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# The Cost-effectiveness of Transplanting Hearts From Hepatitis C-infected Donors Into Uninfected Recipients

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**Background.** The DONATE HCV trial demonstrated the safety and efficacy of transplanting hearts from hepatitis C viremic (HCV+) donors. In this report, we examine the cost-effectiveness and impact of universal HCV+ heart donor eligibility in the United States on transplant waitlist time and life expectancy. **Methods.** We developed a microsimulation model to compare 2 waitlist strategies for heart transplant candidates in 2018: (1) status quo (SQ) and (2) SQ plus HCV+ donors (SQ + HCV). From the DONATE HCV trial and published national datasets, we modeled mean age (53 years), male sex (75%), probabilities of waitlist mortality (0.01–0.10/month) and transplant (0.03–0.21/month) stratified by medical urgency, and posttransplant mortality (0.003–0.052/month). We assumed a 23% increase in transplant volume with SQ + HCV compared with SQ. Costs (2018 United States dollar) included waitlist care ($2200–190 000/month), transplant ($213 400), 4-wk HCV treatment ($26 000), and posttransplant care ($2500–11 300/month). We projected waitlist time, quality-adjusted life-years (QALYs), lifetime costs, and incremental cost-effectiveness ratios (ICERs [$/QALY, discounted 3%/year]; threshold ≤$100 000/QALY). **Results.** Compared with SQ, SQ + HCV decreased waitlist time from 8.7 to 6.7 months, increased undiscounted life expectancy from 8.9 to 9.2 QALYs, and increased discounted lifetime costs from $671 400/person to $690 000/person. Four-week HCV treatment comprised 0.5% of lifetime costs. The ICER of SQ + HCV compared with SQ was $74 100/QALY and remained ≤$100 000/QALY with up to 30% increases in transplant and posttransplant costs. **Conclusions.** Transplanting hearts from HCV-infected donors could decrease waitlist times, increase life expectancy, and be cost-effective. These findings were robust within the context of current high HCV treatment costs.

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## INTRODUCTION

In the United States (US), heart failure affects nearly 6.5 million adults, and its prevalence is projected to increase by 46% between 2012 and 2030.[1,2] Despite therapeutic advances, many heart failure patients ultimately require durable mechanical circulatory support and/or heart transplant, leading to increased transplant waitlist times and reduced survival.[3,4] Hepatitis C viremic (HCV+; ie, HCV

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nucleic acid test positive) donor hearts that are otherwise medically suitable have historically been declined for transplantation because of reported increased mortality and accelerated coronary vasculopathy among recipients.[5,6] Over the past 5 years, organ transplants have increased by 20%, largely from an increase in donors dying from drug overdose.[7] Persons who inject drugs are emerging as the fastest-growing organ donor category, but utilization of these donor organs remains low because of concerns about transmissible infections like HCV.[8] Well-tolerated, highly efficacious direct-acting antivirals (DAAs) have revolutionized HCV treatment and led to a reevaluation of HCV+ donor eligibility.

The Donors of Hepatitis C Nucleic Acid Test Positive Thoracic Allografts for Transplantation Evaluation in Non-HCV Recipients (DONATE HCV) trial demonstrated that thoracic HCV+ donor organs can be safely transplanted into HCV-uninfected recipients using a 4-wk, short-course DAA regimen within hours of transplantation to block viral replication and establishment of HCV infection in the recipient.[9] HCV+ donor eligibility has been shown to reduce waitlist times,[10,11] but the high cost of DAAs remains a barrier for many transplant centers.[12] There are limited data on the cost-effectiveness of transplanting organs from HCV+ donors to heart transplant recipients[13,14] or other solid organ recipients.[15]

We developed a microsimulation model and used DONATE HCV trial and national data to evaluate the potential cost-effectiveness of universal HCV+ heart donor eligibility in the US and its impact on transplant candidate waitlist time and life expectancy.

## MATERIALS AND METHODS

### Analytic Overview

We developed a microsimulation model using TreeAge Pro 2020 software to simulate the clinical and economic outcomes of a cohort of heart transplant candidates newly listed in the US Organ Procurement and Transplantation Network (OPTN) in 2018. The medical urgency tiering system was updated in October 2018, but there are limited data characterized within the new system. We chose to model outcomes with 2017 data because most centers had not yet begun accepting HCV+ hearts.[7] We evaluated 2 strategies: (1) status quo reflecting HCV+ donor ineligibility (SQ) and (2) status quo plus HCV+ donor eligibility (SQ + HCV). In the latter strategy, we only included HCV+ donor hearts that were nucleic acid test positive. Patients receiving an HCV+ heart are treated with a 4-wk DAA regimen. Because we modeled an era before HCV+ donor eligibility, we used the older tiering system to ensure similar comparisons in the 2 cohorts (**Appendix Methods, SDC,** http://links.lww.com/TP/C591; **Table S1, SDC,** http://links.lww.com/TP/C591).

We projected median undiscounted waitlist time, quality-adjusted life-years (QALYs), and costs in the month of transplant and over a lifetime from a healthcare sector perspective for each medical urgency ("emergent," "urgent," and "elective" statuses, listed from greatest to lowest priority for transplant) and the overall cohort (**Figure S1, SDC,** http://links.lww.com/TP/C591). We calculated incremental cost-effectiveness ratios (ICERs, in $/QALY): the difference in discounted lifetime costs divided by the difference in discounted QALYs (discounting 3%/year). We defined "cost-effective" as an ICER below $100 000/QALY and also considered a more stringent threshold of $50 000/QALY.[16]

### Heart Transplant Model

#### Model Structure

At model start, individuals are waitlisted by medical urgency in a user-defined distribution and are simulated in monthly cycles until death (**Figure S2, SDC,** http://links.lww.com/TP/C591). All waitlisted individuals experience monthly probabilities of mortality and transplant, which reflect changes in medical urgency and mortality associated with delisting because of worsening condition while on the waitlist. We assumed that candidates on the waitlist cannot be delisted due to recovery; all candidates remain on the waitlist until transplant or death. Patients selected for transplant experience a 1-time operative mortality; those who survive experience monthly probabilities of postoperative mortality. Patients receiving an HCV+ heart are treated with a 4-wk DAA regimen in the first month following transplantation; we assumed no HCV treatment failures.[9]

We did not simulate heart donors because we developed a stochastic model (ie, probabilistic with time-varying events) in the interest of simulating time-dependent outcomes for individuals waitlisted for heart transplant.

#### Model Validation and Calibration

We internally validated model-projected waitlist times (≤10% difference from reported waitlist times; differences between model-projected and reported waitlist times were 0 months for emergent, +0.7 months for urgent, −1.6 months for elective, and +0.8 months overall) and posttransplant survival (median 13.08 years compared with reported 12.5 years).[4,17] We calibrated model-projected survival to published data at 1, 3, and 5 years posttransplant and mean life expectancy for heart transplant recipients (**Appendix Methods, SDC,** http://links.lww.com/TP/C591).[1,4,18]

### Model Inputs

Because we did not model the heart donor population, we assumed that donor characteristics did not vary between SQ and SQ + HCV except for donor HCV status.

#### Cohort Characteristics

At listing, we modeled a population that was 76% male with a mean age of 53 years (SD: 14 years), based on the 2017 OPTN/Scientific Registry of Transplant Recipients (SRTR) annual report (Tables 1–3).[4] At model start, patients were listed by medical urgency: emergent (28%), urgent (47%), and elective (25%).[11] We estimated the distribution of heart support interventions for emergent and urgent statuses from OPTN/SRTR data (**Table S2, SDC,** http://links.lww.com/TP/C591).

#### Waitlist Mortality and Transplant

Monthly probabilities of waitlist mortality (0.010–0.096) and transplant (0.033–0.206) were stratified by initial medical urgency (Tables 1–3).[4,19,20] These probabilities cover all person-time spent on the waitlist, from initial listing to transplant or death, and include all changes in

**TABLE 1.**

**Input parameters for a model of transplanting hepatitis C-infected hearts into uninfected recipients in the United States**

| Variable | Base case value | Range examined | Source |
|---|---|---|---|
| Cohort characteristics | | | |
| Initial age (SD), mean, years | 53 (14) | 40–70 | 4 |
| Male sex, % | 76 | 50–90 | 4 |
| Medical urgency at listing, % | | | |
| Emergent | 28 | 0–100 | 11 |
| Urgent | 47 | 0–100 | 11 |
| Elective | 25 | 0–100 | 11 |
| Waitlist characteristics | | | |
| Mortality, monthly probability | | | |
| Emergent | | | |
| 0–1 month | 0.096 | 0.5–2.0x | 4,19 |
| >1 month | 0.025 | 0.5–2.0x | 4 |
| Urgent | 0.017 | 0.5–2.0x | 20 |
| Elective | 0.010 | 0.5–2.0x | 20 |
| SQ transplant, monthly probability | | | |
| Emergent | 0.206 | 0.5–2.0x | 4 |
| Urgent | 0.062 | 0.5–2.0x | 4 |
| Elective | 0.033 | 0.5–2.0x | 4 |
| Increase in transplant volume, %[a] | 22.5 | 5–40 | 21 |

[a]Based on available data, we estimated an increase in transplant rate for SQ + HCV associated with a 22.5% increase in transplant volume. See Appendix Methods, SDC, http://links.lww.com/TP/C591, and Figure S3, SDC, http://links.lww.com/TP/C591.
HCV, hepatitis C virus; SQ, status quo; SD, standard deviation.

**TABLE 2.**

**Input parameters for a model of transplanting hepatitis C-infected hearts into uninfected recipients in the United States (continued)**

| Variable | Base case value | Range examined | Source |
|---|---|---|---|
| Transplant characteristics | | | |
| Operative mortality, probability | 0.046 | 0–0.12 | 24 |
| Posttransplant mortality, monthly probability, range by month | 0.003–0.052 | 0.9–1.1x | 17 |
| Quality-of-life | | | |
| Emergent | | | |
| 0–1 month | 0.51 | 0.41–0.61 | 25–29, 31, 32 |
| >1 month | 0.56 | 0.46–0.66 | 25–29, 31, 32 |
| Urgent | | | |
| 0–1 month | 0.52 | 0.42–0.62 | 25–28 |
| >1 month, range by month | 0.60–0.63 | 0.51–0.73 | 25–28 |
| Elective (all months) | 0.67 | 0.57–0.76 | 32 |
| Posttransplant | 0.76 | 0.67–0.87 | 26 |
| Waitlist costs (2018 USD) | | | |
| Emergent[a] | | | |
| 0–1 month | 187 400 | 0.5–2.0x | 26, 33–36 |
| >1 month, range by month | 3500–12 400 | 0.5–2.0x | 26, 33–36 |
| Urgent[a] | | | |
| 0–1 month | 151 700 | 0.5–2.0x | 26, 36 |
| >1 month, range by month | 4100–9100 | 0.5–2.0x | 26, 36 |
| Elective, range by month | 2200–7100 | 0.5–2.0x | 36 |
| Transplant | 213 400 | 0.5–2.0x | 26 |

[a]Monthly costs include incurred hospitalization and treatment costs averaged by waitlist intervention (eg, durable ventricular assist device, intravenous inotropes, intra-aortic balloon pump, total artificial heart, and extracorporeal membrane oxygenation) for each medical urgency. See Appendix Methods, SDC, http://links.lww.com/TP/C591, and Table S2, SDC, http://links.lww.com/TP/C591.
USD, United States dollar.

medical urgency while on the waitlist. We used studies that examined the impact of increased transplant volume on waitlist time to base the impact of SQ + HCV on empiric data; we assumed that transplant rates would increase proportionally to the relative decrease in waitlist time for each status (**Appendix Methods, SDC**, http://links.lww.com/TP/C591; **Figure S3, SDC**, http://links.lww.com/TP/C591). From this relationship between transplant volume, waitlist time, and transplant rates, we estimated that transplant rates would increase by 43% relative to the SQ

**TABLE 3.**

**Input parameters for a model of transplanting hepatitis C-infected hearts into uninfected recipients in the United States (continued)**

| Variable | Base case value | Range examined | Source |
|---|---|---|---|
| Posttransplant costs (2018 USD) | | | |
| 4-wk DAAs for HCV infection | 26 000 | 6700–26 000 | 12 |
| Posttransplant | | | |
| 1–12 months | 11 300 | 0.5–2.0x | 26 |
| >12 months | 2500 | 0.5–2.0x | 53 |

DAA, direct-acting antiviral; HCV, hepatitis C virus; USD, United States dollar.

with a 22.5% increase in transplant volume associated with HCV+ donor eligibility.[9,21] These estimates reflect the greatest plausible values found in the literature and were chosen to demonstrate the greatest plausible clinical and economic impacts of SQ + HCV.

### Operative and Posttransplant Mortality

We used data from the International Society for Heart and Lung Transplantation, published data on class III/IV heart failure mortality, and US life tables to inform mortality at the time of transplant (0.046) and thereafter (0.003–0.052), weighted by the age and sex distribution of our cohort (Tables 1–3 and **Table S2, SDC**, http://links.lww.com/TP/C591).[1,17,22-24]

### Quality-of-life

Monthly preference-based utilities to adjust for quality-of-life for waitlisted patients were derived from data on waitlist interventions: durable ventricular assist device (VAD; emergent status: 0.51–0.60; urgent status: 0.51–0.70),[25-28] intra-aortic balloon pump (0.50), total artificial heart (0.50–0.66),[29] extracorporeal membrane oxygenation (0.50),[30,31] and intravenous inotropes (0.53) (**Table S2, SDC,** http://links.lww.com/TP/C591).[26] We weighted these adjustments to obtain monthly quality-of-life by medical urgency: 0.51 to 0.56 for emergent patients and 0.52 to 0.63 for urgent patients (Tables 1–3). Elective status quality-of-life was 0.67, reflecting class III/IV heart failure patients.[32] Posttransplant quality-of-life was 0.76, reflecting posttransplant care and rehospitalizations for complications, including acute cellular rejection and cardiac allograft vasculopathy.[26]

### Costs

Waitlist care costs were derived from data on waitlist interventions: durable VAD ($3400–$261 400/month),[26] intra-aortic balloon pump ($437 000, 1 time),[33] total artificial heart ($197 000/month for up to 3 months),[33,34] extracorporeal membrane oxygenation ($136 600/month for up to 3 months),[35] and intravenous inotropes ($5100/month) (**Table S2, SDC**, http://links.lww.com/TP/C591).[36] We weighted these costs to estimate costs for each medical urgency: $3500 to $187 400/month for emergent patients and $4100 to $151 700/month for urgent patients (Tables 1–3). Elective status costs were $4100 to $151 700/month, estimated from published data on heart failure patients.[36] The cost of transplant was $213 400.[26] The cost of a 4-wk course of DAAs ranges from $13 200 to $26 000, reflecting the only 2 FDA approved, pan-genotypic DAA regimens presently available in the US for this indication.[12,37] Posttransplant care costs ($2500–$11 300/month) varied by time since transplant and were averaged from published data on posttransplant care and rehospitalizations for complications, including acute cellular rejection and cardiac allograft vasculopathy. All modeled costs reflect 2018 US dollars.

### Sensitivity and Scenario Analyses

We first conducted 1-way sensitivity analyses on all model parameters by varying inputs through plausible ranges. We then varied the most influential parameters simultaneously in 2-way sensitivity analyses. In multiway sensitivity analyses, we widely varied the increase in the rate of heart transplant for each medical urgency to examine scenarios in which policy conclusions would change. In view of limited data regarding long-term (ie, >5-y) outcomes for HCV+ heart transplant recipients, we conducted scenario analyses to examine the potential effect of increased posttransplant mortality for these individuals. We increased posttransplant mortality to determine the theoretical threshold at which SQ + HCV would no longer be cost-effective.

This study was approved by the Mass General Brigham Institutional Review Board. No patient-level data were used; only published data were included.

## RESULTS

### Base Case: Waitlist Time

With SQ, projected undiscounted waitlist time was 8.7 months for all candidates and decreased with greater medical urgency (ie, greater medical urgency was associated with less time on the waitlist; Table 4). Compared with SQ, SQ + HCV reduced waitlist time by 2.0 months for all candidates. Absolute reduction in waitlist time with SQ + HCV was greatest for elective candidates (3.9 months, compared with 2.4 months for urgent and 0.7 months for emergent patients); relative reductions were similar (24%–27%) because of the assumption that transplant rates increased by the same relative percentage across medical urgencies (**Appendix Methods, SDC**, http://links.lww.com/TP/C591; **Figures S3A–D, SDC**, http://links.lww.com/TP/C591).

### Base Case: Life Expectancy

With SQ, undiscounted life expectancy was projected to be 8.85 QALYs for all candidates and increased by 0.33 QALYs with SQ + HCV (Table 4). Life expectancy decreased with greater medical urgency. Urgent candidates experienced the greatest gain in life expectancy with SQ +

**TABLE 4.**

**Clinical and cost-effectiveness outcomes of a model of transplanting hepatitis C-infected hearts into uninfected recipients in the United States**

| Waitlist months | | QALYs | | Lifetime costs (2018 USD)[a] | | ICER[a] |
|---|---|---|---|---|---|---|
| | Undiscounted | Undiscounted | Discounted[b] | Undiscounted | Discounted[b] | $/QALY[c] |
| All candidates | | | | | | |
| SQ | 8.7 | 8.85 | 6.55 | 777 800 | 671 400 | Comparator |
| SQ + HCV | 6.7 | 9.18 | 6.80 | 797 800 | 690 000 | 74 100 |
| Emergent | | | | | | |
| SQ | 2.7 | 8.34 | 6.19 | 795 200 | 701 500 | Comparator |
| SQ + HCV | 2.0 | 8.59 | 6.38 | 812 300 | 716 700 | 81 000 |
| Urgent | | | | | | |
| SQ | 8.9 | 8.92 | 6.60 | 821 800 | 715 300 | Comparator |
| SQ + HCV | 6.5 | 9.32 | 6.90 | 847 900 | 738 700 | 78 000 |
| Elective | | | | | | |
| SQ | 16.1 | 9.30 | 6.87 | 678 300 | 557 700 | Comparator |
| SQ + HCV | 12.2 | 9.59 | 7.09 | 689 800 | 570 600 | 57 800 |

[a] QALYs are rounded to the nearest hundredth decimal. Costs and ICERs are rounded to the nearest $100.
[b] Discounted 3%/year.
[c] ICERs summarize the cost-effectiveness of an intervention. An ICER is the difference in cost divided by the difference in QALY for each strategy compared with the next least costly strategy. A strategy is "cost-effective" if it is not dominated by any other strategy, and it has the largest ICER not exceeding the willingness-to-pay threshold. The willingness-to-pay threshold is a normative value, which varies widely by setting and decision-maker; for interpretability, we have chosen $100000/QALY.
HCV, hepatitis C virus; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life-year; SQ, status quo; USD, United States dollar.

HCV (0.40 QALYs), reflecting a greater absolute decrease in waitlist time compared with emergent candidates, who had the smallest projected gain in life expectancy (0.25 QALYs).

### Base Case: Costs

With SQ, discounted lifetime costs were projected to be $671 400/person for all candidates and increased by $18 600/person with SQ + HCV (Table 4). Lifetime costs increased with greater medical urgency. Urgent candidates had the greatest increase in lifetime costs with SQ + HCV ($23 400/person, compared with $15 200/person for emergent patients and $12 900/person for elective patients), reflecting longer life expectancy than emergent candidates and greater waitlist costs than elective candidates.

When comparing SQ versus SQ + HCV, the distribution of lifetime costs was similar for all candidates (posttransplant care: 53.2% versus 55.0%; waitlist care: 25.5% versus 22.5%; transplant 21.3% versus 22.0%) (Figure 1); these distributions were also similar for each medical urgency (**Figures S4A–C, SDC**, http://links.lww.com/TP/C591). With SQ + HCV, a 4-wk DAA regimen

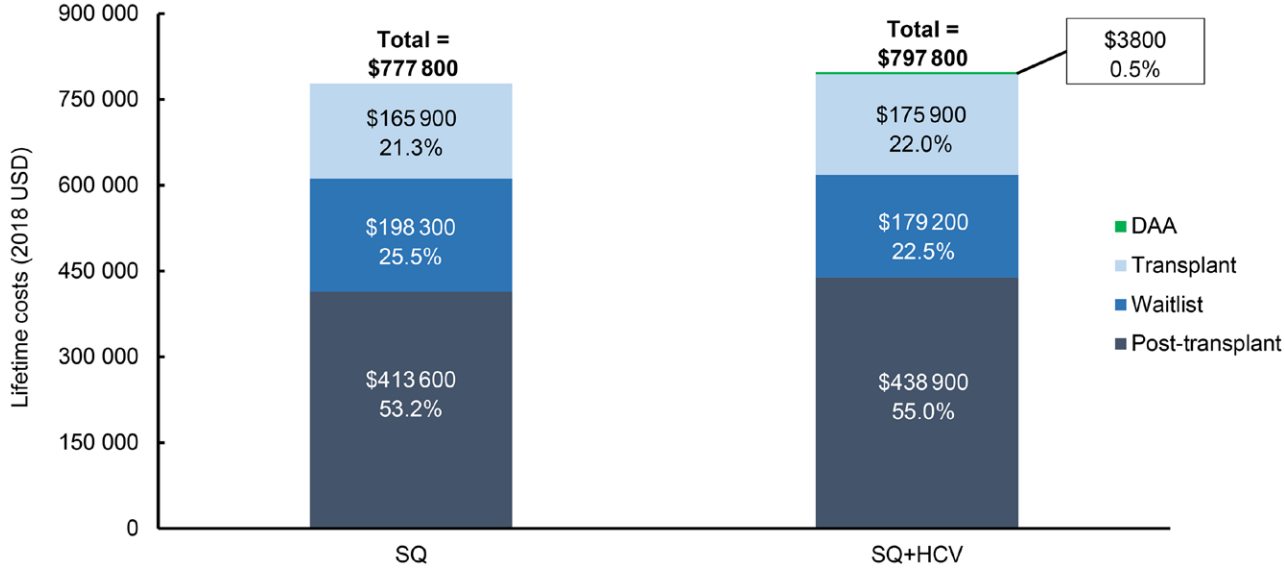


**FIGURE 1.** Cumulative component average lifetime costs for heart transplant candidates when HCV+ hearts are ineligible for transplant (left) and when HCV+ hearts are eligible for transplant (right). Cumulative component costs per person include posttransplant costs (dark gray), waitlist medical intervention costs (dark blue), transplant cost (light blue), and DAA cost (green). The total per-person cost is in bold above each bar. Within each bar are component cost and the percentage of the total cost for that strategy. DAA, 4-wk direct-acting antivirals; HCV, hepatitis C; SQ, status-quo; USD, United States dollar.

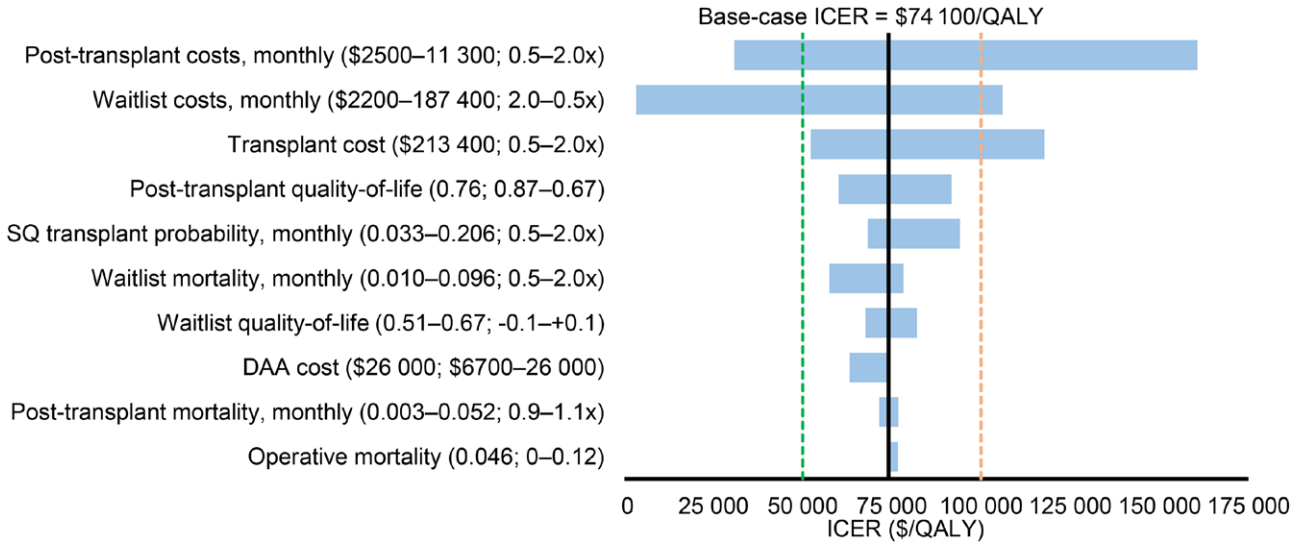


**FIGURE 2.** One-way sensitivity analyses assessing the impact of model input parameter ranges on the cost-effectiveness of transplanting hepatitis C-infected hearts into uninfected recipients in the United States. The horizontal axis shows the ICER ($/QALY) of SQ + HCV compared with SQ. The vertical axis lists input parameters in order of influence on the base-case ICER, with the greatest influencing parameters at the top of the graph. Within the parentheses next to each parameter is the base-case input value followed by the range of values evaluated. The base-case ICER is represented by the solid black vertical line ($74 100/QALY). An ICER was considered "cost-effective" if it was <$100 000/QALY (dashed orange line). A more stringent threshold of $50 000/QALY (dashed green line) was also considered. The ICER of SQ + HCV vs SQ was not sensitive to the increase in transplant volume. HCV; hepatitis C virus; DAA, 4-wk direct-acting antivirals; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life-year; SQ, status-quo.

comprised 0.5% of lifetime costs among all candidates listed, including those who did not receive a transplant, and 1.3% of costs among all recipients accrued specifically during the month of the transplant. SQ + HCV increased transplant and posttransplant care costs compared with SQ because of greater numbers of transplants performed.

### Base Case: Cost-effectiveness

Compared with SQ, the ICER of SQ + HCV was $74 100/QALY for all candidates (Table 4). This ICER increased with greater medical urgency (elective: $57 800/QALY; urgent: $78 000/QALY; emergent: $81 000/QALY) because of smaller absolute decreases in waitlist time because those with the greatest medical urgency are transplanted more quickly than those with lower medical urgency.

### Sensitivity Analyses

When varying each input parameter individually, the ICER of SQ + HCV compared with SQ exceeded the $100 000/QALY willingness-to-pay threshold when the costs of posttransplant care, waitlist care, or transplant were ≥1.3x, <0.7x, or ≥1.6x base-case values, respectively (Figure 2). The ICER fell below the more stringent $50 000/QALY threshold when costs of posttransplant care or waitlist care were <0.8x or >1.3x base-case values, respectively. These parameters were also most influential when examining each medical urgency separately (**Figure S5A–C, SDC,** http://links.lww.com/TP/C591). The ICER was ≤$100 000/QALY under a wide range of costs of DAAs and waitlist care (Figure 3, green and blue shading); SQ + HCV became cost-saving when the costs of waitlist care were doubled while the costs of DAA were simultaneously ≤$20 000.

### Scenario Analyses

In a worst-case scenario, using lower data bounds to estimate the relationship between transplant volume and transplant rates, SQ + HCV reduced waitlist time by 0.8 months or 9% for all candidates (**Table S3, SDC,** http://links.lww.com/TP/C591); in a best-case scenario, using upper data bounds instead, SQ + HCV reduced waitlist time by 2.9 months or 33% for all candidates. In a hypothetical threshold analysis, ≥20% increases in posttransplant mortality among HCV+ heart transplant recipients—corresponding to a decrease in median posttransplant life expectancy from 13.08 life-years to ≤9.83 life-years—resulted in ICERs >$100 000/QALY (**Table S4, SDC,** http://links.lww.com/TP/C591).

## DISCUSSION

We developed a microsimulation model to examine the clinical and economic impacts of transplanting hearts from HCV+ donors into uninfected recipients using a 4-wk, short-course DAA regimen to prevent the establishment of HCV infection. We had 3 key findings.

First, we projected that universal HCV+ heart donor eligibility in the US substantially shortened transplant candidate waitlist time and increased life expectancy. Using available data regarding increases in transplant volume and declines in waitlist time, we estimated that universal HCV+ donor eligibility in the US reduced median waitlist time by nearly a quarter for all candidates, with pessimistic and optimistic estimates ranging from 9% to 33%. Altshuler et al conducted the largest retrospective study to date examining the impact of HCV+ heart donor eligibility on waitlist outcomes.[11] They found that, in regions with high HCV+ donor utilization (ie, comprising >5% of transplants) between January 2017 and October 2018, median waitlist time declined by 1 mo, or 16.5%, compared with

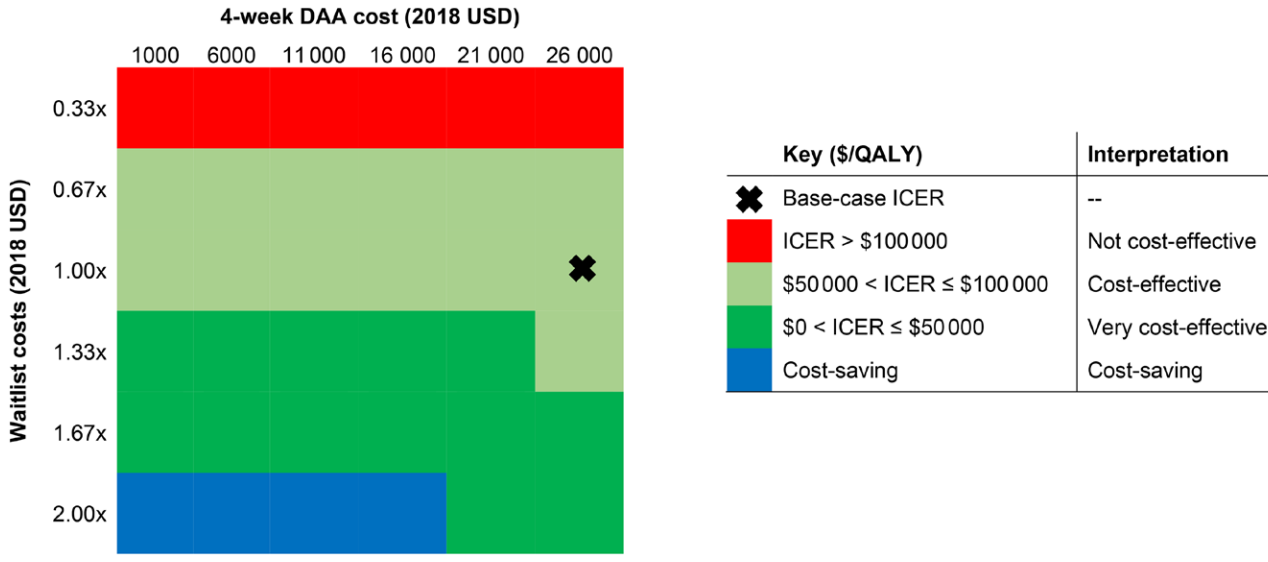


**FIGURE 3.** Two-way sensitivity analyses assessing the joint impact of short-course direct-acting antiviral cost (x-axis) and waitlist costs (y-axis) on the cost-effectiveness of transplanting hepatitis C-infected hearts into uninfected recipients in the United States. The horizontal axis shows the cost of short-course direct-acting antivirals in $5000 increments, and the vertical axis shows waitlist costs ranging from 0.33 to 2.00x base-case input values (see Tables 1–3). The black "X" reflects the base-case ICER of SQ + HCV compared with SQ; red shading reflects ICERs >$100 000/QALY (ie, not cost-effective); light-green shading reflects ICERs >$50 000/QALY and ≤$100 000/QALY (ie, cost-effective); dark-green shading reflects ICERs >$0/QALY and ≤$50 000/QALY (ie, very cost-effective); blue shading reflects negative ICERs (ie, cost-saving). DAA, 4-wk direct-acting antiviral; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life-year; USD, United States dollar.

the pre-HCV era. However, HCV+ heart utilization is still suboptimal in the US,[8,21] despite low refusal rates of HCV+ hearts among patients and the removal of a separate consenting process for increased risk donors. With SQ + HCV, we estimated gains of 0.33 QALYs among all transplant candidates. These are substantial gains in terms of medical interventions for chronically ill patients[38] and are of the same magnitude as projected QALYs gained from other funded medical interventions for heart failure patients (eg, direct VAD as a bridge to transplant and adjunctive ivabradine therapy for heart failure patients with reduced ejection fraction).[39,40] The smallest gain in QALYs with SQ + HCV was projected for emergent candidates because their waitlist time is already short.

Second, SQ + HCV increased lifetime costs by $18 600/person but was associated with an ICER of $74 100/QALY compared with SQ, which is less than commonly accepted willingness-to-pay thresholds in the US.[16] The projected increase in lifetime costs with SQ + HCV was predominately due to more transplants occurring and higher life expectancy leading to increased posttransplant costs rather than the cost of DAAs alone; DAAs comprised just 0.5% of lifetime costs for all transplant candidates. Although the cost of DAAs is perceived as a barrier for some transplant centers,[41] a 4-wk DAA regimen would comprise just 1.3% of the costs incurred by recipients in the month of a transplant if SQ + HCV were brought to scale. The additional per-person costs and resulting ICER of the SQ + HCV intervention fall well within the range of revealed willingness-to-pay thresholds of implemented healthcare interventions for heart failure patients (range: $24 920–$209 400/QALY),[28,39,40] and transplanting other HCV+ and high-risk organs (range: $56 000–$91 700/QALY).[13,42-44]

Third, SQ + HCV was cost-effective across sensitivity analyses that address uncertainties in input parameters and scenarios accompanying the implementation of universal HCV+ donor eligibility or future advances in heart failure care. With greater expenditure on waitlist interventions, as may be seen with growing rates of heart failure in the US,[1,2] lower costs of DAAs could render the SQ + HCV intervention very cost-effective (ie, ICER ≤$50 000/QALY) or cost-saving. Only when transplant or posttransplant care was significantly more costly (ie, ≥60% and ≥30% greater than base-case estimates, respectively) did the ICER of SQ + HCV compared with SQ exceed $100 000/QALY. To examine the impact of potentially increased mortality among recipients of HCV+ organs, we conducted a scenario analysis and found that the ICER remained ≤$100 000/QALY even if median posttransplant life expectancy among these recipients decreased from 13.08 to 9.83 life-years (25% reduction). However, these results are theoretical; although recipients of HCV+ hearts have not been shown to have worse outcomes than recipients of HCV– hearts,[45-47] continued long-term monitoring of these patients is needed. In all sensitivity and scenario analyses examined, the ICER of SQ + HCV compared with SQ remained below that of durable VAD for ambulatory heart failure patients, further suggesting that SQ + HCV would likely be cost-effective in the US.[28,48] Although the cost-effectiveness of SQ + HCV reported in this analysis is specific to the US, our model may also provide insights for international settings. First, the cost-effectiveness of SQ + HCV was independent of the increase in transplant volume, suggesting that transplanting HCV+ hearts may be cost-effective independent of the population prevalence of HCV. Second, the cost of DAAs may be substantially lower in international settings,[49] which would increase the value of SQ + HCV. Third, other considerations such as the availability and provision of medical interventions for heart failure and costs of waitlist, transplant, and posttransplant care may impact the value of SQ + HCV. Setting-specific

cost-effectiveness analyses are needed to determine the cost-effectiveness and nuances of implementing SQ + HCV outside of the US.

Logan et al conducted a Markov model-based analysis that projected that transplanting HCV+ hearts would be cost-effective for adults waitlisted for heart transplant with a durable VAD or intravenous inotropes.[13] We build on this study using a microsimulation model-based analysis, which permits individual patient simulation and time-varying inputs and outcomes (eg, waitlist time and costs), and found that donating HCV+ hearts would be cost-effective for all heart transplant candidates in the US. A second model-based analysis by Wayda et al used national datasets to model the impact of universal HCV+ heart donation for all waitlist candidates between 2014 and 2019, detailing the cost-effectiveness and policy implications of transplanting HCV+ hearts in a real-world cohort. Our analysis adds to this prior work by projecting outcomes of universal HCV+ heart donor eligibility brought to scale with optimal utilization of HCV+ hearts for a present-day cohort without HCV+ heart donor eligibility. Additional distinctions of our analysis include incorporation of the DONATE HCV trial, which used a 4-wk, short-course DAA regimen rather than a 12-wk regimen, and use of published data to estimate the impact of increased transplant volume on transplant rates, which differs from other models that assume a direct mathematical relationship.[13,43]

This study has important limitations that may over- or underestimate the benefit of universal HCV+ heart donor eligibility. First, we assumed that organs would be available and accepted at a constant rate. If this were not true, decreases in waitlist time would be heterogeneous, and changes in waitlist status could also be affected. Although the availability of HCV+ hearts may change in the future, sensitivity analysis showed that smaller or larger increases in transplant volume would not impact the value of SQ+HCV. Second, although the clinical data used to populate the model capture changes in status while on the waitlist, they do not capture the costs and quality-of-life associated with these changes. Third, cost and quality-of-life inputs were averaged for each waitlist status; component costs and quality-of-life data of waitlist interventions may be highly variable. For example, we modeled older generation VADs, which may be more costly and be associated with worse quality-of-life.[48] To address the variability in waitlist costs, we performed wide sensitivity analysis, which demonstrated that decreases in waitlist costs would decrease the value of SQ + HCV. Fourth, by design, we did not model HCV treatment failure or natural history in the case of treatment failure given excellent DAA efficacy in this population (98%–100%) and the 100% efficacy of this treatment regimen demonstrated in the DONATE HCV trial.[9,50,51] To evaluate the hypothetical impact of worse outcomes among recipients of HCV+ donor hearts, such as DAA failure, we performed sensitivity and scenario analyses that showed that SQ + HCV would remain cost-effective even with increased posttransplant costs and when survival was 25% lower than recipients of HCV– hearts. These findings are consistent with prior modeling studies.[13,14] Finally, although the heart donor allocation system changed to a 6-tiered system in October 2018, we chose to model the older 3-tiered system to reflect the era in which HCV+ hearts were not widely used. Importantly, our findings show that SQ + HCV would be cost-effective for all medical urgencies. Our analysis may also illustrate how outcomes may change under the new allocation system. For example, the revised allocation system may have influenced care decisions, as suggested by greater usage of more costly temporary mechanical circulatory support interventions in transplant recipients than in the older allocation system.[52,53] Our sensitivity analyses demonstrate that SQ + HCV would remain cost-effective despite increases in waitlist costs, transplant rates, and posttransplant morbidity and mortality, which may be associated with greater usage of temporary mechanical circulatory support in the current era. Despite these limitations, this analysis unveils the interplay between the clinical benefits and costs of interventions that could increase the availability of donor hearts and therefore has the potential to be applied to other interventions that would increase transplant volume, such as donation after circulatory death.

In this model-based analysis, we found that universal HCV+ heart donor eligibility would decrease waitlist times, improve life expectancy, and increase lifetime costs and could be cost-effective for heart transplant candidates in the US. Importantly, these results were robust even within the current context of costly DAAs used to prevent the establishment of HCV infection among recipients.

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