Chapter IV
Liver and Intestine Transplantation in the United States 1998-2007

Overview

- Liver transplantation numbers in the United States remained constant from 2004-2007, while the number of waiting list candidates has trended down.
- In 2007, the waiting list was its smallest since 1999, with adults ≥50 years representing the majority of candidates.
- Non-cholestatic cirrhosis was most commonly diagnosed. Most age groups had decreased waiting list death rates, however, children <1 year had the highest death rate.
- Use of liver allografts from donation after cardiac death donors increased in 2007. Model for End-stage Liver Disease (MELD)/Pediatric Model for End-stage Liver Disease (PELD) scores have changed very little since 2002, with MELD/PELD <15 accounting for 75% of the waiting list.
- Over the same period, the number of transplants for MELD/PELD <15 decreased from 16.4% to 9.8%. Hepatocellular carcinoma exceptions increased slightly.
- The intestine transplantation waiting list decreased from 2006, with the majority of candidates being children <5 years old.
- Death rates for intestine transplant recipients have improved, but remain unacceptably high. Policy changes have been implemented to improve allocation and recovery of intestine grafts to positively impact mortality.

Introduction

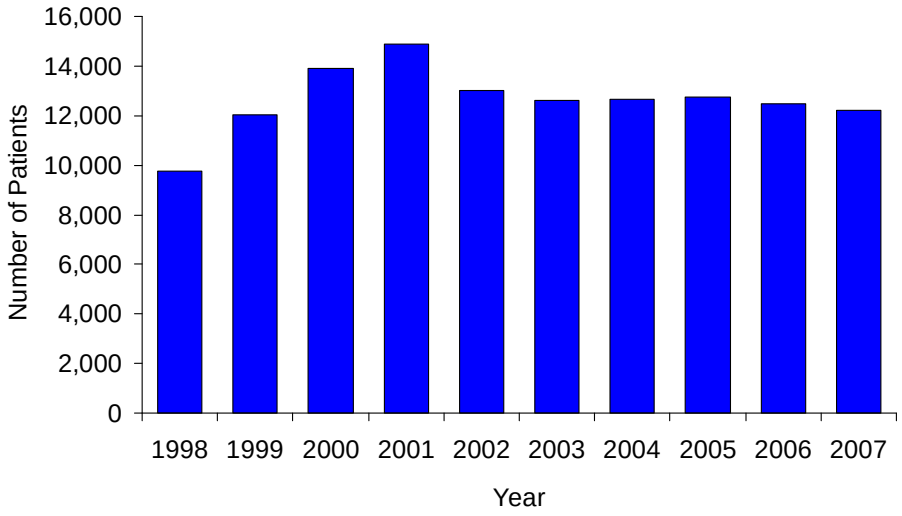
The introduction of the model for end-stage liver disease (MELD) and the pediatric model for end-stage liver disease (PELD) on February 27, 2002 as the basis for allocation of deceased donor livers for transplantation in the United States (US) has transformed the field of liver transplantation. The use of this urgency based allocation system appears to have reduced the number of candidates listed annually while allowing more rational and objective allocation based on risk of waiting list mortality. Equally important, the use of MELD and PELD has helped frame the central role that medical urgency deserves, both regarding the decision to transplant a given patient, as well as in allocation policy.

In this report, we review trends in liver and intestine transplantation over the last decade using data from the 2008 Organ Procurement and Transplantation Network (OPTN)/Scientific Registry of Transplant Recipients (SRTR) Annual Report. Details on the methods of analyses employed may be found in the reference tables themselves or in the technical notes of the 2008 OPTN/SRTR Annual Report, both available online at http://www.ustransplant.org. This chapter focuses on specific areas of interest to the transplant community through analyses presented by the SRTR to the OPTN committees as well as special analyses conducted specifically for this manuscript. In addition to reviewing trends in the waiting list, deceased and living donor transplant recipients, and posttransplant outcomes, special sections are included on issues related to organ acceptance rates, donation after cardiac death, living donor transplantation, and MELD/PELD exceptions. An in depth examination of the state of intestine transplantation is also provided.

Liver Waiting List

There were 12,213 patients active on the liver transplant waiting list on December 31, 2007, a decrease from 2006 (Figure IV-1) *[Table 9.1a]*. This is the smallest waiting list since 1999 when there were 12,044 patients on the waiting list at the year's end. New registrations increased from 11,036 in 2006 to 11,081 in 2007, but the number of inactive patients on the waiting list has remained stable at around 4,200 for the past five years. All of the waiting list characteristics are based on a snapshot of the list on the last day of the calendar year.

Figure IV-1. Number of Candidates on the Liver Waiting List, Active at Year-End, 1998-2007



Source: *2008 OPTN/SRTR Annual Report*, Table 9.1a.

Age, race/ethnicity, gender, and blood type: The liver waiting list continued its aging trend in 2007, with adults aged 50 and older representing 74% of the waiting list, compared to 72% in 2006 and 51% in 1998 *[Table 9.1a]*. Pediatric candidates remained at 3% of the list, the same as 2006, compared to 6% in 1998. A similar trend was observed for younger adults. The racial/ethnic distribution of the waiting list has remained stable for the past five years. In 2007, there were 71.4% white, 6.8% African American, 16.5% Hispanic, 4.5% Asian American, and 0.8% other. Similar to past years, in 2007, men outnumbered women on the waiting list (males: 60%, females: 40%). Blood type distribution among waiting list candidates was also similar to previous years; 49% had blood type O, 38% had blood type A, 11% had blood type B, and 2% had blood type AB. There were fewer females and blood type O candidates in 2007 compared to previous years.

Primary diagnosis at listing and previous transplant: The distribution of major diagnostic categories of liver disease in 2007 was similar to previous years (Table IV-1). Non-cholestatic cirrhosis was the diagnosis for 73% of waiting list candidates, the largest

diagnostic category *[Table 9.1a]*. Cholestatic cirrhosis at 10% was the second largest, followed by other with 9%, acute hepatic necrosis with 3%, malignant neoplasms with 2%, and biliary atresia and metabolic diseases each accounting for less than 2% of the waiting list. These categories are determined by the primary diagnosis code listed for each candidate, so the malignant neoplasms group contains candidates with hepatocellular carcinoma (HCC) and other liver cancers only if these conditions were listed as the primary diagnosis. Note that candidates with MELD/PELD exceptions for HCC often do not have a diagnosis of HCC; only 21% of candidates with initial applications for the HCC MELD/PELD exception in 2006 had a primary diagnosis of malignant neoplasm, while 59% had a primary diagnosis of non-cholestatic cirrhosis *[SRTR Analysis, 2007]*. The OPTN/SRTR registry data does not contain a data field where all liver transplant candidates have the presence or absence of HCC reported; information on HCC in the registry data can come from either the diagnosis codes or the application for a MELD/PELD exception score. Three percent of waiting list candidates had a previous liver transplant in 2007, a decrease from 5% in the late 1990s.

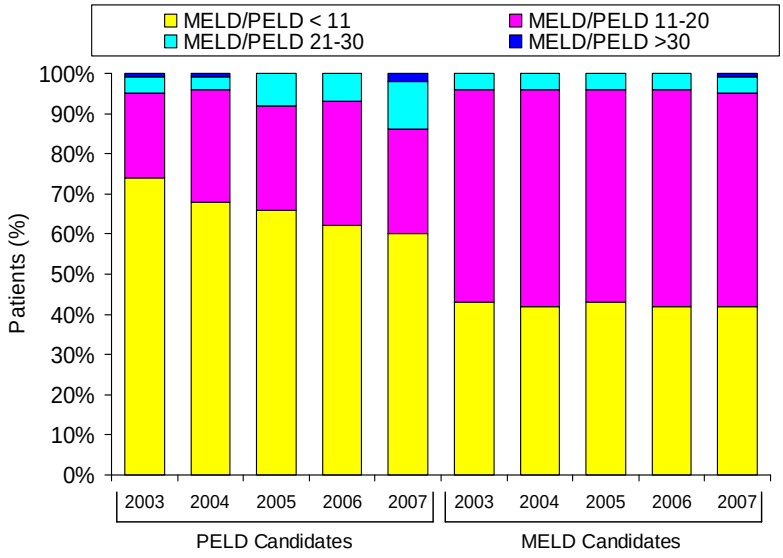
Table IV-1: Liver Waiting List Candidates (Active at End of Year) by Diagnosis, 1998-2007

	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007
Non-cholestatic cirrhosis (%)	70	70	70	70	70	71	72	72	73	73
Hepatitis C (%)	28	29	29	30	30	31	31	31	31	30
Alcoholic cirrhosis (%)	15	15	15	15	15	15	15	15	16	16
Both hep C & alcoholic (%)	8	8	7	6	7	6	7	7	6	7
Autoimmune hepatitis (%)	4	4	4	4	5	4	4	4	4	4
Hepatitis B only (%)	4	4	4	4	3	4	3	3	3	3
Cryptogenic/idiopathic/ NASH (%)	10	10	9	10	10	10	10	11	11	12
Other non-cholestatic (%)	1	1	1	1	1	1	1	1	1	1
Cholestatic liver disease (%)	13	12	12	11	11	11	11	11	10	10
Acute hepatic necrosis (%)	4	5	5	5	5	5	4	4	4	3
Biliary atresia (%)	2	2	2	2	2	2	2	2	1	1
Metabolic disorders (%)	2	2	2	2	2	1	2	2	1	1
Malignant neoplasms (%)	1	1	1	1	1	1	1	1	2	2
Other (%)	7	8	8	9	9	9	8	9	9	9

Notes: Candidates with both Hepatitis B and Hepatitis C are counted in the Hepatitis C category. NASH = non-alcoholic steatohepatitis.

MELD/PELD scores: Adult waiting list MELD scores changed very little since the implementation of MELD/PELD in 2002 (Figure IV-2) *[Table 9.1a]*. Candidates with MELD scores <15 accounted for 75% of the waiting list at the end of 2007, a fraction similar to previous years *[Table 9.1a]*. A change to allocation policy was implemented on January 12, 2005, which substituted the use of the PELD score with the MELD score for adolescents aged 12 to 17. This policy changed the age range of the PELD candidate group from <18 years old (2002-2004) to those <12 years old (2005-2006). There were 66% of PELD candidates with scores <11 in 2005, 62% in 2006, and even fewer in 2007 at 60%. Approximately 2% of children on the waiting list had PELD scores >30 in 2007.

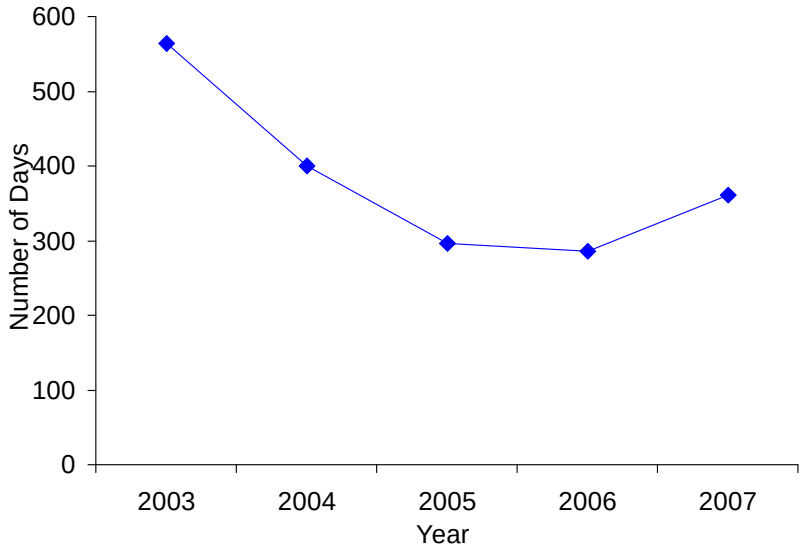
Figure IV-2. Distribution of MELD/PELD Scores Among Candidates on the Liver Waiting List at Year-End, 2003-2007



Source: *2008 OPTN/SRTR Annual Report*, Table 9.1a.

Waiting time and median time to transplant: By the end of 2007, 63% of the waiting list with active status had been listed for more than one year (18% waiting for 1-<2 years and 45% waiting for 2+ years) *[Table 9.1a]*. The median time to transplant (TT) among candidates on the waiting list initially listed in the given calendar year is shown in Figure IV-3 *[Table 1.5]*. The median TT is calculated as the number of days until half of the new waiting list registrants in the calendar year have received a transplant. Median TT for liver waiting list candidates decreased substantially after the implementation of MELD/PELD in 2002 when the median TT was 981 days; in 2003, it decreased to 564 days *[Table 1.5]*.

Figure IV-3. Median Time to Transplant (TT) for New Liver Waiting List Registrations, 2003-2007

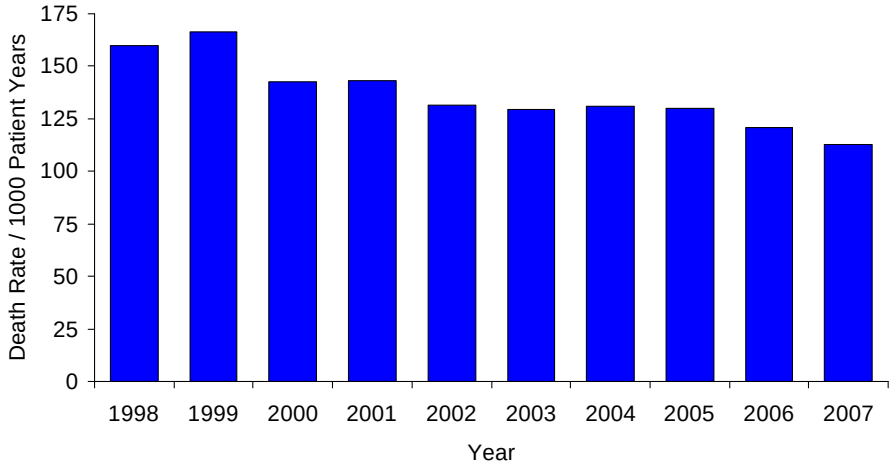


Source: *2008 OPTN/SRTR Annual Report,* Table 1.5.

There was a noticeable drop in median time to transplant between 2004 (400 days) and 2005 (296 days) that coincided with several changes in allocation policy, including the implementation of Share 15, the switch of adolescents to the MELD score instead of the PELD score, and the implementation of a new MELD survival curve (resulting in the exception for stage T2 HCC decreasing to a score of 22). Median TT reached a ten-year low of 286 days in 2006 before increasing again in 2007 to 361 days.

Death rates on the waiting list: Death rates for the waiting list (deaths per 1,000 patient-years at risk) declined in 2007 to 113 from 121 in 2006 (Figure IV-4) *[Table 9.3]* and varied according to demographic and medical factors. Most age groups had decreased death rates. In 2005 patients >65 years had a death rate of 164 and 165 in 2006. In 2007 an improvement was seen with a rate of 129. Children <1 year had, by far, the highest rate of all age groups (447 deaths per 1,000 patient-years). While the death rate in children <1 year remains high, it has declined sharply from past years (738 in 2005 and 905 in 2006).

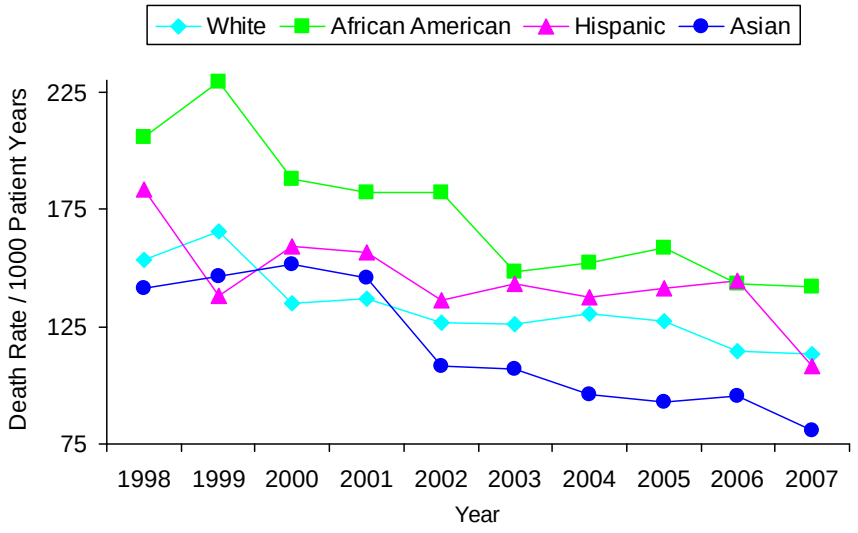
Figure IV-4. Unadjusted Death Rates per 1,000 Patient-Years at Risk, 1998-2007, Liver Waiting List



Source: *2008 OPTN/SRTR Annual Report*, Table 9.3.

All ethnic groups had declining death rates in the last decade (Figure IV-5) *[Table 9.3]*. Asian Americans had the lowest death rate on the waiting list at 81 in 2007 (lower than 2006's rate of 96). With steady rates of 136-145 over the past five years, Hispanics showed a marked decrease in death rates at 108 in 2007. The 2007 death rates for African Americans and whites did not change much from 2006 at 142 and 113, respectively. In 2007, men and women had the same rate of 113, and both were lower than 2006.

Figure IV-5. Unadjusted Death Rates per 1,000 Patient-Years at Risk, 1998-2007, Liver Waiting List by Race/Ethnicity

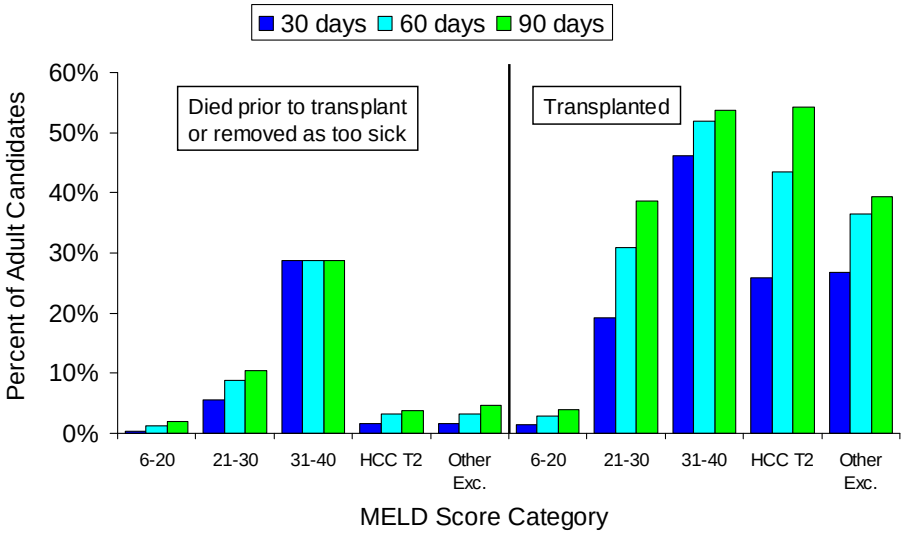


Source: *2008 OPTN/SRTR Annual Report*, Tables 9.3.

All disease etiologies had decreasing death rates over the past ten years when assessed according to diagnostic group. Not surprisingly, in 2007 acute hepatic necrosis had the highest death rate at 160, down from 2006 when it was 190, but down twofold since 1998, likely a result of regional sharing (introduced in 1997 and 1998) and improved patient selection for placement on the waiting list *[Table 9.3]*. The second highest waiting list death rate was 153 for diagnoses classified as other, down slightly from 2006 when it was 166. The remaining categories were: 116 for metabolic disorders; 109 for malignant neoplasms (this category does not contain all candidates with HCC exceptions, only those with a primary diagnosis of liver cancer); 109 for non-cholestatic cirrhosis; 80 for cholestatic cirrhosis, and 44 for biliary atresia. The waiting list death rate was extremely high for candidates listed as Status 1A at 4,364, even though it decreased from 2005 (6,158). Given the ability of MELD and PELD to predict three month waiting list mortality, waiting list death rates increased as MELD and PELD increased, from 35 for MELD scores 6-10 to 596 for MELD scores 21-30 and 3,758 for MELD over 30. Similarly, waiting list death rates increased as PELD scores increased, from 11 for PELD <11, to 768 for PELD scores 21-30 and 2,064 for PELD greater than 30. Patients with exceptions for hepatocellular carcinoma with stage T2 lesions (HCC T2) had a death rate of 99, down from 133 in 2006. Those with exceptions for other diagnoses had a death rate of 81, compared to 101 in 2006.

Patient events on the waiting list: Figure IV-6 shows the incidence of transplant and removal for death, being too sick or medically unsuitable for transplant over three months for adults on the waiting list, by waiting status on January 1, 2007 *[Table 9.2b] (SRTR Analysis)*. Thirty days later, less than 1% of candidates with MELD scores of 20 or less on January 1 had either died or were removed as too sick (0.4%) while 1.4% received transplants *[Table 9.2b]*. Candidates with MELD 21-30 had a removal rate for death or too sick to transplant of 5.6% and a transplant rate of 19%. In the highest MELD score group (MELD >30), 29% of patients died or were removed as too sick to transplant, while almost half (46%) received transplants within 30 days of January 1. About one quarter (26%) of candidates with an HCC T2 exception on January 1 received transplants within 30 days while only 1.6% died or were removed from the list as too sick.

Figure IV-6. Waiting List Candidates With Events Within 30, 60, and 90 Days After Snapshot (January 1, 2007) by MELD



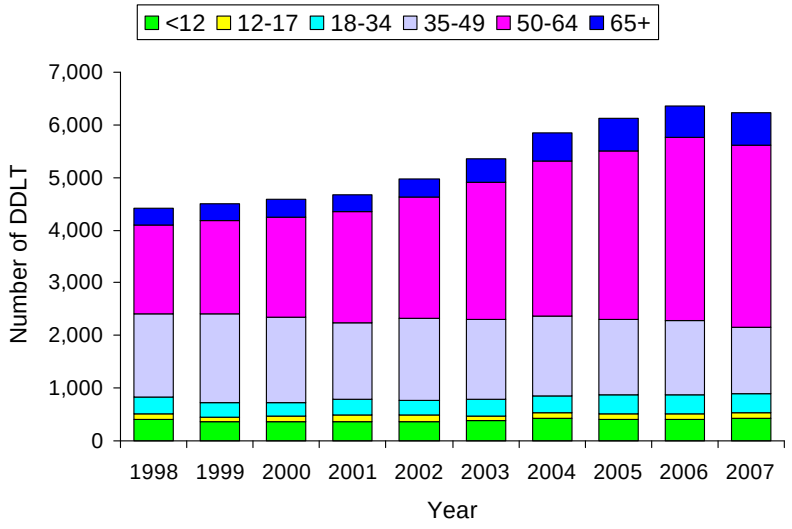
Source: *2008 OPTN/SRTR Annual Report*, Table 9.2b. Uses laboratory MELD score.

Liver Transplant Recipients

The number of liver transplantation procedures performed in the US in 2007 decreased to 6,489 from 6,650 in 2006 *[Table 9.4a, Table 9.4b]*. Deceased donors accounted for 96% of transplants and 4% were from living donors. In 2007 there were 139 fewer deceased donor liver transplants (DDLT) and 22 fewer living donor liver transplants (LDLT) performed, compared to 2006. This slight decrease in the number of transplants was seen across all solid organs, including a decrease in kidney-alone transplants from 16,644 in 2006 to 16,119 in 2007 *[Table 1.7]*. However, the number of combined liver-kidney transplants increased to 444 in 2007 compared to 400 in 2006. *[Table 1.8]*

Age: Figure IV-7 shows the age distribution of DDLT recipients for the past ten years *[Table 9.4a]*. Pediatric (less than 18 years of age) DDLT recipients were only 9% of all DDLT in 2007, and numbers for this group have changed very little (7% for children under 12 and 2% for children age 12-17). Adult DDLT recipients aged ≥50 had the largest increase in DDLT since 1998, matched by decreases in the younger adult categories over the years.

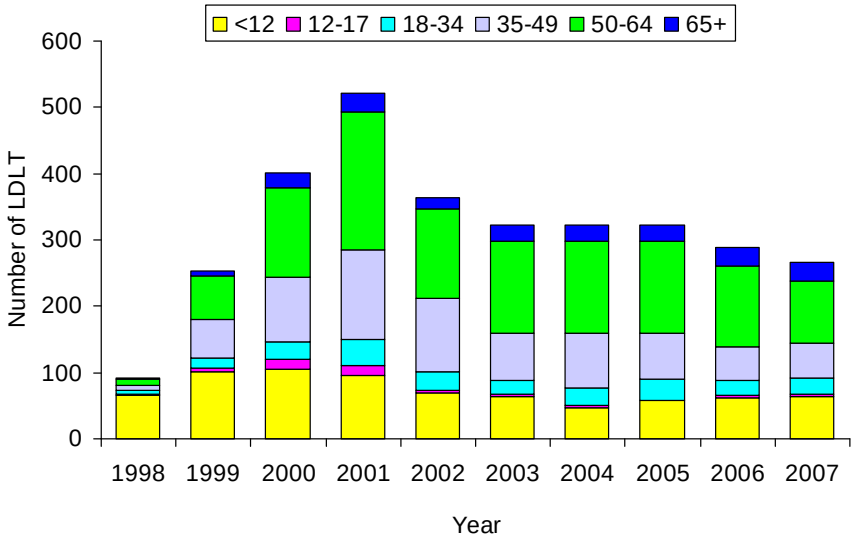
Figure IV-7. Number of Deceased Donor Liver Transplants by Age, 1998-2007



Source: *2008 OPTN/SRTR Annual Report*, Table 9.4a.

LDLT recipients have decreased in numbers since a peak of 522 transplants in 2001 (Figure IV-8) *[Table 9.4b]*. The change in age distribution among LDLT recipients is considerably different from DDLT recipients. The majority of LDLT cases in 1998 were pediatric recipients (73%), but by 2007, recipients under age 18 were only 26% of the total, reflecting expansion of adult-to-adult LDLT. Candidates aged 50-64 (35%) received the most LDLT in 2007.

Figure IV-8. Number of Living Donor Liver Transplants by Age, 1998-2007



Source: *2008 OPTN/SRTR Annual Report*, Table 9.4b.

Gender, race/ethnicity, blood type, and residence: Demographic factors such as gender, race/ethnicity, and blood type among DDLT recipients in 2007 were very similar to the waiting list. Men received more liver transplants in 2007 than women *[Table 9.4a]*, although in 2007, as in 2006, a higher proportion of LDLT were women (42%) than DDLT (33%) *[Table 9.4b]*. DDLT among racial groups in 2007 was also similar to 2006 with 70% white, 14% Hispanic, 10% African Americans, and 5% Asian. Blood group distribution among DDLT was again similar to previous years, however in 2007 a higher proportion of LDLT went to blood type B recipients (12%) compared to 2006 (9%). From 1998 to 2007, fewer DDLT were performed for non-resident aliens (1.9% in 1998 and <1% in 2007).

Insurance: Very little has changed from 2006 to 2007 in primary source of payment among DDLT recipients *[Table 9.4a]*. Private insurance accounted for the majority of DDLT recipients (58%), while Medicare paid for 21% and Medicaid paid for 16%. Alternative payment methods accounted for 5% of DDLT recipients. Private insurance was more common for LDLT recipients at 74%, compared to DDLT recipients. Fewer LDLT recipients had Medicare (11%) or Medicaid (9%) coverage *[Table 9.4b]*.

Previous transplant: In 2007, DDLT recipients that had undergone a previous liver transplant decreased to 7.8% from 8.6% in 2006, the lowest proportion of the decade. There were no LDLT recipients in 2007 with a previous liver transplant, down from a high of 17 in 1999, reflecting challenges and poorer outcomes associated with LDLT in retransplant recipients *[Table 9.4b]*.

Diagnosis: As in 2006, non-cholestatic cirrhosis was most commonly diagnosed in 2007 for both DDLT and LDLT. Among DDLT recipients, 57% were primarily diagnosed with non-cholestatic cirrhosis in 2007, a slight decrease from 59% in 2006 (Table IV-2) *[Table 9.4a]*. The second most common diagnosis among DDLT recipients was malignant neoplasms, which remained stable at 13% (this group contains only those recipients that had liver cancer listed as their primary diagnosis and does not include all HCC MELD/PELD exception holders).

Table IV-2: Liver Deceased Donor Transplant Recipients by Diagnosis, 1998-2007

	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007
Non-cholestatic cirrhosis (%)	63	64	64	64	62	59	60	61	59	57
Hepatitis C (%)	24	26	28	28	29	27	27	24	23	22
Alcoholic cirrhosis (%)	13	13	12	11	11	12	11	12	11	11
Both hep C & alcoholic (%)	8	8	7	8	5	5	6	8	7	7
Autoimmune hepatitis (%)	4	3	4	3	3	3	2	3	2	2
Hepatitis B only (%)	4	4	3	4	4	3	3	2	2	2
Cryptogenic/idiopathic/ NASH (%)	9	9	9	8	7	8	9	10	10	11
Other non-cholestatic (%)	1	1	1	1	1	1	2	3	2	2
Cholestatic liver disease (%)	13	11	10	10	10	10	9	8	9	9
Acute hepatic necrosis (%)	8	9	9	8	7	7	7	7	6	6
Biliary atresia (%)	5	4	4	4	3	3	3	3	2	3
Metabolic disorders (%)	4	3	4	4	3	3	3	3	3	3
Malignant neoplasms (%)	2	2	2	3	7	7	8	10	12	13
Other (%)	6	6	7	8	7	11	9	8	9	10

Notes: Recipients with both Hepatitis B and Hepatitis C are counted in the Hepatitis C category. NASH = non-alcoholic steatohepatitis.

The remaining diagnostic categories were: other diagnoses (10%); cholestatic liver disease (9%); acute hepatic necrosis (6%); metabolic disorders (3%); and biliary atresia (3%). LDLT recipient diagnoses differed greatly from those of DDLT recipients (Table IV-3). Non-cholestatic cirrhosis accounted for only 39% of LDLT recipients, remaining stable from 2006 *[Table 9.4b]*. The second most common diagnosis was cholestatic cirrhosis at 18%, down from 23% in 2006. Similar to last year, the remaining diagnosis categories were: 12% for other (8% in 2006); 12% for malignant neoplasms (9% in 2006); 12% for biliary atresia (12.5% in 2006); 4% for metabolic disorders (2% in 2006); and 3% for acute hepatic cirrhosis (6% in 2006).

Table IV-3: Liver Living Donor Transplant Recipients by Diagnosis, 1998-2007

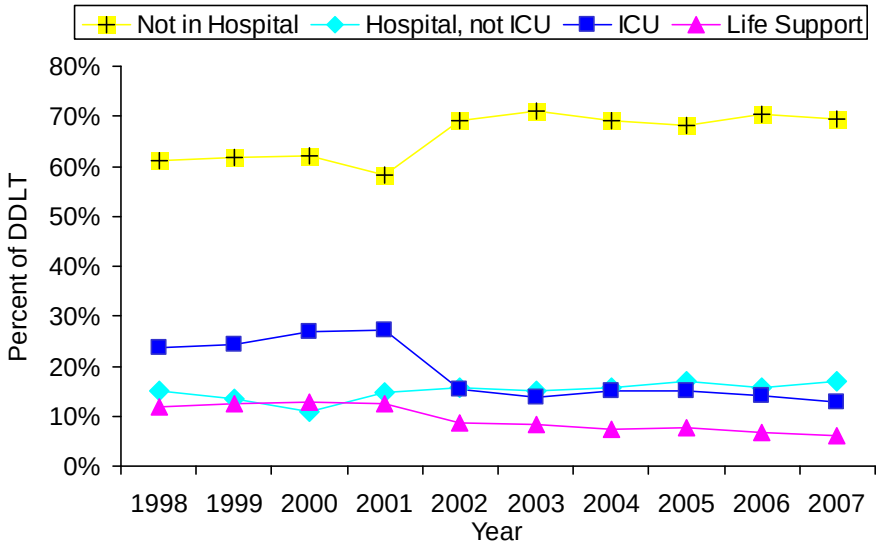
	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007
Non-cholestatic cirrhosis (%)	22	38	44	56	52	46	50	46	39	39
Hepatitis C (%)	9	21	24	27	28	23	22	20	15	17
Alcoholic cirrhosis (%)	3	4	6	8	8	8	9	9	6	5
Both hep C & alcoholic (%)	1	3	2	4	4	2	3	4	3	2
Autoimmune hepatitis (%)	5	4	2	4	3	2	4	2	2	3
Hepatitis B only (%)	1	3	1	3	3	2	1	2	2	2
Cryptogenic/idiopathic/ NASH (%)	2	5	8	7	6	9	11	8	11	9
Other non-cholestatic (%)	0	0	0	1	1	1	0	1	0	1
Cholestatic liver disease (%)	7	11	18	16	21	21	23	21	23	18
Acute hepatic necrosis (%)	7	10	6	5	4	7	3	4	6	3
Biliary atresia (%)	42	20	14	9	9	12	7	8	13	12
Metabolic disorders (%)	5	5	4	3	2	2	3	3	2	4
Malignant neoplasms (%)	2	9	8	6	5	3	7	8	9	12
Other (%)	15	7	7	6	6	8	8	10	8	12

Notes: Recipients with both Hepatitis B and Hepatitis C are counted in the Hepatitis C category. NASH = non-alcoholic steatohepatitis.

Medical condition: Slightly fewer patients were in the intensive care unit (ICU) at the time of their DDLT (13%) in 2007 compared with 2006 (14%). There has been a stable

trend in the past ten years towards a reduction of hospitalized and ICU-bound candidates at the time of transplant (Figure IV-9) *[Table 9.4a]*. Candidates emergently transplanted with deceased donor livers in the Status 1/1A category declined from 11% in 1998 to 6% in 2007. Of all DDLT candidates, only 66 (1.1% of all DDLT) were transplanted as Status 1B (implemented in late August 2005), up from 44 in 2006. Of note, Status 1B is restricted to patients in the pediatric population. Consistent with policies designed to direct more organs to higher MELD patients, such as Share 15, higher proportions of DDLT are going to candidates with higher MELD scores and fewer transplants are performed for candidates with MELD <15. Similar to 2006, only 8.5% of DDLT were for patients without exceptions with MELD 6 to 14. The pediatric DDLT patient distribution remained relatively unchanged with the highest proportion consistently in the PELD <11 category. For patients with HCC exceptions, transplantation increased slightly in 2007 to 15%, up from 14% in 2006.

Figure IV-9. Deceased Donor Transplant Recipients by Hospitalization Status, 1998-2007



Source: *2008 OPTN/SRTR Annual Report*, Tables 9.4a.

In 2007, 2% of LDLT (six cases) were performed for patients on mechanical support, compared to 6% for DDLT *[Table 9.4b]*. Six percent of LDLT recipients were in the ICU (roughly half that of DDLT at 13%) and 14% were hospitalized but not in intensive care compared to 17% for DDLT. Candidates with MELD scores <15 in 2007 were 30% of LDLT, a decrease from 44% in 2006. Patients with MELD >20 were 10% of all LDLT, up from 2006 (6%), while patients with HCC exceptions were up from 3% in 2006 to 6%. Only seven LDLT recipients had never been on the deceased donor transplant waiting list.

Partial liver grafts and ischemia time for DDLT: The number of partial or split liver transplants among DDLT recipients was 4% to 5% from 1998 to 2005. In 2006 it dropped to 2.8% but increased to 3.8% in 2007 *[Table 9.4a]*. Still, there were only 235 DDLT

performed with split livers in 2007. The trend toward shorter cold ischemia time remained steady from 1998-2007. More DDLT were done with less than 11 hours cold ischemia time (82%) in 2007 compared with years past. Between 1998 and 2007, the fraction of DDLT performed with less than six hours of cold ischemia time increased from 17% to 29%, while cold ischemia time between 11 and 15 hours decreased from 16% to 7%.

Liver Transplant Recipient Survival

Adjusted patient survival following DDLT was 94% at three months, 87% at one year, 73% at five years, and 59% at ten years *[Table 9.12a]*. Survival rates were adjusted for recipient age, gender, race, and diagnosis. Adjusted patient survival for LDLT recipients was 96% at three months, 92% at one year, 78% at five years, and 71% at ten years *[Table 9.12b]*. Graft survival for DDLT was 90% at three months, 82% at one year, 68% at five years, and 53% at ten years *[Table 9.8a]*. Graft survival for LDLT recipients was 92% at three months, 85% at one year, 71% at five years, and 62% at ten years *[Table 9.8b]*. Note that the adjustments for these models do not account for the health of the patients prior to transplant. The greater survival of living donor transplant recipients likely reflects their better health at transplant.

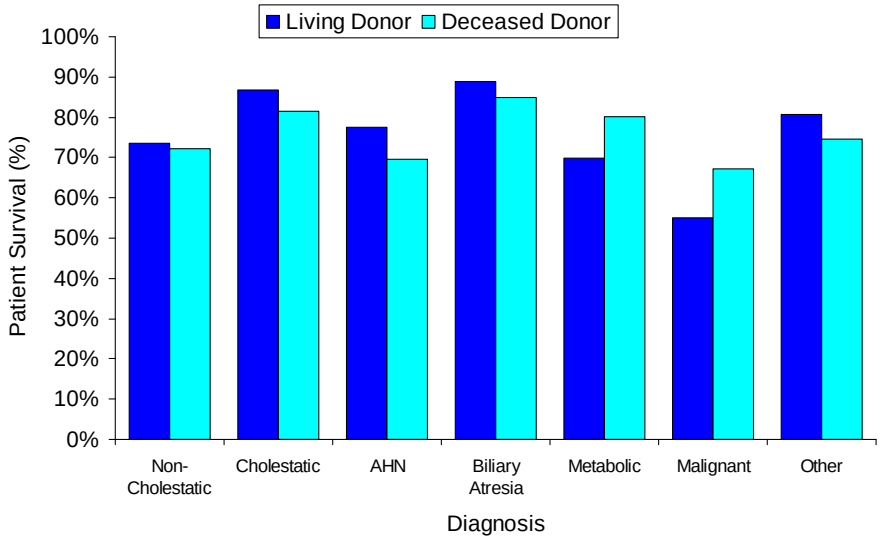
Age: Adjusted patient survival varied according to the recipient's age. Patient survival for DDLT recipients at three months was highest for adults aged 35-49 at 96%, followed by adolescents aged 12-17 at 94% *[Table 9.12a]*. Children <1 year old had the lowest three-month survival rate at 88%. One-year adjusted patient survival for DDLT recipients was lowest for those aged 65 and older at 81%, followed by children <1 year at 83%. The highest one-year survival was 90% for all ages between 1 and 50. At five years, children <1 year old had the highest survival rate for DDLT at 84%. Older recipient age remained strongly associated with poorer long term outcomes. The lowest five-year posttransplant survival was for adults ≥65 years at 64%, with those aged 50-64 having the next lowest survival rate at 71%. This trend is more pronounced for ten-year survival with higher rates for those transplanted as children (77% for <1, 79% for 1-5, and 81% for 6-11) compared to younger adults (66% for 12-34 and 62% for 35-49). Older adults aged 50-64 had the lowest ten-year survival at 56%, and 42% for those ≥65 years. Among LDLT recipients, patients <1 year and ≥65 had the lowest three-month survival at 94% *[Table 9.12b]*. LDLT recipients aged 1-5 had the lowest survival rate of 84% at one year, followed by adults ≥50 years at 85%. Adult LDLT recipients aged 35-49 demonstrated the highest one-year survival at 98%. However, there were too few transplants to calculate three-month or one- year survival for recipients aged 6 to 11 and 12 to 17. Survival at five years after LDLT was highest for both children <1 year old and adults aged 18-34 at 85%, and lowest for those ≥65 years at 71%. At ten years posttransplant, LDLT recipients aged 35 to 49 appear to have the lowest survival rate. However, this estimate is very imprecise with a standard error of 14.6% and is not statistically different than the survival rate of 54% for those ≥65. The highest survival rates at ten years were for the youngest age groups: 82% for <1 year old at transplant, 80% for those aged 1-5, and 83% for those aged 6-11.

Race/ethnicity and gender: DDLT survival was not statistically significantly different across race/ethnicity at three months or at one year. However, one-year survival for both

Asians (89%) and Hispanics (88%) was higher than for African Americans (85%) *[Table 9.12a]*. At five years, African American DDLT recipients had the lowest survival rate (66%) and Asians and Hispanics had the highest (77% for Asians and 75% for Hispanics; not statistically different, p=0.167). African American DDLT recipients had significantly lower survival at ten years following transplant than the other racial groups at 50% compared to 59% for whites, 61% for Hispanics, 68% for Asians, and 60% for other race. Ten-year survival for Asian recipients of DDLT was statistically significantly higher than all the other racial groups. Among LDLT, Asians had the highest survival at three months (100%) but the remaining race categories were not statistically different from each other at three months (95%-96%) *[Table 9.12b]*. Survival at one year was not statistically different among racial groups. At five years, both Hispanics (84%) and other race (92%) exhibited survival rates higher than whites (76%), while Asians (80%) had higher ten-year survival than whites (70%) and African Americans (68%). Men and women DDLT recipients had similar survival rates though statistically significantly different at three months (men: 94% vs. women: 92%) (p<0.001), and at one year (men: 88% vs. women: 86%), (p=0.004) *[Table 9.12a]*. Five- and ten-year survival rates were not statistically different for men and women. Survival rates for LDLT recipients only differed by gender for one-year survival with men at 89% and women at 94% (p=0.03) *[Table 9.12b]*.

Medical factors: At three months, adjusted patient survival for DDLT among primary diagnosis categories was highest for cholestatic cirrhosis at 96%; however, biliary atresia at 92% (with a standard error of 2%) and malignant neoplasms at 95% were not statistically different than cholestatic cirrhosis *[Table 9.12a]*. The lowest three-month survival was for acute hepatic necrosis at 89%, which was not statistically different from biliary atresia, metabolic disorders (91% $\pm$ 1.6%), or malignant neoplasms. Adjusted patient survival rates for DDLT at one year were 92% for cholestatic cirrhosis and 87% for non-cholestatic cirrhosis (p=0.03). Acute hepatic necrosis (84%) and other disorders (83%) did not differ from each other (p=0.76) but were statistically significantly lower than cholestatic (p<0.001 for both) and non-cholestatic cirrhosis (p=0.03 and p=0.02, respectively), while malignant neoplasm (87%) was significantly different from cholestatic cirrhosis only (p=0.001). Biliary atresia (89%) and metabolic disorders (88%) did not differ statistically from any of the other diagnostic categories. Adjusted five-year survival rates according to diagnostic category for DDLT and LDLT are shown in Figure IV-10. DDLT adjusted survival rates at five years were statistically the same for biliary atresia (85%), cholestatic cirrhosis (82%), and metabolic disorders (80%). Other diagnoses (75%) and non-cholestatic cirrhosis (72%) were not statistically different from each other but were significantly lower than biliary atresia, cholestatic cirrhosis, and metabolic disorders. Acute hepatic necrosis (70%) was lower than other diagnoses (p=0.01) but not statistically different than non-cholestatic cirrhosis (p=0.06), while malignant neoplasm (67%) was significantly lower than all diagnostic categories except acute hepatic necrosis (p=0.19).

Figure IV-10. Adjusted Five-Year Patient Survival of LDLT and DDLT Recipients by Diagnosis



Source: *2008 OPTN/SRTR Annual Report*, Tables 9.12a and 9.12b.

For LDLT recipients, adjusted three-month patient survival was not statistically different across diagnosis categories except that cholestatic cirrhosis (94%) and non-cholestatic cirrhosis (96%) were statistically different from acute hepatic necrosis (100%). At one year, survival again did not differ across diagnostic categories except that non-cholestatic cirrhosis (90%) and malignant neoplasms (87%) differed statistically from biliary atresia (99%). At five years, adjusted survival for LDLT was statistically the same for biliary atresia (89%), cholestatic cirrhosis (87%), and other diagnoses (81%). The other diagnoses category only differed statistically from malignant neoplasms (55%). Acute hepatic necrosis (78%) did not differ statistically from non-cholestatic cirrhosis (74%), metabolic disorders (70%), and malignant neoplasms.

Survival among single year cohorts (all recipients of DDLT and LDLT in a given calendar year) over the previous decade, shows a trend toward improving adjusted patient survival for each year of DDLT *[Table 9.13a]*. Three-month adjusted survival has increased from 91% for those transplanted in 1997 to 95% in 2006. One-year survival for DDLT increased from 86% in 1997 to 88% in 2002 and has remained level through 2006, while three-year survival is the same for those transplanted in 2004 as it was in 1997. Survival for LDLT has trended upward, but these improvements are generally not statistically significant *[Table 9.13b]*. The number of people living with a functioning liver transplant continues to increase demonstrating the impact of successful liver transplantation *[Table 9.16]*. Improvements in patient and graft survival have led to more focus on long term outcomes. While such efforts are applicable across all of liver transplantation, there is a particular emphasis on such concerns in the pediatric population (1).

Acceptance Rates for Liver Transplant Programs

One aspect of liver program performance beginning to receive increasing attention is the rate at which organs are accepted for transplant. Because organs are offered to programs for individuals awaiting transplantation, there are two potentially useful metrics:

1. The rate at which **organs** are accepted for any candidate at the program (***organ acceptance rate***)
2. The rate at which **organ offers** are accepted at the program (***offer acceptance rate***)

For example, suppose a program is offered 100 livers specifically for 200 individual candidates during a period. If the program accepts 50 livers for transplant, the *organ acceptance rate* is 50%, while the *offer acceptance rate* is 25%. Because of differences in donor acceptance criteria as well as differences in the characteristics of waiting candidates across programs, liver organ and offer acceptance rates can vary substantially. Additionally, because of the nature of offer/acceptance process and the circumstances under which these data are collected, acceptance rate metrics can be difficult to interpret. The OPTN is beginning to consider how such metrics may be used to monitor program performance in conjunction with transplant rates and waiting list mortality rates. The SRTR is currently generating these data on a recurring basis in order to inform both programs and the OPTN.

Acceptance and Refusals

On the basis of formal OPTN policy, deceased donor livers are offered to potential transplant candidates in decreasing order of medical urgency. It is not uncommon for programs to refuse offers for specific candidates. When this occurs, a reason for refusal must be provided by the transplant center to the OPTN. Typically, organs are refused for reasons such as donor age, donor quality, or positive serology, in keeping with the specific philosophies at each transplant program. Each program has the option to avert certain types of offers based on pre-specified acceptance criteria for the program as a whole and for specific candidates, such as donor age, donor weight, or other specific clinical parameters. For example, a program that sets a general limit of 60 years on donor age would not receive offers for 65-year-old donor livers. Some programs may have liberal acceptance criteria, and as such tend to receive a large number of offers, but may accept fewer organs. Other programs may be more conservative and tend to receive relatively fewer offers, but accept many organs. Even though both types of programs may accept the same *number* of organs, their acceptance *rates* may be very different because of the differences in the number and types of offers received. Additionally, the reasons for turn down reported must accurately reflect the reasons behind the decision.

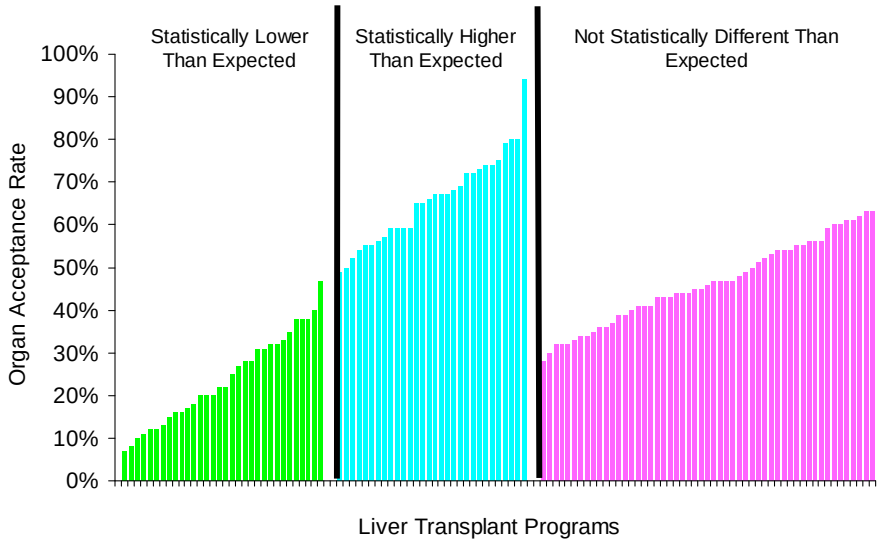
Preliminary Data

Using data generated by the SRTR, the OPTN Membership and Professional Standards Committee has begun to investigate the use of acceptance rates (in combination with other pre-transplant measures) as a performance metric for liver and kidney transplant programs. The goal is to identify programs that are not accepting “good” organs (i.e.,

those organs that most programs would identify as suitable for transplant). In the current analysis, a "good" organ is defined as one that is accepted within either the first 50 offers or the first three transplant programs. Both an actual and expected acceptance rate is generated for each program, with the latter rate derived from logistic regression models of organ acceptance and offer acceptance based on national data. A p-value provides evidence to support the assertion that the actual acceptance rate is significantly different from the expected rate (the rate predicted for that center's caseload and offers, based on national average acceptance behavior).

Based on livers offered for transplant between July 2006 and June 2007, the overall US offer acceptance rate was 19%, and the overall US organ acceptance rate was 45%. For transplant programs offered at least 10 organs during that period, the offer acceptance rate ranged from 0% to 64%, and the organ acceptance rate ranged from 0% to 94%. Of all liver transplant programs (n=122), the offer acceptance rate was not statistically different from expected in 62 programs (51% of programs). For 35 programs, the offer acceptance rate was statistically higher than expected, whereas for 25 programs (one-fifth of all liver programs), the offer acceptance rate was statistically lower than expected. When organ acceptance rates were examined, the results for 58 programs (48% of programs) were not statistically different from expected. The results were statistically higher than expected for one quarter of the programs (n=30) (Figure IV-11).

Figure IV-11. Observed Organ Acceptance Rates Compared to Expected: Liver Transplant Programs, 7/2006 - 6/2007



Source: SRTR/OPTN analyses, liver transplant programs with 10 or more offers only.

Conversely, in approximately one quarter of the programs the organ acceptance rates were statistically lower than expected. The implications of having an acceptance rate that is different from expected for program performance are not yet completely understood. Given the limitations associated with the interpretation of acceptance rates, the OPTN is also examining transplant rates as a program performance metric, as preliminary results

suggest a high degree of correlation between these transplant rates and organ/offer acceptance rates. Exploratory work in this area is ongoing.

Donation after cardiac death (DCD) liver transplantation

Use of liver allografts from donation after cardiac death (DCD) donors has continued to increase steadily and now accounts for 5% of all liver-only transplants, compared to 0.9% of transplants performed in 2000 (see Table IV-4). The number of centers utilizing DCD allografts has also increased quite markedly from 11 centers in 2000 to 62 in 2007. Possible factors contributing to this rise include the continued critical shortage of available organs for transplantation, the report from the Institute of Medicine encouraging increased DCD organ utilization, and the efforts of the Health Resources and Services Administration (HRSA) sponsored Organ Donor Breakthrough Collaborative (2, 3).

Table IV-4. Liver Transplants Using DCD Donors and Number of Liver Transplant Programs that Performed DCD Liver Transplants by Year (1/1/2000 to 12/31/2007)*.

	Total Donors	DCD Donors	DCD Donors	DCD Liver Transplant Programs
	N	N	% of Total	N
Year of Transplant				
2000	4,407	39	0.88	11
2001	4,465	68	1.52	20
2002	4,697	76	1.62	28
2003	5,042	110	2.18	38
2004	5,459	178	3.26	42
2005	5,679	260	4.58	54
2006	5,849	278	4.75	60
2007	5,625	295	5.24	62
Total	41,223	1,304	3.16	86

*Excludes multi-organ transplants

When compared to donation after brain death (DBD) donors, DCD donors were more likely to be between 18 to 49 years of age (54% of DBD donors versus 66% of DCD donors) as demonstrated in Table IV-5. Older donors (≥50) were 32% of the total number of DBD donors but only 22% of the DCD donors (p=0.001). This would suggest that transplant centers are selectively utilizing DCD donors in the younger adult age range or that younger adults are more likely to be declared dead from cardiac death than from brain death. A higher percentage of DCD donors die from an anoxic injury than DBD donors, while stroke is reported as the cause of death in a higher percentage of DBD donors than DCD donors. Additional donor characteristics are presented in Table IV-5.

Table IV-5. Donor Characteristics by Deceased Donor Type (DCD vs. DBD) (1/1/2000 to 12/31/2007)*.

	DBD		DCD		P-value
	N	Percent	N	Percent	DBD vs. DCD
Total	39,919	100.0	1,304	100.0	
Age					<0.0001
Under 2	664	1.7	5	0.4	
2 to 5	687	1.7	10	0.8	
6 to 11	980	2.5	27	2.1	
12 to 17	3,354	8.4	121	9.3	
18 to 39	14,252	35.7	557	42.7	
40 to 49	7,304	18.3	296	22.7	
50 to 59	6,799	17.0	215	16.5	
60 to 69	3,919	9.8	64	4.9	
70 plus	1,960	4.9	9	0.7	
Gender					<0.0001
Female	16,311	40.9	445	34.1	
Male	23,608	59.1	859	65.9	
Race					<0.0001
White	27,734	69.5	1,116	85.6	
Black	5,886	14.7	101	7.7	

	DBD		DCD		P-value
	N	Percent	N	Percent	DBD vs. DCD
Other	1,209	3.0	20	1.5	
Hispanic	5,088	12.7	67	5.1	
Missing	2	0.0	0	0.0	
Cause of Death					<0.0001
Anoxia	4,882	12.2	381	29.2	
Stroke	16,902	42.3	284	21.8	
Trauma	16,985	42.5	561	43.0	
Other	1,139	2.9	78	6.0	
Missing	11	0.0	0	0.0	

*Excludes multi-organ transplants

Recipients of DCD organs were more likely to be adult, male, and white, and to have a higher body mass index (BMI) and diagnosis of cholestatic cirrhosis (Table IV-6). The likelihood that DCD organs came from outside the local organ procurement organization is slightly higher than DBD (Table IV-7). The mean cold ischemia time of 7.6 hours for DCD versus 7.7 hours for DBD donors was not statistically different (p=0.40).

Table IV-6. Recipient Characteristics by Deceased Donor Type (DCD vs. DBD) (1/1/2000 to 12/31/2007)*.

	DBD		DCD		P-value
	N	Percent	N	Percent	DBD vs. DCD
Total	39,919	100.0	1,304	100.0	
Age (years)					<0.0001
Under 1	915	2.3	4	0.3	
1 to 5	1,140	2.9	8	0.6	
6 to 11	590	1.5	3	0.2	
12 to 17	795	2.0	11	0.8	
18 to 24	842	2.1	17	1.3	
25 to 34	1,474	3.7	31	2.4	
35 to 44	4,510	11.3	119	9.1	
45 to 54	14,747	36.9	511	39.2	
55 to 64	11,461	28.7	445	34.1	
65 and older	3,445	8.6	155	11.9	
Gender					0.025
Female	13,902	34.8	415	31.8	
Male	26,017	65.2	889	68.2	
Race					0.0002
White	28,826	72.2	1,000	76.7	
Black	3,797	9.5	111	8.5	
Other	2,141	5.4	39	3.0	
Hispanic	5,155	12.9	154	11.8	
Body Mass Index					<0.0001
Under 20	3,827	9.6	86	6.6	
20 to 24	9,552	23.9	331	25.4	

	DBD		DCD		P-value
	N	Percent	N	Percent	DBD vs. DCD
25 to 29	12,768	32.0	444	34.0	
30 plus	11,246	28.2	417	32.0	
Missing	2,526	6.3	26	2.0	
Medical Condition					<0.0001
In ICU	6,776	17.0	148	11.3	
Hospitalized	5,939	14.9	164	12.6	
Not Hospitalized	27,149	68.0	991	76.0	
Missing	55	0.1	1	0.1	
Mechanical Support					0.08
Not on Mechanical Support	36,434	91.3	1,217	93.3	
On Mechanical Support	3,429	8.6	86	6.6	
Missing	55	0.1	1	0.1	
Previous Liver Transplant					<0.0001
No	36,426	91.2	1,231	94.4	
Yes	3,493	8.8	73	5.6	
Diagnosis					<0.0001
Acute hepatic necrosis	2,916	7.3	61	4.7	
Non-cholestatic cirrhosis	24,278	60.8	874	67.0	
Cholestatic cirrhosis	3,678	9.2	114	8.7	
Metabolic disorders	1,301	3.3	38	2.9	
Malignant neoplasm	3,379	8.5	128	9.8	
Other	4,354	10.9	89	6.8	
Missing	13	0.0	0	0.0	

*Excludes multi-organ transplants

Table IV-7. Transplant Characteristics by Deceased Donor Type (DCD vs. DBD) (1/1/2000 to 12/31/2007)*.

	DBD		DCD		P-value
	N	Percent	N	Percent	DBD vs. DCD
Total	39,919	100.0	1,304	100.0	
Donor Location					0.005
Shared	12,549	31.4	458	35.1	
Local	27,370	68.6	846	64.9	
ABO Compatibility					0.0003
Compatible	3,125	7.8	64	4.9	
Incompatible	311	0.8	7	0.5	
Identical	36,483	91.4	1,233	94.6	
	Mean	SD	Mean	SD	
Cold Ischemia Time	7.7	3.6	7.6	3.5	0.40

*Excludes multi-organ transplants

The recipients of DBD allografts were more likely to be in the ICU at the time of transplant and were also more likely to have MELD scores of 25 or higher (Tables IV-6, IV-8). This suggests that centers are selecting DCD organs for patients who are less critically ill. Alternatively, centers may be utilizing DCD organs as an opportunity to offer transplantation to patients identified as in need of a transplant who are at a lower priority score.

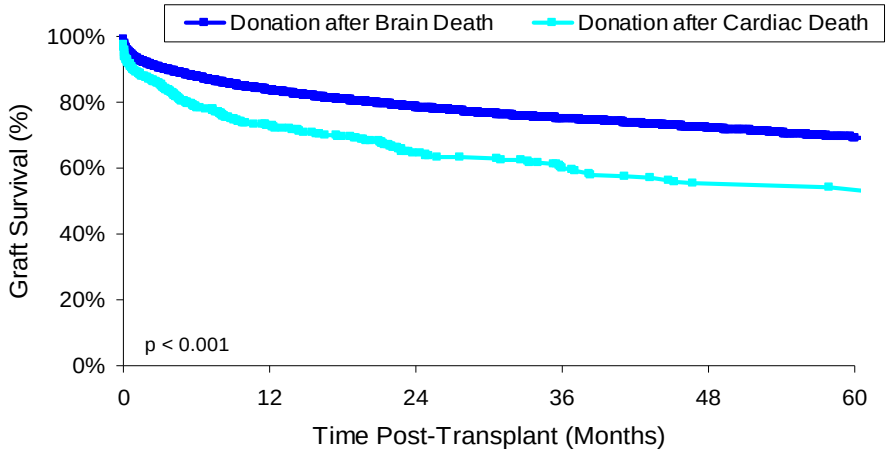
Table IV-8. Distribution of MELD/PELD Score at Transplant by Deceased Donor Type (DCD vs. DBD) (9/1/2001 to 12/31/2007).

			DCD	
	N	Percent	N	Percent
MELD/PELD at Transplant				
Under 10	3,967	12.2	143	11.7
10 to 14	6,070	18.7	274	22.4
15 to 19	7,466	23.0	321	26.2
20 to 24	5,474	16.9	219	17.9
25 to 34	5,773	17.8	171	14.0
35 and higher	3,698	11.4	95	7.8
Total	32,448	100.0	1,223	100.0

Graft survival for DCD liver allografts is inferior to DBD liver allografts (Figure IV-12). This is similar to what was reported previously (4, 5). Covariates included in the graft survival model were: all donor characteristics in Table IV-5; all recipient characteristics from Table IV-6 plus waiting list status 1A/B, pre-existing malignancies, history of diabetes, prior abdominal surgery, portal vein thrombus, Hepatitis B and C status; and transplant characteristics including partial or split liver, ABO compatibility of donor and recipient, donor location (local, regional or national) and cold ischemia time. A recent single center report noted an increased incidence of ischemic biliary complications among recipients of DCD donors where the donor weighed more than 100kg or was over age 50 years with total ischemia time of nine hours or more (6). We ran a model on the subset of recipients of DCD livers only (results not shown) that confirmed a higher risk of graft failure for livers from DCD donors weighing more than 100kg and for livers from DCD donors over age 50 combined with >9 hours of cold ischemia time.

The risk of graft failure did not change based on center experience, suggesting there is not a learning curve with the use of DCD allografts as has been seen with other types of grafts such as living donor grafts (Table IV-9). Given that DCD organ recovery is technically similar to DBD organ recovery other than the need to rapidly cannulate and flush, it is not surprising to observe the lack of a learning curve.

Figure IV-12. Adjusted Graft Survival for DCD and DBD Liver Transplants, 9/1/2001 - 3/31/2006



*Adjusted for donor age, donor cause of death, donor race, donor sex, donor height, recipient age, recipient sex, recipient diabetes, recipient race, recipient diagnosis, recipient medical condition at tx, recipient status 1 at tx, pre-tx dialysis, need for pre-tx mechanical support, recipient history of malignancy, recipient previous abdominal surgery, recipient body mass index, previous liver transplant, recipient MELD/PELD at tx, recipient inotropic blood pressure support, recipient history of portal vein thrombosis, recipient hepatitis B positive, recipient hepatitis C positive, blood type compatibility, regional/national tx, cold ischemia time, and partial/split liver tx.

Source: SRTR Analysis. Data as of May 2008.

Table IV-9. Risk of Graft Failure by DCD Case Number Within Each Center by 5-Case Increments Among DCD Transplants n=1,000 (9/1/2001 to 3/31/2007).

Center Case Numbers	Number of Transplants	Hazard Ratio*	95% Confidence Interval	P-Value
Cases 1-5	262	1.11	(0.78, 1.57)	0.56
Cases 6-10	165	1.11	(0.75, 1.64)	0.60
Cases 11-15	117	1.17	(0.78, 1.78)	0.45
Cases 16-20	83	0.92	(0.57, 1.47)	0.72
Cases 21-25	73	0.86	(0.52, 1.45)	0.58
Cases 26-30	48	0.82	(0.45, 1.50)	0.52
Cases 31-35	38	1.09	(0.59, 2.00)	0.78
Cases 36+ (ref)	214	1.00		Reference

*Adjusted for donor age, donor cause of death, donor race, donor sex, donor height, recipient age, recipient sex, recipient diabetes, recipient race, recipient diagnosis, recipient medical condition at transplant, recipient status 1 at transplant, pre-transplant dialysis, need for pre-transplant mechanical support, recipient history of malignancy, recipient previous abdominal surgery, recipient body mass index (BMI), previous liver transplant, recipient MELD/PELD or Status 1/A/B at transplant, recipient history of portal vein thrombosis, recipient hepatitis B positive, recipient hepatitis C positive, blood type compatibility, regional/national transplant, cold ischemia time, and partial/split liver transplant.

Living donor liver transplantation

Living donor liver transplantation continues to play a small but important role in the management of patients with cirrhosis and even fulminant liver failure. While the total number of candidates waiting for deceased donor liver transplants stopped climbing following the institution of MELD/PELD in 2002, the number of liver transplant candidates has remained relatively constant over the past five years, with 16,438 candidates awaiting transplant at the end of 2007 (including inactive candidates) *[Table 1.3]*. Concomitant with the stabilization of the number of candidates awaiting liver transplantation, there was a steady increase in the number of deceased donor livers recovered between 2000 and 2006 (5,081 recovered organs in 2000 and 7,084 recovered organs in 2006) *[Table 1.2]*. These two trends certainly suggest an improvement in the balance between supply of deceased donor livers and demand for liver transplantation in the US. In 2007, however, the steady rise in the recovery of deceased donor livers may have reached a plateau, as slightly fewer livers (7,029) were recovered in 2007 than in 2006 *[Table 1.2]*. Should a new equilibrium have been reached, centers may re-examine the role of living donor liver transplantation in managing liver transplant candidates.

Characteristics of LDLT recipients

While the total number of living donor liver transplants peaked in the US in 2001 with a total of 522 cases *[Table 9.4b]* among 67 different centers *[SRTR Analysis, 2008]*, a number of transplant centers continue to perform the procedure on a regular basis, including 40 centers with at least one living donor transplant in 2007 *[SRTR analysis, 2008]*. Since 2002, between 266 and 363 living donor liver transplants have been performed annually. Approximately 20% of these cases have been performed in pediatric recipients, a percentage that has held steady since 2001 *[Table 9.4b]*, with the bulk of the remainder of cases involving recipients aged 35 years and older. While the great majority of LDLTs have been performed for managing chronic liver disease, a small number of LDLTs continue to be performed for managing acute liver failure with 15 such cases occurring in 2006, and nine cases performed for acute liver failure in 2007 *[Table 9.4a]*. A recent review from the National Institutes of Health funded Adult-to-Adult Living Donor Liver Transplantation (A2ALL) Living Donor Liver Transplant Consortium described the detailed LDLT experience in a number of centers and found that survival rates for these centers mirrored those in Asia where LDLT is a much more common approach to the management of acute liver failure (7, 8).

In the US, LDLT is typically done for relatively healthy transplant candidates, with 68% of LDLT recipients in 2007 having a MELD/PELD score at transplant of less than 30, and the great majority of those patients having a MELD/PELD score of less than 20 *[Table 9.4b]*. Since LDLT typically occurs at a lower MELD score than DDLT, receipt of an LDLT usually shortens the candidate's time waiting for transplant and thus lowers the risk of mortality on the waiting list (9). The majority of LDLT recipients are transplanted from home (79% of LDLT recipients compared to 70% of DDLT recipients in 2007). Conversely, very few LDLTs are currently being performed for patients on mechanical support (2% of LDLT recipients compared to 6% of DDLT recipients in 2007) or for ICU patients (6% of LDLT recipients compared to 13% of DDLT recipients in 2007) *[Table 9.4a, 9.4b]*.

Outcomes following living donor liver transplantation

While recent reports suggest enhanced waiting list survival with the pursuit of LDLT (9, 10) when compared to waiting for a DDLT, one must also consider LDLT in the context of posttransplant outcomes. Analysis of data accumulating in the OPTN/SRTR database shows that both short-term and long-term patient survival is quite similar between recipients of LDLT and DDLT. Adjusted LDLT recipient three-month survival has been 95% from 2000-2002 and 97% from 2003-2006 *[Table 9.13b]*. Longer-term follow-up on relatively large numbers of living donor liver transplant recipients is now becoming available, such that five-year adjusted patient survival for LDLT is estimated at 78% (± 1.1%) *[Table 9.12b]*, compared to five-year survival for DDLT in the same cohort of 73% (± 0.6%), although these estimates are not adjusted for MELD score at transplant *[Table 9.13a]*. While a number of patient characteristics may influence these assessments of outcomes, it does appear that posttransplant survival after LDLT is quite comparable to that achieved following DDLT. This favorable transplant experience, however, must be balanced by the theoretical and real risks accrued by the healthy donors who are involved in the LDLT process (11).

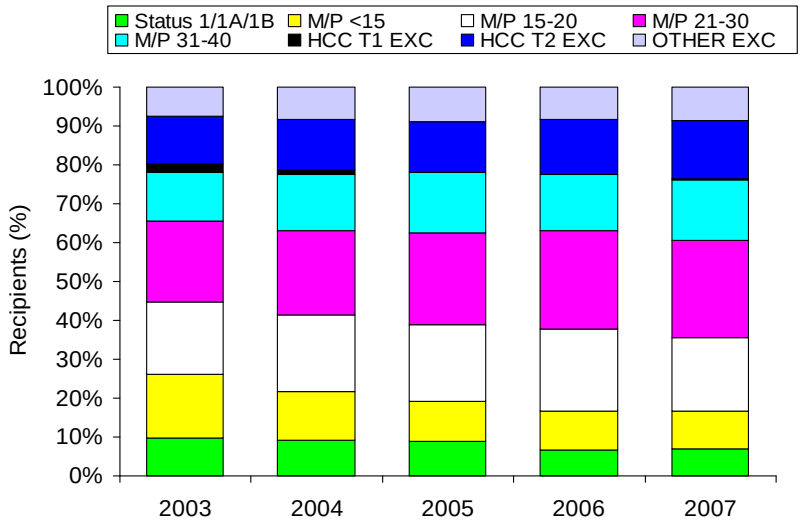
MELD/PELD Exceptions

Deceased donor liver allografts are currently allocated according to MELD score for those >12 years old and PELD score for those <12 years old. This scoring system has been shown to predict three-month pre-transplant mortality with a reasonably high degree of accuracy. This scoring system is most accurate when the liver failure itself is likely to cause death in the near future. There are a number of medical conditions concomitant with end-stage liver disease where the condition itself is more likely to lead to death than the liver failure. The presence of these “exception” cases was identified early in the development of the MELD (12). The most common of these conditions is HCC, where the threat to mortality from cancer metastasizing is greater than that of near-term liver failure. There is a multitude of other disease entities that have similar characteristics. One common theme is the role of non-mortality endpoint for these diseases (such as metastasis), which differs from the mortality endpoint for the majority of patients. A systematic process was developed for assigning MELD exception points for HCC patients, approved as allocation policy by the OPTN, and implemented with the MELD system in 2002. Patients that did not meet pre-defined criteria (e.g., the Milan criteria for HCC) were referred to regional review boards (RRB) for adjudication through a peer-review process. This process has evolved over time but remains decentralized, such that each of the eleven OPTN regions maintains their own RRB. Each region’s RRB has representation from each transplant program in the region and develops mutually-agreed-upon criteria for exception applications. Since these criteria vary by region, there is a common perception that regions differ in their leniency in approving applications. These perceived inconsistencies led the OPTN to convene a study group (the MELD Exceptional Case Study Group, MESSAGE) and a consensus conference in March 2006 (13). Seventeen exceptional medical conditions frequently encountered by RRBs were researched and discussed in a national consensus-building, evidenced-based format. The findings were disseminated to help both transplant professionals and the public understand reasons for adjusting MELD scores to better reflect the severity of these

illnesses and guidelines for these adjustments. The results of that meeting have been implemented in varying degrees across the OPTN regions.

We examined MELD exceptions in place at the time of transplant over the last five years. Figure IV-13 shows the waiting list status at the time of transplant for all DDLT recipients between 2003 and 2007 *[Table 9.4a]*. Over the five years, there was a slight increase in the percentage of patients receiving a DDLT with a MELD/PELD exception other than HCC from 7.6% in 2003 to a high of 9.0% in 2005, to 8.6% in 2007. Patients transplanted with HCC exceptions represented between 13% and 15% of total transplants. Figure IV-6, described previously, shows the fraction of adult (aged 18 and older) candidates on the waiting list that died prior to transplant (left panel) or received a transplant (right panel) within 30, 60, and 90 days of the snapshot date by their waiting list status on the snapshot date, January 1, 2007 *[Table 9.2b]*. Within 90 days, 39% of candidates with exceptions granted for conditions other than Stage T2 HCC had received a transplant compared to 4% of those without exceptions who had MELD scores under 20, 39% of those with MELD 21-30, 54% of those with MELD 31-40, and 54% of candidates with HCC exceptions for Stage T2 at snapshot. Only 2.4% of candidates with MELD exceptions for conditions other than HCC on January 1, 2007 had died within the following 90 days. The fraction of candidates without MELD exceptions at snapshot who died within 90 days varied according to their MELD score as expected; 1.5% for MELD less than 20, 7.4% for MELD 21-30, and 13.5% for MELD 31-40. Only 1.1% of those with MELD exceptions for Stage T2 HCC died within 90 days. Annual death rates per 1,000 patient-years at risk are shown in Table IV-10 *[Table 9.3]*. The death rates of patients with exceptions for conditions other than HCC are consistently comparable to those of patients with MELD scores of 15-20.

Figure IV-13. Waiting List Status at Time of Deceased Donor Liver Transplant



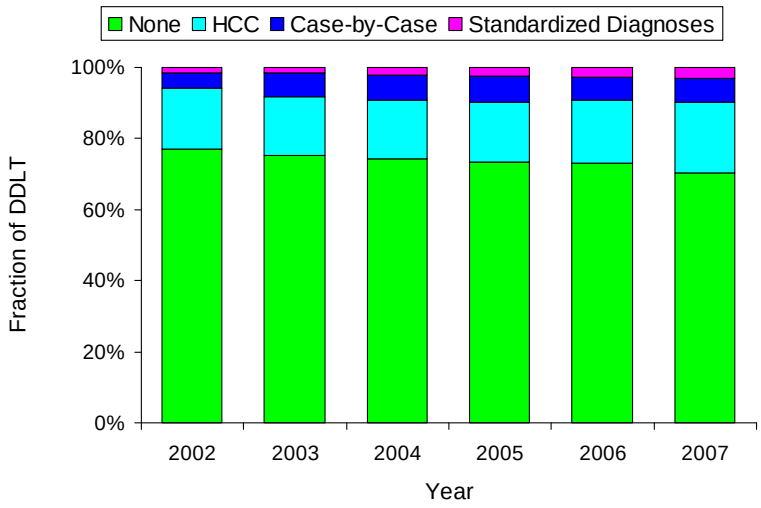
Source: SRTR analysis from *2008 OPTN/SRTR Annual Report*, Table 9.4a.
M/P=recipients with a MELD score and recipients with a PELD score within given range.

Table IV-10: Annual Liver Waiting List Death Rates per 1,000 Patient Years at Risk by Status, 2003-2007

	2003	2004	2005	2006	2007
MELD score, no exceptions					
6 to 10	38	37	36	36	35
11 to 14	72	68	72	66	69
15 to 20	157	166	154	141	125
21 to 30	794	739	721	722	596
31 to 40	4,978	4,969	4,581	3,828	3,758
With MELD score exceptions					
HCC Stage T2	126	173	151	133	99
Non-HCC exceptions	117	97	133	101	81

To examine patterns of exception use in more detail, we divided the exceptions into those for HCC, those for other standardized conditions where criteria are delineated in OPTN Policy, and those for non-standardized conditions that are reviewed on a case-by-case basis by the RRB. Figure IV-14 shows the national use of these three types of exceptions among DDLT recipients across time. The fraction of DDLT recipients with MELD/PELD exceptions in place at the time of transplant has increased from 23% in 2002 to 30% in 2007. The majority of exceptions are granted for HCC, about two-thirds of the total for 2003-2007, while it was slightly higher in 2002 (75%). Exceptions granted on an individual, case-by-case basis have accounted for roughly one-quarter of all exceptions, while those for standardized conditions other than HCC have been between 7% and 11% across time and were 10% of all exceptions in 2007.

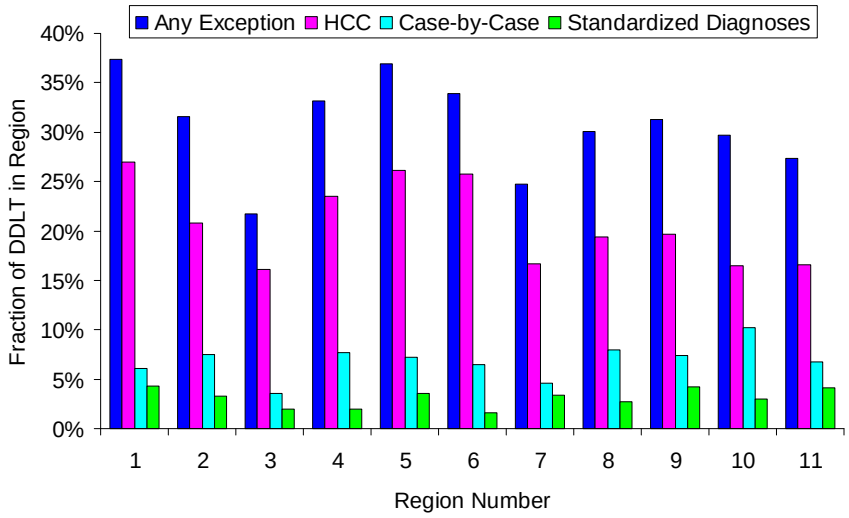
Figure IV-14. Fraction of DDLT with MELD/PELD Exceptions by Type and Year, 2002-2007



Source: SRTR Analysis. Data as of August 2008.

The variability by region regarding the use of these three types of exceptions is displayed in Figure IV-15. In 2007, the percentage of patients transplanted with exceptions scores ranged from 38% (regions 1 and 5) to 22% (region 3). The fraction of patients transplanted with HCC exceptions ranged from less than 20% for 5 regions (16% in region 3, 17% for regions 7, 10, and 11, 19% for region 8), between 20% to 25% for 3 regions (20% for region 9, 21% for region 2, and 24% for region 4), to over 25% of total DDLT for 2007 for 3 regions (26% for regions 5 and 6 and 27% for region 1). Patients transplanted with case-by-case exceptions were between 4% and 10% of all DDLT in 2007(4%: region 3, 5%: 7, 6%: 1, 7%: 5, 6, 9, 11, 8%: 2, 4, 8, 10%: 10). Exceptions for standardized conditions other than HCC accounted for between 2% and 4% of all DDLT within regions in 2007 (2%: regions 3, 4, 6, 3%: 2, 7, 8, 10, 4%: 1, 5, 9, 11).

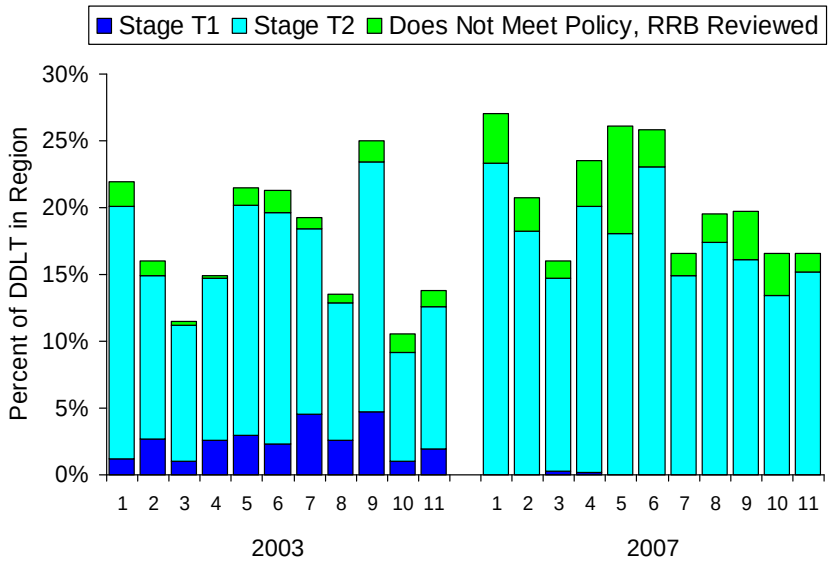
Figure IV-15. Fraction of DDLT with MELD/PELD Exceptions by Type and Region, 2007



Source: SRTR Analysis. Data as of August 2008.

Figure IV-16 shows the three subtypes of HCC exceptions at two points in time – soon after the start of the MELD system in 2003 and the most recent year of data, 2007. In 2003, there was an exception for candidates with HCC tumors that were Stage T1 (14) or with chronic liver disease, a rising alpha-fetoprotein level of 500 ng/ml or higher, and no evidence of a tumor based on imaging studies. By 2007, the exception for Stage T1 lesions was discontinued but those with rising alpha-fetoprotein still qualified for the exception. The exception for candidates with Stage T2 HCC meeting the Milan criteria (15) has been granted without review by the RRBs since May 2003. Increasingly, programs are transplanting patients with HCC that are beyond Milan criteria. These candidates can receive increased MELD priority through an HCC exception application that is reviewed prospectively by the RRB, which is also true of any candidate with HCC that does not meet the requirements of OPTN Policy 4.6.4.4. These trends are evident in Figure IV-16 which shows virtually no T1 HCC transplants in 2007, yet an increasing number of HCC patients transplanted with prospectively reviewed RRB exceptions.

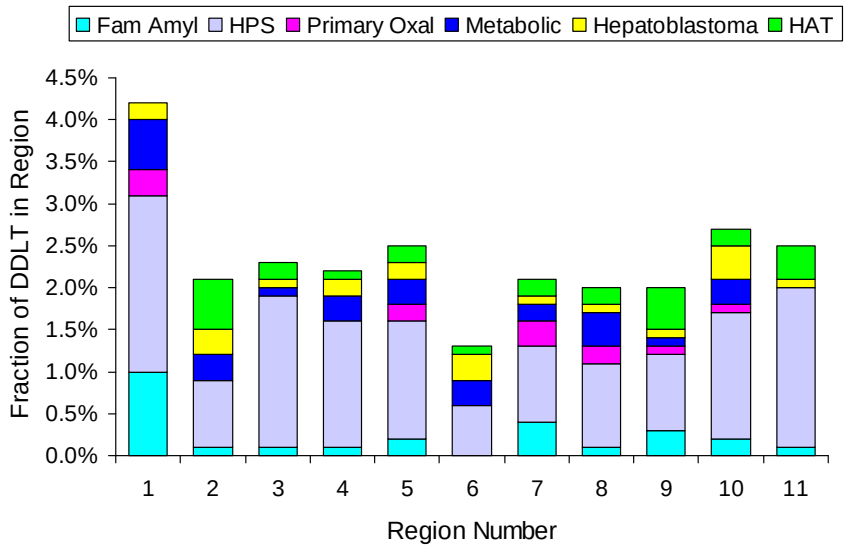
Figure IV-16. Fraction of DDLT with MELD/PELD Exceptions for HCC by Type & Region, 2003 & 2007



Source: SRTR Analysis. Data as of August 2008. In 2007, the T1 HCC exception is for those with AFP $\geq$ 500 ng/ml and rising, with no evidence of tumors upon imaging.

Standardized exceptions for conditions other than HCC are utilized in situations where the transplant community has implemented guidelines in OPTN policy to allow the candidate to have sufficient priority to be transplanted. To a large extent, these are conditions where the MELD score alone does not reflect the risk of mortality or when there are other considerations not related primarily to the risk of mortality. They include familial amyloidotic polyneuropathy, hepatopulmonary syndrome (including portpulmonary hypertension), primary oxaluria, inborn errors of metabolism, hepatoblastoma, and hepatic artery thrombosis after liver transplantation. Patients meeting pre-defined criteria for these conditions are granted automatic exception points, similar to the approach utilized in patients who meet Milan criteria for HCC. Between 2002 and 2007 the number of DDLT recipients with exceptions in place were: 623 for hepatopulmonary syndrome, 126 hepatic artery thrombosis after transplant, 100 for metabolic disorders, 89 for familial amyloidosis, 77 for hepatoblastoma, and 50 for primary oxaluria. For 2007, after implementation of new OPTN Policy following the MESSAGE meeting, the number of cases were: 116 for hepatopulmonary syndrome and portopulmonary hypertension, 47 for hepatic artery thrombosis after liver transplantation, 27 for pediatric hepatoblastoma, 18 for metabolic disorders, 15 for primary oxaluria, and 14 for familial amyloidosis. Figure IV-17 shows the proportion of DDLT by OPTN region that were performed for these conditions from 2002-2007.

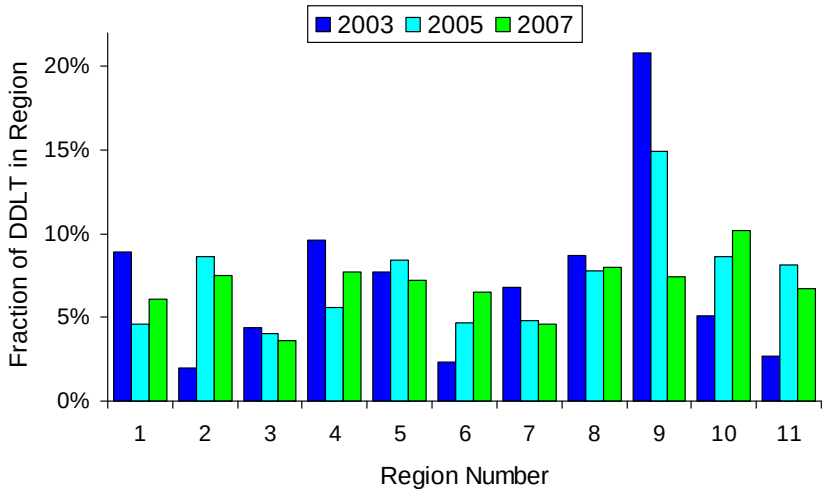
Figure IV-17. Types of Standardized Diagnoses MELD/PELD Exceptions by Region, 2002-2007



Source: SRTR Analysis. Data from 2002-2007 combined, as of August 2008.

Figure IV-18 shows the third group of MELD/PELD exceptions, those applied for and granted on a case-by-case basis with prospective review by the RRB, by region at three points in time – 2003, 2005, and 2007 (these data are presented as fractions of total deceased donor transplants in the region, over the specified time frame). Over the period, the fraction of each region's total DDLT with case-by-case exceptions has become more similar. In 2003, the fraction of regional DDLT with case-by-case exceptions ranged from 2% to 21%, with 5 regions between 2% and 5%; 5 regions between 6% and 10%; and 1 region above 10%. By 2005, the range was 4% to 15%, with only one region with less than 5% and one region with more than 10%; the other nine were between 5% and 9%. In 2007, all regions were between 5% and 10%, except for region 3 with 4%.

Figure IV-18. Case-by-Case MELD/PELD Exceptions by Region and Selected Years



Source: SRTR Analysis. Data as of August 2008.

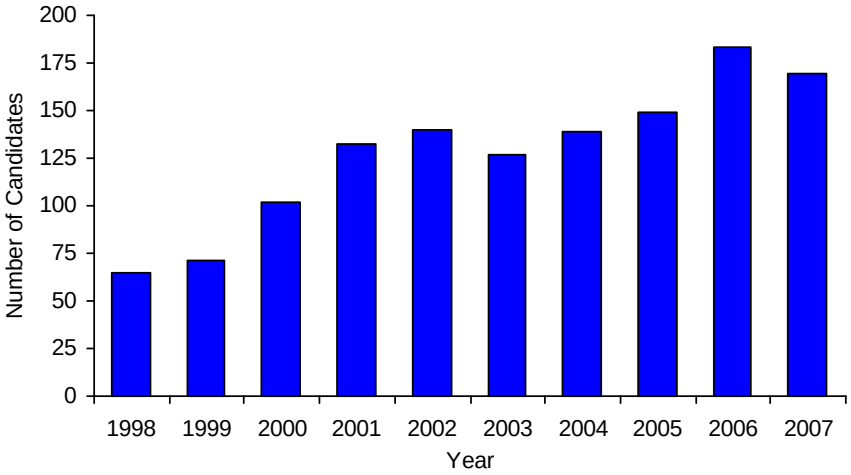
Intestine Transplantation

Intestine transplantation continues to demonstrate ongoing progress in both patient and graft survival, graft function, and quality of life after transplantation. Increasing success, however, has led to new challenges such as determining the optimal timing of referral and transplantation; the best allocation and severity of illness scoring; and how to most effectively reduce the unacceptably high waiting list mortality rates, brought on by increasing demand and insufficient availability of intestine grafts. Assessing long-term outcomes can suggest directions for improvement. This section will summarize five key areas of intestine transplantation: waiting list mortality, donor characteristics, transplant incidence, trends in immunosuppression, and patient and graft outcomes.

Intestine Candidate Selection and Waiting List

Intestine transplant candidates typically suffer from irreversible intestinal dysfunction and dependency on total parenteral nutrition (TPN), often complicated by TPN-associated liver failure or cholestasis, loss of vascular access for TPN due to thrombosis, frequent episodes of line-associated sepsis or dehydration (16, 17). The specific diagnosis and extent of liver damage influences whether candidates are listed for isolated intestine transplants or also listed for liver transplant to receive a combined liver-intestine graft. Candidates on the waiting list for intestine transplantation have increased in number from 93 in 1998 (65 active and 28 inactive) to 222 in 2007 (169 active and 53 inactive). However, for the first time since 2003, the total number of active patients on the waiting list at the end of the year decreased in 2007 compared to 2006 (Figure IV-19) *[Table 1.3]*.

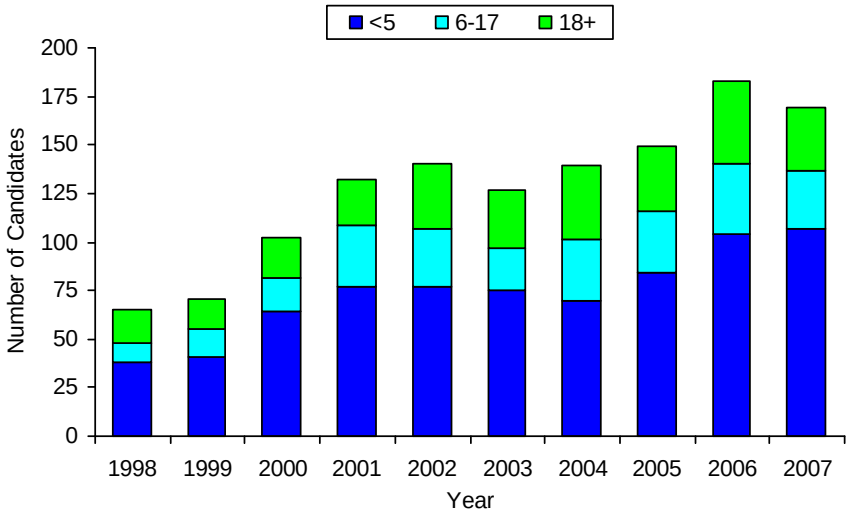
Figure IV-19. Number of Candidates on the Intestine Waiting List, Active at Year-End, 1998-2007



Source: *2008 OPTN/SRTR Annual Report,* Table 10.1a.

The majority of active intestine candidates are children <5 years old (63%) (Figure IV-20) *[Table 10.1a]*. The majority has a primary diagnosis of short gut syndrome (56%) compared to 32% with other diagnoses and 11% with functional bowel problems. Similar to prior years, most candidates were white (60%), male (61%), and had blood type O (42%). However, there has been a trend of an increasing fraction of the waiting list being African American. Since a low of 14% in 2002, this fraction has increased over time to 23% in 2007. In 2007, 8% of active waiting list candidates had received a previous intestine transplant, down from 2006 when 12% of candidates had a previous intestine transplant.

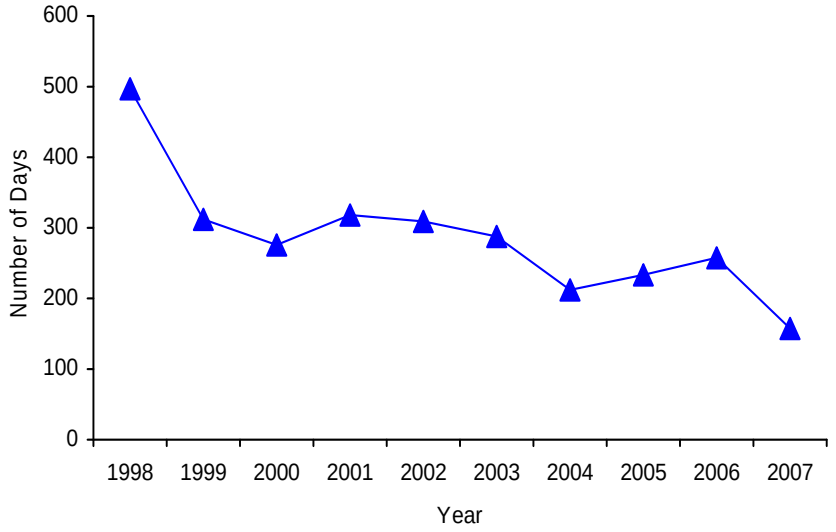
Figure IV-20. Number of Candidates on the Intestine Waiting List by Age, at Year-End, 1998-2007



Source: *2008 OPTN/SRTR Annual Report,* Table 10.1a.

These patients spend a significant amount of time on the waiting list. At the end of 2007, 23% had spent between one and two years on the waiting list and 20% had spent more than two years *[Table 10.1a]*. Median time to transplant decreased significantly in 2007 to 159 days compared to 257 in 2006 (Figure IV-21) *[Table 10.2]*. Discrepancies appear to exist in waiting time across age groups, although the limited sample sizes within age groups are such that it is difficult to evaluate whether these discrepancies reflect true differences or are due to imprecision in the estimates. Adults aged 18-34 and 35-49 years waited a median time to transplant of 77 and 28 days while children <1 year old and 1-5 years old waited a median time of 321 and 214 days. Compared to the overall population in 2007, African Americans and Hispanic candidates waited longer, with a median time to transplant of 250 and 447 days, respectively.

Figure IV-21. Median Time to Transplant (TT) for New Intestine Waiting List Registrations, 1998-2007



Source: *2008 OPTN/SRTR Annual Report,* Table 1.5.

Overall outcomes at one year after being listed for intestine transplant have been relatively stable with some notable exceptions. Table IV-11 shows waiting list outcomes at one year after listing, grouped by year of listing *[SRTR Analysis 2008]*. Among candidates added to the waiting list in 2006 (n=312), 54% of patients had been transplanted within one year of listing, with 17% receiving an isolated intestine transplant and 37% receiving a multi-organ transplant. The number of patients receiving multi-organ transplants within one year of listing increased from 29% in 1998 to 37% in 2006. This may indicate that need for timely referral must continue to be emphasized in order to optimize chances for intestine adaptation and lower the number of patients who ultimately develop parenteral nutrition associated irreversible liver disease requiring transplant. About one-fifth of those added to the list for an intestine transplant in 2006 (21%, n=66) were still on the waiting list one year later. Of those still waiting, 55% were listed at Status 1 (12% of all 2006 new listings), 20% were not Status 1 (4% of all 2006 new listings), and 26% were inactive (5% of all 2006 new listings).

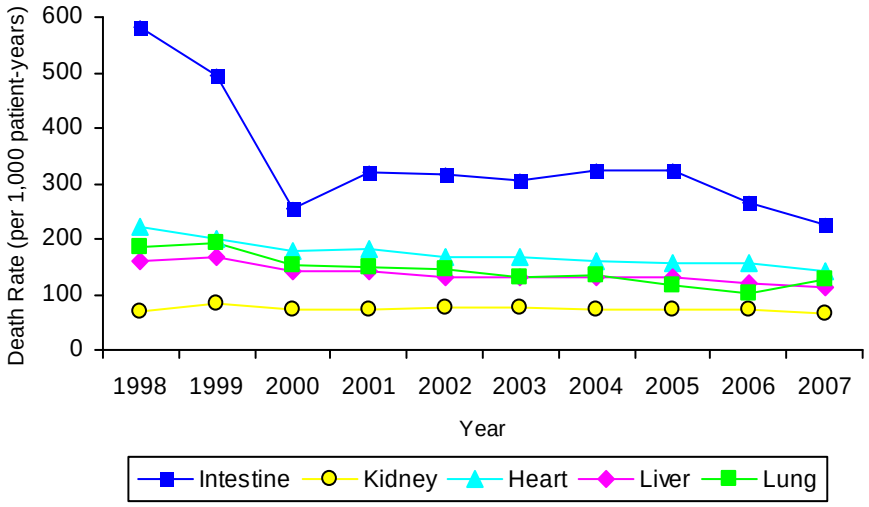
Table IV-11: Outcomes at One Year After Listing for Candidates on the Intestine Transplant Waiting List, 1998 - 2006

	Year of listing								
	1998	**1999**	**2000**	**2001**	**2002**	**2003**	**2004**	**2005**	**2006**
Total listings during calendar year (N)	146	132	155	210	195	196	244	275	312
Status one year after listing (%)	100	100	100	100	100	100	100	100	100
Still on waiting list	15	23	23	21	16	18	18	19	21
Status 1	4	11	13	11	9	11	10	10	12
Not status 1	4	7	5	6	4	3	3	3	4
Inactive	7	5	5	4	3	4	5	6	5
Received transplant	47	49	52	51	50	52	56	54	54
Intestine alone transplant	18	17	20	22	19	21	21	17	17
Multiple organ	29	32	32	29	31	31	35	37	37
Died within one year of listing	27	23	18	20	24	22	18	18	17
Condition worsened/medically unsuitable	3	4	1	1	2	2	2	6	5
No record of subsequent death	2	2	0	1	1	1	0	2	2
Died after removal as too sick	1	2	1	0	1	1	2	4	3
Condition Improved	1	0	3	2	3	3	3	2	2
Removed for other reasons	6	3	5	4	5	4	2	1	2

Slightly more than one quarter (26%) of those added to the waiting list in 2006 had been removed within one year without receiving a transplant *[SRTR Analysis 2008]*. For candidates removed from the list, two-thirds had died within the year (67% of removals), which equates to 17% of all candidates listed for intestine transplant in 2006. This is an improvement from previous years; among those listed in 1998, 27% died without a transplant within one year of listing. The other third of the removals among those listed in 2006 were coded as too sick (n=14), condition improved (n=5), or other (n=7).

Despite overall improved time to transplant, waiting list mortality (expressed as the death rate per 1,000 patient years) at risk remains the highest among all solid organ transplant recipients (Figure IV-22) *[Table 1.6]*. The current death rate for intestine transplant candidates is 226 which, although dramatically better than the rate of 583 reported in 1998, remains higher than all other transplant candidates including those awaiting kidney (65), liver (113), lung (126), heart (142), and heart/lung (195) transplantation. Waiting list death rates are highest among patients aged 35-49 years (437), 50-64 years (400) and those <1 year of age (368) compared to relatively low annual death rates for those age 12-17 (55) *[Table 10.3]*. Death rates improved from 349 to 228 in children aged 1-5 years. Overall higher death rates were seen in white candidates (267) and those with blood type B (282). Patients with functional bowel problems had the lowest death rate among the diagnosis groupings (65).

Figure IV-22. Unadjusted Death Rates per 1,000 Patient Years at Risk for Patients on the Waiting List by Organ, 1998 - 2007



Source: *2008 OPTN/SRTR Annual Report,* Table 1.5.

There are ongoing efforts to address the significant mortality rate facing intestine transplant candidates through refinements in allocation policy (14). The first of these changes was in March 2003 and provided combined liver and intestine candidates additional MELD/PELD points equivalent to 10% mortality risk at three months (Policy 3.6.4.7). This policy allowed the liver to be placed off the intestine list if there were no suitable regional Status 1A/1B liver candidates (policy 3.11.4), and allocated pediatric donor organs age 0-10 to pediatric recipients after Status 1A/1B liver candidates were offered the organ. This MELD risk adjustment, however, had been shown to adequately predict mortality in adults but was not as accurate for combined liver-intestine candidates who were mostly children. As a result, in January 2007 an additional 23 extra PELD points were allocated to combined liver and intestine candidates under age 18 (Policy 3.6.4.7). More recently, policy changes have been approved to allocate combined liver and intestine grafts according to the intestine match run after the liver graft has been sequentially offered though national Status 1A and 1B offers. Any impact of these allocation changes should be apparent in the near future.

Intestine Donation

Intestine donation and acceptance patterns must also be improved to reduce waiting list mortality. Unfortunately, these practices appear relatively static. Although the 205 intestine donors utilized in 2007 is the most ever, the increase over the previous year (185) was only 11% *[Table 1.1]*. Of note, after a peak incidence of seven live intestine donors in 2005, only one live intestine donor was utilized in 2007. The percentage of intestine donors recovered from deceased donors with at least one organ recovered increased from 1.3% (68 of 5,793) in 1998 to 2.5% (205 of 8,091) in 2007 *[Table 2.16]*. Intestinal recovery was always associated with recovery of other organs, usually intestine and kidney or pancreas only (27%) or intestine and other combinations (68%) *[Table 2.16]*. Only 17% of intestines recovered from deceased donors in 2007 were used locally, highlighting both the relatively small number of intestine transplant programs, as well as the efforts that are taken to secure suitable donors *[Table 3.10]*.

Only 7 of the 205 recovered intestines were not used (a discard rate of 3%) *[Table 3.10]*. On the other hand, the most frequently reported reasons for non-recovery of consented intestine donors included “no recipient found” (33%), “poor organ function” (29%), other (20%), and “donor medical or social history” (12%) *[Table 3.12]*. Most intestine donors were children, with 26% being <1 year old and 22% being between one and five years of age *[Table 2.5]*. The most common demographic and medical characteristics of intestine donors were: white race (58%), male (66%), blood type O (58%), and head trauma as cause of death (55%). There have been no intestine donors after cardiac death since an isolated case in 2003. While donors <1 year are often considered with caution, it is noteworthy that the death rate for the first year posttransplant for recipients who received a graft from an infant donor fell to 248 in 2006 compared to 379 in 2004 and 364 in 2005, highlighting the utility of this potentially underutilized donor age group *[Table 10.7]*.

Intestine Recipients

In 2007, 198 patients received a transplant that included an intestine graft, the most ever in one year *[Table 10.4]*. This corresponded to an incidence of intestine transplant (IT) of 0.66 per million population in 2007 with the highest incidence across age groups being for the <1 year age group *[Table 10.5]*. The most frequent categories of demographic and medical characteristics among IT recipients in 2007 were: children aged 1-5 (28%), white race (69%), and short gut syndrome (72%). Ten percent of IT recipients in 2007 had received a previous intestine transplant. Recipients of intestine-only grafts were 29% of all IT recipients (n=57), while the majority (n=141) received intestine-containing multi-organ grafts, usually with the liver (n=33) or liver-intestine-pancreas (n=88) but also with kidney (n=2), pancreas-intestine (n=4) or kidney-pancreas-liver-intestine (n=14). The number of isolated intestine grafts has remained stable for the past two years, while the number of IT recipients also receiving the liver has increased by 30%, from 104 to 135. One can speculate that, despite an increasing awareness of IT, most patients still undergo IT requiring a liver following TPN-induced liver failure rather than isolated intestine transplants prior to liver failure. Optimal timing for referral and evaluation is still being determined.

Primary payment sources for IT were private insurance (41%), Medicaid (44%), Medicare (9%) and other (6%). Most IT recipients (70%) were not in the hospital when the intestine graft became available, a factor which the International Intestine Transplant Registry has found to be associated with improved outcomes (18).

Immunosuppression

Immunosuppression following intestine transplantation continues to evolve. Primary induction therapy continued to be common in intestine transplants in 2007, but not universal with 51% having no induction therapy used *[Table 10.6a]*. The use of induction therapy has varied from 1998-2007, starting at 41% in 1998, peaking at 75% in 2003, and declining to 49% in 2007. In 2007, the most common agent, used alone or in combination, was rabbit antithymocyte globulin (ATG) (Thymoglobulin, Genzyme Corp., Cambridge, MA) used in 24% of all IT recipients, followed by muromonab-CD3 (Orthoclone OKT3, Ortho Biotech, Bridgewater, NJ) used for 18% of recipients, alemtuzumab (Campath-1H, Genzyme Corp., Cambridge, MA) used for 13%, and daclizumab (Zenapax, Roche Group, Nutley, NJ) used 9%. In 1998, induction therapy was used in only 41% of IT recipients, almost all of which used daclizumab. This change to induction therapy and its resultant positive impact on survival have also been noted by the global intestinal transplant community as reported by the International Intestine Transplant Registry (18).

Immunosuppression used for maintenance prior to discharge includes corticosteroids in 77% of IT recipients, the calcineurin inhibitor tacrolimus (Prograf, Astellas, Tokyo, Japan) in almost all IT recipients (97%), and anti-metabolite use in 23%, mostly mycophenolate mofetil (MMF) (CellCept, Roche Group, Nutley, NJ) *[Table 10.6e]*. The most common specific regimen in 2007 was tacrolimus and steroids (56%), followed by tacrolimus alone (11%) and tacrolimus with MMF or mycophenolate sodium (MPA) *[Table 10.6d]*. The most common maintenance regimen at one year posttransplant was

tacrolimus and steroids (47%) followed by tacrolimus alone (33%) *[Table 10.6f]*. By one year, the incidence of patients off steroids completely had increased to nearly 40% *[Table 1.9a]*.

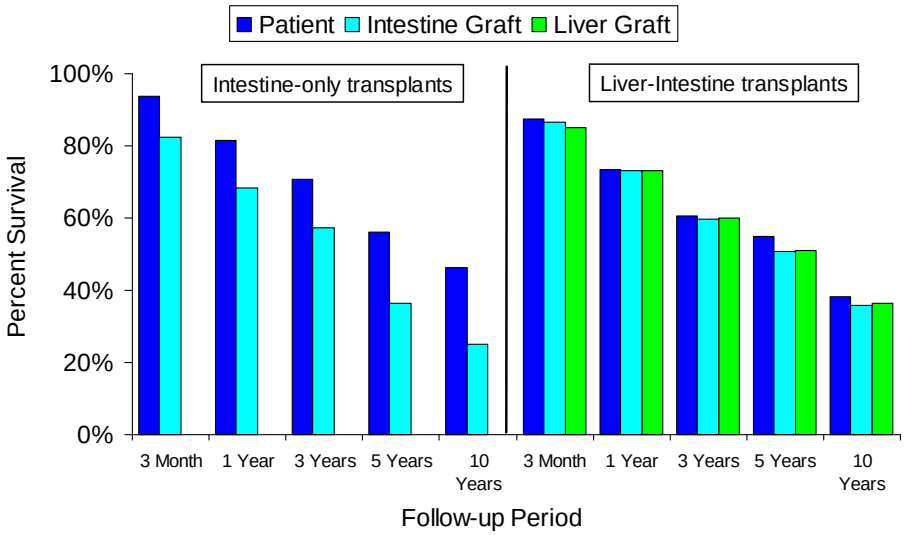
Acute rejection treated with anti-rejection medications at any time between transplant and the one-year follow-up report occurred in 61 of 175 cases in 2006, an incidence of 35% *[Table 10.6i]*. This is a decrease from 68% in 1997, but is about the same as 2005 when it was 33%. Steroids were used in 82% of these acute rejection episodes, and antibodies were used in two-thirds of these reported episodes. This represents an increase in antibody use to its highest level since 1997; antibody use was 40% in 2005 and 46% in 2004. The most common antibody utilized in 1997-2006 remained muromonab-CD3 (41%), followed by rabbit ATG (15%).

Intestine Transplant Survival

Patient and graft survival, as well as death rates per 1,000 patient years at risk, appear to have reached somewhat of a plateau despite significant improvements as compared to 1997. For example, one-year adjusted graft survival for intestine recipients was 70% (± 3.6%) for 2006, which is not statistically different from adjusted graft survival for any year between 2000 and 2006 *[Table 1.11a]*. However, it is better than adjusted one-year graft survival from 1997-1999. One-year adjusted patient survival for IT recipients (isolated intestine or intestine-containing multi-organ) was 78% in 2006, which again is not statistically significantly different than that for 2000-2005, but is a significant increase from 60% in 1997 *[Table 1.12a]*.

Figure IV-23 shows the unadjusted graft and patient survival for IT recipients of intestine-only grafts and combined liver-intestine grafts, at several follow-up time periods. Among recipients of intestine-only grafts, unadjusted patient survival was always higher than graft survival *[Table 1.13]*. At three months after transplant, graft survival was 83% and patient survival was 94%. Graft survival was 68% at one year, 57% at three years, 36% at five years, and 25% at ten years. Patient survival followed a similar pattern and was 81% at one year, 71% at three years, 56% at five years, and 46% at ten years. For recipients of combined liver-intestine grafts, patient and graft survival were statistically the same. Patient survival declined from 88% at three months, 73% at one year, 61% at three years, 55% at five years, and 38% at ten years. Isolated intestine ten-year graft survival is not statistically different from that of pancreas-alone, lung-alone, and heart-lung transplants but lags significantly behind that of other organ transplants. As would be expected given the possibility of graft removal and the current technology of organ replacement therapies, ten-year patient survival for intestine-only recipients (46%) is greater than that of lung-alone (28%) and heart-lung recipients (28%), but less than that of pancreas-alone transplants (73%).

Figure IV-23. Unadjusted Patient and Graft Survival for Intestine-Alone and Liver-Intestine Recipients



Source: *2008 OPTN/SRTR Annual Report*, Table 1.13.

Overall, the one-year posttransplant unadjusted death rate per 1,000 patient years at risk for intestine recipients transplanted in 2006 was 269, similar to the death rate of 253 for those transplanted in 2005 *[Table 10.7]*. Those <1 year of age had the highest posttransplant death rate of 511 for those transplanted in 2006. Other characteristics with higher death rates than the overall death rate were: being African American (417) and being Hispanic (398). Although absolute numbers were small, the percentage of deaths among patients on mechanical support at the time of transplant have been excessive since 1998 when 71% (5 out of 7) died within one year of transplant. The lowest was 40% (2 deaths out of 5 recipients) in 2001 and the highest was 75% in 2006 (3 deaths out of 4 recipients). When evaluated by hospitalization status at the time of transplant, those in the ICU had a death rate of 737 compared to 310 for those in the hospital but not in the ICU and 197 for those not hospitalized.

Importantly, there were 584 recipients living with a functioning graft at the end of 2006; 44% had been transplanted when they were <5 years old and 6% had received more than one intestine transplant *[Table 10.16]*.

Summary and Implications

Improving success with intestine transplantation has been notable over the past ten years. However, several key issues arose upon review of this year's summary analysis: First, the increasing number of patients with functioning grafts will cause a shift of focus from short-term patient survival to optimizing long-term outcomes. Increasingly, causes of patient and graft loss such as chronic rejection will come under scrutiny with a focus on

immunosuppression and research directed towards improving long-term outcomes. The fact that patient and graft survival has stabilized over recent years suggest that efforts must now be intensified to identify ways to improve results for patients. This could include a focus on intestinal rehabilitation, appropriate patient selection, and developing broadly agreed upon criteria for the timing of referral and transplantation. Finally, the transplant community must continually reassess its efforts to improve waiting list mortality in this at-risk population, especially in the very young. The goal of eliminating death on the waiting list is achievable by modest increases in the recovery of intestine-containing grafts and better allocation.

Conclusion

Overall, progress continues in liver and intestine transplantation. Refinements in allocation have resulted in significant improvement in our ability to direct the available organs to those most in need. Though not perfect for all, MELD and PELD have offered a significant improvement in our ability to determine need, and the numbers of patients being transplanted via the non-standard exception mechanism appears stable.

Efforts to increase the pool of potential donors, through the prudent use of living donors, broad-based education efforts such as the Collaborative, and initiatives to evaluate donors previously underutilized (such as DCD and infant donors), will hopefully contribute to narrowing the gap between the number of patients who might benefit from transplantation and the available donor supply. A better understanding of organ acceptance practices may provide additional opportunities to improve donor utilization. Ultimately, organ acceptance practices must also be considered in the context of patient outcomes, both before and after transplantation.

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