

FIGURE 1. The unadjusted Kaplan-Meier 3-year survivals are shown for pediatric recipients (3-17 years) receiving livers from pediatric-aged donors (6-17 years) compared to adult donors (18-49 years) and adult recipients (18-49 years) receiving livers from pediatric aged donors (6-17 years). Results shown include retransplants, all UNOS statuses, and analyses for status 1 and status 2. Graphs on the left show the pediatric recipient data, graphs on the right show the adult recipient data.

exclude patients removed from the list because they became too ill to transplant. The percentage of patients dying was highest in the less than 1-year age range. Combining the <1 and 1- to 5-year groups, the percentage of patients dying is 10%, still higher than any other age range. From this data, the overall percent of children and adults dying in 1998 on the liver list was almost identical, 7.4%, the children (115 of 1541) and 7.3% adults (1202 of 16,442)

We also analyzed the probability of death on the waiting list, divided by status at time of listing and adjusted for race, ABO match, and repeat listing. For adult and pediatric liver recipients added to the waiting list between 1/1/95 and 12/31/97, four possible events could occur: 1) the patient was removed from the waiting list for reasons other than death or transplant, 2) the patient continued to wait, 3) the patient received a cadaveric organ, (living related transplants excluded, reduced and split grafts included), 4) the patient died before transplantation. Patients removed from the list because they were too ill to receive a transplant were counted as pretransplant deaths. Table 4 shows the estimates for the probability of these four possible outcomes in the first 6 months after listing for patients added to the list between 1/1/95 and 12/31/97. Both adult and pediatric patients at status 1 and 3 had similar probabilities of dying on the list. A total of 31% of adults and 27% of children initially listed in status 1, died waiting. In status 2, pediatric patients had a lower probability of dying but a longer waiting time compared to adults. A total of 25.7% of adults at status 2 died compared with 12.4% of children, whereas 14.5% of adults originally listed were still waiting at the end of 6 months compared to 23.7% of children at status 2. In the second 6 months after listing the probability for all four outcomes was similar between adults and children (data not shown).

*Kaplan-Meier patient and graft survivals: effect of donor age on outcome of pediatric and adult liver recipients.* Our first analysis attempted to answer this question by subdividing donor and recipient ages into several age ranges. However, the numbers in each subgroup became too small to allow for a meaningful statistical analysis. It was decided to eliminate several subdivisions of age ranges as well as extremes of donor and recipient age that might bias the results. Therefore, for the first analysis, the 0-5 age range for donors and the 0-2 age range for recipients was eliminated and the 3- to 5-year and 6- to 17-year age range for recipients was combined into one group, i.e., 3-17 years. It was also reasoned that pediatric recipients less than 3 years generally received whole organs from similar age donors based on size considerations. The upper limit of donor and recipient age was set at less than 50 years to exclude the possible negative effects of older donors and recipients. Figure 1, shows the unadjusted Kaplan-Meier 3-year graft survivals for pediatric recipients (3-17 years) receiving livers from pediatric-aged donors (6-17 years) compared to adult donors (18-49 years), and adult recipients receiving livers from pediatric aged donors. Results shown include retransplants, all UNOS statuses and a further analysis for status 1 and status 2. Excluded are reduced, split or living donor transplants. Pediatric recipients receiving livers from younger donors had a significantly improved graft survival, 81% compared with

TABLE 5. The odds of graft survival compared for adult and pediatric donors and recipient: whole grafts only

Recip age (yr)	Donor age (yr)	Num txd	Time points					
			3 Mo post-Tx		1-Yr post-Tx		3 Yr post-Tx	
			Odds ratio	P	Odds ratio	P	Odds ratio	P
3-17	6-17	496	0.62	0.02	0.50	<0.01	0.58	0.03
3-17	18-49	362	1.00	Ref.	1.00	Ref.	1.00	Ref.
18-49	6-17	1699	0.82	0.20	0.77	0.07	0.84	0.36
18-49	18-49	5879	0.78	0.08	0.77	.05	0.84	0.26

TABLE 6. Transplants performed 4/1/94-12/31/97, numbers of whole, reduced, split, and living donors by year 1994-1997

Yr	Type of transplant				Total
	Whole	Reduced	Split	Live	
1994	2669	108	26	45	2848
1995	3771	87	21	45	3924
1996	3865	84	62	46	4057
1997	3935	79	84	60	4158
Total	14240	358	193	196	14987

TABLE 7. Numbers of whole, reduced, split and living donors by age of recipient: 1994-1997

Age	Type of transplant				Total
	Whole	Reduced	Split	Live	
<1	254	131	39	106	530
1-2	304	102	35	47	488
3-5	192	42	13	15	262
6-10	223	35	13	14	285
11-17	375	21	13	7	416
18+	12892	27	80	7	13006
Total	14240	358	193	196	14987

63%,  $P < 0.001$ . In contrast, adult recipients had similar graft survivals irrespective of donor age. These differences remained significant when status at time of listing was considered.

**Multivariate analyses: effect of donor age or outcome of pediatric and adult liver recipients.** The Kaplan-Meier survival curves were unadjusted for risk. Therefore a further multivariate regression analysis was performed to determine if placing younger donor livers into younger recipients reduced the odds of graft failure. As before, this analysis excluded living related donors and split and reduced grafts. Donor and recipient risk factors controlled for were: donor and recipient race, donor cause of death, recipient diagnosis at transplant, medical condition (UNOS status) at transplant, cold ischemia time, ABO match, donor creatinine level, and year of transplant. The odds of graft failure at three months, 1 and 3 years posttransplant were determined (Table 5). At all three time points, the odds of graft failure were significantly less if pediatric recipients (3-17 years) received livers from younger donors (6-17 years). In contrast the odds of graft failure at each time point for adult recipients were similar whether or not the donor was younger or older.

The same multivariate regression analysis was repeated but now applied to all pediatric and adult recipients, with no age exclusions and inclusive of split and reduced grafts. Table 6 shows the number of reduced and split organ transplants performed during the period of this analysis, and

Table 7 the type of transplant according to age. During this time period 66 pediatric-aged donors were split, of which 24 segments were placed in adults.

The results of the unrestricted analysis (Table 8) remained very similar to the restricted analysis: pediatric patients have significantly reduced odds of graft failure if receiving a graft from a pediatric-aged donor whereas the age of the donor had little impact on the odds of graft failure to adult recipients.

An expected outcome of a policy that would direct more livers from pediatric donors to pediatric recipients would be an increased number of relatively large organs being directed to smaller recipients. This would encourage split liver transplantation whereby two recipients benefit from one organ. As well, reduced size transplantation, where part of the liver is discarded, might also occur. Therefore, we investigated the graft survivals of reduced and split size livers. For the time period 4/1/94-12/31/97 the Kaplan-Meier 3-year graft survival estimates for pediatric recipients of primary liver transplants subdivided by the type of organ received are shown (Fig. 2). It can be seen that reduced size grafts had a significantly lower 3-year graft survival compared to all other graft types. In comparison, split liver grafts had an overall 70% 3-year graft survival, not significantly different from either whole or living donor grafts. We were also interested in whether a split liver from a pediatric donor had a different patient and graft survival compared to that from an adult donor. Although the numbers were small, Kaplan-Meier three year adjusted patient survivals for split livers were not different if the liver was from an adult donor ( $n=51$ , patient survival 87%) or a pediatric donor ( $n=32$ , patient survival 89%). However, in comparison, the 3-year Kaplan-Meier graft survival was worse if the split liver was from an adult donor, 62%, as compared to a pediatric donor, 83%.

For all the above analyses of graft survivals, patient survivals were also examined (data not shown), and similar results were observed. Because of the complexity of the analyses derived from data accrued over several years, we did attempt to detect any possible center effects.

**UNOS liver allocation model (UJAM) results.** UJAM was used to investigate whether the proposal to allocate livers from pediatric donors preferentially to pediatric recipients, within urgency status and geographic areas, would have a detrimental impact on adult patients waiting on the list. In particular we believed it was important to investigate whether the number of adults dying either pretransplant or posttransplant would be effected by the proposed new policy. The proposed allocation sequence used in the model is shown in Table 9.

Two models were developed; the first defined a pediatric

TABLE 8. Odds of graft survival compared for pediatric and adult aged donors and recipients; including reduced and split grafts

Recip age (yr)	Donor age (yr)	Num tx'd	Time points					
			3 Mo post-Tx		1 Yr post-Tx		3 Yr post-Tx	
			Odds ratio	P	Odds ratio	P	Odds ratio	P
0-17	0-17	1786	0.66	<0.01	0.62	<0.01	0.65	<0.01
0-17	18+	882	1.00	Ref.	1.00	Ref.	1.00	Ref.
18+	0-17	3225	0.62	<0.01	0.84	0.29	1.06	0.75
18+	18+	15300	0.66	<0.01	0.86	0.33	1.06	0.75

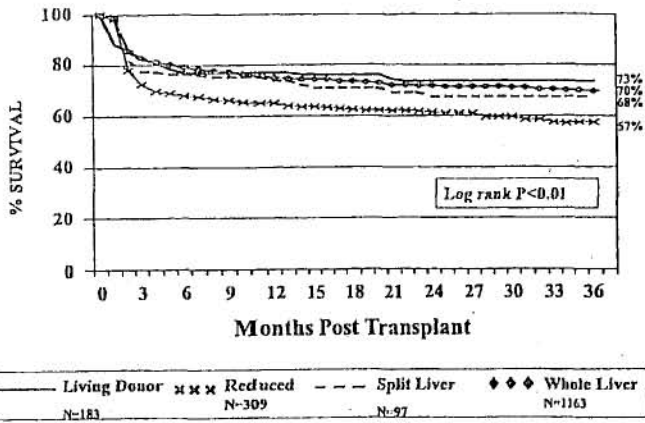


FIGURE 2. The Kaplan-Meier 3-year graft survivals are shown for pediatric recipients of primary liver transplants subdivided by type of organ received.

donor as <18 years, and the second defined a pediatric donor as <18 years and less than a specified weight range. Three weight ranges were investigated, <40, <45, and <50 kg. The second model was developed in response to concerns that small adult recipients might be disadvantaged by the proposed pediatric definition of <18 years without weight restrictions.

Neither model takes into account the data presented above which shows improved patient and graft survivals for children receiving livers from pediatric aged donors. Further, split liver transplant and outcomes were not considered.

Table 10 summarizes the most relevant data from the simulations comparing the current allocation policy to the four proposed pediatric donor definitions: 1) <18 years, 2) <18 years and <40 kg, 3) <18 years and <45 kg, 4) <18 years and <50 kg (Table 11).

The data presented in Table 12 represents the average of each measure for 5 years (1999–2003) and over four simulation runs. The data address: 1) the number of pediatric and adult patients transplanted by age (pediatric recipients divided 0 to 5 years, 6–11 years, 11–17 years) and by status, 2) median waiting time by status, and 3) probability of pre-transplant death within 6 months of listing. The number of repeat transplants, and patient life years under the different proposals is not shown because the model did not account for expected improvements in pediatric graft survival should pediatric recipients receive livers from pediatric aged donors.

In all of the proposed policies, slightly more pediatric patients were transplanted over the 5-year period. The increase over the current policy ranged from 151 over 5 years (30 per year) for the most restrictive policy with donors defined as <18 years and <40 kg, to 297 over 5 years (59 per year) the least restrictive policy defining a pediatric donor as <18 years. Consequently, each of the policies resulted in a corresponding decrease in the number of adult patients receiving transplants.

Investigating the change in the number of transplants by age and status showed that among pediatric patients fewer were transplanted in status 1 under the proposed policies. This is because more pediatric patients were transplanted at less urgent statuses under the proposed policies. In contrast about the same or slightly higher numbers of adult patients

TABLE 9. Proposed order of allocation for a liver from a pediatric donor

1. Local
  - Pediatric status 1
  - Adult status 1
2. Regional
  - Pediatric status 1
  - Adult status 1
3. Local
  - Adult status 2a
  - Pediatric status 2b
  - Adult status 2b
  - Pediatric status 3
  - Adult status 3
4. Regional
  - Adult status 2a
  - Pediatric status 2b
5. National
  - Pediatric status 1
  - Adult status 1
  - Adult status 2a
  - Adult status 2b
  - Pediatric status 3
  - Adult status 3

were transplanted in status 1 because there were fewer pediatric patients competing for organs while in status 1. This is reflected in the increased numbers of children transplanted at status 2B. This was most evident in the policy defining pediatric donors <18 years without weight restriction. The increase in pediatric status 2B patients transplanted was 304 over 5 years compared to current policies. This benefit was diluted as the more restrictive pediatric donor definitions by weight were applied. In contrast, the more stable pediatric patients at status 3 showed only a modest increase, approximately 4–10 more children per year. In examining the data by status for adults, it is also important to note that all of the proposed policies slightly increased the number of adult patients transplanted at status 2A. This effect ranged among 18 to 78 patients over 5 years.

Of all pediatric donor livers, the percent that went into adults was 68.8% under the current policy. Under the least restrictive proposed policy the percentage of adults still receiving pediatric donors was 59.2%, and ranged between 63–64% under the other pediatric donor proposals divided by weight. There was also a decrease in the percentage of adult livers that were transplanted into pediatric patients. This was most pronounced, 3.9%, in the policy defining pediatric donors <18 years, without weight restriction. Only a negligible increase in the percentage of adult livers that were transplanted into adults was demonstrated.

The percentage of local, regional, and national transplants was essentially unchanged as was the average and median distance the organ traveled. The percentage of organs that traveled greater than 1000 miles increased from 1.6 to 1.7%.

Deaths pretransplant and posttransplant and total deaths for the proposed policies was examined and no significant changes were noted with all four policies proposed as compared to the current policy.

When the probability of pre transplant death within 6 months of listing was analyzed, there were minimal differences, none of which was statistically significant, between