

# Liver Transplantation for Status 1: The Consequences of Good Intentions

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Status 1 is the listing category reserved for patients awaiting liver transplantation who are at risk of imminent death. This high allocation priority was intended to benefit patients with acute liver failure and children with severe chronic liver failure. However, the status 1 criteria were not well defined. The aims of this study, which used the Organ Procurement and Transplantation Network/Scientific Registry of Transplant Recipients database for patients wait-listed between February 27, 2002, and September 30, 2003, were to determine the indication and numbers of children and adults at status 1 (including regional variations); examine death rates on the waiting list for children at vs. not at status 1; and examine time to death, transplant, or removal from the waiting list for both pediatric and adult status 1 candidates. During the study period, 40.3% of children and 6.1% of adults were transplanted at status 1. The indication was acute liver failure in 52.1% of adults and 31% of children. Among status 1 transplants, Regional Review Board exceptions were granted for 16.7% of children and 10.1% of adults. Death rates for children listed at status 1 by exception per patient-year at risk were substantially lower (0.51) than those of children with acute liver failure (4.06) or with chronic liver disease and Pediatric End-Stage Liver Disease score  $\geq 25$  (4.63). The percentage of adults who died while on the waiting list within 90 days of listing was more than twice that of children, whereas the percentages transplanted were similar. Patients listed and transplanted at status 1 were a heterogeneous population with an overrepresentation of children with varying degrees of chronic liver disease and other exceptions, and an associated wide variation in waiting list mortality. Recent changes in status 1 criteria provide stricter definitions, particularly for children, including the removal of the "by exception" category, with the intent that all candidates listed at status 1 share a similar mortality risk. *Liver Transpl* 13:699-707, 2007. © 2007 AASLD.

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The intent of the status 1 listing designation for patients awaiting liver transplantation is to efficiently and rapidly direct donor organs to patients at risk of imminent death. Although this concept is well accepted and supported by liver transplant professionals familiar with these patients' rapid progression to death, defining this patient population and judging what constitutes "imminent" death has been more difficult. If defined by

diagnosis, the patients most obviously eligible for such a designation are those with acute liver failure, classically defined<sup>1</sup> as no preexisting liver disease with the acute onset of liver failure within 8 weeks. However, also eligible for this category are patients with liver failure after liver transplantation that is the result of the complications of primary nonfunction (PNF) or hepatic artery thrombosis (HAT), as well as patients with

**Abbreviations:** HAT, hepatic artery thrombosis; PNF, primary nonfunction; OPTN, Organ Procurement and Transplantation Network; RRB, Regional Review Board; PELD, Pediatric End-Stage Liver Disease; MELD, Model for End-Stage Liver Disease; ICU, intensive care unit.

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This study was approved by the U.S. Health Resources and Services Administration (HRSA) Scientific Registry of Transplant Recipients project officer. HRSA has determined that this study satisfies the criteria for the IRB exemption described in the "Public Benefit and Service Program" provisions of 45 CFR 46.101(b) (5) and HRSA Circular 03.

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acute decompensated Wilson disease. More difficult to categorize are those patients with chronic liver disease, irrespective of diagnosis, who are in the rapidly terminal phase of their disease and have a life expectancy of only a few days.

In attempts to incorporate prioritization for such gravely ill patients into liver allocation algorithms, Organ Procurement and Transplantation Network (OPTN) policies for these most urgent patients have evolved through several iterations over the years. In 1987, "UNOS-Stat" identified any candidate expected to live <24 hours. In 1991, the designation of status 1 was further refined to include adults or children in an intensive care unit (ICU) with either acute or chronic liver disease and with a life expectancy of <7 days. However, in response to the growing numbers of severely decompensated adults with chronic liver disease and the increasingly evident donor organ shortage, a less urgent category (status 2A) was established in 1997 for adults with chronic liver disease. Children with chronic liver disease could still be listed at status 1. With the establishment of the Regional Review Board (RRB) process in 1997, any patients with approval of the RRB could be listed as status 1, including patients whose liver function was relatively well preserved but in whom the extrahepatic manifestations of their disease were life-threatening. For children with metabolic diseases such as Crigler-Najjar syndrome and urea cycle enzyme deficiencies, this exception was considered important because it allowed timely transplantation before devastating central nervous injury occurred.

A major change in the philosophy of liver allocation occurred as a result of the Institute of Medicine's report in 1999,<sup>2</sup> and as a consequence, the so-called Final Rule, issued by the U.S. Health Resources and Services Administration in 1999, required that organs be allocated to patients on the liver waiting list as ranked by the severity of their disease, irrespective of time spent waiting for an organ. This mandate resulted in the development of severity of illness scores for both children and adults with chronic liver disease: the Pediatric End-Stage Liver Disease (PELD) score for children<sup>3</sup> and the Model for End-Stage Liver Disease (MELD) score for adults.<sup>4,5</sup> These scores, which were developed by using statistical models that were based on large national databases, predicted the risk of death while on the waiting list. Each candidate's position on the waiting list was determined by his or her MELD or PELD score. All patients with chronic liver disease would therefore be ranked by MELD or PELD score, but review of individual cases for assignment of an exception score by the RRB was preserved. As a consequence, status 2A for adults with severe chronic liver disease was abolished. However, children (<18 years of age) with severely decompensated chronic liver disease could be listed at status 1, provided they were located in an ICU and had at least one of the following conditions: ventilator dependence, upper gastrointestinal bleeding, hepatorenal syndrome, stage 3 or 4 encephalopathy, refractory ascites, or biliary sepsis requiring pressor support. The status 1 provision for pediatric candidates was in-

tended to address the high waiting list mortality rate among children, particularly those younger than 2 years of age. This high death rate arose not only from the fragility of very small children, but from the difficulty in finding small donor livers for small recipients in a timely fashion.

The MELD- and PELD-based liver allocation system was initiated on February 27, 2002, and included the following status 1 definitions: adults and children with acute liver failure including HAT, PNF, and decompensated Wilson disease; children with chronic liver disease as defined by specific criteria (adults with chronic liver disease were excluded); and adults and children with exceptional conditions (not defined) with retrospective RRB approval.

To understand the effect of the current status 1 definition on liver transplantation in the MELD and PELD era, we performed 3 analyses. First, the number of patients transplanted at status 1 was compared with those transplanted at their MELD or PELD score. The subcategories of status, regional differences, and donor organ type were also examined. Second, we assessed the waiting list death rates for status 1 and non-status 1 children. Third, we assessed the time to death, transplant, or removal from the waiting list for both pediatric and adult status 1 candidates.

## MATERIALS AND METHODS

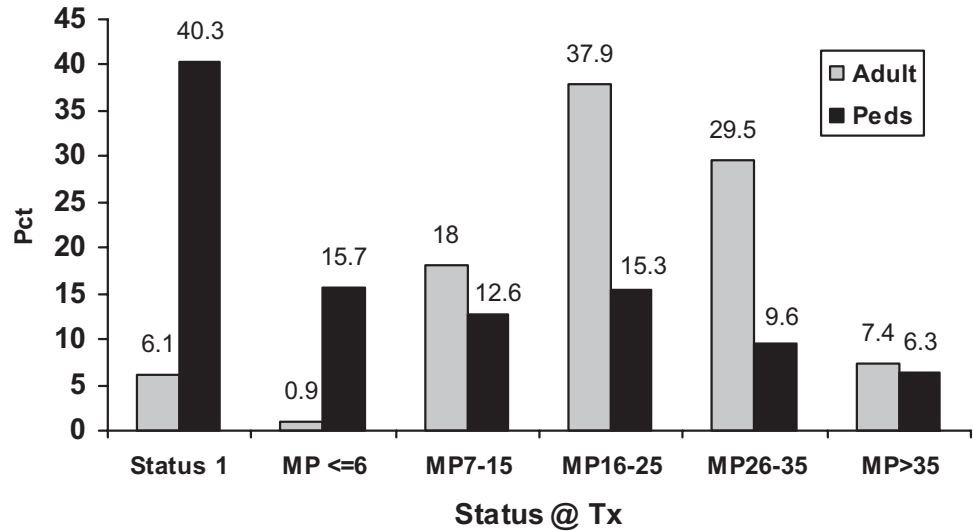
### Data Sources

The data used in this study were obtained from the OPTN/Scientific Registry of Transplant Recipients database, which contains information on all wait-listed candidates and transplant recipients in the United States. Data on mortality were supplemented with information from the Social Security Death Master File.<sup>6</sup> We examined characteristics of donors and recipients of liver transplants that took place between February 27, 2002, and September 30, 2003. The analyses of adult and pediatric candidates on the liver waiting list included candidates placed on the waiting list during this period, with follow-up extending through December 31, 2003. Candidates waiting for a combined liver-intestine transplant were excluded.

### Analytic Methods

Status 1 liver candidates and recipients were divided into 4 main indications for status 1 designation: those with acute liver failure, those with PNF or HAT, those with chronic liver disease (meeting criteria), and those at status 1 by exception (granted by an RRB). The percentages of children and adults transplanted within the 4 subgroups of status 1 were examined both nationally and by region. Pediatric status 1 candidates with chronic liver disease were further subdivided into 2 groups by using their calculated PELD score with a threshold of 25.

For candidates on the liver waiting list, we examined rates of removal from the waiting list over the first 90 days after being made status 1 for reasons of death,



**Figure 1. Adult and pediatric liver recipients by MELD or PELD score and status 1.**

transplantation, recovery, or becoming too sick to transplant. Removal rates were assessed for children and adults in each status 1 subcategory.

For the third analysis, mortality rates on the waiting list for children were compared among 5 subgroups of status 1. Candidates were followed from the time at which they first became active as status 1 until death, transplantation, or the end of the study, whichever was earliest. In order to avoid missing deaths occurring shortly after removal from the waiting list or a switch to inactive status, candidates were followed for 30 days after moving to inactive status or removal from the waiting list for reason other than transplantation. Death rates were calculated as the number of deaths divided by the total number of patient-years spent in that category.

## RESULTS

During the study period, 365 (40.3%) of 906 pediatric liver transplant recipients were status 1 at the time of transplant, compared with 476 (6.1%) of 7800 adult recipients. Among pediatric status 1 recipients, 31.0% were transplanted for acute liver failure, 13.4% for PNF or HAT, 31% for chronic liver disease (meeting standard criteria), and 16.7% by exception. In contrast, 52.1% of adults transplanted at status 1 had acute liver failure, 33.2% had PNF or HAT, and 10.1% had exceptions. One child and 11 adults were transplanted for decompensated Wilson disease. Figure 1 shows the percentages of children and adults transplanted by MELD or PELD score and at status 1 during the study period.

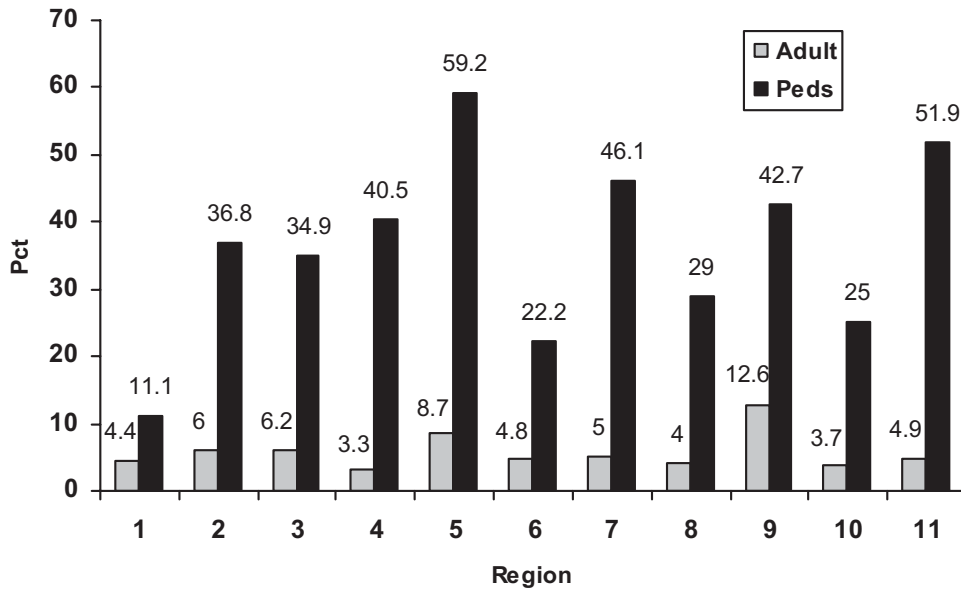
Regional differences in the percentages of children and adults transplanted at status 1 are shown in Figure 2. In the 9 regions where an average of >20 pediatric liver transplants per year were performed, the percentage of children transplanted at status 1 ranged 11.1 to 59.2% (median, 36.8%). The percentage of adults transplanted at status 1 over all 11 regions ranged 3.3 to 12.6% (median, 4.9%).

Table 1 shows the mean calculated MELD and PELD

scores for adults and children transplanted at status 1 for those with acute liver failure, PNF or HAT, chronic liver disease meeting criteria, and "by exception." The mean PELD score for the combined group of children listed at status 1 for acute liver failure and PNF or HAT was statistically significantly higher than for those status 1 children with chronic liver disease criteria (mean PELD 25.8 vs. 22.0, respectively;  $P = 0.02$ ) and for those children transplanted at status 1 by exception (mean PELD 13.4,  $P < 0.0001$ ). The mean PELD for pediatric status 1 recipients with chronic liver disease was also significantly higher than that of children transplanted at status 1 by exception ( $P < 0.001$ ).

## Death Rates on the Waiting List for Children Transplanted at Status 1

Table 2 shows the number of patient-years, number of deaths, death rate per year, median PELD score, and median days to death (among candidates who died) for each status 1 category. The highest death rates were seen for children with acute liver failure, PNF or HAT, and those with chronic liver disease whose PELD scores were at least 25. The death rate was substantially lower for children who were status 1 by exception. For comparison, Figure 3 shows death rates on the waiting list for all children listed during the same period at a PELD score. The death rate for children at status 1 by exception was comparable to that of children wait-listed with a PELD score of 22-26. The dropoff in the mortality risk at PELD scores  $\geq 35$  is explained by the movement of these children into the status 1 category. (When not censoring at movement to status 1, the death rate for PELD  $\geq 35$  is 2.66.) Among candidates who died, children with acute liver failure, PNF, or HAT died at a median of 4.5-5.5 days after listing, whereas children with chronic liver disease or those listed by exception died between 18 and 24 days after status 1 listing.



**Figure 2. Regional differences in liver transplantation at status 1.**

**TABLE 1. MELD or PELD Scores at Transplant Among Liver Recipients Listed at Status 1, February 27, 2002, to September 30, 2003**

Characteristic	Adult		Child	
	n	Mean	n	Mean
Acute disease	406	31.6	162	25.8*
Acute liver failure	248	34.5	113	27.2
PNF or HAT	158	27.1	49	22.7
Wilson disease	11	40.5	1	7.0
Chronic disease <sup>†</sup>			113	22.0 <sup>‡</sup>
By RRB exception	48	24.8	61	13.4

**Abbreviations:** MELD, Model for End-Stage Liver Disease; PELD, Pediatric End-Stage Liver Disease; PNF, primary nonfunction; HAT, hepatic artery thrombosis; RRB, Regional Review Board.

\**P* = 0.02 compared with mean PELD for recipients with chronic disease (22.0) at time of transplantation; *P* < 0.0001 compared with mean PELD for recipients with status 1 by RRB exception (13.4).

<sup>†</sup>Excluding hepatoblastoma (N = 11), urea cycle defects (N = 15), and cases where the reason for status 1 was not given (N = 13).

<sup>‡</sup>*P* < 0.001 compared with mean PELD for recipients with status 1 by RRB exception (13.4).

**Time to Removal From the Waiting List for Status 1 Children and Adults**

Status 1 liver-only candidates (adults and children) added to the liver waiting list were divided into the following subcategories: acute liver failure, PNF or HAT, RRB exception, MELD or PELD score ≥25, and MELD or PELD score <25. Events after being placed on the liver waiting list were compared among pediatric and adult status 1 subcategories. Table 3 lists the number and percentage of adults and children in each category. The percentage of adults transplanted for acute liver failure (54.2%) was considerably higher than the percentage for children (39.3%). In contrast, only 11.4% of adults were listed at status 1 by exception or for any reason other than acute liver failure or PNF or HAT, compared with 41.3% of children. In particular, the

second most common category for status 1 listing for children was the category of chronic liver disease with PELD score <25 (19.8%).

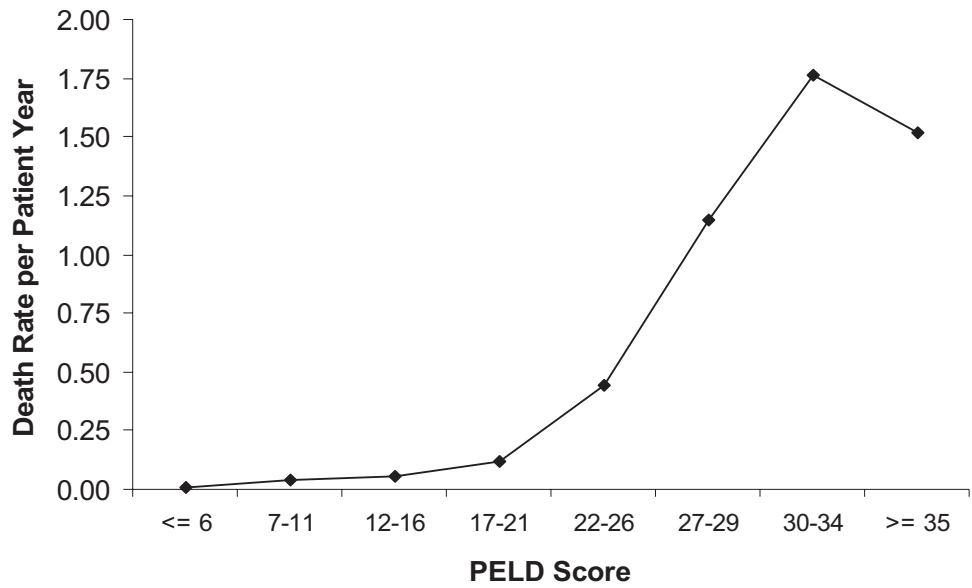
For patients in each status 1 category, we examined, from day 0—90 after listing, the number of patients transplanted (either at the same status as listed or at a different status), number of patients who died (at the same status, at a different status, or after removal from list), number of patients removed from the list before transplant (because of improvement, becoming too sick to transplant, or for any other reason), and number of patients remaining on the list (at the same status, at a different status, or becoming inactive on the list). A summary of these data is displayed graphically (Fig. 4) over the first 90 days after listing for the major outcome groups: patients who died, were transplanted, were re-

**TABLE 2. Waiting List Death Rates for Pediatric Status 1 Candidates by PELD Score and Status 1 Category**

Status 1 category	Patient-years at risk	No. of deaths	Death rate per patient-year at risk	Median calculated PELD score at status 1 listing	Median days from status 1 listing to death
Acute liver failure	5.9	24	4.06	29	5.5
PNF or HAT	3.0	12	4.04	23	4.5
Chronic disease: PELD ≥25	1.5	7	4.63	32	21.0
Chronic disease: PELD <25	4.1	10	2.42	8	15.5
By RRB exception*	3.9	2	0.51	8	24

**Abbreviations:** PELD, Pediatric End-Stage Liver Disease; PNF, primary nonfunction; HAT, hepatic artery thrombosis; RRB, Regional Review Board.

\*Excluding hepatoblastoma and urea cycle defects.



**Figure 3. Death rates for all children on the waiting list between February 27, 2002, and September 30, 2003.**

**TABLE 3. Status 1 Listings by Category Among Adults and Children, February 27, 2002, to September 30, 2003**

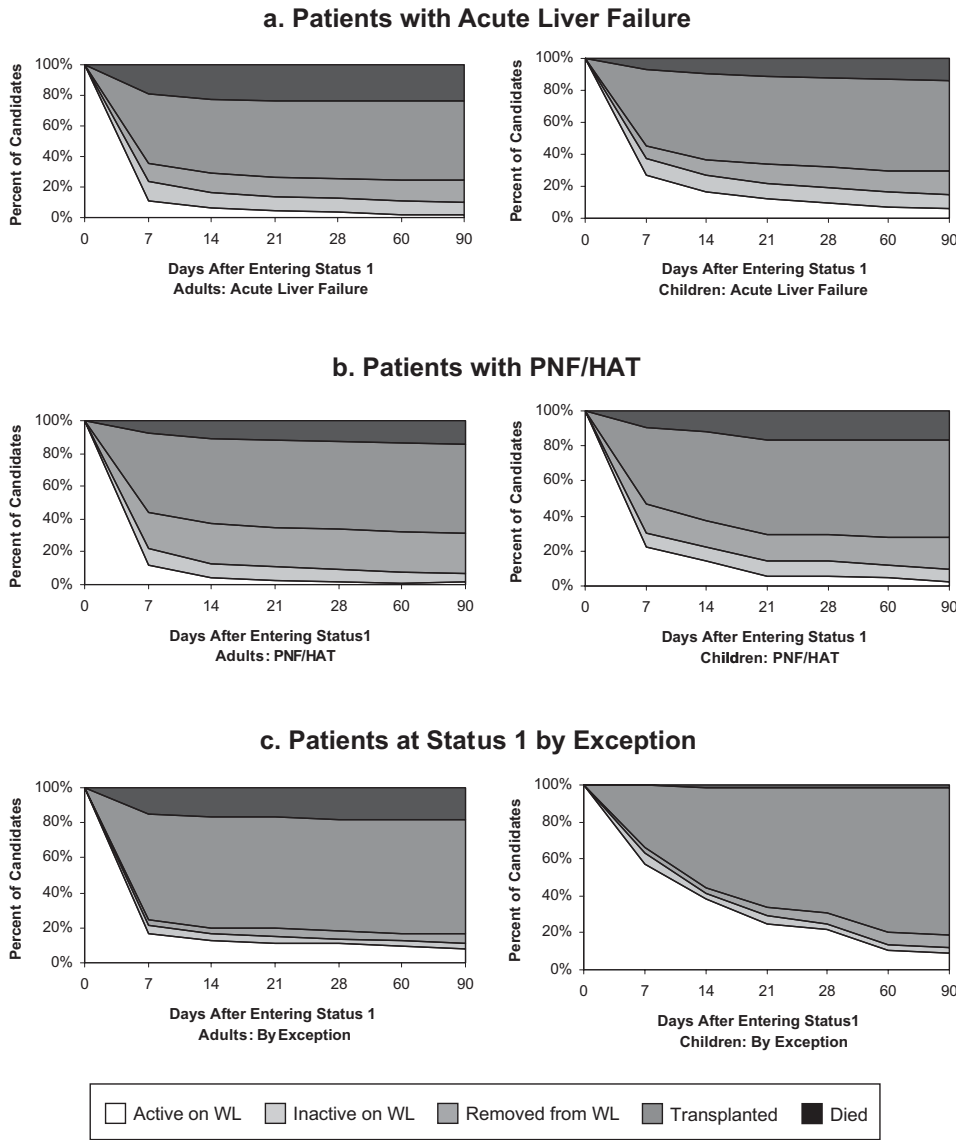
Age group	Acute failure, n (%)	PNF or HAT, n (%)	By RRB exception, n (%)	PELD or MELD ≥25, n (%)	PELD or MELD <25, n (%)
Adults (n = 878)	476 (54.2%)	302 (34.4%)	65 (7.4%)	27 (3.1%)	8 (0.9%)
Children (n = 486)	191 (39.3%)	86 (17.7%)	65 (13.4%)	48 (9.9%)	96 (19.8%)

**Abbreviations:** PNF, primary nonfunction; HAT, hepatic artery thrombosis; RRB, Regional Review Board; PELD, Pediatric End-Stage Liver Disease; MELD, Model for End-Stage Liver Disease.

moved from the list, made inactive on the list, or remained active on the list. Figure 4 shows the events over 90 days after listing for adults and children, comparing those with acute liver failure (Fig. 4a), PNF or HAT (Fig. 4b), and RRB exception (Fig. 4c).

These figures demonstrate that most removals from the waiting list occurred between 7 and 14 days after listing. Table 4 provides the actual numbers of patients and their outcome in status 1 or with change of status

on the waiting list 14 days after status 1 listing. For both adults and children with fulminant liver failure who were transplanted, almost all remained at status 1 until transplant. However, approximately half of both adults and children who died were at another status or had been removed from the waiting list. The death rates for children and adults listed at status 1 for fulminant liver failure were 4.06 and 7.59, respectively, per patient-year at risk.



**Figure 4. Events on the waiting list for first 90 days after listing: status 1 adults (left) and children (right).**

**TABLE 4. Events Within 14 Days of Status 1 Listing**

Event	Died (%)	Transplanted (%)	On list, active (%)	On list, removed or inactive (%)
<b>Fulminant</b>				
Adults (n = 476)	22.7	48.5	6.3	22.5
Children (n = 191)	9.9	53.4	16.8	19.9
<b>PNF or HAT</b>				
Adults (n = 302)	10.6	52.3	4.6	32.5
Children (n = 86)	11.6	51.2	14.0	23.3
By RRB exception, children (n = 65)	1.5	55.5	38.4	6.2
<b>PELD</b>				
≥25 (n = 48)	8.4	60.4	22.9	8.4
<25 (n = 96)	6.2	44.8	46.8	2.0

**Abbreviations:** PNF, primary nonfunction; HAT, hepatic artery thrombosis; RRB, Regional Review Board; PELD, Pediatric End-Stage Liver Disease.

## DISCUSSION

The intent of the status 1 category for liver transplant candidates was to give the highest priority to a select group of the sickest patients awaiting liver transplantation. This goal has been largely achieved for adult candidates: the status 1 criteria for adults remain restricted to the manifestations of acute liver failure, and a relatively small percentage of adults are transplanted at status 1. In comparison, children with chronic liver disease, meeting rather loosely defined criteria, have been eligible for status 1 or have been assigned status 1 through the exception process after RRB approval. As a result, 40.3% of all children transplanted over the time period of this study were status 1 at the time of transplant. This percentage is similar to the 48% reported in the pre-PELD era,<sup>7</sup> suggesting that pediatric transplant specialists gained little confidence that the PELD system would accurately prioritize the sickest children with chronic liver disease for transplantation.

Shneider et al.<sup>8</sup> and Salvalaggio et al.<sup>9</sup> reported that 53% and 52% of children, respectively, were not transplanted at their calculated PELD score. Additionally, the granting of pediatric exception cases was noted to be subject to wide regional variation.<sup>9</sup> The result is a large, heterogeneous population of children listed or subsequently upgraded to status 1, with a correspondingly wide range of probability of death while on the waiting list. This variation is clearly shown by our finding that the death rate for children at status 1 ranged 0.51 to 4.6 deaths per patient-year at risk. The inability to discriminate the risk of death within this diverse population of children listed at status 1 has meant that waiting time has driven the allocation of deceased donor livers within the status 1 pediatric candidate pool. Not only has this contravened the federal directive to prioritize candidates for transplantation on the basis of urgency,<sup>2</sup> but it has resulted in more children with less urgent need being transplanted ahead of children with acute liver failure. Additionally, some adolescent pediatric donor livers that were suitable for an adult with acute liver failure have been directed to children with chronic liver disease despite their having a much lower risk of death. Particularly relevant to the bypassing of adults with acute liver failure in favor of children with chronic liver disease is the observation in this study that twice as many adults as children died at status 1 (20% vs. 10%, respectively).

In the analysis of events on the waiting list over the first 90 days after listing at status 1, it is apparent that for both children and adults with acute liver failure or PNF or HAT, the majority of deaths and transplants occurred within 14 days, which is consistent with the original intent of the status 1 definition: directing donor livers to those thought to face death imminently. The most obvious difference in events on the list over the first 90 days is evident in the comparison of children listed at status 1 by RRB exception to children or adults with acute liver failure listed at status 1. For children listed at status 1 by exception, the percentage who died within 14 days was very small (1.5%) compared with the

percentages of children and adults with acute liver failure (9.9% and 22.6%, respectively). By 90 days, 80.0% of children listed at status 1 by exception received a transplant—a much higher proportion than seen for any other category of status 1, either adults or children. This result is explained by a lower overall risk of death on the waiting list for the status 1 by exception subgroup. This same subgroup also had the smallest percentage of children removed from the list for reasons other than death or transplant, and had the largest fraction of patients still active on the list 90 days after listing.

As a consequence of the results presented in these analyses, proposals to redesign eligibility criteria for status 1, for both adults and children, were made by the OPTN Liver and Intestinal Organ Transplantation and Pediatric Transplantation Committees. The intent of these changes was to restrict the status 1 designation to groups of patients with highly urgent transplant need and similar probabilities of death on the waiting list. Another goal was to refine the eligibility criteria defining status 1 to be both objective and verifiable. Given that the pathophysiology and tempo of clinical deterioration is different for acute liver failure (including acute liver failure secondary to HAT or PNF), and that the highest early death rates for both adults and children, but especially for adults, were seen for those with acute liver failure, a new category of status 1A was established for these patients that would supersede any child with chronic liver failure. The criteria for status 1A for both adults and children are shown in Table 5.

A new status 1B category was designated for children who have chronic liver disease, have a PELD score of at least 25, and meet specific criteria. As the data in this study show, a PELD score of at least 25 was associated with a risk of death similar to that of children with acute liver failure, although the mean time to death was longer for children with chronic liver disease. The eligibility criteria for status 1B are shown in Table 5. Because grading of hepatic encephalopathy is at best subjective and is often impossible to assess in small children, the Glasgow Coma Score was accepted in its place. This score of neurologic status is a routine part of the daily monitoring record of ICU patients. Although the score was developed for the assessment of neurologic function after head trauma,<sup>10</sup> Tissieres et al.<sup>11</sup> found a correlation between a Glasgow Coma Score of <8 (as well as bilirubin, international normalized ratio of prothrombin time, and unreactive bilateral mydriasis) and mortality in children with acute liver failure. The advantage of the Glasgow Coma Score is that the clinical observations that make up the score are objective. For the status 1B criteria, a maximum Glasgow Coma Score of 10 was chosen as the required measure of neurologic assessment that most closely approximated the clinical description of grade 3 hepatic encephalopathy.

An essential feature of the new status 1A and 1B definitions, and one that is true to the primary goal of reserving this designation for patients with comparable risks of dying on the waiting list, is their exclusion of

TABLE 5. Status 1A and 1B Criteria for Adults and Children\*

Status 1A (adults and children)	Must have diagnosis of fulminant liver failure and must be in ICU plus at least one of the following: On ventilator Renal failure requiring dialysis of continuous veno-venous hemofiltration or continuous veno-venous hemodialysis INR >2.0
Status 1B (children only)	Must be in ICU with chronic liver disease and must have PELD >25 and at least one of the following: On ventilator Gastrointestinal bleeding requiring at least 30 mL/kg of packed red blood cell transfusion in the previous 24 hours Renal failure requiring dialysis of continuous veno-venous hemofiltration or continuous veno-venous hemodialysis Glasgow Coma Score < 10

**Abbreviations:** ICU, intensive care unit; INR, international normalized ratio of prothrombin time; PELD, Pediatric End-Stage Liver Disease.

\*Additional definitions for status 1A listing for primary nonfunction and hepatic artery thrombosis are also provided. The complete policy can be found at the Organ Procurement and Transplantation Network (<http://www.optn.org/>).

exception cases that were previously eligible for status 1 listing by the RRB. The RRBs now have the increased responsibility to more accurately determine how to award additional MELD or PELD points when prioritizing exceptional cases within their region. Voigt et al.<sup>12</sup> showed that RRBs' assignment of MELD or PELD points could accurately distinguish high- and low-risk patients, whereas referring physicians predicted pre-transplant mortality poorly. Regional variation in how these decisions are made will, we hope, decrease with the adoption of the MELD exception guidelines recently approved by the OPTN and circulated to the wider transplant community. However, such guidelines are not well established for children, and they cannot take into account every exceptional circumstance. As RRBs are made up of physicians and surgeons within the region, the potential conflict between local or center interests and what is in the best interest of the region remains an inherent flaw in the RRB system.

The new status 1 criteria were incorporated into the liver allocation system in the United States on August 24, 2005, coinciding with broader sharing for pediatric candidates listed at status 1. Broader sharing is also important for timely allocation of deceased donors to these most urgent patients. In a single-center experience, Humar et al.<sup>13</sup> showed that region-wide sharing for status 1 candidates decreased waiting list mortality from 32% to 5% over an 8-year period. Organs from pediatric donors (age <18 years) are now offered first to pediatric status 1A candidates within the service area of the procuring organ procurement organization (local), then to status 1A-listed children in the region, followed by local then regional status 1A adult candidates, followed by local then regional status 1B candidates, and then to children aged 0-11 throughout the region ranked by descending PELD score. The complete algorithm for deceased donor liver allocation is available at <http://www.optn.org/>.

It is too early to evaluate the effects of these changes

in allocation policy, particularly with respect to waiting list death rates. Also to be considered is that adults and children with acute liver failure not meeting status 1 criteria will be ranked by MELD or PELD scores. Although MELD and PELD were both developed to predict mortality in patients with chronic liver disease, there is some evidence that they accurately assess prognosis in acute liver failure. Yantorno et al.<sup>14</sup> showed that a MELD score >30 in adults and children with acute liver failure predicted mortality better than either the Clichy or London criteria, with a diagnostic accuracy of 95%. In another study, Kremers et al.<sup>15</sup> demonstrated that MELD score was statistically significantly associated with poor survival probability for nonacetaminophen-associated acute liver failure but that it did not predict mortality for patients with PNF listed within 7 days after transplant.

Further studies are needed to understand whether MELD and PELD scores are the most appropriate means to determine the urgency for transplantation for patients with acute liver failure not meeting status 1 criteria. In such analyses, a more appropriate endpoint might be the score's accuracy in predicting a switch to status 1, rather than its ability to predict death on the waiting list. In a preliminary univariate analysis of the Studies of Pediatric Liver Transplantation database, PELD score at listing was associated with moving to an ICU (used as a surrogate for status 1) among children with acute liver failure. In a preliminary multivariate analysis of the same database, the factors significantly associated with waiting list death were the need for dialysis or any form of renal replacement therapy ( $P < 0.0001$ ) and location in an ICU at the time of listing (Sue McDiarmid, personal communication, June 2006). A modified MELD or PELD score for acute liver failure may more accurately prioritize acute liver failure patients on the waiting list. Such a modification could be important for patients who do not qualify for status 1A listing, and it might also allow better prioritization of



patients within status 1, for whom waiting time is a metric now used to rank organ offers.

In conclusion, these analyses make clear that the original intent of the status 1 designation has been subverted by the inclusion of substantial numbers of candidates, particularly children, with widely varying risks of death on the waiting list. As long as waiting time governed organ allocation in this diverse group of patients, the concept of medical urgency was largely lost. The new definitions of status 1A and 1B seek to promote access to donor organs to those patients with a similarly high risk of death, and appropriately distinguishes those with acute liver failure from children with severe chronic liver failure. Essential to the success of this concept is the broader regional sharing of pediatric deceased donor livers to this most urgent group of patients. Additional benefits anticipated but as yet unproven are a decrease in deaths on the waiting list, and a potential improvement in posttransplant outcomes if the patients with most urgent need receive more timely liver transplants with better-quality organs.

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