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Cost-Effectiveness of Direct-Acting Anti-viral Treatment in Hepatitis C-infected Liver Transplant Candidates with Compensated Cirrhosis and Hepatocellular Carcinoma

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Abstract

Background—HCV(+) donors represent an effective strategy to increase liver donor availability to HCV-infected recipients. However, many HCV(+) transplant candidates are now receiving treatment with direct acting anti-virals (DAA) that lower the risk of posttransplant HCV recurrence but could make the patient ineligible for HCV(+) livers.

Methods—We compared pretransplant DAA treatment versus deferred DAA treatment using a cost-effectiveness decision analysis model to estimate incremental cost-effectiveness ratios (ICERs; cost per quality-adjusted life year [QALY] gained) from the societal perspective across a range of HCV(+) liver availability rates. For practical considerations, the population modelled was restricted to well-compensated HCV(+) cirrhotics listed for liver transplantation with HCC MELD exception points.

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Results—Under base case conditions, the deferred DAA treatment strategy was found to be the "dominant" strategy. That is, it provided superior health outcomes at cost savings compared to the pretransplant DAA treatment strategy. The pretransplant DAA treatment strategy trended towards cost-effectiveness as HCV(+) donor liver availability declined. However, only in 1 scenario that was highly optimized for favorable outcomes in the pretransplant DAA treatment arm (low availability of HCV(+) organs, low cost of DAA treatment, high cost of HCV recurrence) was the ICER associated with HCV DAA treatment *before* transplant <$150,000/QALY gained.

Conclusions—Deferring HCV treatment until after liver transplant and maintaining access to the expanded pool of HCV(+) donors appears to be the most cost-effective strategy for well-compensated HCV-infected cirrhotics listed for liver transplantation with HCC, even in geographic areas of relatively low HCV(+) donor availability.

INTRODUCTION

The high demand for liver transplantation has necessitated multiple strategies to broaden the pool of donor livers. One key strategy is to transplant livers from donors with a positive hepatitis C (HCV) antibody in HCV-infected liver transplant candidates. Compared with HCV(−) donor livers, transplantation with HCV(+) donor livers results in similar rates of HCV recurrence, graft survival, and patient survival.[1–4] Thus, HCV(+) donor livers represent a viable strategy for expanding the donor pool available to HCV-viremic candidates.

The availability of direct-acting anti-viral agents (DAAs) against HCV – which are both safe and effective at curing HCV for patients with well-compensated cirrhosis awaiting liver transplantation – has introduced a new dilemma for HCV-infected liver transplant candidates. On the one hand, HCV cure *prior to transplant* eliminates the possibility of HCV recurrence after transplant, and, as a result, may increase patient and graft survival.[5–10] Pretransplant HCV treatment may also reduce the risk of hepatic decompensation.[11,12] On the other hand, according to current policies in the majority of transplant centers, patients who achieve an undetectable HCV viral load prior to transplant are ineligible to receive livers from HCV(+) donors, reducing their access to the pool of HCV(+) donors and potentially prolonging their waiting time and increasing their risk of waitlist mortality.

In this study, we developed a cost effectiveness decision analysis model to quantify the trade-offs of pretransplant HCV treatment with DAAs versus deferring HCV treatment until *after* transplant for the option of early access to transplant with an HCV(+) donor liver. We hypothesized that for a well-compensated cirrhotic with hepatocellular carcinoma (HCC) whose need for liver transplantation is determined not by portal hypertensive complications but by the presence of cancer, the decision to undergo HCV treatment *before* transplant depends upon the geographic availability of HCV(+) donor livers in a candidate's listing region.

METHODS

The cost-effectiveness decision analysis model, shown in Figure 1, was created and analyzed using Excel 2016. The model estimated from a societal perspective the direct costs of DAA treatment, liver transplant, and each modelled health state (eg HCV, HCC), along with the

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quality-adjusted life-years (QALYs) associated with each outcome. The population modeled was US adult HCV-infected liver transplant candidates with HCC and well-compensated cirrhosis who are listed for liver transplantation. Candidates were modeled to receive pretransplant DAA treatment or defer DAA treatment until after transplant. We made the following assumptions about the population:

1. HCV cure would not eliminate the need for liver transplant, as the candidate still needed liver transplant for cure of HCC, and
2. Patients who achieved an undetectable HCV RNA would *not* be eligible for liver transplantation with a liver from an HCV(+) donor.

In order to obtain the QALYs gained and the costs for each strategy, the annual utilities and costs associated with the trajectory of each outcome were summed. The final model outcome was the incremental cost effectiveness ratio (ICER) calculated as:

$$\mathrm{ICER}=\frac{[\text{Costs of pre- transplant DAA} - \text{Costs of deferred DAA treatment}]}{[\text{Effect of pre- transplant DAA} - \text{Effect of deferred DAA treatmen}]}$$

where

- The costs of each strategy included the costs of pretransplant DAA treatment, posttransplant DAA treatment, and costs of HCC and HCV management.
- The effect on health status was measured in terms of quality-adjusted life years (QALYs) achieved from listing on the waitlist.

DAA treatment

Our base case modeled DAA treatment with 12 weeks of Ledipasvir/Sofosbuvir (LDV/SOF; Harvoni) + Ribavirin (RBV) based on data from the SOLAR-1 and SOLAR-2 studies.[6,7] Efficacy data on this treatment in patients with well-compensated cirrhosis was used for the base case, while sensitivity analyses were performed across a range of efficacies established from similar DAA regimens with a plausible lower limit being defined by an earlier, less effective DAA regimen.[5] There was no difference with regards to cost between the pretransplant and posttransplant DAA treatments modeled.

Clinical Outcomes

The time horizon of the model began at the time of listing and limited by the available survival data in the literature, extended up to 5 years after transplant. Waitlist outcomes were modeled as occurring at 1 year from listing consistent with data obtained from the United Network for Organ Sharing/Organ Procurement Transplantation Network (UNOS/OPTN) for this patient population and were as follows:

1. Deceased donor liver transplant (DDLT).
2. Delisting due to sickness. Patients who were delisted due to sickness were modeled to ultimately die from complications of advanced HCC. It was assumed that the patient would live an additional 2 years after delisting if the patient was

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HCV-viremic or 3 years if the patient had achieved HCV cure based on the avoidance of potential complications of comorbid HCV. In this case, the costs associated with HCC and/or HCV and utilities associated with pretransplant HCC were extended until death.

3. Death. This outcome was defined as death of any cause.

If the patient underwent liver transplant, outcomes were as follows:

1. Death within 90 days. Patients who died within this period would not receive DAA treatment after transplant.
2. Posttransplant survival beyond 90 days. Subsequent outcomes were as follows:
   a. Avoidance of HCV recurrence (only possible in pretransplant DAA treatment arm).
   b. HCV recurrence (possible in either arm). We assumed that HCV would recur within the first year posttransplant and be treated with DAA 1-year posttransplant. The effects of HCV recurrence were modeled via both QALY and cost penalties over the first year posttransplant (Table 1). Subsequent outcomes were as follows:
      i. Posttransplant cure of HCV. The QALY and cost penalties for HCV recurrence stopped at 1-year posttransplant.
      ii. Failure to achieve cure of HCV posttransplant. The QALY and cost penalties for HCV recurrence extended for the remainder of the patient's survival, where survival was modeled for death of any cause.

Input parameters for the model

Base case conditions, sensitivity ranges, and sources for all model parameters are reported in Table 1. Model parameters included outcome probabilities, health-outcome utilities, and costs. To ensure accurate representation of our target population, probabilities of waitlist outcomes, including the probability of receiving an HCV(+) vs. HCV(−) liver, were directly determined using data on HCV(+) adult patients with HCC on the waitlist with terminal outcomes from June 1, 2010 to May 31, 2015 obtained from the UNOS/OPTN. Notably, patients receiving a living donor liver transplant were not included in this analysis. For waitlist outcome probabilities in HCV(+) patients (eg probability of DDLT), we employed the national average of this cohort as the base case and used UNOS regional level variation to define the range for sensitivity analyses. To compute the theoretical waitlist outcomes for a candidate who achieved undetectable HCV RNA while on the waitlist, we assumed that the probability of transplant was the probability of receiving only an HCV(−) liver. The decrease in the probability of DDLT that resulted from loss of access to HCV(+) livers was distributed proportionally across the other waitlist outcomes. For inputs derived from literature review, base case parameters were selected based on a combination of factors including relevance to the study cohort and the modeled HCV treatment regimen. Drug costs were estimated using approximate whole acquisition prices. All costs were obtained from

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US sources and adjusted to 2015 US$ using the Consumer Price Index Factors available from the US Bureau of Labor Statistics (stats.bls.gov/cpi/). All future QALYs and costs were discounted by 3% year, the standard rate.[13,14]

Scenarios

We considered scenarios over a range of probabilities that a patient would be transplanted with a liver from an HCV(+) donor. This depended upon 2 factors: 1) the probability that a patient will be transplanted, and 2) the probability that, if transplanted, they receive an HCV(+) liver. The range of probabilities for the latter was based on our own analyses of HCV(+) liver availability relative to the number of HCV(+) candidates by UNOS region.[15] Figure 2 shows the percentage of HCV(+) recipients receiving an HCV(+) liver nationally and by region, based on UNOS/OPTN data from 4/1/2010-3/31/2015.

The greater the availability of HCV(+) livers, the greater the expanded pool of eligible donors available to the HCV(+) candidate if DAA treatment is deferred until after transplant. Based on this principle, we developed 2 scenarios centered around the probability of receiving an HCV(+) liver: 1) high probability of receiving an HCV(+) liver, and 2) low probability of receiving an HCV(+) liver. Scenarios that yielded cost *savings* per QALY gained were considered "dominant." Given the dominance of the deferred DAA treatment arm in the scenarios with relatively high probabilities of receiving an HCV(+) liver, we focused our analyses in scenarios of lower HCV(+) liver availability, where there would be a greater chance of achieving cost-efficacy in the pretransplant DAA treatment arm.

Sensitivity analyses

One-way deterministic sensitivity analyses were performed varying the (1) DAA efficacy parameters (2) waitlist outcome probabilities, (3) posttransplant outcome probabilities, (4) outcome utility weights, (5) treatment costs, and (6) annual costs of care using the ranges reported in Table 1. The possibility that pretransplant DAA treatment would prevent deteriorating liver function from precluding locoregional therapy was also explored via 1-way sensitivity analyses. The impact of locoregional therapy was implemented by decreasing the probabilities of delisting due to sickness and death on the waitlist in the pretransplant DAA treatment arm by a percentage. The amount that the probabilities of delisting due to sick and death on the waitlist was decreased by locoregional therapy was redistributed to increasing probability of DDLT. Multi-way deterministic sensitivity analyses were used to assess the efficacy in different scenarios. Sensitivity analyses were also performed to assess the impact of all assumptions.

RESULTS

Under base case parameters and in a modelled population of well-compensated HCV(+) adult cirrhotics listed for liver transplantation with HCC MELD exception points and average age of listing of 58 years, treatment with DAAs *prior* to transplant produced 2.95 QALYs from the time of listing, which was inferior to the 3.04 QALYs produced by deferring HCV treatment until *after* transplant. In our model, the average cost associated with the pretransplant DAA treatment arm was also greater, at $580,502, compared to

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$531,619 for the deferred DAA treatment strategy. Therefore, in our base case, deferring HCV treatment until after transplant, compared to treating HCV before transplant, achieved a superior health outcome at a decreased cost ("dominant").

Table 2 shows the ICERs over a range of probabilities that a patient would be transplanted and if they were transplanted, that they would be transplanted with an HCV(+) liver. The increased cost of the pretransplant DAA treatment arm ranged from $48,883 in regions of high availability of HCV(+) livers to $98,027 in regions of low availability of HCV(+) livers. In the pretransplant DAA treatment arm, the net QALYs ranged from 0.09 QALYs lost in regions of high availability of HCV(+) livers to 0.15 QALYs gained in regions of low availability of HCV(+) livers. The ICER ranged from the deferred DAA treatment arm being the dominant strategy to $663,624/QALY gained in regions of low availability of HCV(+) livers.

We then performed multiple 1-way sensitivity analyses, the most influential of which are shown in Figure 3, based on the ranges of inputs reported in Table 1. Specifically, the sensitivity analyses that we show in Figure 3 are: 1) the probability that a patient will be transplanted, 2) the probability of receiving an HCV(+) liver given transplant, 3) the probability of posttransplant virologic response, 4) the probability of sustained virologic response for posttransplant DAA treatment, 5) the HCV recurrence utility penalty, 6) cost of DAA treatment, 7) cost of HCV recurrence, 8) locoregional therapy benefit in the pretransplant DAA treatment arm, and 9) increasing probability of perioperative death. In Figure 3, each parameter is represented by a single vector. From these univariate sensitivity analyses, we identified that the parameters of greatest influence were: 1) the probability of receiving any transplant, 2) the probability of receiving an HCV(+) liver given transplant, 3) HCV recurrence utility and cost penalties, and 4) the cost of DAA treatment. The assessment that pretransplant DAA treatment is not cost-effective was robust to all univariate sensitivity analyses, as the 1-way sensitivity analyses failed to diminish the dominance of the base case scenario. Among the 1-way sensitivity analyses that produced health benefit, none achieved a pretransplant DAA treatment ICER ≤ $1 million/QALY gained.

Lastly, in an attempt to identify scenarios favoring pretransplant DAA treatment, we re-evaluated the ICERs associated with pretransplant DAA treatment versus deferred DAA treatment, this time using inputs optimized for pretransplant DAA treatment favorability (using the factors of greatest influence in our sensitivity analyses). Specifically, we used the upper bounds for HCV recurrence utility and cost penalties and the lower bound for the cost of DAA treatment from Table 1, while maintaining all other parameters at base case conditions. We observed similar trends in incremental cost and QALYs gained as HCV(+) donor liver availability decreased (Table 3). As expected, in this optimized scenario analysis we also observed an absolute decrease in costs and increase in QALYs gained leading to lower pretransplant DAA treatment ICERs relative to those presented in the previous scenario analyses above.

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DISCUSSION

Using cost-effectiveness analysis, we compared the strategies of pretransplant DAA treatment to deferring HCV treatment until after transplant in well-compensated HCV-infected cirrhotics listed for liver transplantation with HCC MELD exception points. At a threshold of <$150,000/QALY gained to define cost-effectiveness, as suggested by Neumann et al to better reflect today's health care and economic climate, pretransplant DAA treatment in HCV(+) candidates with HCC is ***not*** cost effective, even in scenarios of relatively low HCV(+) donor availability.[31] This conclusion was robust to thorough and comprehensive sensitivity analyses. In regions with relatively high availability of HCV(+) donors, deferring HCV treatment until after liver transplant emerged as the dominant strategy.

Through our scenario simulations, we demonstrated that the pretransplant DAA treatment strategy becomes more cost-effective as HCV(+) donor liver availability declines. This occurs because as HCV(+) availability decreases, the potential benefit of avoiding the deleterious effects of HCV recurrence in the pretransplant DAA treatment arm begin to outweigh the benefit of the expanded pool of available HCV(+) donor livers. Only in the 1 scenario, that was highly optimized for favorable outcomes in the pretransplant DAA treatment arm, did the ICER associated with HCV DAA treatment before transplant dip below the $150,000/QALY gained threshold. This occurred because the minimal health benefit of pretransplant DAA treatment was achieved at a substantial incremental cost since *all* patients in the pretransplant DAA treatment arm receive DAA treatment regardless of their ultimate transplant status. Of note, as the results of our scenario analyses were so heavily in favor of deferred DAA treatment, further probabilistic sensitivity analyses were deemed to be noninformative and thus, are not presented.

Our conclusions make intuitive sense. For a patient with well-compensated cirrhosis listed with HCC MELD exception points, pretransplant DAA treatment is costly in terms of both the price of DAA treatment for those who do not reach transplant as well as the health consequence of decreased probability of transplant, with little upside with respect to HCV disease regression. With respect to internal validity, we employed several measures to ensure that we accurately represented our target population. First, we were able to accurately model waitlist outcomes for our population of interest by using data from UNOS directly. Furthermore, expert clinicians evaluated the results of our sensitivity analyses to ensure that our model performed in a logical manner.

Furthermore, given that we used conservative inputs to optimize the pretransplant DAA treatment arm, we believe this assessment will hold true, if not strengthen, in the face of forecasted changes in the HCV treatment landscape. For example, in our base case, we employed a 100% efficacy of pretransplant DAA treatment, which was greater than our posttransplant DAA treatment efficacy of 95%. Given early evidence that posttransplant DAA treatment may in fact be intrinsically better within the population of HCV candidates with HCC,[32] this modeled advantage for pretransplant DAA treatment may be better modeled as an advantage for deferred DAA treatment. Another modeled advantage of pretransplant DAA treatment was avoidance of HCV recurrence. However, with new efforts

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to employ DAA treatment preemptively in the peri-operative setting,[33] the modeled costs of HCV recurrence may also be partially obviated within the deferred DAA treatment arm. Lastly, with growing efforts to employ marginal donor livers such as those from HCV(+) donors, the modeled availability of HCV(+) donor livers is likely an underestimate of the future availability.

We acknowledge several limitations to our model, largely based on our assumptions that are inherent in conducting this cost-effectiveness analysis. We assumed that HCV cure would not eliminate the need for liver transplantation in this population of patients with HCC. Therefore, this model does not apply to patients with cirrhosis listed for liver transplantation without MELD exception points – for whom HCV cure may lead to clinically meaningful disease regression (that would favor the pretransplant DAA treatment arm). Given that this model was based on US data and transplant system, we also acknowledge that it does not apply readily to other settings where factors such as diverging rules governing access to DAA treatment or substantially lower costs could alter the cost effectiveness of pretransplant DAA treatment. However, we'd like to specifically address the case that posttransplant DAA treatment is restricted in some jurisdiction to HCV infection having progressed to stage 2 or more fibrosis, which we'd only expect to strengthen our conclusion that pretransplant DAA treatment is not cost effective. As modelled currently, any instance of HCV recurrence, which is predominantly an issue in the deferred arm, gets treated with costly DAA treatment regardless of severity. However, if we limit posttransplant treatment to those with grade 2 fibrosis, the level at which we expect substantial health consequences, we would bypass the substantial expense of DAA treatment in the cases of HCV recurrence with minimal consequence, which would only serve to make the deferred treatment arm more cost-effective.

We also forced assumptions into the model on the time course of a patient with HCC on the waitlist and the input parameters. However, in areas of ambiguity, assumptions were made that would favor the pretransplant DAA treatment arm so we do not believe that they would have substantially changed our overall conclusions regarding the benefit of the deferred DAA treatment arm. For example, in our model, if a patient achieved a sustained virologic response with pretransplant DAA treatment but was subsequently delisted for tumor progression outside of Milan criteria, we assumed that this patient would achieve 1 additional year of life relative to those who did not receive DAA treatment to account for any added benefit of SVR even in the absence of transplant for a patient with HCC. Despite the limitations inherent in these assumptions, our results are consistent with a recent cost-effectiveness analysis of pretransplant DAA therapy which also concluded that posttransplant DAA therapy was the most cost-effective strategy in this population.[13]

In conclusion, our model suggests that deferring HCV treatment until after liver transplant and maintaining access to HCV(+) donors is the preferred strategy in the management of well-compensated HCV-infected cirrhotics listed for liver transplantation with HCC MELD exception points. Through sensitivity analyses, we established that this conclusion is even generalizable to geographic areas of relatively low HCV(+) donor availability. While many centers have started to shift their HCV treatment strategies until after transplant, our analyses *quantify* this benefit and provide powerful justification for the deferred DAA

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treatment strategy to the patients who oftentimes cannot fathom waiting any longer to achieve HCV cure. These data are particularly relevant in light of the recently implemented 6-month delay between the first and the second HCC MELD exception point extension as well as the MELD 34 cap for HCC MELD exception points, both of which are anticipated to increase drop-out rates for patients listed for liver transplantation for HCC. Further analyses are needed to evaluate the cost-effectiveness of pretransplant DAA treatment in the general HCV-infected liver transplant population. We believe that our model and the considerations presented in this paper will not only be helpful in guiding decision making in the HCV(+) HCC populations but will provide a strong conceptual framework to build off for these broader analyses.

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List of abbreviations

DAA	direct acting antiviral
DDLT	deceased donor liver transplant
HCC	hepatocellular carcinoma
HCV	hepatitis C virus
ICER	incremental cost-effectiveness ratio
LT	liver transplant
OPTN	Organ Procurement Transplantation Network
QALY	quality-adjusted life-year
SVR	sustained virologic response
UNOS	United Network for Organ Sharing

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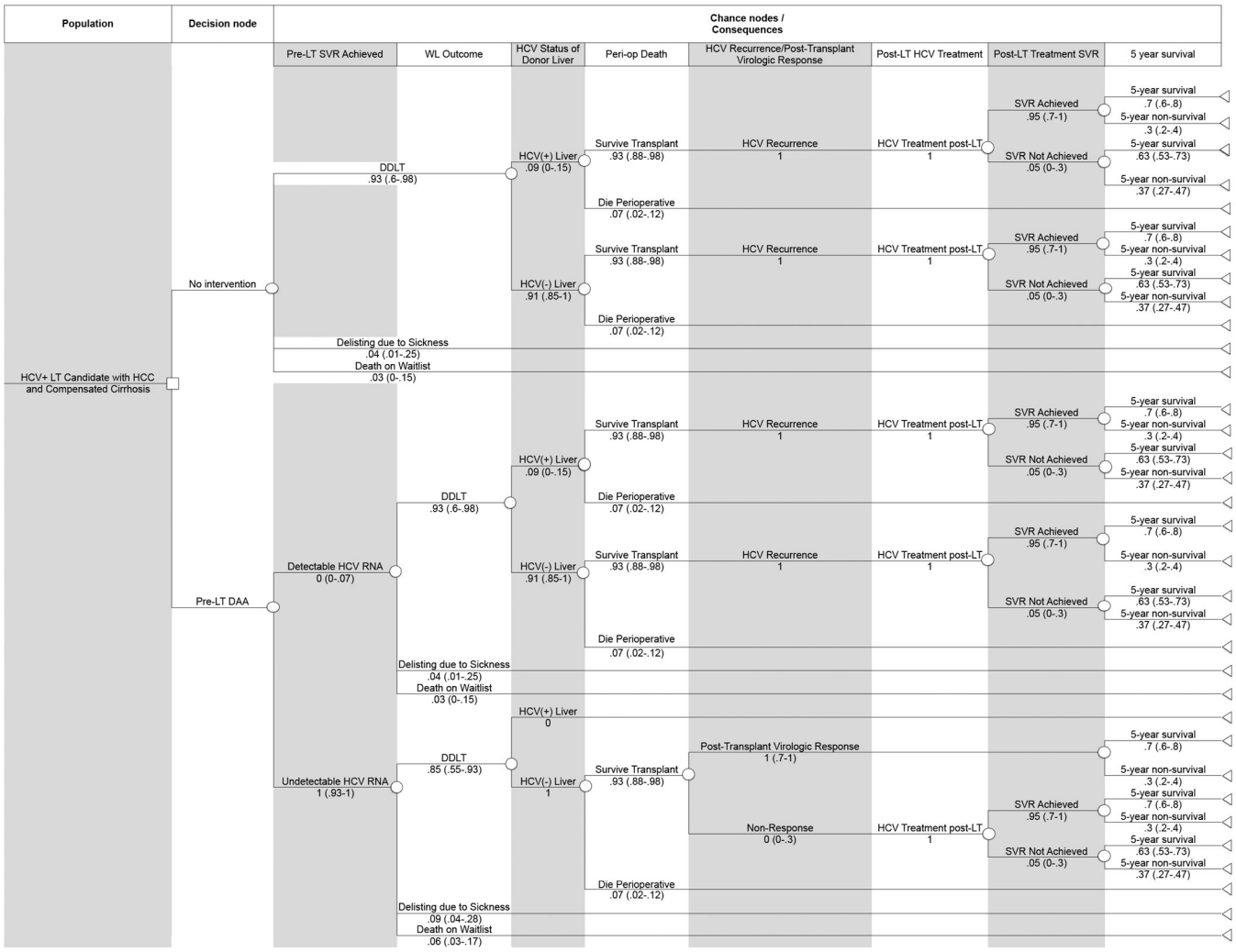

Figure I. Model Schematic

Schematic of the **cost effectiveness** decision analysis model for pretransplant DAA treatment versus deferred DAA treatment of HCV(+) liver transplant candidates with HCC and well-compensated cirrhosis. Under each node is the base case probability and range used in sensitivity analyses.

DAA, direct acting antiviral; DDLT, deceased donor liver transplant; HCC, hepatocellular carcinoma; LT, liver transplant; SVR, sustained virologic response

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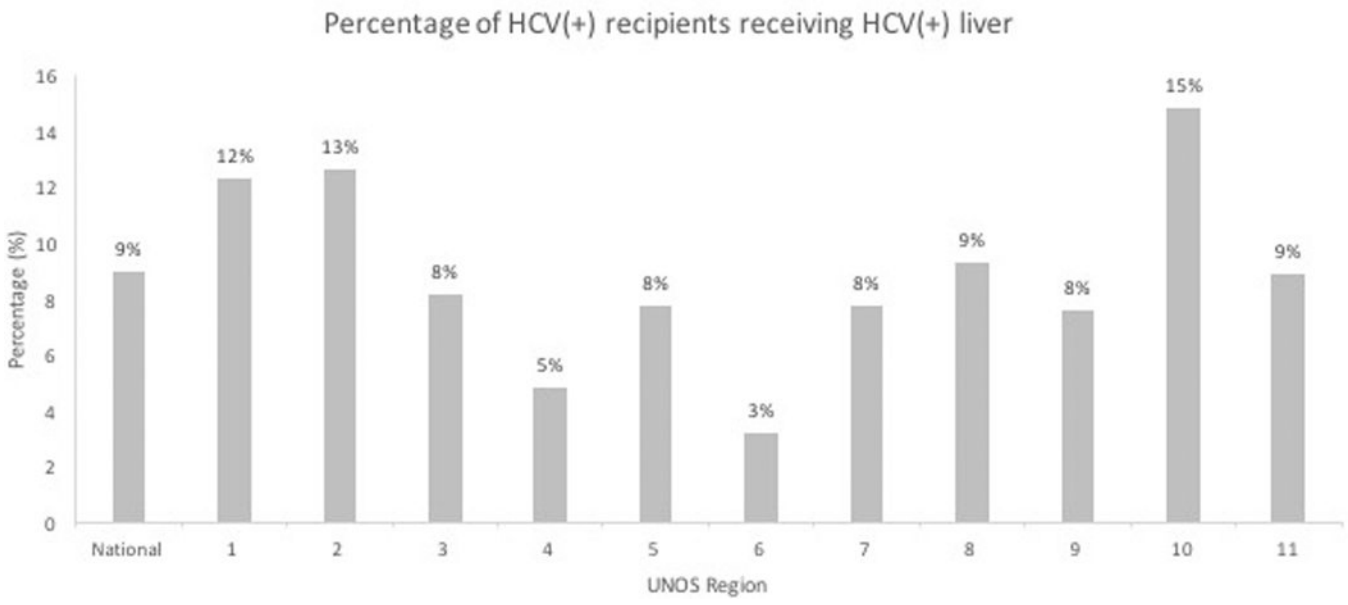

Figure II. Percentage of HCV(+) recipients receiving an HCV(+) liver

Percentage of HCV(+) recipients receiving an HCV(+) liver, nationally and by UNOS region of listing. UNOS data on all US adult deceased donor LT recipients 4/1/10-3/31/15.

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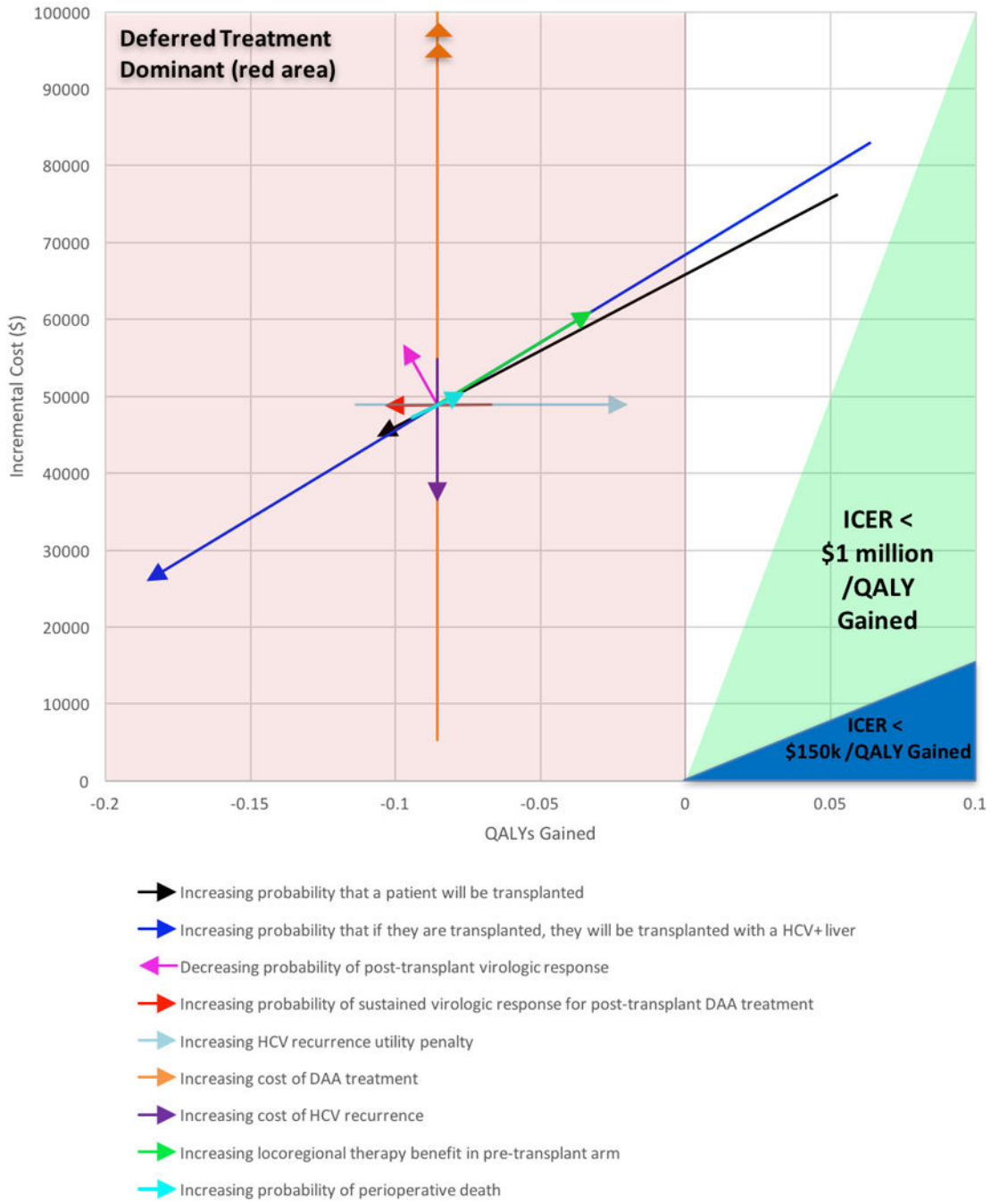

Figure III. Supernova Sensitivity Analysis

Each parameter is represented by a single vector. The end points represent the QALYs gained and incremental costs at the lower and upper bounds of our sensitivity analysis of each parameter. The base case result is where the vectors intersect. For any given parameter, the horizontal change of the vector represents its effect on health outcomes and the vertical change represents its effect on cost. The arrow points in the direction of decreasing or increasing the value of the parameter as specified in the legend. For example, the violet arrow indicates that with decreasing probability of posttransplant virologic response, the

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deferred strategy becomes incrementally less favorable than the base case, with higher net costs and more lost QALYs. A double arrow indicates results outside of the bounds visualized. Longer lines indicate that under the sensitivity bounds outlined in Table 1, a particular parameter has greater potential for influence. The red shaded area denotes conditions in which the deferred DAA treatment was the dominant option (ie associated with both QALYs gained and cost savings), the green shaded area denotes the area in which the ICER would be <$1 million/QALY gained, and the blue shaded area denotes the area in which the ICER would be <$150,000 /QALY gained.

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Table I

Model parameters

Model parameters	Base case value (range)	References
Model assumptions		
Discount rate cost/outcomes	.03 **(0–.05)**	-
Time horizon	5-years postwaitlist outcome	-
Perspective	Societal	-
DAA Efficacy		
Probability of achieving undetectable HCV RNA on waitlist	1 (.93-1)	(5–7)
Probability of posttransplant virologic response	1 (.7-1)	(5–7)
Probability of sustained virologic response with posttransplant DAA treatment	.95 (.7-1)	(6,7,16)
Waitlist outcome probabilities if detectable HCV		
Probability of DDLT	.93 (.6−.98)	UNOS/OPTN
Probability of HCV(+) Donor Liver	.09 (0−.15)	UNOS/OPTN
Probability of delisting due to sickness	.04 (.01−.25)	UNOS/OPTN
Probability of death	.03 (0−.15)	UNOS/OPTN
Waitlist outcome probabilities if undetectable HCV		
Probability of DDLT	.85 (.55−.98)	UNOS/OPTN
Probability of HCV(+) Donor Liver	0	Assumption
Probability of delisting due to sickness	.09 (.01−.28)	UNOS/OPTN
Probability of death	.06 (0−.17)	UNOS/OPTN
Locoregional therapy benefit in pretransplant treatment arm	0% (0–20%)	Assumption
Probability of peri-operative death	.07 (.02−.12)	(17)
Probability of 5-year survival if SVR achieved posttransplant	.7 (6−.8)	(18)
Probability of 5-year survival if SVR not achieved posttransplant	.63 (.53−.73)	(18)
Utility weights		
Pretransplant	.53 (.52−.61)	(19,20)
Posttransplant Year 1	.69 (.61−.71)	(19,20)
Posttransplant Year 2 and onwards	.73(.62−.84)	(20,21)
HCV recurrence penalty	−.03 (−.1-0)	(22)
Treatment cost ($2015)		
SOF + RBV (24 wks)	$86,184	(23,24)
LDV/SOF + RBV (12 wks)	$97,675	(25)
DAA Cost Range	$50,000-$200,000	**Exploratory**1
Annual Costs of Care ($2015)		
HCC	$51,253 ($26,000-$61,000)	(26–29)
Liver Transplant (1st year)	$320,583 ($287,000-$496,000)	(17,27,28)

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Model parameters	Base case value (range)	References
Liver Transplant (successive year)	$40,258 ($40,200-$48,600)	(17,27,28)
HCV Recurrence	$6,680 ($350-$20,000)	(30)

[1] This range was defined outside the bounds of DAA costs found in literature intentionally in an effort to explore threshold points of cost-effectiveness.

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Table II

Incremental cost-effectiveness ratios (ICERs) over a range of HCV(+) liver availability rates under otherwise base case conditions

Probability of Deceased Donor Liver Transplant	Probability of HCV(+) liver given DDLT	Cost Δ ($)[1]	QALY Δ[1]	ICER ($/QALY)[2]
.93	.09[3]	48,883	−.09	Deferred-treatment arm is dominant
	.045	65,912	−.01	Deferred-treatment arm is dominant
	0	82,941	.06	1,305,644
.75	.09	63,871	−.01	Deferred-treatment arm is dominant
	.045	77,555	.05	1,551,588
	0	91,238	.11	830,721
.6	.09	76,133	.05	1,465,205
	.045	87,080	.1	872,216
	0[4]	98,027	.15	663,624

"Dominant" = resulted in improved outcomes at reduced costs; QALY, quality-adjusted life years; DDLT, deceased donor liver transplant

[1]Cost Δ and QALY Δ is the Cost/QALY of the deferred strategy subtracted from that of the pretransplant DAA strategy

[2]The ICER is the ratio of the difference in costs/difference in QALYs

[3]The base-case scenario featuring relatively high probability of deceased donor liver transplant and probability of HCV(+) given DDLT

[4]Scenario featuring relatively low probability of deceased donor liver transplant and probability of HCV(+) liver given DDLT

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Table III

Incremental cost-effectiveness ratios (ICERs) over a range of HCV(+) liver availability rates under optimized conditions for pretransplant

Probability of Deceased Donor Liver Transplant	Probability of HCV(+) liver given DDLT	Cost Δ ($)[1]	QALY Δ[1]	ICER ($/QALY)[2]
.93	.09[3]	−7,144	−.02	N/A
	.045	8,107	.05	147,930
	0	23,402	.13	180,600
.75	.09	9,586	.04	224,329
	.045	21,877	.10	212,766
	0	34,168	.16	209,732
.6	.09	23,310	.09	247,882
	.045	33,143	.14	233,221
	0[4]	42,976	.19	225,972

Optimized conditions included using the upper bounds for HCV recurrence utility and cost penalties and the lower bound for cost of DAA treatment. QALY, quality-adjusted life years; DDLT, deceased donor liver transplant

[1]Cost and QALY Δ is the Cost/QALY of the deferred strategy subtracted from that of the pretransplant DAA strategy

[2]The ICER is the ratio of the difference in costs/difference in QALYs

[3]The base-case scenario featuring relatively high probability of deceased donor liver transplant and probability of HCV(+) given DDLT

[4]Scenario featuring relatively low probability of deceased donor liver transplant and probability of HCV(+) liver given DDLT