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Cost-effectiveness of Transplanting HCV-Infected Livers into Uninfected Recipients with Preemptive Antiviral Therapy

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Abstract

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Background & Aims: Guidelines do not recommend transplanting hepatitis C virus (HCV)-infected livers into HCV-uninfected recipients. Direct-acting antivirals (DAAs) can be used to treat donor-derived HCV infection. However the added cost of DAA therapy is a barrier. We evaluated the cost effectiveness of transplanting HCV-positive livers into HCV-negative patients with preemptive DAA therapy.

Methods: A previously validated Markov-based mathematical model was adapted to simulate a virtual trial of HCV-negative patients on the liver transplant waitlist. The model compared long-term clinical and economic outcomes in patients willing to accept only HCV-negative livers vs those willing to accept any (HCV-negative or HCV-positive) liver. Recipients of HCV-positive livers received 12 weeks of preemptive DAA therapy. The model incorporated data from the United Network for Organ Sharing and published sources.

Results: For patients with a model for end-stage liver disease (MELD) score ≥ 22 , accepting any liver vs waiting for only HCV-negative livers was cost effective, with incremental cost-effectiveness ratios ranging from \$56,100 to \$91,700/quality-adjusted life year. For patients with a MELD score of 28 (the median MELD score of patients undergoing transplantation in the United States), accepting any liver was cost effective at an incremental cost-effectiveness ratio of \$62,600/quality-adjusted life year. In patients with low MELD scores that may not accurately reflect disease severity, accepting any liver was cost effective, irrespective of MELD score.

Conclusions: Using a Markov-based mathematical model, we found transplanting HCV-positive livers in HCV-negative patients with preemptive DAA therapy to be a cost-effective strategy that could improve health outcomes.

Keywords

ICER; QALY; viremic donor; prevention; simulation modeling

INTRODUCTION

Over the last decade there has been a steady rise in the number of patients with end stage liver disease in need of transplantation. With limited liver donor availability, we have not seen a parallel increase in the number of annual liver transplants performed.¹ As this shortage of transplant viable organs persists, it is of paramount importance that all transplantable organs are identified and allocated to those most in need. Hepatitis C virus (HCV)-infected donor organs are a potentially underutilized resource. This is becoming increasingly recognized as persons who inject drugs emerge as the fastest-growing donor category, and HCV-positive organs begin to compromise a larger portion of the donor organ supply.² With the advent of highly effective direct-acting antivirals (DAAs), the number of patients in need of liver transplantation as the result of HCV related liver disease is expected to decline, while an increasing number of HCV-uninfected patients, remain on the waitlist.^{3,4}

Current guidelines do not recommend the use of HCV-positive donor livers for transplantation into HCV-negative recipients. This is because viremic donor livers carry a universal risk of HCV transmission, and if liver allograft HCV infection develops and cannot be successfully treated, there is a higher risk of complications, including potential graft failure.^{5,6} Given this concern, HCV-positive donor livers have historically been reserved for

HCV-infected waitlist patients. However, while HCV treatment in the interferon era was poorly tolerated and associated with complications that led to worse post-transplant outcomes, this is not the case with new HCV treatment regimens. If allograft HCV infection can be successfully cured with DAA therapy, then it may be time to revisit HCV-positive organ allocation policies.

Emerging data demonstrate excellent DAA efficacy in treating donor derived HCV infection in lung, kidney, and liver transplant (LT) recipients.⁷⁻⁹ A recent modeling study also highlighted the clinical importance of this approach, demonstrating the potential benefits seen at various MELD scores when patients on the LT waitlist become open to accepting HCV-positive livers.¹⁰ Despite the currently limited data, it is postulated that DAAs will continue to exhibit successful post-transplant HCV cure.¹¹

While there is clear clinical rationale and physician consensus to support strategies aimed at increasing the static donor organ pool, the added cost of DAA therapy remains a logistical barrier. The current environment restricts reimbursement for treatment of donor derived HCV infection, allowing payers to deny coverage and place the burden of DAA cost on individual patients. Although accepting HCV-positive organs could reduce a patient's time to transplant and waitlist associated mortality, it could also increase post-LT complications associated with HCV allograft infection. The tradeoffs of such a strategy have not been studied. However, such information can prove critical in helping inform policy level decisions surrounding HCV-positive organ use. To evaluate these tradeoffs, we conducted a model-based analysis, providing some of the first cost-effectiveness data on the use of preemptive DAA therapy in HCV-negative waitlist patients receiving HCV-infected donor livers.

METHODS

Model Overview

We adapted a previously validated Markov-based mathematical model, SIM-LT (*Simulation of Liver Transplant*), to conduct our cost-effectiveness analysis (Figure 1).^{10,12,13} SIM-LT simulated a virtual trial of HCV-negative patients on the LT waiting list in order to compare long-term clinical and economic outcomes in patients willing to accept only HCV-negative livers *versus* those willing to accept any, i.e. HCV-negative or HCV-positive, liver. The model incorporated data from the United Network for Organ Sharing (UNOS) and has been validated with reported values from the Organ Procurement and Transplantation Network (OPTN).^{10,12} SIM-LT was developed from the healthcare payer's perspective with a lifetime horizon.

Baseline population

We created a hypothetical cohort of HCV-negative decompensated cirrhotic patients (without hepatocellular carcinoma) who were active on the LT waiting list. At baseline, the mean age of patients in the model was 50, and MELD scores ranged between 12 and 40.

SIM-LT waiting list

We simulated the lifetime course of decompensated cirrhotic patients waiting for LT. Patients' MELD scores could naturally change on the waiting list. To estimate the natural disease course and MELD fluctuations, we used a previously published study based on UNOS data to estimate weekly changes in MELD.^{10,12,13} We aggregated data in paired groups of consecutive MELD scores as 12–13, ..., 38–39, and 40. We also estimated waitlist mortality by MELD score from the same data source (Supplementary Table S1). While patients were on the waiting list they could undergo LT, die from background mortality, or die from liver-related mortality based on their MELD scores.

Interventions

For each patient on the LT waiting list, we simulated two scenarios: 1) accept *only* HCV-negative livers, i.e. the current practice, and 2) accept *any* liver, i.e. HCV-negative or HCV-positive, followed by preemptive DAA treatment if an HCV-positive liver was accepted.

In both scenarios, the probability of receiving a liver transplant was based on MELD scores and geography (Supplementary Table S2, Supplementary Section S1).¹⁴ Patients could experience graft failure at any time after LT. If a patient had early acute-graft failure they were listed as status 1A for retransplantation. We assigned the average probability of liver transplant and liver-related mortality to these patients, estimated from UNOS data.¹²

In the '*accept only HCV-negative livers*' scenario, patients moved to the Post-LT (non-viremic) health state after successful HCV-negative liver transplant (Figure 1).

In the '*accept any liver*' scenario, if the incoming liver was HCV-negative, the patient moved to the Post-LT (non-viremic) health state post-transplant. If the incoming liver was HCV-positive, then preemptive antiviral treatment with DAAs was initiated. The status of the patient following LT was determined by their response to DAA therapy, i.e. ongoing viremia or achievement of sustained virologic response (SVR). If patients were successfully treated, they moved to the Post-LT (SVR) state; otherwise, they were given salvage therapy. The SVR rate of the salvage therapy was assumed to be the same as with preemptive therapy. If patients failed salvage therapy, they followed the natural progression of disease and were assumed to have chronic HCV (Figure 1).

Preemptive therapy in our analysis was defined as antiviral treatment at the time of or shortly after liver transplantation (i.e. administered within the days to weeks following transplant once allograft function stabilized). We incorporated DAA efficacy data from recent trials, including pan-genotypic regimens, and used SVR rates seen with 12 weeks of therapy in post-LT patients (Supplementary Table 3).¹⁵ We also accounted for the potential increased likelihood of fibrosing cholestatic hepatitis and graft failure in patients receiving HCV-positive livers (Supplementary Section S1).

The likelihood of undergoing transplant in the '*accept any liver*' scenario was higher than the current practice of accepting only HCV-negative organs. We therefore increased the rate of receiving a liver by 5.9%,¹⁶ i.e. the proportion of HCV-positive organs among all liver donors in the U.S. In the sensitivity analysis, we varied this rate from 2.9 to 26.7%,

corresponding to the lowest and highest HCV-positive organ rates observed in UNOS regions.¹⁷

Costs

Patients in both strategies incurred costs that included the cost of wait list patient care, the cost of transplantation, and the cost of post-LT patient management. In the ‘*accept any liver*’ scenario, patients transplanted with an HCV-positive liver incurred the additional cost of DAA therapy. Previously published studies were used to determine the health-state costs in our model.^{18,19} Because in practice the price of DAAs is lower than listed values, we applied a 23.1% discount on the wholesale acquisition cost of glecaprevir and pibrentasvir, \$39,600,²⁰ in our base case analysis, and further conducted sensitivity analysis on a wide range of potential DAA prices (\$10,000-\$95,000). All costs were converted to 2017 US dollars (Supplementary Table S3).

Health-related quality of life

For each health state in our model, we assigned health-related quality-of-life (QoL) weights, with 0 denoting death and 1 denoting perfect health. We derived EuroQol-5D instrument (Rotterdam, Netherlands) values from a previous study and adjusted them to the US population norm with age and sex (Supplementary Table S4).¹³

In order to evaluate patients with MELD scores that may not accurately reflect disease severity (e.g. a patient with MELD 18 with refractory ascites and high associated morbidity), we conducted an additional analysis by decreasing a patient’s QoL on the waiting list, using a QoL weight of 0.56.²¹

Model Outcomes

For each scenario, we estimated total costs and quality adjusted life years (QALYs) by MELD score, and the incremental cost-effectiveness ratio (ICER) of accepting *any* versus *only HCV-negative* livers. All future costs and QALYs were discounted at 3% per year. We projected outcomes for each UNOS region by adjusting the likelihood of LT and mortality on the waiting list using region-specific transplantation and death rates (Supplementary Table S5). In addition, we incorporated HCV-positive donor organ rates within each region (Supplementary Table S6) and adjusted the likelihood of transplant. Specific details are provided in Supplementary Section S1. A 1-way sensitivity analysis was performed to identify most sensitive model parameters. We also performed additional analyses to evaluate model outcomes under varying assumptions and scenarios, including incorporation of blood type and the Share 35 rule.

RESULTS

Cost-Effectiveness Analysis

The clinical and economic benefit of accepting any liver was dependent on the MELD scores at which patients were willing to accept an HCV-positive liver. For patients having MELD 22, accepting any liver versus waiting for only HCV-negative livers was cost-effective with an ICER between \$56,100 and \$91,700 per additional QALY (Figure 2, Supplementary

Table S7). For MELD scores 18–20, even though a willingness to accept an HCV-positive liver was clinically beneficial, the ICER was above the commonly accepted willingness to pay (WTP) threshold of \$100,000/QALY. For perspective, at the current median MELD at transplant in the U.S., i.e. MELD 28, accepting any liver was deemed cost-effective with an ICER of \$62,600 per additional QALY.

In patients with poor quality of life, and low MELD scores that may not accurately reflect disease severity, accepting any liver was clinically beneficial, i.e., QALYs were higher, irrespective of MELD score (Figure 3). The ICER of accepting any liver for these patients ranged from \$57,000–\$66,000, below the WTP threshold of 100,000/QALY.

Cost-Effectiveness by UNOS Regions

Results for each individual UNOS region, accounting for differences in HCV-positive donor organ rates as well as regional variations in transplant wait times and waitlist mortalities, demonstrated that at MELD 22 or 24 and above, accepting any liver was a cost-effective strategy in all regions (Figure 4). In regions 1–9 and 11, accepting any liver was cost-effective at the median MELD at transplant for each given region. In region 10, the median MELD at transplant was 22 and accepting any liver became a cost-effective strategy at MELD 24.

Sensitivity Analysis

In the accept any liver strategy, the highest clinical benefit was observed at MELD score 28, and the strategy was cost-effective in patients having MELD $\geq$ 22. One-way sensitivity analysis was performed and the 10 most sensitive model parameters are shown with tornado diagrams (Figure 5). At MELD 28, the model parameters that most influenced the cost-effectiveness of accepting any liver were the cost of LT and post-LT care. At MELD 22, the cost of LT, cost of post-LT care, DAA price, and the QoL on the waiting list were sensitive model parameters that could impact cost-effectiveness results. Supplementary Tables S8–S9 show all model parameters in a decreasing order based on their impact on the ICER at MELD scores 22 and 28.

The cost-effectiveness of accepting any liver varied by blood type—for patients having blood type O and A, accepting any liver was cost-effective when MELD $\geq$ 22. It was cost-effective for blood type B when MELD $\geq$ 24 and the blood type AB when MELD $\geq$ 28 (Supplementary Figure S1). Regional Share 35 policy did not change model outcomes—accepting any liver remained cost-effective in patients with MELD $\geq$ 22 (Supplementary Figure S2).

The cost of transplant can vary widely between transplant centers and the price of DAAs remains dynamic. We conducted a 2-way sensitivity analysis demonstrating how the cost-effectiveness of accepting *any* liver versus only HCV-negative livers would change with different combinations of DAA price and LT costs. Figure 6 shows these outcomes for MELD scores 22, 28 and 34. The figure uses the standard cost of LT utilized in cost-effectiveness analyses, which is different from the billed and reimbursement charges that hospitals and physicians receive for providing transplant care.

A threshold analysis on the efficacy of preemptive DAA treatment demonstrated that our model outcome, i.e. accepting *any* liver, is cost-effective when SVR rates remain above 75% (Supplementary Figure S3).

DISCUSSION

DAAs have provided us the opportunity to better utilize HCV-positive donor organs. We can now consider previously discarded HCV-positive livers for active use, expand the historically static liver donor pool, and allocate these viable organs in a manner that maximizes our ability to perform lifesaving transplants. While there are clear potential benefits to accepting HCV-positive organs, concerns surrounding the additional risks, including cost associated with preemptive DAA therapy, could impede clinical implementation. We conducted a model-based analysis to evaluate these tradeoffs, and provided the first publicly available data on the economic impact of this proposed course of action. Our results demonstrate that for the median MELD at transplant in the United States, it is not only clinically beneficial but also cost-effective for HCV-negative waitlist patients to accept HCV-positive donor livers. As MELD score rises, it becomes increasingly cost-effective to utilize this strategy, provided DAA efficacy in this setting remains robust.

The rising cost of health care management has raised concerns regarding the affordability and budget impact of costly treatments. Given that out of pocket DAA expense is prohibitively high for the vast majority of patients, payer coverage in this setting will be critical.²² The cost-effectiveness data provided here can be used to inform policy and support DAA coverage for this new use of therapy, emphasizing that while this strategy will result in an increase in initial spending, it is an advantageous investment that can improve long-term health outcomes.

We recognize that larger studies providing definitive clinical data on DAA efficacy in donor derived HCV infection are required before the preemptive use of DAAs is accepted as the standard of care and incorporated into transplant guidelines. Encouragingly, smaller studies are already demonstrating promising results, and it is strongly postulated that DAAs will continue to exhibit excellent efficacy for this indication.²³ Furthermore, our threshold analysis showed that preemptive treatment with DAAs remains cost-effective until the SVR rate drops below 75%, which is highly unlikely.

Liver transplant waitlist priority is determined based on MELD score, a surrogate for mortality; quality of life is not factored in to national waitlist ranking. This factor impacts model generalizability, as our base case results represent the average waitlist patient without case specific quality of life adjustments. We acknowledge that some of the patients who may benefit most from accepting HCV-positive livers are those with lower MELD scores that do not accurately reflect disease severity. For example, patients with refractory complications of portal hypertension, or recurrent cholangitis, who experience significant morbidity and higher mortality at lower MELD scores than the more general LT waitlist. While our primary results suggest accepting an HCV-positive organ is a cost-effective strategy starting around MELD 22, a separate analysis demonstrated how a reduced QoL can make accepting an HCV-positive organ a uniformly cost-effective strategy, irrespective of MELD. Of note, costs

that are accruing for low QoL patients while on the waitlist – hospitalizations, antibiotic courses, large volume paracentesis procedures – were not factored into the model for this select group of patients, but if incorporated would only further increase the cost-effectiveness of accepting HCV-positive organs at lower MELD scores. This highlights the primary take-away from our analysis, which is not a specific MELD threshold at which a patient or provider should consider accepting an HCV-positive organ, but that movement towards routine utilization of HCV-positive livers is a clinically beneficial and cost-effective strategy.

There are limitations to our model predictions. First, there are no published data on the graft failure rates in donor HCV-positive to recipient HCV-negative liver transplant; to obtain a value for model input, survival data was used as a proxy for graft failure.²⁴ Pre- and post-transplant risks, accounting for factors like steatosis that can impact allograft function, were included. Using a conservative approach, a likely overestimation of graft failure was incorporated with a high HR of 1.44, in order to maintain model robustness and ensure the risks associated with receipt of an HCV-positive organ were not minimized. The model did not incorporate risks associated with accepting HCV-positive livers with advancing levels fibrosis. Second, long-term data on transplant recipients who achieved SVR is extremely limited, and not incorporated in the model. Instead, we assumed that patient and graft survival would be similar to those of HCV-negative LT recipients. Third, our baseline population was HCV-uninfected patients awaiting transplant, we did not extend model outcomes to include HCV-positive waitlist populations. Fourth, HCV-positive region specific donor organ rates represent both viremic and non-viremic livers; outcome analysis based on specific nucleic acid testing (NAT)-positive and NAT-negative rates were not performed. Fifth, providing donor organs to an increasing number of patients may have secondary effects on general waitlist mortality, this was not incorporated into the model given lack of data. Sixth, donor age has an impact on long-term post-transplant survival, with recipients of younger donors experiencing better long-term outcomes.²⁵ Individual donor age was not factored into the current model, however if incorporated it would further support the use of viremic organs. Our model did not include patients with HCC, as these patients have a different natural disease history and require evaluation in a separate analysis.

Our current model evaluates preemptive DAA therapy, an approach that is likely to be uniformly agreed upon in NAT-positive donor organs exhibiting a universal rate of HCV transmission. The timing of DAA initiation in non-viremic, NAT-negative, donor organs may present an additional challenge.²² A recent study found the risk of HCV transmission from seropositive, non-viremic donors to be 16%, with the highest risk conferred by donors who died of drug overdose.²⁶ As opposed to preemptive therapy, there are potential cost-saving benefits to a reactive approach to DAA initiation in non-viremic donors. However, until additional studies can further evaluate the clinical outcomes associated with these high-risk organs, administration of preemptive therapy irrespective of NAT status is likely to minimize patient harm.

In conclusion, we found that preemptive DAA therapy in donor HCV-positive to recipient HCV-negative liver transplant is a cost-effective strategy that can improve health outcomes.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

DAAs	Direct-acting antivirals
HCV	Hepatitis C virus
ICER	Incremental cost-effectiveness ratio
LT	Liver transplant
MELD	Model for end-stage liver disease
NAT	Nucleic acid testing
OPTN	Organ Procurement and Transplantation Network
QoL	Quality-of-life
QALYs	Quality adjusted life years
SIM-LT	Simulation of liver transplant candidates
SVR	Sustained virologic response
UNOS	United Network for Organ Sharing

REFERENCES

1. Kim WR, Lake JR, Smith JM, et al. OPTN/SRTR 2015 Annual Data Report: Liver. Am J Transplant 2017;17 Suppl 1:174–251. [PubMed: 28052604]
2. Levitsky J, Formica RN, Bloom RD, et al. The American Society of Transplantation Consensus Conference on the Use of Hepatitis C Viremic Donors in Solid Organ Transplantation. American Journal of Transplantation:n/a-n/a.
3. Pais R, Barritt ASt, Calmus Y, et al. NAFLD and liver transplantation: Current burden and expected challenges. J Hepatol 2016;65:1245–1257. [PubMed: 27486010]
4. Kwong A, Kim WR, Mannalithara A, et al. Decreasing Mortality and Disease Severity in Hepatitis C Patients Awaiting Liver Transplantation in the United States. Liver Transpl 2017.
5. Berenguer M Treatment of hepatitis C after liver transplantation. Clin Liver Dis 2005;9:579–600, vi. [PubMed: 16207565]

6. Berenguer M, Palau A, Aguilera V, et al. Clinical benefits of antiviral therapy in patients with recurrent hepatitis C following liver transplantation. *Am J Transplant* 2008;8:679–87. [PubMed: 18294165]
7. Shah AP, Cameron A, Singh P, et al. Successful treatment of donor-derived hepatitis C viral infection in three transplant recipients from a donor at increased risk for bloodborne pathogens. *Transpl Infect Dis* 2017;19.
8. Khan B, Singer LG, Lilly LB, et al. Successful Lung Transplantation From Hepatitis C Positive Donor to Seronegative Recipient. *Am J Transplant* 2017;17:1129–1131. [PubMed: 27873483]
9. Saberi B, Hamilton JP, Durand CM, et al. Utilization of hepatitis C virus RNA–positive donor liver for transplant to hepatitis C virus RNA–negative recipient. *Liver Transplantation* 2018;24:140–143. [PubMed: 28779557]
10. Chhatwal J, Samur S, Bethea ED, et al. Transplanting HCV-positive livers into HCV-negative patients with preemptive antiviral treatment: A modeling study. *Hepatology* 2018;In Press.
11. Bowring MG, Kucirka LM, Massie AB, et al. Changes in Utilization and Discard of Hepatitis C-Infected Donor Livers in the Recent Era. *Am J Transplant* 2017;17:519–527. [PubMed: 27456927]
12. Chhatwal J, Samur S, Kues B, et al. Optimal timing of hepatitis C treatment for patients on the liver transplant waiting list. *Hepatology* 2017;65:777–788. [PubMed: 27906468]
13. Samur S, Kues B, Ayer T, et al. Cost Effectiveness of Pre–vs Post–Liver Transplant Hepatitis C Treatment With Direct-Acting Antivirals. *Clinical Gastroenterology and Hepatology* 2018;16:115–122. e10. [PubMed: 28634131]
14. Massie AB, Caffo B, Gentry SE, et al. MELD Exceptions and Rates of Waiting List Outcomes. *Am J Transplant* 2011;11:2362–71. [PubMed: 21920019]
15. AASLD-IDSA. Recommendations for testing, managing, and treating hepatitis C <http://www.hcvguidelines.org> [04/25/2018].
16. Based on OPTN data as of January 27, 2018 Retrieved from <http://optn.transplant.hrsa.gov>.
17. Gonzalez SA, Trotter JF. The Rise of the Opioid Epidemic and Hepatitis C Positive Organs: A New Era in Liver Transplantation. *Hepatology*:n/a-n/a.
18. Saab S, Hunt DR, Stone MA, et al. Timing of hepatitis C antiviral therapy in patients with advanced liver disease: a decision analysis model. *Liver Transpl* 2010;16:748–59. [PubMed: 20517909]
19. McAdam-Marx C, McGarry LJ, Hane CA, et al. All-cause and incremental per patient per year cost associated with chronic hepatitis C virus and associated liver complications in the United States: a managed care perspective. *J Manag Care Pharm* 2011;17:531–46. [PubMed: 21870894]
20. RedBook Online 2014 Available from: <http://www.redbook.com/redbook/online/>. Accessed November 10, 2015.
21. Younossi ZM, Boparai N, McCormick M, et al. Assessment of utilities and health-related quality of life in patients with chronic liver disease. *American Journal Of Gastroenterology* 2001;96:579. [PubMed: 11232711]
22. Verna EC, Goldberg DS. Hepatitis C viremic donors for hepatitis C nonviremic liver transplant recipients: Ready for prime time? *Liver Transpl* 2018;24:12–14. [PubMed: 29160931]
23. Kling CE, Limaye AP, Landis CS, et al. Expanding access to transplantation with hepatitis C-positive donors: A new perspective on an old issue. *Clin Transplant* 2017;31.
24. Cholankeril G The Use of HCV Positive Donors in HCV Negative Liver Transplant Recipients. AASLD Liver Meeting, Abstract ID: 1630 2016.
25. Lue A, Solanas E, Baptista P, et al. How important is donor age in liver transplantation? *World J Gastroenterol* 2016;22:4966–76. [PubMed: 27275089]
26. Bari K, Luckett K, Kaiser T, et al. Hepatitis C Transmission from Seropositive, Non-Viremic Donors to Non-Hepatitis C Liver Transplant Recipients. *Hepatology* 2017.

What You Need to Know**Background:**

There is a continued increase in the number of donor organs that are positive for HCV infection. HCV-infected livers have not been routinely offered to uninfected patients on the liver transplant waitlist. Approval and cost of DAA therapy are barriers.

Findings:

Providing HCV-negative patients on the liver transplant waitlist the option of accepting an HCV-positive liver, with a plan for preemptive DAA therapy, is a cost-effective strategy that can improve health outcomes.

Implications:

HCV-positive livers should be considered for transplantation into HCV-uninfected patients on the waitlist.

Figure 1. Model schematic for HCV-negative patients on the liver transplant waitlist.
For each patient profile, the model simulated two scenarios: (1) accept *any* liver, and (2) accept *only* HCV-negative livers.

Figure 2. Change in QALYs for patients willing to accept *any* liver irrespective of HCV status. The shaded area shows where accepting any liver is cost-effective. Orange bar depicts median MELD score at transplant in the US.

Figure 3. Change in QALYs for patients with a low QoL on the waitlist if they accept *any* liver versus accept only HCV-negative livers.

It is cost-effective to accept *any* liver in patients with a QoL of 0.56, by extension accepting *any* liver is always cost-effective when QoL on the waiting list = 0.56.

Figure 4. Change in QALYs for patients willing to accept *any* liver irrespective of HCV status in 11 UNOS regions.

Grey shaded area demonstrates MELD scores at which accepting *any* liver is cost-effective. Orange bars depict median MELD score at transplant within a given region. The map shows the 11 UNOS regions.

Figure 5. Tornado Diagrams Showing 10 Most Sensitive Model Parameters for MELD 22, and 28.

Dashed Line depicts commonly accepted willingness-to-pay threshold.

Abbreviations: LT, Liver transplant; DAA, Direct-acting antivirals; QoL, Quality of life; SVR, Sustained virologic response; GF, Graft Failure; LRD, Liver related death; WL, Waiting List, MELD, Model for end-stage liver disease; TP, Transition probability, ICER, Incremental cost-effectiveness ratio.

Figure 6. Two-way sensitivity analysis showing the relationship between the cost of LT and the DAA price below which accepting *any* liver is cost-effective at a willingness-to-pay threshold of \$100,000-per-QALY.