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CAQ CORNER: Evolution of Liver Allocation Policy

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This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1002/lt.26497

Abbreviations:

Child Turcotte and Pugh	CTP
Donor Specific Area	DSA
International Normalized Ratio	INR
Liver Transplantation	LT
Model for End-stage Liver Disease	MELD
National Organ Transplantation Act	NOTA
Organ Procurement Organization	OPO
Organ Procurement and Transplantation Network	OPTN
Simultaneous Liver-Kidney Transplantation	SLKT

Introduction

The United States (US) urgency-based liver transplantation (LT) policy has two components: allocation and distribution of donor livers. The Model for End Stage Liver Disease (MELD) score, the metric of waitlist mortality, was implemented on Feb 29, 2002. Since then, there have been several evidence-based dynamic changes to the allocation and distribution scheme in attempts to be fair, just, and equitable. (Figure 1)

Allocation:

Pre- MELD Allocation:

The National Organ Transplantation Act (NOTA sections 371-376 of the Public Health Services Act) was enacted in 1984 to govern and provide regulatory oversight for transplantation through the creation of an Organ Procurement and Transplantation Network (OPTN). Prior to NOTA, there were no formal guidelines for allocation. After the passage of NOTA and until 1996, allocation of donor livers was stratified as urgent (Status 1: fulminant hepatic failure) and non-urgent. The non-urgent status was further subdivided into hospitalized in intensive care unit (ICU) setting (Status 2), non- ICU setting (Status 3) and ambulatory (status 4).[i] Later, status 2,3 and 4 were reclassified as Status 2A, 2B and 3, respectively. Candidates were ranked based upon their waiting time in these status-based categories with broad ranges of disease severity. The location-based status designation was susceptible to covert and overt manipulation. As a result, the allocation policy was amended and the Child-Pugh (CTP) score of 7 was adopted as the minimal listing criteria for LT.[ii] However, this did not improve the inequities and

inefficiencies in the allocation associated with gaming the system due to the subjectivity of criteria and waiting times. The US Department of Health and Human Services stated in a Final Rule in 1999 that organ allocation rules should be based on objective medical criteria, ideally based on continuous measures of medical urgency.[iii] The Final Rule clearly advocated for a system that would promote equity by reducing disparities in waiting list outcomes.

MELD- Based Allocation:

MELD score, originally developed to risk stratify patients undergoing an elective transjugular intrahepatic portosystemic shunt procedure,[iv] was further refined and validated in other datasets including hospitalized patients, ambulatory patients with cholestatic and non-cholestatic liver disease with excellent performance characteristics. MELD score performed superior to CTP score (C-statistic: 0.82) in predicting 3-month mortality among 3437 waitlisted candidates.[v]

MELD score is based upon serum creatinine, serum bilirubin and international normalized ration (INR) of prothrombin time (Figure 2) was implemented for allocation with few caveats: 1) the etiology of the liver disease was dropped to avoid subjectivity but the coefficient was kept 2) the lower bound of serum creatinine and serum bilirubin was set at 1.0 mg/dl to avoid negative score 3) the upper bound of creatinine was set at 4.0 mg/dl if the candidate is on dialysis or creatinine > 4.0 mg/dl to avoid undue advantage to kidney disease 4) the upper bound of MELD score was set at 40.

Introduction of MELD in the US was associated with 12% reduction in waiting list registrations (particularly among those with MELD <10), 3.5% reduction in waiting list mortality, and an increase in LT rates distributed across all demographic and epidemiologic strata with unchanged early patient and graft survival despite sicker patients receiving a higher proportion of donor livers.[vi]

Kim et al. and others[vii] showed that hyponatremia was an independent predictor of waitlist mortality and addition of serum sodium to the MELD score could reduce waiting list mortality by as much as 7%.[viii] Sharma et al. demonstrated that the survival benefit of LT increased significantly with decreasing serum sodium at MELD scores ≥12.[ix] However, the survival benefit of LT was not affected by serum sodium for patients with MELD ≤11). The MELD-Na based policy (Figure 2) went into effect in January 2016.

Despite best efforts and modifications, the MELD score does not account for many other factors (e.g., frailty, albumin) and gender differences leading to disparities in transplantation. Over time, modifications of the MELD score have been proposed, most recently the MELD 3.0 incorporating gender and serum albumin has been developed to improve mortality prediction.[x]

Candidates with age < 12 years receive a pediatric end stage liver disease (PELD) score. The components of the PELD score include age, serum bilirubin, serum albumin, INR, and growth failure.

Waitlist Maintenance:

Mandatory MELD score reassessment and recertification by the transplant center is required by OPTN, the governing body overseeing organ transplant. MELD scores must be submitted periodically for recertification with updates at more frequent intervals required at higher MELD, for example every 7 days for those with MELD score ≥24. Recertification must be based on the most recent laboratory test results and diagnosis, including the dates of the laboratory tests. Failure to do so in accordance with the schedule may result in re-assignment to a previous lower MELD score. The candidate may remain at that previous lower score for the period allowed based upon the recertification schedule for the previous lower score, minus the time spent in the uncertified score. If the candidate remains uncertified past the recertification due date for the previous lower score, the candidate will be assigned a MELD score of 6.

Adult Status 1A:

Adult candidates with severe, life-threatening liver dysfunction (life expectancy < 7 days without LT) in the absence of prior liver disease are given the highest medical priority for allocation of deceased donor liver ahead of all candidates with MELD scores via 1A status. (Table 1). In this category, patients are rank ordered based on waiting time. Although MELD score is not used to allocate livers in this category, MELD las are updated every 7 days.

Pediatric Status 1A/1B:

Like their adult counterparts, pediatric LT candidates are stratified according to medical necessity and, depending on objective clinical criteria, may achieve priority in listing for life saving LT as pediatric status 1A or 1B candidates, superseding calculated and/or exception MELD/PELD scores. (Table 1)

MELD/PELD Exceptions:

As in the case with any mathematical model or risk score, MELD score does not reflect the disease severity in certain conditions such as hepatopulmonary syndrome (HPS), portopulmonary hypertension (PoPH), cholangiocarcinoma (CCA) and hepatocellular carcinoma (HCC). Hence a system of exception score has been in place to award increased priority to candidates whose disease severity is not captured by calculated MELD score. These broadly fall into standardized and non-standardized MELD/PELD exception scores (Table 2).[xi] The candidates' transplant team submit a vignette with request for standard MELD exception or customized exception score request to the National Liver Review Board (NLRB). The NLRB, implemented in 2019, consists of volunteer, independent medical experts (transplant hepatologists and transplant surgeons). The review board decide whether the requested score is reasonable based on the patient's current medical condition and the likelihood that the recipient will do well once transplanted. The board makes its decision based solely on the medical facts supplied by the transplant hospital, aided by their own medical judgment and guidance from the OPTN. The review board may grant or deny the exception score requested. If the initial request is denied, the transplant team listing the candidate can choose to appeal up to three times.

Median MELD at Transplant (MMaT)/ Median PELD at Transplant (MPaT):

The MMaT/MPaT are used in assigning standard MELD/PELD disease exception scores. The MMaT/MPaT score is calculated by using the median of the MELD (age ≥ 12 years)/PELD (age < 12 years) scores at the time of LT of all recipients who were transplanted at hospitals within

250 nautical miles of the candidate's listing hospital in a prior 365-day period. The MMaT/MPaT calculations exclude status 1A /1b transplants and the recipients of living donor, donation after cardiac death (DCD) and donor procured > 500 nautical miles from the transplant hospital. The OPTN recalculates the MMaT/MPaT every 6 months based on an updated cohort of LT within 250 nautical miles of the transplant hospital over a prior 365-day period if there ≥10 qualifying transplants and over a prior 730-day period if there were < 10 qualifying transplants.

Standard MELD/PELD Exceptions:

The OPTN Liver and Intestinal Organ Transplantation Committee has developed guidance for adult MELD exception candidates. These standardized recommendations were proposed after reviewing the 2006 MELD Exception Study Group (MESSAGE) Conference.[xii] The objective criteria of standardized MELD/PELD exception conditions and criteria to qualify for exception status are shown in Table 2.

Non-Standard MELD/PELD Exceptions:

Certain decompensation events such as ascites, hepatic encephalopathy and gastrointestinal bleeding lack adequate evidence to support granting specific MELD exception scores. However, there are additional complications where MELD score does not reflect the disease severity and are not covered under standard MELD/PELD exception. These non-standard MELD/PELD exception are shown in Table 2.

Organ Distribution

Distribution can be defined as the ordering of waiting lists candidates to which organs are offered, in essence the list of patients to which a particular organ is presented.[xiii]

Donor Specific Area (DSA)- OPTN region- Nation:

Historically, deceased donor liver distribution was based on a local – regional - national gradient to the most degree. DSA is the distinct, non- overlapping geographic area served by each of the fifty-eight federally certified organ procurement organizations (OPO). DA's may include one or more transplant programs of a given organ, and one or more donor hospitals.[xiv] These DSAs were grouped into 11 (OPTN) regions before viewing the nation.

Geographic variability in access to LT, measured by median MELD at transplant, is a major contributor to inequitable access across the OPTN regions. Based on SRTR report in 2019, the median MELD score varied from 19 to 36 by recipient DSA.[xv] The 'regional Share 15', 'regional Share Status 1' and 'regional Share 35' were the major changes in the distribution scheme to mitigate this variability.

Merion et al. demonstrated significant overall survival benefit from LT for patients with MELD score ≥ 18.[xvi] Based upon 1 year of post-LT mortality risk, the survival benefit of LT diminished for patients with MELD scores < 15. Hence, the 'regional Share 15' policy was implemented where, after initial offer within the local DSA to patients with a MELD >15, it would be offered regionally before being offered locally to patients with a MELD < 15.

In line with the tenants of the 'Final Rule' prioritizing access to organ transplantation for the sickest patients, **regional Share for Status 1** was implemented in 2010 where patients listed as Status 1 would receive priority for transplant ahead of all other patients listed within that OPTN region. This policy change improved the access to LT by increasing the probability of LT and

reduced the waiting list mortality for adult status 1 candidates without negatively affecting waitlist mortality for non-status 1 patients in the same region.[xvii]

Regional Share 35 rule was implemented to prioritize access to the sickest patients in the OPTN region. Sharma et al. demonstrated that candidates listed for LT with a MELD score range of 36 -40 had similar waitlist mortality risk and post LT survival compared to Status 1A and yet were not prioritized for LT within the region as their Status 1A/1B counterparts.[xviii] These results were validated by OPTN Liver and Intestinal Committee, thus 'Regional Share 35' was implemented in 2013 to improve the access for high MELD patients within the OPTN region. These policy changes increased transplant rates for patients with MELD ≥35, with a corresponding decrease in waitlist mortality by 30% for the sickest patients and by 8% overall.[xix]

Acuity Circle Distribution System:

Despite the earlier changes in distribution scheme and creation of NLRB, significant geographical variability persisted in the median MELD scores across different regions.[xx] Coupled with legal challenges towards a broad geographical rational of organ distribution, a donor liver distribution system based on concentric geographical circles (like donor lung distribution) around a donor site hospital was examined. Simulation modeling of concentric circle demonstrated improved access to LT and increased travel time as a tradeoff. This change in distribution system was accepted by OPTN after public comment and implemented in 2020.[xxi] (Figure 3)

Under acuity circles, all livers from adult deceased donors are first offered to compatible Status 1A and 1B candidates listed at transplant hospitals within a radius of 500 nautical miles of the donor hospital. Subsequently, livers from deceased adult (age ≥18 years) donors are distributed based on the deceased donor's age and mechanism of death to patients stratified by MELD score ranges through concentric zones of distribution at 150 nautical miles, 250 nautical miles and 500 nautical miles of the donor hospital in a tiered approach. To increase priority for pediatric candidates over their adult counterparts at similar levels of medical urgency, livers from pediatric (age<18 years) are initially offered to compatible pediatric candidates listed at any transplant hospital within a 500 nautical-mile radius of the donor hospital. (Figure 4)

Recent data report from the OPTN demonstrated increased liver transplant rates for Status 1A/1B candidates and those with MELD/PELD scores of ≥ 29, increased rates of deceased donor liver alone transplants and decreased geographic variability in median urgency scores at transplant.[xxii] Going forward, all organ allocation systems will transition to a continuous distribution model where all candidates are considered collectively vs specific groups, with candidates receiving priority on a sliding scale formula based on a composite allocation score of medical urgency, post-transplant survival, candidate biology, patient access and placement efficacy (https://unos.org/news/innovation/building-more-flexible-system-for-organ-allocation/).

Simultaneous Liver-Kidney Transplantation (SLKT):

SLKT is a therapeutic option for LT candidates with advanced chronic kidney disease (CKD), sustained irreversible acute kidney injury and inherited metabolic diseases such as primary hyperoxaluria and comprised of 8-10% of all LT. Since the implementation of MELD in 2002, the incidence of SLKT has increased significantly.[xxiii]

There was a continued controversy within the transplant community that multi-organ transplants were drawing deceased donor kidneys away from the kidney transplant candidate pool. Moreover, mostly low Kidney Donor Profile Index are utilized in multiorgan transplantation including SLKT. Therefore, OPTN convened a working group that consisted of members of OPTN Kidney, Liver and Intestinal, OPO, Ethics, Minority Affairs, and Operations and Safety committees to develop SLKT policy through data review, discussion, deliberation, and compromise. This policy was ratified by the OPTN Board of Directors in June 2016 and was implemented August 10,2017.[xxiv]

The current policy is based on medical eligibility criteria[xxv] (Table 3) and has a 'safety net' option. The medical eligibility criteria are stratified by the presence of CKD, acute kidney injury or select metabolic diseases (Table 1). The "safety net" is for those LT recipients who remained dialysis dependent, or subsequently develop advanced, persistent renal dysfunction within 60–365 days of LT alone. 'Safety net' candidates are assigned significant allocation priority in the kidney allocation system to receive an expedited kidney after liver transplant, appearing ahead of other local adult candidates.

Data suggest that 2017 policy change was successful in establishing a more directed utilization of deceased donor kidneys for SLKT without affecting the post-transplant outcomes. There was no significant change in the overall rate of SLKT over time but a reduction in SLKT utilization in patients with eGFR >30 mL/min was seen.[xxvi]

Conclusion:

MELD and PELD have proved to be useful tools in the development of liver allocation in the United States, contributing to transparency of the allocation system and use of objective elements. Evidence-based incremental changes are the best path forward to further refine and inform future policy recommendations.

Key Points:

1. MELD score is the mortality risk score used to allocate diseased donor liver for decompensated cirrhosis
2. MELD score performed better than CTP score in predicting waitlist mortality
3. Addition of serum sodium to MELD score improved the waitlist mortality by 7%
4. Creation of NLRB and implementation of acuity circles have improved the variability in MELD scores across the OPTN region
5. SLKT policy has medical eligibility criteria and 'safety net' option.

Table 1: Liver Transplant Candidate Allocation

Adult Candidates (≥ 18 years at time of registration)	Pediatric Candidates (< 18 years at time of registration)
Adult Status 1A	Pediatric Status 1A
a. Fulminant liver failure (onset of hepatic encephalopathy within 56 days of the first signs or symptoms of liver disease in a candidate without a pre-existing diagnosis of liver disease. Candidate must be admitted in the intensive care unit with at least *one* of the following conditions: • Is ventilator dependent • Requires dialysis, continuous veno-venous hemofiltration (CVVH), or continuous veno-venous hemodialysis (CVVHD) • Has an international normalized ratio (INR) > 2.0 b. Anhepatic candidates c. Primary non-function of a transplanted whole liver or liver segment from a deceased or living donor within 7 days of transplant, with aspartate aminotransferase (AST) greater than or equal to 3,000 U/L and at least *one* of the following: • International normalized ratio (INR) ≥ 2.5 • Arterial pH ≤ 7.30 • Venous pH ≤ 7.25 • Lactate ≥ 4 mmol/L e. Hepatic artery thrombosis (HAT) within 7-days of transplant, with AST ≥ 3,000 U/L and at least *one* of the following: • INR ≥ 2.5 • Arterial pH ≤ 7.30 • Venous pH ≤ 7.25	a. Fulminant liver failure (onset of hepatic encephalopathy within 56 days of the first signs or symptoms of liver disease in a candidate without a pre-existing diagnosis of liver disease. Candidate must have *one* of the following conditions: • Is ventilator dependent • Requires dialysis, continuous veno-venous hemofiltration (CVVH), or continuous veno-venous hemodialysis (CVVHD) • Has an international normalized ratio (INR) greater than 2.0 b. Primary non-function of a transplanted liver within 7 days of transplant, evidenced with at least two of the following: • Aspartate aminotransferase (AST) ≥ 2,000 U/L. • International normalized ratio (INR) ≥ 2.5 • Total Bilirubin ≥ 10 mg/dl • Acidosis, defined as one of the following: • Arterial pH ≤ 7.30 • Venous pH ≤ 7.25 • Lactate ≥ 4 mmol/L c. Diagnosis of hepatic artery thrombosis (HAT) in a transplanted liver within 14 days of transplant d. Acute decompensated Wilson's disease
	Pediatric Status 1B
	a. Biopsy-proven hepatoblastoma without evidence of metastatic disease.

• Lactate ≥ 4 mmol/L f. Acute decompensated Wilson's disease	b. Organic acidemia or urea cycle defect and an approved MELD or PELD exception meeting standard criteria for metabolic disease for at least 30 days. c. Chronic liver disease with a calculated MELD or PELD greater than 25 (and/or is a combined liver-intestine candidate), and has at least *one* of the following criteria: • Is on a mechanical ventilator • Has gastrointestinal bleeding requiring at least 30 mL/kg of red blood cell replacement (10 ml/kg for liver-intestine candidates) within the previous 24 hours • Has renal failure or renal insufficiency requiring dialysis, continuous veno-venous hemofiltration (CVVH), or continuous veno-venous hemodialysis (CVVHD) • Has a Glasgow coma score (GCS) less than 10 within 48 hours before the status 1B assignment or extension.

Table 2: Liver Transplant Standard and Non-Standard Exception Scoring

Specific Standardized MELD/PELD Score Exceptions	
Hepatocellular Carcinoma (HCC) • Indication that candidate is not eligible for resection and imaging evidence ruling out extrahepatic spread/macrovascular disease/metastatic disease with dynamic contrast enhanced computed tomography (CT) or magnetic resonance imaging (MRI) and CT chest. • Candidates with T2 (one lesion ≥ 2 cm and ≤ 5 cm in size or up to three lesions each ≥ 1 cm and ≤ 3 cm in size) HCC lesions and an alpha-fetoprotein (AFP) level ≤ 1000 ng/mL. • Candidates with T2 HCC but with an AFP > 1000 ng/mL may be treated with local-regional therapy. If AFP level falls < 500 ng/mL after treatment, the candidate is eligible for a standardized MELD/PELD exception as long as AFP level remains below 500 ng/mL. Candidates with an AFP level ≥ 500 ng/mL following local-regional therapy at any time must be referred to the NLRB for consideration of a MELD/PELD exception. • Candidates with HCC beyond T2 but within downstaging inclusion protocol (one lesion > 5 cm and ≤ 8 cm or up to three lesions each > 3 cm and ≤ 5 cm with a total diameter of all lesions ≤ 8 cm or up to five lesions each < 3 cm with a total diameter of all lesions ≤ 8 cm) and subsequently meet T2 criteria post local-regional therapy. • Candidates with lesions that do not initially meet the downstaging protocol inclusion criteria who are later downstaged and then meet eligibility for T2 lesions are not automatically eligible for a standardized MELD/PELD exception and must be referred to the NLRB for consideration of a MELD/PELD exception.	HCC Exception Scores • Candidates ≥ 18 years: ○ Initial Request/First Extension: ▪ Higher between MELD of 6 or calculated MELD ○ Subsequent Extensions: ▪ MMaT-3 • Candidates ≥ 12 and < 18 years: ○ Initial request & any extension: ▪ MELD 40 • Candidates < 12 years: ○ Initial request & any extension: ▪ MELD 40
Cholangiocarcinoma (CCA) • Candidate meets the diagnostic criteria for unresectable (because of technical considerations or underlying liver disease) hilar CCA with a malignant appearing stricture on cholangiography and at least *one* of the following:	CCA Exception Scores • Candidates ≥ 18 years: ○ Initial request & any extension: ▪ MMaT- 3

• Biopsy or cytology results demonstrating malignancy • Carbohydrate antigen 19-9 > 100 U/mL in absence of cholangitis • Aneuploidy • Hilar mass < 3 cm in radial (perpendicular to the duct) diameter • No history of transperitoneal aspiration or biopsy of the primary tumor, cross sectional imaging of the chest and abdomen excluding intrahepatic/extrahepatic metastasis, administration of neoadjuvant therapy before transplantation and negative regional hepatic lymph node involvement and peritoneal metastases by operative staging after completion of neoadjuvant therapy.	• Candidates ≥ 12 and < 18 years: ○ Initial request & any extension: ▪ MMaT • Candidates < 12 years: ○ Initial request & any extension: ▪ MPaT
Portopulmonary Hypertension Candidate will receive a MELD/PELD score exception if *all* the following are met: ▪ Documentation of portal hypertension at the time of initial exception ▪ Document via heart catheterization initial mean pulmonary arterial pressure (MPAP) ≥ 35 mmHg and initial pulmonary vascular resistance (PVR) ≥ 240 dynes*sec/cm5 (or greater than or equal to 3 Wood units (WU)) from same test date. ▪ Other causes of pulmonary hypertension have been assessed and determined to not be a significant contributing factor ▪ Initial transpulmonary gradient to correct for volume overload ▪ Documentation of treatment ▪ Document via heart catheterization within 90 days prior to submission of the initial exception either of the following: • Post-treatment MPAP < 35 mmHg and post-treatment PVR < 400 dynes*sec/cm5 (or less than 5 Wood units (WU)) from same test date. • Post-treatment MPAP ≥ 35 mmHg and < 45 mmHg and post-treatment PVR < 240 dynes*sec/cm5 (or less than 3 Wood units (WU)) from same test date.	Portopulmonary Hypertension Exception Scores • Candidates ≥ 18 years: ○ Initial request & any extension: ▪ MMaT- 3 • Candidates ≥ 12 and < 18 years: ○ Initial request & any extension: ▪ MMaT • Candidates < 12 years: ○ Initial request & any extension: ▪ MPaT
Hepatopulmonary Syndrome (HPS) Candidate will receive a MELD/PELD score exception if *all* the following are met: ▪ Ascites, varices, splenomegaly, or thrombocytopenia. ▪ A shunt, shown by either contrast echocardiogram or lung scan.	HPS Exception Scores • Candidates ≥ 18 years: ○ Initial request & any extension: ▪ MMaT- 3

▪ PaO2 < 60 mmHg on room air within 30 days prior to submission of the initial exception request. ▪ No clinically significant underlying primary pulmonary disease.	• Candidates ≥ 12 and < 18 years: ○ Initial request & any extension: ▪ MMaT • Candidates < 12 years: ○ Initial request & any extension: ▪ MPaT
Cystic Fibrosis (CF) Candidate will receive a MELD/PELD score exception diagnosis if *all* the following are met: ▪ Diagnosis confirmed by genetic analysis ▪ Forced expiratory volume at one second (FEV1) < 40 percent of predicted FEV1 within 30 days prior to submission of the initial exception request.	CF Exception Scores • Candidates ≥ 18 years: ○ Initial request & any extension: ▪ MMaT- 3 • Candidates ≥ 12 and < 18 years: ○ Initial request & any extension: ▪ MMaT • Candidates < 12 years: ○ Initial request & any extension: ▪ MPaT
Familial Amyloid Polyneuropathy (FAP) Candidate will receive a MELD/PELD score exception diagnosis if *all* the following are met: ▪ Concurrently listed for heart transplant or echocardiogram performed within 30 days prior to submission of the initial exception request an ejection fraction >40 percent. ▪ Able to walk without assistance ▪ Confirmed transthyretin (TTR) gene mutation ▪ Biopsy proven amyloid	FAP Exception Scores • Candidates ≥ 18 years: ○ Initial request & any extension: ▪ MMaT- 3 • Candidates ≥ 12 and < 18 years: ○ Initial request & any extension: ▪ MMaT • Candidates < 12 years: ○ Initial request & any extension: ▪ MPaT
Primary Hyperoxaluria Candidate will receive a MELD/PELD score exception diagnosis if *all* the following are met: ▪ Concurrently listed for kidney transplantation	Primary Hyperoxaluria Exception Scores • Candidates ≥ 18 years: ○ Initial request & any extension: ▪ MMaT

▪ Alanine glyoxylate aminotransferase (AGT) deficiency proven by liver biopsy using sample analysis or genetic analysis ▪ Estimated glomerular filtration rate (eGFR) by six variable Modification of Diet in Renal Disease formula (MDRD6), or glomerular filtration rate (GFR) measured by iothalamate or iohexol, ≤ 25 mL/min on 2 occasions at least 42 days apart	• Candidates ≥ 12 and < 18 years: ○ Initial request & any extension: ▪ MMaT+3 • Candidates < 12 years: ○ Initial request & any extension: ▪ MPaT+3
Metabolic Disease Candidate will receive a MELD/PELD score exception diagnosis if *all* the following are met: ▪ Evidence of urea cycle disorder or organic acidemia	Metabolic Disease Exception Scores • Candidates ≥ 12 and < 18 years: ○ Initial request & any extension: ▪ MMaT • Candidates < 12 years: ○ Initial request & any extension: ▪ MPaT
Hepatic Artery Thrombosis (HAT) Candidate will receive a MELD score exception for HAT if the candidate is at least 18 years old at registration and has HAT within 14 days of transplant but does not meet criteria for status 1A	HAT Disease Exception Score ▪ MELD 40

Non-Standardized MELD/PELD Score Exceptions	
Adult MELD Exception Review	Pediatric PELD Exception Review
• Budd Chiari Syndrome • Hepatic Epithelioid Hemangioendothelioma • Hepatic Hydrothorax • Hereditary Hemorrhagic Telangiectasia • Multiple Hepatic Adenomas • Neuroendocrine Tumors (NET) • Polycystic Liver Disease (PLD) • Primary Sclerosing Cholangitis or Secondary Sclerosing Cholangitis • Diffuse Ischemic Cholangiopathy	• Growth Failure or Nutritional Insufficiency • Infections • Complications of portal hypertension, including ascites and gastrointestinal bleeding • Pruritus • Metabolic Liver Diseases • Metabolic Bone Disease

Table 3: Current SLKT Policy

Candidate's Transplant Nephrologist Confirms a Diagnosis of	Transplant Program Must Document at least 1 of the following
Chronic kidney disease (CKD) with a measured or calculated GFR ≤60 mL/min for > 3 months	At least one of the following: • That the candidate has begun regularly administered dialysis as a patient with ESRD in a hospital-based, independent non-hospital-based, or home setting. • At the time of registration on the kidney waiting list, that the candidate's most recent measured or calculated CrCl or GFR is ≤30 mL/min. • On a date after registration on the kidney waiting list, that the candidate's measured or calculated CrCl or GFR is≤30 mL/min
Sustained acute kidney injury (AKI)	At least one of the following, or a combination of both of the following, for the last 6 weeks: • That the candidate has been on dialysis at least once every 7 days. • That the candidate has a measured or calculated CrCl or GFR ≤25 mL/min at least once every 7 days. If the candidate's eligibility is not confirmed at least once every 7 days for the last 6 weeks, the candidate is not eligible to receive a liver and a kidney from the same donor.
Metabolic disease	A diagnosis of at least one of the following: • Hyperoxaluria • Atypical hemolytic uremic syndrome from mutations in factor H or factor I • Familial nonneuropathic systemic amyloidosis • Methylmalonic aciduria

Figure 1 Evolution of Liver Transplant Allocation and Distribution in the United States

Figure 2: Formula to calculate MELD score, MELD-Na score and PELD score

Figure 3 Shift Towards Acuity Circle Distribution

Figure 4 Current Acuity Circle Distribution of Deceased Donor Livers

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Figure 1 Evolution of Liver Transplant Allocation and Distribution in the United States

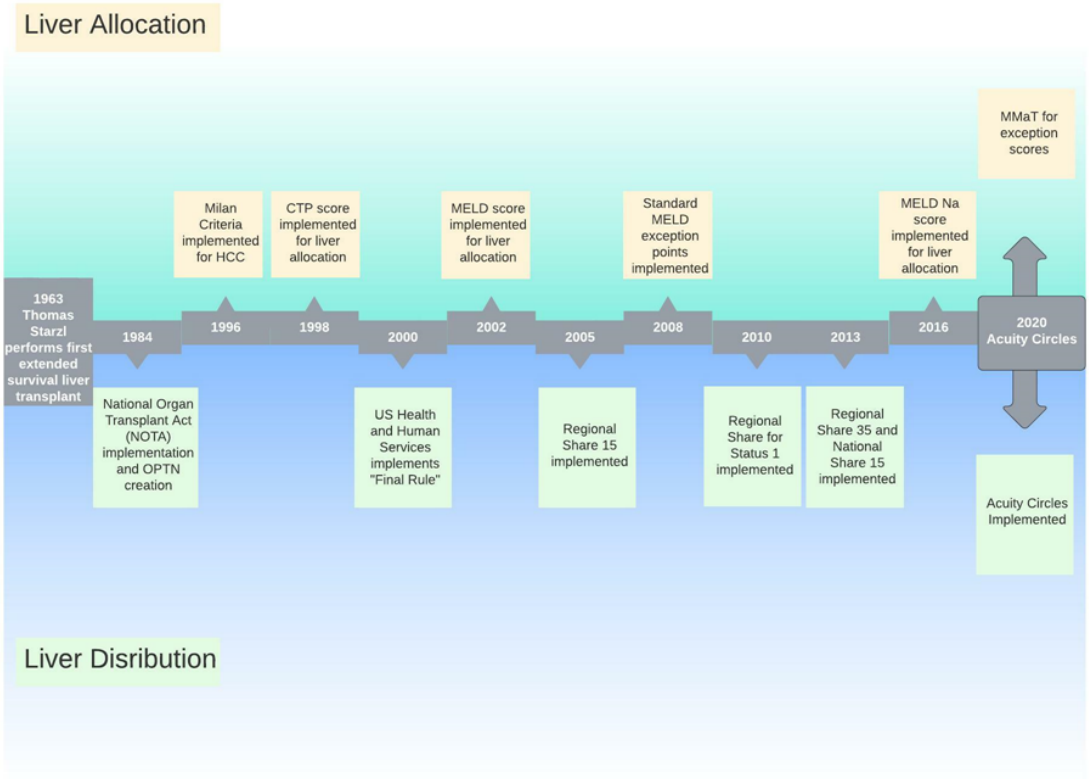


Figure 2: Formula to calculate MELD score, MELD-Na score and PELD score

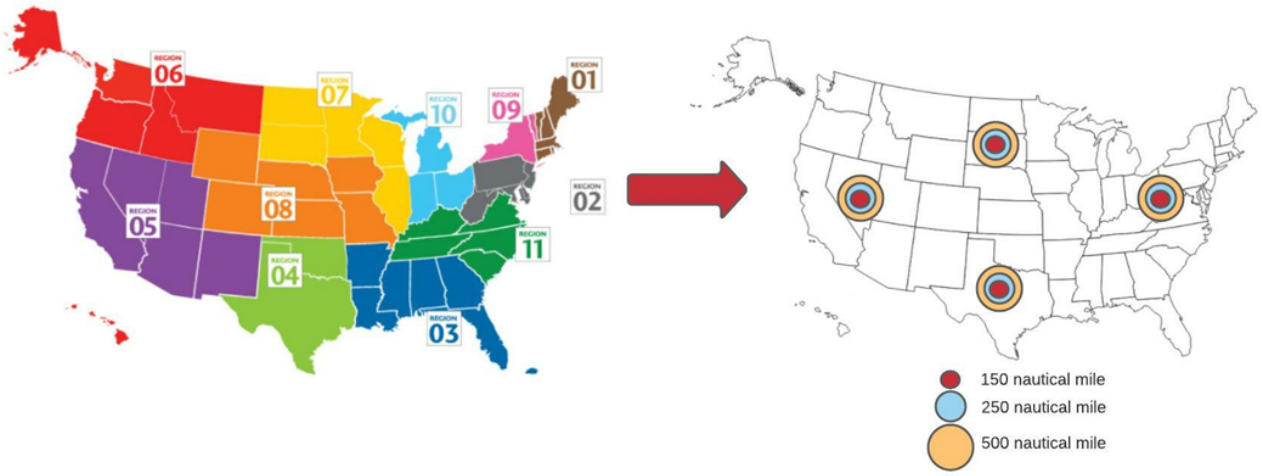
MELD score: 0.957 x Log_e(creatinine mg/dL) + 0. 378 x Log_e(bilirubin mg/dL) + 1.120 x Log_e(INR) + 0.643

MELD-Na = MELD(i) + 1.32(137-Na) – [0.033*MELD(i)*(137-Na)]*

PELD Score: *0.436 (Age (<1 YR.)) – 0.687 x Log_e (albumin g/dL) + 0.480 x Log_e (total bilirubin mg/dL) + 1.857 x Log_e (INR) +0.667 (Growth failure*)*

**> 2 Standard deviations based on age and gender using the most recent Centers for Disease Control and Prevention's (CDC) National Center for Health Statistics pediatric clinical growth chart*

Figure 3 Shift Towards Acuity Circle Distribution



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