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Financial Evaluation of Kidney Transplant With Hepatitis C Viremic Donors to Uninfected Recipients

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Background. Kidney transplantation with hepatitis C viremic (dHCV+) donors appears safe for recipients without HCV when accompanied by direct acting antiviral (DAA) treatment. However, US programs have been reluctant to embrace this approach due to concern about insurance coverage. While the cost of DAA treatment is currently offset by the reduction in waiting time, increased competition for dHCV+ organs may reduce this advantage. This analysis sought to demonstrate the financial benefit of dHCV+ transplant for third-party health insurers to expand coverage availability. **Methods.** An economic analysis was developed using a Markov model for 2 decisions: first, to accept a dHCV+ organ versus wait for a dHCV uninfected organ; or second, accept a high kidney donor profile index (KDPI) (>85) organ versus wait for a better quality dHCV+ organ. The analysis used Medicare payments, historical survival data, cost report data, and an estimated cost of DAA of \$29874. **Results.** In the first analysis, using dHCV+ kidneys reduced the cost of end-stage kidney disease care if the wait for a dHCV uninfected organ exceeded 11.5 months. The financial breakeven point differed according to the cost of DAA treatment. In the second analysis, declining a high-KDPI organ in favor of a waiting dHCV+ organ was marginally clinically beneficial if waiting times were <12 months but not cost effective. **Conclusions.** dHCV+ transplant appears to be economically and clinically advantageous compared with waiting for dHCV-uninfected transplant but should not replace high-KDPI transplant when appropriate. Despite the high cost of DAA therapy, health insurers benefit financially from dHCV+ transplant within 1 year.

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INTRODUCTION

The need for kidney transplant continues to greatly exceed the available organ supply, as over 90 000 US residents are currently waiting for an organ. Consequently, every year thousands of patients die or are removed from the transplant waiting list before being offered an organ. At the same time, the rate of discard of potentially transplantable kidney allografts remains substantial.² Active donor infection with hepatitis C virus (dHCV+), defined as evidence of active viral replication by nucleic acid testing,

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has historically increased the risk of kidney nonutilization.³ While use of dHCV+ organs in patients with active HCV has increased, the population of potentially acceptable HCV-infected recipients remains small, limiting use of these organs if only infected patients are transplanted.

The landscape of HCV treatment changed in 2014 with the introduction of the first effective direct acting antiviral agents (DAAs), although the need for ribavirin limited their use in patients with renal dysfunction.4 DAA treatment of HCV has been shown to be highly effective in achieving a sustained viral response (SVR), defined as no detectable virus at 12 weeks. Recently, new regimens have been developed that overcome early limitations, allowing treatment all HCV genotypes in patients with kidney failure and after transplant. In this context, 2 landmark trials demonstrated that dHCV+ kidneys can be safely used in HCV-uninfected patients who are treated with DAAs shortly after transplant.^{5,6} Patients transplanted under these protocols waited <2 months for transplant, compared with 4-7 years for patients waiting for non-HCV infected organs. While clinically beneficial, broader use of these protocols had been limited by cost, as early commercially available DAA regimens exceeded \$80 000.7 Fortunately, competition has reduced the price of treatment substantially. Despite this reduction in cost, transplant programs remain reluctant to expand use of these organs due to concern about insurance coverage.7

To facilitate broad adoption of dHCV+ organ utilization, transplant centers need assurance that third-party health insurers will provide coverage for necessary DAAs. However, from a financial perspective, private insurance carriers do not bear the costs of life-long renal replacement therapy nor benefit from expansion of organ supply associated with the use of these organs. Therefore, the incremental cost of DAAs to clear HCV infection acquired from dHCV+ organs needs to be offset by a sufficient reduction dialysis time. The economic breakeven point needed is a function of the cost of DAA therapy, which is rapidly declining as shorter courses of treatment are demonstrated to be effective. To better understand the financial implications of using dHCV+ kidney transplant in HCV-uninfected recipients, we sought to estimate the minimal waiting time reduction required to justify acceptance of dHCV+ organs over a range of DAA treatment prices.

MATERIALS AND METHODS

Data Sources and Approval

This study used data from the US Renal Data System, the Scientific Registry of Transplant Recipients (SRTR), and transplant hospital Medicare Costs Reports (Table 1). The US Renal Data System database includes payment data for all patients on maintenance renal replacement therapy with Medicare as their primary insurance, including professional charges and payments for hospitalizations. The SRTR system includes data on all donors, waitlisted candidates, and transplant recipients in the United States, submitted by the members of the Organ Procurement and Transplantation Network. The Health Resources and Services Administration, US Department of Health and Human Services, provides oversight of the activities of the Organ Procurement and Transplantation Network and SRTR contractors. National Medicare Cost Report data were obtained under a Freedom

TABLE 1.

Data elements included in cost-effectiveness models

Model	Data element	Basecase value	Source
IVIOUGI			
Dialysis	Cost per mo of dialysis	\$4753	Medicare (part A/B)
	Waitlist mortality (age 48)	0.41%	SRTR
	Waitlist mortality (age 65)	0.67%	SRTR
KDPI=20-85	Cost of transplant	\$29765	Medicare (part A/B)
KDPI=20-85	Cost report payment	\$68 567	Medicare cost report
KDPI=20-85	Total cost of transplant	\$98332	
KDPI=20-85	Annual cost after transplant (first yr)	\$34292	Medicare (part A/B)
KDPI=20-85	Annual cost after transplant 13-24 mo	\$14049	Medicare (part A/B)
KDPI=20-85	Graft failure rate (pts/mo)	0.170%	SRTR annual report
KDPI=20-85	Death rate (pts/mo)	0.190%	SRTR annual report
KDPI> 85	Cost of transplant	\$31 557	Medicare (part A/B)
KDPI> 85	Cost report payment	\$68 567	Medicare cost report
KDPI> 85	Total cost of transplant	\$100124	
KDPI> 85	Annual cost after transplant (first yr)	\$43316	Medicare (part A/B)
KDPI> 85	Annual cost after transplant 13-24 mo	\$19340	Medicare (part A/B)
KDPI> 85	Graft failure rate (pts/mo)	0.3%	SRTR annual report
KDPI> 85	Death rate (pts/mo)	0.3%	SRTR annual report
dHCV+	Cost of transplant	\$33332	Medicare (part A/B)
dHCV+	Cost report payment	\$68 567	Medicare cost report
dHCV+	Cost of DAA (Mavyret)	\$27610	Average wholesale
	. , ,		price
dHCV+	Cost of labs (PCR X6, LFTs X4)	\$2265	Medicare (part A/B)
dHCV+	Total cost of transplant	\$131733	
dHCV+	Annual cost after transplant (first yr)	\$34292	Medicare (part A/B)
dHCV+	Annual cost after transplant 13–24 mo	\$14049	Medicare (part A/B)
dHCV+	Graft failure rate (pts/mo)	0.150%	SRTR annual report
dHCV+	Death rate (pts/mo)	0.150%	SRTR annual report

DAA, direct acting antiviral; KDPI, kidney donor profile index; LFTs, liver function tests; SRTR, Scientific Registry of Transplant Recipients.

of Information Act request. This study was approved by the Saint Louis University Institutional Review Board.

This analysis was conducted from the health insurer (Medicare) perspective using methods described in previous publications.⁸ Medicare claims for 18 037 kidney transplant procedures performed from 2014 to 2016 were reviewed. Payments for technical services (part A) and professional services/immunosuppression (part B) were aggregated for 3 categories of costs that relate to distinct periods:

- First, the cost of maintaining a patient on the kidney transplant waiting list (pretransplant) including the cost of hemodialysis for patients not listed preemptively. Medicare payments were aggregated for patients who were listed on the national US waiting list to determine an average monthly cost.
- Second, the cost of the transplant episode including the transplant and initial postoperative care was determined as the mean payment (parts A and B). In addition, mean national payment per kidney via the Medicare cost report was included based on data from 154 transplant centers obtained via a freedom of information act request (full data not shown). For patients who receive DAA treatment for HCV infection, the cost of medication, physician visits, and laboratory tests were included during this period.
- Third, posttransplant cost for technical services (part A) and professional services/ immunosuppression (part

- B) were aggregated. Posttransplant cost did not include medication coverage under part D.
- The cost of graft failure and patient death were derived from Medicare payments for the month of the graft loss.

The basecase cost of DAA therapy was calculated from clinical trial protocols and Medicare allowable payments. The basecase included a 12-week course of glecaprevir/pibrentasvir, which has an average wholesale price of \$9203 per 4-week course (Micromedex Redbook, Accessed February 17, 2020), 3 visits to a hepatologist including liver function tests (\$240 per visit), and HCV PCR tests at week 0, 2, 4, 8, 12, and 24 (\$257 per test). Total cost of basecase DAA treatment was \$29875. Sensitivity analyses examined costs from \$5000 to \$65000 per treatment course.

Mortality rates for patients on the transplant waiting list and patient and graft survival after transplant were derived from transplant registry (SRTR) data based on kidney donor profile index (KDPI) for high- (>85) and lower-KDPI (≤85) organs, as reported in the SRTR annual report. Because patients who consent for high KDPI organs systematically differ from patients who do not consent to receive these organs, waitlist survival was modeled separately. For the lower KDPI analysis, waitlist survival was modeled for a 48-year-old patient; for the high KDPI analysis, waitlist mortality was modeled for a 65-year-old patient. Similarly, graft failure rates were derived from transplant registry analyses. Differences in patient and graft survival were calculated at 36 months after initial offer for this analysis.¹

Analyses

A multistate Markov model was constructed including waitlist, transplanted, graft failure with return to dialysis, and death states. Transition probabilities were determined from published literature as summarized in Table 1. Patients can transition to death before transplant at rates based on the waitlisted population, after transplant with a functioning graft, or after graft failure. A 36-month model was constructed without discounting given the offsetting medical cost inflation and time value of money over this short period of analysis. A 36-month analysis was chosen as this coincides with current Medicare payment policy for transplant and provides a reasonable period for a health insurer to derive financial benefit.

Logically, patients offered a dHCV+ donor and dHCVuninfected donor at the same time with equal or better KDPI will choose the uninfected organ. Therefore, decision analytic models were constructed to compare cost and outcomes for 2 scenarios. The first considered a waitlist patient offered the choice of accepting a dHCV+ organ (with DAA treatment) or waiting for a dHCV-uninfected organ of similar or better quality as defined by KDPI. For this analysis, we calculated the point of cost equivalence between accepting a dHCV+/ lower KDPI (≤85) kidney with waiting for a dHCV-uninfected organ of similar quality. The second scenario examined the choice of accepting a dHCV-uninfected/high KDPI kidney or waiting for a longer lasting lower-KDPI dHCV+ organ. This decision analysis reflects patients' desire to wait for a lower KDPI kidney with the hope longer graft survival and the promise that a dHCV+ donor organ can be identified with only a short incremental waiting time.

Aggregated costs for kidney transplant were calculated for dHCV-uninfected/lower KDPI transplant, dHCV-uninfected/

high KDPI transplant, and dHCV+ transplant using the input data summarized in Table 1 to determine the time to cost equivalence. Patients with a graft failure were assumed to return to dialysis until the end of the period of analysis. Secondary analysis included patient survival and the cost-effectiveness as determined by the cost per year of life saved to 36 months. Strategies which both increased life expectancy and lower spending were labeled as dominant. Sensitivity analyses examined the economic impact of varying the anticipated reduction in waiting time (between 0 and 30 mo) and the anticipated costs of DAA treatment.

RESULTS

In the base analysis, cost of dHCV+ kidney transplant (\$131772) significantly exceeded the cost of dHCV-uninfected/ lower KDPI kidney transplant (\$98332) and dHCV-uninfected/ high KDPI transplant (\$100124). This cost reflects the need for DAA therapy (\$29874 per treatment). The cost of dialysis for 36 months was \$171108. Three-year graft and patient survival were essentially equivalent for dHCV-uninfected (87% and 93%) and dHCV+ (89% and 95%) lower KDPI kidney transplant but were lower for dHCV-uninfected/high KDPI transplant recipients (77% and 88%). Survival on dialysis at 36 months was 86.3% for lower-KDPI only consented candidates and 78.5% for high KDPI consented patients.

In the basecase analysis, the total cost of care over 36 months was compared for patients who underwent transplant with a dHCV+/lower KDPI kidney and those who waited for a dHCV-uninfected organ. At 11.5 months, the cost of care was equivalent between the 2 strategies (\$201049 for immediate dHCV+ kidney transplant, \$200779 for a delayed dHCVuninfected kidney transplant). Accepting dHCV+ transplant resulted in improved 3-year expected survival (94.7%), compared with waiting for a dHCV-uninfected organ (91.0%). Accepting a dHCV+ organ which reduced waiting times for transplant <11.5 months was associated with higher costs but greater survival compared with waiting for dHCV-uninfected transplant (Table 2). However, if a dHCV-uninfected organ was available in <6 months, dHCV+ was no longer cost effective (>\$100000 per life-year saved) over a 36-month analysis (Table 2). Sensitivity analysis confirmed that as the cost of DAA decreased, necessary waiting time reduction to achieve breakeven cost similarly decreased. For example, if the time to transplant with a dHCV- organ was only 6 months, the cost of DAA would need to decrease to <\$15000 to remain cost effective.

In the second analysis, accepting a dHCV-uninfected/high KDPI organ now was compared with waiting for a dHCV+/lower KDPI organ. Over the 36 months, accepting a high KDPI organ was associated with lower total cost unless DAA treatment was <\$5000 even if offered simultaneously. Waiting for a dHCV+/lower KDPI organ for up to 12 months was associated with a small survival benefit at 36 months, while immediate acceptance KDPI organ is preferred for longer waiting periods. However, given the high incremental cost of DAA therapy, declining a dHCV-uninfected/high KDPI organ to wait for a dHCV/lower KDPI was not cost effective (Table 3).

DISCUSSION

Use of dHCV+ kidney transplant in recipients without HCV infection has been demonstrated to improve access to

TABLE 2.

Two-way sensitivity analysis showing the cost per year of life saved by accepting a dHCV+ kidney rather than waiting for a dHCV-uninfected kidney

Cost of DAA	Anticipated reduction in waiting time							
	3	6	9	12	18	24	30	
\$5000	\$100 038	dHCV+ DOM						
\$10000	\$184516	dHCV+ DOM						
\$15000	\$268 994	\$63 365	dHCV+ DOM					
\$20 000	\$353 472	\$127840	dHCV+ DOM					
\$25 000	\$437950	\$192315	\$41 202	dHCV+ DOM	dHCV+ DOM	dHCV+ DOM	dHCV+ DOM	
\$30 000	\$522428	\$256791	\$93399	dHCV+ DOM	dHCV+ DOM	dHCV+ DOM	dHCV+ DOM	
\$35000	\$606 906	\$321 266	\$145596	\$26506	dHCV+ DOM	dHCV+ DOM	dHCV+ DOM	
\$40 000	\$691 384	\$385741	\$197794	\$70 400	dHCV+ DOM	dHCV+ DOM	dHCV+ DOM	
\$45 000	\$775 862	\$450216	\$249991	\$114294	dHCV+ DOM	dHCV+ DOM	dHCV+ DOM	
\$50 000	\$860340	\$514691	\$302 189	\$158 188	dHCV+ DOM	dHCV+ DOM	dHCV+ DOM	
\$55 000	\$944818	\$579167	\$354386	\$202 082	\$8573	dHCV+ DOM	dHCV+ DOM	
\$60000	\$1 029 296	\$643642	\$406 583	\$245 976	\$41 953	dHCV+ DOM	dHCV+ DOM	

The cost of DAA therapy varies from \$5000 to \$60000 and the time to first dHCV- kidney from 3 mo to 30 mo. The total period of analysis is 36 mo

Green, cost effective; blue, survival improved but not cost effective; black, survival not improved despite higher cost.

DAA, direct acting antiviral; dHCV+, hepatitis C viremic donor kidney; DOM, dominant strategy with lower cost and improved survival.

TABLE 3.

Two-way sensitivity analysis showing the cost per year of life saved by accepting a high KDPI kidney rather than waiting for a dHCV+/lower KDPI kidney

Waiting time for low KDPI/dHCV+ kidney							
3	6	9	12	18	24	30	
\$65 938	\$203216	\$542 235	\$2 686 885	High KDPI DOM	High KDPI DOM	High KDPI DOM	
\$100617	\$252873	\$628 622	\$3 004 685	High KDPI DOM	High KDPI DOM	High KDPI DOM	
\$135297	\$302530	\$715 009	\$3 322 485	High KDPI DOM	High KDPI DOM	High KDPI DOM	
\$169976	\$352188	\$801 396	\$3640285	High KDPI DOM	High KDPI DOM	High KDPI DOM	
\$204655	\$401 845	\$887783	\$3 958 084	High KDPI DOM	High KDPI DOM	High KDPI DOM	
\$239335	\$451 502	\$974170	\$4275884	High KDPI DOM	High KDPI DOM	High KDPI DOM	
\$274014	\$501 159	\$1 060 557	\$4593684	High KDPI DOM	High KDPI DOM	High KDPI DOM	
\$308694	\$550816	\$1146944	\$4911484	High KDPI DOM	High KDPI DOM	High KDPI DOM	
\$343373	\$600 473	\$1 233 331	\$5 229 283	High KDPI DOM	High KDPI DOM	High KDPI DOM	
\$378 053	\$650130	\$1319717	\$5 547 083	High KDPI DOM	High KDPI DOM	High KDPI DOM	
\$412732	\$699788	\$1 406 104	\$5 864 883	High KDPI DOM	High KDPI DOM	High KDPI DOM	
\$447 411	\$749 445	\$1 492 491	\$6 182 683	High KDPI DOM	High KDPI DOM	High KDPI DOM	
	\$65 938 \$100 617 \$135 297 \$169 976 \$204 655 \$239 335 \$274 014 \$308 694 \$343 373 \$378 053 \$412 732	\$65 938 \$203 216 \$100 617 \$252 873 \$135 297 \$302 530 \$169 976 \$352 188 \$204 655 \$401 845 \$239 335 \$451 502 \$274 014 \$501 159 \$308 694 \$550 816 \$343 373 \$600 473 \$378 053 \$650 130 \$412 732 \$699 788	3 6 9 \$65 938 \$203 216 \$542 235 \$100 617 \$252 873 \$628 622 \$135 297 \$302 530 \$715 009 \$169 976 \$352 188 \$801 396 \$204 655 \$401 845 \$887 783 \$239 335 \$451 502 \$974 170 \$274 014 \$501 159 \$1 060 557 \$308 694 \$550 816 \$1 146 944 \$343 373 \$600 473 \$1 233 331 \$378 053 \$650 130 \$1 31 9717 \$412 732 \$699 788 \$1 406 104	3 6 9 12 \$65 938 \$203 216 \$542 235 \$2 686 885 \$100 617 \$252 873 \$628 622 \$3 004 685 \$135 297 \$302 530 \$715 009 \$3 322 485 \$169 976 \$352 188 \$801 396 \$3 640 285 \$204 655 \$401 845 \$887 783 \$3 958 084 \$239 335 \$451 502 \$974 170 \$4 275 884 \$274 014 \$501 159 \$1 060 557 \$4 593 684 \$308 694 \$550 816 \$1 146 944 \$4 911 484 \$343 373 \$600 473 \$1 233 331 \$5 229 283 \$378 053 \$650 130 \$1 319717 \$5 547 083 \$412 732 \$699 788 \$1 406 104 \$5 864 883	3 6 9 12 18 \$65 938 \$203 216 \$542 235 \$2 686 885 High KDPI DOM \$100 617 \$252 873 \$628 622 \$3 004 685 High KDPI DOM \$135 297 \$302 530 \$715 009 \$3 322 485 High KDPI DOM \$169 976 \$352 188 \$801 396 \$3 640 285 High KDPI DOM \$204 655 \$401 845 \$887 783 \$3 958 084 High KDPI DOM \$239 335 \$451 502 \$974 170 \$4 275 884 High KDPI DOM \$274 014 \$501 159 \$1 060 557 \$4 593 684 High KDPI DOM \$308 694 \$550 816 \$1 146 944 \$4 911 484 High KDPI DOM \$378 053 \$650 130 \$1 319717 \$5 547 083 High KDPI DOM \$412 732 \$699 788 \$1 406 104 \$5 864 883 High KDPI DOM	3 6 9 12 18 24 \$65 938 \$203 216 \$542 235 \$2 686 885 High KDPI DOM High KDPI DOM \$100 617 \$252 873 \$628 622 \$3 004 685 High KDPI DOM High KDPI DOM \$135 297 \$302 530 \$715 009 \$3 322 485 High KDPI DOM High KDPI DOM \$169 976 \$352 188 \$801 396 \$3 640 285 High KDPI DOM High KDPI DOM \$204 655 \$401 845 \$887 783 \$3 958 084 High KDPI DOM High KDPI DOM \$239 335 \$451 502 \$974 170 \$4 275 884 High KDPI DOM High KDPI DOM \$274 014 \$501 159 \$1 060 557 \$4 593 684 High KDPI DOM High KDPI DOM \$308 694 \$550 816 \$1 146 944 \$4 911 484 High KDPI DOM High KDPI DOM \$378 053 \$650 130 \$1 319717 \$5 547 083 High KDPI DOM High KDPI DOM \$412 732 \$699 788 \$1 406 104 \$5 864 883 High KDPI DOM High KDPI DOM	

The cost of DAA therapy varies from \$5000 to \$60000 and the time to first dHCV+ kidney from 3 mo to 30 mo. The total period of analysis is 36 mo. Green, cost effective; blue, survival improved but not cost effective; black, survival not improved despite higher cost.

DAA, direct acting antiviral; DOM, dominant strategy with lower cost and improved survival; KDPI, kidney donor profile index.

kidney transplant, but the financial implications of this strategy are not well defined. Based on this cost analysis of national US transplant registry and Medicare data, widespread use of dHCV+ kidney allografts appears justified if acceptance is associated with shorter waiting times to transplant. Given the current cost of DAA therapy, a reduction in waiting time of at least 11.5 months is necessary to demonstrate a cost savings. Waiting time reductions of at least 6 months were cost-effective at 36 months (based upon a threshold of \$100000 per life-year), with greater benefit possible as the period of analysis is extended. This calculus is likely to change as demand for dHCV+ organs increases and the cost of DAA treatment decreases. In contrast, declining a high KDPI/dHCV- organ in hope of being offered a lower KDPI/dHCV+ kidney did not appear to be cost effective. As dHCV+ transplant is more costly and waitlist mortality is high, it is neither clinically advantageous nor financially sound over a short-time horizon to delay transplant if the high-KDPI kidney is otherwise appropriate.

In the Transplanting Hepatitis C Kidneys into Negative Kidney Recipients (THINKER) trial, Reese et al⁹ reported 1-year outcomes of 10 uninfected patients who received dHCV+ kidneys followed by elbasvir–grazoprevir DAA therapy at the onset of viremia, and 10 additional patients. All patients achieved SVR with excellent kidney function (mean creatinine 1.2 mg/dL) at 6 months without evidence of acute rejection. Patient-reported quality of life was excellent, with an improvement in the mean physical component summary on the RAND-36 scale 6.7 (*P*=0.012) points from baseline. In the Exploring Renal Transplants Using Hepatitis C Infected Donors for HCV-negative Recipients (EXPANDER-1) trial, Durand et al⁶ described 10 uninfected patients who underwent dHCV+ transplant with preemptive DAA treatment. All participants attained SVR at 12 weeks without evidence of

acute rejection and had excellent renal function at the time of the trial report.

The favorable results of these trials have led to broader adoption of similar protocols outside of the clinical trial setting. In 2020, members of the Cleveland Clinic-Florida transplant program reported their results of dHCV+ transplant across multiple organs (liver, heart, kidney). 10,11 In their protocol, DAA treatment was delayed until patients were viremic and insurance approval was obtained (median 72 d). The report described transplants in 64 patients with a mean waiting time of 23.5 days from consent to transplant. While DAA therapy was not complete for all patients at the time of reporting, 48 patients achieved SVR and only 1 was found to have resistant HCV infection requiring an alternative treatment regimen. Three patients who underwent kidney transplant from dHCV+ donors with very low viral loads did not become viremic and thus were not treated. Importantly, 2 patients developed fibrosing sclerosing hepatitis after delay in DAA initiation (8 and 14 wks), both of whom recovered with DAA therapy and achieved SVR.

The clinical success of a strategy of dHCV+ kidney transplant combined with DAA treatment has led to significant reductions in organ discard nationally. The proportion of patients on the kidney waiting list willing to accept a dHCV+ organ increased from 3% in 2007 to 14% in 2018.3 As expected, acceptance varies by waiting time. Among newly listed patients, 22% were willing to accept a dHCV+ organ while only 13% of patients with 5 years or more waiting time were willing to accepted a viremic organ. This growing acceptance of dHCV+ kidney transplants has contributed to 500% increase in the annual number of these transplant performed between 2007 and 2018. One result of these broader acceptance practices is increased competition for organs, longer waiting times for a DHCV+ organ, and a reduction in the cost savings associated with accepting viremic organs. Before the introduction of DAA, 52.3% of all HCV+ kidneys were recovered but not transplanted, compared with 16.7% of non-HCV+ kidneys. Following the introduction of DAAs, discard of HCV+ kidneys decreased to 37.6% from 2104 to 2017.12 The economic benefits of this practice are contingent on reducing the time to transplant as compared with waiting for an uninfected organ. Consequently, alternative allocation systems may need to be devised to appropriately transplant these organs into patients most likely to benefit.

Although waiting time benefit is likely to be reduced over time, overall cost of DAA is also likely to diminish. Recent studies suggest that "ultra-short" preemptive treatment (immediately before transplant) followed by a 4-day course of treatment can achieve SVR in up to 93% of patients. 13 The current study examines the intersection of these trends to establish a financial justification for broader adoption of these protocols in the United States and international contexts. While single payer systems have the benefit of lifetime recovery of the cost of HCV therapy improving the cost effectiveness of this treatment, from a purely financial standpoint, currently a patient who is able to get an uninfected kidney in <12 months and, instead, is transplanted with an HCV+ kidney uses additional resources. Conversely, any system that reduces waiting by at least 11.5 months provides a dominant strategy, as it is both cost saving and life extending. Therefore, impact on expected waiting time should be considered in determining the optimal

patient to receive these valuable organs regardless of payment system.

Previous analyses of the cost-effectiveness of transplantation of dHCV+ organs differ from the current study in several ways. Kadetz et al assess the cost effectiveness of this approach in Canada. This analysis considered the lifetime cost-effectiveness of DHCV+ transplant compared with staying on the waiting list for a year¹⁴ and reported an incremental cost effectiveness ratio of \$56018 per QALY. Unlike the current study, the Canadian study did not assess the minimal waiting time necessary for cost equivalence/savings for the health insurer given the national healthcare system in Canada which benefits from long-term cost savings. In addition, they assume that 100% of waitlisted patients are on dialysis, while this analysis included the benefits for all waitlisted patients, including those not on dialysis. Other analyses have likewise considered lifetime cost effectiveness analyses rather than financial analyses of direct cost of care which is most relevant to health insurers who need to determine if they will support the incremental cost of DAAs.¹⁵ Finally, no study has reported 2 way sensitivity analyses which examines the impact of simultaneous changes in the cost of DAAs and the wait time reduction resulting achieved by accepting these organs. Eckman et al suggest a reduction in time to transplant of >3 years, which will likely not be true given wider use of organs, while reductions of <0.7 years were not cost effective. Furthermore, this cost savings assumes patients are on dialysis. The authors also did not consider the implications of lower cost of DAA therapy. 15

This study is limited by a 3-year window to calculate cost and benefits. This window was chosen based on the availability of accurate Medicare payment data, as kidney transplant-specific Medicare benefits expire at 36 months in the absence of age older than 65 years or disability. Thus, to provide an accurate tradeoff between waitlist cost (both on and off dialysis) and posttransplant expenditures, we limited the analytic window. We sought to demonstrate the economic benefit of this treatment strategy over this brief period to assess the short-term implications of dHCV+ on total cost of care, which is relevant for payment decisions for private health insurers and budgeting for national health systems. Second, we assume SVR with a pan-genotypic medication (glecaprevir/pibrentasvir). Possibly, a small number of patients may require additional therapy, although in realworld experience retreatment is rare, particularly if treatment is started promptly.¹⁶ In addition, some patients who are transplanted with dHCV+ donors with low viral loads may not require treatment, further reducing the cost of these protocols. Finally, we did not perform bootstrapping analyses to determine significance levels but instead present sensitivity analyses around the key variables.

In conclusion, use of dHCV+ kidney transplant in uninfected recipients appears to be clinically and financial beneficial in the context of current organ availability and DAA cost. As the cost of therapy decreases, the waiting time reduction needed to achieve cost savings will also diminish, requiring reexamination of this strategy in even in patients likely to undergo transplant rapidly with a dHCV- organ. Finally, in patients who consent to receive a high-KDPI organ, it is not cost-effective to decline transplant with a dHCV-uninfected/high KDPI organ to wait for a dHCV+/lower KDPI organ.

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