Supplementary Appendix Accompanying Manuscript
Optimal Timing of Hepatitis C Treatment for Patients on the Liver Transplant Waiting List

Jagpreet Chhatwal, PhD,[1,2,3] Sumeyye Samur, PhD[1,2] Brian Kues, PhD,[4] Turgay Ayer, PhD,[4] Mark S. Roberts, MD, MPP,[5,6] Fasiha Kanwal, MD, MSHS,[7,8] Chin Hur, MD, MPH[1,2,3] Drew Michael S. Donnell, MS,[5,6] Raymond T. Chung, MD[2,3]

[1]Massachusetts General Hospital Institute for Technology Assessment, Boston, MA

[2]Harvard Medical School, Boston, MA

[3]Liver Center and Gastrointestinal Division, Massachusetts General Hospital, Boston, MA

[4]Department of Industrial and Systems Engineering, Georgia Institute of Technology, Atlanta, GA

[5]Department of Health Policy and Management, University of Pittsburgh Graduate School of Public Health, Pittsburgh, PA

[6]University of Pittsburgh School of Medicine, Pittsburgh, PA

[7]Department of Medicine, Gastroenterology and Hepatology, Baylor College of Medicine, Houston, TX

[8]Houston Veterans Affairs Health Services Research and Development Center of Excellence, Michael E. DeBakey Veterans Affairs Medical Center, Houston, TX

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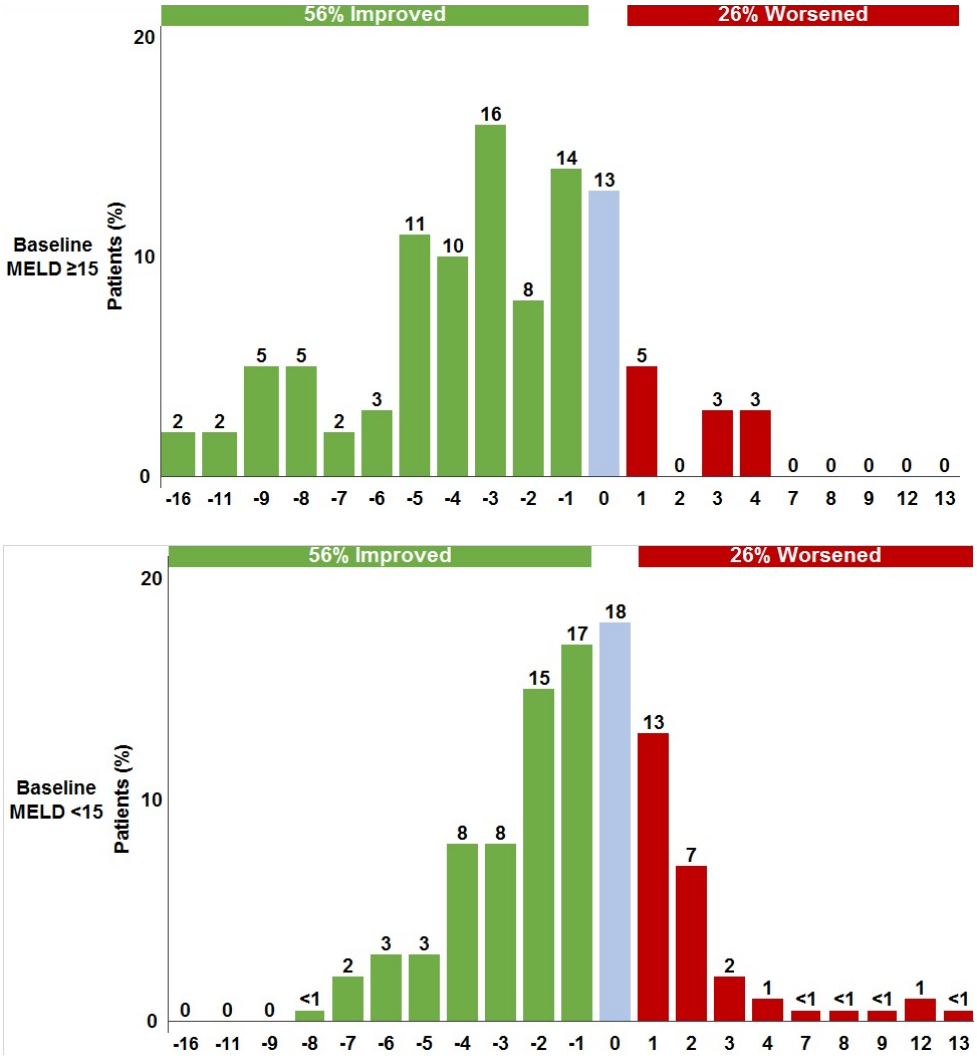

Figure S1. Change in MELD scores because of HCV treatment in decompensated cirrhosis patients on the live transplant waiting list. The top panel shows percentage change in patients having MELD score ≥ 15 and the bottom panel in patients having MELD < 15. For example, if a patient having MELD 20 achieves SVR, the likelihood of her MELD score will remain unchanged is 13%, will decrease to 19 is 14%, will increase to 21 is 5%, etc.
Source: SOLAR 1 and 2 trials (1-3).

Table S1. Annual mortality on the liver transplant waiting list

MELD Score	Annual Mortality
6–7	0.000014
8–9	0.000697
10–11	0.000691
12–13	0.000022
14–15	0.000681
16–17	0.000235
18–19	0.003659
20–21	0.007021
22–23	0.009891
24–25	0.011323
26–27	0.047260
28–29	0.078599
30–31	0.159678
32–33	0.192294
34–35	0.211013
36–37	0.273120
38–39	0.344884
40	0.481372

Source: Alagoz et al. (4) and UNOS data

Table S2. Three-month Liver Transplantation Probabilities based on MELD score

MELD Score	90-day Probability of Liver Transplant
<14	0
14–15	0.008161
16–17	0.012561
18–19	0.026286
20–21	0.036498
22–23	0.052484
24–25	0.066997
26–27	0.078408
28–29	0.082616
30–31	0.084809
32–33	0.087066
34–35	0.084809
36–37	0.068787
38–39	0.066997
40	0.052484

Source: Massie et al. (5)

S1. Mean waiting time and mortality while on the transplant waiting list after a graft failure

After a graft failure, patients entered the transplant waiting list. Because we did not know their MELD score, we assigned the average probability of liver transplant and liver-related mortality to these patients, which were estimated from UNOS data. Specifically, standard statistical estimates of waiting times for liver transplantation were obtained from the UNOS STAR database. From the initial dataset (n = 220,598), we restricted the cohort to adult registrants (at least 18 years of age) with a diagnosis at listing of HCV who listed for transplantation between January 2006 and June 2010. Expert clinical evaluation of a previously developed classification of end-stage liver diseases guided the inclusion criterion for the diagnoses of HCV (6). Subsequently, we selected the subset of registrants who underwent a solid liver transplant or died while waiting, defined by the UNOS removal codes. Patients who previously received a solid organ transplant of any type were then excluded. The final cohort provided an aggregate sample of $9{,}701$adult registrants. We found that the mean time on the transplant waiting list was 155 days, and mean time to liver-related death was 240 days. Using the mean time, we estimated the probability of liver transplant and death in patients on the waiting list using the following formula:

$$weekly = 1 - \sqrt[\frac{mean\ days}{7}]{1/2}$$

The weekly probability of death and liver transplant in patients having graft failure was estimated as 0.020 and 0.0308, respectively. The corresponding annual probabilities were 0.652 and 0.805, respectively.

Table S3. Health-Related Quality-of-Life Utilities of the United States Population

Age Group	Male	Female
20–29	0.928	0.913
30–39	0.918	0.893
40–49	0.887	0.863
50–59	0.861	0.837
60–69	0.84	0.811
70–79	0.802	0.771
80–89	0.782	0.724

Source: Hanmer et al.(7)

Section S2. Transplant Rate and Mortality by UNOS Region

We used UNOS-reported transplantation and death rates for each region to adjust the probability of receiving a LT and probability of death on the waiting list. Particularly, we estimated the ratio of observed transplant rate of each region and overall rate in the United States. Using the ratio, we estimated region-specific rates as follow: *Transplant-Region* = (1 – *Transplant-U.S.*)$^{\text{Ratio-Region}}$

Table S4. Transplantation Rates by UNOS Region

Region	Transplantation (Rate per 100 Person Years)	Ratio (Region / U.S.)	Death (Rate per 100 Person Years)	Ratio (Region / U.S.)
1	30.5	0.709	19	1.061
2	34	0.791	18.4	1.028
3	110.2	2.563	20.1	1.123
4	29.8	0.693	15.9	0.888
5	28.7	0.667	16.9	0.944
6	50.5	1.174	21.3	1.190
7	47.8	1.112	19.2	1.073
8	37.9	0.881	16	0.894
9	26.4	0.614	17.2	0.961
10	68.8	1.600	20	1.117
11	76.9	1.788	18.9	1.056
U.S.	**43.0**		**17.9**	

Table S5. Liver Transplant Model Variables: Baseline Values, Ranges, and Parameters for Distributions Used in Deterministic and Probabilistic Sensitivity Analyses

Parameter	Base Case	Range	Distribution	Parameter 1[a]	Parameter 1[b]
Sustained virologic response rate					
Pre-LT SVR rate	0.840	0.700-0.930	Beta	21.29	4.05
Post-LT SVR rate	0.950	0.900-0.980	Beta	68.39	3.60
Transition probabilities					
Liver transplant to liver-related death (3 months of 1st LT)	0.124	0.118-0.129	Beta	2069.63	14620.96
Liver transplant to liver-related death (3 months of repeated LT)	0.264	0.240-0.287	Beta	372.25	1037.79
Liver transplant to graft failure (3 months of 1st LT)	0.167	0.161-0.173	Beta	2478.90	12364.79
Liver transplant to graft failure (3 months of repeated LT)	0.312	0.287-0.336	Beta	446.36	984.28
Sustained virologic response to liver-related death (1st year)	0.110	0.082-0.137	Beta	54.59	441.72
Sustained virologic response to liver-related death (subsequent year)	0.032	0.024-0.04	Beta	59.47	1798.87
Sustained virologic response to graft failure	0.050	0.037-0.062	Beta	58.34	1108.50
F0-F2 to liver-related death (1st year of 1st LT)	0.124	0.118-0.129	Beta	2069.63	14620.96
F0-F2 to liver-related death (Subsequent year of 1st LT	0.041	0.040-0.042	Beta	6163.39	144530.78
F0-F2 to liver-related death (1st year of repeated LT)	0.264	0.240-0.287	Beta	372.25	1037.79
F0-F2 to liver-related death (Subsequent year of repeated LT)	0.072	0.070-0.075	Beta	2053.37	26465.67
F3-F4 to liver-related death (1st year of 1st LT)	0.124	0.118-0.129	Beta	2069.63	14620.96
F3-F4 to liver-related death (Subsequent year of 1st LT	0.041	0.040-0.042	Beta	6163.39	144530.78
F3-F4 to liver-related death (1st year of repeated LT)	0.264	0.240-0.287	Beta	372.25	1037.79
F3-F4 to liver-related death (Subsequent year of repeated LT)	0.072	0.070-0.075	Beta	2053.37	26465.67
F0–F2 to graft failure (1st year of 1st LT)	0.167	0.161-0.173	Beta	2478.90	12364.79
F0–F2 to graft failure (1st year of repeat LT)	0.312	0.287-0.336	Beta	446.36	984.28
F3–F4 to graft failure (1st year of 1st LT)	0.290	0.315-0.525	Beta	3.86	9.46
F3–F4 to graft failure (1st year of repeat LT)	0.312	0.287-0.336	Beta	446.36	984.28
F0–F2 to graft failure (subsequent year of 1st LT)	0.051	0.050-0.052	Beta	9482.36	176446.24
F0–F2 to graft failure (subsequent year of repeat LT)	0.095	0.093-0.098	Beta	3486.21	33210.74

F3–F4 to graft failure (subsequent year of 1st LT)	0.051	0.050-0.052	Beta	9482.36	176446.24
F3–F4 to graft failure (subsequent year of repeat LT)	0.095	0.093-0.098	Beta	3486.21	33210.74
Graft failure to liver-related death	0.652	0.489-0.815	Beta	20.74	11.06
Graft failure to repeat transplant	0.805	0.604-1	Beta	11.96	2.90
F0–F2 to F3–F4	0.044	0.040-0.055	Beta	58.72	1275.76
Decrease in transplant rate due to achieving SVR	0.08	0.050-0.150	Beta	4.54	52.17
Health-related quality-of-life weights					
Transplant waiting list	0.800	0.570-0.990	Beta	12.82	3.21
Liver transplant	0.600	0.370-0.730	Beta	32.13	21.42
F0–F2	0.828	0.716-0.865	Beta	326.86	68.04
F3–F4	0.801	0.693-0.837	Beta	377.66	93.83
Antiviral Treatment	0.890	0.770-0.930	Beta	208.31	25.75
Sustained virologic response	0.890	0.770-0.930	Beta	208.31	25.75
Graft failure	0.800	0.570-0.990	Beta	12.82	3.21

[a] Parameter 1 corresponds to α parameter for beta distribution
[b] Parameter 2 corresponds to β parameter for beta distribution

Section S3. Validation of Transplant Survival Rates

We validated the predicted 1-year and 5-year transplant survival rates with those from Organ Procurement Transplant Network (OPTN) data. Because OPTN data provides survival rates in the pre-DAA era, we simulated the scenario using pre-DAA therapies. Specifically, we assumed that 20% of HCV patients after LT were eligible for HCV treatment with peginterferon-based therapies in the pre-DAA era. The SVR rate in post-LT patients was 23% (8).

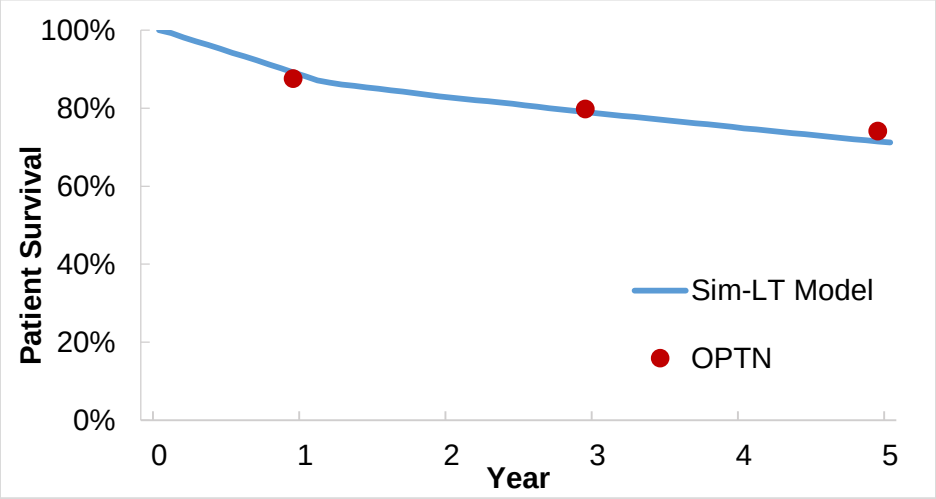

Figure S2. Validation of model-predicted post-liver transplant patient survival with OPTN data

Section S4. Additional Model Outcomes

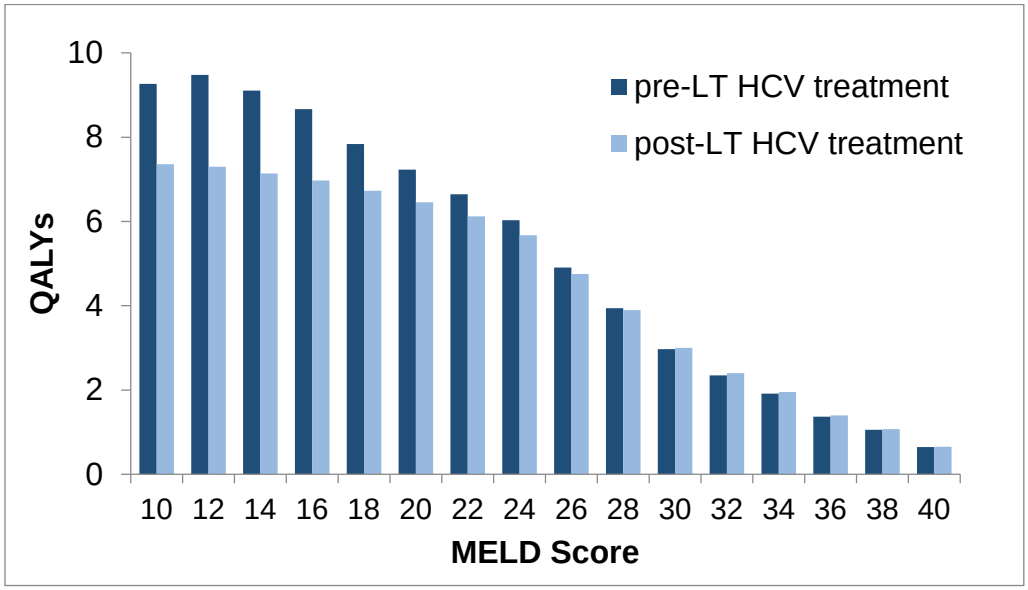

Figure S3. Comparison of quality-adjusted life years (QALYs) by MELD score under *pre*-LT versus *post*-LT treatment of hepatitis C in decompensated cirrhosis patients on the waiting list.
Abbreviation: LT, liver transplant

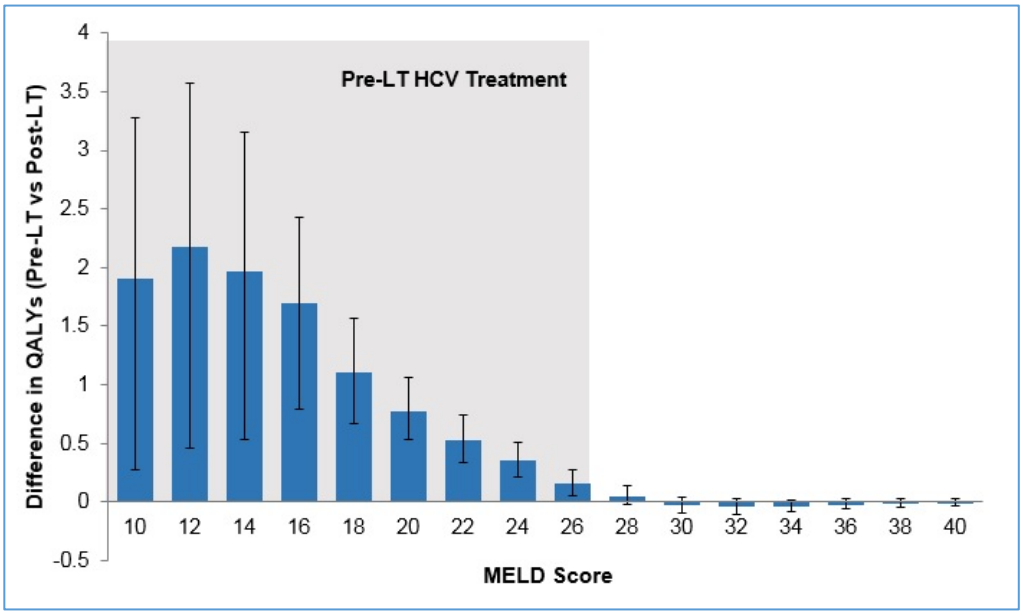

Figure S4. Difference in quality-adjusted life years (QALYs) if HCV is treated *pre*-LT versus *post*-LT in patients with decompensated cirrhosis on the transplant waiting list. The error bars represent 95% confidence interval generated by probabilistic sensitivity analysis. Patients having MELD ≤ 27 will benefit from pre-LT HCV treatment (shown by the shaded region).

The increase in the likelihood of receiving an LT in HCV-positive patients could be occurring at a different rate, we therefore conducted an addition analysis by increasing the likelihood of LT from the base case value to evaluate at what rate the decision to treat HCV would change. **Figure S5** shows that the threshold MELD score to treat HCV pre-LT fell below 26 when the rate of LT in HCV+ patients increases by 10% (because the 95% CI in gain in life years with pre-LT HCV treatment does not remain positive). Similarly, we found that the threshold to treat HCV pre-LT changed to MELD score < 24 when the rate of LT in HCV+ patients increased by 40% (**Figure S6**).

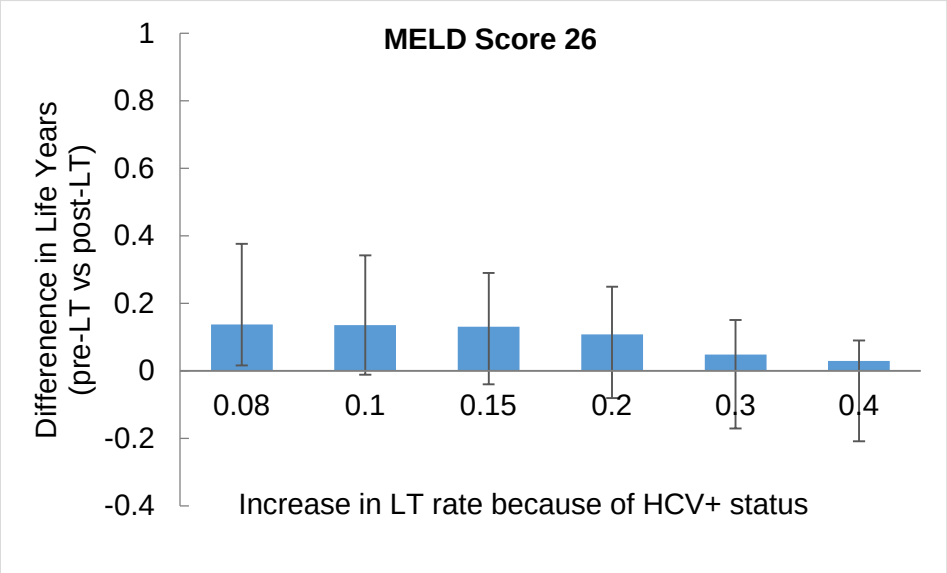

***Figure S5*. Difference in life years if HCV is treated *pre*-LT versus *post*-LT in patients with MELD score 26 on the transplant waiting list.** The error bars represent 95% confidence interval generated by probabilistic sensitivity analysis.

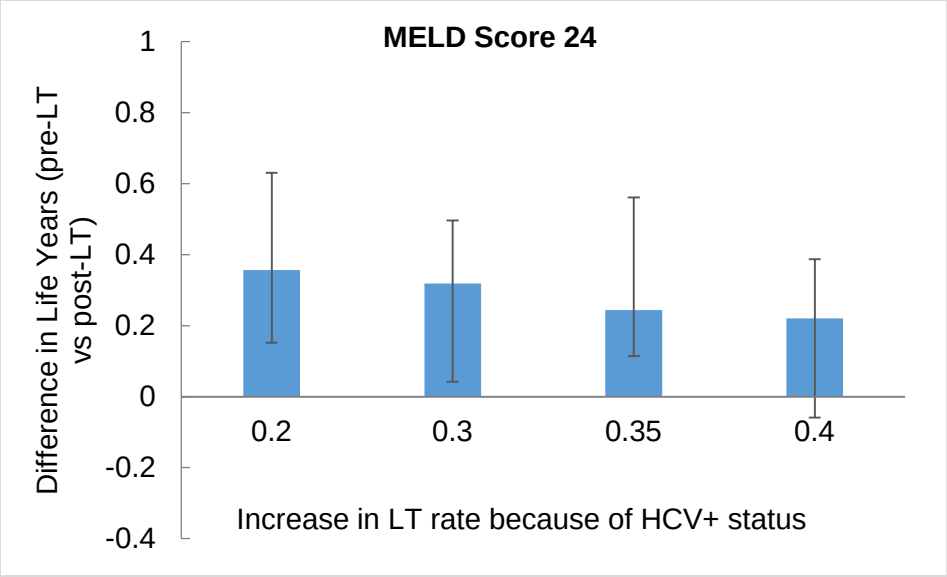

***Figure S6*. Difference in life years if HCV is treated *pre*-LT versus *post*-LT in patients with MELD score 24 on the transplant waiting list.** The error bars represent 95% confidence interval generated by probabilistic sensitivity analysis.

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