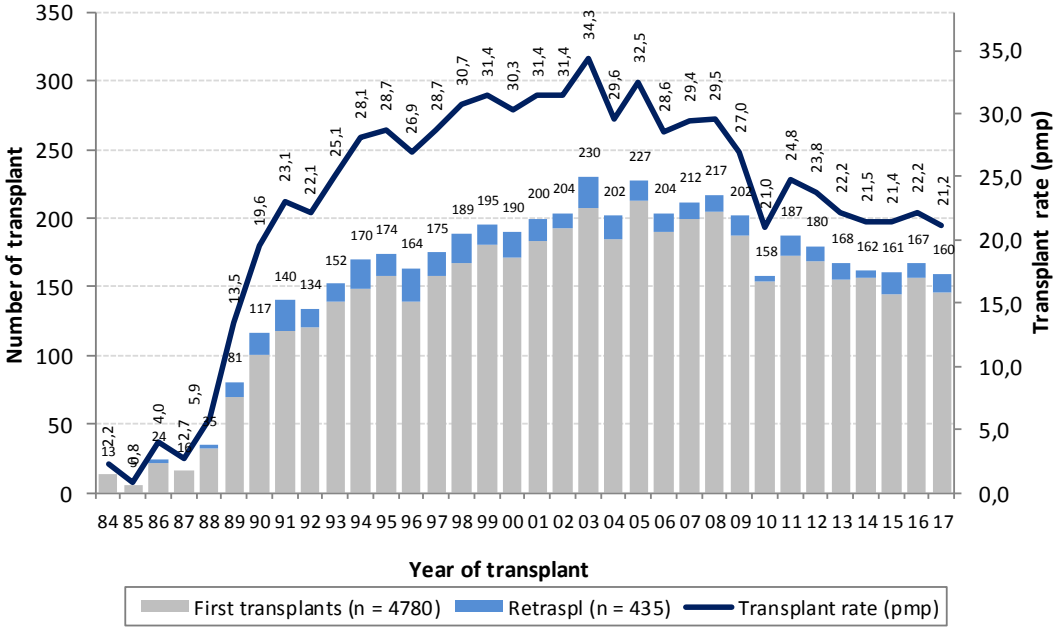
Annual rate of liver transplants in Catalonia
Total number of transplants performed in a year in authorized hospitals, independently of place of residence of recipient and origin of donor with respect to the population of Catalonia (population census of 1991 and 1996, and annual census updates from 1997 onward Instituto Nacional de Estadística), figures per million population (pmp).

Evolution of Liver Transplants

In Catalonia, a total of 5215 liver transplants were carried out on 4785 patients (435 were retransplants) between 1984 and 2017. Whereas in 2017, a total of 160 transplants were carried out (14 retransplants).

The annual evolution of the number of liver transplants has shown a growing trend (Figure 1), to stabilize at 200 annual transplants, but a decreasing tendency in recent years. During the last year seven less transplants has been performed than previous year.

Figure 1. Annual Evolution of Number of Transplants and Rate of Liver Transplants, 1984-2017



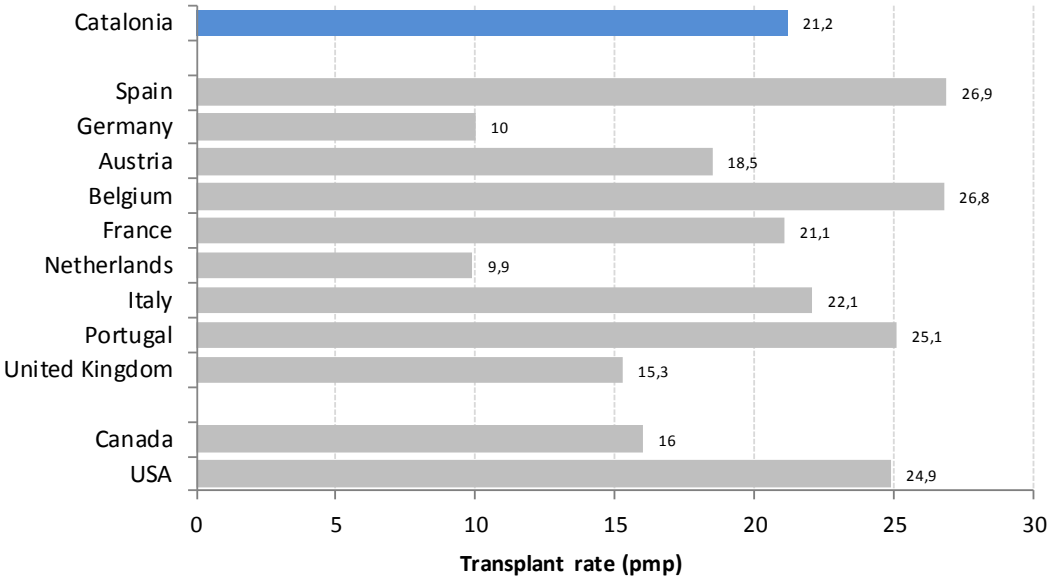
Number of transplants = 5215

The same trend can be seen in the annual rate of liver transplant (Figure 1), which reached 21.2 transplants per million population (pmp) in 2017, the rate vary considerably among countries (Figure 2).

These data should be interpreted taking into account the different factors that affect the transplant workload in each country, such as the health care system, indication criteria, population structure and cultural aspects.

A total of 86.0% (4117) of patients who underwent transplant were residents in Catalonia, 13.0% (621) were resident in the rest of Spain and 0.8% (37) were from abroad. This information was not available for 10 patients.

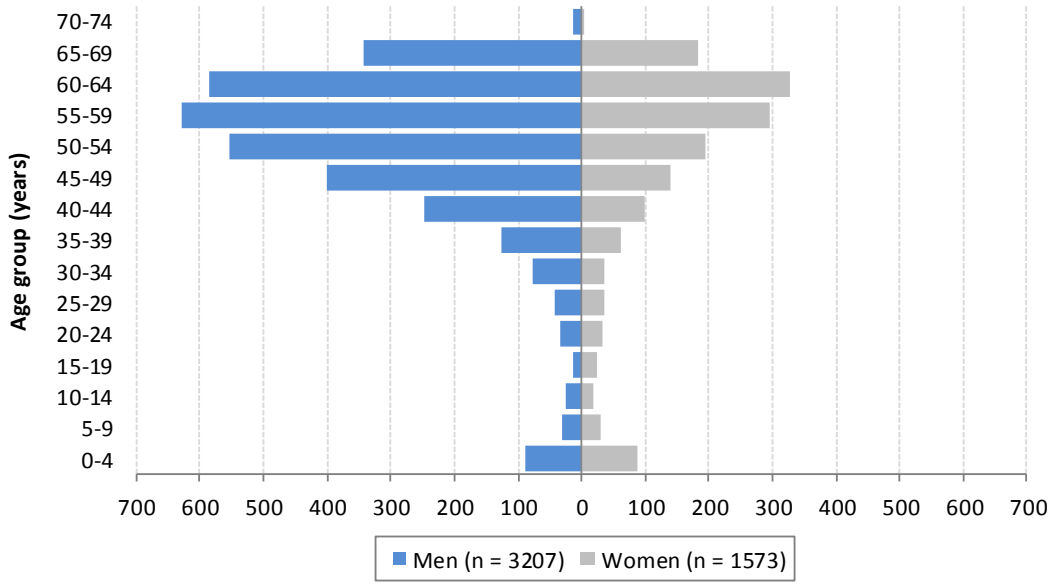
Figure 2. Liver Transplant Rates in Different Countries, 2017



Source: *Newsletter Transplant*. International Figures on Organ Donation and Transplantation - 2017. 2018. Vol. 23.

Of the 5215 transplants carried out in Catalonia throughout the entire period, 4888 were performed in adult patients (4499) and 327 were performed in paediatric patients (287). In 2017, 150 transplants were carried out on adults and 10 on children.

Figure 3. Number of Patients who Received Liver Transplants by Age Group and Sex. 1984-2017

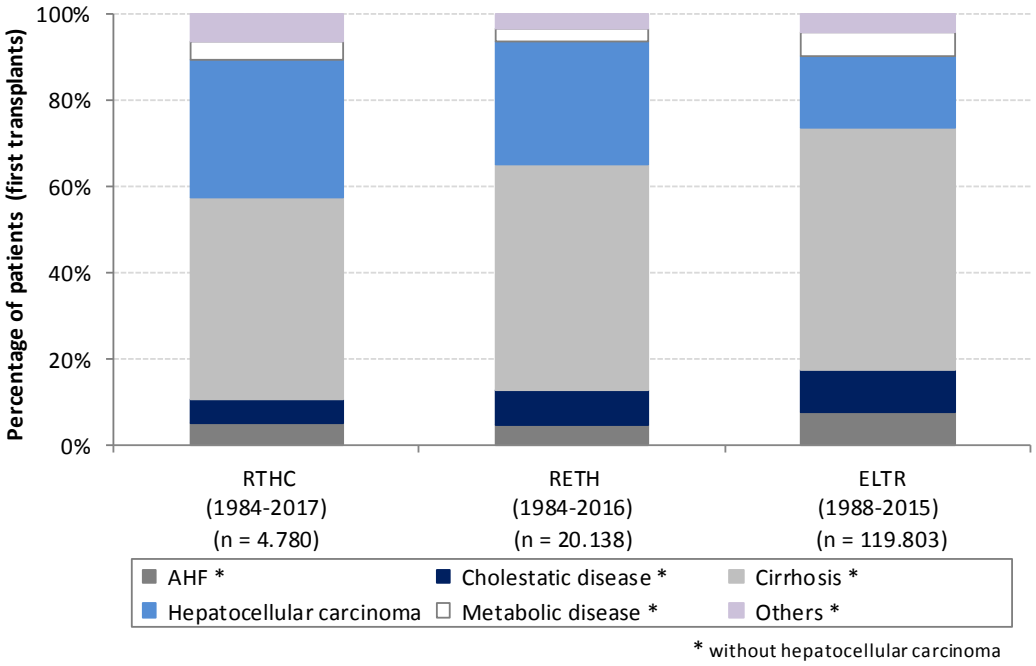


Number of patients (first transplants) = 4780

The mean age of patients who received a first liver transplant was 50 years and the median was 54 years (SD, 15.6 y; range, 0-73 y). The age group with the highest number of cases was the 55-59 years group (Figure 3), which represents 19,4% of all patients. In 2017, patients over the age of 60 years represented 30.8% of patients; this figure was 11.6% in 1992. Overall, this group represents 26.7% of patients who received a first transplant.

Differences can be seen in the distribution of the indications in different areas in our region, which may be due to different inclusion criteria for patients on the waiting list and to differences in the way the data is processed (Figure 4). For example, in the case of the European registry (ELTR), the category of tumours includes hepatocellular carcinomas and other liver cancers, whereas the Spanish liver transplant registry (RETH) and the Catalan registry (RTHC) only includes hepatocellular carcinomas, with or without cirrhosis, in this category.

Figure 4. Indications of the First Liver Transplant in Patients of All Ages. Comparative Data From the European Registries (ELTR)[1], Spanish Registry (RETH)[2] and Catalan Registry (RTHC). 1984-2017

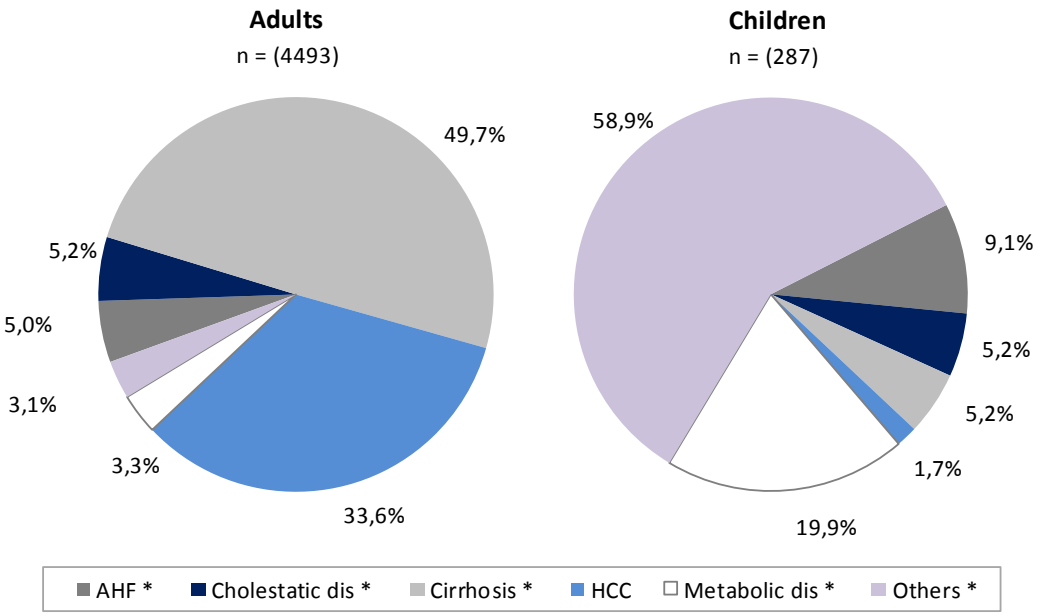


The most frequent indication in Catalonia is cirrhosis (47.0%), followed by hepatocellular carcinoma (31.7%), although there are differences according to recipient age (Figure 5). In paediatric patients, the most frequent indications are congenital biliary diseases, grouped in the “others” category.

Given the differences between the characteristics of the transplants performed in adult patients and in children, both in terms of indications and of the transplant itself and its course, the results obtained in each of these populations are analyzed separately.

[1] European Liver Transplant Registry 1988-2015 (available at: http://www.eltr.org)
[2] Spanish Liver Transplant Registry, annual Report of Results, 1984-2016 (available at: http://www.sethepatico.org).

Figure 5. Percentage of Patients who Received Liver Transplants by Principal Diagnosis and Age Group. 1984-2017



Number of patients (first transplants) = 4780

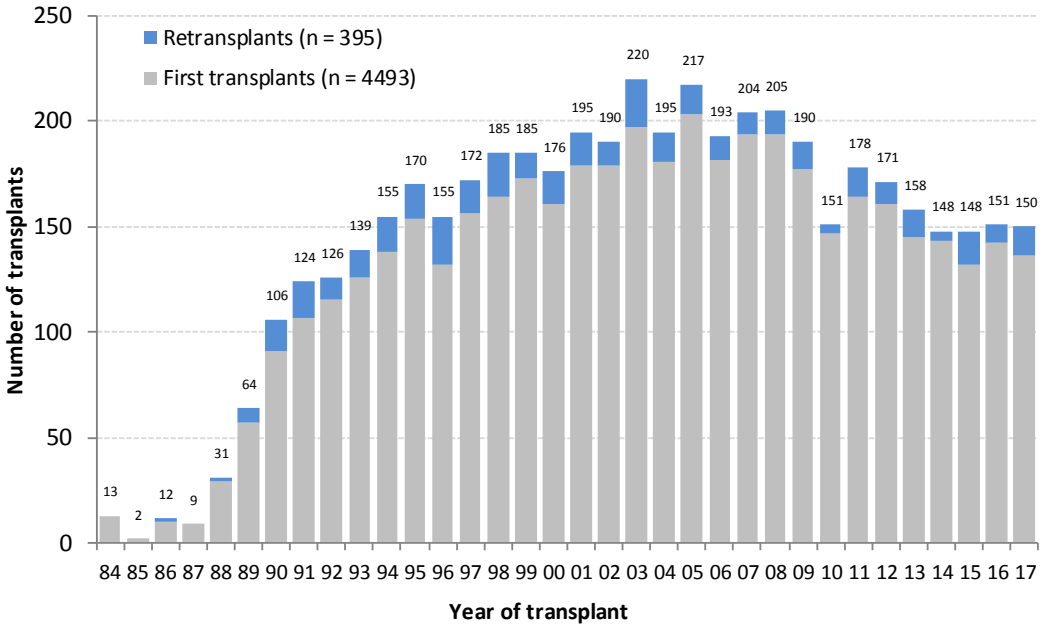
* without hepatocellular carcinoma

Liver Transplants in Adults

Of the 5215 transplants carried out in Catalonia throughout the 1984-2017 period, 4888 were performed in adult patients: 4493 first transplants and 395 retransplants. These transplants were carried out on 4499 patients; five patients received the first transplant outside Catalonia and one was not an adult when the first transplant was received (Figure 6).

In 2017, a total of 150 were performed in adult patients: 136 first transplants and 14 retransplants.

Figure 6. Evolution of Number of Liver Transplants: Adult Patients. 1984-2017



Number of transplants = 4888

Recipient Characteristics

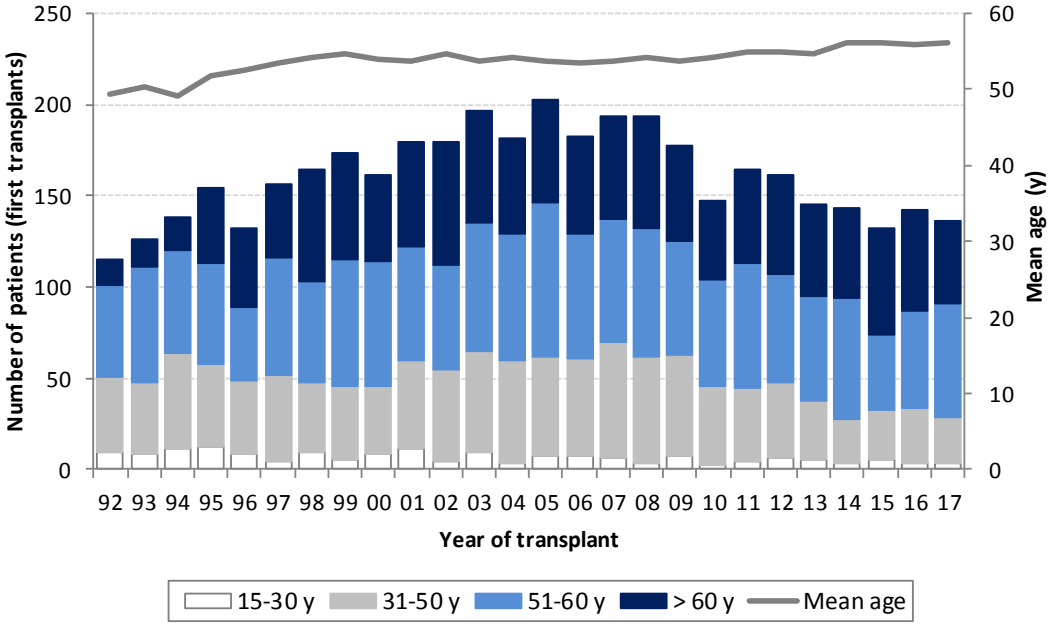
- **Sex and age**

Of the 4493 patients who received a first transplant in Catalonia during the 1984-2017 period, 3060 (68.1%) were men and 1433 (31.9%) were women. The proportion of women has decreased over the years and has gone from 44.0% in the 1984-1991 period to 25.8% in the 2012-2017 period. Specifically, in 2017, the proportion of women was 26.5%.

The mean age of patients who received a first liver transplant in the 1984-2017 period was 53 years, the median was 55 years and the maximum was 73 years.
The mean age has gone from 49.4 years in 1992 (range, 17-65 y; 95% CI, 47.3-51.5y) to 56.0 years in 2017 (range, 20-70 y; 95% CI, 54.5-57.6 y) (Figure 7), the early years show a progressive increase in the mean age, which stops in 1999, to stabilize at between 53 and 54 years.

With regard to distribution by age groups, the percentage of patients over 60 years of age has increased from 12.2% in 1992 to 33.1% in 2017.

Figure 7. Evolution of the Age of Patients who Received a First Liver Transplant: Adult Patients. 1992-2017



Number of patients (first transplants), 1992-2017 = 4175

♦ Indications

The indications are grouped into six categories: acute liver failure (ALF), cholestatic liver disease, cirrhosis (without hepatocellular carcinoma), hepatocellular carcinoma, metabolic disease and others, in accordance with the code recorded in the principal diagnosis. With the exception of patients with hepatocellular carcinoma, who were grouped in a separate category, the principal and secondary diagnoses were taken into account, although some cases may involve incidental tumours.

In the 1984-2017 period, almost three-quarters of transplanted patients (with a first transplant) belong to only two of these six groups: 49.7% presented cirrhosis (without hepatocellular carcinoma) and 33.6% presented hepatocellular carcinoma (Figure 8). These percentages are 42.6% and 42.6%, respectively, in the first transplants carried out in 2017.

Hepatocellular carcinomas are the indications that have most increased over the years and currently represent three times the percentage observed in 1992, although the trend has not grown throughout all of these years (Figure 9).

Figure 8. Principal Diagnosis of First Liver Transplant: Adult Patients. 1984-2017

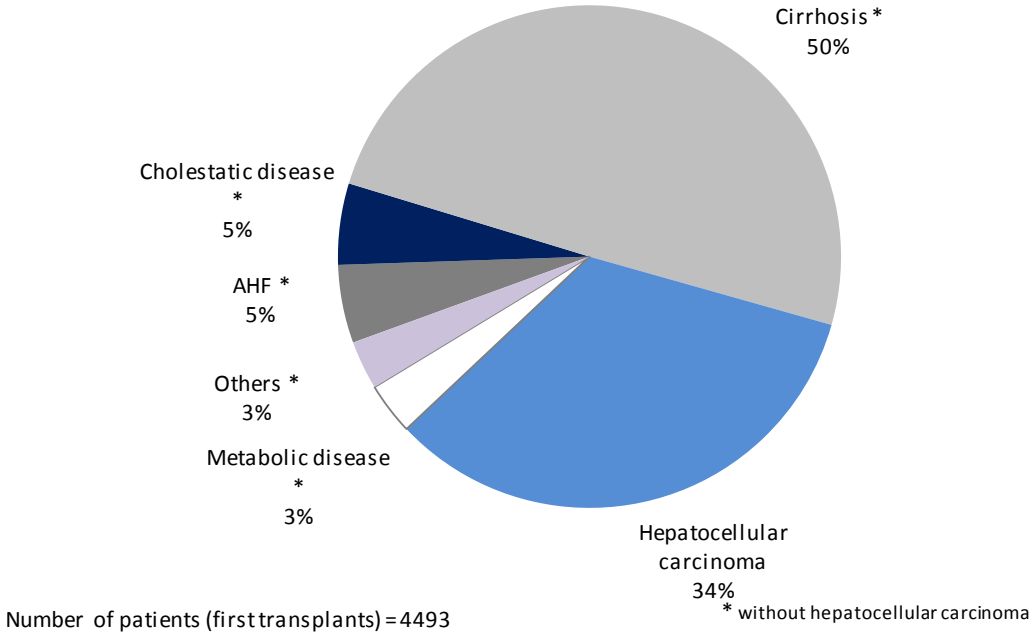
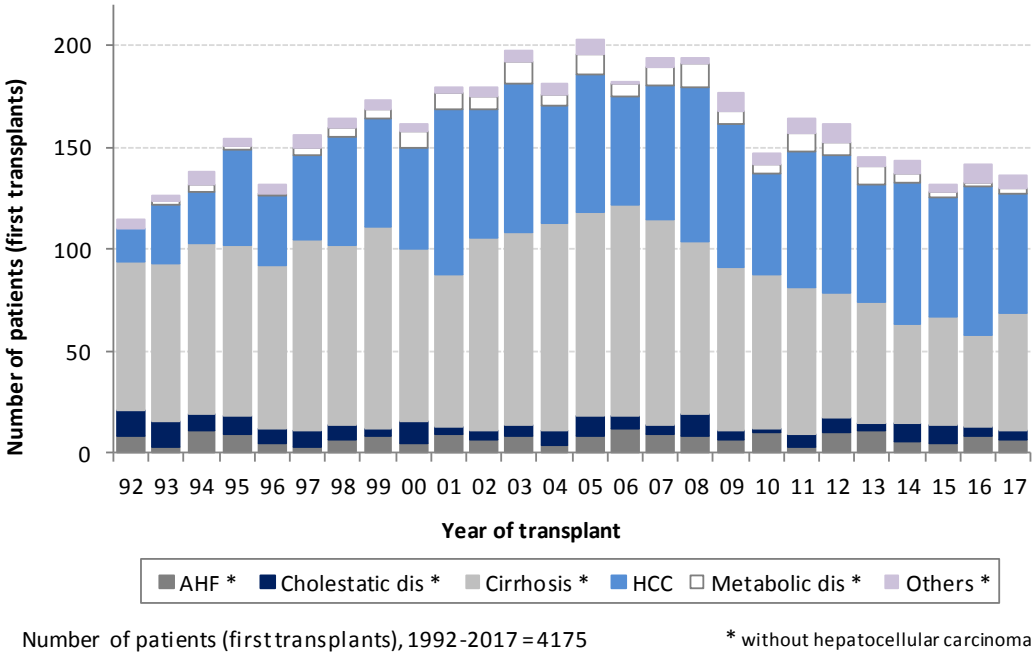
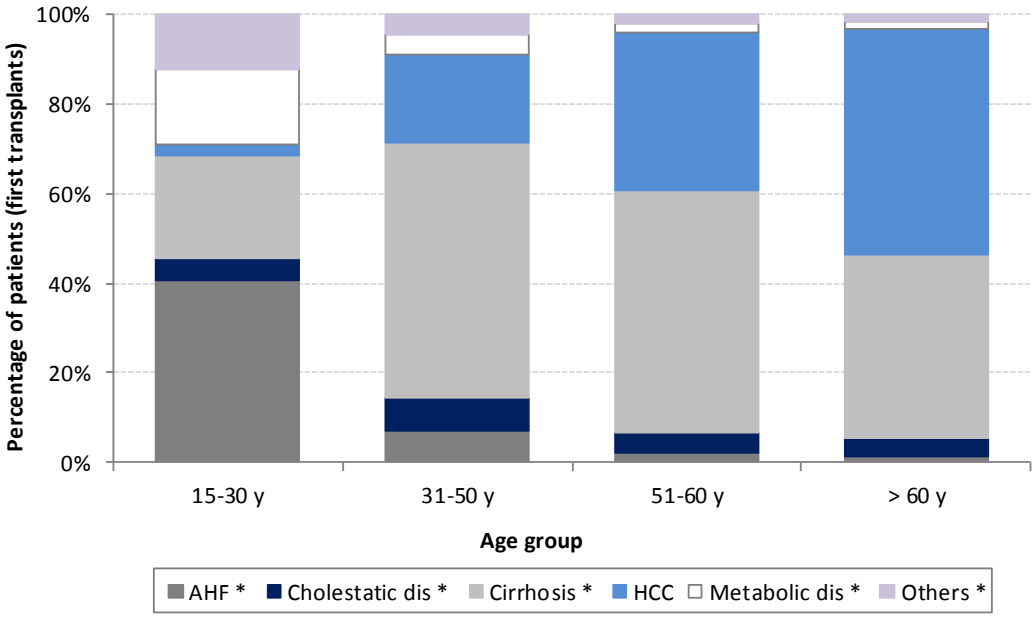


Figure 9. Evolution of Principal Diagnosis of First Liver Transplant: Adult Patients. 1992-2017



Cirrhosis is the most frequent group of indications in patients over 30 years of age, but as age increases, the proportion of transplants in which the indication is hepatocellular carcinoma, which represents 50.4% of all diagnoses in patients over 60 years of age (Figure 10).

Figure 10. Principal Diagnosis of First Liver Transplant by Age Group: Adult Patients. 1984-2017



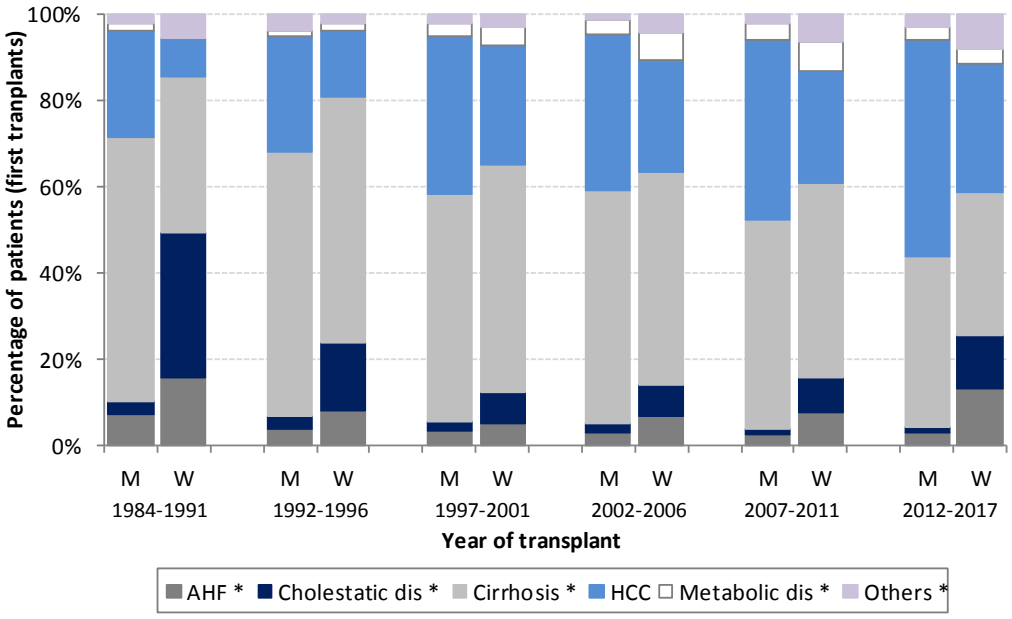
Patients with acute liver failure are the youngest, in contrast to patients with hepatocellular carcinoma, who are the oldest (p<0.001) (Table 1).

Table 1. Mean and Confidence Interval of Age for Principal Diagnosis: Adult Patients. 1984-2017

	n	mean	95% CI	range
Acute liver failure	226	38,1	36,2 – 40	12 – 69
Cholestatic liver disease	235	51,2	49,9 – 52,6	19 – 70
Cirrhosis	2.232	53,1	52,8 – 53,5	15 – 71
Hepatocellular carcinoma	1.509	57,8	57,4 – 58,2	25 – 73
Metabolic disease	150	43,4	41,1 – 45,6	19 – 73
Others	141	45,4	43,1 – 47,7	11 – 68
Total	4.493	53,3	53 – 53,6	11 – 73

The diagnoses of cholestatic liver disease and acute liver failure are more frequent in women than in men, in contrast, hepatocellular carcinoma occurs more frequently in men than in women (Figure 11).

Figure 11. Principal Diagnosis of First Liver Transplant by Period and Recipient Sex: Adult Patients. 1984-2017



Number of patients (first transplants) = 4493

* without hepatocellular carcinoma

Acute liver failure

This indication represents 5.0% (226) of transplanted patients in the 1984-2017 period. In most cases (80.1%, 181 patients), it is fulminant or subfulminant hepatitis - either viral or due to unknown causes.
In 2017, 5.1% (7) of transplanted patients presented acute liver failure; due to fulminant or subfulminant hepatitis.

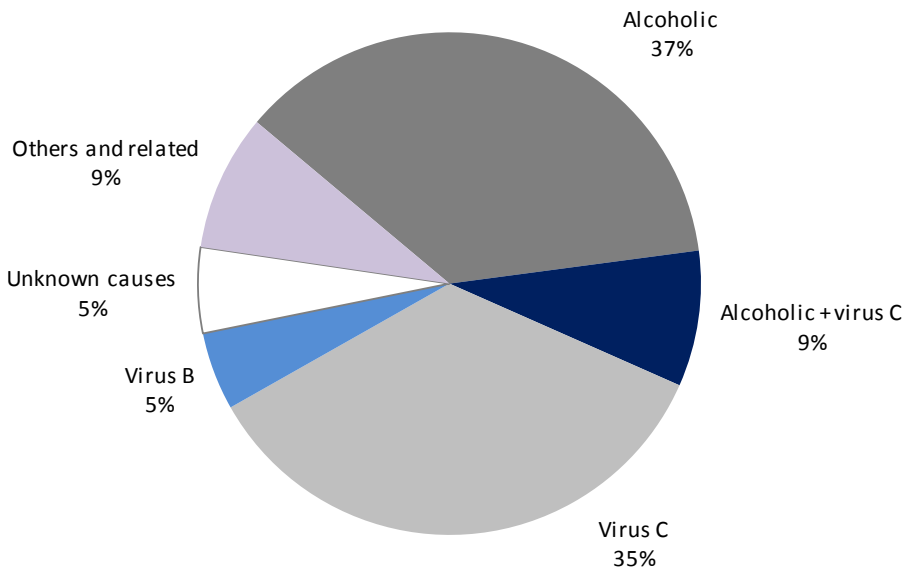
Cholestatic liver disease

Cholestatic liver disease is one of the less frequent diagnosis groups, with 235 (5.2%) cases for the same period. Primary biliary cirrhosis represents 65.5% (154) of all cases and sclerosing cholangitis represents 28.1% (66).
Some 2.9% (4) of patients who received a transplant in 2017 presented a cholestatic disease, two had a sclerosing cholangitis, one a primary biliary cirrhosis and one a secondary biliary cirrhosis.

Cirrhosis (without hepatocellular carcinoma)

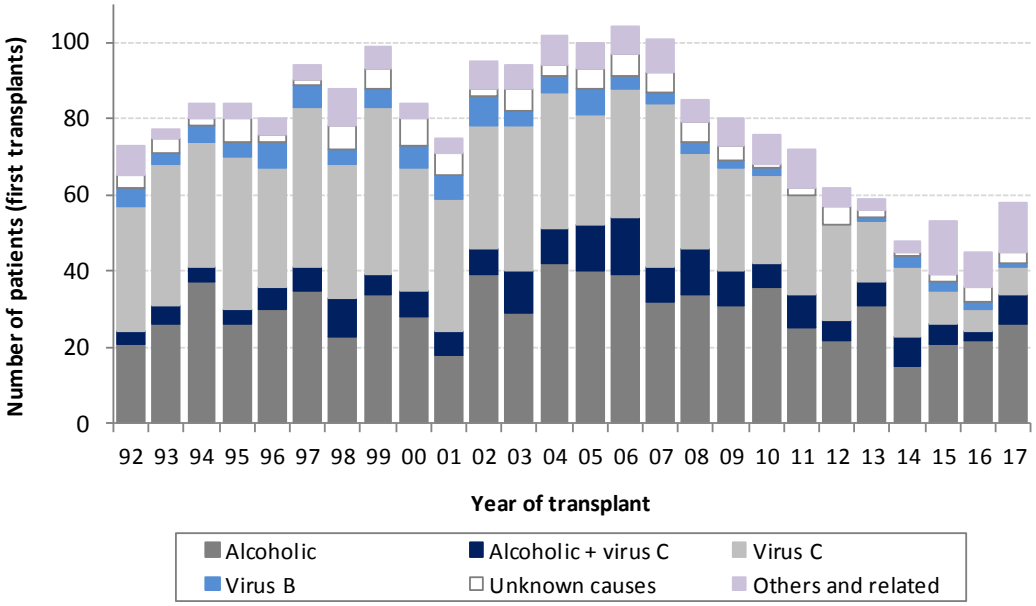
This is the most frequent indication, with 2232 patients - 49.7% of the total. Alcoholic cirrhosis and cirrhosis due to the hepatitis C virus are the most frequent (Figure 12).
Cirrhosis (without hepatocellular carcinoma) represents 42.6% (58) of patients who received a first liver transplant in 2017; 44.8% (26) of whom had alcoholic cirrhosis, 12,1% (7) had cirrhosis due to hepatitis C virus and 13.8% (8) had both alcoholic cirrhosis and cirrhosis due to hepatitis C virus (Figure 13). In the last year we observe an increase in the number of transplanted patients with NASH cirrhosis included in the “Others and related” category, and a decrease in the number of transplanted patients with cirrhosis due to hepatitis C virus.

Figure 12. Principal Diagnosis of Cirrhosis in the First Transplant: Adult Patients. 1984-2017



Number of patients (first transplants) with Cirrhosis as main diagnosis = 2232

Figure 13. Evolution of Principal Diagnosis of Cirrhosis in the First Liver Transplant: Adult Patients. 1992-2017

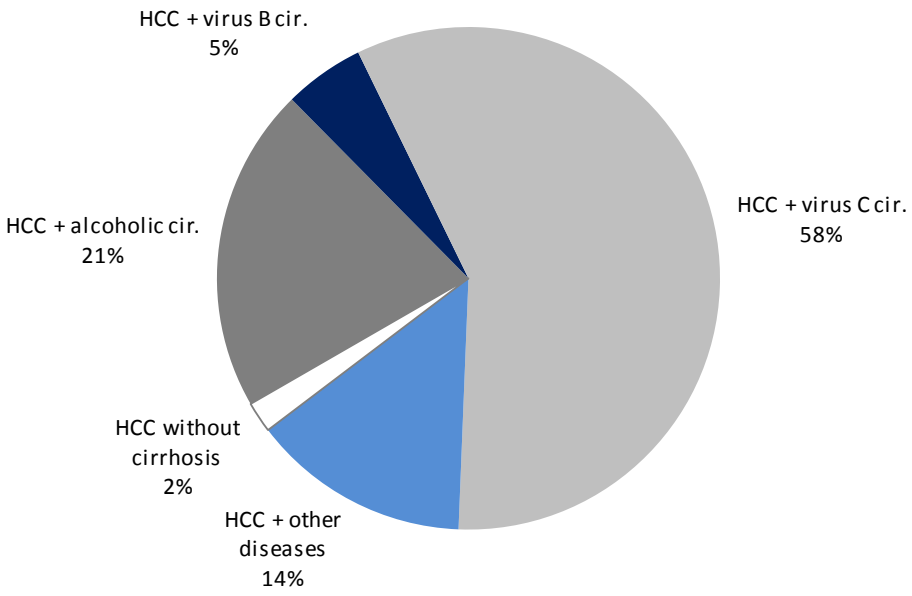


Number of patients (first transplants) with Cirrhosis as main diagnosis, 1992-2017 = 2072

Hepatocellular carcinoma

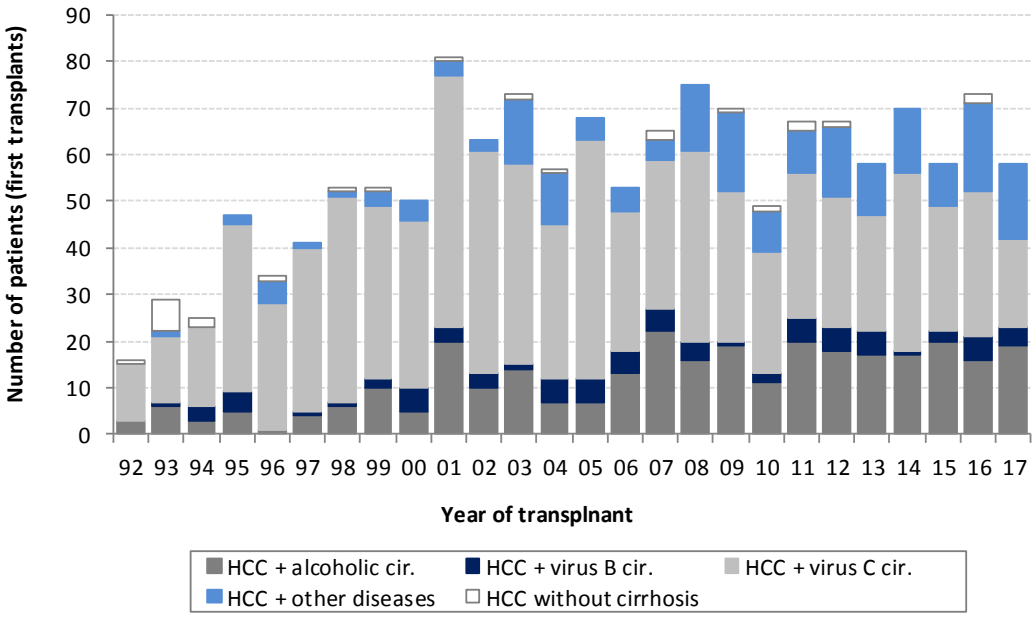
This type of carcinoma represents 33.6% (1509) of patients who received transplants in the 1984-2017 period and is the second most frequent indication. Of these cases, 98.0% are accompanied by cirrhosis - in most cases, cirrhosis due to the hepatitis C virus (Figures 14 and 15). Of the patients who received a transplant in 2017, 42.6% (58) had a hepatocellular carcinoma.

Figure 14. Principal Diagnosis of Hepatocellular Carcinoma in the First Liver Transplant: Adult Patients. 1984-2017



Number of patients (first transplants) with Hepatocellular carcinoma as main diagnosis = 1509

Figure 15. Evolution of Principal Diagnosis of Hepatocellular Carcinoma in the First Liver Transplant: Adult Patients. 1992-2017



Number of patients (first transplants) with Hepatocel. carcinoma as main diagnosis, 1992 -2017 = 1453

In fact, 44.7% (2007) of patients who received a transplant in the 1984-2017 period presented cirrhosis due to the hepatitis C virus, either in isolation (39.1%), combined with other cirrhosis (11.7%) or with hepatocellular carcinoma (48.9%).

Metabolic disease

Of patients who received a transplant in this period, 150 cases (3.3%) had a metabolic disease, in most cases (75.3%, 113 patients), the disease was a familial amyloidotic polyneuropathy.

Of the 136 patients who received a transplant in 2017, 3 (2.2%) had a metabolic disease as the principal diagnosis; specifically a familial amyloidotic polyneuropathy.

Others

This is the least frequent group of indications, with 141 patients (3.1%), in the 1984-2017 period.

Of the other indications for transplant, 47 presented some type of malignant tumour, 36 a benign tumour or polycystic disease, 24 presenting a congenital liver disease, 18 Budd-Chiari disease, and 16 more presented another type of liver disease.

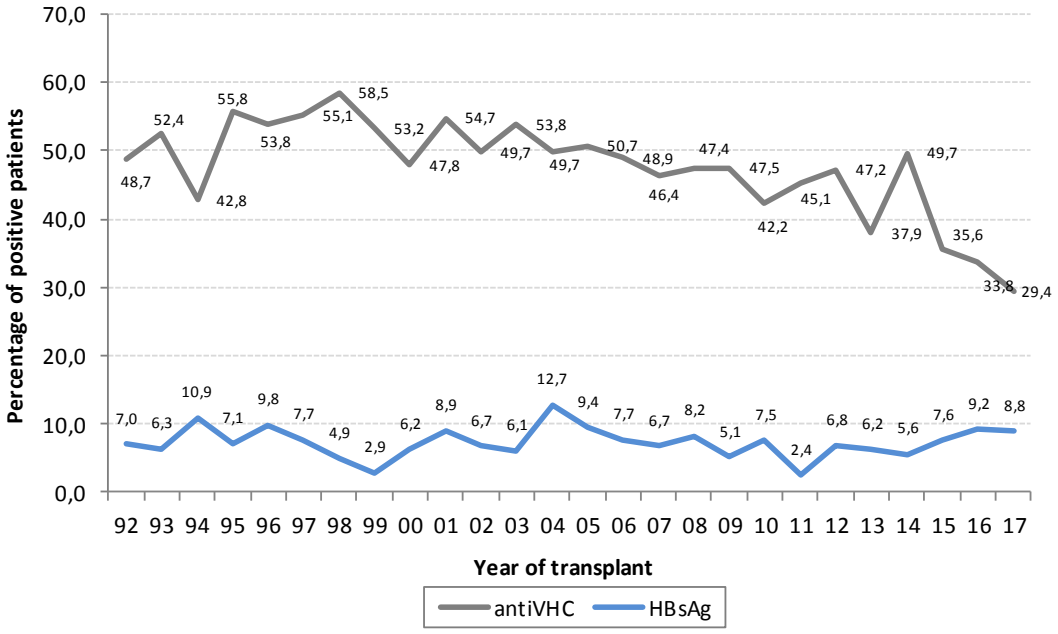
Six patients (4.4%) who received transplants in 2017 had an indication belonging to this group; two with polycystic disease, two with malignant tumour, one with Caroli disease and one with Budd-Chiari.

♦ Infection by hepatitis B and C viruses

The proportion of HB_SAg-positive adult patients in the 1984-2017 period was 7.6%; this number has remained relatively stable in recent years (Figure 16).

A total of 46.8% of patients who received a transplant in the 1984-2017 period were HCV-positive. A decrease in the percentage of patients with HCV-positive has been observed recently due to the appearance of the direct-acting antivirals.

Figure 16. Annual Evolution of Percentage of Adult Patients who Tested Positive for HVB and HCV. 1992-2017



Number of patients (first transplants), 1992-2017 = 4175

- **HIV infection**

The first four liver transplants in patients infected with HIV were performed in 2002, since then, 98 transplants (92 patients) have been performed - 3 of them in 2017.

Of these patients, 56.5% (52) had cirrhosis as an indication, principally due to HCV, and 38.0% (35) had a hepatocellular carcinoma.

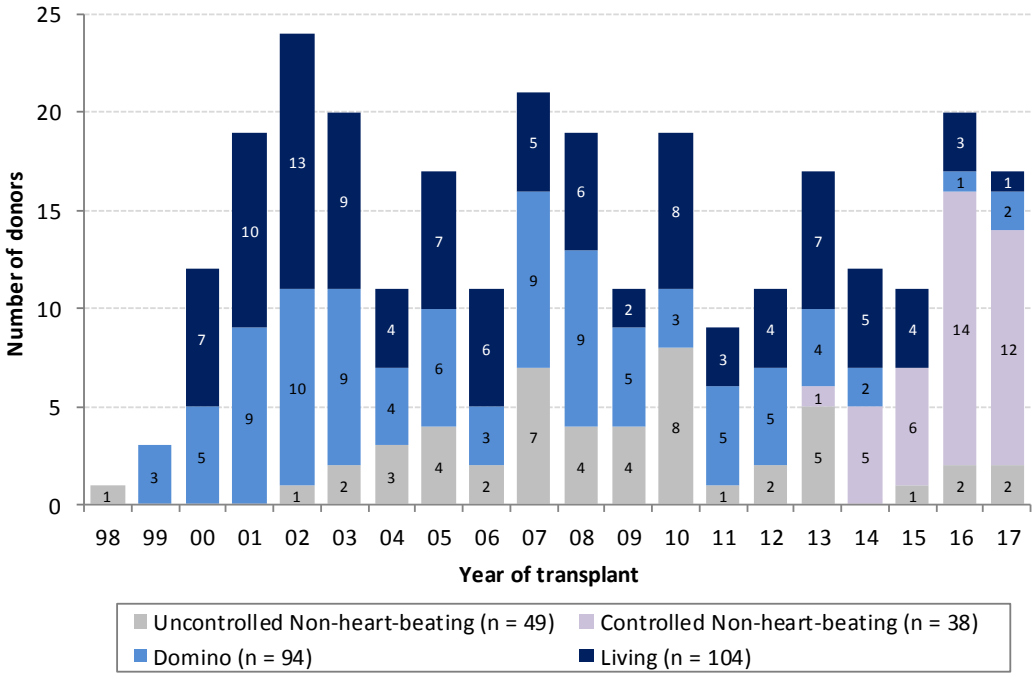
Donor Characteristics

♦ Type

94.2% of all transplants in 1984-2017 period were performed using organs from brain-death cadaveric donors (taken into account the 1992-2017 period was 93.7%).

Since 1998 other types of donors have been used; non-heart-beating donors, domino and living (Figure 17). Together, non-heart-beating, domino and living donors represent 11.3% of all donors in 2017 (Table 2).

Figure 17. Evolution of Number of Living, Domino and Non-heart-beating Donor Transplants in Adult Patients. 1998-2017



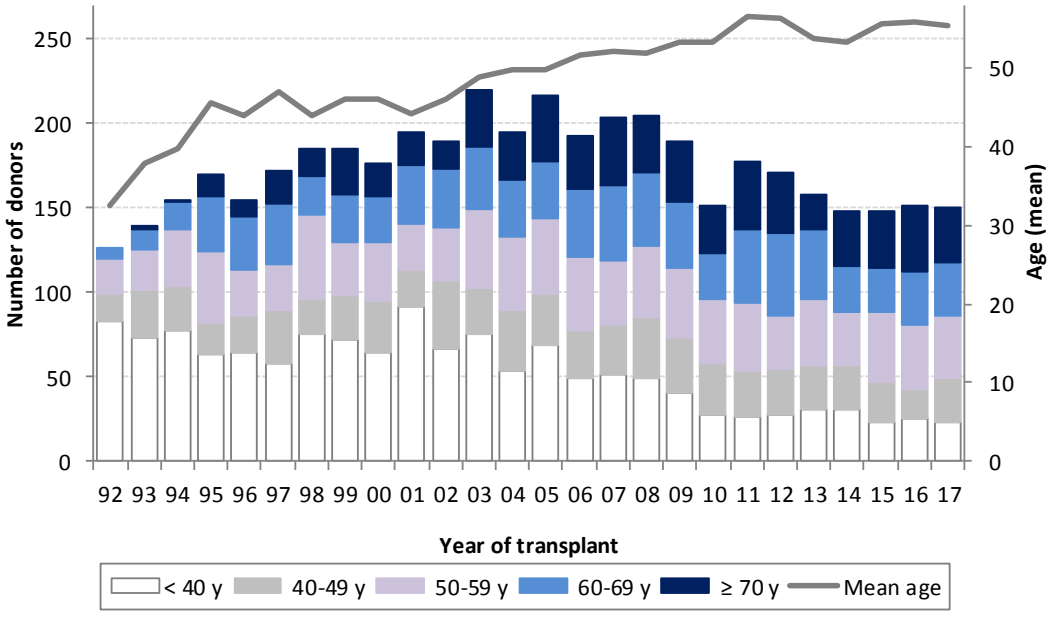
♦ Age and sex

The mean age of liver donors was 49 years in the 1992-2017 period; this figure has increased gradually over the years and has gone from 33 years (95% CI, 29.9-35.3 y; maximum age, 65 y) in 1992 to 56 years (95% CI, 52.9-58.2 y; maximum age, 84 y) in 2017 (Figure 18).
This increase has occurred in the oldest donors, given that, in 2017, 21.3% (32) were 70 years old or more, whereas this age group did not exist in 1992. In contrast, donors under the age of 40 years, who represented 65.9% (83) of all cases in 1992, had fallen to 15.3% (23) by 2017.

Table 2. Evolution of Donor Type: Transplants in Adult Patients. 1998-2017

	Brain Death Cadaver	Non-Heart-Beating	Domino	Living	Total
	n %	n %	n %	n %	
1998	184 (99,5%)	1 (0,5%)	-	-	185
1999	182 (98,4%)	-	3 (1,6%)	-	185
2000	164 (93,2%)	-	5 (2,8%)	7 (4,0%)	176
2001	176 (90,3%)	-	9 (4,6%)	10 (5,1%)	195
2002	166 (87,4%)	1 (0,5%)	10 (5,3%)	13 (6,8%)	190
2003	200 (90,9%)	2 (0,9%)	9 (4,1%)	9 (4,1%)	220
2004	184 (94,4%)	3 (1,5%)	4 (2,1%)	4 (2,1%)	195
2005	200 (92,2%)	4 (1,8%)	6 (2,8%)	7 (3,2%)	217
2006	182 (94,3%)	2 (1,0%)	3 (1,6%)	6 (3,1%)	193
2007	183 (89,7%)	7 (3,4%)	9 (4,4%)	5 (2,5%)	204
2008	186 (90,7%)	4 (2,0%)	9 (4,4%)	6 (2,9%)	205
2009	179 (94,2%)	4 (2,1%)	5 (2,6%)	2 (1,1%)	190
2010	132 (87,4%)	8 (5,3%)	3 (2,0%)	8 (5,3%)	151
2011	169 (94,9%)	1 (0,6%)	5 (2,8%)	3 (1,7%)	178
2012	160 (93,6%)	2 (1,2%)	5 (2,9%)	4 (2,3%)	171
2013	141 (89,2%)	6 (3,8%)	4 (2,5%)	7 (4,4%)	158
2014	136 (91,9%)	5 (3,4%)	2 (1,4%)	5 (3,4%)	148
2015	137 (92,6%)	7 (4,7%)	-	4 (2,7%)	148
2016	131 (86,8%)	16 (10,6%)	1 (0,7%)	3 (2,0%)	151
2017	133 (88,7%)	14 (9,3%)	2 (1,3%)	1 (0,7%)	150

Figure 18. Evolution of Donor Age in Transplants in Adult Patients. 1992-2017



Number of transplants, 1992-2017 = 4527

Taking into account the type of donor, the living donors are the youngest (Table 3).

Table 3. Donor Characteristics: Transplants in Adult Patients. 1998-2017

	Brain Death Cadaver	Uncontrolled Non-Heart-Beating	Controlled Non-Heart-Beating	Domino	Living
n	4242	49	38	94	104
Age (years)					
Mean	50	43	48	42	34
95% CI	49,1 - 50,2	39,1 - 47,9	43,5 - 51,8	39,5 - 44,8	32,4 - 36
Range	3 - 87	12 - 65	20 - 66	22 - 73	17 - 57
Sex					
Men	2563 (60,4%)	43 (87,8%)	28 (73,7%)	58 (61,7%)	64 (61,5%)
Women	1679 (39,6%)	6 (12,2%)	10 (26,3%)	36 (38,3%)	40 (38,5%)

In the 1992-2017 period, 60.9% (2756) of donors were men and 39.1% (1771) were women, in 2017, 57.3% (86) were men and 42.7% (64) were women.

The mean age of male donors in the 1992-2017 period was 47 years (SD, ±18.4 y; 95% CI, 46.4-47.8 y; maximum age, 87 y) and that of women was 52 years (SD, ±17.4 y; 95% CI, 51.3-52.9 y; maximum age, 86 y).

- **Cause of death**

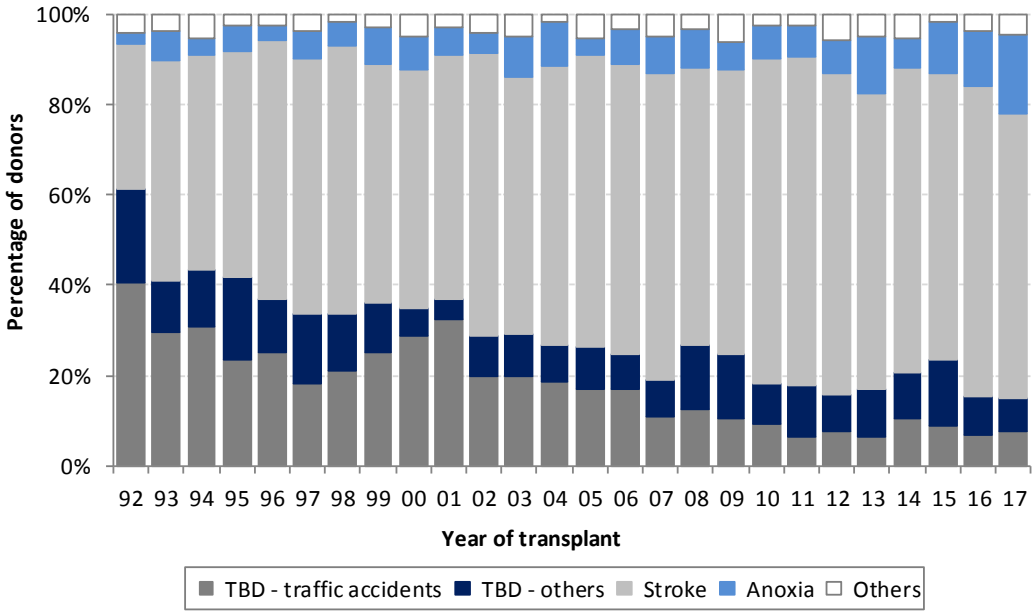
In brain-death cadaveric donors, in parallel with the increase in donor age, there has also been an increase over the years in the proportion of deaths due to due to cerebrovascular accident (CVA) or stroke, in detriment to deaths due to traumatic brain damage (TBD).

In 1995, for example, 41.7% of all donors had died due to TBD and 50.0% due to stroke, whereas in 2017, these figures were 15.0% and 63.2%, respectively (Figure 19).

During 1992-2017 period, the mean donor age was 33 years (95% CI, 32.0-34.6 y; range, 5-87 y) in deaths due to TBD following traffic accident, 45 years (95% CI, 43.3-46.9 y; range, 3-85 y) in deaths due to TBD caused by other incidents and 56 years (95% CI, 55.9-57.0 y; range, 7-86 y) in deaths due to stroke.

The mean age of donors who died due to TBD was 28 years (26 years due to a traffic accident and 33 years caused by other incidents) in 1992 and 44 years (34 years due to a traffic accident and 53 years caused by other incidents) in 2017. The mean age of donors who died due to stroke was 41 years in 1992 and 63 years in 2017.

Figure 19. Evolution of Cause of Donor Death: Transplants in Adult Patients. 1992-2017



Number of cadaveric donors (brain death), 1992-2017 = 4242

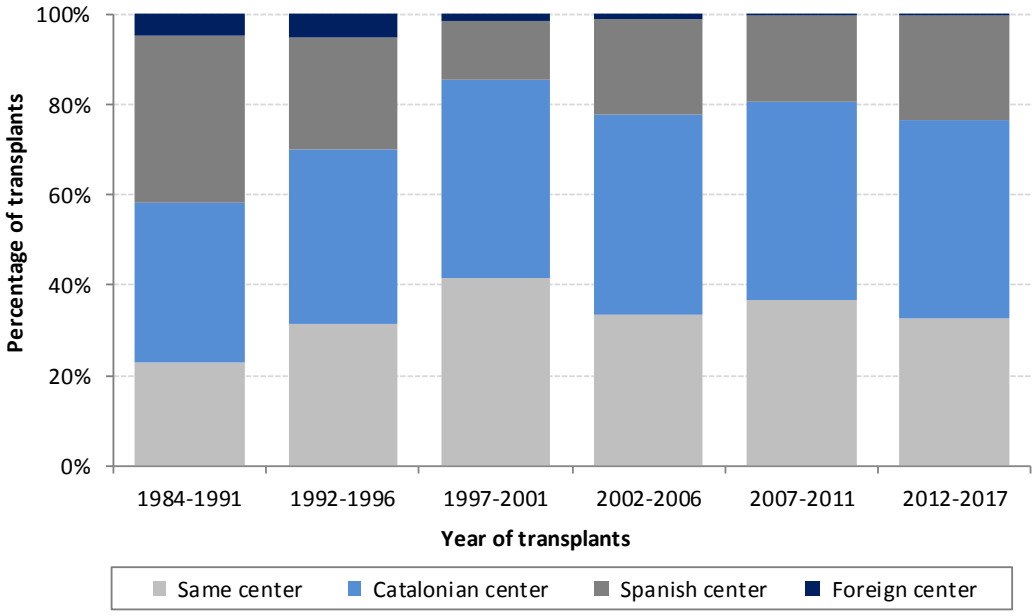
♦ Origin

If we compared transplants from deceased donors in the different periods, there is an increase in the proportion of organs generated in the same transplant centre and a reduction in organs from the rest of Spain or from abroad. The proportion of organs from the rest of Spain increased in the last two periods in comparison with the previous period, due to the progressive increase in organs from the autonomous community of the Balearic Islands, which are included in this category as they correspond to Catalonia as part of the region (Figure 20).

During the 1984-1991 period, 22.7% of transplanted livers from deceased donors came from the same transplant centre and 35.5% from other centres in Catalonia, these proportions have increased to 32.8% and 43.9% respectively in the 2007-2017 period.

In 2017, 36.1% (53) of deceased-donor livers came from the same centre, 44.2% (65) from other centres in Catalonia and 19.7% (29) from other centres in Spain.

Figure 20. Evolution of Donor Origin: Transplants in Adult Patients. 1984-2017



Number of cadaveric donors = 4690

Transplant Characteristics

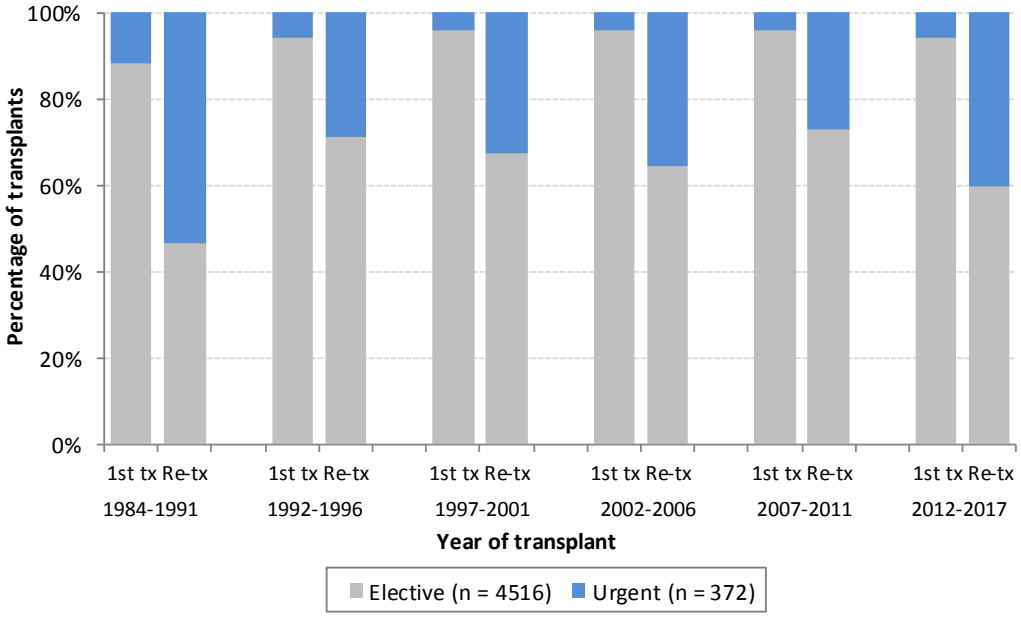
♦ Emergency

Of the 4888 liver transplants in adults in the 1984-2017 period, 372 (7.6%) were urgent. Of these, 62.6% (233) were first transplants, 35.5% (132) were second transplants and the remaining 1.9% (7) were third and fourth transplants.

In 2017, 11 (7.3%) urgent transplants were performed, seven first transplants and four retransplants.

In the 2012-2017 period, 40.3% of the retransplants were urgent, a higher percentage than the last four periods (Figure 21).

Figure 21. Evolution of Urgent Liver Transplants and Number of Transplants: Adult Patients. 1984-2017



Number of transplants = 4888

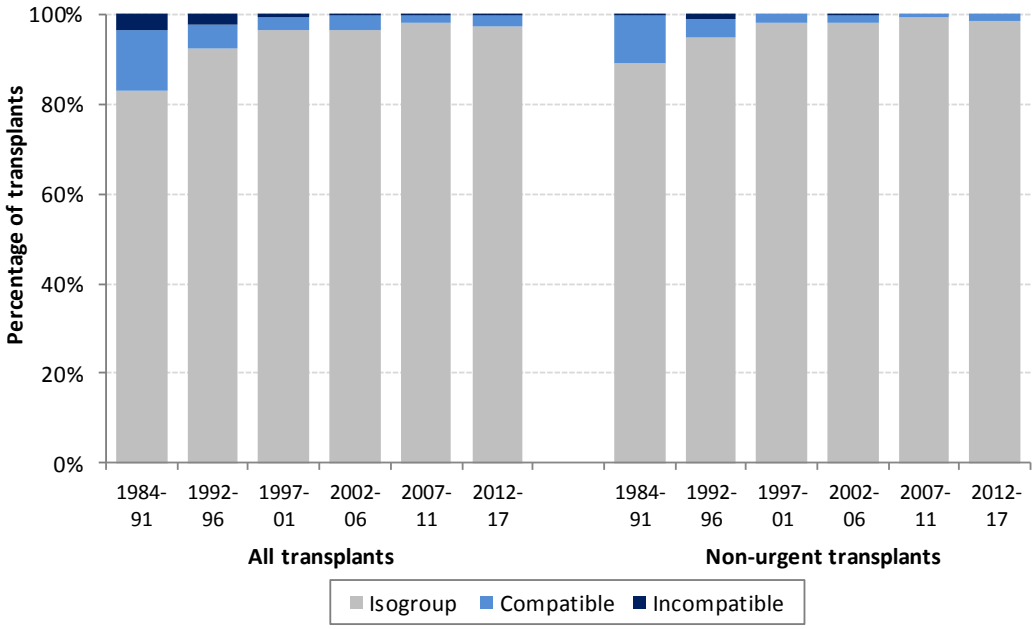
♦ Sex compatibility

In the 1992-2017 period, the proportion of transplants with organs from donors of the same sex as the recipient was 57.4%; transplants performed on men with a liver from a woman represent 25.3% and those on a female recipient from a male donor, 17.3%.

♦ Blood-group compatibility

The blood group of the receiver and the donor were the same in 95.4% of transplants, compatible in 3.8% and incompatible in 0.8%. Over the years, there has been a reduction in compatible or incompatible transplants, especially in non-urgent transplants (Figure 22).

Figure 22. Evolution of ABO Compatibility: Transplants in Adult Patients.1984-2017.



Number of transplants = 4888

♦ Graft type

In 95.2% of the transplants in the registry, a whole organ from a cadaver donor (brain death and non-heart-beating) was used, whereas 0.5% were split transplants. If we also take into account the organs from domino donors, these percentages are 97.1% and 0.5%, respectively. The reduced grafts from live donors represent 2.1%. Both split transplants and organs from live donors have oscillated over the last period (Table 4).
Split transplants are usually performed between an adult and a child; two adults have been transplanted in only one case. Overall, 27 transplants were performed with split grafts, benefitting 25 adults and 27 children. [3]

♦ Simultaneous transplants

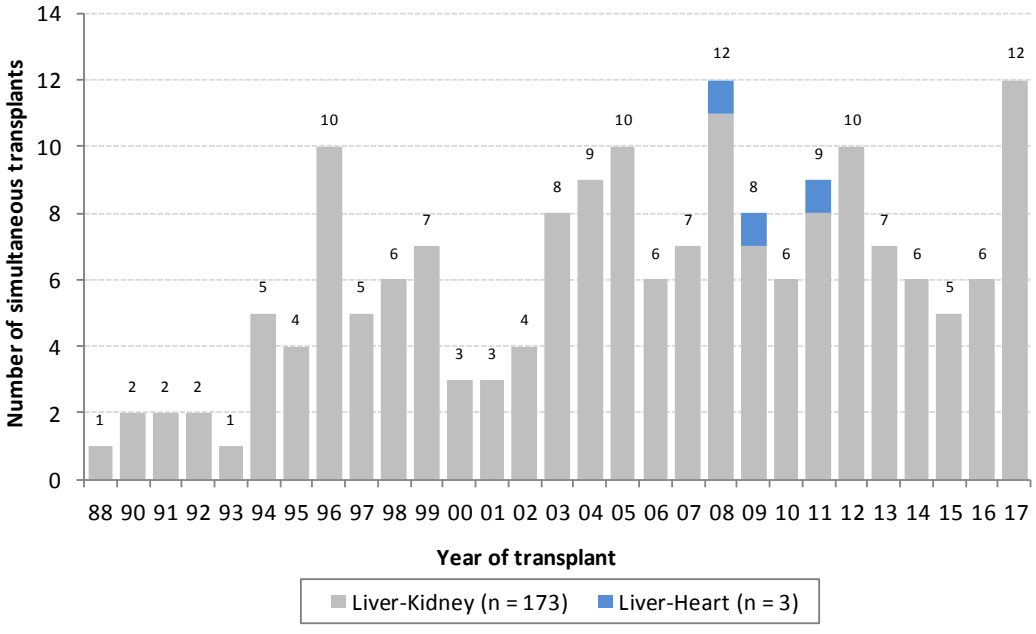
The first combined liver and kidney transplant was performed in 1988 and 173 of these transplants have been carried out since then. In 2017, a total of 12 of these transplants were performed –six more than in the previous year. The first combined liver and heart transplant was carried out in 2008 and the third one in 2011 (Figure 23).

[3] Two of the split transplants was not performed in a Catalonian hospital

Table 4. Evolution of Graft Type: Transplants in Adult Patients. 1997-2017

	Full size	Reduced	Reduce-Living	Split	Total
	n %	n %	n %	n %	
1997	170 (99,4%)	1 (0,6%)	-	-	171
1998	183 (98,9%)	-	-	2 (1,1%)	185
1999	183 (98,9%)	-	-	2 (1,1%)	185
2000	165 (93,8%)	1 (0,6%)	7 (4,0%)	3 (1,7%)	176
2001	183 (93,8%)	1 (0,5%)	10 (5,1%)	1 (0,5%)	195
2002	175 (92,1%)	-	13 (6,8%)	2 (1,1%)	190
2003	208 (94,5%)	-	9 (4,1%)	3 (1,4%)	220
2004	191 (97,9%)	-	4 (2,1%)	-	195
2005	206 (95,4%)	1 (0,5%)	7 (3,2%)	2 (0,9%)	216
2006	185 (95,9%)	-	6 (3,1%)	2 (1,0%)	193
2007	198 (97,1%)	-	5 (2,5%)	1 (0,5%)	204
2008	198 (96,6%)	-	6 (2,9%)	1 (0,5%)	205
2009	188 (98,9%)	-	2 (1,1%)	-	190
2010	142 (94,0%)	-	8 (5,3%)	1 (0,7%)	151
2011	175 (98,3%)	-	3 (1,7%)	-	178
2012	167 (97,7%)	-	4 (2,3%)	-	171
2013	150 (94,9%)	-	7 (4,4%)	1 (0,6%)	158
2014	142 (95,9%)	-	5 (3,4%)	1 (0,7%)	148
2015	144 (97,3%)	-	4 (2,7%)	-	148
2016	148 (98,0%)	-	3 (2,0%)	-	151
2017	148 (98,7%)	1 (0,7%)	1 (0,7%)	-	150

Figure 23. Evolution of Number of Simultaneous Transplants (Liver-Kidney and Liver-Heart): Transplants in Adult Patients. 1988-2017



Number of simultaneous transplants = 176 (3,6% of total)

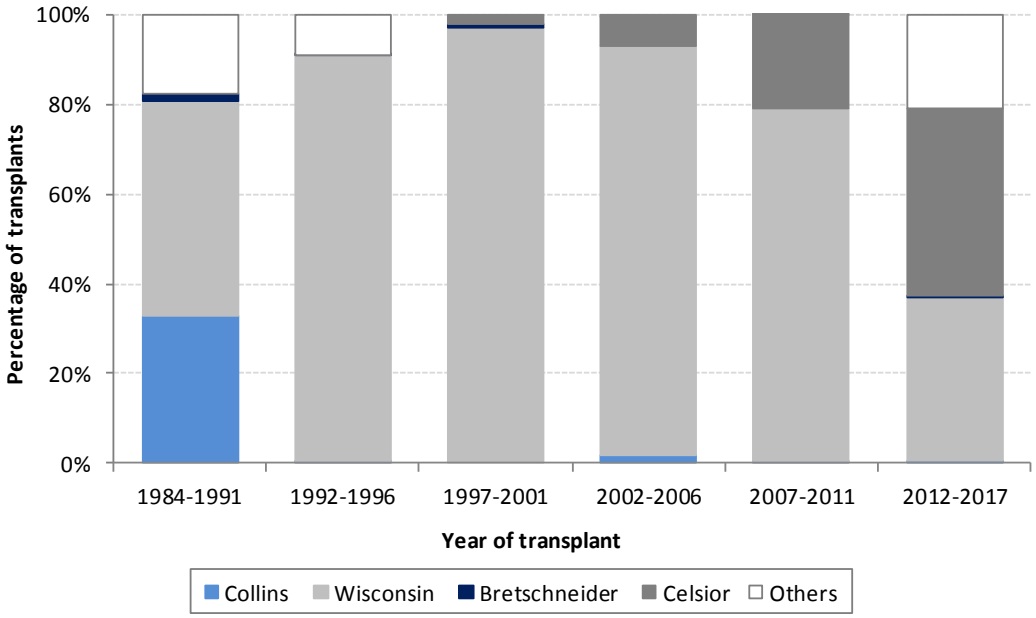
♦ Technique used in anhepatic phase

In 92.2% of the transplants carried out in the 1984-2017 period, the piggy back technique was used (with or without portacaval anastomosis). The number of transplants using the classic technique has fallen over the years; it was widely used in the early years but is currently practically not used at all.

♦ Preservation liquid

The University of Wisconsin preservation solution is the most commonly used (76.8% of all transplants in the 1984-2017 period) (Figure 24), although there has been an increase in the use of Celsior solution in recent years.

Figure 24. Evolution of Preservation Liquid Type: Transplants in Adult Patients. 1984-2017

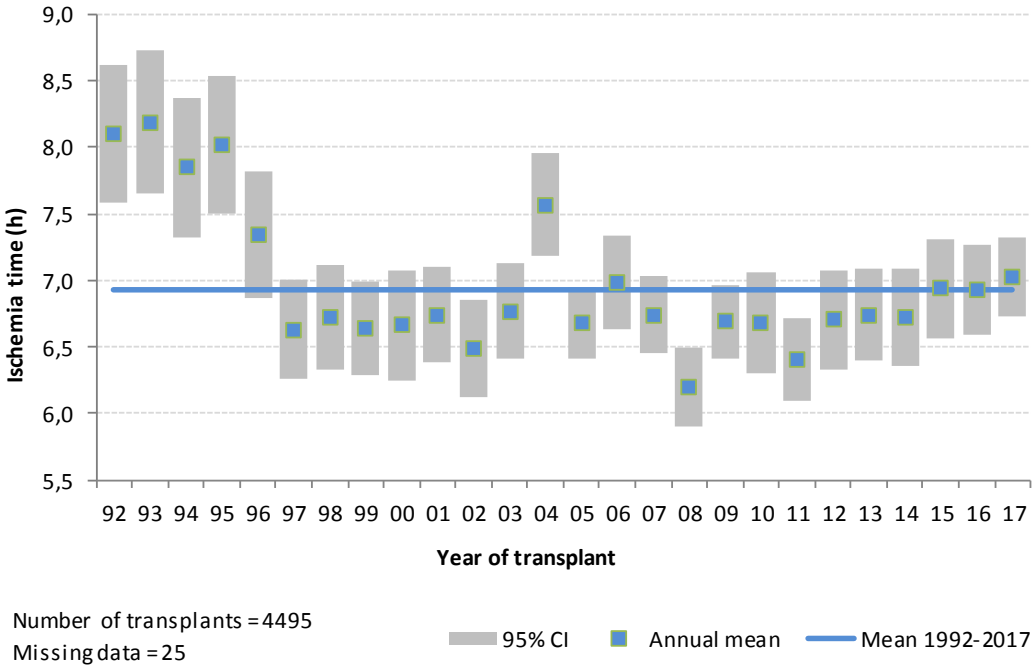


Number of transplants = 4816 Missing data = 72

♦ Ischemia time

The mean time in ischemia has fallen over the years (Figure 25), for the entire period, the mean ischemic time was 6.9 hours (median, 6.5 h; range, 0.5-24.0 h). From 1992 to 2017, ischemic time fell significantly ($p<0.0001$) and went from a mean of 8.1 hours (95% CI, 7.6-8.6 h; range, 3.2-15.7 h) to 7.0 hours (95% CI, 6.7-7.3 h; range, 1.6 -12).

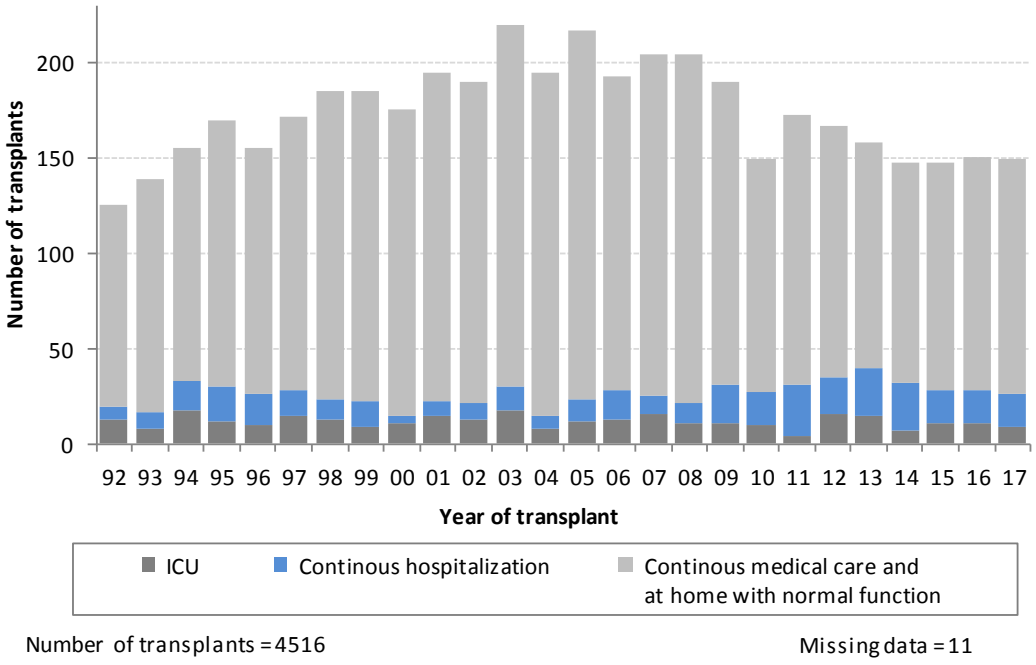
Figure 25. Evolution of Mean Ischemia Time: Transplants in Adult Patients. 1992-2017



♦ Patient status before transplant

A total of 83.8% of patients who received a transplant in the 1984-2017 period were at home, leading a normal life and/or receiving ongoing medical care before transplant, 8.5% required conventional hospital care and 7.5% had been admitted to an ICU.

Figure 26. Evolution of Patient Status Before Transplant: Transplants in Adult Patients. 1992-2017

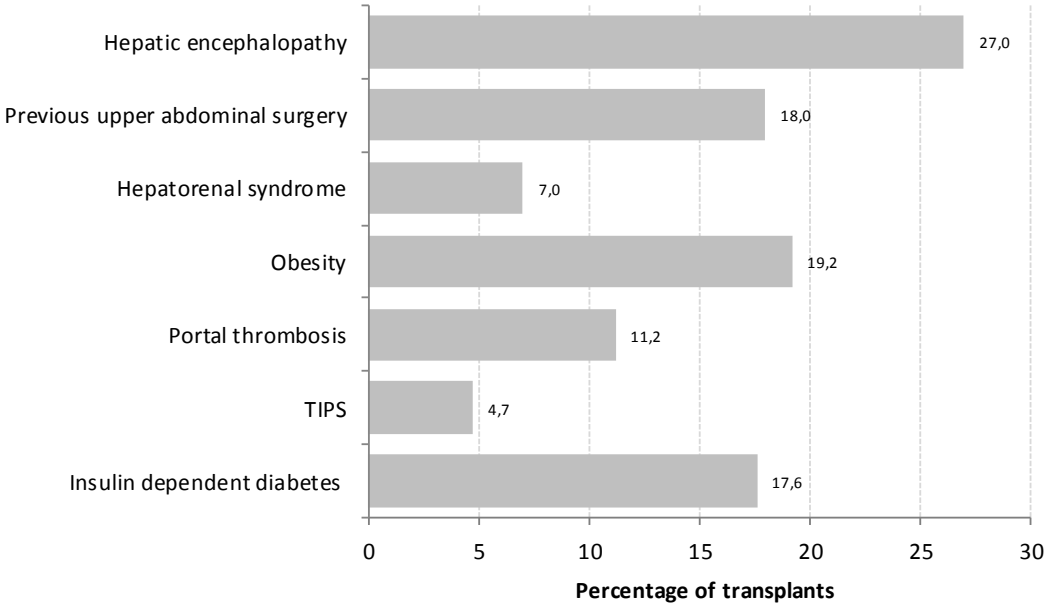


Taking into account only patients who received an elective transplant, excluding urgent transplants, the proportion of patients who were leading a normal life and/or receiving ongoing medical care before transplant has remained stable over the years (Figure 26).

♦ Pre-transplant risk factors

Figure 27 shows that hepatic encephalopathy, obesity, diabetes and prior abdominal surgery are the most frequent pretransplant risk factors in transplanted patients (first transplants) in the 2003-2017 period.

Figure 27. Pre-Transplant Risk Factors: Adult Patients. 2003-2017

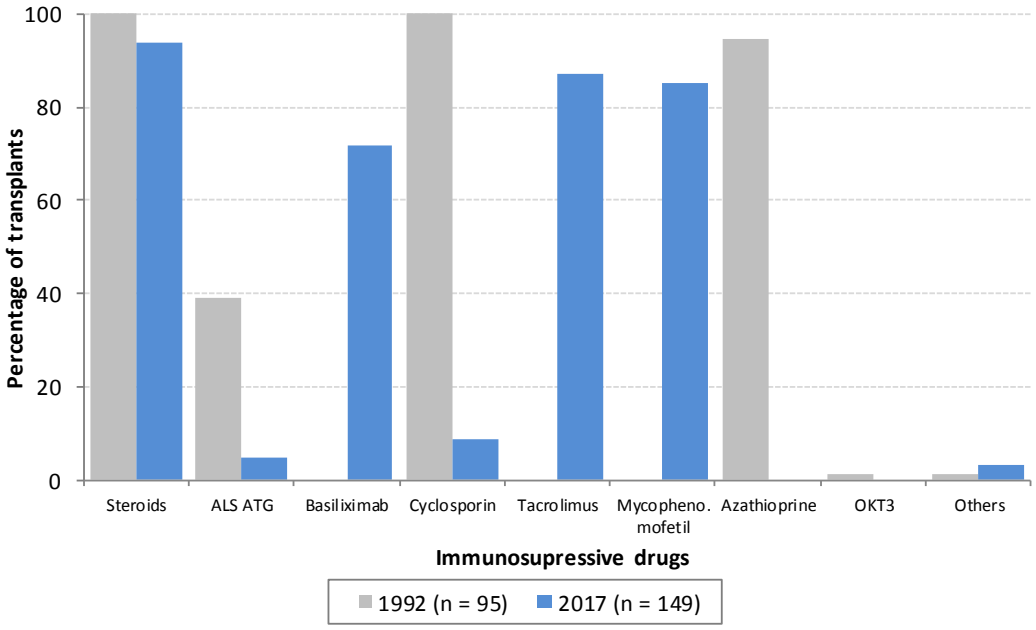


Number of transplants = 2173

♦ Immunosuppressors

The study of immunosuppressors was carried out using data collected from 1992 and 2017 for transplants with information on all drugs. Figure 28 shows the distribution of the drugs used in the first month after transplant in 1992 and 2017.

Figure 28. Immunosuppressant Drugs Used During the First Month Following Transplant: Adults Patients, transplants 1992 and 2017



Only transplants for which information on all variables was available have been considered

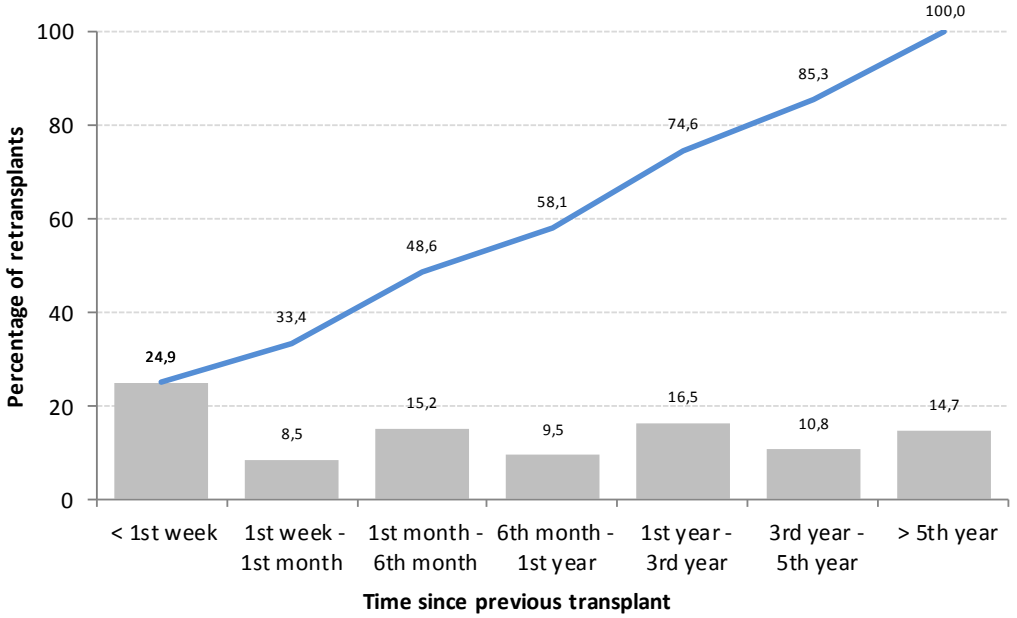
Retransplants

A total of 395 of the 4888 liver transplants carried out from 1984 to 2017 in adult patients (8.1%) have been retransplanted (368 first transplants, 25 second transplants and two third transplants). Six of these patients received the first transplant outside Catalonia or before reaching adult age.

Some 92.0% (4137) of these patients received a single transplant. 7.5% (337) received two, 0.5% (23) received three and 0.1% (2) received four.

Of these transplants, 24.9% took place less than a week before having received the previous transplant, whereas 41.9% were retransplanted at least a year after the first transplant (Figure 29).

Figure 29. Percentage of Retransplants by Time Elapsed Since Previous Transplant: Adult Patients. 1984-2017



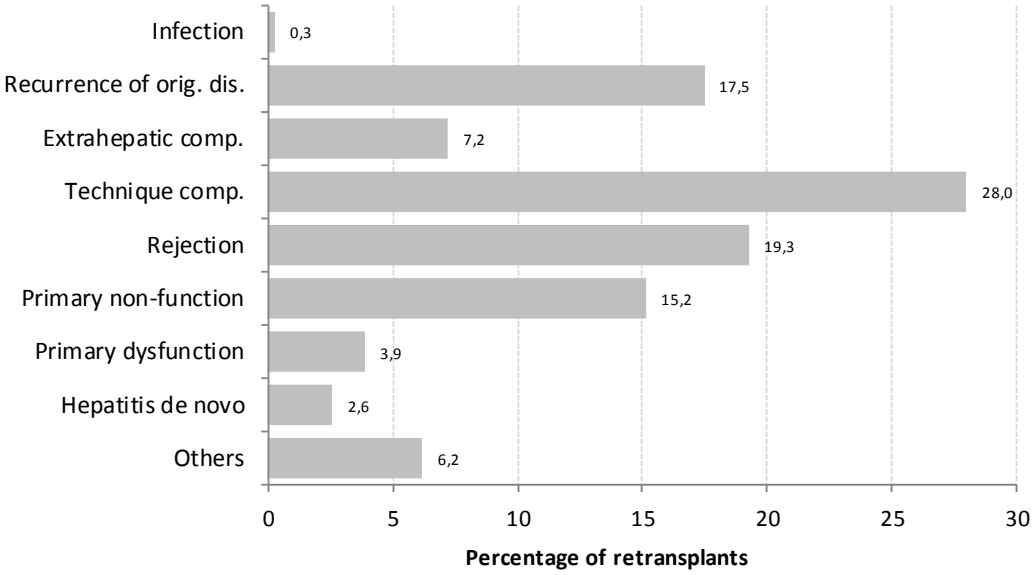
Number of valid retransplants = 389

Six retransplants were excluded because the first transplant was performed outside Catalonia or in a child.

Technical complications were the main cause of graft failure (e.g., arterial thrombosis), followed by (mostly chronic) rejection (Figure 30). Recurrence of the underlying disease was the main cause of failure in the long term (Figure 31).

In terms of the underlying disease of patients who received a retransplant, the three most frequent disease groups are cirrhosis (49.4%), hepatocellular carcinoma (25.4%) and acute liver failure (10.3%). In the remaining 14.9%, the underlying disease was a metabolic disease or other, less frequent, liver disease.

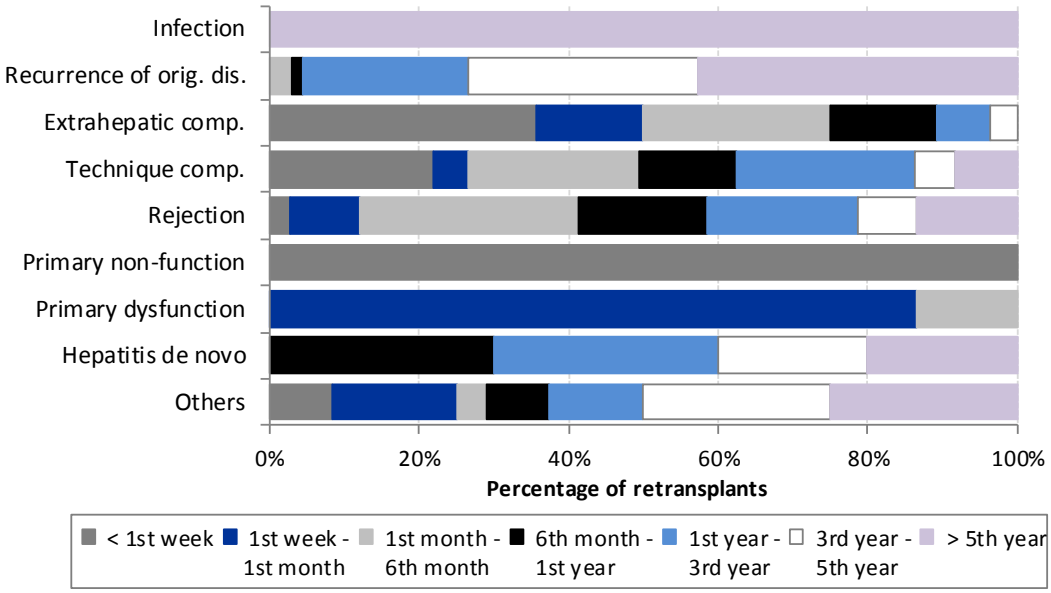
Figure 30. Causes of Graft Failure: Adult Patients. 1984-2017



Number of valid retransplants = 389

Six retransplants were excluded because the first transplant was performed outside Catalonia or in a child.

Figure 31. Percentage of Retransplants by Cause of Graft Failure and Time Elapsed Since Previous Transplant: Adult Patients.1984-2017.



Number of valid retransplants = 389

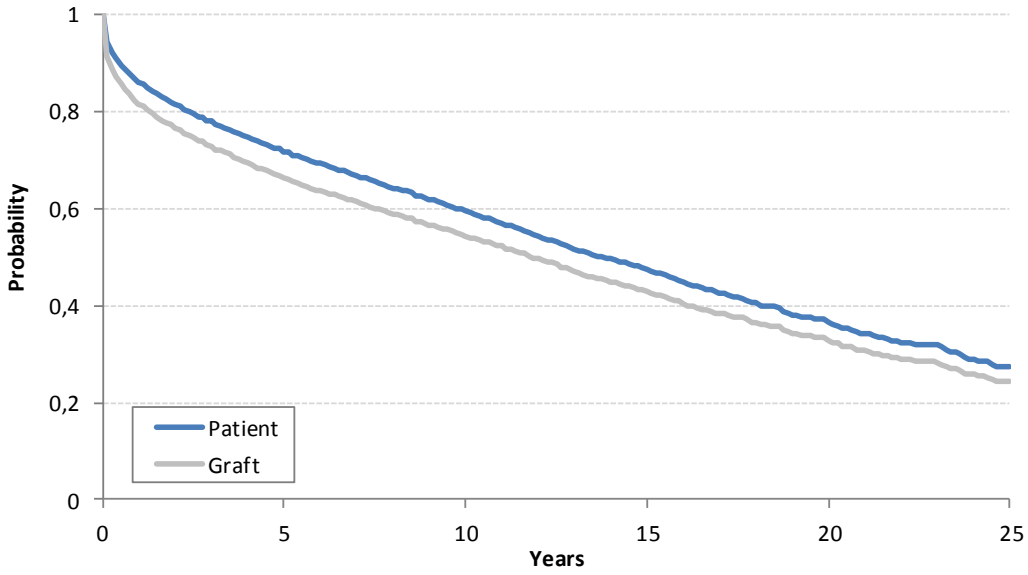
Six retransplants were excluded because the first transplant was performed outside Catalonia or in a child.

Survival

Overall survival of adult patients who received a liver transplant in the 1984-2017 period was 86% at one year, 78% at three years, 72% at five years and 59% at 10 years. In terms of graft survival, these probabilities fall to 82%, 73%, 66% and 54%, respectively (Figure 32).

Overall survival is affected by the characteristics of the transplants carried out in the first years, since the number of cases was small and the technique used was new, and by factors inherent to the transplants carried out thereafter, such as the inclusion of patients with diseases with a poorer outcome and older patients, changes in the use of immunosuppressants, advances in surgical techniques and in preservation techniques, etc.

Figure 32. Survival of Patient and Graft: Transplants in Adult Patients. 1984-2017



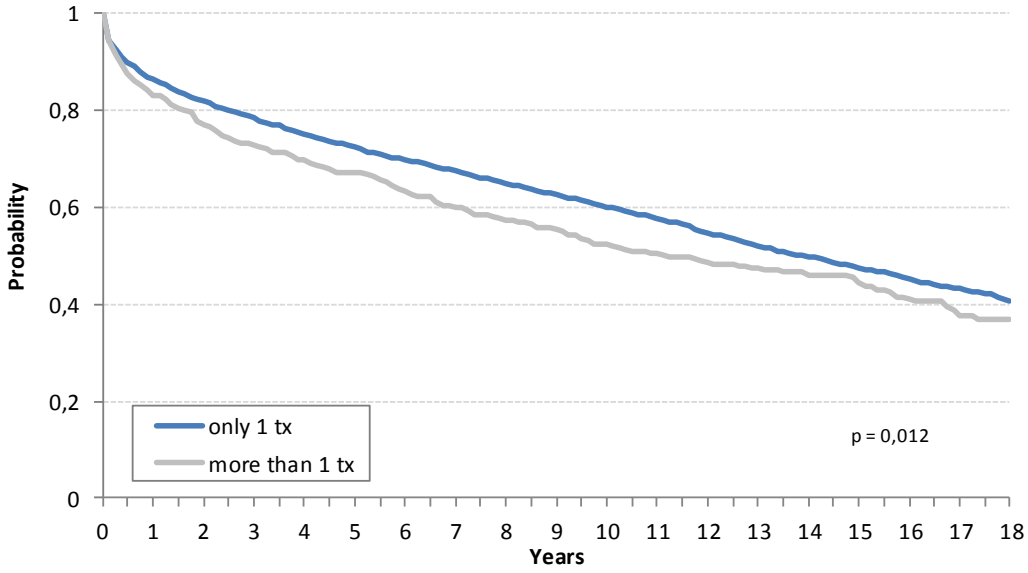
	n	3r month	1st year	3rd year	5th year	10th year	15th year	20th year
Patient	4.486	92%	86%	78%	72%	59%	47%	37%
Graft	4.876	89%	82%	73%	66%	54%	43%	33%

Patient survival presents statistically significant differences (p=0.012) when the number of transplants received is taken into account, although the survival rate during the initial years is not very different between those who received a single transplant and those who received more than one. At five and 10 years, the differences are 0.05 and 0.08, respectively (Figure 33).

- **Period in which transplant was performed**

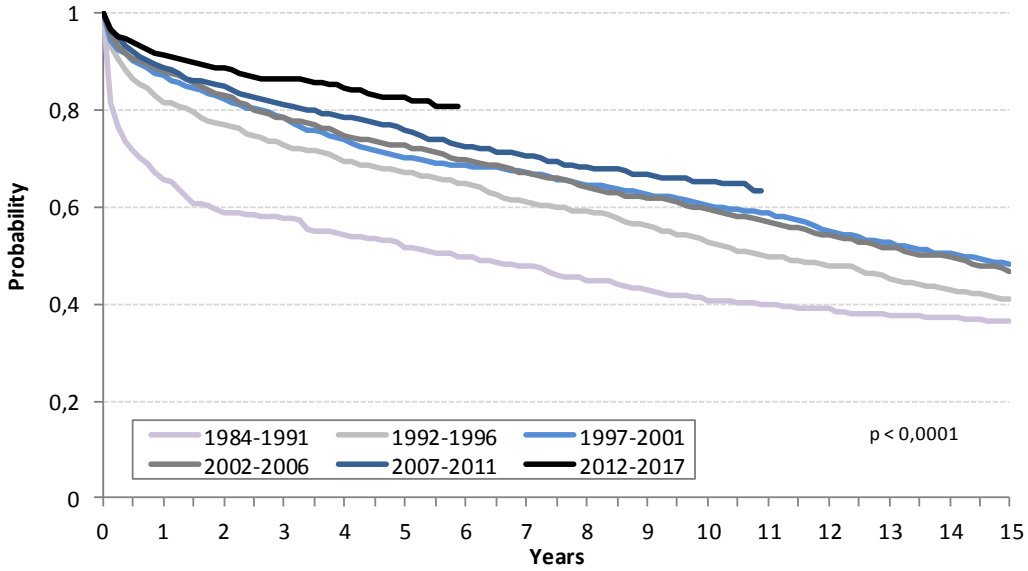
To adjust the results as much as possible to the context of each stage, five periods were defined to analyse survival: 1984-1991, 1992-1996, 1997-2001, 2002-2006, 2007-2011 and 2012-2017.

Figure 33. Survival of Patient by Number of Transplants Received: Adult Patients. 1984-2017



	n	1st year	3rd year	5th year	10th year
only 1 tx	4.124	86%	78%	72%	60%
more than 1 tx	362	83%	73%	67%	52%

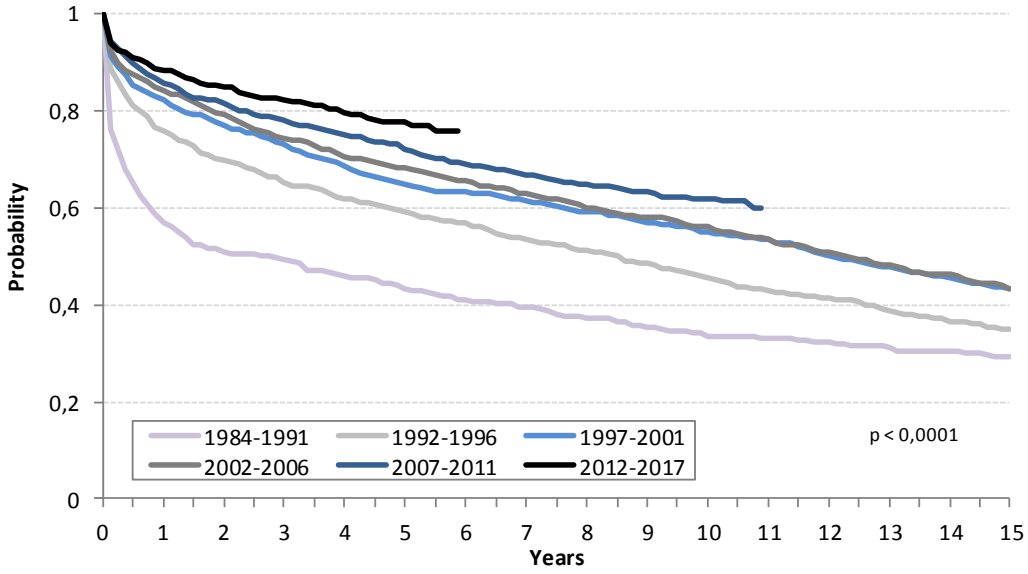
Figure 34. Survival of Patient by Period in which First Liver Transplant was Received: Adult Patients. 1984-2017



	1984-1991	1992-1996	1997-2001	2002-2006	2007-2011	2012-2017
n	315	662	832	942	876	859
1st year	66%	82%	87%	88%	88%	91%
3rd year	58%	73%	78%	78%	81%	87%
5th year	52%	67%	70%	73%	76%	83%
10th year	41%	53%	60%	60%	65%	-

Statistically significant differences can be seen by period in both patient survival and graft survival (p<0.0001) (Figures 34 and 35). All combinations of two periods are statistically significant, except the survival between 1997-2001 and 2002-2006 period.

Figure 35. Graft Survival by Period: Transplants in Adult Patients. 1984-2017



	1984-1991	1992-1996	1997-2001	2002-2006	2007-2011	2012-2017
n	358	742	911	1.013	926	926
1st year	57%	76%	82%	84%	86%	88%
3rd year	49%	65%	73%	74%	78%	82%
5th year	43%	59%	65%	68%	72%	78%
10th year	33%	45%	55%	56%	62%	-

The following survival analyses were carried out using data on transplants carried out from 1997, since the current behaviour of liver transplants fits more closely with the survival pattern observed in the last three periods.

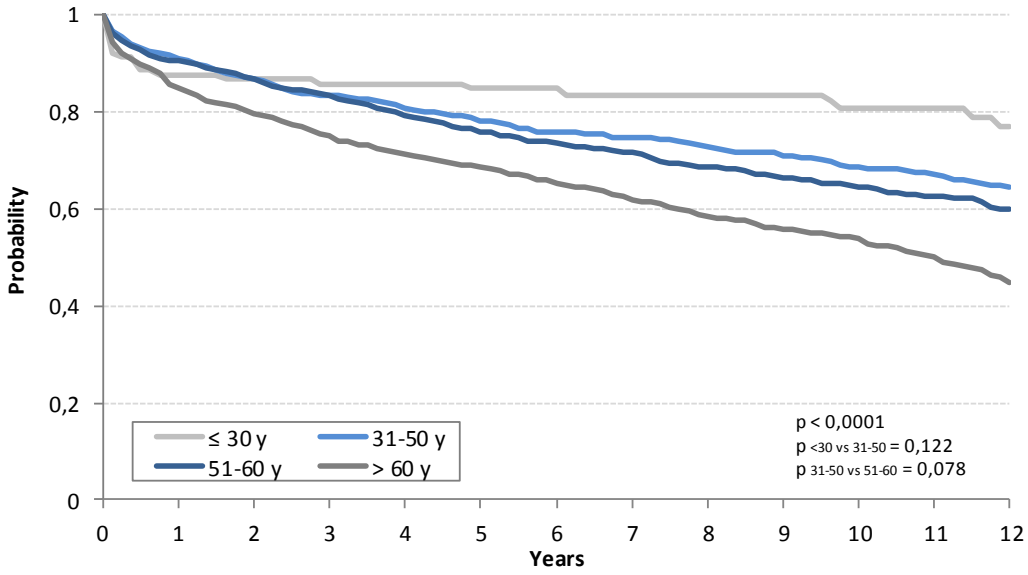
Patient survival in the 1997-2017 period was 89% at one year, 81% at three years, 75% at five years and 63% at 10 years. Graft survival for these same times was 85%, 77%, 70% and 59%, respectively.

- **Recipient age group**

In the long term, the oldest patients have the lowest survival rates. Specifically, in patients over the age of 60 years, survival at ten years is 69%, 0.07 less than in those aged between 51 and 60 years (Figure 36).

The differences in survival by age of recipient are statistically significant when compared with the four groups overall (p<0.0001). Comparisons between two age groups show no differences between the ≤30 years and the 31-50 years groups (p=0.122), and also between the 31-50 years and 51-60 years group (p=0,078); differences between the other age groups are statistically significant.

Figure 36. Survival of Patient by Age Group in Which First Liver Transplant was Received: Adult Patients. 1997-2017



	n	1st year	3rd year	5th year	10th year
≤ 30 y	114	88%	86%	85%	81%
31-50 y	934	91%	83%	78%	69%
51-60 y	1.331	90%	83%	76%	65%
> 60 y	1.130	85%	75%	69%	54%

- **Indication**

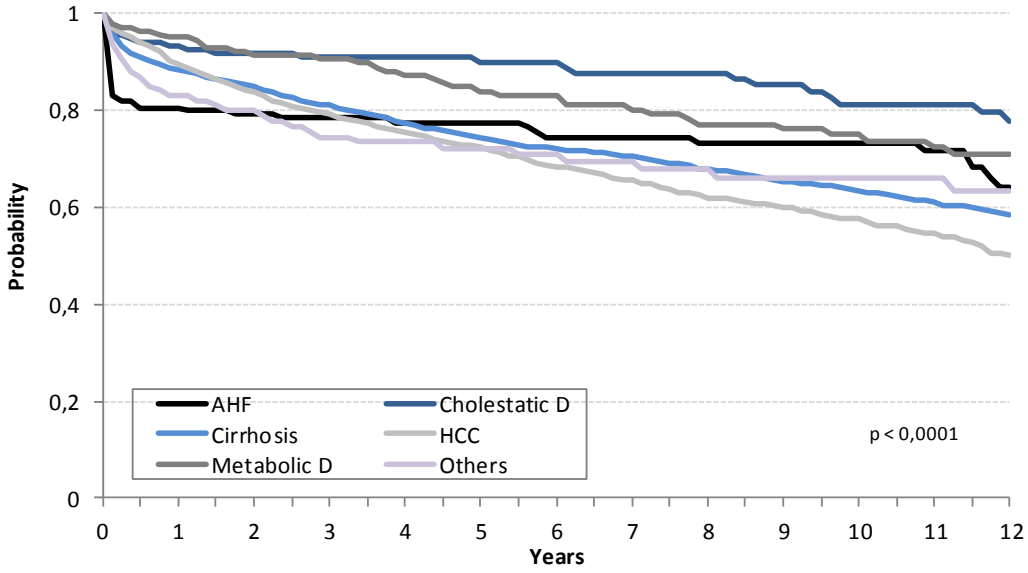
In terms of transplant indication, patients with a higher survival rate in the long term are those who present a metabolic disease or cholestatic liver disease as an indication. The differences between the different indications are statistically significant (p<0.0001) (Figure 37).

Patients with hepatocellular carcinoma and cirrhosis present very similar survival rates (p=0.057); after the first year, patients with cirrhosis present a slightly higher survival rate than patients with hepatocellular carcinoma - at five years, 74% of patients with cirrhosis survive compared to 72% of those with a tumour.

The same pattern occurs in graft survival, although there is a more pronounced fall in the first two years in transplants where the indication is a cholestatic disease (Figure 38).

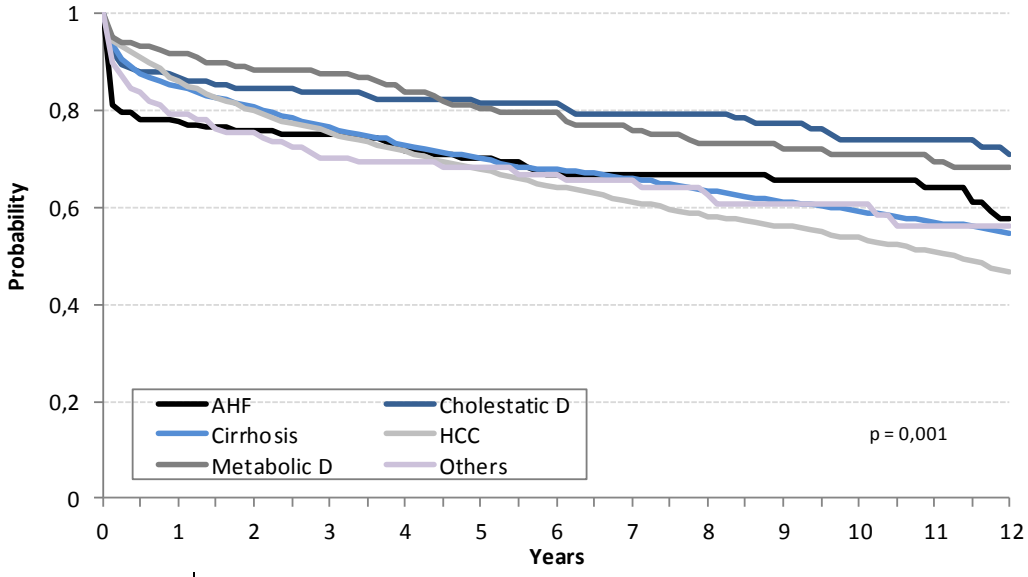
On comparing the survival of patients who present alcoholic cirrhosis, viral cirrhosis and hepatocellular carcinoma without another accompanying disease, the differences are statistically significant (p=0.006). The differences between viral cirrhosis and hepatocellular carcinoma are not statistically significant (p=0.507) (Figure 39).

Figure 37. Patient Survival by Indication: Adult Patients. 1997-2017



	AHF	Cholestatic Disease	Cirrhosis	HCC	Metabolic Disease	Others
n	155	133	1.673	1.302	138	108
1st year	80%	93%	88%	89%	95%	83%
3rd year	78%	91%	81%	79%	90%	74%
5th year	77%	90%	74%	72%	84%	72%
10th year	73%	81%	63%	58%	75%	66%

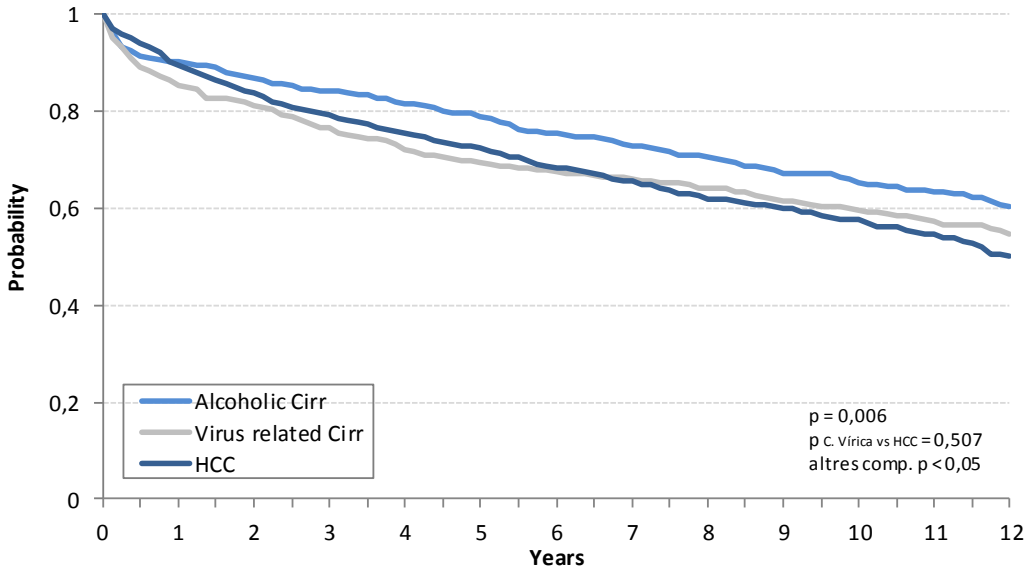
Figure 38. Graft Survival by Indication: Transplants in Adult Patients. 1997-2017



	AHF	Cholestatic Disease	Cirrhosis	HCC	Metabolic Disease	Others
n	176	151	1.803	1.383	146	117
1st year	78%	87%	85%	86%	92%	79%
3rd year	75%	84%	77%	75%	87%	70%
5th year	70%	81%	70%	68%	80%	68%
10th year	65%	74%	59%	54%	71%	61%

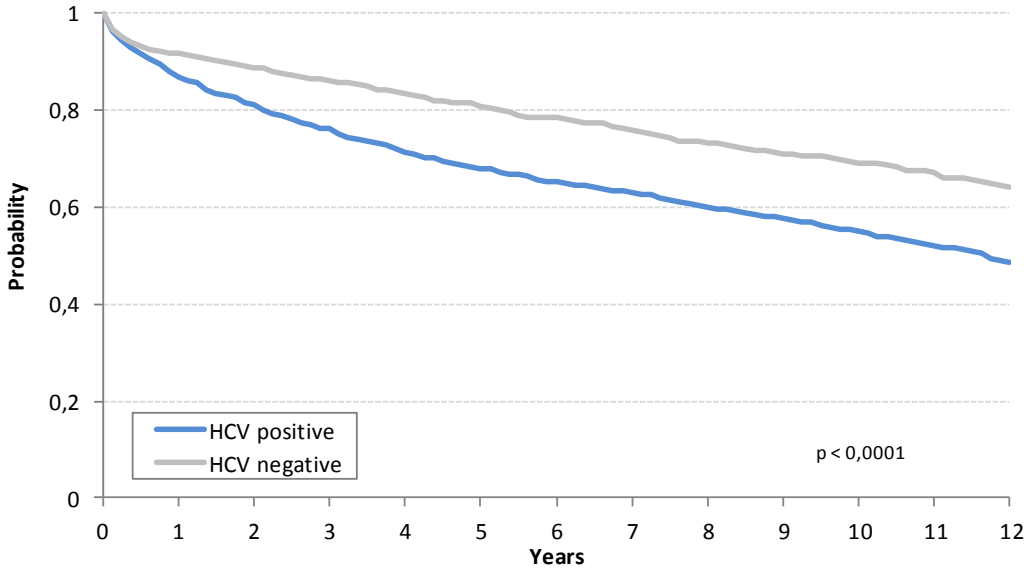
Those patients diagnosed with cirrhosis (with or without hepatocellular carcinoma) and positive C virus had lower survival rates than patients with only cirrhosis (p < 0,0001) (Figure 40).

Figure 39. Patient Survival by Indication (Three Groups): Adult Patients. 1997-2017



	n	1st year	3rd year	5th year	10th year
Alcoholic Cirr	621	90%	84%	79%	65%
Virus related Cirr	688	85%	77%	69%	60%
HCC	1.302	89%	79%	72%	58%

Figure 40. Patient Survival by HCV serology: Adult Patients With First Elective Transplant diagnosed with cirrhosis, 1997-2017

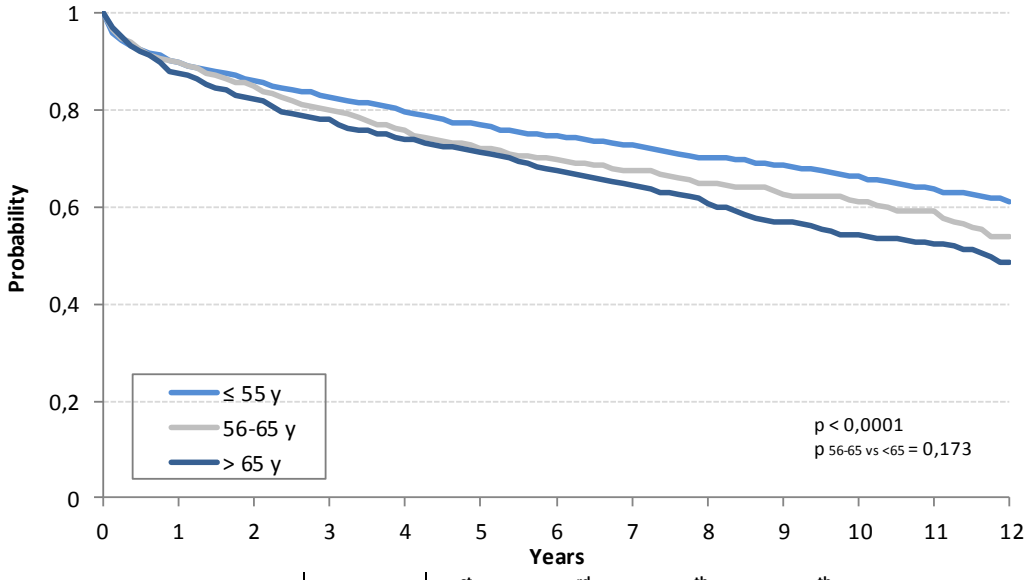


	n	1st year	3rd year	5th year	10th year
HCV positive	1.650	87%	76%	68%	55%
HCV negative	1.304	92%	86%	81%	69%

♦ Donor age

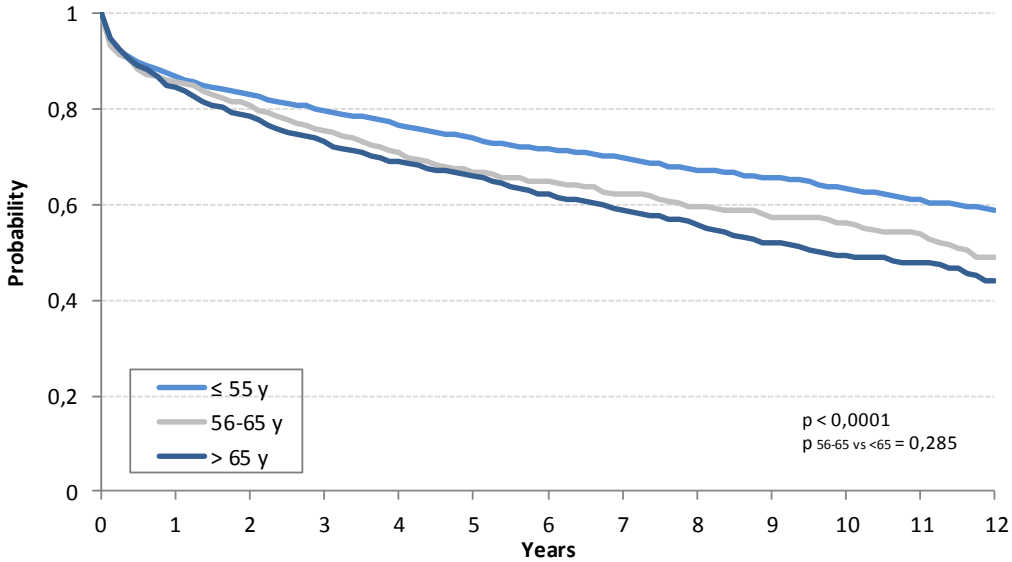
Patient survival by donor age group for the first transplant shows statistically significant differences in the overall comparison (p<0.0001) (Figure 41), and between the different groups, except the 56-65 years group and the group of patients over the age of 65 years (p=0.173).

Figure 41. Survival of Patient by Donor Age Group: Adult Patients With First Elective Transplant. 1997-2017



	n	1st year	3rd year	5th year	10th year
≤ 55 y	1.838	90%	83%	77%	66%
56-65 y	683	90%	80%	72%	61%
> 65 y	829	88%	78%	71%	54%

Figure 42. Graft Survival by Donor Age Group: Elective Transplants in Adult Patients. 97-06.



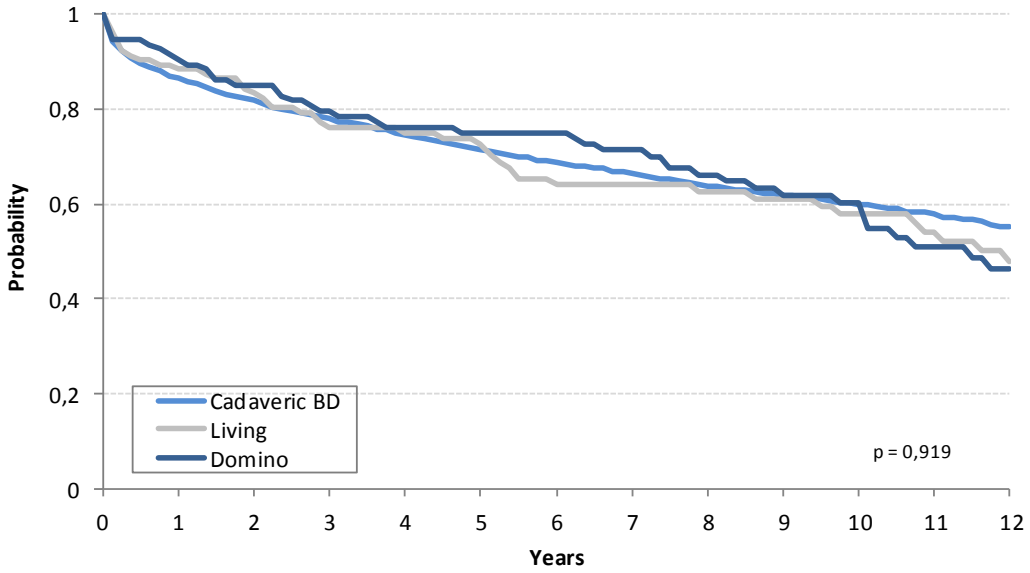
	n	1st year	3rd year	5th year	10th year
≤ 55 y	1.943	87%	80%	74%	63%
56-65 y	710	86%	75%	67%	56%
> 65 y	871	84%	73%	66%	49%

In terms of graft survival, there are statistically significant differences (p<0.0001) in the overall comparison and between all the groups, except between the 56-65 years group and the group of patients over the age of 65 years (p=0.285) (Figure 42).

- **Donor type**

No statistically significant differences were found in graft survival by type of donor (cadaver, live or domino), although it appears that short-term survival is better in domino transplants (Figure 43).

Figure 43. Graft Survival by Donor Type: Elective Transplants in Adult Patients. 1999-2017



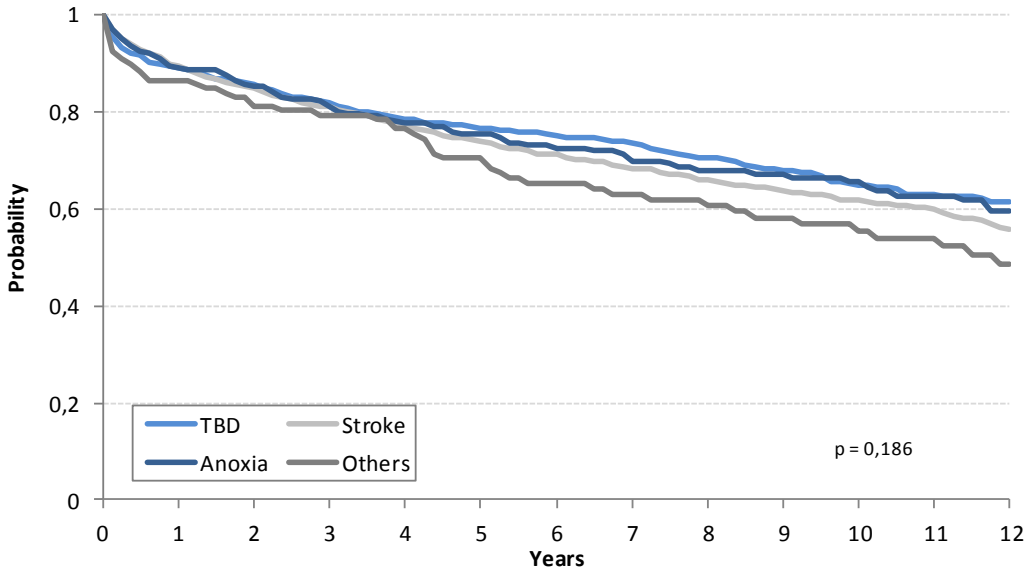
	n	1st year	3rd year	5th year	10th year
Cadaveric BD	2.913	86%	78%	71%	60%
Living	103	88%	76%	73%	58%
Domino	94	90%	80%	75%	60%

- **Cause of donor death**

No statistically significant differences (p=0.186) were observed in patient survival when cause of first-transplant donor death was taken into account (Figure 44).

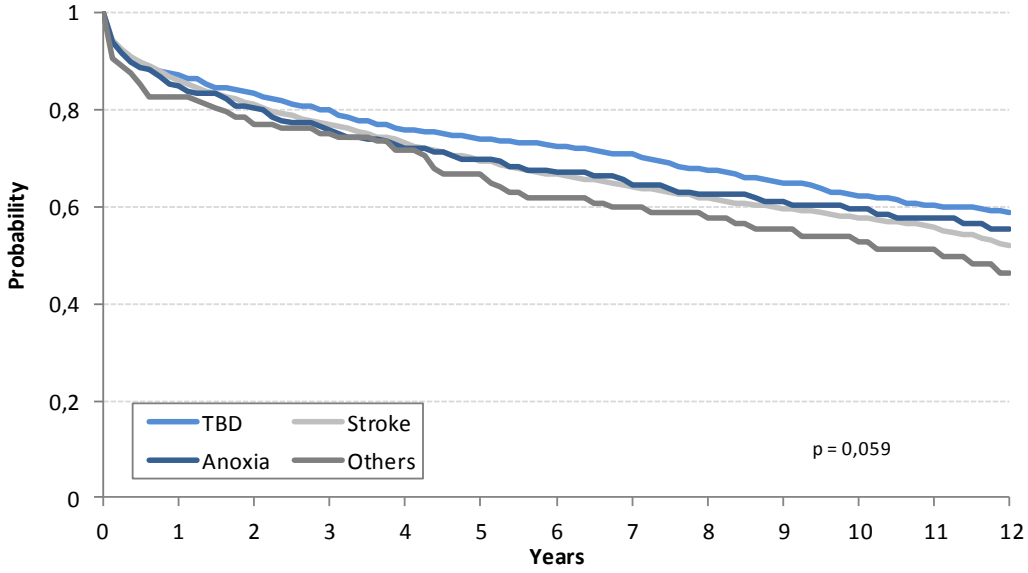
There were statistically significant differences in graft survival by cause of donor death (p=0.059) (Figure 45).

Figure 44. Survival of Patient by Cause of Donor Death (Brain Death): Adult Patients With First Elective Transplant. 1997-2017



	n	1st year	3rd year	5th year	10th year
TBD	786	89%	82%	76%	65%
Stroke	1.907	89%	81%	74%	62%
Anoxia	260	89%	81%	75%	65%
Others	120	87%	79%	70%	55%

Figure 45. Graft Survival by Cause of Donor Death: Elective Transplants in Adult Patients. 1997-2017

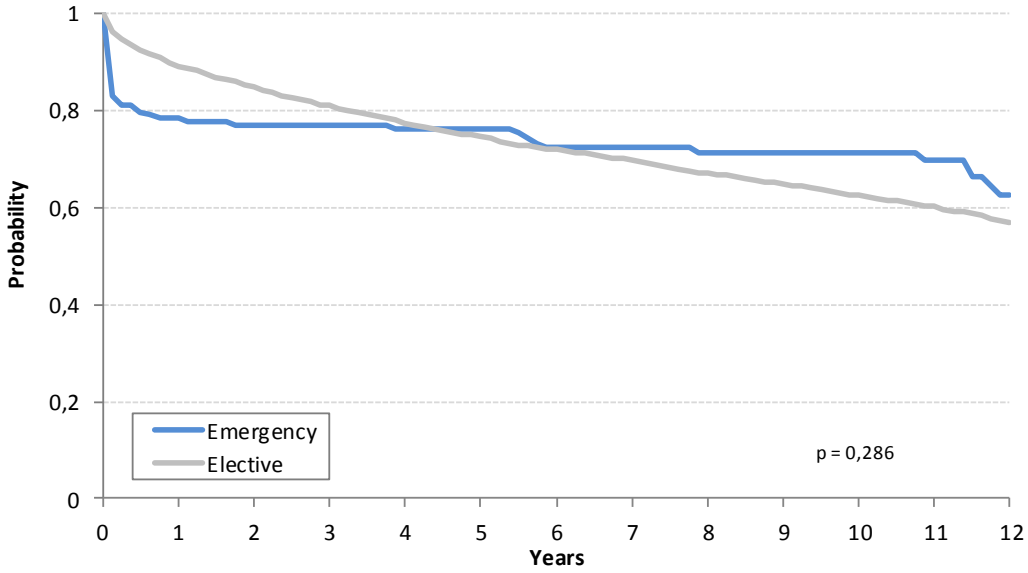


	n	1st year	3rd year	5th year	10th year
TBD	831	87%	80%	74%	62%
Stroke	2.010	86%	77%	70%	58%
Anoxia	272	85%	76%	70%	59%
Others	129	83%	75%	67%	53%

♦ Emergency

Patients who received an emergency first transplant have a survival probability 0.11 lower than the rest of patients, although it is practically the same, at five years, as that for patients who underwent an elective transplant (p=0.286) (Figure 46).

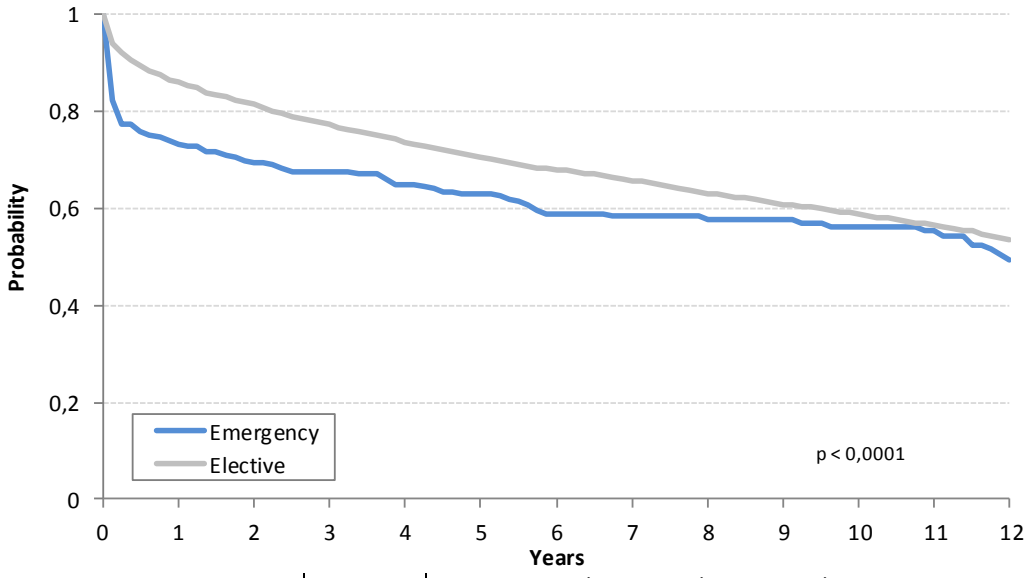
Figure 46. Patient Survival by Emergency: Adult Patients. 1997-2017



	n	1st year	3rd year	5th year	10th year
Emergency	159	78%	77%	76%	71%
Elective	3.350	89%	81%	74%	62%

Differences for graft survival were statistically significant (p<0.0001) (Figure 47).

Figure 47. Graft Survival by Emergency: Transplants in Adult Patients. 1997-2017

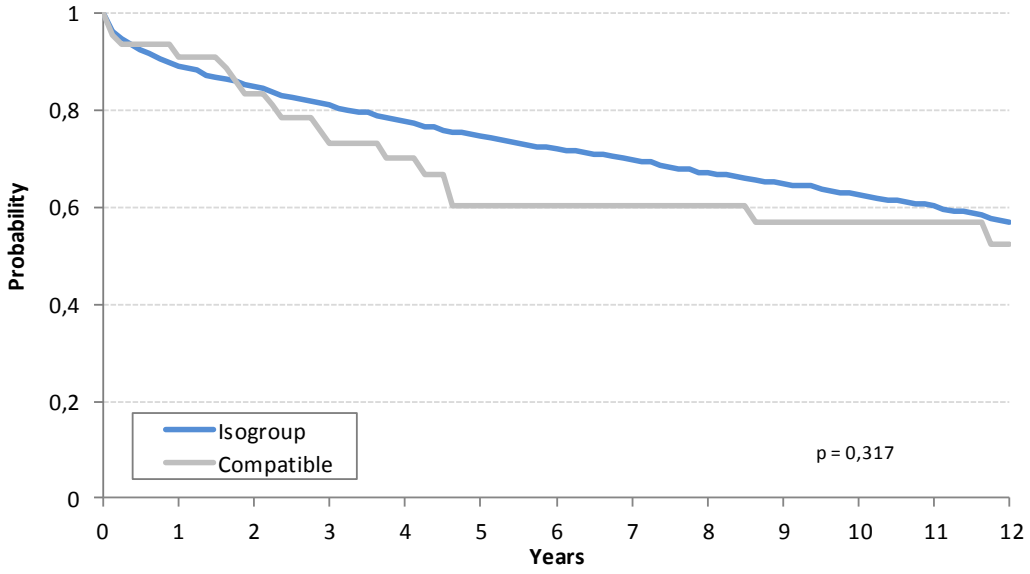


	n	1st year	3rd year	5th year	10th year
Emergency	252	73%	67%	63%	56%
Elective	3.524	86%	77%	71%	59%

♦ ABO compatibility

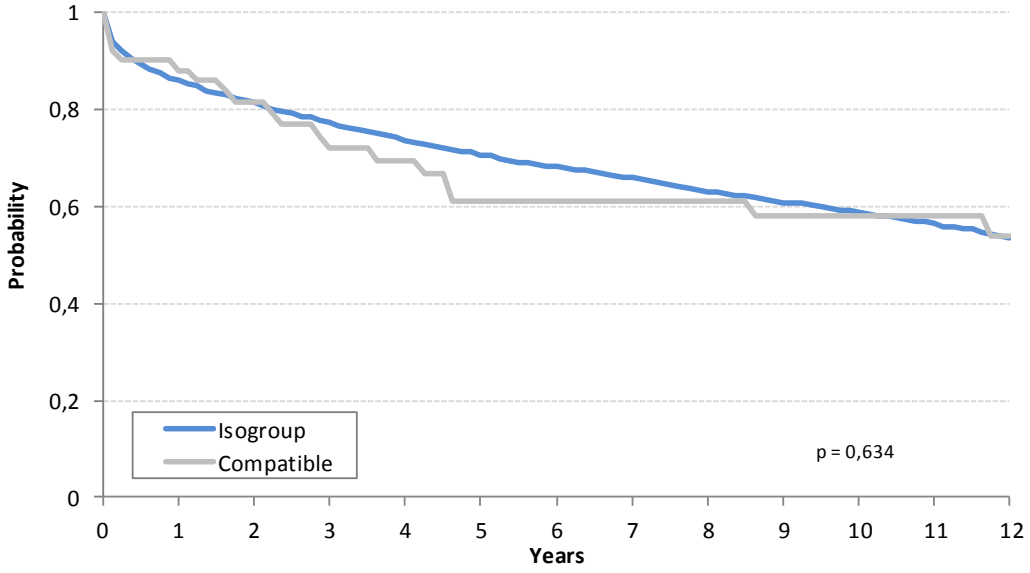
Patients who received a liver from an identical ABO donor have a higher survival rate than those for whom compatibility was not perfect; the differences aren't significant (p=0.317) (Figure 48).

Figure 48. Survival of Patient by ABO Compatibility: Adult Patients With First Elective Transplant. 1997-2017



	n	1st year	3rd year	5th year	10th year
Isogroup	3.302	89%	81%	75%	63%
Compatible	46	91%	73%	60%	57%

Figure 49. Graft Survival by ABO Compatibility: Elective Transplants in Adult Patients. 1997-2017



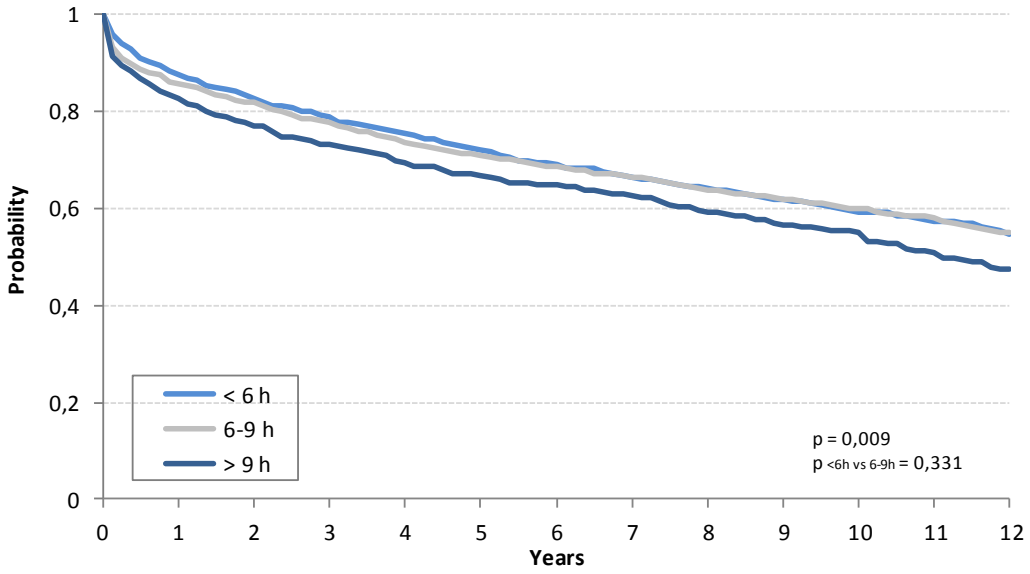
	n	1st year	3rd year	5th year	10th year
Isogroup	3.471	86%	77%	71%	59%
Compatible	51	88%	72%	61%	58%

Neither were differences statistically significant for graft survival (Figure 49).
It must be remembered that there is a low number of non-identical compatible cases and that incompatible cases were not included.

- **Ischemic time**

Overall, the differences observed in graft survival by hours elapsed in ischemia are statistically significant (p=0.009). Those grafts with over nine hours ischemic time have poorer survival rates (Figure 50).

Figure 50. Graft Survival by Ischemic Time: Transplants in Adult Patients. 1997-2017



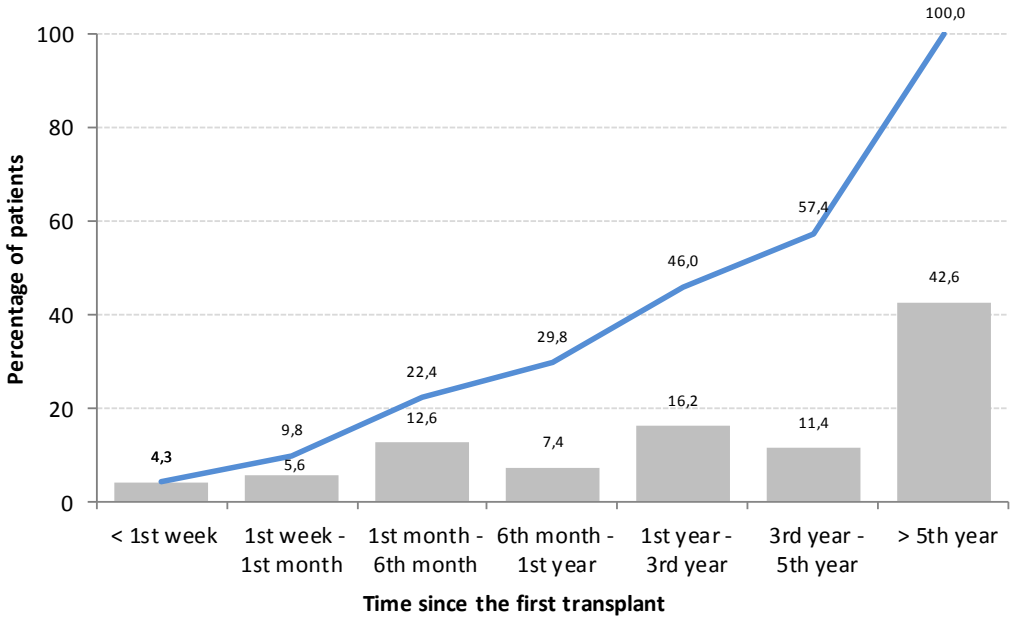
	n	1st year	3rd year	5th year	10th year
< 6 h	1.488	88%	79%	72%	59%
6-9 h	1.449	86%	78%	71%	60%
> 9 h	561	83%	73%	67%	55%

Mortality

Of the 4499 adult patients in the registry, 52.4% (2356) were still alive as at 31 December 2017 and 46.4% (2088) had died. This information was not available due to lost follow-up in 1.2% (55).

In 9.8% (205) of deceased patients, death occurred during the first month after the first transplant (Figure 51).

Figure 51. Patients Deceased by Time Elapsed Between Death and First Transplant: Adult Patients. 1984-2017



Number of deceased patients = 2086

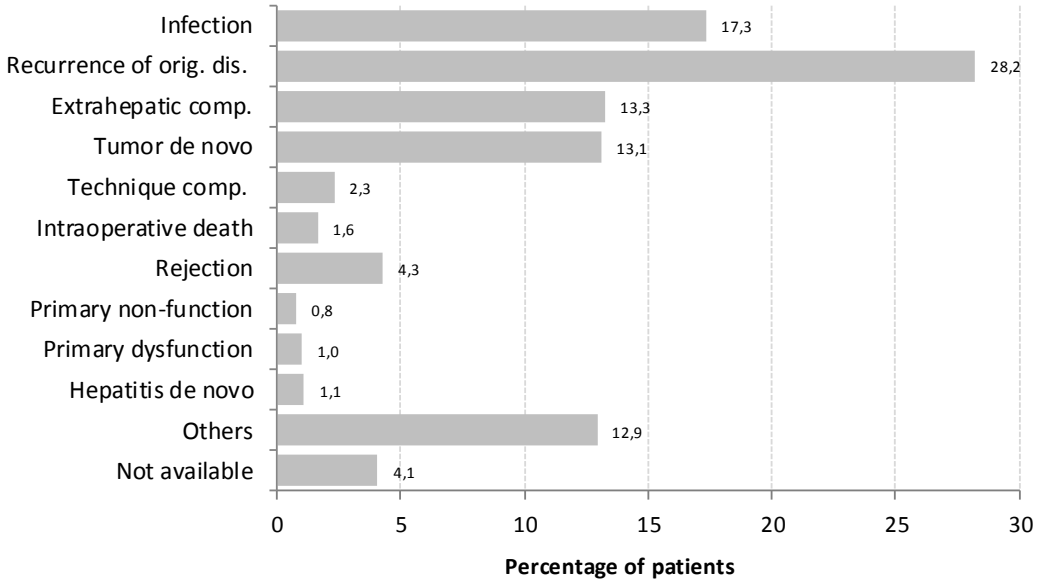
Two patients were excluded because the first transplant was performed outside Catalonia or in a child.

The main causes of death in adult patients were recurrence of the underlying disease (28.2%) and infections (17.3%) (Figure 52). Recurrence of the underlying disease was the main cause of death in the long term (Figure 53).

Mortality was analysed in percentages in relation to the period (year of death). The 1984-1991 period has a considerably higher mortality rate (20.3%); mortality is less than half of this figure for the following periods (1992-1996, 7.6%; 1997-2001, 5.6%; 2002-2006, 5.2%; 2007-2011, 4.5%; 2012-2017: 4.1%). Figure 54 shows the distribution of the main causes of death by period; a reduction can be seen in mortality due to infection, extrahepatic complications and rejection.

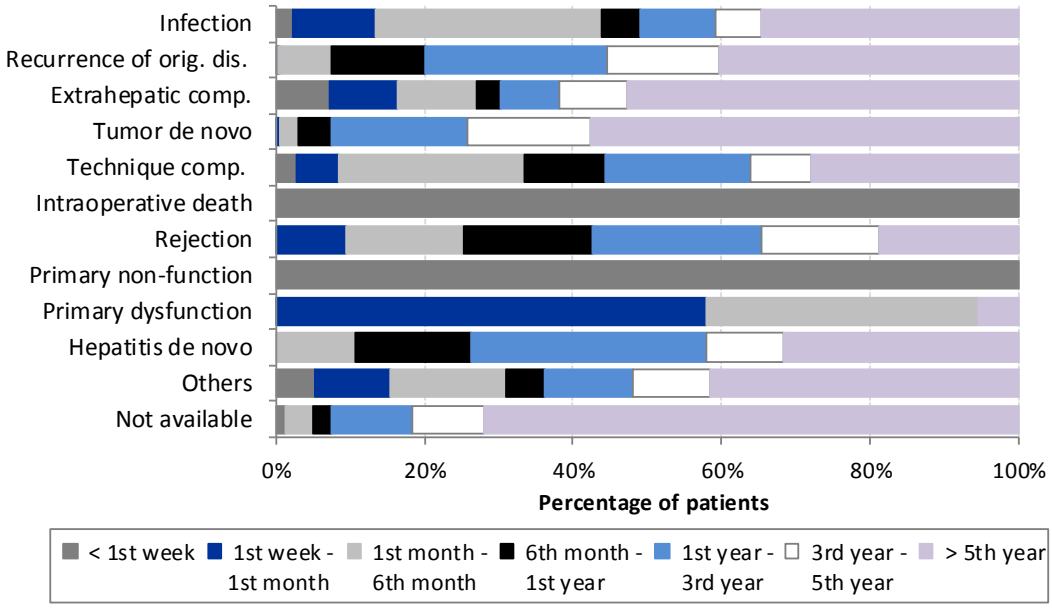
Recurrence of the underlying disease, infections, extrahepatic complications and de novo tumours are the main causes of death in adult patients who received a single liver transplant. Recurrences, infections and extrahepatic complications are also the main cause of death in patients who received a second transplant; in these cases, however, they are followed by rejection and technical complications (Table 5).

Figure 52. Causes of Death: Adult Patients. 1984-2017



Number of deceased patients = 2088

Figure 53. Mortality by Cause of Death and Time Elapsed Since First Transplant: Adult Patients who Received a Single Liver Transplant. 1984-2017



Number of deceased patients = 1878

Figure 54. Distribution of the Main Causes of Death by Period (Year of Death) in Percentages (per 100 People/Year): Adult Patients. 1984-2017

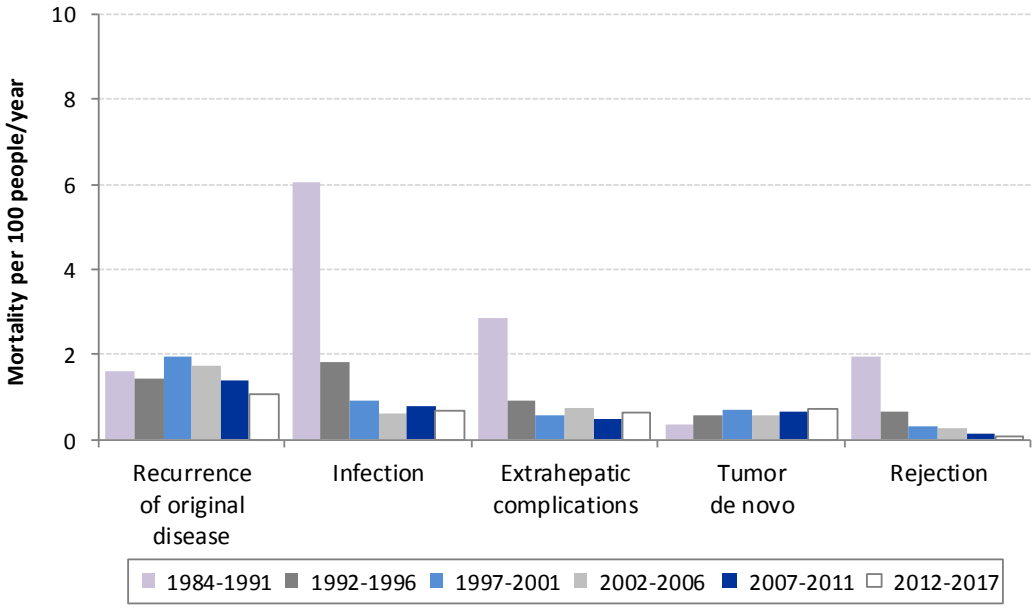


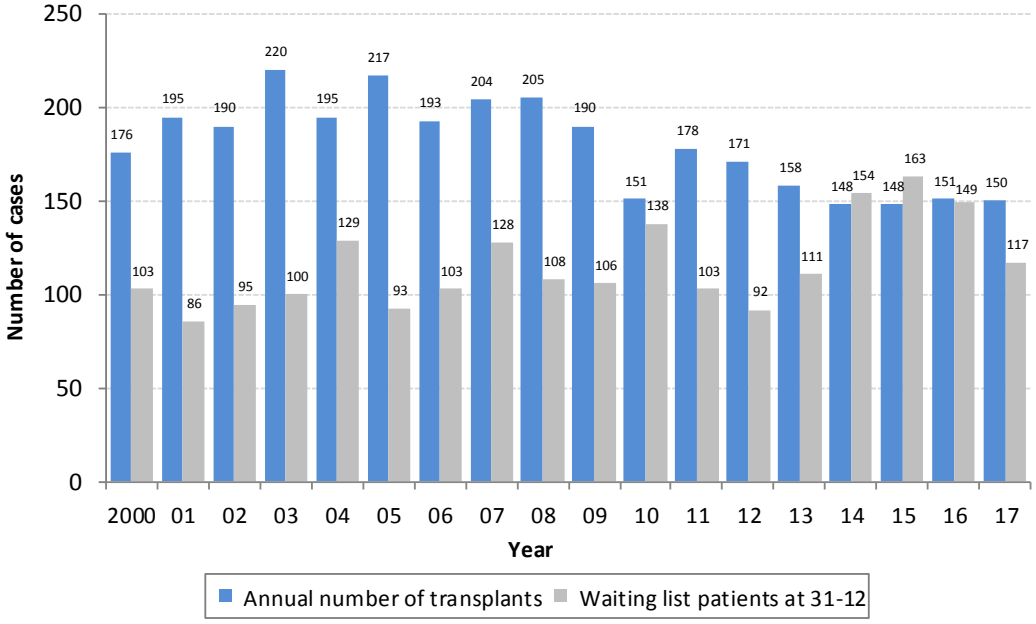
Table 5. Evolution of Cause of Death by Number of Transplants Received: Adult Patients. 1984-2017

	One transplant	Two transplant
	n %	n %
Infection	304 (16,2%)	53 (27,5%)
Recurrence of orig, disease	546 (29,1%)	37 (19,2%)
Extrahepatic complications	249 (13,3%)	27 (14,0%)
Tumor de novo	259 (13,8%)	15 (7,8%)
Technical complications	36 (1,9%)	11 (5,7%)
Intraoperative death	28 (1,5%)	6 (3,1%)
Rejection	75 (4,0%)	13 (6,7%)
Primary non-function (<8 days)	13 (0,7%)	3 (1,6%)
Primary dysfunction (>7 days)	19 (1,0%)	2 (1,0%)
Hepatitis de novo	19 (1,0%)	4 (2,1%)
Others	248 (13,2%)	20 (10,4%)
Unknown	82 (4,4%)	2 (1,0%)
Total	1878 (100%)	193 (100%)

Waiting List

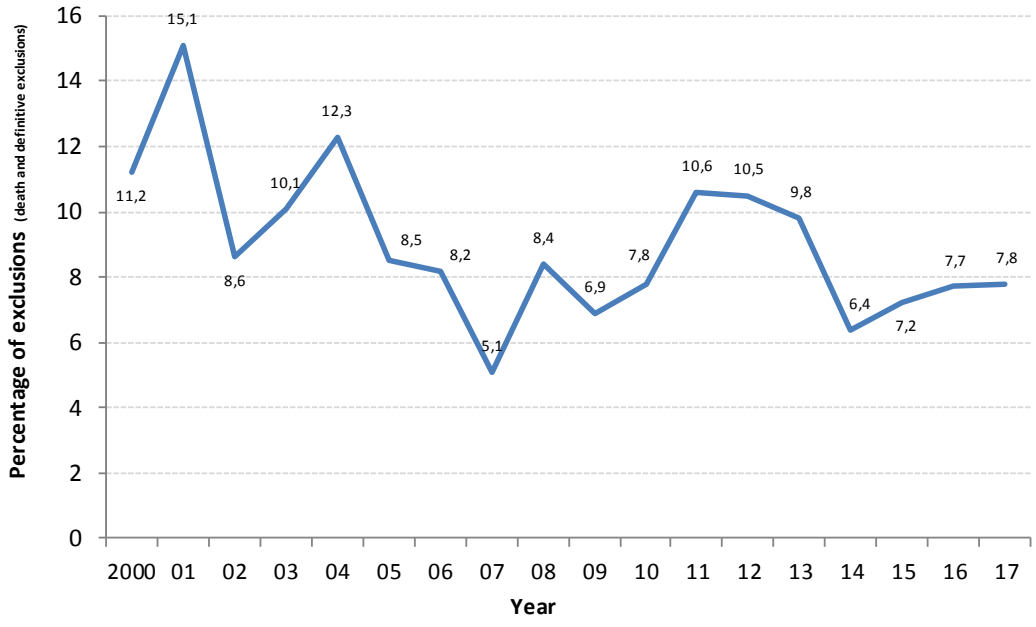
The number of patients on the waiting list at the end of 2017 was lower than in previous years, going from 149 to 117 (Figure 55).

Figure 55. Evolution of Number of Transplants and Number of Patients on Waiting List at End of Year: Adult Patients. 2000-2017



Source: Donor and Transplant Registry

Figure 56. Evolution of Mortality Percentage on Waiting List: Adult Patients. 2000-2017



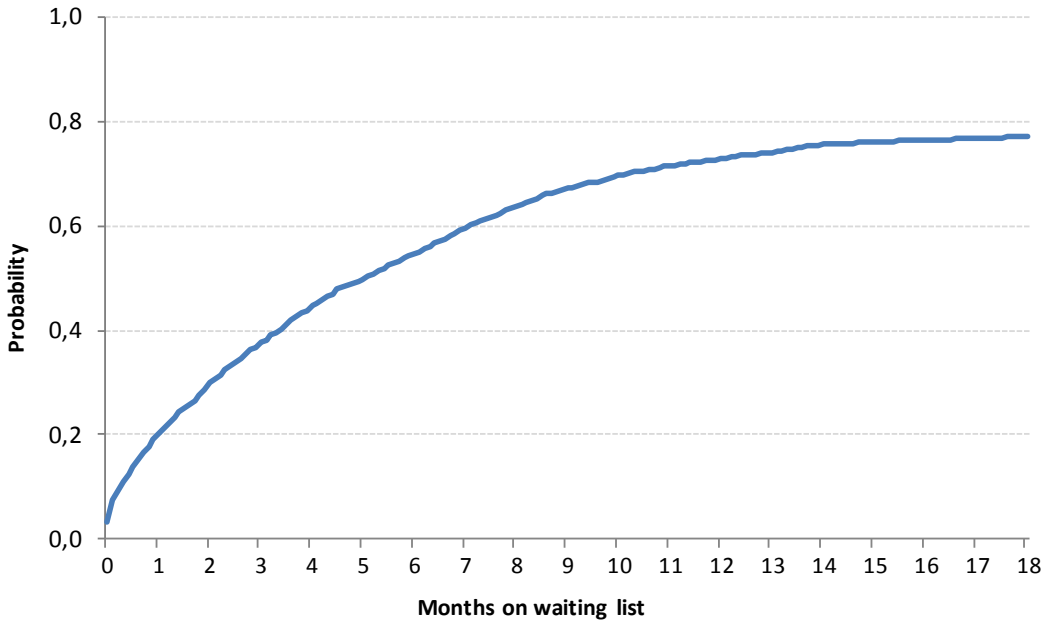
Source: Donor and Transplant Registry

In 2017, the mean number of days waiting for a liver transplant was 214 days, excluding urgent transplants, the waiting time was 231 days.

In 2017, 167 adults were included in the list and 46 were excluded (transplant not included), the percentage of transplant on the list was 46.4%. Of the total number of exclusions, 15 were due to death, which represented a mortality rate on the waiting list of 4.7%, and 10 were due to definitive exclusions (3.1%). Compared to 2016, there was no change in exclusions due to death and definitive exclusions in 2017 (Figure 56).

In the 2000-2017 period, the probability of receiving a liver transplant was 55% after six months on the waiting list and 73% after one year (Figure 57).

Figure 57. Probability of Receiving a Transplant: Adult Patients. 2000-2017



Source: Donor and Transplant Registry

Living donor liver transplant

The first living donor liver transplant in adults was performed in 2000 and 104 of these transplants have been carried out since then. In 2017, one transplant was performed.

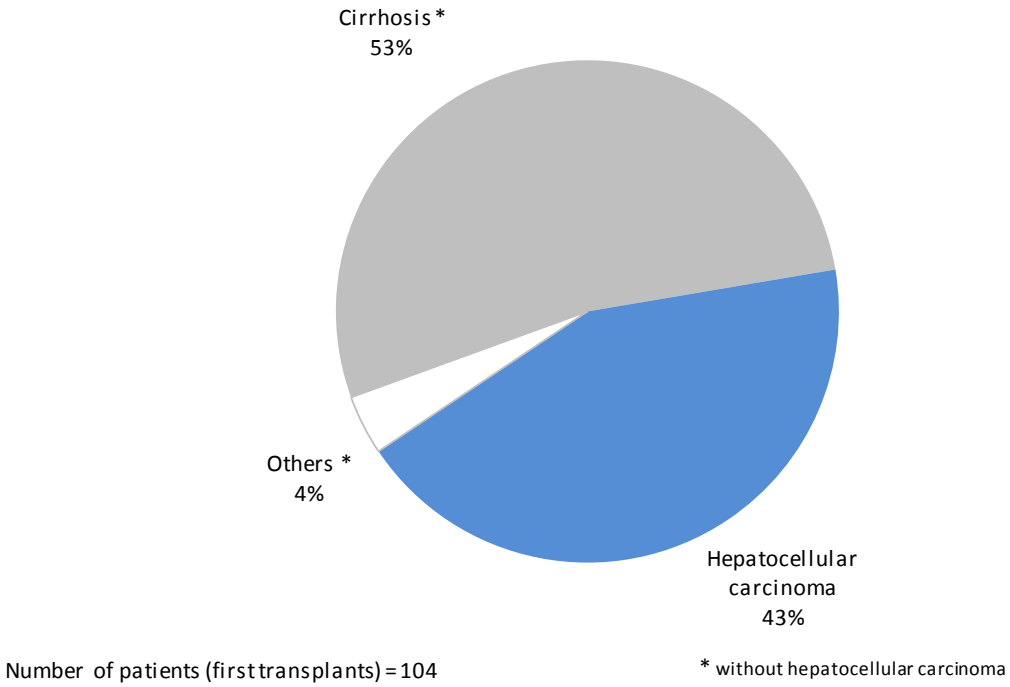
Recipient Characteristics

A total of 69.2% (72) of the patients who received a living donor transplant were men and 30.8% (32) women.

The mean age of recipients was 55 years, the median was 57 years and the range was 23-69 years, with regards to distribution by age groups; 2.9% (3) of patients were under 30 years, 23.1% (24) 31-50 years, 39.4% (41) 51-60 years and 34.6% (36) over 60 years.

Cirrhosis (without hepatocellular carcinoma) is the most frequent indication, representing 52.9% of all patients, the second one (43.3%) is hepatocellular carcinoma (Figure 58). 62.5% of the patients who received a living donor transplant are HCV positive.

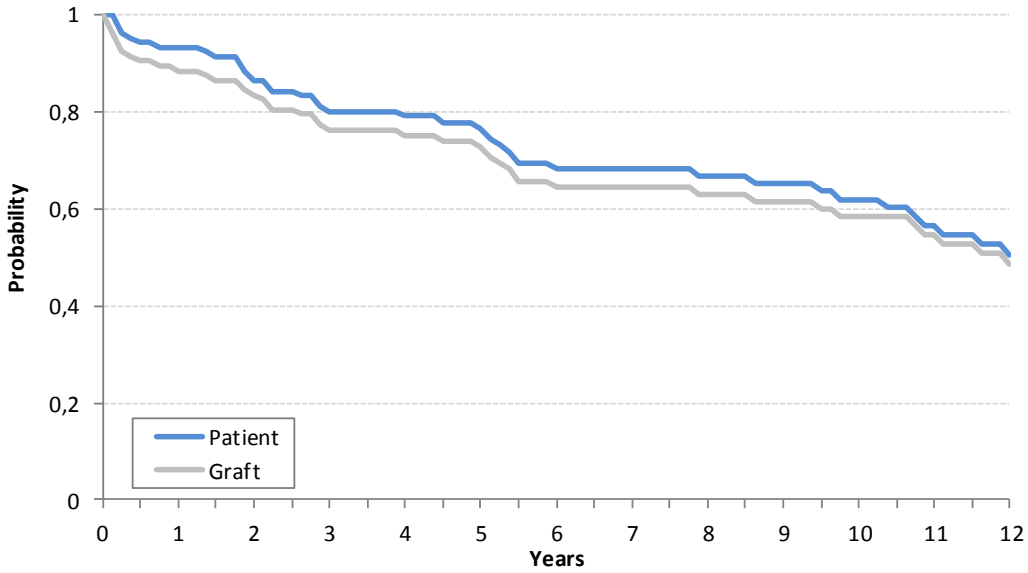
Figure 58. Principal Diagnosis of Patients Who Received a Living Donor Liver Transplant: Adult Patients.2000-2017.



Survival and Mortality

Overall survival of adult patients who received a living donor liver transplant in the 2000-2017 period was 93% at one year and 77% at five years. In terms of graft survival, these probabilities are 88% and 73% respectively (Figure 59).

Figure 59. Survival of Patient and Graft: Living Donor Transplants in Adult Patients. 2000-2017



	n	3r month	1st year	3rd year	5th year	7th year	10th year
Patient	104	96%	93%	80%	77%	68%	62%
Graft	104	92%	88%	76%	73%	64%	58%

Nine (8.7%) grafts failed and needed a retransplant from a brain-death cadaveric donor, three of them before the first week (national emergency) and one between the first week and the first month (local emergency).

Of the 104 adult patients, 56.7% (59) were still alive as of 31st December 2017 and 43.3% (45) had died.

Of the 45 deceased patients, 7 (15.6%) died between the first month and the first year of transplant, 13 (28.9%) died between the first and third year, 3 (6.7%) died between the third and fifth year and 22 (48.9%) died after the fifth year.
The most frequent causes of death were recurrence of the underlying disease (44.4%), infections (17.8%) and technical complications (8.9%).

Domino donor liver transplant

The first domino donor liver transplant in adults was performed in 1999 and 94 of these transplants have been carried out since then; 89 first transplants and 5 retransplants. In 2017, two transplants were performed.

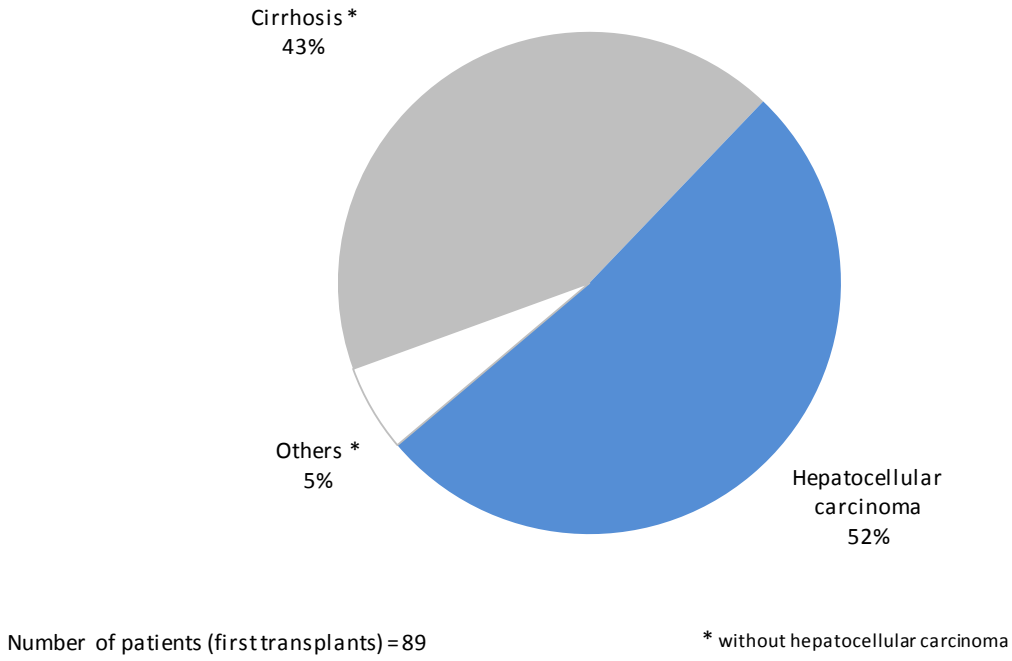
Recipient Characteristics

Of the 89 patients who received a first domino donor liver transplant, 61 (68.5%) were men and 28 (31.5%) women.

For these patients, the mean and median age was 63 years and the range 52-69 years, 76.4% (68) of patients were over 60 years.

Cirrhosis (without hepatocellular carcinoma) and hepatocellular carcinoma were the most common indications and represent 42,7% and 51,7%, respectively, of the patients who received a first domino donor liver transplant (Figure 60). 60.7% of the patients are HCV positive.

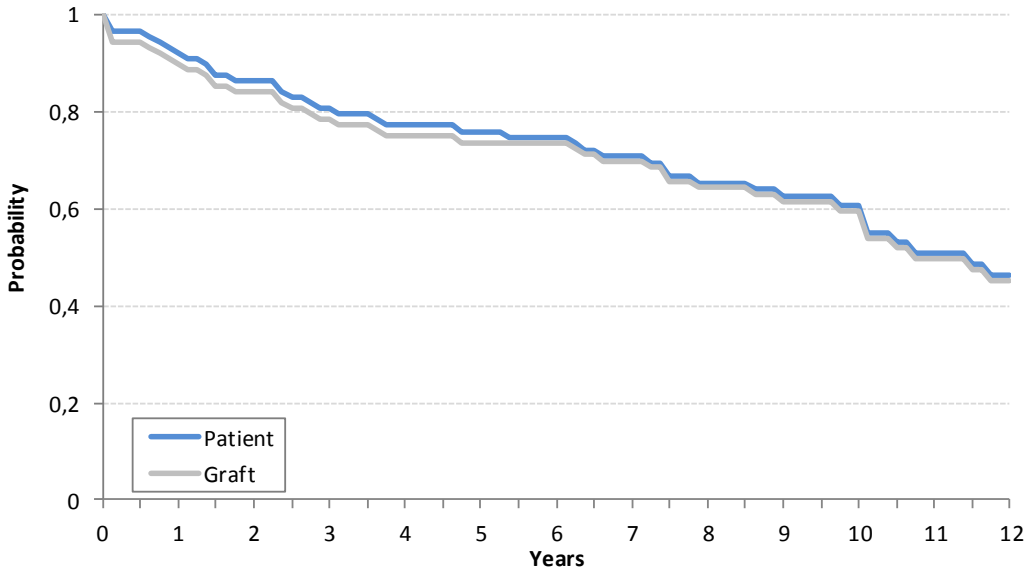
Figure 60. Principal Diagnosis of Patients Who Received a First Domino Donor Liver Transplant: Adult Patients.1999-2017.



Survival and Mortality

Overall survival of adult patients who received a first domino donor liver transplant in the 1999-2017 period was 92% at one year and 76% at five years. In terms of graft survival, these probabilities are 90% and 74% respectively (Figure 61).

Figure 61. Survival of Patient and Graft: Domino Donor Transplants in Adult Patients. 1999-2017



	n	3r month	1st year	3rd year	5th year	7th year	10th year
Patient	89	97%	92%	81%	76%	71%	61%
Graft	89	94%	90%	78%	74%	70%	60%

Two (2.2%) grafts failed and needed a retransplant from a brain-death cadaveric donor before the first week (emergency).

Of the 94 adult patients, 51.1% (48) were still alive at 31st December 2017 and 48.9% (46) had died.

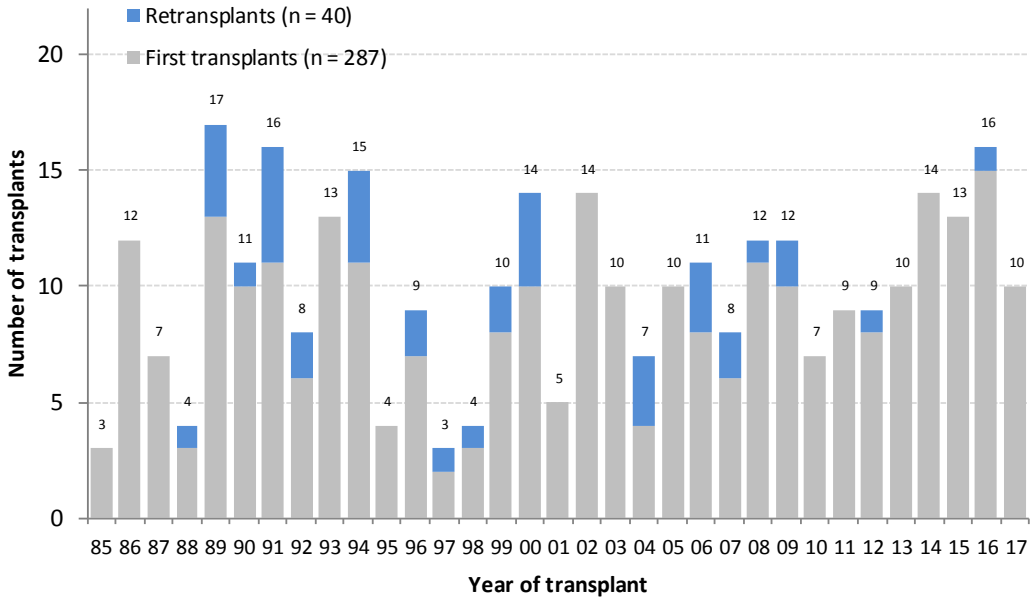
Of the 46 deceased patients, 7 (15.2%) died between the first month and the first year of transplant, 10 (21.7%) died between the first and third year, 4 (8,7%) died between third and fifth year and 25 (54.3%) died after the fifth year.
The most frequent causes of death were recurrence of the underlying disease (34.8%), infections (15.2%), tumour de novo (8.7%) and extrahepatic complications (8.7%).

Liver Transplants in Children

Of the 5215 transplants carried out in Catalonia in the 1984-2017 period, 327 were performed in children (287 first transplants and 40 retransplants). In 2017, a total of 10 transplants were performed, all first transplants.

The paediatric transplant workload varies from one year to another and there is no clear trend upwards or downwards in the workload (Figure 62).

Figure 62. Evolution of Number of Liver Transplants: Paediatric Patients. 1985-2017



Number of transplants = 327

Recipient Characteristics

- **Sex and age**

A total of 51.2% (147) of patients who received a first transplant were boys and 48.8% (140) were girls.

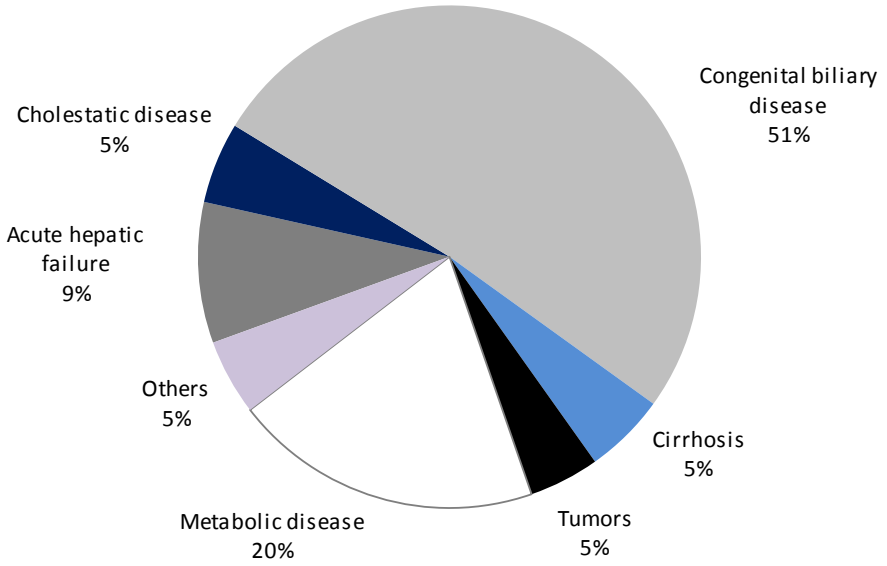
The mean age for the 1984-2017 period was four years (95% CI.3.9-5.0 y; range. 17 days-17 years), although 49.8% (143) of patients were 2 years of age or younger.

In 2017, 7 (70.0%) patients were boys and 3 (30.0%) were girls. The mean age was 4 years with the range from age 8 months to 10 years. Five patients (50.0%) were 2 years of age or younger.

♦ Indications

Indications are stratified into six groups: acute liver failure, cholestatic liver disease, congenital biliary disease, cirrhosis, tumours, metabolic disease and others (Budd-Chiari and polycystic disease), in accordance with the code recorded in the principal diagnosis.
Congenital biliary disease is the most frequent indication, with 51.2% (147) of transplanted patients, mostly corresponding to biliary atresia (133 of 147 cases). The second most frequent indication (57 patients; 19.9%) was metabolic diseases (Figure 63).

Figure 63. Principal Diagnosis of First Liver Transplant: Paediatric Patients. 1985-2017



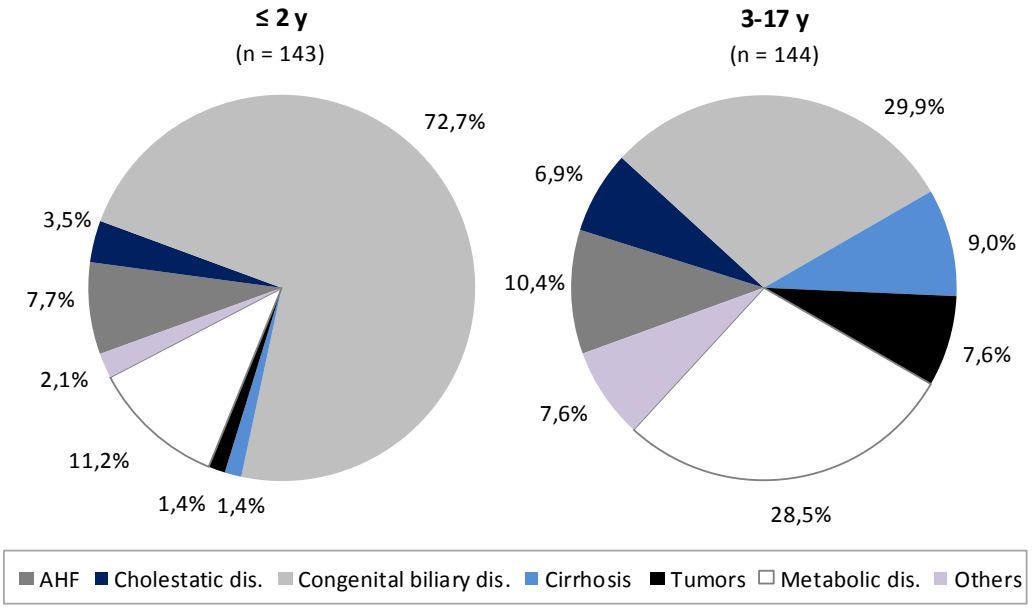
Number of patients (first transplants) = 287

By age, 72.7% (104) of children aged 2 years or younger had a congenital biliary disease, whereas only 29.9% (43) of children aged between 3 and 17 years had this indication (Figure 64). This means that 70.7% of patients with a congenital biliary disease are aged 2 years or younger.

Over the years, congenital biliary disease has remained the most frequent indication, representing 55.9% of indications for the 1984-1991 period and 38.6% for the 2012-2017 period. The percentage of patients with a metabolic disease had decreased in the first periods and risen in the last one, representing, in the 2012-2017 period, 28,6% of all the patients. Given the small number of cases, it was not possible to evaluate the evolution of the other liver diseases (Figure 65).

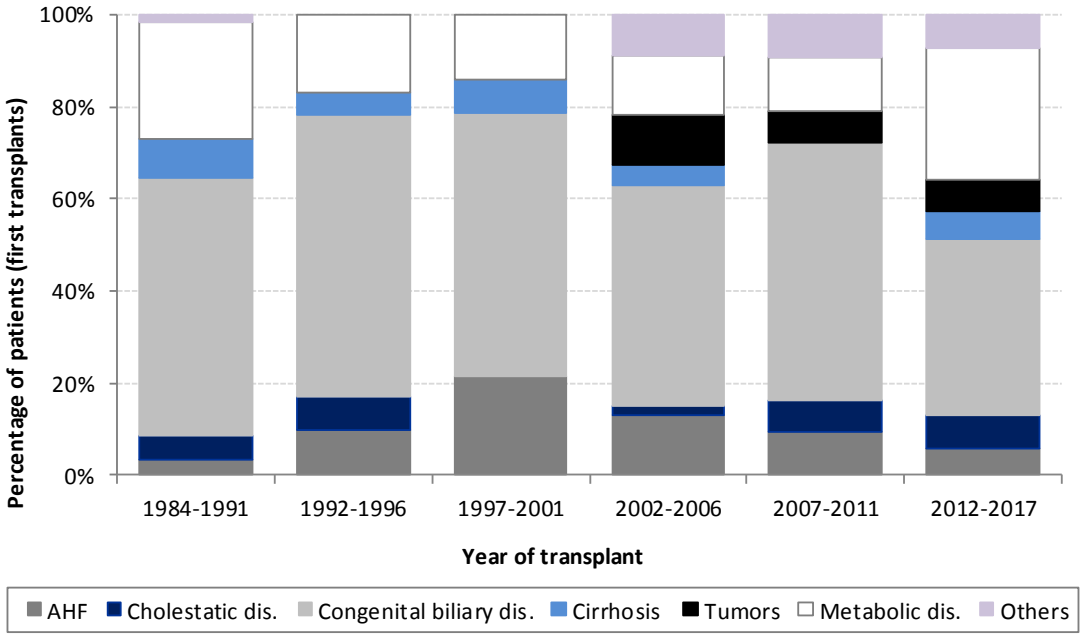
In 2017, 60,0% (6) of the patients have a congenital biliary disease, 20,0% (2) a metabolic disease, 10,0% (1) a cholestatic liver disease and 10,0% (1) a tumour.

Figure 64. Principal Diagnosis of First Liver Transplant by Age Group: Paediatric Patients. 1985-2017



Number of patients (first transplants) = 287

Figure 65. Principal Diagnosis of First Liver Transplant by Period: Paediatric Patients. 1985-2017



Number of patients (first transplants), 1992-2017 = 228

Donor Characteristics

- **Age and sex**

The mean donor age in the 1992-2017 period was 17 years (95% CI.15.3-19.2 y; range. 1-63 y). Over the years, the mean age has oscillated, with a slight tendency to increase due to the increased maximum donor age (split graft transplant, emergency 0 transplants and living donors).

In the same period, 57.3% of donors were men and 42.7% were women.

- **Donor type**

The first living donor transplant was performed in 2003, a total of 43 of these transplants has been performed. Organs from living donors represented 13.1% of all organs transplanted in the 1984-2017 period: the remaining 86.9% (284) came from cadaver donors due to brain death (16.7% and 83.3% respectively in 1992-2017 period).

- **Cause of death**

In the 1992-2017 period, 47.9% (102) of donors died due to craneoencephalic trauma, 24.9% (53) due to cerebrovascular accident, 15.9% (34) due to anoxia and 11.3% (25) due to other causes.

- **Origin**

A total of 14.0% (30) of deceased donors in paediatric transplants carried out in the 1992-2017 period came from the same centre and 23.8% (51) came from another centre in Catalonia, whereas 48.6% (104) came from the rest of Spain and 13.6% (29) from abroad.

Transplant Characteristics

- **Emergency**

Of the 327 transplants carried out in the 1984-2017 period, 16.8% (55) were urgent, of these, 63.6% (35) were first transplants and 36.4% (20) were retransplants.

- **Graft type**

In 62.1% (203) of paediatric transplants carried out in the 1984-2017 period, a whole organ from a cadaver donor was used, a reduced organ was used in 16.2% (53) and a split graft in 8.3% (27). Reduced grafts from living donors represent 13.1% (43).

- **Simultaneous transplants: liver-kidney**

The first simultaneous liver and kidney transplant was carried out in 2000 and 12 of these transplants have been performed since then.

- **Patient status before transplant**

Prior to transplant, 66.1% of patients who underwent a transplant in the 1984-2017 period were living at home leading a normal life and/or receiving ongoing medical care, 11.6% required conventional hospital care and 19.6% were admitted to an ICU.

Retransplants

Of the 327 paediatric transplants performed in the 1984-2017 period, 40 (12.2%) were retransplants (287 first transplants, 34 second transplants and six third transplants). One patient required a retransplant after becoming an adult.

Some 88.2% (253) of these patients received a single transplant, 9.8% (28) received two and the remaining 2.1% (6) received three.

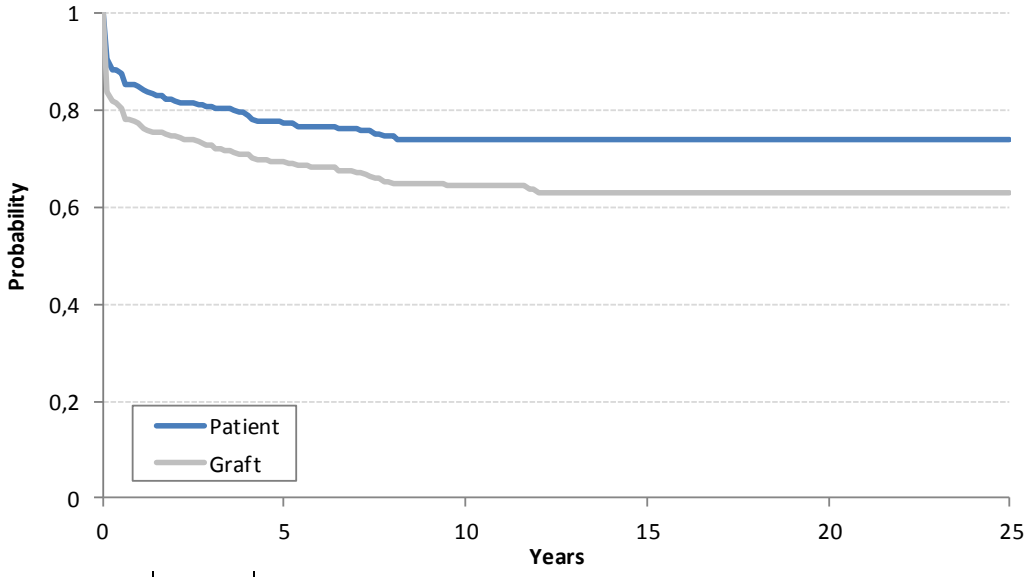
Of the 40 failed grafts, 10 (25.0%) failed before the first week, 10 (25.0%) after the first week and before three months, five (12.5%) after the fourth month and before one year and the remaining 15 (37.5%) after one year.

The principal cause of failure was rejection (14; 35.0%), followed by technical complications (11; 27.5%) and primary non-function (8; 20.0%). In most cases of graft failure that occurred during the first month, the cause was primary non-function, whereas chronic rejection was the principal cause in cases where failure occurred at a later stage.

Survival

Overall survival of children who received a liver transplant in 1984-2017 period was 85% at one year and 74% at 10 years (Figure 66). Graft survival is slightly lower than patient survival - 0.08 less in the first year and 0.10 lower at 10 years.

Figure 66. Survival of Patient and Graft: Paediatric Patients. 1985-2017

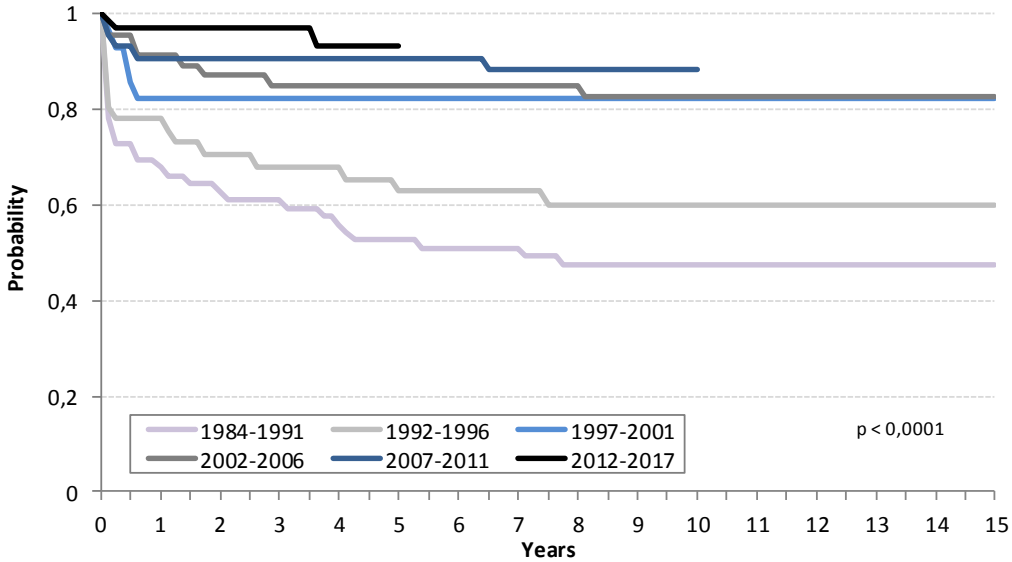


	n	3r month	1st year	3rd year	5th year	10th year	15th year	20th year
Patient	287	88%	85%	81%	77%	74%	74%	74%
Graft	327	82%	77%	73%	69%	64%	63%	63%

- **Period in which transplant was performed**

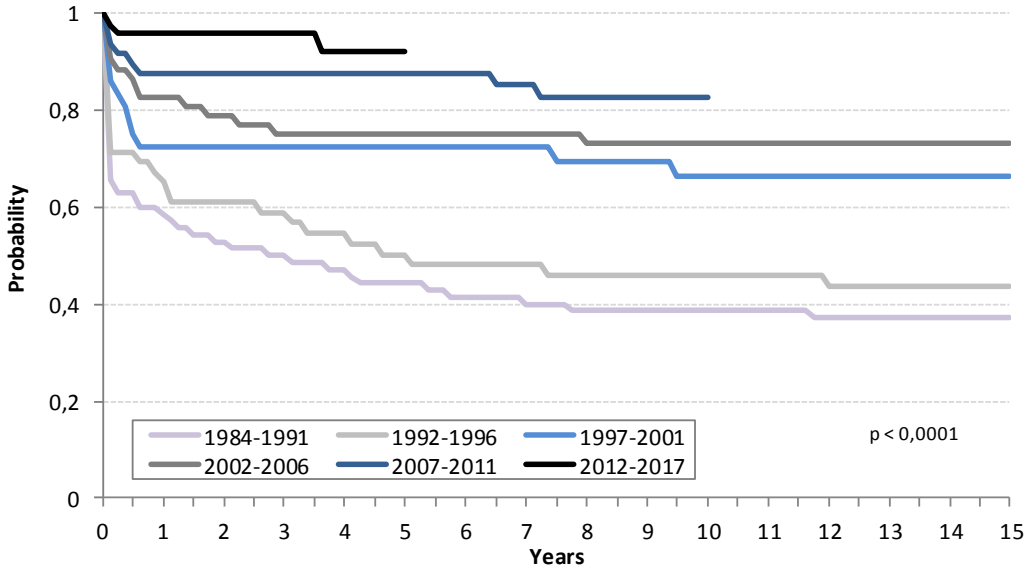
When survival is analysed by the period in which the transplant was performed, the probability of survival increases considerably in the first and third year in the later periods (Figures 67 and 68).

Figure 67. Survival of Patient by Period: Paediatric Patients. 1985-2017



	1984-1991	1992-1996	1997-2001	2002-2006	2007-2011	2012-2017
n	59	41	28	46	43	70
1st year	68%	78%	82%	91%	91%	97%
3rd year	61%	68%	82%	85%	91%	97%
5th year	53%	63%	82%	85%	91%	93%
10th year	47%	60%	82%	83%	88%	-

Figure 68. Survival of Graft by Period: Paediatric Patients. 1985-2017



	1984-1991	1992-1996	1997-2001	2002-2006	2007-2011	2012-2017
n	70	49	36	52	48	72
1st year	59%	65%	72%	83%	88%	96%
3rd year	50%	59%	72%	75%	88%	96%
5th year	44%	50%	72%	75%	88%	92%
10th year	39%	46%	66%	73%	83%	-

The differences in both patient and graft survival for the different periods studied are statistically significant, but this difference was not found between the first and second period or between the four last periods.

To provide a more up-to-date vision of the results, we analysed survival rates using data on transplants carried out from 1997. In the 1997-2017 period, patient survival was 92% in the first year and 89% in the third and fifth year.

- **Age**

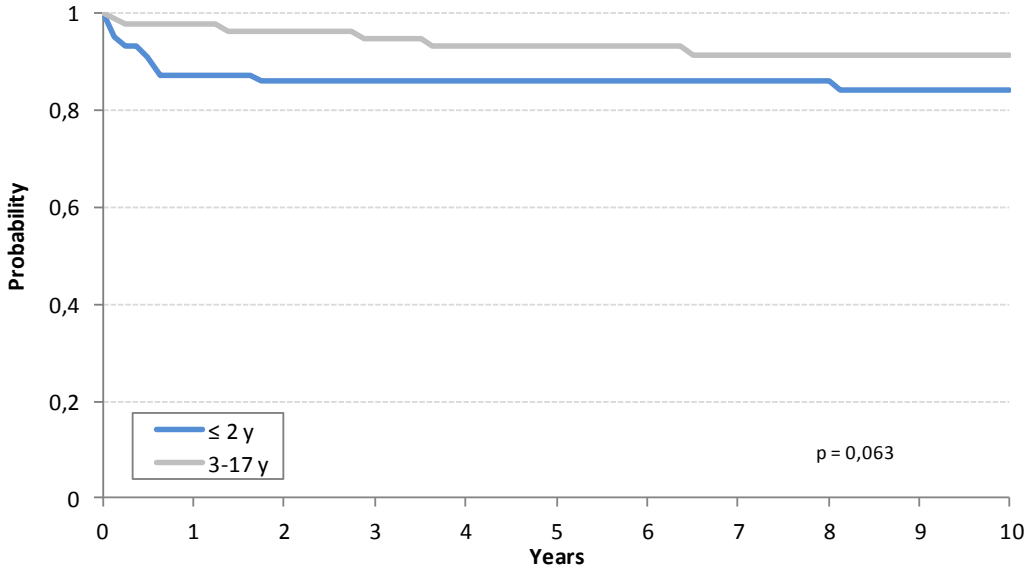
When the child's age is taken into account, the children aged 2 years or younger have a lower survival rate than children aged between 3 and 14 years (p = 0.063) (Figure 69).

- **Indication**

Given the small number of transplants carried out on children, it was not possible to analyse survival in the different groups of indications; two unique groups were therefore created for children with or without congenital biliary disease.

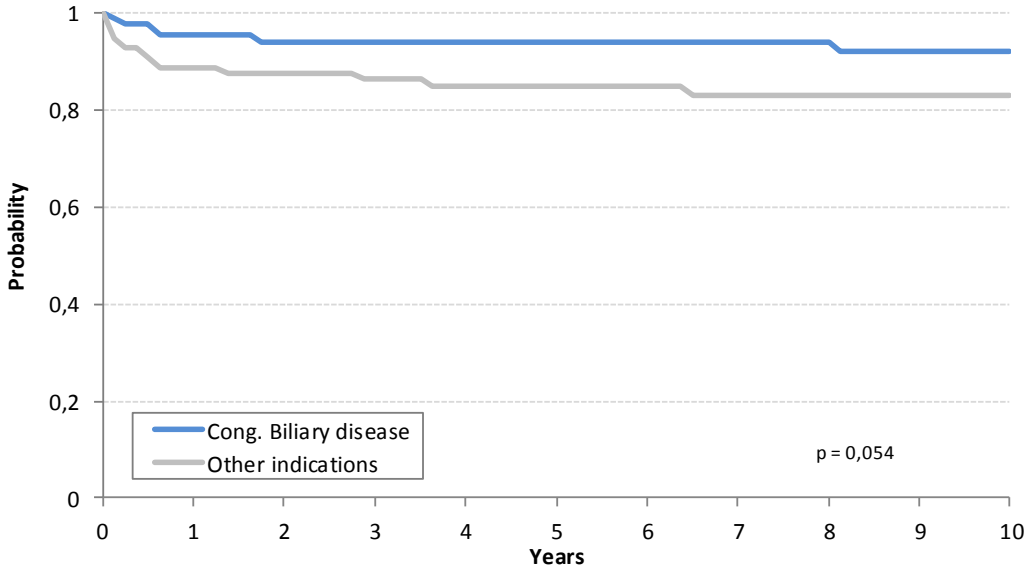
Children who received a liver transplant in the 1997-2017 period due to a congenital biliary disease had a higher survival rate than patients with other indications, although the differences between the two groups were not significant (Figure 70).

Figure 69. Survival of Patient by Age: Paediatric Patients. 1997-2017



	n	1st year	3rd year	5th year	10th year
≤ 2 y	102	87%	86%	86%	84%
3-17 y	85	98%	95%	93%	91%

Figure 70. Survival of Patient by Indication (congenital biliary disease or others): Paediatric Patients. 1997-2017



	n	1st year	3rd year	5th year	10th year
Cong. Biliary disease	89	95%	94%	94%	92%
Other indications	98	89%	86%	85%	83%

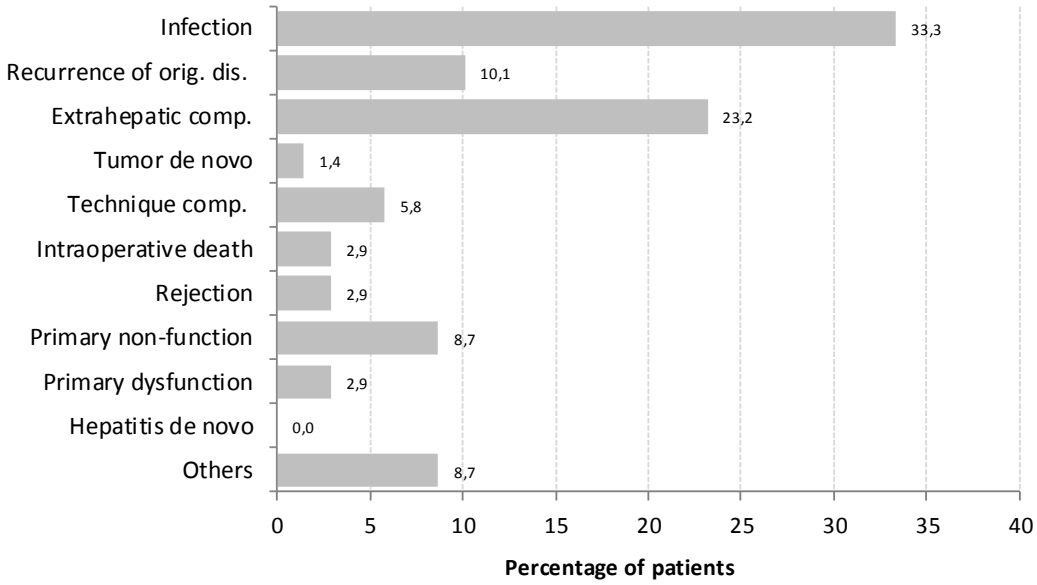
Mortality

Some 70.4% (202) of the 277 patients transplanted were living as at 31 December 2017 and 24.0% (69) had died. This information was not available due to lost follow-up in 5.6% (16)

Of the 69 deceased patients, 23 (33.3%) died before one month after the first transplant and 26 (37.7%) died after the first year.

The most common causes of death were infections and extrahepatic complications (Figure 71).

Figure 71. Cause of Death: Paediatric Patients. 1985-2017



Number of deceased patients = 69

Waiting List

A total of 233 patients were included in the waiting list in the 2000-2017 period; 82.4% received a transplant and 17 patients died while awaiting a transplant.
In 2017, there were 11 inclusions on the waiting list; nine patients remained on the list as at 31 December.

Source: Donor and Transplant Registry.

Living donor liver transplant

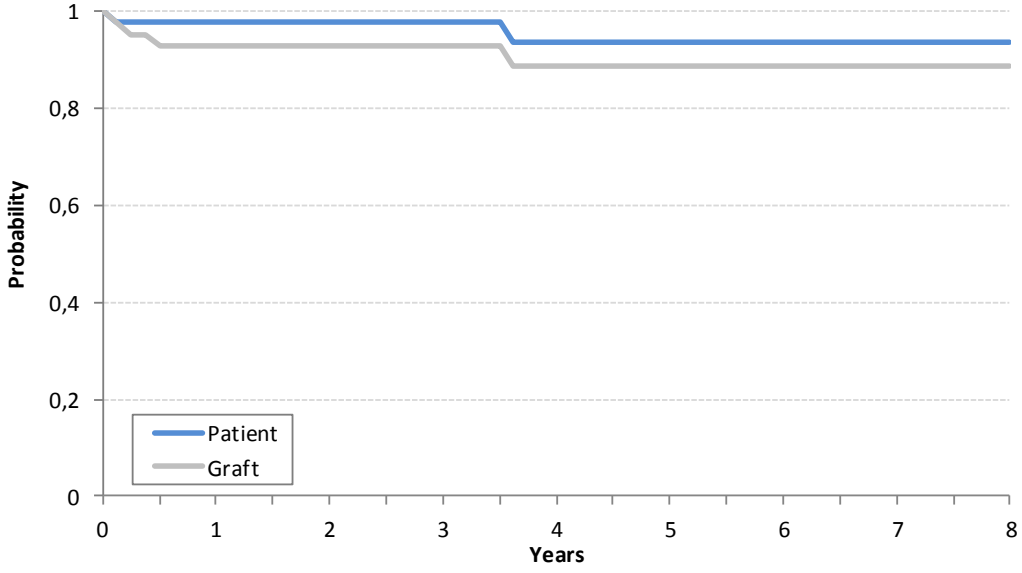
In 2003 the first living donor liver transplant in children was performed and 43 of these transplants have been carried out since them. In 2017, four transplants were performed.

Of these 43 patients, 60.5% (26) were boys and 39.5% (17) girls, the mean age was 2 and the median was one year and the range was between 4 months and 8 years. 69.8% (30) of patients were 2 years of age or younger

23 (53.5%) patients have biliary atresia (congenital biliary disease), 8 (18.6%) metabolic disease, 6 (14.0%) tumour (hepatoblastoma or hepatocellular carcinoma) and 6 (14.0%) other type of liver disease.

Overall survival of children who received a living donor liver transplant in the 2003-2017 period was 98% at one year and 94% at five year (Figure 72). Two (4.7%) grafts failed and needed a retransplant.

Figure 72. Survival of Patient and Graft: Living Donor Transplants in Paediatric Patients. 2003-2017



	n	3r month	1st year	3rd year	5th year	7th year
Patient	43	98%	98%	98%	94%	0%
Graft	43	95%	93%	93%	89%	0%