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Journal

Hepatology, 61(5)

ISSN

0270-9139

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Publication Date

2015-05-01

DOI

10.1002/hep.27704

Peer reviewed

Delayed Hepatocellular Carcinoma MELD Exception Score Improves Disparity in Access to Liver Transplant in the US

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Abstract

The current system granting liver transplant candidates with hepatocellular carcinoma (HCC) additional model for end-stage liver disease (MELD) points is controversial due to geographic disparity and uncertainty regarding optimal prioritization of candidates. The current national policy assigns a MELD exception score of 22 immediately upon listing of eligible patients with HCC. The aim of this study was to evaluate potential effects of delays in granting these exception

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

Supplementary Material Supplementary Methods: Methods used to create the liver simulated allocation model input file.

points on transplant rates for HCC and non-HCC patients. We used Scientific Registry of Transplant Recipients data and liver simulated allocation modeling (LSAM) software and modeled (1) a 3-month delay before granting a score of 25; (2) a 6-month delay before granting a score of 28, and (3) a 9-month delay before granting a score of 29. Of all candidates waitlisted between January 1 and December 31, 2010 ($n = 28,053$), 2773 (9.9%) had an HCC MELD exception. For HCC candidates, transplant rates would be 108.7, 65.0, 44.2, and 33.6 per 100 person-years for the current policy and for 3-, 6-, and 9-month delays, respectively. Corresponding rates would be 30.1, 32.5, 33.9, and 34.8 for non-HCC candidates.

Conclusion—A delay of 6 to 9 months would eliminate the geographic variability in the discrepancy between HCC and non-HCC transplant rates under current policy, and may allow for more equal access to transplant for all candidates.

Keywords

Allocation; geographic disparity; model for end-stage liver disease; Scientific Registry of Transplant Recipients; waiting list

Historically, hepatocellular carcinoma (HCC) accounted for a small proportion of liver transplants in the US, in part because the prior organ allocation system based on waiting time limited access to liver transplant and in part because posttransplant recurrence of the malignancy resulted in poor patient survival. In the past two decades, the seminal paper by Mazzaferro et al (1) established the efficacy of liver transplant for patients with HCC within specific size criteria, known as the Milan criteria.

The model for end-stage liver disease (MELD)-based allocation system, implemented in 2002, assigns "exception" scores for patients with HCC within the Milan criteria. The HCC exception score, adjusted every 3 months, was intended to reflect candidates' expected waitlist mortality due to progression of the tumor. It was quickly determined that the initial scores assigned to waitlisted HCC candidates overestimated the likelihood of disease progression and/or death while waiting, and the policy was adjusted to decrease the score in 2003 and again in 2005 (2;3). The current system of allocation for candidates with HCC has been in place since the 2005 adjustment.

Even under the current policy, analyses of waitlist survival demonstrate that candidates with HCC are much less likely than candidates without HCC to die or to be removed from the list while waiting (4). In addition, candidates with HCC undergo transplant at a higher rate than candidates without HCC, indicating a substantial advantage over non-HCC candidates, who principally have complications of end-stage liver disease and thus high native MELD scores (5). Despite the increased transplant rate, posttransplant survival for patients with HCC remains inferior to survival of patients without HCC (6;7). Because liver allocation for HCC candidates is currently based on an assigned score derived from an estimation of waitlist survival that does not appear to accurately reflect the actual waitlist dropout rate, and because this has resulted in over- prioritization of candidates with HCC in most areas of the US, policy makers have considered various proposals to make the allocation system more equitable between candidates with and without HCC.

Based on the observation that in some regions of the US with high median MELD scores at the time of liver transplant, the transplant rate for HCC and non-HCC patients is similar (4), we hypothesized that delaying granting the MELD exception score may result in more equitable transplant rates across the country. In this study, we considered maintaining the initial exception score of 22 for HCC candidates but with a mandatory waiting period (3, 6, or 9 months) until a candidate would become eligible to receive organ offers. The primary aim of the study was to evaluate the impact of a potential new policy instituting such delays, compared with the current allocation policy, on the transplant rate for HCC and non-HCC patients. Secondly, we modeled the impact of the delays on mortality rates of HCC and non-HCC patients

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), and has been described elsewhere (8). The Health Resources and Services Administration (HRSA), US Department of Health and Human Services, provides oversight of the activities of the OPTN and SRTR contractors.

Study Rationale and Design

Because the median MELD score at the time of liver transplant varies considerably by region, simply lowering the initial assigned HCC exception score across all regions would result in significantly longer waiting times for HCC patients in high MELD regions, thus producing a negative effect in areas where transplant rates are already similar between HCC and non-HCC patients. To account for the variability in MELD at the time of transplant without disproportionately affecting HCC patients in high MELD regions, we considered assigning an initial score of 22 but with a mandatory waiting period before a patient would become eligible for offers with this exception score. The score would continue to rise at the current schedule every 3 months, while the candidate would not be eligible for offers at that score until the delay period was completed. Waitlisted candidates could still receive offers based on their calculated MELD scores during this delay. This mandatory delay would have no effect in high-MELD regions as HCC candidates already wait substantially longer than the proposed mandatory delay period. However, the mandatory delay time would affect low-MELD regions and could reduce the disparity in access to transplant between HCC and non-HCC patients.

Using the liver simulated allocation modeling (LSAM) software, we modeled the effect of instituting a mandatory delay before a candidate with HCC who was eligible for standard MELD exception scores could receive offers. Thus, we considered four scenarios: (1) current policy without a delay (exception MELD 22, corresponding to 15% risk of 90-day mortality at listing); (2) 3-month delay (with approved exception MELD 25, corresponding to 25% risk of 90-day mortality); (3) 6-month delay (with approved exception MELD 28, corresponding to 35% risk of 90-day mortality); and (4) 9-month delay (with approved

exception MELD 29, corresponding to 45% risk of 90-day mortality). Table 1 summarizes the waiting periods and subsequent escalation of the exception scores for the four scenarios.

LSAM Modeling

Details of the simulated modeling process using the LSAM software have been described (9). Actual candidate and donor data are needed to implement LSAM. The data set used for this analysis included candidates who were on the liver transplant waiting list at any time between January 1, 2010, and December 31, 2010, and all donor organs offered during that same period.

LSAM uses observed candidates to form input files to which simulation algorithms are applied to predict outcomes under the proposed policy change. In this study, in order to estimate waitlist outcomes for candidates who underwent transplant after only a short waiting time in reality, it was necessary to append the status histories of several candidates together to create the input file. To best approximate the outcomes, the status histories that matched based on expected mortality were selected and assembled together. The numerical details of the methods used to create the input file are found in the supplementary material. Subsequent events including transplant and posttransplant outcomes were predicted following the standard LSAM procedures.

Four sets of LSAM runs, each consisting of 10 iterations, were performed for the four scenarios described in Table 1. Under the current liver allocation system, candidates meeting specified conditions, corresponding to the Milan criteria, were assigned a MELD exception score of 22 and received additional MELD points equivalent to a 10 percentage point increase in mortality every 3 months until they underwent transplant or stopped extending their exception scores due to becoming unsuitable for transplant (e.g., tumor progression beyond the Milan criteria) or other reasons (10). For the subsequent scenarios with specified delays, calculated biological MELD scores or MELD scores based on non-HCC exceptions were used for allocation for HCC candidates during the delay periods. For example, for the 3-month delay scenario, HCC candidates were assigned a MELD exception score of 25 after waiting for 3 months, which subsequently increased according to the same schedule as for current patients.

The primary outcome of interest was the transplant incidence rates for HCC and non-HCC candidates. After 10 iterations for each scenario were implemented using LSAM, means, standard deviations, and ranges of the numbers of waitlist removals due to liver transplant were calculated; theses were then used to compute the transplant incidence rate. Secondarily, we assessed the numbers of deaths and mortality rates.

In calculating the transplant incidence rate, time on the waiting list began at the latter of the registration date or January 1, 2010, and ended at the earliest of first transplant, removal, death, or December 31, 2010. Thus, the incidence of liver transplant was calculated as:

$$Incidence\ rate\ of\ LTx = \frac{\Sigma\ transplants}{\Sigma\ Time\ on\ waitlist}$$

In calculating the denominators of the incidence rate, for candidates who received their first standard MELD exception score for HCC before 2010 or at the time of first listing, the entire time on the waiting list was considered "HCC time." For candidates who received their first standard MELD exception score for HCC during 2010, the period prior to receiving the score was counted as "non-HCC time" and the period afterward as "HCC time." For candidates who never received an HCC exception score, the entire time on the waiting list was considered "non-HCC time."

The incidence of waitlist deaths (including deaths occurring within 90 days after waitlist removal) was calculated similarly. Time on the waiting list or within 90 days after removal began at the latter of the registration date or January 1, 2010, and ended at the earliest of first transplant, death, 90 days after removal, or December 31, 2010.

Results

Table 2 summarizes characteristics of liver transplant candidates in 2010; data from these candidates constituted the basis for the LSAM modeling. The data set included 28,053 pediatric and adult candidates, including 2773 (9.9%) who had an HCC exception score at least once before or during 2010. Not surprisingly, candidates with HCC were older and more likely to be male and of non-white race than non-HCC candidates. In both groups, hepatitis C virus infection was the most common underlying cause of liver disease, but the preponderance was stronger among HCC candidates. As expected, compared with non-HCC counterparts, HCC candidates had substantially lower biological MELD scores, and their allocation MELD scores were boosted higher by the exception scores.

In 2010, 5863 livers originating from 5786 unique donors were transplanted. The mean (± standard deviation) donor age was 38.8 (± 18.3) years. The majority (59.3%) of donors were male and white. Donation after circulatory death accounted for 4.6% of donors. Causes of death included anoxia (23.2%), cerebrovascular accident/stroke (37.3%), head trauma (36.7%), and other (2.7%).

Table 3 summarizes the descriptive outcomes of the simulations performed for the four scenarios. As expected, compared with the current policy of no delays, progressively increasing the length of delay resulted in fewer transplants for candidates with HCC exception scores, but the total number of transplants remained steady. The proportion of transplants in HCC exception candidates decreased from 20.0% under the current policy to 10.4% with a 6-month delay and 8.2% with a 9-month delay. A reciprocal increase occurred in the number of non-HCC transplants, from 4712 under the current policy to 5226 and 5345 with 6- and 9-month delays, respectively.

Similarly, transplant rates for HCC candidates decreased from 108.7 per 100 candidates per year under the current policy to 44.2 per 100 candidates per year with a 6-month delay and 33.6 per 100 candidates per year with a 9-month delay. Transplant rates for non-HCC patients increased with increasing duration of delay; rates for HCC and non-HCC patients became similar (33.6 versus 34.8, respectively) in the 9-month delay scenario.

Regarding the match MELD at transplant, there was a modest, gradual decrease for non-HCC patients, but no change for HCC patients. There was a similar decrease in the laboratory MELD score at transplant for non-HCC patients. As expected, with longer delays, the laboratory MELD for HCC patients at transplant increased. Even with the longest delay, however, the laboratory MELD remained substantially lower for HCC than for non-HCC patients.

Finally, we examined the potential indirect effect of the delay on waitlist deaths. Mortality estimates suggest that the effect on mortality would be more modest than the effect on transplants. Compared with the current policy, 6- and 9-month delays resulted in approximately 40 more deaths among HCC candidates and approximately 70 fewer deaths among non-HCC candidates, a net reduction of 30 deaths overall. Death rates for both HCC and non-HCC candidates did not change appreciably.

Figure 1 and Table 4 display data for the 11 regions. Figure 1A demonstrates that when the data are compared across regions, under the current policy there is a negative correlation between the median match MELD score and the gap between HCC and non-HCC transplant rates, indicating that in regions where patients with relatively low MELD scores can undergo liver transplant, patients with HCC exception scores have better access. Table 4 describes the gap between transplant rates for HCC and non-HCC patients for the four scenarios for the US as a whole and by region. As the delay increased, the gap between HCC and non-HCC rates decreased progressively for the US as a whole, as shown in Table 3, and became essentially zero with the 9-month delay scenario. In Figure 1B, with delays of 6 or 9 months, the aforementioned negative correlation disappeared and HCC and non-HCC rates became much more homogeneous across regions. With a 9-month delay, HCC candidates in low-MELD regions may be slightly disadvantaged, as some candidates with biological MELD scores of less than 29 would undergo transplant before HCC candidates became eligible to receive an organ.

Discussion

The result of our analysis of four scenarios using LSAM demonstrates that instituting a delay in the receipt of HCC exception points may significantly reduce disparities in access to liver transplant between HCC and non-HCC candidates. Within the constraints of modeling, the application of a mandatory delay resulted in 1) closer alignment in transplant rates for HCC and non-HCC patients; 2) modest but consistent reduction in the match and laboratory MELD scores in non-HCC patients, and 3) equilibration across geographic regions of transplant rates for HCC and non-HCC patients. Our results also showed that while the delay renders transplant rates similar between HCC and non-HCC patients, it may not affect mortality rates of these two groups appreciably. The lack of increase in mortality accompanying reduction in transplant rates in HCC patients in this study further supports that priority granted for HCC patients in the current allocation system remains excessive.

The current system of liver allocation for candidates with HCC MELD exception scores allows them to undergo transplant at a higher rate with a lower chance of waitlist dropout than non-HCC candidates (4). The intent of granting MELD exception scores was not to

provide advantage to one group of candidates over another, but to recognize that for certain patients the underlying liver disease does not contribute to short-term mortality. As stated by Freeman et al on standard MELD exceptions, other factors than MELD contribute to defining the need for liver transplantation (11). Given that more than one-fourth of deceased donor livers were allocated to patients with HCC in 2012, the level of priority HCC patients receive has a major impact on waitlisted candidates in general.

Over the past several years, a progressive rise in median MELD score at transplant has been observed (7). An important driver of this trend may be the substantial number of patients receiving priority scores for HCC, combined with the critical shortage of available donor livers. An additional potential benefit of instituting a mandated delay in HCC patients is that longer waiting times before transplant for candidates with HCC may allow for selection of candidates with more favorable tumor biology and thus may ultimately improve outcomes.

In the recent past, several alternative methods of changing allocation for HCC candidates have been considered. One proposal would be to cap the score an HCC candidate could achieve at some arbitrary limit, for example 28, 29, or 31. When this approach was modeled, it did not equalize transplant rates, and would seem at least in the short run to unfavorably affect HCC exception score patients in high MELD regions. Another alternative would be to cap the score at the median MELD score for each donation service area, although this would require frequent recalibration of the system since median MELD scores are not static, presenting an implementation challenge. The idea of simply lowering the initial score was met with concerns over the differential impact on high MELD regions, as previously discussed. Lastly, the initial exception score could be set based on the median MELD at transplant for each region. However, such a complex system would be difficult to program and monitor and may potentially worsen geographic disparity in access to liver transplant.

An ideal solution for HCC candidates may take into account not only HCC exception eligibility and MELD score, but also the biological behavior of the tumor and treatment response by incorporating radiographic and other characteristics of the tumor. An example may be to require patients to undergo ablative therapy before being granted an exception score and then to grant a different priority depending on the residual disease. However, such a system would be difficult to implement and monitor. More importantly, patients with tumors that do not respond as well to ablative therapies may be preferentially selected, because such tumors have been shown to have a higher risk of recurrent disease, leading to unfavorable outcomes (12–14). Finally, the lack of granularity of the currently available OPTN data makes it impossible to model such a system before implementation.

Our analysis is based on registry data and extrapolation to future implementation must be done with caution. This analysis has limitations pertaining to how LSAM may be used to predict HCC-related waitlist and post-waitlist outcomes. As indicated, waitlist outcomes in HCC candidates were approximated by linking the status histories of several candidates together. The accuracy of this estimation process may improve if more information could be incorporated to represent tumor biology, such as detailed imaging characteristics or treatment response. Thus, predicting mortality in patients with HCC is not as reliable as, for example, predicting the number of transplants; this is the reason mortality prediction was a

secondary aim of the study. In addition, LSAM does not predict how transplant surgeons and physicians would adapt their practices in response to policy changes to provide the best outcome of their patients. For example, LSAM is unable to address how the risk profiles of donor and recipient will be balanced and affect organ acceptance. Changes in the diagnosis and treatment of HCC in the future are not predictable. Despite these uncertainties, the similarities between the modeling results and the actual experience in high MELD regions are reassuring regarding the relevance of the model.

In conclusion, the current system allows for higher waitlist dropout and lower transplant rates for non-HCC patients, which has resulted in a significant disparity in access to transplant. The results of this study based on LSAM suggest that the transplant and waitlist dropout rates for HCC and non-HCC patients may become similar with a delay of 6 to 9 months in application of HCC exception points. While this strategy does not affect the most essential problem, which is the critical shortage of available organs for transplant, it has the potential to allow for more equitable access to transplant for HCC and non-HCC patients.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Abbreviations

HCC	hepatocellular carcinoma
MELD	model for end-stage liver disease
LSAM	liver simulated allocation modeling

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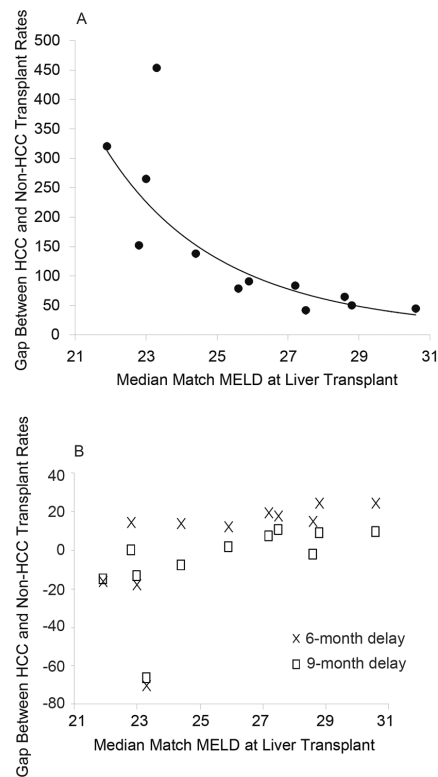
Figure 1.
Panel A. Median match MELD at liver transplant and the gap in transplant rates between HCC and non-HCC patients by region. In regions where patients undergo transplant at lower MELD scores, the disparity between HCC and non-HCC patients was larger than in high MELD regions. Each dot represents one of the 11 OPTN regions.

Panel B. Effect of 6- and 9-month delays in application of HCC exception scores on the gap in transplant rates between HCC and non-HCC patients by region. The negative correlation seen in Panel A is no longer apparent. HCC, hepatocellular carcinoma; MELD, model for end-stage liver disease; OPTN, Organ Procurement and Transplantation Network.

Table 1

Waiting periods and subsequent escalation of HCC exception scores for the four scenarios simulated by LSAM

Months after Listing	Current System	Scenarios		
		3-Month Delay[*]	6-Month Delay[*]	9-Month Delay[*]
0–3	22	Lab MELD or non-HCC exception score	Lab MELD or non-HCC exception score	Lab MELD or non-HCC exception score
3–6	25	25	Lab MELD or non-HCC exception score	Lab MELD or non-HCC exception score
6–9	28	28	28	Lab MELD or non-HCC exception score
9–12	29	29	29	29
12–15	31	31	31	31
15–18	33	33	33	33
18–21	34	34	34	34
21–24	36	36	36	36
24–27	39	39	39	39

HCC, hepatocellular carcinoma; LSAM, liver simulated allocation modelling; MELD, model for end-stase live disease.

[*] Delays in applying HCC exception scores.

Table 2

Characteristics of liver transplant candidates in 2010

	HCC Exception Score			
Characteristic	**Yes**	**No**	**Total**	***P*** [*]
n	2773	25,280	28,053	
Age, yrs.	58.5 (7.4)	52.1 (14.7)	52.7 (14.3)	< 0.0001
Male sex	75.0	60.2	61.7	< 0.0001
Race				
White	63.8	70.4	69.7	< 0.0001
Black	9.1	8.2	8.3	
Other	27.1	21.4	22.0	
Diagnosis				
HBV	3.5	2.7	2.7	< 0.0001
HCV	39.0	34.3	34.7	
Non-cholestatic	8.1	22.7	21.2	
Alcoholic	6.4	15.9	15.0	
HCC[†]	38.1	2.7	6.2	
Other	5.0	21.8	20.2	
MELD at listing				
Lab	11.6 (4.2)	14.8 (8)	14.5 (7.8)	< 0.0001
Allocation	18.9 (6.3)	14.9 (7.8)	15.3 (7.8)	< 0.0001
Listed before January 2010	45.6	59.5	58.1	< 0.0001

Note: Data from these candidates constituted the basis for the LS AM modeling. Unless otherwise specified, values are mean (standard deviation) or percentage. Statistical methods: numerical variables (age and lab and allocation MELD), the student's t-test; categorical variables (remaining variables), the chi-square test.

HBV, hepatitis B virus; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; MELD, model for end-stase liver disease.

[*] Comparison between candidates who received HCC exception scores before or during 2010 and those who did not receive exception scores during the same period.

[†] No underlying liver disease specified.

Table 3

Descriptive outcomes of the LSAM simulations performed for the four scenarios

Outcomes	Scenario			
	Current System	3-Month Delay*	6-Month Delay*	9-Month Delay*
Liver transplant				
Total, *n* (SD, range)	5891 (17.1, 5868–5923)	5855 (29.9, 5810–5917)	5830 (28.6, 5787–5869)	5823 (15.0, 5797–5844)
HCC patients, *n* (SD, range)	1179 (14.7, 1162–1202)	820 (16.3, 793–843)	603 (10.9, 586–620)	479 (18.6, 438–501)
Non-HCC patients, *n* (SD, range)	4712 (25.2, 4670–4746)	5035 (25.2, 4982–5074)	5226 (21.5, 5192–5260)	5345 (27.4, 5309–5403)
% of HCC patients (SD, range)	20.0 (0.27, 19.7–20.4)	14.0 (0.25, 13.6–14.4)	10.4 (0.15, 10.1–10.6)	8.2 (0.33, 7.5–8.6)
Rate of liver transplant[†]				
HCC patients (SD, range)	108.7 (1.6, 106.41–11.4)	65.0 (1.7, 62.1–67.8)	44.2 (0.92, 42.6–45.5)	33.6 (1.4, 30.5–35.4)
Non-HCC patients (SD, range)	30.1 (0.18, 29.8–30.4)	32.5 (0.18, 32.1–32.8)	33.9 (0.17, 33.7–34.2)	34.8 (0.20, 34.5–35.4)
Average match MELD at transplant				
HCC patients (SD, range)	24.9 (0.07, 24.8–25.0)	25.5 (0.12, 25.2–25.6)	25.5 (0.18, 25.2–25.7)	24.4 (0.25, 24.1–24.8)
Non-HCC patients (SD, range)	25.8 (0.10, 25.7–26.0)	25.2 (0.05, 25.1–25.3)	24.9 (0.09, 24.8–25.1)	24.8 (0.07, 24.7–24.9)
Average lab MELD at transplant				
HCC patients (SD, range)	13.7 (0.09, 13.5–13.8)	14.8 (0.11, 14.6–15.0)	15.9 (0.31, 15.5–16.7)	17.4 (0.36, 16.8–17.9)
Non-HCC patients (SD, range)	24.5 (0.11, 24.3–24.7)	24.0 (0.05, 23.9–24.0)	23.7 (0.08, 23.6–23.8)	23.5 (0.07, 23.4–23.6)
Death				
HCC patients, *n* (SD, range)	158 (4.7, 152–167)	178 (6.2, 169–190)	201 (4.5, 194–206)	198 (4.7, 193–208)
Non-HCC patients, *n* (SD, range)	1991 (18.1, 1955–2019)	1947 (14.3, 1925–1970)	1927 (10.4, 1913–1943)	1915 (18.4, 1883–1939)
Rate of death per 100 person-years				
HCC patients (SD, range)	13.2 (0.4, 12.8–13.9)	12.9 (0.4, 12.2–13.6)	13.5 (0.3, 12.9–13.8)	12.8 (0.3, 12.4–13.5)
Non-HCC patients (SD, range)	11.8 (0.11, 11.6–12.0)	11.7 (0.08, 11.5–11.8)	11.6 (0.07, 11.5–11.7)	11.6 (0.12, 11.3–11.7)

HCC, hepatocellular carcinoma; LSAM, liver simulated allocation modelling; MELD, model for end-stage live disease; SD, standard deviation.

*
Delays in applying HCC exception scores.

[†]
Per 100 person-years.

Table 4

Gap between transplant rates, HCC and non-HCC candidates

OPTN/UNOS Region	MELD at Liver Transplant		Scenario			
	Mean (SD) Match	Mean (SD) Lab	Current System	3-Month Delay*	6-Month Delay*	9-Month Delay*
All	25.6 (7.6)	22.1 (9.9)	78.6 (1.7, 76.2–81.4)	32.5 (1.7, 29.7–35.4)	10.3 (0.85, 8.8-11.5)	−1.2 (1.6, −4.7–0.85)
1	28.8 (7.9)	24.0 (11.2)	50.2 (9.2, 35.3–59.2)	35.6 (5.7, 26.3–46.3)	24.3 (6.2, 14.5–36.0)	8.8 (5.1, 0.33–18.3)
2	25.9 (7.4)	21.9 (10.1)	91.0 (7.5, 80.5–105.6)	41.8 (3.7, 34.5–48.3)	12.5 (3.0, 6.6–16.1)	1.9 (3.5, −3.3–6.2)
3	23.3 (6.6)	21.1 (8.5)	453.9 (31.4, 399.8–500.9)	−51.4 (7.3, −63.2 to −37.2)	−70.1 (7.4, −83.0 to −61.6)	−66.7 (8.0, −77.6 to −56.4)
4	27.2 (7.1)	23.5 (10.1)	83.8 (5.9, 71.6–91.0)	54.3 (3.2, 48.5–58.4)	19.5 (3.2, 15.5–25.4)	7.4 (2.3, 3.3–10.8)
5	30.6 (7.7)	25.6 (11.7)	44.5 (2.7, 38.5–48.5)	36.1 (2.5, 31.8–39.2)	24.8 (1.7, 22.8–28.3)	9.4 (1.7, 5.9–11.8)
6	22.8 (6.5)	19.6 (8.1)	152.0 (19.8, 128.1–184.2)	40.4 (16.2, 17.7–59.2)	14.7 (15.1, −1.3–38.0)	0.0 (13.5, −17.9–21.9)
7	28.6 (7.8)	25.0 (10.8)	64.5 (6.9, 55.3–72.8)	43.0 (7.3, 35.3–54.1)	15.1 (5.7, 3.4–20.8)	−2.4 (2.7, −5.9–2.6)
8	24.4 (6.7)	20.7 (9.2)	137.8 (12.9, 120.5–153.6)	66.7 (4.6, 59.7–74.1)	14.2 (5.2, 3.1–21.2)	−7.7 (2.6, −11.9 to −3.9)
9	27.5 (7.4)	21.6 (10.6)	41.6 (4.9, 30.4–46.2)	28.7 (3.2, 24.3–35.2)	18.0 (3.2, 13.5–22.5)	10.6 (3.0, 6.4–16.2)
10	23.0 (6.7)	20.4 (8.6)	265.0 (37.4, 207.2–344.1)	18.2 (11.5, 0.17–41.3)	−17.8 (6.0, −23.1 to −8.1)	−13.3 (8.9, −26.9-3.7)
11	21.9 (6.2)	19.6 (7.8)	320.5 (25.7, 285.0–373.3)	10.9 (6.2, 1.5–23.7)	−16.1 (4.8, −24.9 to −8.7)	−14.9 (6.7, −21.9-0.72)

Note: Values are mean (SD) or rate per 100 person-years (SD, range).

HCC, hepatocellular carcinoma; MELD, model for end-stage live disease; OPTN, Organ Procurement and Transplantation Network; SD, standard deviation; UNOS, United Network for Organ Sharing.

*
Delays in applying HCC exception scores.