Received: 27 September 2019 | Revised: 5 March 2020 | Accepted: 5 April 2020

DOI: 10.1111/ajt.15925

AJT

ORIGINAL ARTICLE

Improving the predictive ability of the pediatric end-stage liver disease score for young children awaiting liver transplant

Evelyn Hsu[1] | David P. Schladt[2] | Andrew Wey[2] | Emily R. Perito[3] | Ajay K. Israni[2,4,5]

[1]Department of Pediatrics, University of Washington School of Medicine, Seattle Children's Hospital Center for Clinical and Translational Research, Seattle, Washington

[2]Scientific Registry of Transplant Recipients, Hennepin Healthcare Research Institute, Minneapolis, Minnesota

[3]University of California San Francisco School of Medicine, Benioff Children's Hospital, San Francisco, California

[4]Department of Medicine, Hennepin Healthcare, University of Minnesota, Minneapolis, Minnesota

[5]Department of Epidemiology and Community Health, University of Minnesota, Minneapolis, Minnesota

Correspondence
Ajay Israni
Email: isran001@umn.edu

Funding information
Health Resources and Services Administration, Grant/Award Number: HHSH250201000018C

The current pediatric end-stage liver disease (PELD) score underestimates pediatric waitlist mortality. Children frequently require PELD exception points to achieve appropriate priority ranking. We developed a new PELD score using serum sodium, creatinine, and updated original PELD components to more accurately rank children and equalize children's mortality risk with the age-standardized mortality rate of adults. We included children aged younger than 12 years with chronic liver disease, listed for deceased donor livers January 1, 2005-December 31, 2017. Pediatric candidates (n = 5111) were followed from listing to the earliest of waitlist mortality (death or removal from the list due to being too sick to undergo transplant, n = 339) or 180 days. We incorporated linear splines for the current components of PELD and added sodium and creatinine to the equation. The updated PELD-Na-Cr had a cross-validated AUC ROC of 0.854, vs 0.799 for the original PELD. PELD-Na-Cr required 9.44 additional points to equalize children's mortality risk with the age-standardized mortality rate of adults. PELD-Na-Cr better ordered the sickest children and should better prioritize children relative to adults. As a result, PELD-Na-Cr could increase pediatric transplant rates and reduce pediatric liver transplant waitlist mortality.

1 | INTRODUCTION

Allocation of organs to children on the liver transplant waiting list in the United States is determined by the pediatric end-stage liver disease (PELD) score for children aged younger than 12 years and the model for end-stage liver disease (MELD) score for children aged 12-17 years. MELD is based on an objective formula that accurately predicted 3-, 5-, 9-, and 12-month mortality in adults awaiting liver transplant for end-stage liver disease.[1] MELD has gone through several iterations since its implementation in 2002, most significantly the incorporation of MELD-Na[2] in 2016.

The PELD score was derived separately in June 2000 using a cohort of 779 patients from the Studies in Pediatric Liver Transplantation (SPLIT) registry, which at the time included 29 North American pediatric liver transplant programs. In the PELD derivation cohort, the area under the curve of receiver operating characteristic (AUC ROC) at 90 days after listing was 0.92 for predicting death, and 0.82 for predicting death or intensive care unit admission.[3] A validation study in a smaller cohort from Pittsburgh reported the AUC ROC for death as 0.89.[4] However, recent analyses show that PELD significantly underestimates mortality in children awaiting liver transplant, particularly compared with the MELD score for adults.[5] In addition, the current growth failure variable generates a problematic "growth failure gap," in which children's weight or height z-scores can be more than 2 standard deviations below the norm, but they do not receive PELD's "growth failure" points. This

Abbreviations: AUC, area under the curve; CDC, Centers for Disease Control and Prevention; Cr, creatinine; INR, international normalized ratio; MELD, model for end-stage liver disease; Na, sodium; OPTN, Organ Procurement and Transplantation Network; PELD, pediatric end-stage liver disease; ROC, receiver operating characteristic; SPLIT, Studies in Pediatric Liver Transplantation; SRTR, Scientific Registry of Transplant Recipients; UNOS, United Network for Organ Sharing.

Evelyn Hsu and David P. Schladt shared first authorship.

particularly disadvantages infants and children at the older range of each 3-month age group.[6]

Despite these shortfalls, PELD has not been systematically re-reviewed or re-fit for children with chronic liver disease using an independent dataset since its derivation 18 years ago. We hypothesized that, using data collected between PELD implementation and the present, PELD's ability to discriminate medical urgency among pediatric candidates, to discriminate among candidates with varying levels of growth failure, and to address subsets of patients who are currently ignored (eg, those with low sodium levels) could be improved. This study aimed to use national liver transplant databases over a 13-year period to assess whether PELD modification could improve prediction of 180-day mortality in children with chronic liver disease awaiting deceased donor liver transplant.

2 | METHODS

This study used data from the Scientific Registry of Transplant Recipients (SRTR). The SRTR data system includes data on all donors, waitlisted candidates, and transplant recipients in the US, submitted by the members of the Organ Procurement and Transplantation Network (OPTN). The Health Resources and Services Administration, US Department of Health and Human Services, provides oversight of the activities of the OPTN and SRTR contractors.

2.1 | Cohort description

Children from the SRTR database who were aged younger than 12 years at the time of listing and were active on the liver transplant waiting list between January 1, 2005, and December 31, 2017, were included in the cohort. We excluded children whose first active status was 1, 1A, or 1B (Figure 1). We excluded 968 (15.9%) listings with specific primary or secondary diagnoses that fit criteria for non-chronic liver disease diagnoses for transplant (Table S1). Six candidates were excluded due to incomplete data necessary for the PELD calculation, leaving 5111 listings of 4876 unique children. All analyses were based on pediatric candidate listings for transplant, and thus included more than one listing for children who underwent

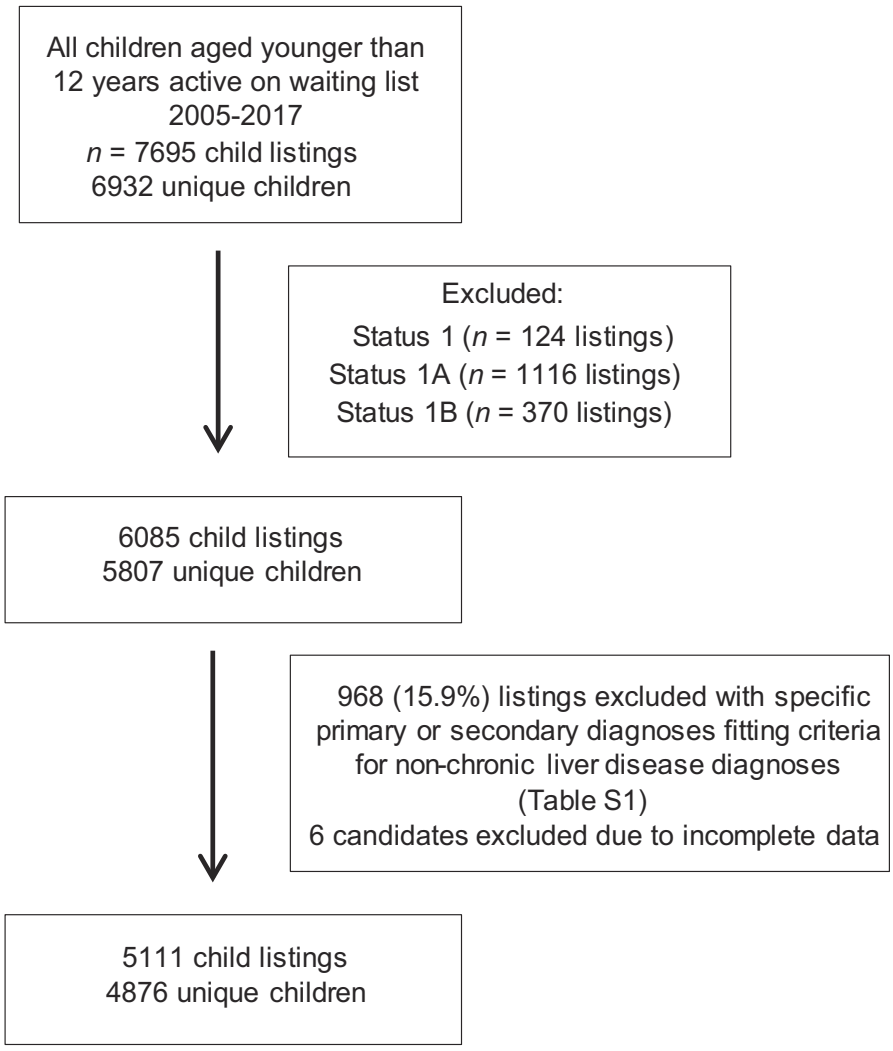

FIGURE 1 Creation of the study cohort using Scientific Registry of Transplant Recipients standard analysis files (SAFs). The final analytic dataset included 5111 pediatric listings for liver transplant for 4876 individuals

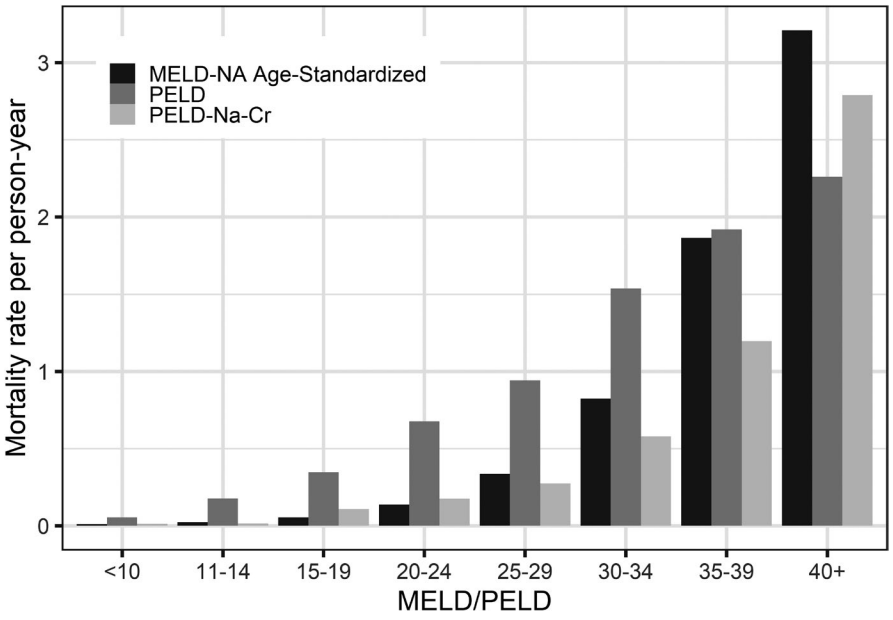

FIGURE 2 Mortality rates in person-years, based on assigned allocation score. MELD-Na standardized for age represents the mortality rate in a given MELD range adjusted as if all adults were aged 18 years; it is lower than the PELD through scores of 35 and roughly equivalent at 35-39. PELD-Na-Cr is adjusted to scores that are similar to age-standardized MELD-Na through the entire spectrum of scores. MELD, model for end-stage liver disease; PELD, pediatric end-stage liver disease

transplant and were re-listed. We included children listed for re-transplant because we expected calculated PELD to accurately reflect their severity of illness.

2.2 | Statistical analysis

A Cox proportional hazards (Cox PH) regression modeled the effect of risk factors on time to waitlist mortality within 180 days after listing (n = 339). Waitlist mortality was defined as death on the waiting list (n = 246) or removal from the list due to being too sick to undergo transplant (n = 93). Death after removal was not considered due to very limited follow-up data, as most children aged younger than 1 year are not tracked by Social Security or the Centers for Medicare & Medicaid Services. The cohort was followed from first active status and censored at transplant, removal for other reasons, or 180 days after date of first active listing, as MELD-Na studies used this interval for adult patients.[7,8] All risk factors used the values at first active status.

2.3 | Model fitting

To refit PELD, we considered the following objective, verifiable variables: age, albumin, total bilirubin, international normalized ratio (INR), and the minimum of the height or weight Z-score based on 2000 Centers for Disease Control and Prevention (CDC) growth charts.[9,10] We plotted the non-linear association of each variable with mortality from a multivariable model (Figure S1). The factors, other than CDC Z-scores, used a natural-log transformation to account for extreme observations. Knots for splines were visually selected from inflection points in penalized splines. Backward selection with Cox PH regression was performed univariately for each risk factor and their associated splines with a retention *P* value of .05. Next, this process was repeated with creatinine (0.2-4.0 mg/dL) and sodium (up to 140 mmol/L), and their associated splines (Figure S1). For candidates on dialysis, creatinine was set to 4.0 mg/dL, as is done when calculating MELD-Na in adults.

All risk factors and splines were then combined into a multivariable model. Backward selection was again performed with a retention *P* value of .05. Since serum creatinine was missing from 180 listings (3.5%) at the time of first active status, 10 iterations of multiple imputation were completed to fill in the missing data. The model was fit to each iteration of multiple imputation, and Rubin's rules were used to combine the beta coefficients and variances across the 10 iterations.[11]

2.4 | Model fit evaluation

The time-dependent AUC ROC at 180 days was used to measure the predictive accuracy of the original PELD and our updated PELD-Na-Cr The time-dependent AUC ROC measures the probability that candidates who died by 180 days had higher PELDs than candidates who did not die. For the new PELD score, n-fold cross-validation estimated the time-dependent AUC ROC to avoid overfitting. We then performed bootstrap with 1000 resamples to estimate the *P* value for the difference between AUC ROC of PELD vs PELD-Na-Cr and the 95% confidence intervals of the AUC ROCs.

2.5 | Converting PELD model into a score

We then converted the PELD-Na-Cr model (the linear equation from the Cox regression) into a usable PELD-Na-Cr score in two steps. First, the linear model was standardized to have the same mean and standard deviation as the original PELD score: mean (standard deviation [SD]) = 11.5 (11.7). Second, we estimated the required shift in the standardized PELD-Na-Cr score to equalize

TABLE 1 Calculating the PELD-Na-Cr score for young children on the liver waiting list and value contribution of different variables

	Term in current PELD equation	Term in linear PELD-Na-Cr equation	If the child's value is:	Then the value's contribution to PELD-Na-Cr is:
Age (years)	0.436 if age < 1 year 0 if age ≥ 1 year	−0.284 * ln(Age > 0.3 years)	≤0.3	−0.284 * ln(0.3)
			>0.3	−0.284 * ln(age)
Albumin (g/dL)	−0.687*ln(albumin)	−2.017 * ln(albumin 2.3 to 4.4)	<2.3	−2.017 * ln(2.3)
			2.3-4.4	−2.017 * ln(child's albumin)
			>4.4	−2.017 * ln(4.4)
Total bilirubin (mg/dL)	0.480*ln(bilirubin)	1.127 * ln(bilirubin < 2.5) + 1.535* ln(bilirubin > 9.0)	<2.5	1.127 * ln(child's bilirubin) + 1.535 * ln(9)
			2.5-9.0	1.127 * ln(2.5) + 1.535 * ln(9)
			>9.0	1.127 * ln(2.5) + 1.535 * ln(child's Bili)
INR	1.857*ln(INR)	2.588 * ln(INR < 1.7) + 2.972 * ln(INR > 6.5)	<1.7	2.588 * ln(child's INR) + 2.972 * ln(6.5)
			1.7-6.5	2.588 * ln(1.7) + 2.972 * ln(6.5)
			>6.5	2.588 * ln(1.7) + 2.972 * ln(child's INR)
Minimum of height or weight Z-score	0.667 if Z < −2 0 if Z ≥ −2	−0.224 * (min Z-score −5 to 0)	<−5	−0.224 * (−5)
			−5-0	−0.224 * (child's minimum z-score)
			>0	−0.224 * (0)
Creatinine (mg/dL)	—	0.623 * ln(creatinine 0.2 to 4)	<0.2	0.623 * ln(0.2)
			0.2-4.0	0.623 * ln(child's creatinine)
			>4.0	0.623 * ln(4.0)
Sodium (meq/L)	—	−29.05 * ln(sodium < 123)	<123	−29.05 * ln(child's sodium)
			≥123	−29.05 * ln(123)
PELD score	PELD = sum of all terms * 10 → rounded to nearest whole number	PELD-Na-Cr = (sum of all terms + 131.605)*7.62 + 20.98 → rounded to nearest whole number		

Abbreviations: Cr, creatinine; INR, international normalized ratio; Na, sodium; PELD, pediatric end-stage liver disease.

the mortality rate of children with the age-standardized mortality rate for adults. Specifically, we estimated an initial mortality rate for each PELD-Na-Cr value and then smoothed the initial estimates to obtain a final mortality rate for each PELD-Na-Cr value. The required shift for ensuring that pediatric candidates had similar waitlist mortality rates as age-standardized adults was the average difference between the smoothed PELD-Na-Cr and MELD-Na for the same pediatric and age-standardized 180-day mortality rates (Figure 2). The age-standardized expected mortality rate was the mortality rate if every adult candidate had been aged 18 years, which was estimated from a Cox PH model that included age and MELD-Na, and used only adults waitlisted between January 11, 2016, and December 31, 2017. Analyses were conducted using SAS version 9.4 (SAS Institute) and R software version 3.5 (www.r-project.org).

3 | RESULTS

The final PELD-Na-Cr derivation cohort included 5111 candidate listings from 4876 children (Table S2); 51.0% of the listings were for candidates aged younger than 1 year. The most common primary diagnosis was biliary atresia (45.7%). Mean (SD) albumin was 3.15 g/dL (0.69); 31.4% of children had growth failure as defined by current United Network for Organ Sharing (UNOS) PELD calculations, and the mean (SD) minimum CDC height or weight Z-score was −2.04 (1.76).

Age, albumin, total bilirubin, INR, minimum CDC height or weight Z-score, creatinine, and serum sodium were significantly predictive of waitlist mortality in multivariable modeling. Since the factors in the PELD-Na-Cr model are all splines, use of the factors in calculation differs from use of factors in calculating the PELD. For example, the age effect is a spline that begins at 0.3 years. For children aged 0.3 years or older, age is used directly in the equation, but children aged younger than 0.3 years would be treated in PELD-Na-Cr calculation as if they were aged 0.3 years. This is equivalent to a using a floor value of 0.3; ie, all values less than 0.3 are set to 0.3 (Table 1).

For PELD-Na-Cr, the AUC ROC at 180 days was 0.854 (95% CI 0.832-0.878), significantly better than the AUC ROC for the original PELD score performed in our updated cohort, 0.799 (0.773-0.825), for a difference of 0.055 (95% CI 0.039-0.074), $P < .001$. The updated PELD-Na-Cr score correctly ordered 5.5% more pediatric candidates by their risk of mortality at 180 days than the current PELD score. The discriminatory ability of PELD was thus notably improved by considering non-linear effects and by adding serum creatinine and sodium to the model.

After standardizing PELD-Na-Cr, matching the predicted mortality rate to the age-standardized mortality rate for adults by MELD-Na required adding 9.44 points to the PELD-Na-Cr score.

TABLE 2 PELD-Na-Cr equation and parameters, using sample cases

	Sample case 1: 6-year-old child with albumin 2.1 g/dL, total bilirubin 10.0 mg/dL, INR 2.5, weight z-score −2.0, creatinine 0.8 mg/dL, sodium 122 meq/L				Sample case 2: 6-month-old child with albumin 3.0 g/dL, total bilirubin 6.0 mg/dL, INR 1.4, weight z-score 0, creatinine 0.1 mg/dL, sodium 135 meq/L			
	Case 1 value	Value in equation	Term contribution to PELD equation	Total variable contribution to PELD equation	Case 2 value	Value in equation	Term contribution to PELD equation	Total variable contribution to PELD equation
Age	6.0	6.0	−0.284 * ln(6.0) = −0.509	−0.509	0.5	0.5	−0.284 * ln(0.5) = 0.197	0.197
Albumin	2.1	2.3	−2.017 * ln(2.3) = −1.680	−1.680	3.0	3.0	−2.017 * ln(3) = −2.216	−2.216
Bilirubin	10.0	2.5	1.127 * ln(2.5) = 1.033	4.567	6.0	2.5	1.127 * ln(2.5) = 1.033	4.405
	10.0	10.0	1.535 * ln(10) = 3.534		6.0	9.0	1.535 * ln(9) = 3.373	
INR	2.5	1.7	2.588 * ln(1.7) = 1.373	6.936	1.4	1.4	2.588 * ln(1.4) = 0.871	6.434
	2.5	6.5	2.972 * ln(6.5) = 5.563		1.4	6.5	2.972 * ln(6.5) = 5.563	
Minimum of height or weight Z-score	−2.0	−2.0	−0.224 * (−2.0) = 0.112	0.448	0	0	−0.224 * (0) = 0	0
Creatinine	0.8	0.8	0.623 * ln(0.8) = −0.139	−0.139	0.1	0.2	0.623 * ln(0.2) = −1.003	−1.003
Sodium	122	122	−29.05 * ln(122) = −139.557	−139.557	135	123	−29.05 * ln(123) = −139.794	−139.794
PELD-Na-Cr				34				18

Abbreviations: Cr, creatinine; INR, international normalized ratio; Na, sodium; PELD, pediatric end-stage liver disease.

The algorithm for determining the PELD-Na-Cr score for a specific candidate is thus as follows:

First, obtain the linear predictor from the Cox PH model:

−0.284 * ln(max(Age(years), 0.3))
−2.017 * ln(min(max(Albumin (g/dL), 2.3), 4.4))
+1.127 * ln(min(Total Bilirubin (mg/dL), 2.5))
+1.535 * ln(max(Total Bilirubin (mg/dL), 9))
+2.588 * ln(min(INR, 1.7))
+2.972 * ln(max(INR, 6.5))
−0.224 * min(max(CDC Minimum Height or Weight Z-score, −5), 0)
+0.623 * ln(min(max(Creatinine (mg/dL), 0.2), 4))
−29.05 * ln(min(Sodium (mEq/L), 123))

Next, add 131.605, then multiply by 7.62, and add 20.98. Finally, round to the nearest whole number.

For example, for a hypothetical candidate aged 1.2 years, an albumin of 3.1 g/dL, a total bilirubin of 10.4 mg/dL, an INR of 2.7, a CDC height Z-score of −1.2, a CDC weight Z-score of −2.0, a serum creatinine of 1.0 mg/dL, and a sodium of 137 mEq/L, the linear predictor would be:

−0.284*ln(1.2)
−2.017*ln(3.1)
+1.127*ln(2.5)
+1.535*ln(10.4)
+2.588*ln(1.7)
+2.972*ln(6.5)
−0.224*(−2.0)
+0.623*ln(1.0)
−29.05*ln(123) = −130.116

PELD-Na-Cr Score = (−130.116 + 131.605)*7.62 + 20.98 = 32.32, which would be rounded to 32. The same candidate would have a PELD score of 22. We include sample cases (Table 2) to demonstrate calculation of the PELD-Na-Cr score and the relative contribution of clinical variables to the equation (Table 1).

In our derivation cohort, mean (SD) PELD score was 11.5 (11.7), and mean (SD) PELD-Na-Cr score was 21.0 (11.7). Most pediatric candidates had higher scores with PELD-Na-Cr than with PELD (Table 3). In Table 3, candidates in the diagonal (dark gray) boxes had similar values for both scores. Candidates in boxes above the diagonal line had PELD-Na-Cr scores higher than PELD scores, and those below the line had PELD-Na-Cr scores lower than PELD score. The 1787 (35%) candidates in the boxes above the diagonal line had PELD-Na-Cr scores higher than 25.

4 | DISCUSSION

Children die awaiting liver transplant in the United States. Over 13 years, in a cohort of almost 5000 young children with chronic liver disease on the liver transplant waiting list, 7% died while waiting.

TABLE 3 PELD vs. PELD-Na-Cr scores

PELD	PELD-Na-Cr									
	<10	11-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50+
<10	928	599	506	170	24	4	1	0	0	0
11-14	0	23	198	400	164	21	5	1	0	0
15-19	0	1	38	192	354	195	41	7	4	0
20-24	0	1	4	42	138	215	126	34	8	4
25-29	0	0	3	14	46	80	113	46	18	7
30-34	0	1	2	7	19	37	44	37	20	9
35-39	0	0	0	4	9	17	21	20	20	9
40-44	0	0	0	0	4	6	4	9	6	4
45-49	0	0	0	0	0	2	1	6	4	8
≥50	0	0	0	0	0	0	0	3	4	3

Note: Abbreviations: Cr, creatinine; Na, sodium; PELD, pediatric end-stage liver disease.

For PELD-Na-Cr, we used multiple imputations and the average of 10 imputations is displayed.

Reducing pediatric waitlist deaths and ensuring that children have equitable access to liver transplant requires ongoing re-evaluation of our priority ranking system, which is based on the PELD score. This analysis provides an evidence-based approach for updating the PELD score based on more than a decade's worth of data, and for incorporating serum sodium and creatinine, well-known predictors of waitlist mortality. Our work (1) demonstrates that young children die on the waiting list, (2) illustrates a new model that improves the classification of all children at risk of dying on the waiting list, and (3) suggests the potential impact of this model for allocation outcomes for young children.

The strength of this analysis is that the data were comprehensive and prospectively collected for children with chronic liver disease, from a national transplant database that identifies every individual listed for liver transplant in the United States with high fidelity and completion, and represents all programs and geographic areas. Only candidates registered on the waiting list under the current allocation system were included, making this the largest, most inclusive dataset applicable to waitlisted children in the United States. This is the first work performed to re-examine the prognostic factors that determine mortality of children aged younger than 12 years on the liver transplant waiting list since implementation of the MELD/PELD scoring system in 2002, nearly 2 decades ago.

We found that discriminatory ability, ie, the ability to rank children based on their risk of death on the list, was improved by updating the coefficients used for PELD calculation and adding the variables creatinine and sodium. Mortality estimates in our model confirmed previously shown findings that PELD underestimates mortality in young children relative to adults. Equalizing mortality estimates to those of adults aged 18 years required adding almost 10 points to every score.

By censoring for removal due to transplant, PELD estimates the cause-specific hazard of waitlist mortality or removal due to being too sick.[12] There is no a priori reason for correlations among the cause-specific hazards of living donor transplant, deceased donor transplant, or waitlist mortality. However, the sub-hazard of waitlist mortality (ie, a Fine-Grey competing risks analysis) depends, by definition, on the likelihood of living and deceased donor transplant. As previously suggested,[5] analyses of waitlist mortality in transplantation should account for competing risks. However, analyses focused on allocation should estimate the cause-specific hazard of waitlist mortality because a sub-hazard analysis may systematically underestimate the waitlist mortality of candidates at high risk of death and transplant.

Our study had a number of limitations. Due to the smaller number of children listed for liver transplant compared with the number of adults, the entire cohort was used for derivation, as opposed to "saving" part of the dataset for validating the PELD-Na-Cr system. This analysis did not investigate PELD as a predictor of survival benefit, which is an important outcome in children and is incorporated into other solid organ allocation systems, such as kidney allocation. Survival benefit, which accounts for both pre- and posttransplant survival, is critical for children given their expected decades of posttransplant survival. Lastly, PELD-Na-Cr improves prediction for children, equalizing their predicted mortality rate to that of adults aged 18 years, but this analysis does not verify that implementation of PELD-Na-Cr as presented would be sufficient to ensure sufficient access to transplant for children. Our reclassification table demonstrates that most children would have PELD-Na-Cr scores higher than their current PELD scores, but many would still have scores lower than the median national PELD at transplant and the median regional MELD at transplant.

This analysis also excludes children listed as Status 1A and 1B; children in both categories--particularly those with decompensated chronic liver disease at Status 1B--are at the highest risk for death on the waiting list and will continue to be prioritized above children priority-ranked by their PELD score. The differentiation between children listed at Status 1B for inborn errors of metabolism and hepatoblastoma and those with decompensated chronic liver disease at Status 1B is not addressed in this work and remains an important issue facing pediatric liver allocation that needs to be assessed.

All patients waiting for liver transplant deserve an allocation model that is optimized to reduce mortality. Young children on the liver transplant waiting list deserve an accurate allocation system that maintains equitable access to transplant while reducing waitlist mortality. As their advocates, physicians and surgeons are morally obligated to ask for vigilance and accuracy when optimizing allocation models. With the exception of the United States, most countries in the world with a formalized liver transplant process have definitively prioritized liver allocation to children. In Eurotransplant, Canada, and Brazil, modifications to allocation by MELD or PELD have been introduced in an effort to prioritize children and recognize the necessity of prompt transplants for children with end-stage liver disease.[13] These measures have resulted in low waitlist mortality and excellent clinical outcomes for children, with increased likelihood of technical variant or split graft use for all candidates.

The PELD-Na-Cr increases accuracy. It will require further assessment with simulations to determine its impact on equitable access to transplant for all young children. Although further refinement and validation is necessary, updating PELD could potentially better discriminate young children with the greatest medical urgency while reducing barriers to access to life-saving transplants.

ACKNOWLEDGMENTS

This work was conducted under the auspices of the Hennepin Healthcare Research Institute (HHRI), contractor for the Scientific Registry of Transplant Recipients (SRTR), as a deliverable under contract no. HHSH250201000018C (US Department of Health and Human Services, Health Resources and Services Administration, Healthcare Systems Bureau, Division of Transplantation). As a US Government-sponsored work, there are no restrictions on its use. The data reported here have been supplied by HHRI as the contractor for SRTR. The interpretation and reporting of these data are the responsibility of the author(s) and in no way should be seen as an official policy of or interpretation by the SRTR or the US Government. The authors gratefully acknowledge the participation of adult and pediatric liver transplant programs that enter information into the UNOS/OPTN database. The authors thank SRTR colleague Nan Booth, MSW, MPH, ELS, for manuscript editing.

DISCLOSURE

The authors of this manuscript have no conflicts of interest to disclose as described by the *American Journal of Transplantation*.

DATA AVAILABILITY STATEMENT

Data are available from the Scientific Registry of Transplant Recipients.

ORCID

Andrew Wey https://orcid.org/0000-0002-2584-3018 .

REFERENCES

1. Kamath PS, Wiesner RH, Malinchoc M, et al. A model to predict survival in patients with end-stage liver disease. *Hepatology*. 2001;33(2):464-470.
2. Elwir S, Lake J. Current status of liver allocation in the United States. *Gastroenterol Hepatol (NY)*. 2016;12(3):166-170.
3. McDiarmid SV, Anand R, Lindblad AS. Principal Investigators and Institutions of the Studies of Pediatric Liver Transplantation (SPLIT) Research Group. Development of a pediatric end-stage liver disease score to predict poor outcome in children awaiting liver transplantation. *Transplantation*. 2002;74(2):173-181.
4. Mazariegos G, Anand R, Mcdiarmid S, et al. Validation of PELD severity score in a pediatric transplant candidate database. *Am J Transplant*. 2002;2(S3):249-276 [abstract 451].
5. Chang C-C, Bryce CL, Shneider BL, et al. Accuracy of the pediatric end-stage liver disease score in estimating pretransplant mortality among pediatric liver transplant candidates. *JAMA Pediatr*. 2018;172(11):1070-1077.
6. Swenson SM, Roberts JP, Rhee S, Perito ER. Impact of the pediatric end-stage liver disease (PELD) growth failure thresholds on mortality among pediatric liver transplant candidates. *Am J Transplant*. 2019;19(12):3308-3318. [Epub ahead of print].
7. Biggins SW, Kim WR, Terrault NA, et al. Evidence-based incorporation of serum sodium concentration into MELD. *Gastroenterology*. 2006;130(6):1652-1660.
8. Biggins SW, Rodriguez HJ, Bacchetti P, Bass NM, Roberts JP, Terrault NA. Serum sodium predicts mortality in patients listed for liver transplantation. *Hepatology*. 2005;41(1):32-39.
9. Kuczmarski RJ, Ogden CL, Guo SS, et al. 2000 CDC growth charts for the United States: methods and development. *Vital Health Stat 11*. 2002;May(246): 1-190.
10. Centers for Disease Control and Prevention. A SAS Program for the 2000 CDC Growth Charts (ages 0–20 years). https://www.cdc.gov/nccdphp/dnpao/growthcharts/resources/sas.htm. Accessed March 4, 2020.
11. Marshall A, Altman DG, Holder RL, Royston P. Combining estimates of interest in prognostic modelling studies after multiple imputation: current practice and guidelines. *BMC Med Res Methodol*. 2009;9:57.
12. Kalbfleisch JD, Prentice RL. *The statistical analysis of failure time date*. Hoboken NJ: John Wiley and Sons; 2002.
13. Hsu EK, Mazariegos GV. Global lessons in graft type and pediatric liver allocation: A path toward improving outcomes and eliminating wait-list mortality. *Liver Transpl*. 2017;23(1):86-95.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

How to cite this article: Hsu E, Schladt DP, Wey A, Perito ER, Israni AK. Improving the predictive ability of the pediatric end-stage liver disease score for young children awaiting liver transplant. *Am J Transplant*. 2021;21:222–228. https://doi.org/10.1111/ajt.15925