

At-a-Glance

Proposal to Delay HCC Exception Score Assignment

- **Affected/Proposed Policy:** 9.3.G Candidates with Hepatocellular Carcinoma (HCC)

- **Liver and Intestinal Organ Transplantation Committee**

Candidates with a MELD/PELD score exception for HCC receive high priority on the liver waiting list, especially as their exception scores may increase automatically every three months. These candidates have significantly lower dropout rates (i.e., removal from the waiting list for death or for reasons related to the HCC) than non-HCC candidates, with the exception of those areas of the country with lengthy waiting times. The proposed solution to address the disparities in drop-out rates between patients with HCC exceptions and those without is to delay the score assignment by 6-months. Simulation modeling has shown that this would equalize the transplant and drop-out rates for those with and without HCC exceptions. In areas of the country with shorter waiting times to transplant, the delay will also allow a window of time for centers to observe candidates with rapidly growing tumors who may have very poor outcomes with a transplant. At least one study indicates that candidates with HCC exceptions in regions with shorter waiting times to transplant, where this “biologic test” is not met due to rapid transplantation, have worse post-transplant outcomes.

- **Affected Groups**

Transplant Administrators
Transplant Data Coordinators
Transplant Physicians/Surgeons
Transplant Program Directors
Organ Candidates

- **Number of Potential Candidates Affected**

From 2008 through 2012, an average of 1,774 candidates were listed with an HCC exception that met policy criteria each year; this number was 1,937 in 2012. This represented 13.8% of candidates added to the liver waiting list during the period.

- **Expected Impact on Strategic Plan and Adherence to OPTN Final Rule**

This proposal would increase access to transplants for candidates without HCC exceptions.

Proposal to Delay HCC Exception Score Assignment

Affected/Proposed Policy: 9.3.G Candidates with Hepatocellular Carcinoma (HCC)

Liver and Intestinal Organ Transplantation Committee

Public comment response period: March 14, 2014 – June 13, 2014

Summary and Goals of the Proposal

Candidates with a MELD/PELD score exception for HCC receive high priority on the liver waiting list, especially as their exception scores may increase automatically every three months. These candidates have significantly lower dropout rates (i.e., removal from the waiting list for death or being too sick) than non-HCC candidates, with the exception of those areas of the country with lengthy waiting times. The proposed solution to address the disparities in drop-out rates between patients with HCC exceptions and those without is to delay the score assignment by 6-months. Simulation modeling has shown that this would reduce the disparity in the transplant and drop-out rates for those with and without HCC exceptions. In areas of the country with shorter waiting times to transplant, the delay will also allow a window of time for centers to observe candidates with rapidly growing tumors who may have very poor outcomes with a transplant.

Background and Significance of the Proposal

The priority assigned to candidates with HCC exceptions has been modified several times since first included in OPTN policy in 1998. In that year, the liver allocation policy was modified such that patients with Stage 1 or 2 HCC whose condition met specified criteria could be listed in Status 2B. When the MELD/PELD system was implemented in early 2002, patients with stage T2 could be registered with a MELD/PELD score equivalent to a 30% probability of candidate death within 3 months, which was a MELD score of 29¹. Candidates were eligible for a MELD score equal to an additional 10 percentage point increase in their mortality risk every 3 months. An assessment of the first 6-months of this policy revealed that patients with a calculated MELD score of 29 had a transplant rate of 27% versus 42.9% for Stage T2 HCC patients. Based on these data, the score assigned for Stage T2 exceptions was reduced to 24 (mortality risk of 15%) in 2003. A subsequent update in the MELD score mortality curve in 2005 reduced the initial MELD score assignment to 22.

Despite these reductions in priority, candidates with HCC exceptions still have significantly higher transplant rates and lower dropout rates (i.e., removal from the waiting list for death or being too sick) than non-HCC candidates^{2,3}. The proposed solution to address the disparities in drop-out rates between patients with HCC exceptions and those without is to delay the exception score assignment for 6 months following the initial application submission. Under this proposal, HCC applications would be submitted as they are currently, but candidates would be listed at their calculated MELD/PELD scores for the first three months (initial application) and for the first three-month extension as long as the candidate continues to meet the policy criteria. Currently, the median calculated MELD/PELD score at the time of an initial HCC exception application meeting policy criteria is 11. At six months (the second extension), candidates will receive a score of 28.

¹ Candidates with Stage T1 HCC were also eligible for automatic upgrades, but this priority was removed in 2004.

² Washburn K, Edwards E, Harper A, Freeman RB. Hepatocellular Carcinoma Patients Are Advantaged in the Current Liver Transplant Allocation System. *American Journal of Transplantation* 2010; 10: 1652–1657

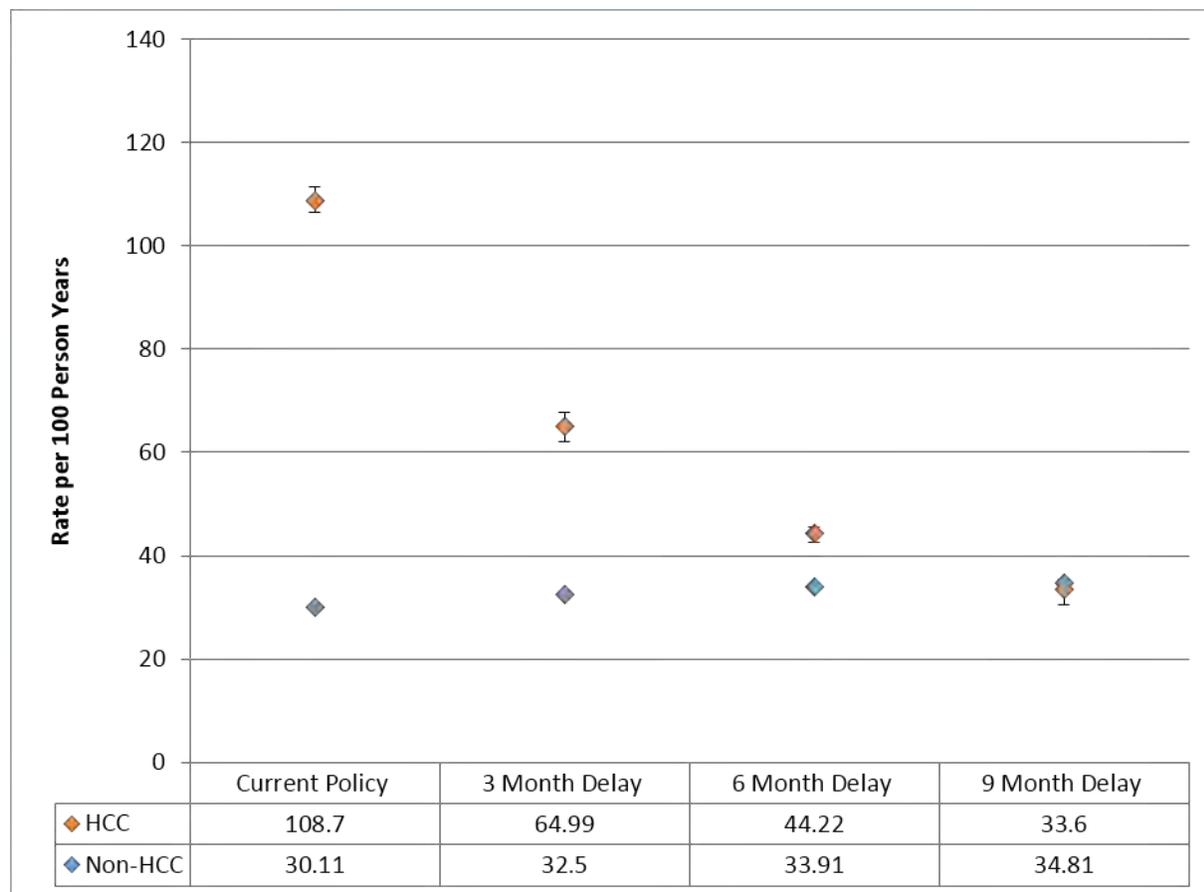
³ Massie AB, Caffo B, Gentry SE, Hall EC, Axelrod DA, Lentine KL, Schnitzler MA, Gheorghian A, Salvalaggio PR, Segev DL. MELD Exceptions and Rates of Waiting List Outcomes. *Am J Transplant*. 2011 Nov;11(11):2362-71.

Currently, candidates receive scores of 22, 25, and 28 at these time intervals (initial application, first extension at the months, second extension at 6 months).

Supporting Evidence and/or Modeling

LSAM modeling suggests that this would result in similar transplant rates between those with HCC exceptions and those without, at least in regions with lower waiting times (Figure 1).⁴

Figure 1: Comparison of Transplant Rates per 100 Person-years: Current Policy versus Delayed Scores



This equalization occurs naturally in areas with longer waiting times, and may serve as a test for the biology of HCC. In those regions with longer waiting times, candidates whose tumors rapidly progress (and will likely have poor outcomes) wait long enough such that they can be removed from waiting list if the prognosis with a transplant deteriorates. At least one study indicates that candidates with HCC exceptions in regions with shorter waiting times to transplant, where this “biologic test” is not met due to rapid transplantation, have worse post-transplant outcomes.⁵ A

⁴ J. Heimbach, R. Hirose, K. Olthoff, W. Kim, D. Schladt, H. Xiong, J. Liu, A. Harper, P. Stock Delayed HCC MELD Exception Score Improves Disparity in Access to Liver Transplant. Presented at the 2013 American Transplant Congress.

⁵ K. Halazun, E. Verna, B. Samseith, J. Guarrera, T. Kato, R. Brown Jr, J. Emond A Priority Pass to Death—Prioritization of Liver Transplant for HCC Worsens Survival, Center for Liver Disease And Transplantation, Columbia University Medical Centre, New York, NY. Presented at the 2013 American Transplant Congress, Seattle, WA.

delay would not impact regions with longer waiting times, where drop-out rates are already similar and the built in delay for the “biologic test” already exists.

As noted above, several studies have shown that candidates with HCC exceptions are advantaged relative to candidates without HCC exceptions. Washburn, et al, reported that candidates without HCC exceptions had significantly higher drop-out rates than those with HCC exceptions ($p < 0.0001$). Massie, et al, reported that both HCC and other exceptions “were associated with decreased risk of waitlist mortality compared to non-exception patients with equivalent listing priority (multinomial logistic regression odds ratio [OR] = 0.47 for HCC, OR = 0.43 for other, $p < 0.001$) and increased odds of transplant (OR = 1.65 for HCC, OR = 1.33 for other, $p < 0.001$).”

Alternatives Considered

The Committee initially considered the current proposal which delays any additional priority for the first 6 months. In subsequent Committee discussions, several Committee members suggested that candidates with controlled disease could be assigned a lower score after the first three months (e.g., a score of 14 or 15) to be eligible for local offers (score of 15) or for extended criteria donors (score of 14). The Committee ultimately agreed that candidates should be listed at the calculated MELD/PELD score during the 6-month delay period, and that the center could appeal to the RRB in cases when higher priority is required.

In its effort to assign more appropriate priority to candidates with HCC, the Committee is also proposing another modification to the HCC exception policy, which would cap the HCC score at 34. The two proposals are being circulated for public comment separately, but could be combined into one programming effort if both are approved.

Expected Impact on Living Donors or Living Donation

Not applicable.

Expected Impact on Specific Patient Populations

No expected impact on specific patient populations.

Expected Impact on OPTN Strategic Plan, and Adherence to OPTN Final Rule

The proposal is intended to reduce waiting list mortality in candidates without HCC exceptions by increasing their access to donated livers.

Plan for Evaluating the Proposal

This proposal is intended to reduce the disparity in waiting list drop-out rates (removals for death/“too sick”/other removals due to HCC) between HCC and non-HCC candidates, particularly in regions with relatively short waiting times to transplant. As such, drop-out rates for these groups will be compared at 6-months, 1 year, 2-years and, if deemed necessary by the Committee, up to 3-years post-implementation of the policy. A review of the existing data at 6 months after implementation will be performed to determine if a sufficient number of events have occurred to support the analysis. For each analysis, a comparable time period prior to implementation will serve as the baseline. Event rates (transplant rates, drop-out rates) will be compared overall and, if possible, by region. To detect unintended consequences, event rates pre- and post-policy will

also be estimated by age (pediatric vs. adult) and by ethnicity. Note: A reasonable lag time (6-8 weeks) should be expected for each report to allow time for more complete data reporting and for analyzing/collating the results. Disclaimer: Since these are observational data, it should be noted that any observed differences in the results (pre- vs. post-implementation) may be due to external factors and are not necessarily due to the impact of the policy.

Additional Data Collection

This proposal does not require additional data collection.

Expected Implementation Plan

This proposal will require programming in UNetSM.

Communication and Education Plan

Communication Activities			
Type of Communication	Audience(s)	Deliver Method(s)	Timeframe
Policy Notice following Board Approval	Liver candidates, transplant surgeons, transplant physicians, transplant coordinators, transplant administrators	OPTN and UNOS websites	1 month after Board approval
System Notice upon implementation	All UNet SM Users	Blast e-mail, UNet SM notice	30 days before the implementation, and again upon implementation

Education/Training Activities			
Education/Training Description	Audience(s)	Deliver Method(s)	Timeframe and Frequency
Brief Training Session	All UNet SM Users	Webinar	Prior to Implementation

Compliance Monitoring

At transplant hospitals, UNOS site surveyors will continue to review a sample of recipient medical records, and any material incorporated into the medical record by reference, for documentation that data reported through UNetSM is consistent with source documentation.

Policy or Bylaw Proposal

Proposed new language is underlined (example) and language that is proposed for removal is struck through (~~example~~).

9.3.G Candidates with Hepatocellular Carcinoma (HCC)

Upon submission of the required information to the OPTN Contractor, candidates with Hepatocellular Carcinoma (HCC) that have stage T2 lesions and meet the criteria according to Policies 9.3.G.i through vi below will be listed at their calculated ~~receive an initial~~ MELD or PELD score ~~equivalent to a 15 percent risk of 3-month mortality.~~

9.3.G.vi *Extensions of HCC Exceptions*

In order for a candidate to maintain an HCC approved exception, the transplant program must submit an updated MELD/PELD exception application every three months. The candidate will receive the additional priority until transplanted or is found unsuitable for transplantation based on the HCC progression. Upon submission of the first extension, the candidate will be listed at the calculated MELD/PELD score. Upon submission of the second extension, the candidate will be assigned a MELD/PELD score equivalent to a 35 percent risk of 3-month mortality (MELD 28/PELD 41). For each subsequent extension, A ~~the~~ candidate will receive additional MELD or PELD points equivalent to a 10 percentage point increase in the candidate's mortality risk every three months. ~~until the candidate receives a transplant or is unsuitable for transplantation based on the candidate's HCC progression.~~

To receive the extension, the transplant program must submit an updated MELD exception application ~~every three months~~ that contains all of the following:

1. Submit an Hepatocellular Carcinoma (HCC) MELD/PELD score exception application with an updated narrative
2. Document the tumor using a CT or MRI
3. Specify the type of treatment if the number of tumors decreased since the last application.

Invasive studies such as biopsies or ablative procedures and repeated chest CT scans are not required after the initial application is approved. If a candidate's tumors have been resected since the previous application, then the transplant program must submit the extension application to its RRB for prospective review.

Candidates with Class 5T lesions will receive a MELD or PELD equivalent to a 10 percentage point increase in the candidate's mortality risk every three months, without RRB review, even if the estimated size of residual viable tumors falls below stage T2 criteria due to ablative therapy.