liver

The number of adult recipients of deceased donor liver transplants peaked in 2006, and has remained relatively stable over the past 2 years (Figure LI 4.1). In 2009, only 168 of 5,748 transplanted livers (2.9%) were from living donors. Concerns about donor safety, and generally good outcomes after deceased donor liver transplant, have limited use of living donors. The proportion of livers transplanted from living donors is greater for pediatric than for adult recipients (Figure 8.8). In 2009, only 51 of 572 pediatric liver transplants (8.9%) used organs from living donors. Most recovered livers were transplanted. For example, in 2009, livers were recovered from 85% of all deceased donors, and 76% of deceased donors were transplanted.
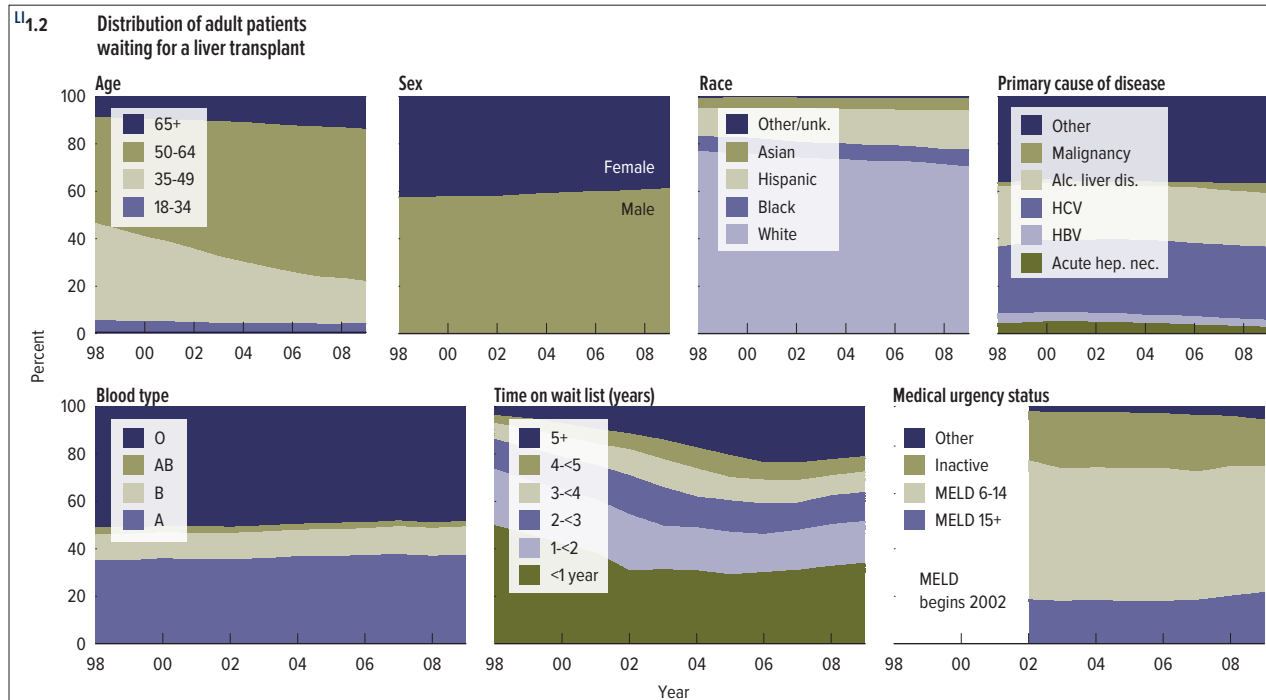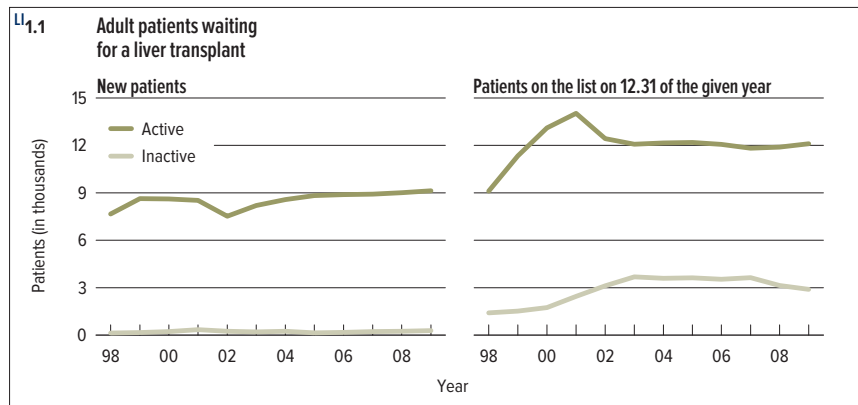
Implementation of the model for end-stage liver disease (MELD) system in 2002 led to a sharp reduction in liver transplant waiting list registrations (Figure 1.1). After transplant, the most common reason for removal from the waiting list is death (Figure 1.5). In 2009, reasons for removal were transplant (56.9%), death (22.8%), becoming too ill for transplant (3.1%), improving enough not to need transplant (5.6%), transferring to another center (1.8%), and other (9.8%). High mortality on the liver transplant waiting list is thus a major challenge.

In adjusted analysis of deceased donor liver graft survival (Figure 6.2), 6-month graft survival increased from 74.3% in 1991 to 89.8% in 2009; 1-year graft survival increased from 70.0% in 1991 to 84.9% in 2008; 3-year graft survival increased from 62.4% in 1991 to 75.0% in 2006; 5-year graft survival increased from 56.6% in 1991 to 67.1% in 2004; and 10-year graft survival increased from 43.4% in 1991 to 51.3% in 1999. Living donor liver graft survival has improved similarly (Figure 6.3).

Without treatment, patients with Anna's condition often only live about two years. We are just so appreciative that another family made the generous decision to share life with our daughter.

Kim, mother of liver recipient

OPTN :SRR
SCIENTIFIC REGISTRY OF
TRANSPLANT RECIPIENTS

LI 1.1   **Adult patients waiting for a liver transplant**

New patients

Patients on the list on 12.31 of the given year

— Active
— Inactive

Patients (in thousands)

Year

LI 1.2   **Distribution of adult patients waiting for a liver transplant**

Percent

Age
- 65+
- 50-64
- 35-49
- 18-34

Sex
- Female
- Male

Race
- Other/unk.
- Asian
- Hispanic
- Black
- White

Primary cause of disease
- Other
- Malignancy
- Alc. liver dis.
- HCV
- HBV
- Acute hep. nec.

Blood type
- O
- AB
- B
- A

Time on wait list (years)
- 5+
- 4-<5
- 3-<4
- 2-<3
- 1-<2
- <1 year

Medical urgency status
- Other
- Inactive
- MELD 6-14
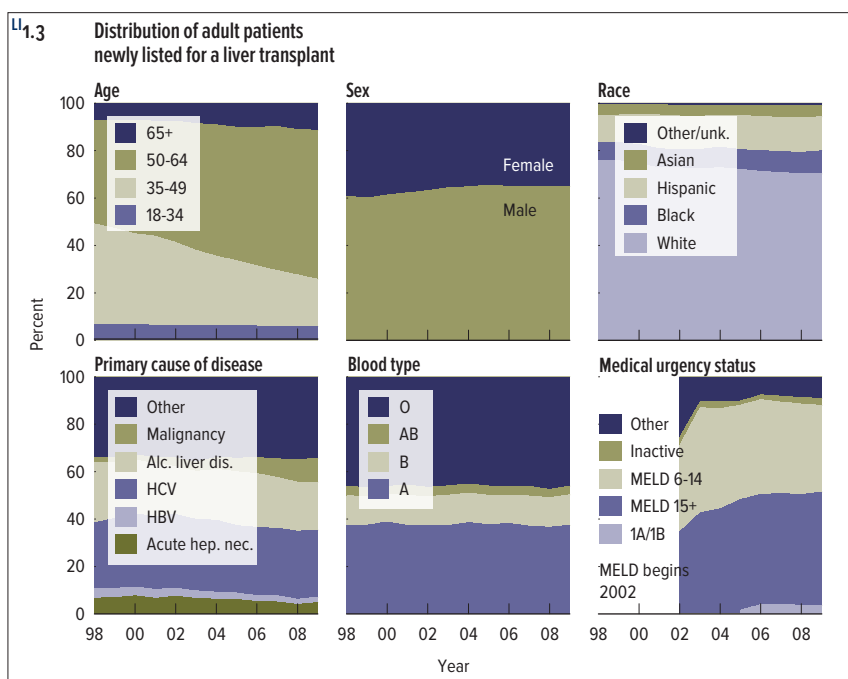- MELD 15+

MELD begins 2002

Year

wait list

On February 27, 2002, use of the MELD score as the main criterion for liver allocation began. MELD is a numerical score based on 3 objective variables: the serum concentrations of total bilirubin and creatinine, and the international normalized ratio (INR) for prothrombin time. By adopting MELD, the allocation policy operationalized the "sickest-first" policy.

Implementation of the MELD system led to a sharp reduction in liver transplant waiting list registrations (Figure 1.1) because, unlike under the previous allocation scheme, accrual of waiting time was no longer necessary. The impact of the MELD system is more pronounced when the number of prevalent patients is considered (Figure 1.1). The number of patients waiting for a liver

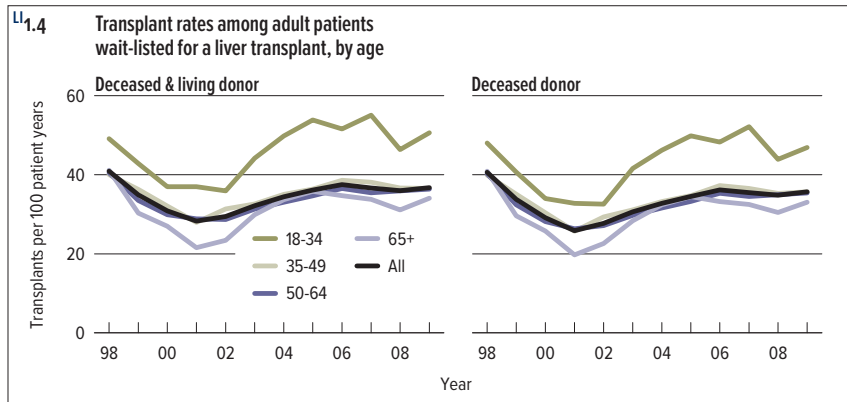transplant had been increasing continuously, but has essentially remained flat since 2002.

The age distribution of wait-listed registrants has changed noticeably in that the age group 50 to 64 years has increased substantially in the past decade (Figures 1.2 and 1.3). This likely reflects changes in the epidemiology of liver disease in the United States. The most common cause of disease among liver transplant candidates is the end-stage consequences of chronic hepatitis C virus (HCV) infection (Figures 1.2 and 1.3), which mostly affects Americans in their 50s and 60s. Thus, the age shift seen in these figures partly reflects the aging of the cohort of HCV-infected patients over time. Another contributing factor may be the increasing number of wait-listed registrants with obesity-related

LI 1.3   **Distribution of adult patients newly listed for a liver transplant**

Age

- 65+
- 50-64
- 35-49
- 18-34

Sex

Female

Male

Race

- Other/unk.
- Asian
- Hispanic
- Black
- White

Primary cause of disease

- Other
- Malignancy
- Alc. liver dis.
- HCV
- HBV
- Acute hep. nec.

Blood type

- O
- AB
- B
- A

Medical urgency status

- Other
- Inactive
- MELD 6-14
- MELD 15+
- 1A/1B

MELD begins 2002

Year

Percent

98 00 02 04 06 08

fatty liver disease. The rapid increase in the prevalence of obesity in the US is well recognized. One of the complications of obesity is so-called nonalcoholic liver disease, which is grouped under Other diagnosis. Some of these patients develop end-stage liver disease, most commonly after they pass middle age. Related to these epidemiologic trends is a clear rising trend in the incidence of hepatocellular carcinoma (HCC). Some patients with HCC who meet the eligibility criteria (the "Milan criteria") can be cured of the malignancy by liver transplant. The proportion of wait-listed registrants for this indication has increased noticeably.
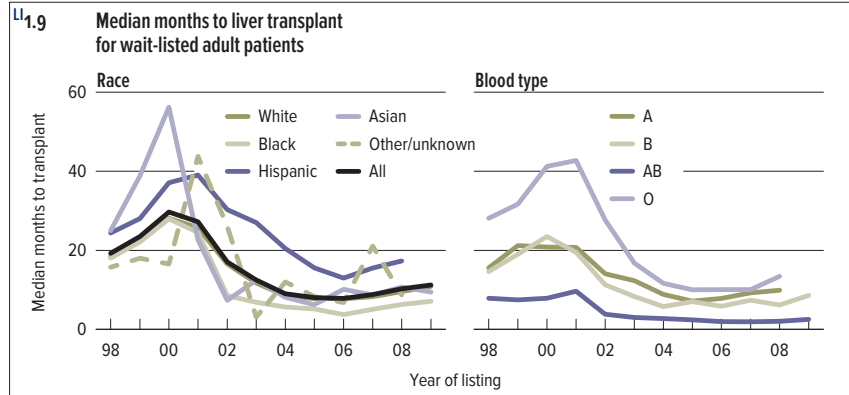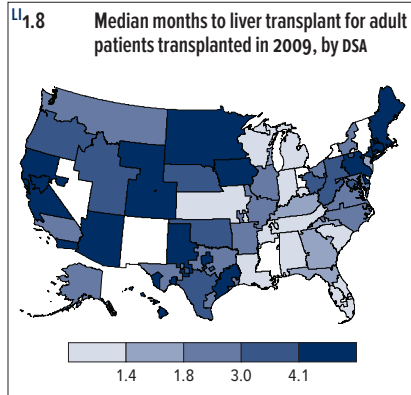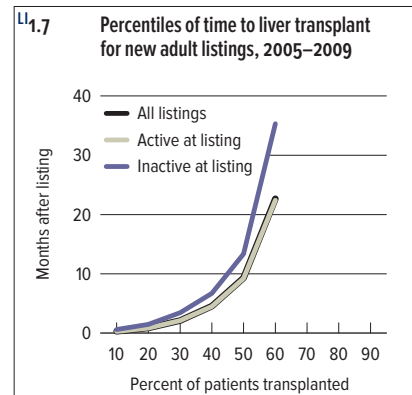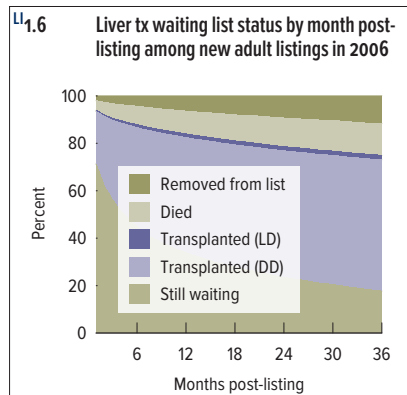
Although the MELD system provides no advantage to patients who are registered early in the course of disease progression, a substantial number of wait-listed registrants are not at an immedi-

ate risk of death, as reflected by their low (< 15) MELD scores. By design, these patients are not selected for liver transplant and will accumulate significant time, not infrequently longer than 5 years, on the waiting list before their disease progresses to a MELD score high enough for liver transplant.

OPTN :SRTR
SCIENTIFIC REGISTRY OF
TRANSPLANT RECIPIENTS

LI1.4 Transplant rates among adult patients wait-listed for a liver transplant, by age

LI1.5 Liver transplant waiting list activity among adult patients

|	2007	2008	2009
Listings at start of year	16,085	15,990	15,641
Listings added during year	10,261	10,344	10,478
Listings removed during year	10,356	10,693	10,494
Listings at end of year	15,990	15,641	15,625
Removal reason			
Deceased donor transplant	5,951	5,791	5,807
Living donor transplant	191	173	168
Patient died	2,336	2,451	2,396
Trans. to another center	263	190	184
Too sick to transplant	269	280	327
Improved, tx not needed	476	585	586
Other	870	1,223	1,026

LI1.6 Liver tx waiting list status by month post-listing among new adult listings in 2006

LI1.7 Percentiles of time to liver transplant for new adult listings, 2005–2009

LI1.8 Median months to liver transplant for adult patients transplanted in 2009, by DSA

LI1.9 Median months to liver transplant for wait-listed adult patients

wait list

The rate of liver transplant, which had been decreasing before implementation of MELD in 2002, has been stable since then (Figure 1.4). Other factors contributed to this trend reversal, such as an increased number of donor organs, including expanded criteria donors (ECD).

A similar trend is shown in the median time to transplant. Implementation of the sickest-first policy using the MELD score reversed the previous trend of increasing time to transplant (Figure 1.9). This affected all race and blood type categories. The slight upturn in the curve is a potential cause of concern and may suggest that the degree to which optimization of organ allocation can affect transplant rates is limited. The most common reason for being removed from the waiting list but not undergoing liver transplant is death. In 2009, reasons for removal from the waiting list were transplant (56.9%), death (22.8%), becoming too ill for transplant (3.1%), improving enough not to need transplant (5.6%), transferring to another center (1.8%), and other (9.8%). The high mortality rate on the liver transplant waiting list is thus a major challenge. A substantial degree of variability remains in transplant rates (Figure 1.4), and an improved organ distribution policy may be necessary for waiting times to continue to decrease (Figure 1.9).

LI 1.10 Pre-transplant mortality rates among adult patients wait-listed for a liver transplant
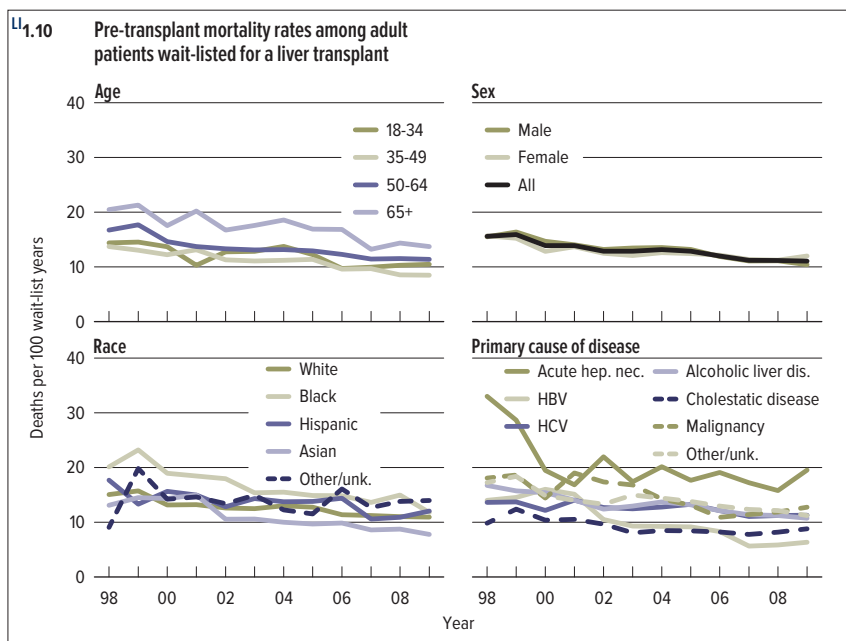
| LI 1.11	Characteristics of adult patients on the liver tx waiting list on December 31, 2009		
	Level	N	%
Age	18-44	1,726	11.5
	45-64	11,230	74.9
	65-74	1,967	13.1
	75+	78	0.5
Gender	Male	9,178	61.2
	Female	5,823	38.8
Race	White	10,555	70.4
	Black	1,065	7.1
	Hispanic	2,485	16.6
	Asian	752	5.0
	Other/unk.	144	1.0
Primary cause of disease	Acute hepatic necrosis	413	2.8
	HBV	448	3.0
	HCV	4,606	30.7
	Alcoholic liver disease	3,390	22.6
	Cholestatic disease	1,427	9.5
	Malignancy	632	4.2
	Other/unk.	4,085	27.2
Transplant history	Listed for first tx	14,542	96.9
	Listed for sub. tx	459	3.1
Blood type	A	5,622	37.5
	B	1,780	11.9
	AB	356	2.4
	O	7,243	48.3
Time on wait list	<1 year	5,095	34.0
	1-<2	2,649	17.7
	2-<3	1,835	12.2
	3-<4	1,298	8.7
	4-<5	961	6.4
	5+	3,163	21.1
Status	Active	12,069	80.5
	Inactive	2,932	19.6
Medical urgency status	1A/1B	5	0.0
	MELD> 30	83	0.6
	MELD 21-30	631	4.2
	MELD 15-20	2,538	16.9
	MELD 11-14	3,610	24.1
	MELD 6-10	4,363	29.1
	HCC T1	3	0.0
	HCC T2	571	3.8
	Other exceptions	265	1.8
	Inactive	2,932	19.6

Figures 1.5 to 1.9 summarize outcomes of waiting. In 2007–2009, the liver transplant waiting list was essentially in a steady state, with roughly the same number of candidates listed and removed each year.

Encouragingly, wait-list mortality has continued to decline in the past decade (Figure 1.10). Further, this decrease occurred for both sexes and all race and age groups, and it affected both acute and chronic liver disease patients. Patients with acute hepatic necrosis by nature are faced with a high risk of mortality, which remains higher than in patients with end-stage complications of chronic liver disease. Status 1 patients are ranked ahead of pa-tients listed with a MELD score at the local and regional level. As of 2009, patients with cholestatic liver disease and hepatitis B virus (HBV) experienced a lower risk of death than others with chronic liver disease.
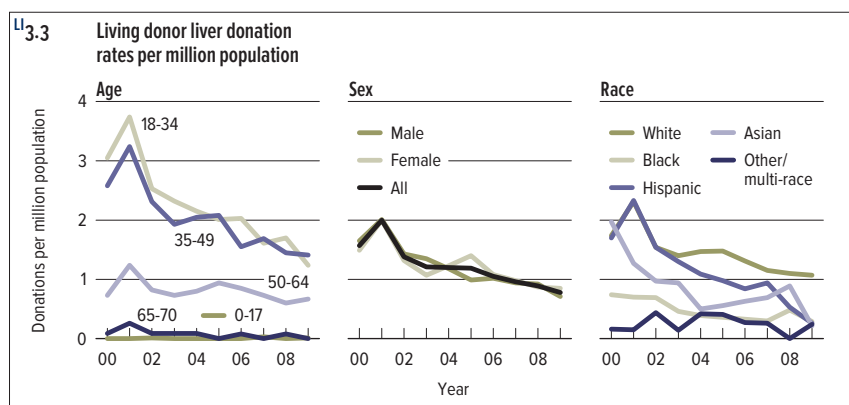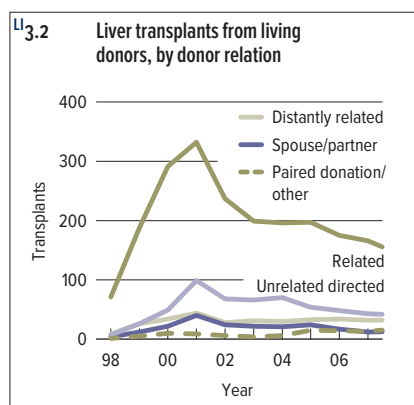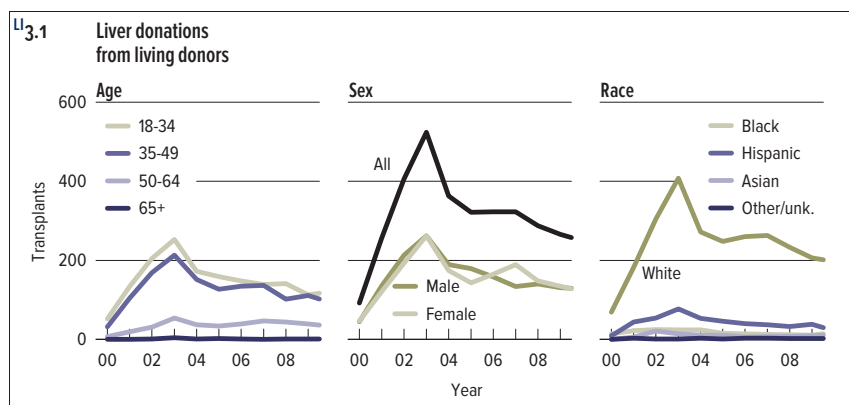
Figure 1.11 is a snapshot of wait-listed patients at the end of 2009. The most typical profile of a wait-listed registrant was age between 45 and 64 years, male, and white, with HCV and blood type O. More than half (53%) of the wait-listed patients had a low (< 15) MELD score, and a substantial number were inac-tive status.

LI2.1   Liver donations from deceased donors per million population
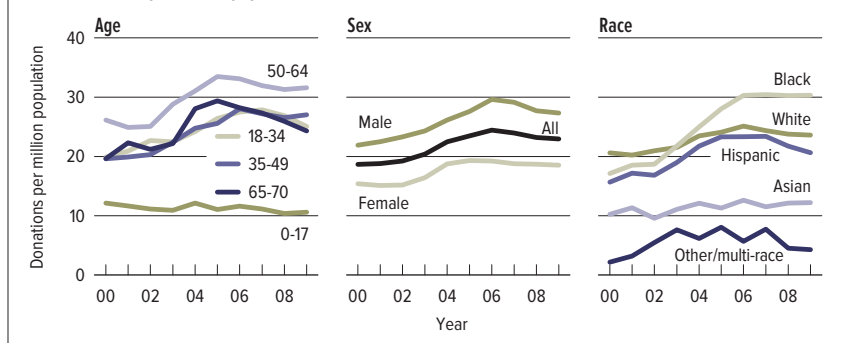
LI2.2   Deceased donor liver donation rates (per million population, age <70), by state
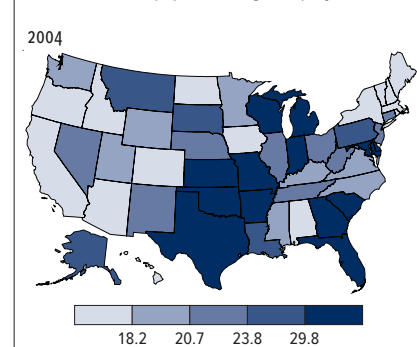
LI2.3   Livers recovered per donor & livers transplanted per donor
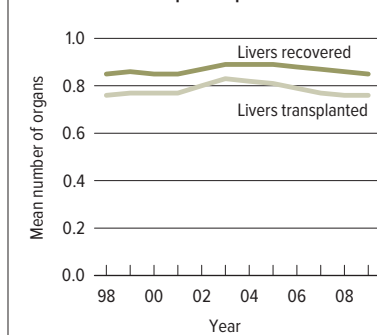
LI2.4   Deceased donor livers transplanted with another organ
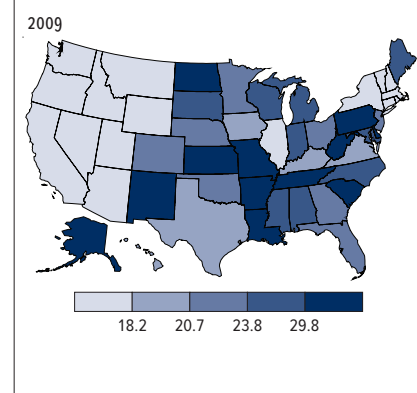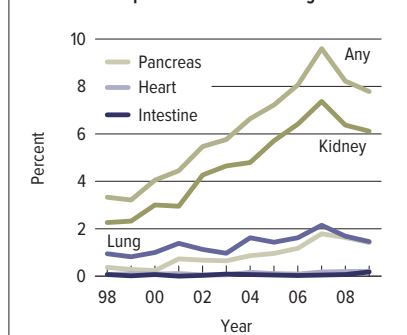
LI2.5   Discard rates for livers recovered for transplant
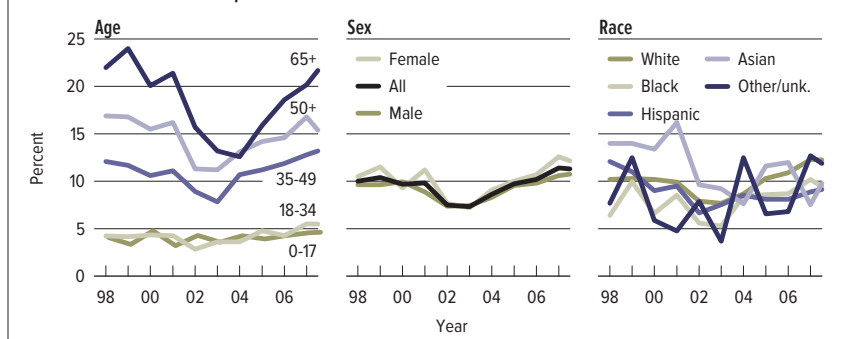
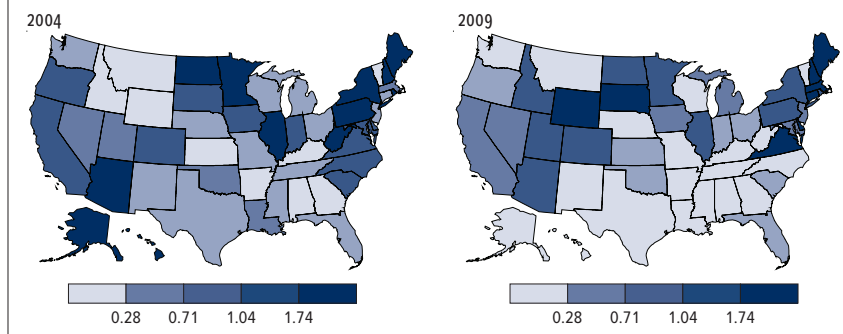**LI2.6   Liver donors who are DCD**
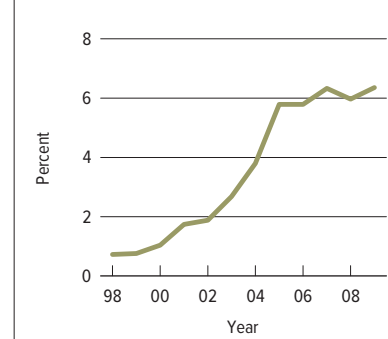
deceased donation

The overall donation rate rose until 2006, when it reached a plateau (Figure 2.1). Rates in older patients (aged 50 years or older) are declining, especially, since 2004, in those aged 65 to 70 years. Rates are highest for blacks, followed by whites, Hispanics, and Asians; the reasons for variability likely include incidence of brain death and age distribution of decedents, and the influence of cultural and belief systems. Some of these factors may underlie the geographic variability in donation rates (Figure 2.2). Rates are lower in the western regions and in the northeast, regions known for the longest waiting times for liver transplant. However, many reasons may account for longer waiting times, including access to transplantation.

Livers are recovered from nearly 90% of donors (Figure 2.3). Both the recovery and transplant rates seem to be falling. The discard rate is highest for older donors: 20% of recovered livers from donors aged 65 years or older were discarded in 2009 (Figure 2.5). This may reflect recognition of the deleterious outcome of older donor organs in recipients with HCV infection, and the trend toward increasing numbers of ECDs being sought, some of whose organs may be found unacceptable. The proportion of donation after circulatory death (DCD) donors increased rapidly in the early 2000s, then remained stationary (Figure 2.6). The increasing trend toward multi-organ transplant in liver recipients is well recognized (Figure 2.4). This may be attributable in part to the MELD system, although the rising trend began before MELD was implemented in 2002.
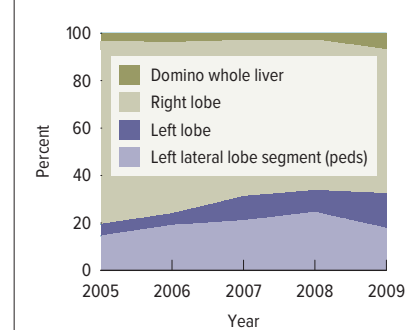
LI3.1   Liver donations from living donors

LI3.2   Liver transplants from living donors, by donor relation

LI3.3   Living donor liver donation rates per million population

live donation

The number of living donor liver transplants performed in 2009 (n = 219) reflects a continued decrease since the peak in 2001 and a further decrease since 2008 (n = 249). This trend likely reflects ongoing concern related to the relatively higher risks of donor morbidity and mortality compared with risks for living kidney donors. Demographic characteristics of living liver donors have not changed regarding age, sex, race (Figure 3.1), or donor relation (Figure 3.2). In 2009 most living donors (83%) were younger than 50 years old, reflecting the concern regarding higher rates of morbidity in older living donors. Although related donors remain the majority of living donors, the numbers decreased more in proportion to unrelated, distantly related, unrelated directed, and paired exchange donors (Figure 3.2). Rates of living donations (per million population) have also declined (Figure 3.3).
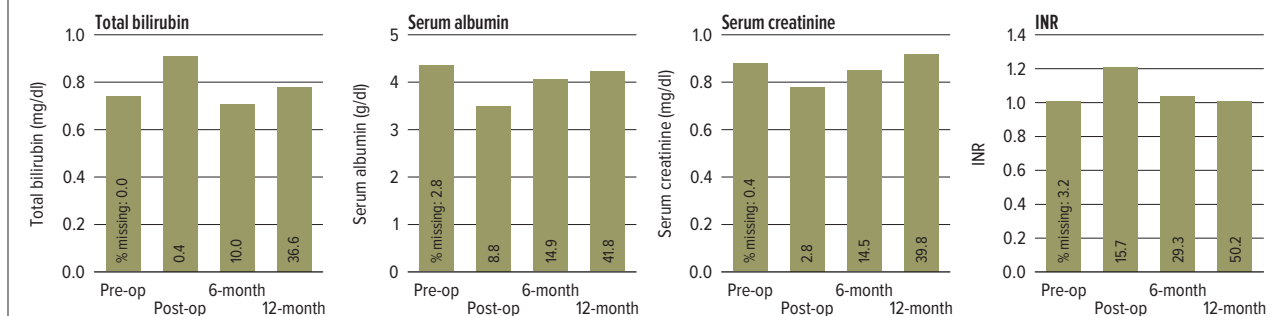
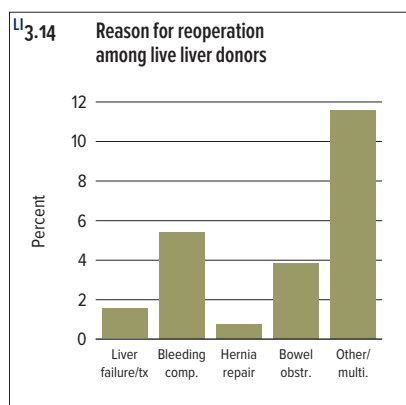**LI3.4**   **Living donor liver donation rates (per million population, age <70), by state**

2004

2009

0.28   0.71   1.04   1.74

0.28   0.71   1.04   1.74

LI3.5   **Living donor liver transplant graft type**

Domino whole liver
Right lobe
Left lobe
Left lateral lobe segment (peds)

Percent

2005   2006   2007   2008   2009

Year

LI3.6   **Mean pre- & post-operative total bilirubin, serum albumin, serum creatinine, & INR among liver donors, 2008**

Total bilirubin

Serum albumin

Serum creatinine

INR

Pre-op   6-month   Post-op   12-month

live donation

Significant geographic disparities remain regarding rates of living donor liver donation. Certain regions in the southeast and Pacific Northwest have extremely low or absent rates of living donor liver transplants (Figure 3.4), possibly reflecting shorter waiting times for deceased donor organs at the local center. Many centers performing living donor liver transplants proceed with a living donor only if the donor risks are justified by long waiting times and higher MELD requirements or if a deceased donor organ cannot be allocated within a safe time period.

Although fewer living donor transplants were performed in 2009, the number of left-lobe transplants increased relative t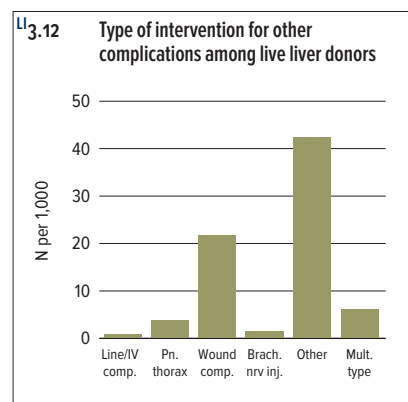o right-lobe transplants (Figure 3.5). Right lobes continue to represent most living donor transplants, at 63% and 60.7% of all living donor transplants in 2008 and 2009, respectively. Left lobes made up only 9.2% of living donor transplants in 2008, increasing to 14.6% in 2009. The relative increase in left-lobe transpl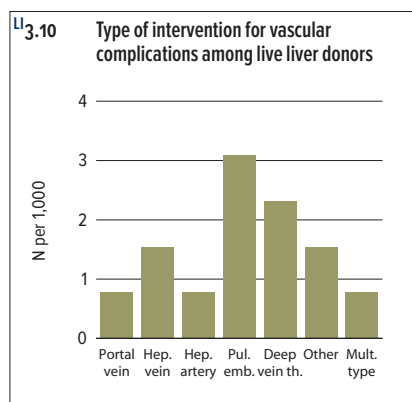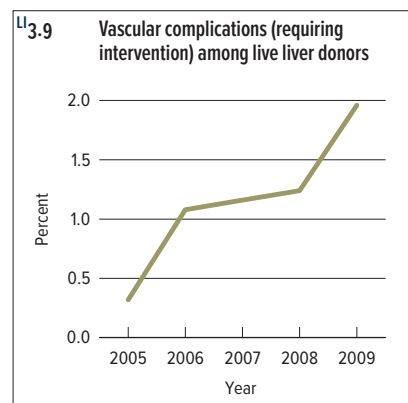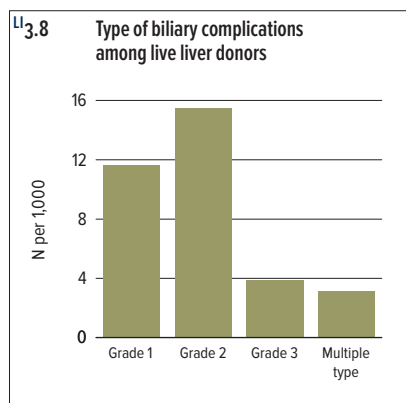ants is consistent with the overall concern in the transplant community to minimize donor morbidity, as donation of the left lobe is considered a relatively safer procedure. Also of interest was a significant decrease in the number of left lateral segment living donor transplants performed in 2009 (n = 39), down from 2008 (n = 61). It is unclear whether the decrease in living donation to children relates to increased access to split deceased donor livers; this will be important to monitor in

LI 3.7 Biliary complications among live liver donors

LI 3.8 Type of biliary complications among live liver donors

LI 3.9 Vascular complications (requiring intervention) among live liver donors

LI 3.10 Type of intervention for vascular complications among live liver donors

LI 3.11 Other complications (requiring intervention) among live liver donors

LI 3.12 Type of intervention for other complications among live liver donors

LI 3.13 Re-operation within the first six weeks among live liver donors

LI 3.14 Reason for reoperation among live liver donors

LI 3.15 Readmission to the hospital in the first year among live liver donors, 2008

the coming years. When children were given increased access to deceased donor kidneys, the number of living donor transplants decreased substantially. The relation between access to deceased donor livers and rates of living donation should be monitored over the next several years, and will undoubtedly affect rates of living donation and the development of new allocation algorithms.

Twelve-month follow-up for living donors from 2008 shows no significant impact on donor serum bilirubin, serum albumin, serum creatinine, or INR (Figure 3.6). The number of biliary complications following donation has remained fairly constant (1.8% to 2.9%), although the frequency in 2007 was aberrantly higher at 7.8% (Figure 3.7). Most biliary complications were reported as

grade 2 (Figure 3.8). Vascular complications following living liver donation were infrequent (< 2.0%) and largely related to deep venous thrombosis and pulmonary embolus (Figures 3.9 and 3.10). In 2009, no living donor deaths occurred within 30 days of transplant; 1 reported death occurred within 1 year of transplant. Rates of other complications and hospitalization have been relatively low (Figures 3.11 to 3.15).

LI 4.2   Adult liver transplants

Age

Transplants (in thousands)

50-64
35-49
65+
18-34

98 00 02 04 06 08

Sex

Male
Female

98 00 02 04 06 08

Race

White
Hispanic
Black
Asian
Other/unknown

98 00 02 04 06 08

Primary cause of disease

- Acute hepatic necrosis
- HCV
- Alcoholic liver disease
- Cholestatic disease
- Metabolic liver disease
- Malignancy
- Other/unk.

98 00 02 04 06 08

Year

LI 4.1   Total adult liver transplants

Transplants (in thousands)

All
Deceased donor

Living donor

98 00 02 04 06 08

LI 4.3   Liver transplant rates in adult candidates

Transplants per 100 pt years on WL

All
Deceased

Living, all

98 00 02 04 06 08
Year

LI 4.4   Use of DCD livers among adult recipients, by recipient age

Percent

- 18-34
- 35-49
- 50-64
- 65+
- All

98 00 02 04 06 08
Year

LI 4.5   Percent of adult, deceased donor liver transplants that are DCD, by DSA, 2009

1.3   1.9   2.9   5.7

transplant The number of adult recipients of deceased donor livers peaked in 2006 and has remained relatively stable over the past 2 years (Figures 4.1 and 4.3). The average age of adult recipients increased steadily over the past 10 years; in 2009, approximately 75% were aged older than 50 years (Figure 4.2). Male recipients predominated, at a 2:1 male-to-female ratio (Figure 4.2). Most liver transplant recipients are white, 71.8% in 2009. The most frequent cause of liver disease leading to transplant remains HCV infection (25.6%); however, the number of patients listed in the unknown/other category continues to increase, representing 23.6% of patients in 2009 (Figure 4.2). This likely represents the increasing role of nonalcoholic steatohepatitis as the cause of liver disease leading to transplant.

Although the frequency of DCD livers increased substantially among adult recipients in 2000–2006, use of DCD livers has stabilized at approximately 5% of all recipients (Figure 4.4). Lack of further increase in overall use of DCD organs may in part reflect increasing concern about the higher rate of biliary complications observed with these donors. Regions of the country where there is high use of DCD are likely also regions with longer waiting times to receive a deceased donor liver (Figures 4.5 and 4.6). Marked

LI 4.6 Deceased donor liver tx rates per 100 pt years on the waiting list, adult pts, 2009

25.0   34.0   47.0   62.0
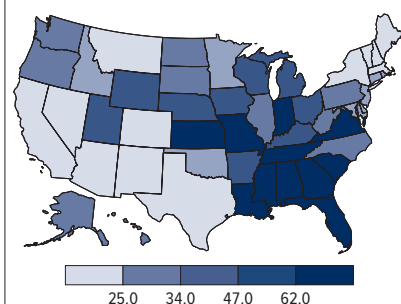
LI 4.7 Insurance coverage among adult liver transplant recipients at time of transplant

Other/unknown
Private
Other gvmt
Medicaid
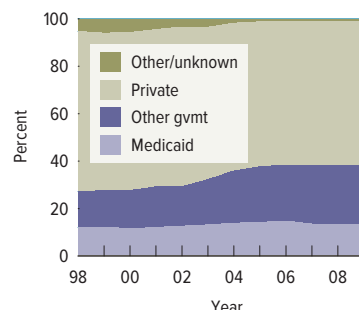
LI 4.9 Median MELD score for adult deceased donor liver transplants, by DSA, 2009

23.0   24.0   25.0   26.5

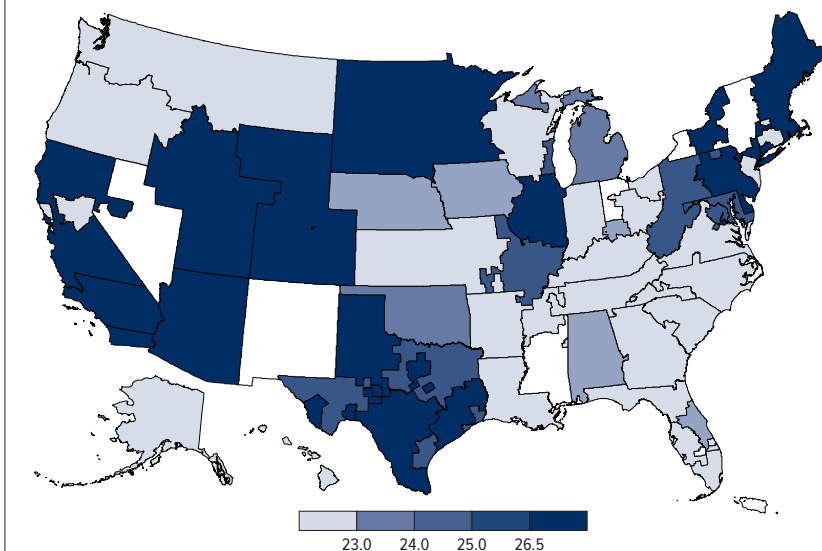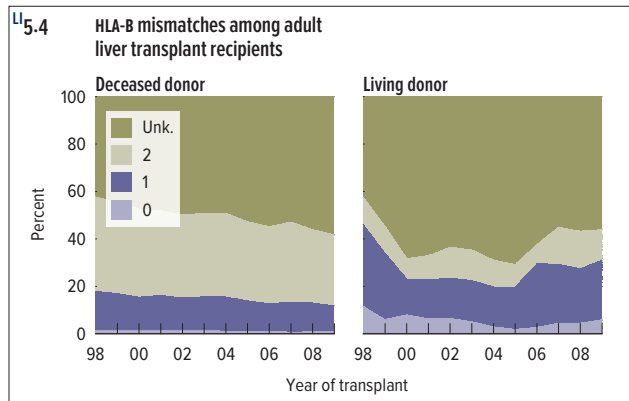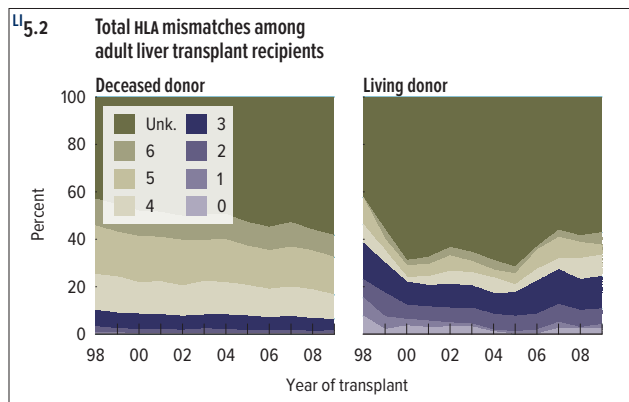| LI 4.8	Characteristics of adult liver transplant recipients, 2009		
	Level	N	%
Age	18-34	352	6.1
	35-49	1,092	19.0
	50-64	3,608	62.8
	65+	696	12.1
Sex	Female	1,861	32.4
	Male	3,887	67.6
Race	White	4,126	71.8
	Black	572	10.0
	Hispanic	720	12.5
	Asian	282	4.9
	Other/unknown	48	0.8
Primary cause of disease	Acute hep. necrosis	246	4.3
	HCV	1,470	25.6
	Alcoholic liver dis.	999	17.4
	Cholestatic dis.	455	7.9
	Metab. liver dis.	143	2.5
	Malignancy	1,077	18.7
	All others	1,358	23.6
Blood type	A	2,112	36.7
	B	769	13.4
	AB	264	4.6
	O	2,603	45.3
Time on waiting list	<30 days	2,015	35.1
	31-60 days	683	11.9
	61-90 days	424	7.4
	3-<6 months	877	15.3
	6-<12 months	753	13.1
	1-<2 years	511	8.9
	2-<3 years	197	3.4
	3+ years	288	5.0
BMI	<18.5	142	2.5
	18.5-24.9	1,601	27.9
	25.0-29.9	1,957	34.0
	30.0-34.9	1,150	20.0
	35.0-39.9	508	8.8
	40.0+	209	3.6
	Unknown	181	3.1
Medical condition	Hosp.: ICU	676	11.8
	Hosp.: not ICU	1,052	18.3
	Not hospitalized	4,020	69.9
Patient wait listing status before tx	Status 1A/1B	260	4.5
	MELD 30-40	1,443	25.1
	MELD 15-29	3,864	67.2
	MELD 6-14	180	3.1
	Other status	1	0.0
Primary payer	Private	3,457	60.1
	Medicaid	779	13.6
	Other	1,512	26.3
Procedure type	Whole liver	5,519	96.0
	Partial, rest not tx	156	2.7
	Split liver	73	1.3
Donor type	Deceased	5,580	97.1
	Living	168	2.9
Pt on life support	Yes	377	6.6
Prev. abdom. surg.	Yes	2,524	43.9
Diabetes	Yes	28	0.5
Portal vein throm.	Yes	360	6.3
Incident tumor at tx	Yes	176	3.1
Spon. bac. perit. (SBP)	Yes	357	6.2
Total		5,748	100

geographic disparity remains in deceased donor transplant rates across the country, with higher rates in the northwest and southeast (Figure 4.6). These maps of DCD organ use, transplant rates, and median MELD scores at the time of transplant can be superimposed. Regions of the country with high transplant rates, low DCD use rates, and high median MELD scores at the time of transplant are roughly similar. Private payers constitute the largest insurance coverage group for liver transplant, and in 2009 represented 60.1% of the providers.

OPTN :SRR
SCIENTIFIC REGISTRY OF TRANSPLANT RECIPIENTS

LI5.1   PRA at time of liver transplant in adult recipients

LI5.2   Total HLA mismatches among adult liver transplant recipients

LI5.3   HLA-A mismatches among adult liver transplant recipients

LI5.4   HLA-B mismatches among adult liver transplant recipients

LI5.5   HLA-DR mismatches among adult liver transplant recipients

donor-recipient matching

The role of anti-human leukocyte antigen (HLA) antibodies and HLA matching has historically not held high interest in the field of liver transplantation (Figures 5.1 to 5.5). This is reflected in the lack of recipient panel reactive antibody and HLA information for more than half of recipients, and in the high frequency of HLA-A, HLA-B, and HLA donor-recipient mismatching in deceased donor liver transplants (Figures 5.2 to 5.5). HLA typing has not been a requirement for listing for liver transplant unless the candidate is also listed for kidney transplant. Recent data suggesting a role for antibody-mediated rejection in liver transplant may increase the importance of

HLA matching and the monitoring of anti-HLA antibodies.

The cytomegalovirus (CMV) status of donor and recipient was identified for almost all donors and for over 90% of recipients, reflecting the importance of this information for guiding post-transplant prophylaxis. CMV matching between donor and recipient is not used in the allocation process, as shown by the relatively high frequency (18.6%) of CMV-positive deceased donors used with CMV-negative recipients (Figure 5.6). Similarly, Epstein-Barr virus (EBV) serologic status is not used in the allocation process, but post-transplant EBV monitoring may be particularly important in the pediatric population (Figure 5.7).

Ongoing concern about transmission of HBV from core antibody (HBcAb)-positive recipients is responsible for the low use

LI 5.6 Adult liver donor-recipient cytomegalovirus (CMV) serology matching, 2005–2009

10.3	18.6	0.1	29.0	24.4	11.0	6.4	41.8
20.6	40.9	0.3	61.8	23.0	21.0	9.1	53.1
2.8	6.3	0.1	9.2	2.4	1.3	1.5	5.1
33.7	65.8	0.5	100	49.9	33.2	17.0	100

LI 5.7 Adult liver donor-recipient Epstein-Barr virus (EBV) serology matching, 2005–2009

RECIPIENT	DECEASED DONOR				LIVING DONOR			
	Neg.	Pos.	Unk.	Total	Neg.	Pos.	Unk.	Total
Negative	0.5	7.6	2.4	10.5	0.8	4.6	2.9	8.2
Positive	2.4	35.8	17.2	55.4	2.4	40.0	17.7	60.0
Unknown	1.1	20.8	12.2	34.1	2.4	13.4	15.9	31.7
Total	4.0	64.2	31.8	100	5.6	57.9	36.5	100

LI 5.8 Adult liver donor-recipient hepatitis B core antibody (HBcAb) serology matching, 2005–2009

RECIPIENT	DECEASED DONOR				LIVING DONOR			
	Neg.	Pos.	Unk.	Total	Neg.	Pos.	Unk.	Total
Negative	61.3	2.6	0.2	64.1	60.5	1.6	7.8	69.8
Positive	18.7	2.2	0.1	21.0	12.0	0.9	1.6	14.5
Unknown	14.2	0.7	0.0	15.0	4.5	0.0	11.3	15.7
Total	94.3	5.5	0.3	100	77.0	2.4	20.6	100

LI 5.9 Adult liver donor-recipient hepatitis B surface antigen (HBsAg) serology matching, 2005–2009

RECIPIENT	DECEASED DONOR				LIVING DONOR			
	Neg.	Pos.	Unk.	Total	Neg.	Pos.	Unk.	Total
Negative	83.8	0.0	0.2	84.0	75.3	0.0	6.3	81.6
Positive	5.4	0.0	0.0	5.4	3.2	0.0	0.3	3.5
Unknown	10.5	0.0	0.1	10.6	4.1	0.0	10.9	14.9
Total	99.7	0.0	0.3	100	82.5	0.0	17.5	100

LI 5.10 Adult liver donor-recipient hepatitis C serology matching, 2005–2009

RECIPIENT	DECEASED DONOR				LIVING DONOR			
	Neg.	Pos.	Unk.	Total	Neg.	Pos.	Unk.	Total
Negative	47.4	0.1	0.1	47.5	48.6	0.1	5.1	53.8
Positive	37.6	2.5	0.1	40.1	24.7	0.1	3.1	27.9
Unknown	11.9	0.4	0.0	12.4	6.5	0.0	11.7	18.2
Total	96.8	3.0	0.2	100	79.8	0.2	20.0	100

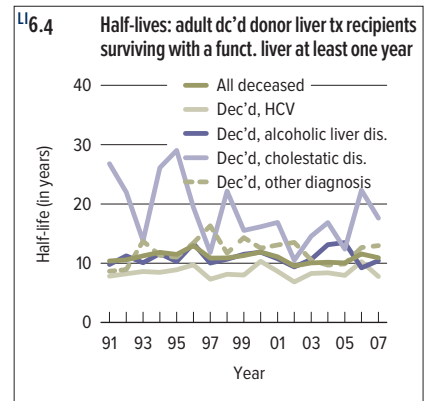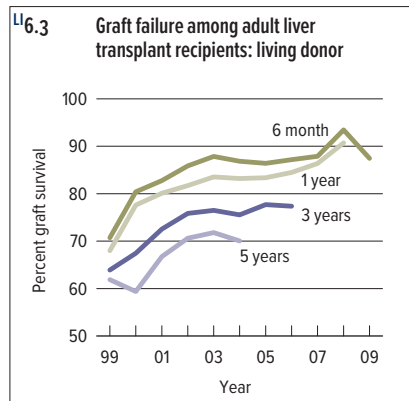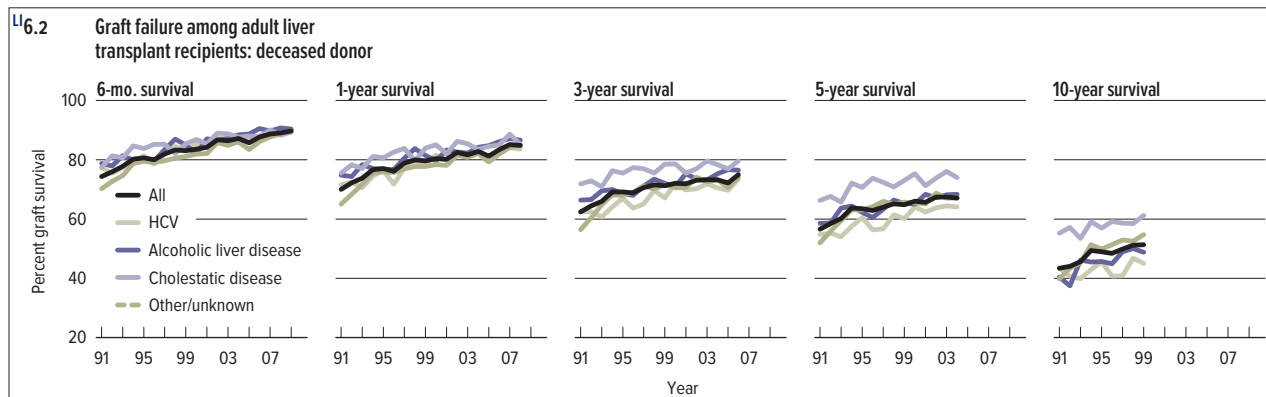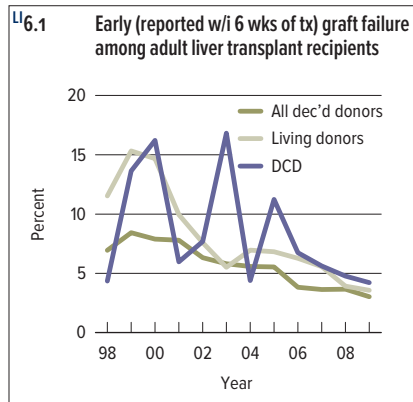**LI 5.11 Adult liver donor-recipient human immunodeficiency virus (HIV) serology matching, 2005–2009**

RECIPIENT	DECEASED DONOR				LIVING DONOR			
	Neg.	Pos.	Unk.	Total	Neg.	Pos.	Unk.	Total
Negative	80.5	0.0	0.1	80.5	69.0	0.0	6.6	75.6
Positive	0.5	0.0	0.0	0.5	0.2	0.0	0.1	0.3
Unknown	19.0	0.0	0.0	19.0	4.8	0.0	19.4	24.2
Total	99.9	0.0	0.1	100	73.9	0.0	26.1	100

rates of core positive donors, particularly in surface antibody negative recipients. Nonetheless, 2.6% of deceased donor transplants were performed between core antibody positive donors and core antibody negative recipients. The risk/benefit ratio of transmitting HBV through a core positive donor favors use of these organs to expedite transplant over the risk of HBV transmission, particularly with the efficacy and availability of prophylactic antiviral agents directed against hepatitis (Figure 5.8). No known cases of surface antigen positive donors being used for liver transplants occurred between 2005 and 2009 (Figure 5.9).

Only 3.0% of deceased liver donors were reported as HCV positive between 2005 and 2009 (Figure 5.10). Most of these organs were transplanted into HCV-positive recipients, as expected, but this reflected only 2.5% of all deceased liver donor transplants. Interestingly, 0.1% of all deceased donor transplants involved transplanting an HCV-positive donor liver into an HCV-negative recipient. The latter mismatches presumably occurred in the scenario of the urgent requirement for a donor liver in the setting of fulminant failure.

In 2005–2009, 0.5% of recipients of deceased donor livers and 0.3% of recipients of living donor livers were serologically positive for human immunodeficiency virus (HIV) (Figure 5.11). This number will likely increase in the next decade, given the success of antiretroviral therapy against HIV and the high rate of HBV and HCV co-infection (> 30%) in this population. Of note, no HIV-positive donors were reported during this time period.

LI6.1   Early (reported w/i 6 wks of tx) graft failure among adult liver transplant recipients

LI6.2   Graft failure among adult liver transplant recipients: deceased donor

LI6.3   Graft failure among adult liver transplant recipients: living donor

LI6.4   Half-lives: adult dc'd donor liver tx recipients surviving with a funct. liver at least one year


outcomes

The ultimate goal of liver transplant is to prolong survival and improve quality of life. Over the past 2 to 3 decades, the outcome has improved substantially.

Regardless of donor type, incidence of graft failure reported within the first 6 weeks after transplant among adult recipients has declined in the past decade (Figure 6.1). Early graft failures in deceased donor recipients decreased from 6.9% in 1998 to 3.0% in 2009. This is remarkable because over this decade, more recipients had a high level of disease severity (in part as a result of the MELD-based organ allocation system) and more donors were less than ideal, including donors aged 50 years or older.

Figure 6.2 compares longer term liver transplant outcome by year of transplant and liver disease diagnosis. It is encouraging that transplant outcome is better in more recent years. This occurred across all diagnosis categories, suggesting that improvement in medical management may underlie this trend. Figure 6.3 demonstrates similar data for adult living donor recipients, in that survival numbers have in general improved over the past decade.

Overall, in deceased donor recipients who survived 1 year with a functioning graft, the expected half-life of the organ is 10 years (Figure 6.4). The half-life of living donor organs in adult recipients has been stable over the past 10 years, although numbers are relatively small.
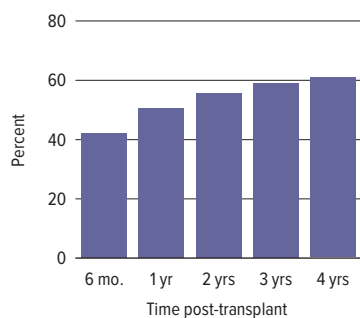
LI6.5 **Adult recipients alive & with a functioning liver transplant on June 30 of the year**
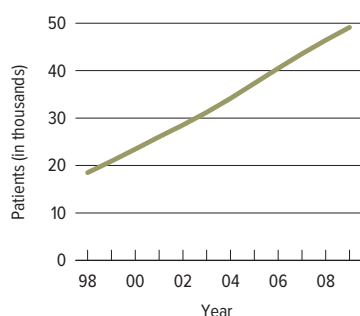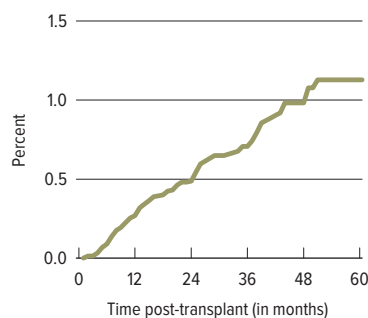

LI6.6 **Incidence of first acute rejection among adult pts receiving a liver tx in 2005–2009**
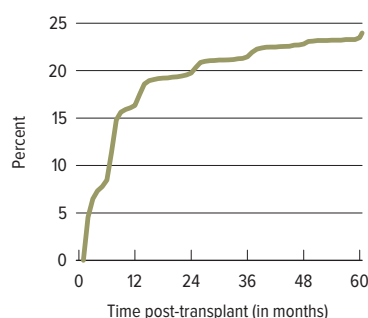
LI6.7 **Reported hospitalizations among adult pts receiving a liver transplant in 2005–2009**

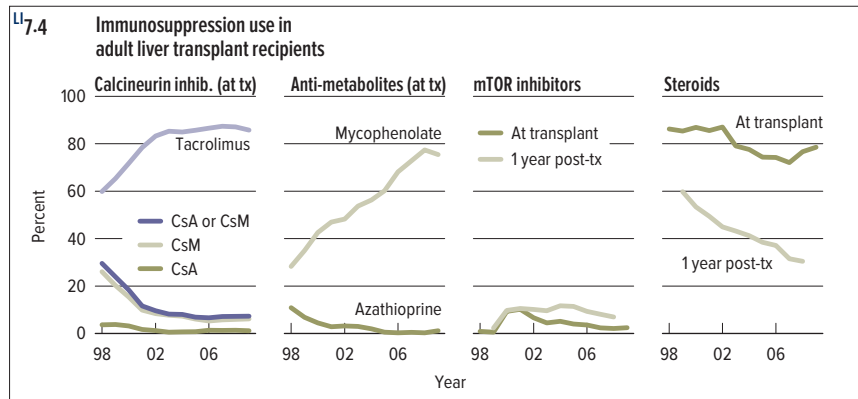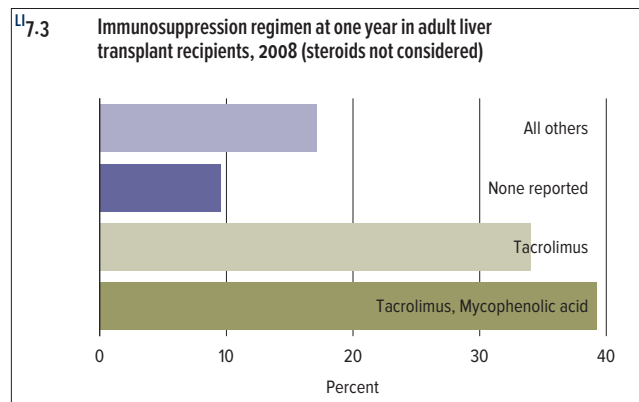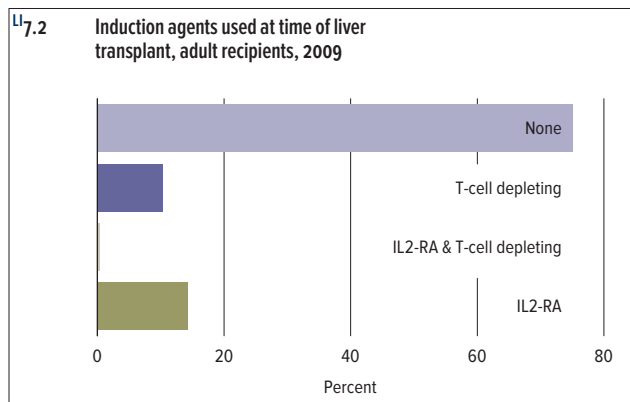**LI6.8** **Incidence of PTLD among adult patients receiving a liver transplant in 2005–2009**

These improvements in outcomes have resulted in a rapid increase in the number of recipients with a functioning liver graft. The number of American transplant recipients living with a liver graft as of June 2009 was nearly 50,000, more than double a decade earlier (Figure 6.5).

Incidence of acute rejection is highest in the first year post-transplant (Figure 6.6). Except for recipients with HCV infection, early acute cellular rejection has no detrimental impact on long-term survival. On the other hand, rejections that occur 12 to 60 months after transplant may represent future opportunities to further improve the outcome of liver transplant.

Given the severity of illness in patients undergoing liver transplant in recent years, re-hospitalization remains common, especially in the first few months (Figure 6.7).

Post-transplant lymphoproliferative disorder (PTLD) is a serious and potentially devastating complication that occurs in liver transplant recipients as a result of immunosuppression and/or EBV infection (Figure 6.8). Although cumulative incidence is not high (approximately 1% at 4 years), the incidence increased steadily through the first 5 years post-transplant.

OPTN :SRR
SCIENTIFIC REGISTRY OF
TRANSPLANT RECIPIENTS

LI7.1   Initial immunosuppression regimen in adult liver transplant recipients, 2009 (steroids not considered)

LI7.2   Induction agents used at time of liver transplant, adult recipients, 2009

LI7.3   Immunosuppression regimen at one year in adult liver transplant recipients, 2008 (steroids not considered)

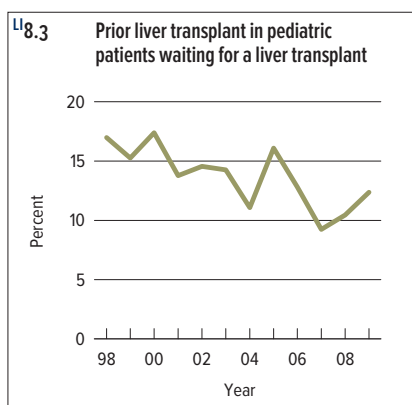**LI7.4   Immunosuppression use in adult liver transplant recipients**

immunosuppression

Immunosuppressive strategies based on tacrolimus and mycophenolate continue to be the dominant early regimen (Figures 7.1 and 7.3). In 2009, the alternative calcineurin inhibitor cyclosporine was used relatively infrequently (7.3%) compared with tacrolimus (85.8%) (Figure 7.4). Similarly, mycophenolate has almost completely replaced azathioprine as the antiproliferative agent of choice. Although 76.7% of patients were using a steroid at the time of transplant in 2008, only 30.5% remained on steroids 1 year after transplant (Figure 7.4). Mammalian target of rapamycin (mTOR) inhibitors were used infrequently, with only 2.5% of patients reported to be on this agent in 2009 (Figure 7.4).

The controlled rejection in liver transplant recipients is suggested by the relatively low use rates for interleukin-2 (IL2-RA) receptor inhibitors (14.3%) or T-cell depleting agents (10.3%) as induction agents (Figure 7.2). Over the past decade, the trend has been toward less use of corticosteroids. By 1 year post-transplant, many patients are weaned off corticosteroids (Figure 7.4).

LI 8.1 Pediatric patients waiting for a liver transplant

New patients

Patients on the list on 12.31 of the given year

Legend: Active, Inactive

Y-axis: Patients (0–1,000)
X-axis: Year (98, 00, 02, 04, 06, 08)

LI 8.2 Distribution of pediatric patients waiting for a liver transplant

Age

Legend: 11+, 6-10, 1-5, <1

Race

Legend: Other/unk., Asian, Hispanic, Black, White

Y-axis: Percent of patients (0–100)
X-axis: Year (98, 00, 02, 04, 06, 08)

LI 8.3 Prior liver transplant in pediatric patients waiting for a liver transplant

Y-axis: Percent (0–20)
X-axis: Year (98, 00, 02, 04, 06, 08)

LI 8.4 Liver transplant waiting list activity among pediatric patients

	2007	2008	2009
Listings at start of year	945	888	705
Listings added during year	822	832	784
Listings removed during year	879	1015	792
Listings at end of year	888	705	697
Removal reason			
Deceased donor transplant	558	566	538
Living donor transplant	68	69	50
Patient died	82	93	63
Patient refused transplant	1	1	2
Trans. to another center	19	23	22
Improved, tx not needed	95	179	88
Pt too sick to transplant	16	20	12
Other	40	64	17

LI 8.5 Liver tx waiting list status by month post-listing among new pediatric listings in 2006

Legend: Removed from list, Died, Transplanted (LD), Transplanted (DD), Still waiting

Y-axis: Percent (0–100)
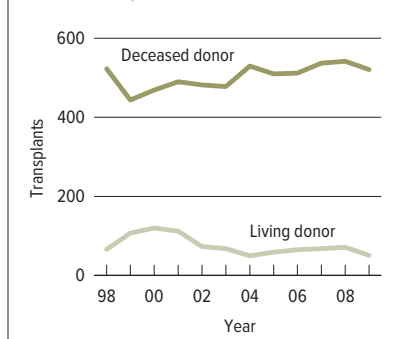X-axis: Months post-listing (6, 12, 18, 24, 30, 36)
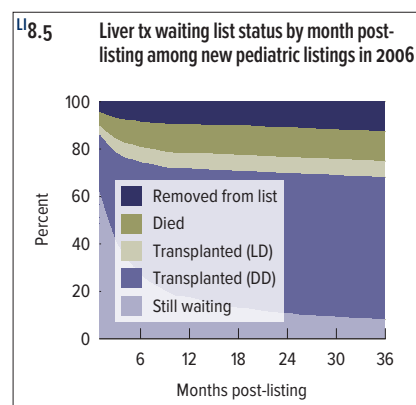
pediatric transplant

Since 1998, the number of children and adolescents new to the liver transplant waiting list has remained between 691 and 800 (Figure 8.1). Among prevalent patients on the waiting list for a liver transplant in 2009, almost equal numbers were active and inactive. The age distribution of patients on the waiting list has changed little; children aged 11 years or older account for 46% of patients (Figure 8.2). In 2009, 59% of patients on the waiting list were white, 16% were black, and 19% were Hispanic. In 2009, 12.4% of patients on the list were waiting for a re-transplant (Figure 8.3). Death as the reason for removal from the list remained stable in 2007–2009 at less than 10% (Figure 8.4). For the 2006 cohort of patients on the waiting list, after 3 years, 60.4% received a deceased donor transplant, 6.8% received a living donor transplant, 12.8% were removed from the list, 12.5% died, and 7.5% were still waiting (Figure 8.5).

OPTN SRTR SCIENTIFIC REGISTRY OF TRANSPLANT RECIPIENTS

LI8.6   Median months to liver transplant for wait-listed pedatric patients, by blood type

Legend: A, B, AB, O, All

X-axis: Year of listing (98, 00, 02, 04, 06, 08)
Y-axis: Median months to transplant
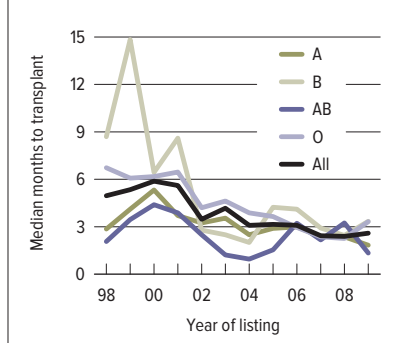
LI8.7   Pre-tx mortality rates among pediatric pts wait-listed for a liver transplant, by age

X-axis: Year (98, 00, 02, 04, 06, 08)
Y-axis: Deaths per 100 wait-list years
Labels: <6, Overall, 11-17, 6-10

LI8.8   Pediatric liver transplants

Labels: Deceased donor, Living donor
X-axis: Year (98, 00, 02, 04, 06, 08)
Y-axis: Transplants

LI8.9   Pediatric liver transplant rates, by age

Legend: 1-5, 6-10, 11+, Overall
Label: <1
X-axis: Year (98, 00, 02, 04, 06, 08)
Y-axis: Transplants per 100 pt years on WL

LI8.11   Pediatric liver transplants from living donors

Labels: Related, Distantly related, Unrelated directed, Other
X-axis: Year (98, 00, 02, 04, 06, 08)
Y-axis: Transplants
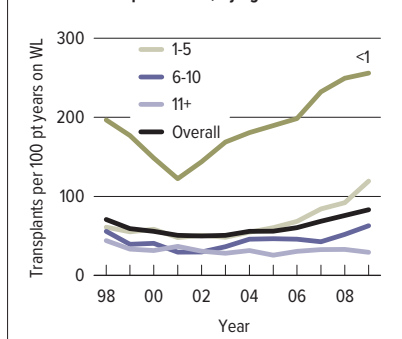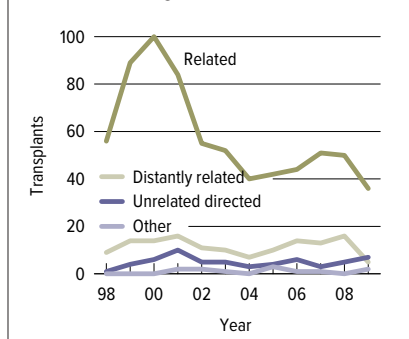
LI8.12   Use of DCD donors in pediatric liver transplant recipients

X-axis: Year (98, 00, 02, 04, 06, 08)
Y-axis: Percent

LI8.10   Characteristics of pediatric liver transplant recipients, 2007–2009

|	Level	N	%
Age	<1	542	30.3
	1-5	692	38.7
	6-10	232	13.0
	11-17	324	18.1
Sex	Female	891	49.8
	Male	899	50.2
Race	White	927	51.8
	Black	319	17.8
	Hispanic	387	21.6
	Asian	117	6.5
	Other/unk.	40	2.2
Primary cause of disease	Acute hep. necrosis	186	10.4
	HCV	7	0.4
	Cholestatic disease	809	45.2
	Metabolic liver dis.	184	10.3
	Malignancy	282	15.8
	All others	322	18.0
Transplant history	First transplant	1,617	90.3
	Subsequent	173	9.7
Blood type	A	629	35.1
	B	245	13.7
	AB	68	3.8
	O	848	47.4
Primary payer	Private	802	44.8
	Medicaid	789	44.1
	Other public	135	7.5
	Other	64	3.6
Time on wait list	<30 days	744	41.6
	31-60 days	294	16.4
	61-90 days	180	10.1
	3-<6 months	256	14.3
	6-<12 months	158	8.8
	1 - <2 years	110	6.1
	2- <3 years	17	0.9
	3+ years	25	1.4
	No listing date	6	0.3
Medical condition	Hospitalized: ICU	456	25.5
	Hosp.: not ICU	322	18.0
	Not hospitalized	1,012	56.5
Medical urgency status	1A	274	15.3
	1B	207	11.6
	MELD/PELD 30+	521	29.1
	MELD/PELD 15-29	532	29.7
	MELD/PELD <15	250	14.0
	Other/unknown	6	0.3
Procedure type	Whole liver	1,149	64.2
	Partial liver, remainder not tx	363	20.3
	Split liver	278	15.5
Donor type	Deceased	1,600	89.4
	Living	190	10.6
Previous ab. surg.	Yes	1,042	58.2
Portal vein throm.	Yes	65	3.6
Inc. tumor at tx	Yes	17	0.9
Sp. bact. perit. (SBP)	Yes	40	2.2
All patients		1,790	100

pediatric transplant

Among pediatric patients, the median number of months waiting for a liver-alone transplant for all blood types was 2.6 in 2009 (Figure 8.6). Pre-transplant mortality declined for patients wait-listed for a liver-alone transplant, from 14.4 deaths per 100 wait-list years in 1998 to 8.2 in 2008 (Figure 8.7). Patients on the waiting list aged younger than 6 years have the highest death rate, but this improved from 23.2 deaths per 100 wait-list years in 1998 to 14.9 in 2008. The number of deceased donor liver transplants has remained steady, while the number of living donor transplants decreased from a peak of 120 in 2000 to 51 in 2009 (Figure 8.8). The rate of pediatric liver transplant has increased since 2002 to the current rate of 83.1 transplants per 100 patient-years on the waiting list (Figure 8.9). Patients aged 1 to 5 years are the most common recipients. Whites accounted for more than half of recipients. The most common etiology of liver disease was cholestatic disease. Among children and adolescents who underwent transplant in 2007–2009, 58% were on the waiting list for 60 days or less. Fifteen percent of patients were status 1A at transplant, and 29% had a MELD/pediatric end-stage liver disease (PELD) score of 30 or higher. Sixty-four percent of patients received a whole liver.
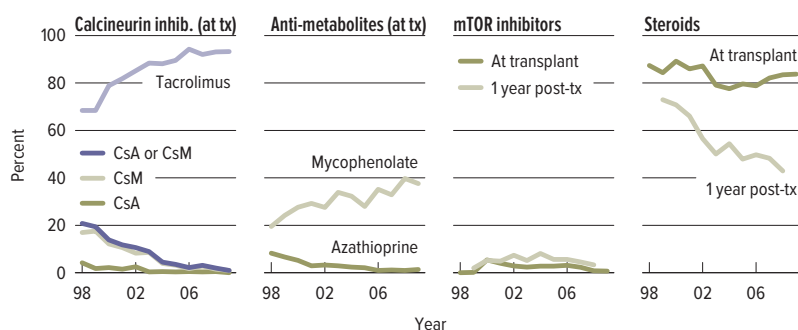
LI8.13 Insurance coverage among pediatric liver transplant recipients at time of transplant
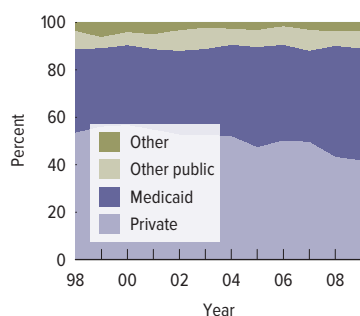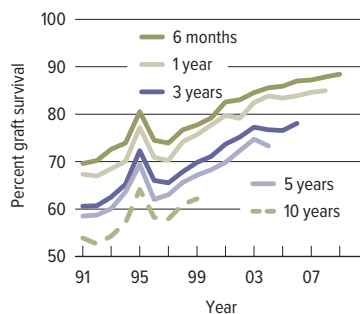

LI8.14 Pediatric liver transplant recipients with reported PTLD, 2000–2009
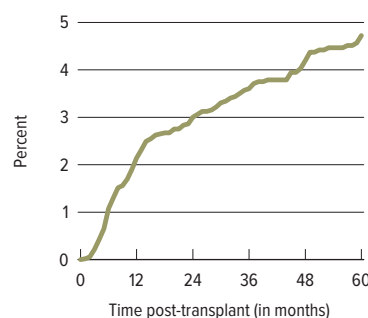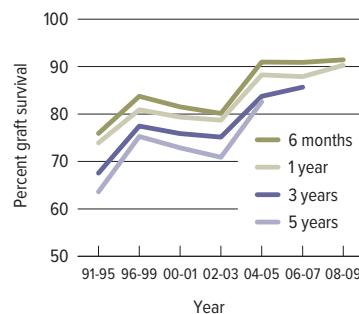

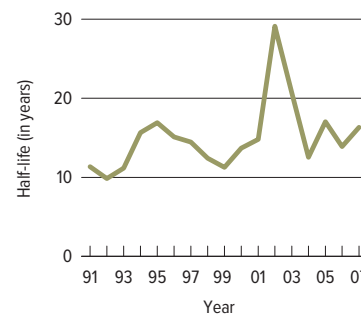LI8.15 Immunosuppression use among pediatric liver transplant recipients

LI8.16 Graft failure among pediatric liver transplant recipients: deceased donor

LI8.17 Graft failure among pediatric liver transplant recipients: living donor
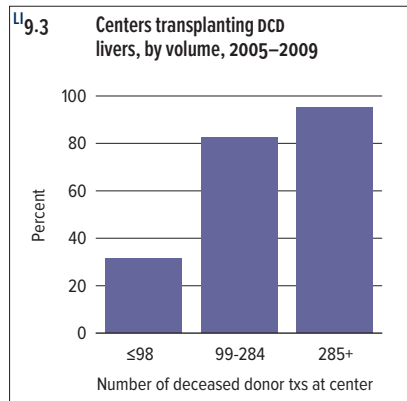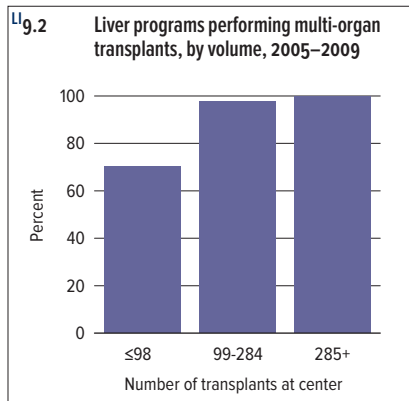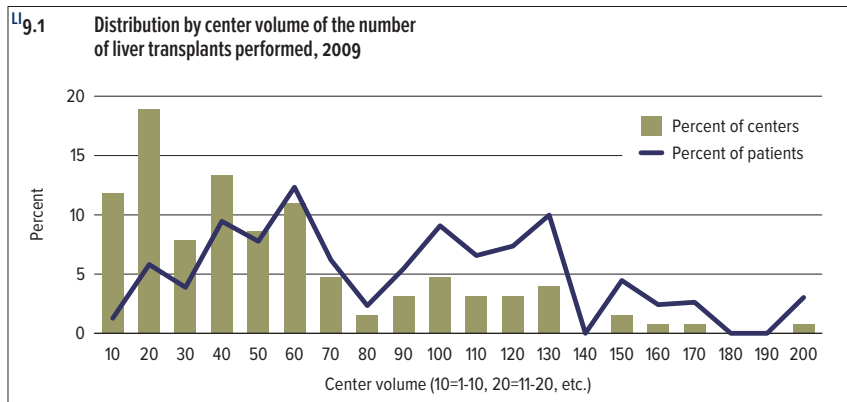

LI8.18 Half-lives for pediatric liver tx pts surviving with a functioning liver at least one year

Among living donor liver transplants, 72% were from related donors in 2009 (Figure 8.11). Only a small number of transplants were from DCD donors (Figure 8.12).

Private insurance coverage for liver transplant recipients declined from 56.5% in 2000 to 41.6% in 2009; Medicaid coverage increased from 33.6% to 47.2% (Figure 8.13). For children and adolescents who underwent transplant in 2000–2009, cumulative incidence of PTLD was 1.1% at 6 months, 2.1% at 1 year, 3.0% at 2 years, and 4.7% at 5 years after transplant (Figure 8.14). In 2009, 93.4% of patients received tacrolimus as part of the initial maintenance immunosuppressive medication regimen, and 37.6% received MMF (Figure 8.15). Among patients transplanted in 2008, 83.5% received steroids at the time of transplant; only 43.0% continued to use

steroids at 1 year post-transplant. Graft survival has continued to improve. Graft survival for deceased donor transplants in 2009 was 88.4% at 6 months; for transplants in 2008, 84.9% at 1 year; for transplants in 2006, 78.1% at 3 years; for transplants in 2004, 73.3% at 5 years; and for transplants in 1999, 62.2% at 10 years (Figure 8.16). Graft survival for living donor transplants in 2008–2009 was 91.4% at 6 months and 90.3% at 1 year; for transplants in 2006–2007, 85.7% at 3 years; and for transplants in 2004–2005, 82.6% at 5 years (Figure 8.17). The rate of late graft failure is traditionally measured by the graft half-life conditional on 1-year survival, defined as the time to when half of grafts have failed among those surviving a year. The graft half-life for deceased donor liver transplants in 2007 was 16.3 years (Figure 8.18).

LI9.1   **Distribution by center volume of the number of liver transplants performed, 2009**

LI9.2   **Liver programs performing multi-organ transplants, by volume, 2005–2009**

LI9.3   **Centers transplanting DCD livers, by volume, 2005–2009**

center characteristics

In 2009, 127 unique transplant centers performed liver transplants in the US. This included 58 centers that performed pediatric transplant. Figure 9.1 displays the distribution of the number of transplant procedures performed at each center. The minimum volume was 1 and the maximum was 192; the median was 40. Eighteen centers performed more than 100 transplants, and 13 centers performed fewer than 10 transplants for the year. Some of the low-volume centers were dedicated pediatric transplant centers. As expected, high-volume centers tend to be willing to accept more complicated cases, such as multi-organ or DCD organ transplants. Figure 9.2 displays tertiles of center volume. Essentially all centers with a volume of 99 or higher in 2005–2009 performed multi-organ transplants, most of which were simultaneous liver and kidney grafts. Similarly, Figure 9.3 shows that higher-volume centers performed more DCD transplants during the same period.

LI10.1   Centers performing adult liver transplants in 2009, within Donation Service Areas (DSAS)
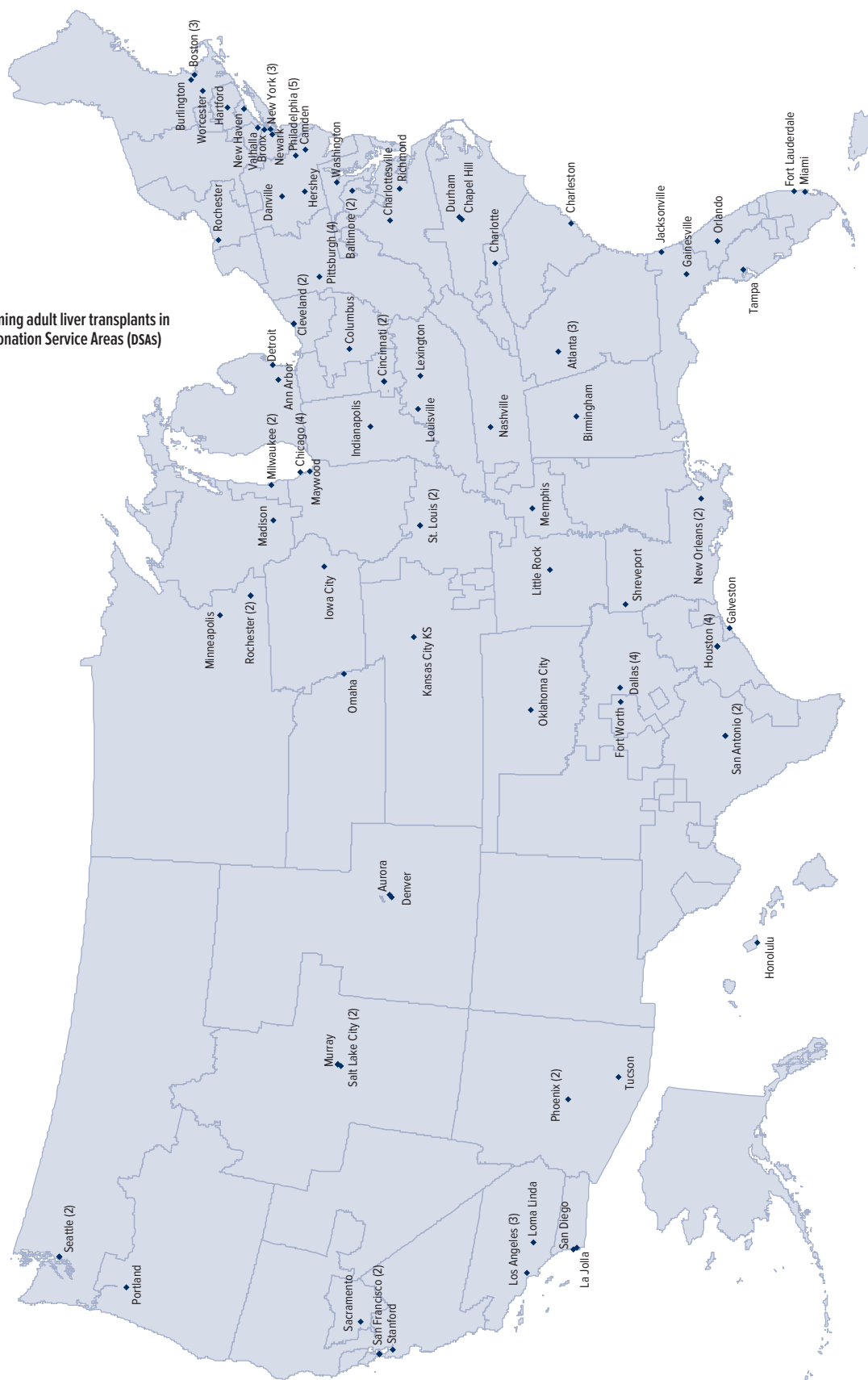
LI10.2   **Centers performing pediatric liver transplants in 2009, within Donation Service Areas (DSAs)**

- Seattle
- Boston
- Minneapolis
- Rochester
- Madison
- Milwaukee
- Ann Arbor
- Valhalla
- New Haven
- New York (2)
- Cleveland
- Philadelphia
- Wilmington
- Chicago (4)
- Pittsburgh
- Baltimore
- Washington
- Salt Lake City
- Iowa City
- Omaha
- Indianapolis
- Cincinnati
- Charlottesville
- Richmond
- San Francisco
- Palo Alto
- Stanford
- Aurora
- Kansas City
- St Louis (2)
- Durham
- Nashville
- Charlotte
- Los Angeles (2)
- Memphis
- Atlanta
- Charleston
- San Diego
- Tucson
- Birmingham
- Dallas
- Gainesville
- New Orleans
- Houston (2)
- San Antonio
- Miami

LI10.3   **Centers performing adult liver transplants in 2009, within OPTN regions**

- Seattle (2)
- Portland
- Burlington
- Boston (3)
- Worcester
- Hartford
- Rochester
- New Haven
- Minneapolis
- Valhalla
- Bronx
- New York (3)
- Rochester (2)
- Madison
- Milwaukee (2)
- Detroit
- Danville
- Newark
- Philadelphia (5)
- Camden
- Chicago (4)
- Ann Arbor
- Cleveland (2)
- Maywood
- Hershey
- Murray
- Iowa City
- Pittsburgh (4)
- Washington
- Salt Lake City (2)
- Omaha
- Indianapolis
- Columbus
- Baltimore (2)
- Sacramento
- Aurora
- Cincinnati (2)
- Charlottesville
- San Francisco (2)
- Denver
- Richmond
- Stanford
- Kansas City KS
- St. Louis (2)
- Louisville
- Lexington
- Durham
- Chapel Hill
- Los Angeles (3)
- Nashville
- Charlotte
- Loma Linda
- San Diego
- Phoenix (2)
- Oklahoma City
- Little Rock
- Memphis
- Charleston
- La Jolla
- Atlanta (3)
- Tucson
- Birmingham
- Fort Worth
- Dallas (4)
- Shreveport
- Jacksonville
- Gainesville
- Houston (4)
- New Orleans (2)
- Orlando
- San Antonio (2)
- Galveston
- Tampa
- Honolulu
- Fort Lauderdale
- Miami