Supporting Information Accompanying Manuscript
Cost-Effectiveness of Pre versus Post Liver Transplant Hepatitis C Treatment with Direct-Acting Antivirals

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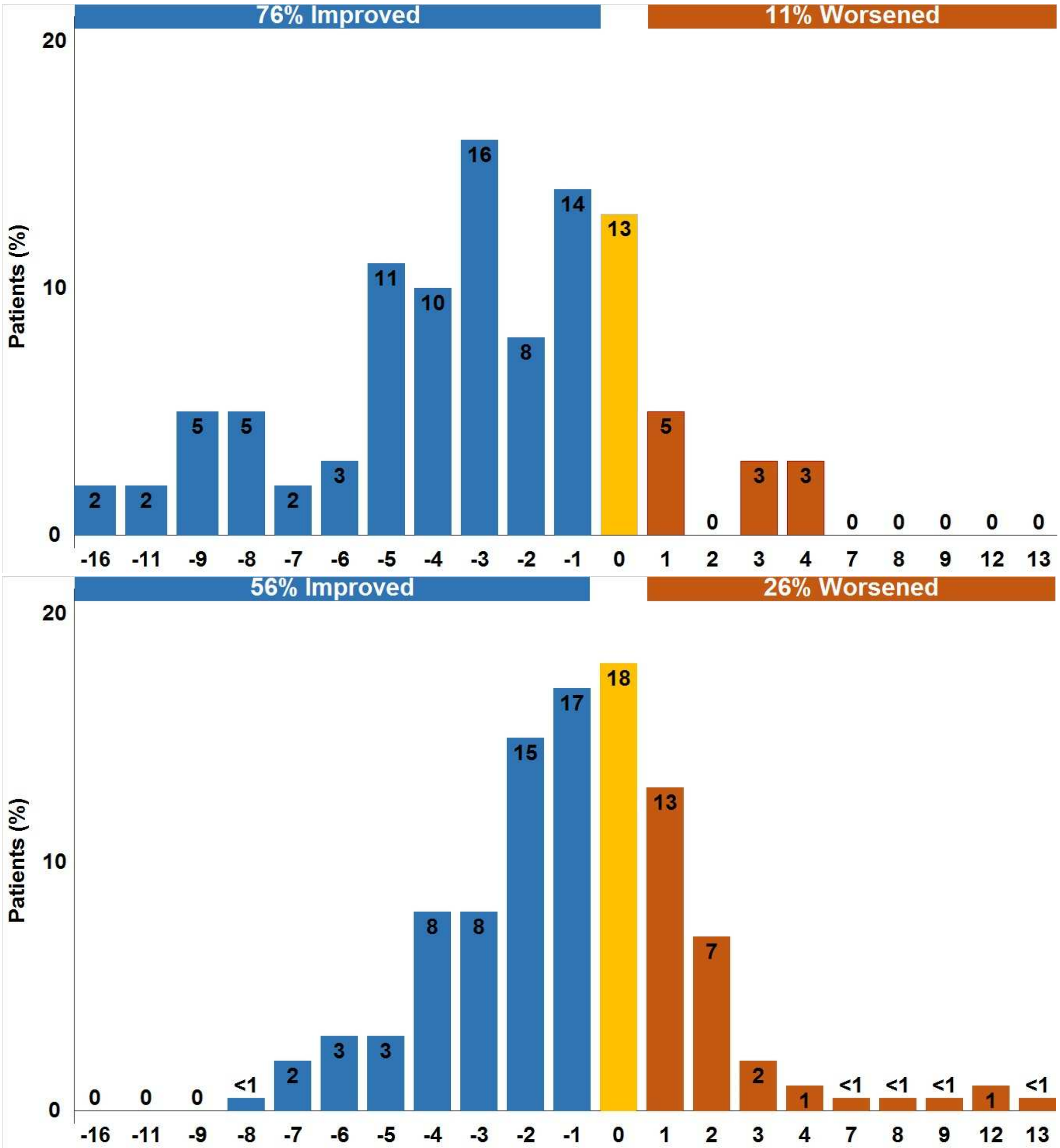

Figure S1. Change in MELD scores because of HCV treatment in decompensated cirrhosis patients on the live transplant waiting list. The top panel shows percentage change in patients having MELD score ≥ 15 and the bottom panel in patients having MELD < 15. Source: SOLAR 1 and 2 trials (1-3).

Table S1. Weekly mortality on the liver transplant waiting list

MELD Score	Weekly 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. Weekly Liver Transplantation Probabilities based on MELD score

MELD Score	Weekly 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)

Table S3. 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 (1-3)	0.840	0.700-0.930	Beta	21.29	4.05
Post-LT SVR rate (1-3)	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) (6)	0.110	0.082-0.137	Beta	54.59	441.72
Sustained virologic response to liver-related death (subsequent year) (6)	0.032	0.024-0.04	Beta	59.47	1798.87
Sustained virologic response to graft failure (7)	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) (8)	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 (9)	0.652	0.489-0.815	Beta	20.74	11.06
Graft failure to repeat transplant(9)	0.805	0.604-1	Beta	11.96	2.90
F0–F2 to F3–F4 (10)	0.044	0.040-0.055	Beta	58.72	1275.76
Decrease in transplant rate due to achieving SVR (11)	0.08	0.050-0.150	Beta	4.54	52.17
Health-related quality-of-life weights					
Transplant waiting list (12, 13)	0.800	0.570-0.990	Beta	12.82	3.21
Liver transplant (14)	0.600	0.370-0.730	Beta	32.13	21.42
F0–F2 (13, 14)	0.828	0.716-0.865	Beta	326.86	68.04
F3–F4 (13, 14)	0.801	0.693-0.837	Beta	377.66	93.83
Antiviral Treatment (14)	0.890	0.770-0.930	Beta	208.31	25.75
Sustained virologic response (14)	0.890	0.770-0.930	Beta	208.31	25.75
Graft failure (12)	0.800	0.570-0.990	Beta	12.82	3.21
Costs					
12-week HCV treatment **(15)**	95,523	0.570-0.990	Gamma	61.46	1,554.08
Monitoring cost if treated in WL (weekly) **(16)**	74	0.370-0.730	Gamma	61.46	1.20
WL (annual) **(16)**	20,841	15,630-26,050	Gamma	61.46	339.07
LT-1st year (annual) (17)	180,358	103,102-739,100	Gamma	0.40	450,582.1
Post-LT (annual) (17)	44,388	33,291-55,485	Gamma	61.46	722.16

* Based on OPTN data as of March 4, 2016
[a] Parameter 1 corresponds to α parameter for beta distribution, k *(shape)* parameter for gamma distribution
[b] Parameter 2 corresponds to β parameter for beta distribution, θ *(scale)* parameter for gamma distribution

Table S4. 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.(18)

Section S1. 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:

$$\textit{Region-specific-probability} = (1 - \textit{National probability})^{\text{Ratio}}$$

Table S5. Transplantation and Death Ratios by UNOS Regions

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**	

Section S2. Cost-Effectiveness Results by UNOS Regions

We conducted a subgroup analysis to evaluate the cost-effectiveness results for each of the 11 UNOS region. In particular, we plotted the clinical and cost effectiveness of the timing of HCV treatment by patient's MELD score in each region (**Figure S2–S12**). The dotted lines on each plot show the clinical threshold below which pre-LT treatment is more effective than post-LT treatment. Different shaded regions represent the cost-effectiveness of the timing of HCV treatment. Note that a strategy is cost-saving when it results in more QALYs for lower costs than the comparator, and it is cost-effective when it provides more QALYs for higher costs *and* the ICER is below the commonly accepted willingness to pay threshold, i.e. $100,000-per-QALY.

We found that below MELD score 19 pre-LT treatment was cost-effective, and above MELD score 27 post-LT treatment was cost-effective irrespective of the UNOS region. For MELD scores between 19 and 27, the price of DAAs in the UNOS region determined the cost-effectiveness of pre-LT HCV treatment. We found that price threshold for DAAs below which pre-LT treatment was cost-effective varied between $8,600 and $74,000 depending on the MELD score and the region.

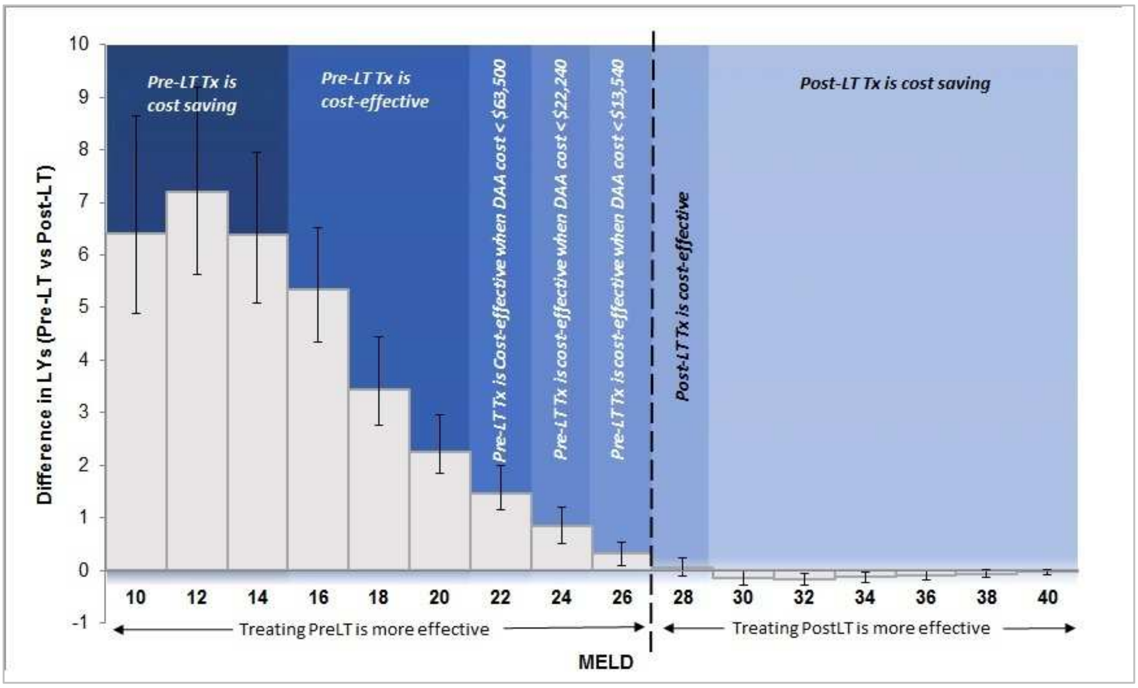

Figure S2. Clinical and cost-effectiveness of treatment timing for Region 1

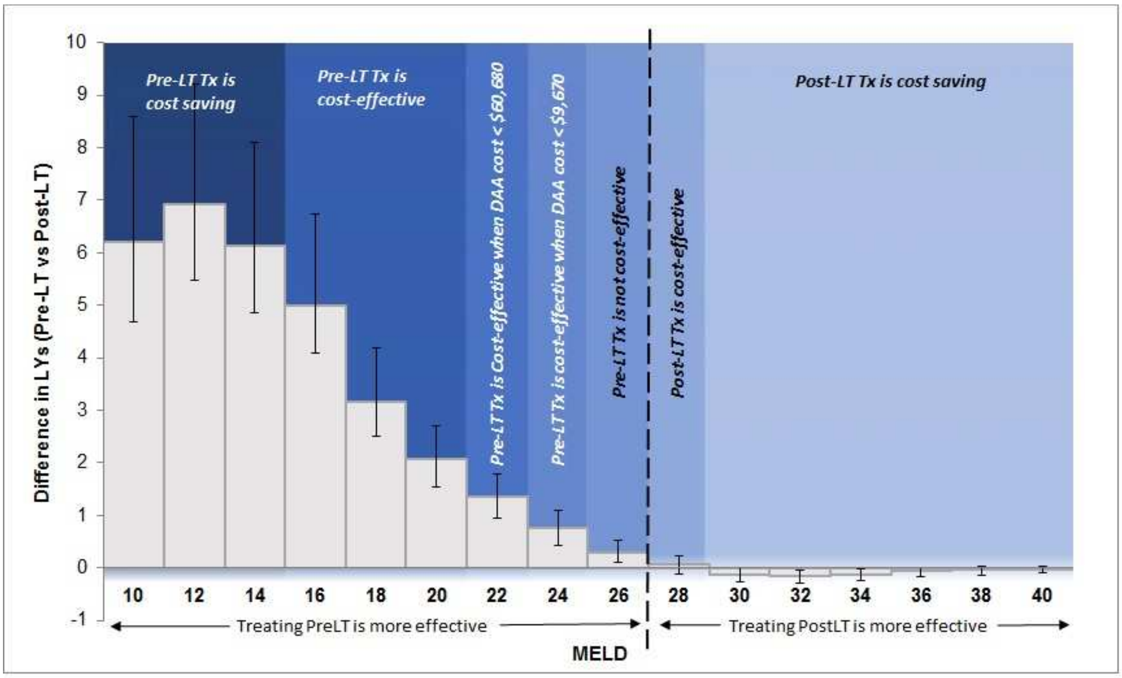

Figure S3. Clinical and cost-effectiveness of treatment timing for Region 2

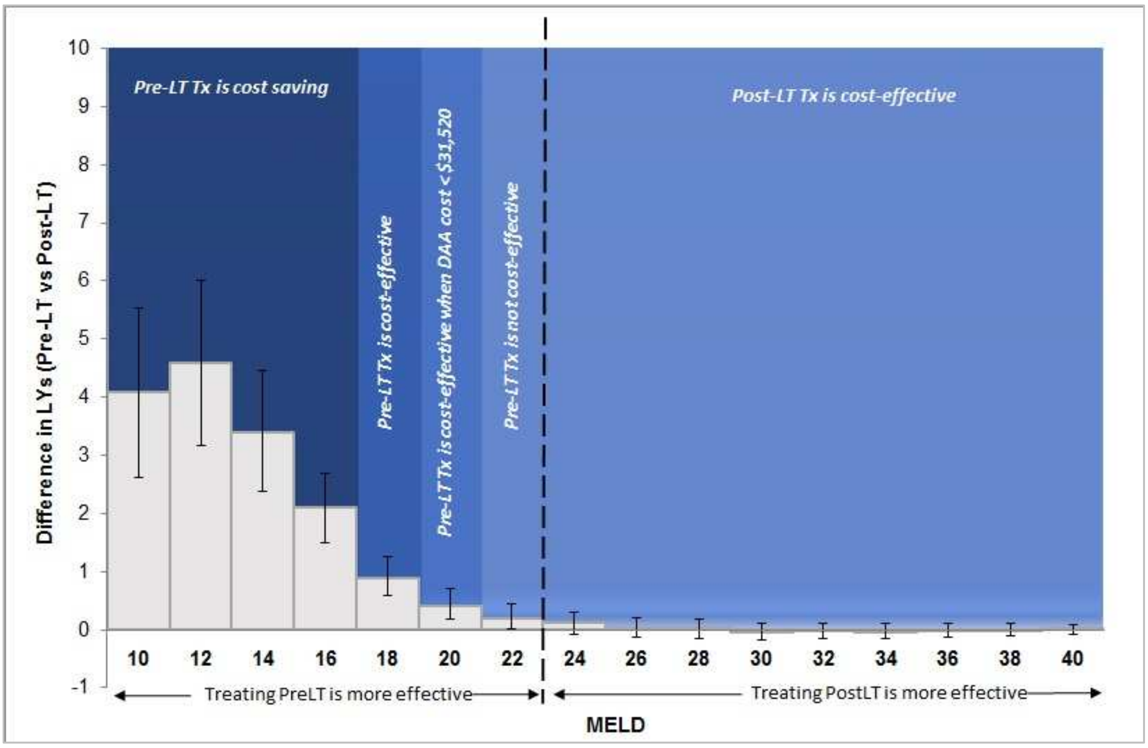

Figure S4. Clinical and cost-effectiveness of treatment timing for Region 3

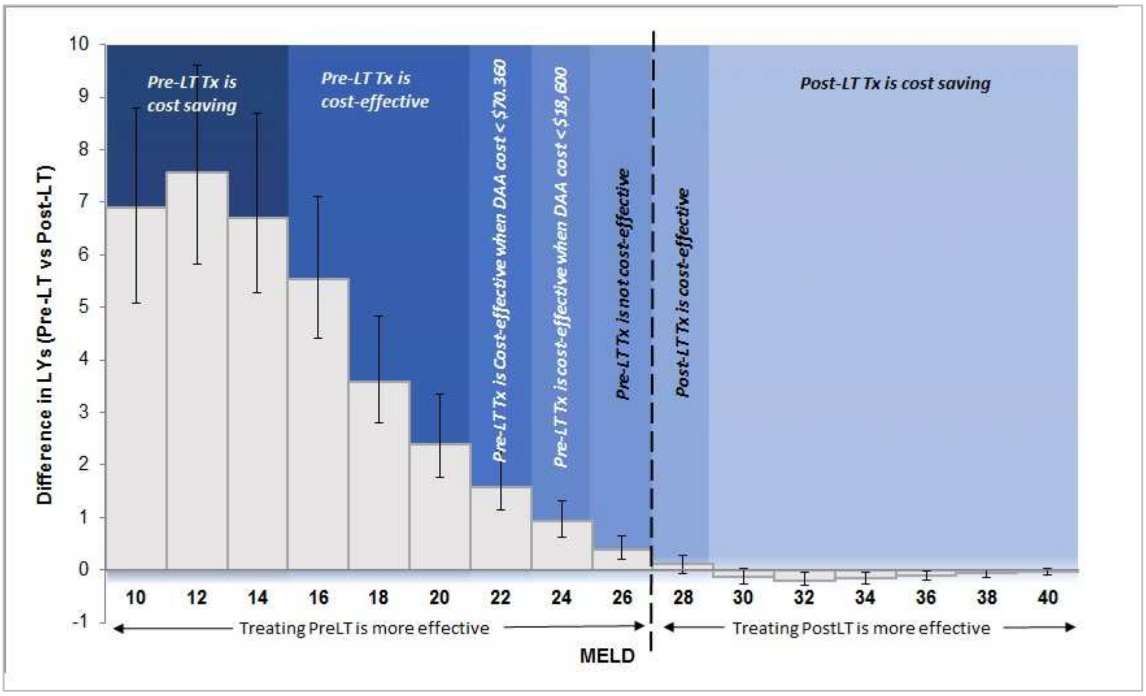

Figure S5. Clinical and cost-effectiveness of treatment timing for Region 4

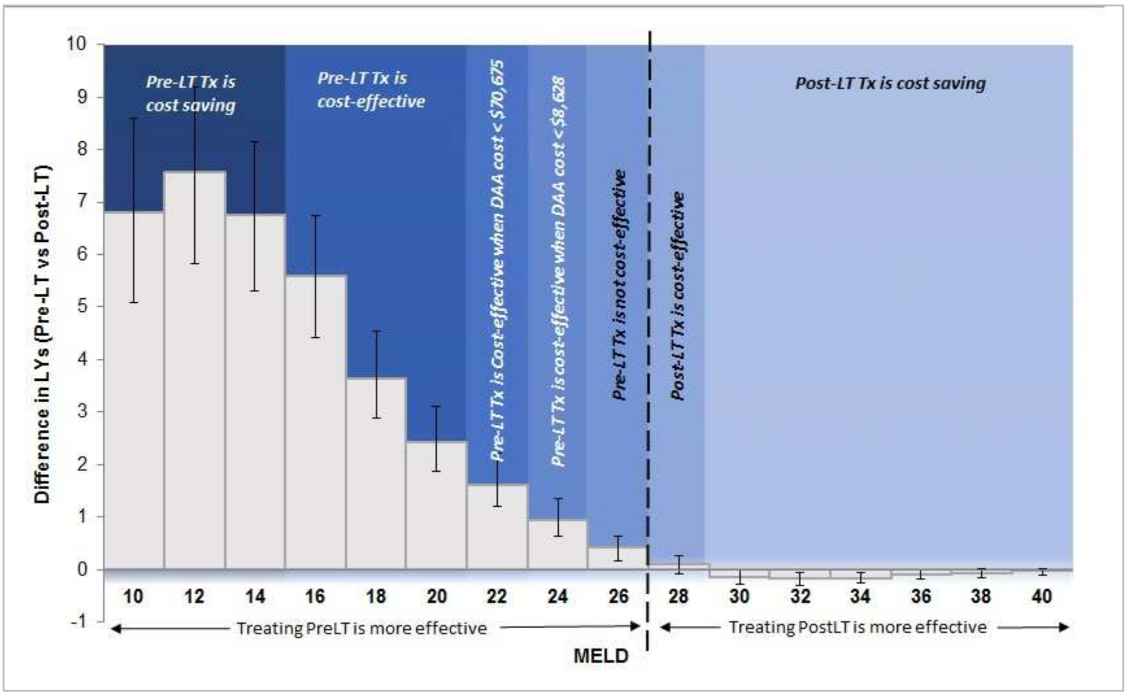

Figure S6. Clinical and cost-effectiveness of treatment timing for Region 5

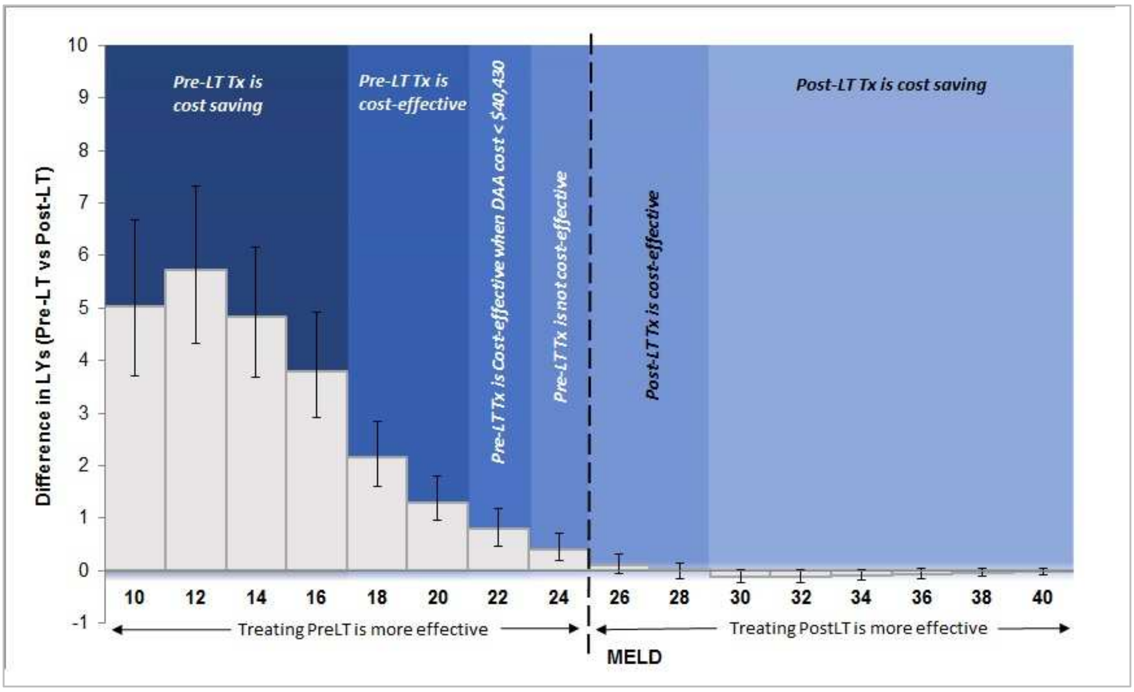

Figure S7. Clinical and cost-effectiveness of treatment timing for Region 6

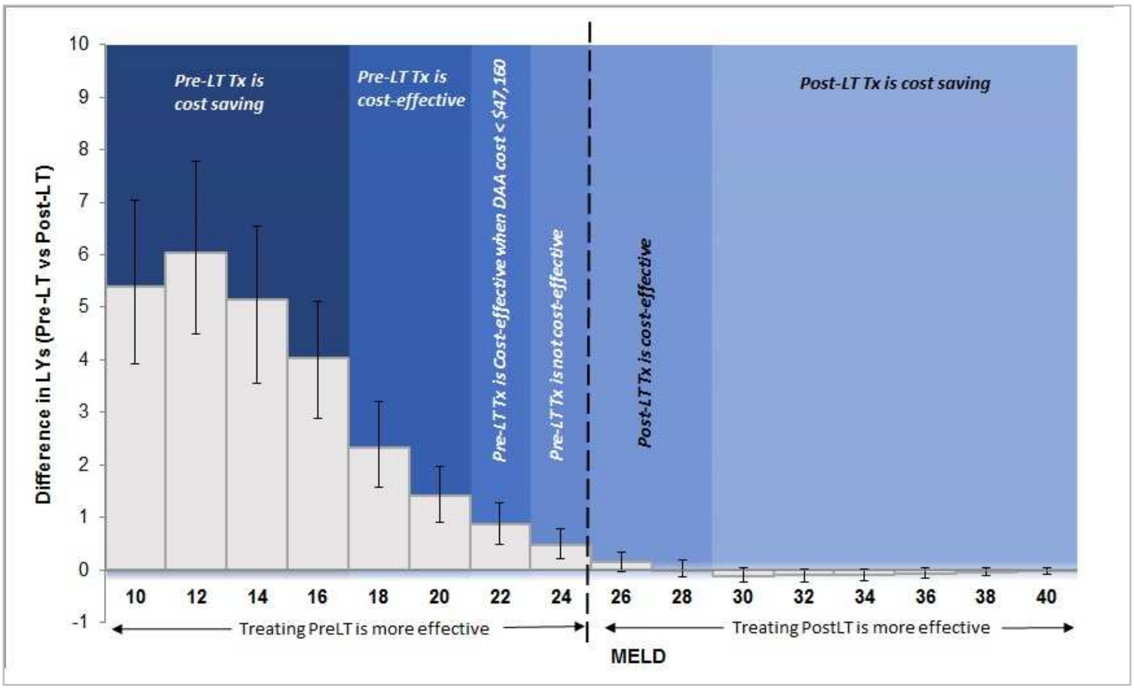

Figure S8. Clinical and cost-effectiveness of treatment timing for Region 7

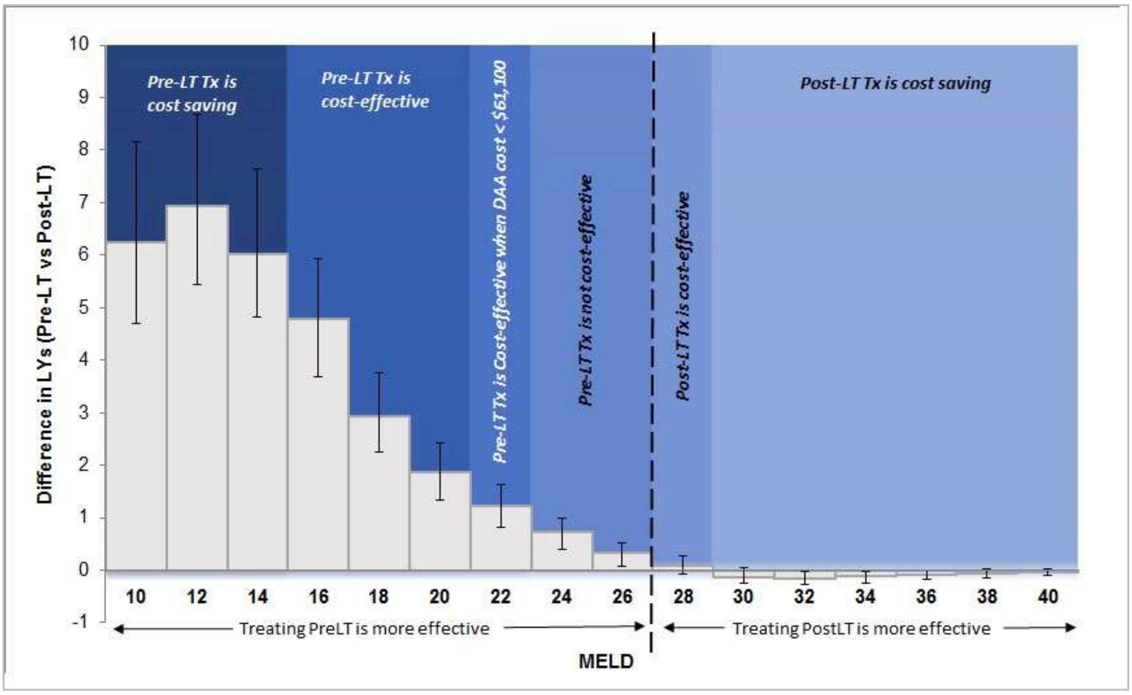

Figure S9. Clinical and cost-effectiveness of treatment timing for Region 8

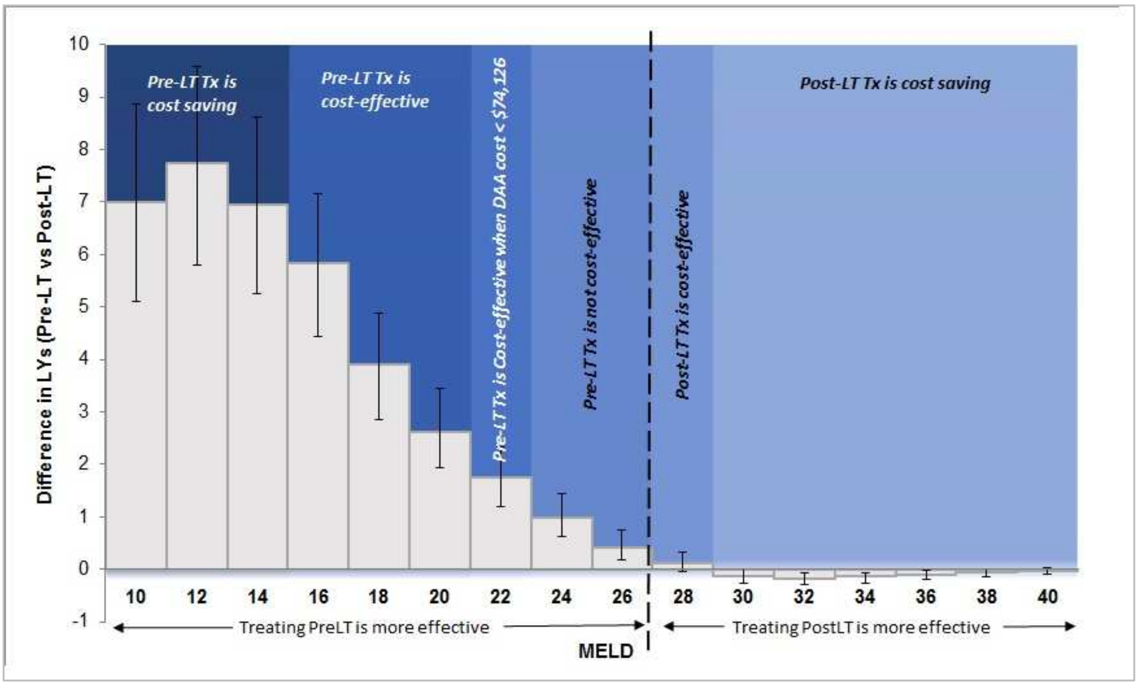

Figure S10. Clinical and cost-effectiveness of treatment timing for Region 9

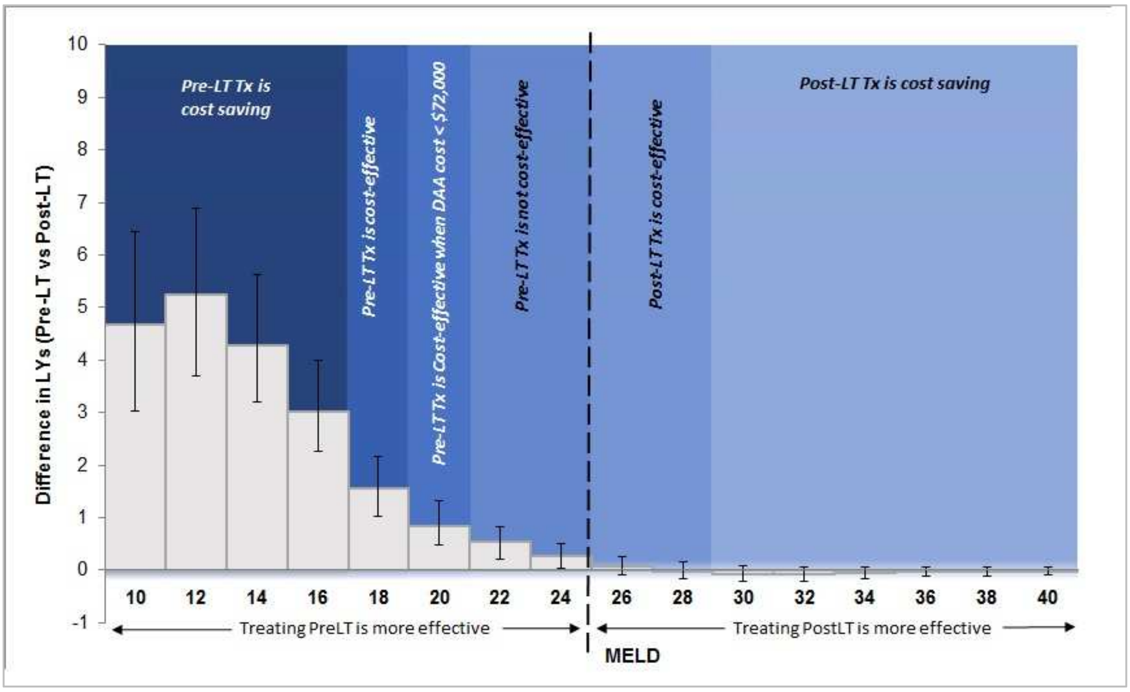

Figure S11. Clinical and cost-effectiveness of treatment timing for Region 10

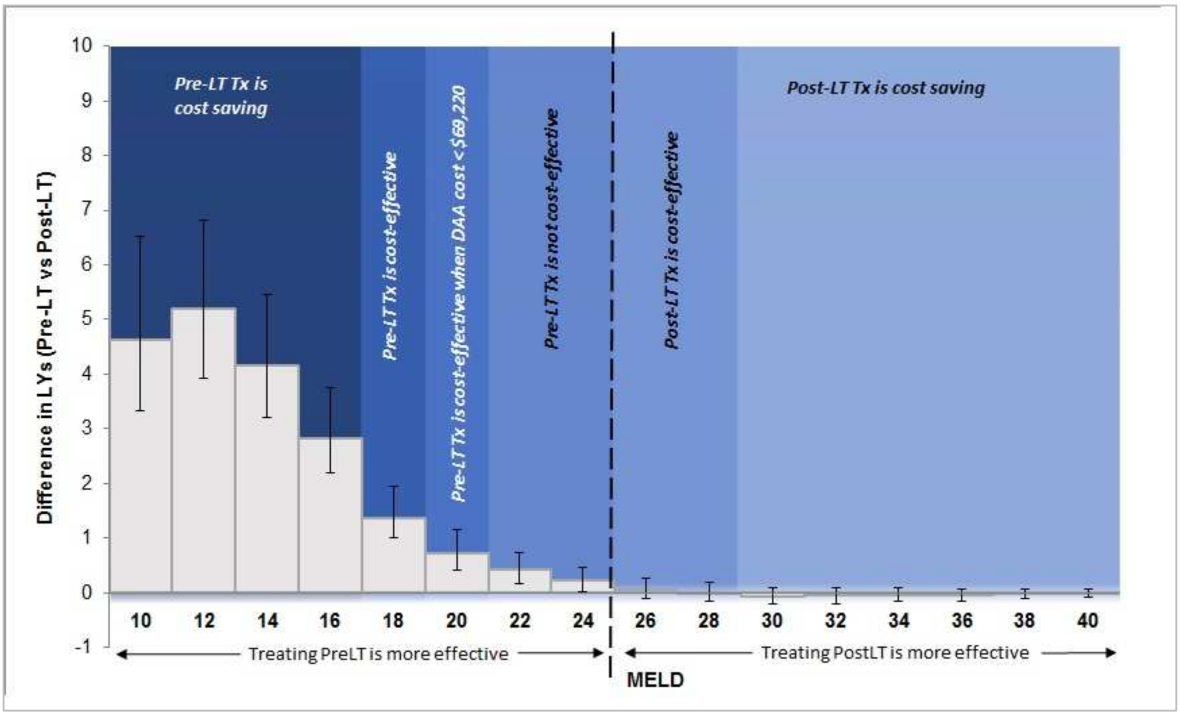

Figure S12. Clinical and cost-effectiveness of treatment timing for Region 11

Finally, we also compared net monetary benefit of treating HCV pre-LT versus post-LT for all UNOS regions. The net monetary benefit in pre-LT treatment was higher in regions with longer time on the LT waiting list, i.e. Region 4-5 and 9, and vice versa **(Figure S13)**.

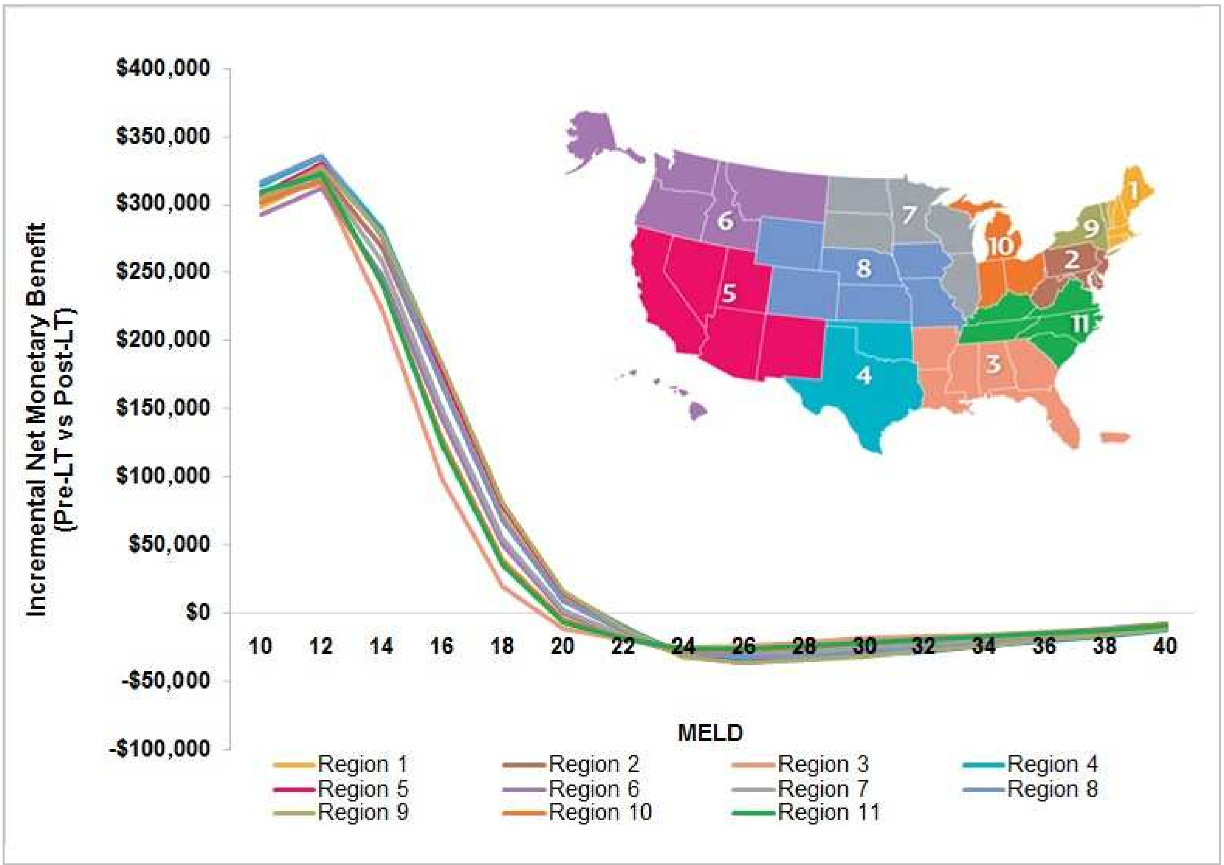

Figure S13. Comparison of incremental net-monetary benefit of treating HCV pre-LT versus post-LT in different UNOS regions. The net-monetary benefit of pre-LT treatment was higher in regions with longer time on the LT waiting list and vice versa.

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