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# Model for End-Stage Liver Disease–Based Organ Allocation: Managing the Exceptions to the Rules

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Since February 27, 2002, the Model for End-Stage Liver Disease (MELD) score has prioritized waitlisted liver transplant candidates in the United States. The MELD score effectively predicts 90-day waitlist mortality,[1,2] yet there are conditions for which it does not accurately predict this risk.[3-5] In these cases, transplant centers may apply for exception points through a regional peer review system of regional review boards (RRBs) that consist of physicians, coordinators, and nonmedical representatives.[6]

Exception point applications are divided into (1) recognized exceptional diagnoses (REDs) where data are thought sufficient to bypass formal RRB approval, provided patients meet prespecified clinical criteria (eg, hepatocellular carcinoma [HCC]), and (2) non-REDs, where a formal RRB review and vote determine approval.[6]

The number of exception applications has risen since 2002, and by 2010, 33% of all transplant recipients received exception points.[7,8] In response to the increase, the MELD Exception Study Group conducted the only formal evaluation of exception policies in 2006. They published guidelines for granting exception points, including calls for further research into conditions for which limited data existed.[3]

Managing allocation of exception points is of great importance, because waitlist candidates receiving exception points have lower waitlist mortality and increased odds of transplantation.[9-12] Herein we highlight specific examples of pitfalls in exception allocation and propose modifications to improve efficiency and fairness.

## Hepatocellular Carcinoma

Waitlist candidates with HCC within Milan criteria receive standardized exception points that are based on a concern for increased waitlist dropout because of tumor growth.[13] Since 2002, this policy has been modified 3 times to better reflect the true risk of waitlist dropout for HCC patients. Under the current system, formalized data on tumor number, size, and

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explant pathology are submitted through UNet by each transplant center by using a common classification system.[13] Despite modifications and standardized data collection, flaws exist in the HCC exception point system. Compared with non-HCC candidates with comparable MELD scores, HCC waitlist candidates continue to have decreased waitlist dropout, despite a similar odds of transplantation.[13] There also is marked geographic variability in the risk of waitlist dropout for HCC because the system does not account for regional variability in access to transplantation.[11,12,14] Thus, despite a formal and stringent system, ongoing reassessment of HCC exception allocation is needed.

## Primary Sclerosing Cholangitis

Excluding HCC, 12% of primary sclerosing cholangitis transplant recipients receive exception points.[8] Published consensus recommendations state that exception points for primary sclerosing cholangitis patients with bacterial cholangitis be limited to those with documentation of a history of bacteremia and/or septic complications while on suppressive antibiotic therapy.[5,8] Since 2007, only 3% of such applications contained this documentation, and 75% did not meet the recommendations, yet 80% were approved.[6] These data highlight the need to provide an oversight mechanism to ensure that recommendations are followed.

## Hepatopulmonary Syndrome

Hepatopulmonary syndrome (HPS) is classified as a RED, with exception criteria driven by studies published before and early in the MELD exception era that found increased preoperative and postoperative mortality in those with severe hypoxemia.[15-18] The only published analysis of national transplant data found that HPS patients granted exceptions may be advantaged on the basis of improved waitlist survival with similar post-transplant survival compared with other waitlist candidates.[19] However, the data do not include parameters to verify the presence of HPS and do not account for variability in HPS screening. Moreover, a recent U.S. prospective multicenter screening study found increased mortality in HPS patients relative to non-HPS patients across a spectrum of severity of oxygenation abnormalities.[16] Thus, there is a need to collect data to define and validate clinical parameters that identify HPS patients at highest risk of adverse outcomes and to guide modification of exception allocation.

## Portopulmonary Hypertension

Moderate and severe portopulmonary hypertension (POPH), sufficiently responsive to medical therapy, has been a RED since 2006,[20] which was based on case reports and small series showing resolution of POPH in a small subset of patients after liver transplantation.[21-23] However, data on cardiopulmonary testing before or on medical therapy, specific medical POPH therapies used, and information on evaluation for other causes of pulmonary arterial hypertension are not collected in national transplant data. Therefore, the opportunity to define whether liver transplantation is beneficial in POPH and to identify predictors of successful post–liver transplantation outcome is lost. These observations highlight the need to prospectively collect data on a large number of waitlist candidates to develop evidence-

based criteria for exception point allocation, particularly when exceptions are based on limited data.

## Potential Solutions

To achieve the goal of MELD exception policy and to remain responsible stewards of a scarce resource, the transplant community needs to standardize allocation and evaluation of outcomes for MELD exceptions. The examples cited above highlight deficiencies in both of these areas. We propose 3 actions to address these deficiencies.

First, we recommend the formation of a national MELD exception review board that would operate within the United Network for Organ Sharing transplant framework. Such a board would be charged with ensuring uniformity in the review of and access to exception points by overseeing the development of standardized and evidence-based policies across regions for exception points.[10] A specific mandate for the board would be to ensure that the allocation of exception points accommodates the geographic variability in access to transplantable organs, in accordance with the Institute of Medicine 1999 report emphasizing the uniform allocation of organs across geographic areas.[24]

Second, allocation of exception points for both REDs and non-REDs must be accompanied by accurate and complete documentation of relevant disease states and contributing factors. This would ensure compliance with policies and help to define the impact of each MELD exception protocol on outcomes.[10] This could be patterned after the current system of HCC exception points.

Third, we propose a network of multi-center collaborations, who would report to the national board. These collaborative groups would be charged with developing evidence-based guidelines for each MELD exception diagnosis and undertake periodic reviews of policies that are based on disease and outcome data. This would ensure that patients afforded exception points merit them, and that the number of assigned exception points is aligned with the true risk of waitlist dropout.

We acknowledge that the proposed actions would require significant change. However, we believe that centralization and standardization of the exception system that integrate ongoing evidence-based peer review would be more equitable and also more transparent to patients, physicians, and the greater public.

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