Original Research Article

MDM Policy & Practice

MDM Policy & Practice
2021, Vol. 6(2) 1–20

DOI: 10.1177/23814683211056537
journals.sagepub.com/home/mdm
SAGE

Incorporating Patients' Values and Preferences Into Decision Making About Transplantation of HCV-Naïve Recipients With Kidneys From HCV-Viremic Donors: A Feasibility Study

Mark H. Eckman, Adeboye A. Adejare, Heather Duncan, E. Steve Woodle, Charuhas V. Thakar, Rita R. Alloway, and Kenneth E. Sherman

Abstract

Introduction. While use of (hepatitis C virus) HCV-viremic kidneys may result in net benefit for the average end-stage kidney disease (ESKD) patient awaiting transplantation, patients may have different values for ESKD-related health states. Thus, the best decision for any individual may be different depending on the balance of these factors. Our objective was to explore the feasibility of sampling health utilities from hemodialysis patients in order to perform patient-specific decision analyses considering various transplantation strategies. **Study Design.** We assessed utilities on a convenience sample of hemodialysis patients for health states including hemodialysis, and transplantation with either an HCV-uninfected kidney or an HCV-viremic kidney. We performed patient-specific decision analyses using each patient's age, race, gender, dialysis vintage, and utilities. We used a Markov state transition model considering strategies of continuing hemodialysis, transplantation with an HCV-unexposed kidney, and transplantation with an HCV-viremic kidney and HCV treatment. We interviewed 63 ESKD patients from four dialysis centers (Dialysis Clinic Inc., DCI) in the Cincinnati metropolitan area. **Results.** Utilities for ESKD-related health states varied widely from patient to patient. Mean values were highest for -transplantation with an HCV-uninfected kidney (0.89, SD: 0.18), and were 0.825 (SD: 0.231) and 0.755 (SD: 0.282), respectively, for hemodialysis and transplantation with an HCV-viremic kidney. Patient-specific decision analyses indicated 37 (59%) of the 63 ESKD patients in the cohort would have a net gain in quality-adjusted life years from transplantation of an HCV-viremic kidney, while 26 would have a net loss. **Conclusions.** It is feasible to gather dialysis patients' health state utilities and perform personalized decision analyses. This approach could be used in the future to guide shared decision-making discussions about transplantation strategies for ESKD patients.

Keywords

decision analysis, end-stage kidney disease, hepatitis C, kidney transplantation, utilities, values and preferences

Date received: June 22, 2021; accepted: October 5, 2021

Introduction

In the United States, an estimated 110,000 patients start dialysis each year. Of the 500,000 patients receiving dialysis for end-stage kidney disease (ESKD), 24,273 (4%) received kidney transplants in 2019. A total of 101,337

Corresponding Author

Mark H. Eckman, University of Cincinnati Medical Center, PO Box 670535, Cincinnati, OH 45267-0535, USA; Telephone: (513) 558-7581 (mark.eckman@uc.edu).

patients with ESKD were waitlisted for kidney transplantation in 2019. While the number of patients receiving kidney transplants has increased to 24,273 in 2019, from 18,912 in 2016, 4,130 patients died and 4,259 were too sick to undergo transplantation.[1] Waiting times for kidney transplants is greater than 1 year for roughly 50% of waitlisted patients and 3 years or more for 24.3% of patients.

Given limited organ availability, the majority of patients face the prospect of indefinite hemodialysis and premature mortality (up to 16% per year). The scarcity of kidneys for transplantation and high mortality while awaiting transplant have led some physicians and patients to consider transplantation of organs that otherwise might not be considered, such as those from donors who have antibodies to the hepatitis C virus (HCV). Many of these organs come from individuals who have died from drug overdoses. The increase in overdose-related deaths ("opioid epidemic") has resulted in increased organ availability, from 514 kidney donations in 2013 to 1,313 donations in 2018.[2] Overdose-related deaths more frequently occur in younger donors who generally have healthier kidneys. Outcomes of transplantation with these organs have been superior to outcomes from donors who have died from medical causes.[3] Indeed, the number of waitlisted candidates receiving kidneys from HCV-viremic donors has increased from 3.1% in 2007 to 14.2% in 2018.[4] In addition, 59.2% of such kidneys were transplanted into HCV-naïve recipients. Finally, effective treatments for HCV infection have become available, resulting in almost certain cure for patients receiving HCV-viremic kidneys. Thus, the availability of effective treatments for HCV creates a medical challenge that lends itself well to individualized decision analytic models that incorporate individual patient values and preferences for health outcomes.

While use of HCV-viremic kidneys may result in net benefit for the average ESKD patient awaiting transplantation, there is great variability in waiting list times as well as competing mortality risks that may result in dying while awaiting transplantation. In addition, patients may have widely varying values for health states, including life following transplantation with either an HCV-uninfected or an HCV-viremic kidney. Thus, the best decision for any individual may be different depending on the balance between individual patient's health state valuations and waiting time for a kidney. If the medical care system is to best utilize the available kidneys from this hopefully self-limited epidemic of opioid deaths, there is an urgent need to develop decision-making tools that incorporate the key decision variables.

Using more contemporary data from the Multi-center study to Transplant Hepatitis-C InfeCted kidneys (MYTHIC) trial,[5] we updated a previously published Markov state transition decision model,[6] by decreasing posttransplant treatment time for HCV from 12 weeks to 8 weeks using a glecaprevir/pibrentasvir regimen starting 3 days posttransplant, and by using the sustained virologic response of 1.0 reported in the MYTHIC trial. We also added a strategy of continuing hemodialysis. In addition, we created patient-specific inputs to the decision model for age, gender, race, dialysis vintage, and personalized health state utility values (weights). For ESKD patients receiving hemodialysis who are on kidney transplant waiting lists, interventions included transplantation with an HCV-unexposed kidney versus transplantation with an HCV-viremic kidney and HCV treatment. As part of a larger study examining the impact of race on various utility assessment presentation methods, we performed utility assessments on a convenience sample of 63 patients undergoing dialysis at several of our Cincinnati neighborhood dialysis centers, and then used those health state assessments to perform individualized decision analyses.

Methods

Our institutional review board approved the study protocol (2019-0792).

Simulation Model

We used a computer program (Decision Maker) to develop a 31-state Markov transition model, analyze decision trees, and perform sensitivity analyses, using a lifelong time horizon. We considered three strategies for a patient population with kidney failure, making the hypothetical assumption that they had just been waitlisted for deceased donor transplants: continue dialysis, transplantation with an HCV-unexposed kidney, or transplantation with an HCV-viremic kidney and HCV

Division of General Internal Medicine and the Center for Clinical Effectiveness (MHE), Department of Biomedical Informatics (AA), Division of Digestive Diseases (KES), Division of Nephrology (HD, CT, RRA), Division of Transplantation, Department of Surgery (ESW), University of Cincinnati, Cincinnati, Ohio. The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article. The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: Investigator-initiated grant funding from Bristol-Myers Squibb, Grant Number CV-185-764; NICHD (NIH), Grant Number R01HD094213; NCATS (NIH) Grant Number UL1TR001425.

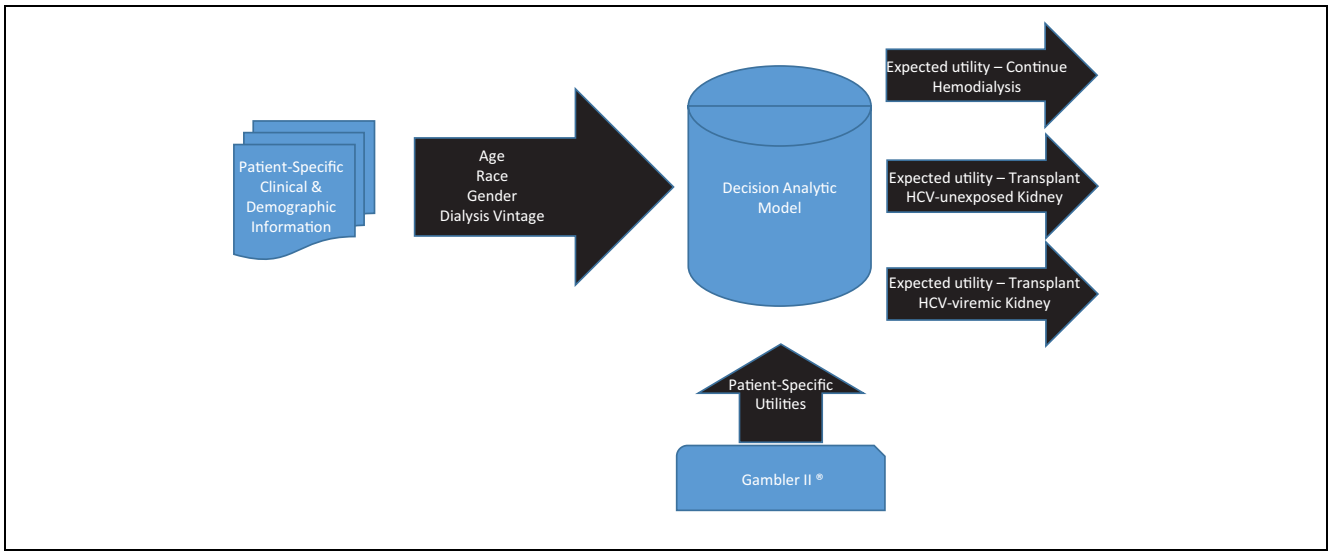

Figure 1 Figure 1 Schematic of patient-level decision model. Patient-specific demographic and clinical information, including age, race, gender, and dialysis vintage are used to parameterize variables in the decision model, along with patient-specific utilities for health states. Utilities for life on dialysis, and life following transplantation with either an HCV-unexposed or an HCV-viremic kidney were assessed using the Gambler II. Output from the decision model is an estimate of quality-adjusted life expectancy in QALYs for each of the three strategies - 1) continue hemodialysis; 2) transplant HCV-unexposed kidney; and 3) transplant HCV-viremic kidney.
Abbreviations: QALYs, quality-adjusted life years.

treatment (Figures S1–S3). We used a cycle length of 1 month, and a lifelong time horizon for our simulation. Using patient-specific information about age, race, gender, dialysis vintage, and health state utilities, we performed patient-specific decision analyses on each of the 63 patients in our cohort (Figure 1). Table 1 summarizes probabilities, rates, and utilities obtained from our literature review and used in the decision model.

Patients in both transplantation strategies continue to receive hemodialysis until a kidney becomes available. Average wait times were 4.0 years and 1.56 years for HCV-unexposed and HCV-viremic kidneys, respectively.[7] Kidney failure has a significant impact on quality of life. We used the patient-specific standard gamble utility weights we assessed to adjust life expectancy accrued in each Markov state in our simulation model for patients receiving hemodialysis and after kidney transplantation with either an uninfected kidney or an HCV-infected kidney. We used data from the US Renal Data System to calculate excess mortality attributable to hemodialysis.[8] Among dialysis patients on transplant waiting lists, annual mortality rates increase the longer a patient remains on dialysis. We captured this patient-to-patient variability by using individual patient's dialysis vintage to model how long patients had been receiving dialysis at the beginning of the simulation. We used US population mortality tables, patient-specific demographics (age, gender, race), and excess mortality rates among either kidney transplant or hemodialysis patients to determine overall death rates as patients aged through the simulation.[9–11] As described earlier, the annual excess mortality rate among patients receiving hemodialysis increased for those with a longer dialysis vintage (see Table 1). We assume that all patients are HCV-naïve at the start of the simulation, and that those receiving HCV-viremic kidneys are treated with glecaprevir/pibrentasvir, a pangenotypic regimen that has been used in patients with ESKD. We used published data to model the decreased quality of life during the time in which patients receive treatment for HCV infection with glecaprevir/pibrentasvir.[12–16] Utilities for multiple health states were combined in a multiplicative fashion.

We present results of the patient-specific decision analyses, using patient-specific inputs as described above and in Figure 1. In order to demonstrate the impact of parameter uncertainty on any given patient's personalized decision analysis, we also performed probabilistic sensitivity analyses on two prototypical patients who were interested in kidney transplantation, by conducting 10,000 second-order Monte Carlo iterations for each of these patients. Ten thousand second-order Monte Carlo iterations are generally deemed sufficient to achieve stable

Table 1 Data Required in the Analysis: Probabilities, Rates, and Quality of Life[a]

Variable	Base-Case Value, Mean, [95% CI]	Distribution Type
Literature-based data		
Annual rate for receiving deceased donor kidney[b,c]		
HCV-unexposed	0.1733 [0.1359–0.4077]	Log normal
HCV-viremic	0.4456 [0.3466–0.6238]	Log normal
Average waiting time for deceased donor kidney, years[b]		
HCV-unexposed	4.0 [1.7–5.1][7]	Log normal
HCV-viremic	1.56 [1.1–2.0][7]	Log normal
Cumulative probability of 30-day mortality post-KTx		
HCV-viremic kidney	0.015 [0.009–0.020][35]	Beta
HCV-unexposed kidney	0.0085 [0.002–0.017][35]	Beta
Annual excess mortality rate on maintenance HD[d]	0.074 [0.073–0.075][10,8]	Beta
Relative risk of dialysis-related mortality[8]		
<2 years	0.59	
2 to <5 years	1.0	
≥ 5 years	1.5	
Annual excess mortality rate post-KTx[d]	0.02 [0.019–0.021][8]	Beta
HCV treatment-related parameters		
Glecaprevir-pibrentasvir SVR[e]	1.0 [0.956–1.0][36,37]	
Quality of life		
Treatment with DAA	0.96[13,16]	

Abbreviations: CI, confidence interval; DAA, direct-acting antiviral; HCV, hepatitis C virus; HD, hemodialysis; KTx, kidney transplant; SVR, sustained virologic response.

[a]Values in brackets represent 95% CIs unless noted otherwise.

[b]Interquartile range.

[c]Average rates for receiving deceased donor kidney were calculated from average weighting times, as $(-\ln(0.5))/(\text{mean waiting time})$.

[d]Excess annual mortality rates were calculated by adjusting US Renal Data System all-cause mortality rates using relative survival at 10 years based on an age-matched US population sample.

[e]After 8-week course 100 mg of glecaprevir and 40 mg of pibrentasvir (3 times daily).

results.[17] Their health state utilities were held constant, while distributions were used for other key model parameters, based on the 95% confidence intervals shown in Table 1. Beta distributions were used for probabilities, and log normal distributions were used for rates and waiting times that could have values greater than unity.

Utility Assessment

We used a web-based health utility assessment (HUA) platform we developed, the Gambler II,[18] to perform standard gamble assessments for three health states used in the decision analytic model: 1) life on dialysis, 2) life following kidney transplantation with an HCV-unexposed kidney, and 3) life following transplantation with a kidney from an HCV-viremic deceased donor. The Gambler II uses icons, text descriptions, and video clips of patient actors to describe each health state. Text descriptions and standardized scripts used by the patient actors and Gambler II screenshots are shown in Supplement 2. In addition to text instructions for using the Gambler II, there are videos providing instructions at each stage of the process. As shown in Supplement 2 (Figures S1 to S8), the Gambler II first presents icons and text descriptions for each health state. Users may also double click on each health state icon to launch a $\sim$1.5-minute video clip of a demographically matched patient actor describing the health state. Users can relaunch these videos at any stage of the HUA process. Users are next asked to rank each of the intermediate health states being assessed between best and worst health anchor states of Well and Dead, by clicking on the respective icon and dragging it into position on a categorical scale. The Gambler II next performs an assessment using a visual analog scale, or a "feeling thermometer," asking the users to click and drag the health state icons to the appropriate place on the thermometer. Next, the Gambler II proceeds with the standard gamble assessment for each of the health state utilities. We use the analogy of a pill bottle that contains 100 pills guaranteed to cure the health state in question. For example, in the assessment of the health state kidney transplantation, the user is told the following:

Table 2 Characteristics of ESKD Patients in Our Cohort

Variable	Base-Case Value, *N* (%) [SD]
Number	63
Interested in kidney transplant	47 (75)
Mean age, years	57.8 [12.3]
Male sex	33 (52)
Racial distribution	
White	19 (30)
African American	44 (70)
Mean dialysis vintage, years	5.94 [8.1]
Quality of life	
Hemodialysis	0.83 [0.23]
Transplant HCV-unexposed kidney	0.89 [0.18]
Transplant HCV-viremic kidney	0.76 [0.28]

Abbreviations: ESKD, end-stage kidney disease; HCV, hepatitis C virus.

> As a treatment for your ESKD, you are being offered a Kidney Transplant. Imagine you were offered a medication that could cure your ESKD without needing a Kidney Transplant. You have the choice between receiving a Kidney Transplant or taking the medication (represented by the bottle of pills on the right). However, a certain number of pills in this bottle of 100 contain a deadly poison.

The assessment typically starts at a 50:50 gamble, by asking,

> If 50 of the 100 pills in the bottle contained the medicine, while 50 of the 100 pills were contaminated by poison (assume you cannot differentiate between the medicine and the poison pills), would you take a pill from this bottle? If you are indifferent between the two choices click on the middle "Equal" button.

As the users click on either the pill bottle representing the gamble, or the icon representing the intermediate health state, the gamble resets, and continually presents a new gamble. The user indicates when they are indifferent between the gamble and the health state being assessed, and the value of the gamble is used to calculate the utility weight. If the anchor states have values of 1 (Well) and 0 (Dead), then the utility of the intermediate health state equals the (1 − probability of death) the user is willing to accept in the gamble to be Well. For instance, if the user is willing to accept a 15% chance of death (15 poison pills in the bottle of 100) for the health state Kidney Transplant, then the utility weight of this state would be 0.85.

We used the standard gamble utility assessment method for the utility weights in the personalized decision analyses, as the gamble holistically incorporates risk attitude, and risk attitude is an important component in this particular decision.[19] In addition, for the health state, life following transplantation with an HCV-viremic kidney, we performed a separate gamble using life following transplantation with a non-HCV-viremic kidney and death as the two anchor states. We framed the gamble in this manner as we were specifically interested in assessing how much of a risk of death patients would be willing to take to avoid transplantation with an HCV-viremic kidney compared with receiving a noninfected kidney.

We recruited a convenience sample of 63 ESKD patients (see Table 2) undergoing intermittent hemodialysis at four dialysis centers (Dialysis Clinic Inc., DCI) in the Cincinnati metropolitan area. Patients were eligible for the study if they were between 21 and 80 years of age, could read and understand English, and did not have cognitive deficits that would interfere with their ability to consent to participate.

We present results in Table 2 using simple descriptive statistics for means and standard deviations. In subanalyses stratifying by race, we had insufficient evidence to assume nonnormal distributions and therefore used two-sample *t* tests with 2 tails. We used the chi-squared test for significance of frequency data.

Results

Patient Characteristics

Patient-level information for the 63 patients from whom we assessed health state utilities are summarized in Supplemental Table 1. Mean age was 57.8; 33 (52%) were male and 30 (48%) were female. Forty-four (70%) were African American and 19 (30%) were White. The mean dialysis vintage for the group was 5.94 years. Forty-seven (75%) were interested in receiving a kidney transplant.

Health-Related Quality of Life

As shown in Figure 2, standard gamble utilities varied widely from patient to patient. Mean utility weights were highest for transplantation with an HCV-uninfected kidney (0.89, SD: 0.18), and were 0.825 (SD: 0.231) and 0.755 (SD: 0.282) for hemodialysis and transplantation with an HCV-viremic kidney, respectively. However, 30 patients rated transplantation with an HCV-viremic kidney higher than dialysis. Utility values for transplantation with an HCV-viremic kidney were calculated as the product between the utility weight for transplantation with an HCV-unexposed kidney times a weighting factor

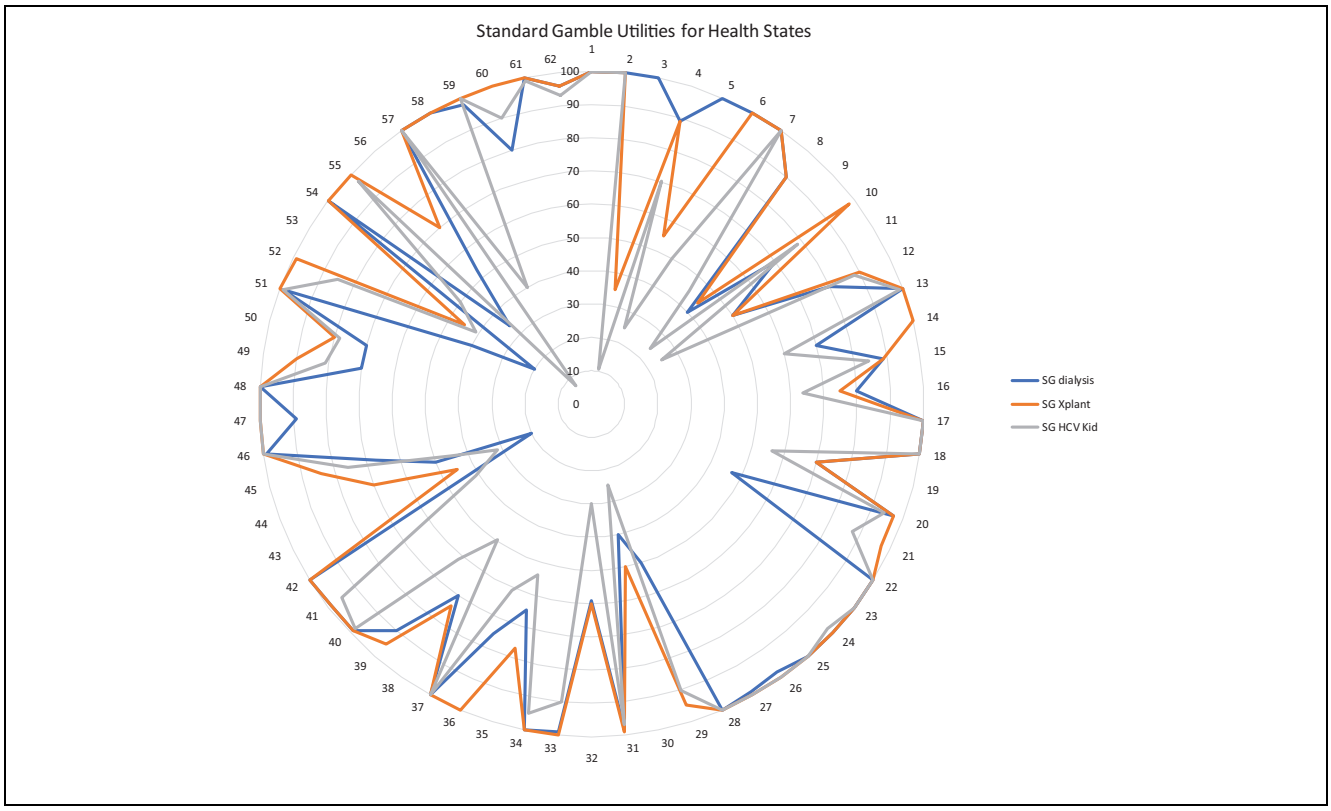

Figure 2 Health state utilities. Radar plot showing utilities for the three health states - 1) hemodialysis; 2) transplantation with an HCV-unexposed kidney; and 3) transplantation with an HCV-viremic kidney, for each of the 63 patients in the study, using the standard gamble utility assessment method. For all patients, Xplant is either best or as good as dialysis. The radar plot highlights the substantial patient-to-patient variation in utility values.
Abbreviations: SG, standard gamble; Xplant, transplantation with an HCV-unexposed kidney; HCV Kid, transplantation with an HCV-viremic kidney.

capturing the worry and concern individual patients had related to receiving an HCV-viremic kidney.

Patient-Specific Decision Analyses

As shown in Figure 1, we performed patient-specific decision analyses using individual patient's health state utilities for hemodialysis, life following kidney transplantation, and life following transplantation with an HCV-viremic kidney (Figure 2) along with individual patient's age, race, gender, and dialysis vintage. The output of the decision model was an estimate of quality-adjusted life expectancy for each of the three strategies. Figure 3 shows results for patient-specific decision analyses on all 63 patients, reported as the gain (or loss) in quality-adjusted life years (QALYs) of transplantation with an HCV-viremic kidney versus an HCV-unexposed kidney. Thirty-seven (59%) of the 63 ESKD patients in the cohort would have a net gain in QALYs from transplantation of an HCV-viremic kidney, while 26 would have a net loss. In addition, continuing dialysis was best for one patient in this cohort. We performed a second analysis in which we removed the 13 patients who were not interested in receiving a kidney transplant. In this analysis, 33 of 50 (66%) patients interested in receiving a transplant would have fared best with receipt of an HCV-viremic kidney. We also performed a subanalysis looking only at patients who were not interested in transplantation (Figure 4). In this analysis, 8 of 13 (62%) patients would have fared best with transplantation of an HCV-unexposed kidney, transplantation with an HCV-viremic kidney was recommended for four patients (31%), and continued dialysis was recommended for one patient (8%).

Since the major factor driving analysis results was the degree of worry and concern patients had over receiving an HCV-viremic kidney, we performed a separate analysis in which compared the weighting factor for concern

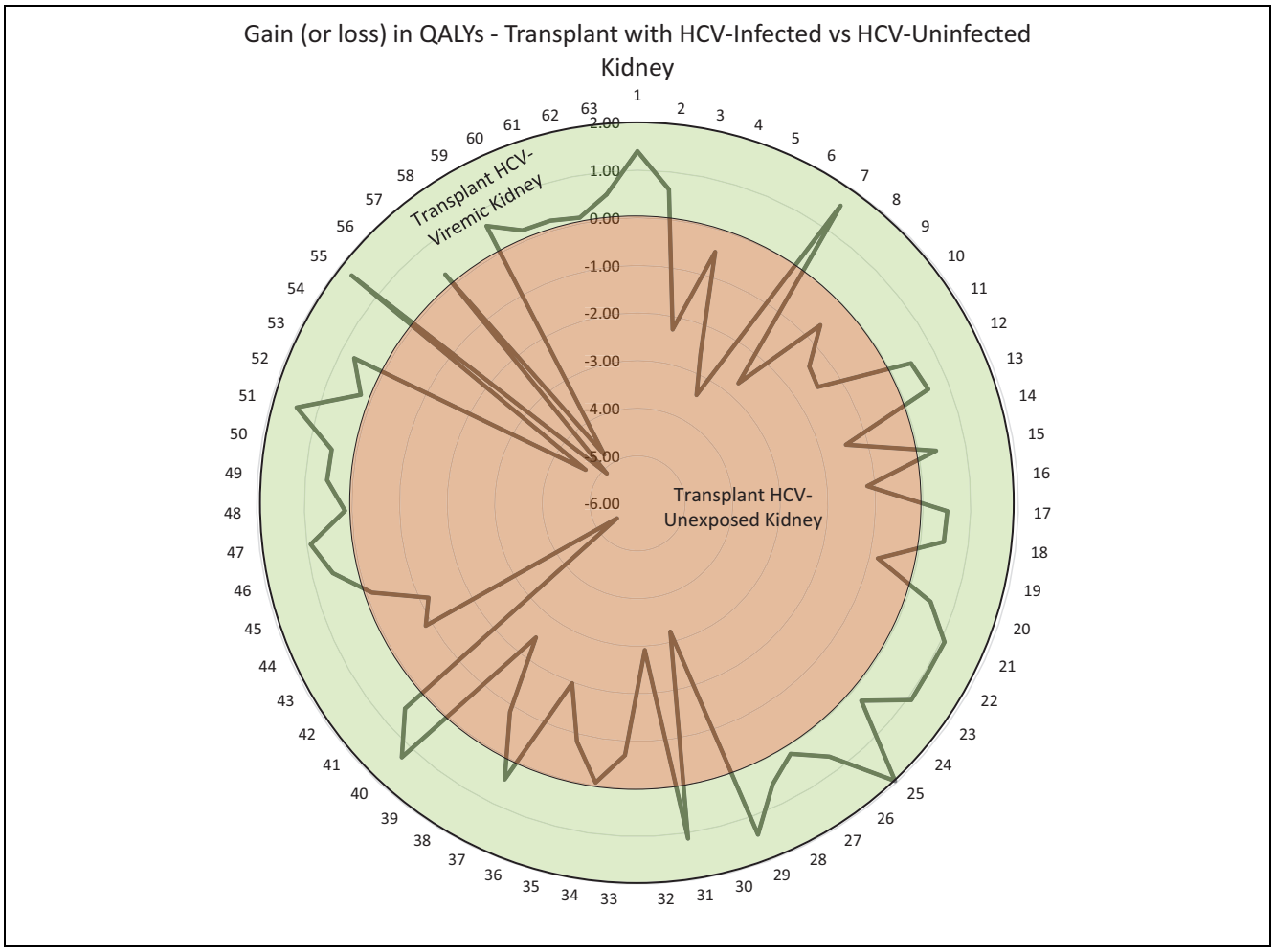

Figure 3 Figure 3 Results of the patient-level decision analyses for all 63 patients in the cohort. The green shaded zone indicates patients with a gain in QALYs while the pink shaded zone indicates patients with a loss in QALYs for transplantation with an HCV-viremic kidney versus an HCV-unexposed kidney.
Abbreviations: QALYs, quality-adjusted life years; HCV, hepatitis C virus.

over an HCV-viremic kidney with the net gain (or loss) in QALYs from transplantation with an HCV-viremic kidney. Note, the weighting factor capturing worry and concern about receiving an HCV-viremic kidney ranges between zero and one, where one represents no worry. As shown in Figure 5, all patients who had a net gain from transplantation with an HCV-viremic kidney, had a value for $Q_{\text{worry}} \geq 0.9$.

We also performed subanalyses stratifying by race. The mean values for Q_{worry} among African American and White patients were 0.84 and 0.78 ($P = 0.32$), respectively. Patient-specific decision analyses suggested transplantation with an HCV-viremic kidney in 28 (64%) African American patients and in 9 (47%) White patients ($P = 0.23$), and in 24 (71%) and 7 (54%), respectively, of African American and White patients who were interested in receiving a kidney transplant ($P = 0.28$).

We performed probabilistic sensitivity analyses on two prototypical patients who were interested in kidney transplantation. The first patient (see patient 29 in Supplemental Table 1) is a 39-year-old African American male who has been on dialysis for 3 years has little concern about receiving an HCV-viremic kidney. His utilities for dialysis, HCV-unexposed kidney, and HCV-exposed kidney were 0.50, 0.95, and 0.90, respectively. Mean results and standard deviations for this patient were 11.83 (0.21), 10.43 (0.32), and 4.46 (0.02) QALYs for transplantation with an HCV-viremic kidney, transplantation with an HCV-unexposed kidney,

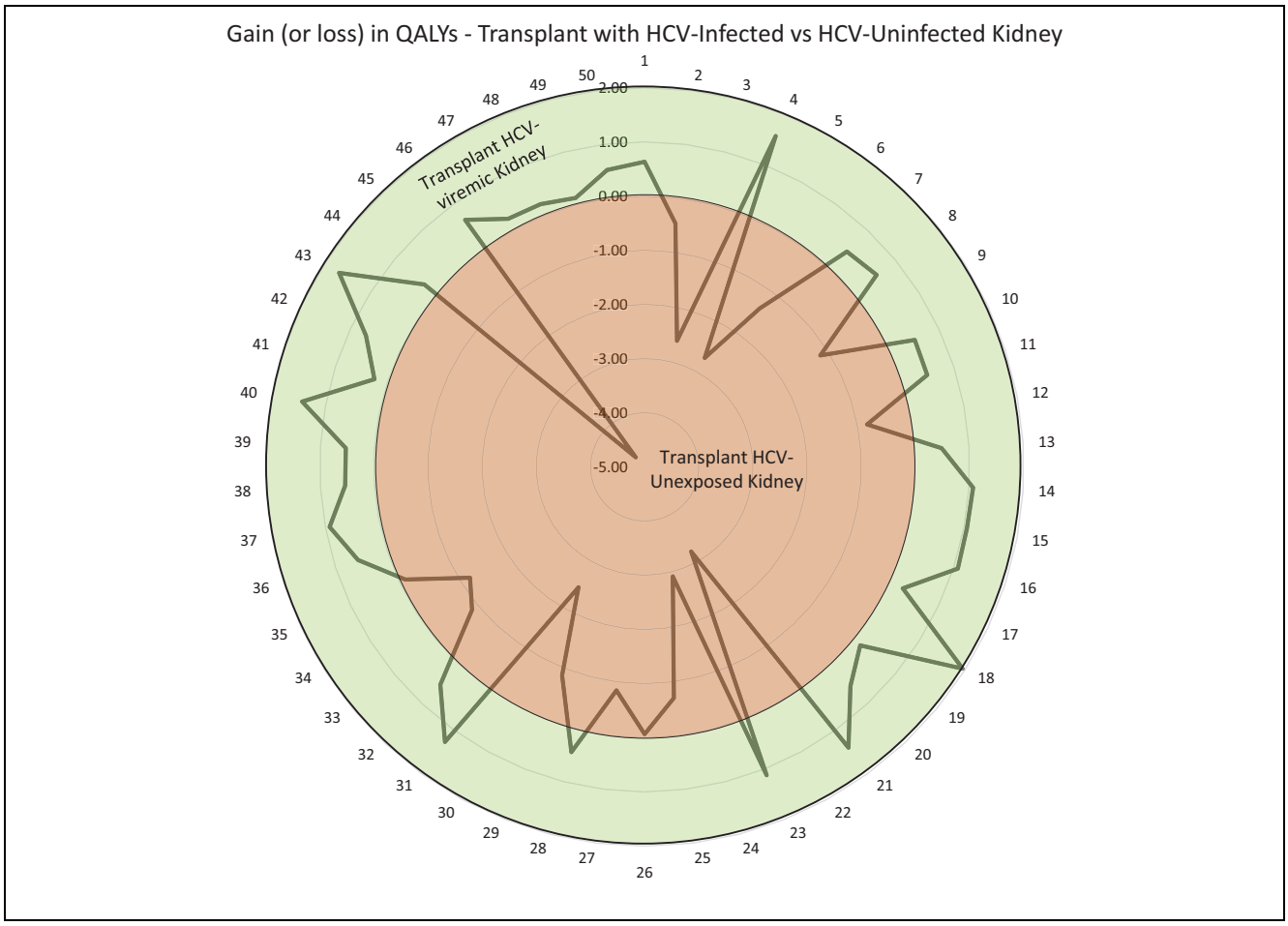

Figure 4 Results of the patient-level decision analyses for the 13 patients in the cohort who were not interested in receiving a kidney transplant. The green shaded zone indicates patients with a gain in QALYs while the pink shaded zone indicates patients with a loss in QALYs for transplantation with an HCV-viremic kidney versus an HCV-unexposed kidney.
Abbreviations: QALYs, quality-adjusted life years; HCV, hepatitis C virus.

and dialysis, respectively. Transplantation with an HCV-viremic kidney was best in 100% of simulations resulting in an average gain of 1.40 (SD: 0.12) QALYs compared with transplantation of an HCV-unexposed kidney. Supplemental Figure S4 shows the distribution of gain between transplantation with an HCV-viremic versus an HCV-unexposed kidney for this patient.

The second patient (see patient number 44 in Supplemental Table 1) is a 48-year-old African American female who has been on dialysis for 7 years and has significant concerns about receiving an HCV-viremic kidney. Her utilities for dialysis, HCV-unexposed kidney, and HCV-exposed kidney were 0.50, 0.70, and 0.46, respectively. Mean results and standard deviations for this patient were 5.84 (0.09), 7.02 (0.22), and 3.36 (0.01) QALYs for transplantation with an HCV-viremic kidney, transplantation with an HCV-unexposed kidney, and dialysis, respectively. Transplantation with an HCV-unexposed kidney was best in 100% of simulations resulting in an average gain of 1.19 (SD: 0.14) QALYs compared with transplantation of an HCV-viremic kidney. Supplemental Figure S5 shows the distribution of loss between transplantation with an HCV-viremic versus an HCV-unexposed kidney for this patient.

Discussion

A possible silver lining of the opioid epidemic is the increased availability of higher quality organs coming from younger individuals who have died from drug overdoses. Unfortunately, some of these organs are from donors who were infected with the HCV. Given the

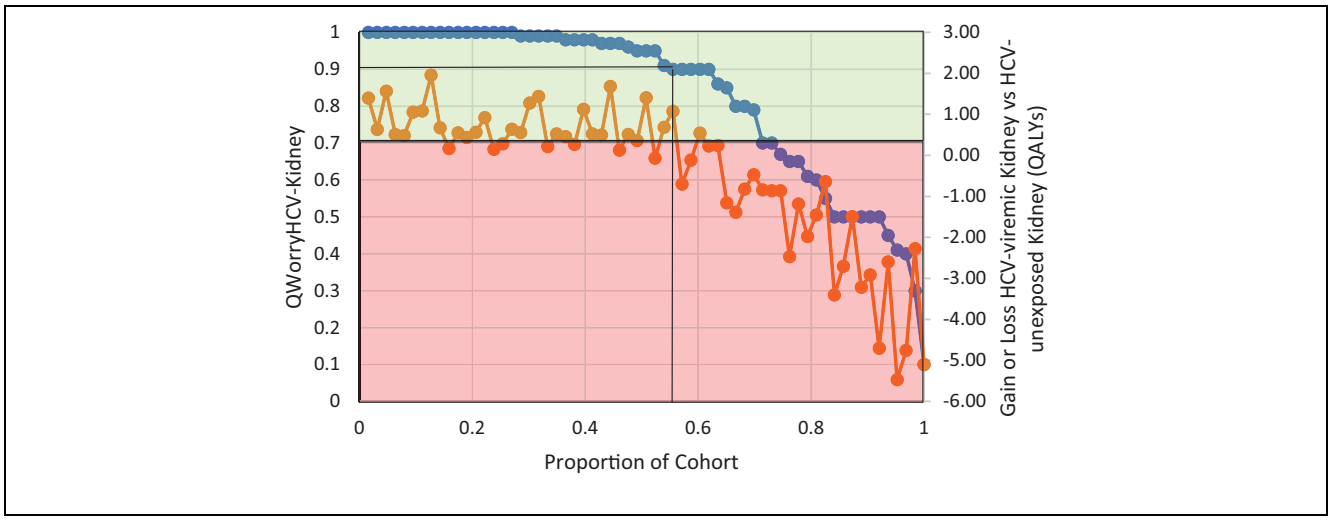

Figure 5 Comparison of gain (loss) HCV-viremic vs HCV-unexposed kidney and weighting factor for concern and worry about receiving an HCV-viremic kidney. The x-axis shows the proportion of the cohort of 63 patients. The blue line corresponding to the primary y-axis, to the left shows the weighting factor for worry and concern about transplantation with an HCV-viremic kidney (QWorryHCV-Kidney) ranging between zero and one. A weighting factor of 1.0 indicates no worry or concern, while progressive smaller numbers < 1.0 indicate concern. These are based on standard gamble utility results with best and worst anchor states of transplantation with an HCV-unexposed kidney and death, respectively. For example, a value of 0.9 would correspond to a willingness to accept a 0.1 (1.0 – 0.9) chance of death to avoid receiving an HCV-viremic kidney. The orange line, corresponding to the secondary y-axis, to the right, shows the gain (or loss) in QALYs for transplantation with an HCV-viremic kidney versus and HCV-unexposed kidney. The area to the top, shaded in green, corresponds to the 59% of patients who have a net gain in QALYs for transplantation with an HCV-viremic kidney. Patients in this region all have QWorryHCV-Kidney values ≥ 0.9. The pink shaded region below, corresponds to patients with a net loss in QALYs, who would do better with transplantation with an HCV-unexposed kidney. These patients have QWorryHCV-Kidney values ≤ 0.9.
Abbreviations: QALYs, quality-adjusted life years; HCV, hepatitis C virus.

overall scarcity of organs for transplantation, use of these HCV-infected organs for transplantation is increasingly being considered. Indeed, the proportion of transplant candidates willing to accept a kidney from an HCV-
viremic donor has steadily increased over the past few years to over 30% in 2019.[1] However, as our study has shown, there is wide variability in individual patient values and preferences for health states relevant to the decision to accept an HCV-viremic kidney transplant. The other key dynamic in this decision is how acceptance of transplantation with an HCV-viremic kidney might favorably impact waiting time for transplantation. Thus, patients and their clinicians must weigh the relative risks and benefits of earlier transplantation, reducing the time patients must continue to receive dialysis, and acceptance of transplantation with an HCV-viremic kidney. These tradeoffs and the importance of individual preferences make this decision an ideal setting for shared decision-making facilitated by patient-specific decision analysis.

One of our major goals was to test the feasibility of using a utility assessment platform, The Gambler II, along with a decision analytic model capable of performing personalized decision analyses by incorporating individual patient's utility weights for health states of hemodialysis, and transplantation with either an HCV-uninfected or HCV-infected kidney, along with patient-specific demographic information (age, sex, race, and dialysis vintage), and predictions of organ availability in real-world clinical settings. Our longer-term goal is to develop a Kidney Transplantation Decision Support Tool (KTDST) that will seamlessly integrate a utility assessment tool, a decision analytic model (computational engine), and a patient-facing interface that will present a personalized report for the patient that can be used to facilitate a shared decision-making discussion about the various kidney transplantation strategies (see Figure 6). Although the current study has focused on the utility assessment process and the impact of variability in patient values and preferences, the other major dynamic

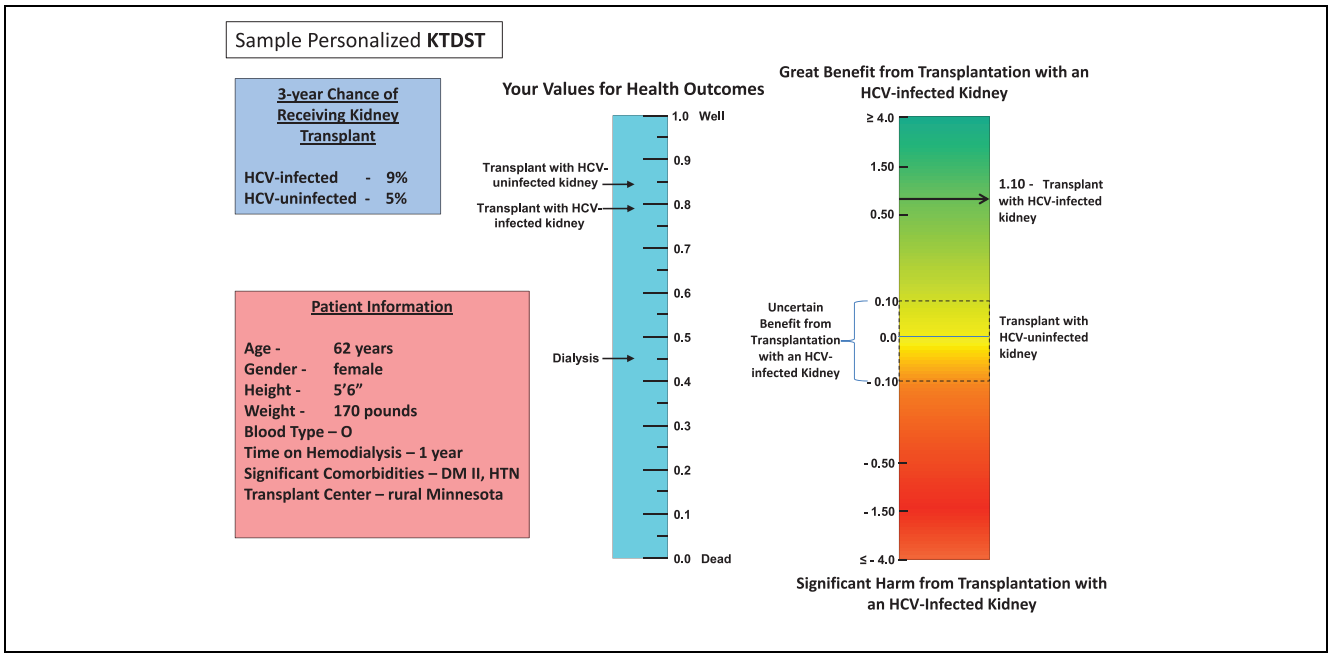

Figure 6 Sample personalized report from the Kidney Transplant Decision Support Tool (KKDST). This mock-up of a personalized report envisions how patient information could be used to predict 3-year chance of receiving an organ, and then incorporate that prediction along with the patient's personal utility weights for the relevant health states, age, race, sex, and dialysis vintage to generate an estimate of net benefit in quality-adjusted life years of transplantation with an HCV-infected kidney versus transplantation with an HCV-uninfected kidney. In this example a 62-year-old woman with a 9% and 5% 3-year chance of receiving an HCV-infected and an HCV-uninfected kidney, respectively, and utilities of 0.98, 0.85, 0.78, and 0.45 for treatment with antiviral agents for HCV, transplant with HCV-uninfected kidney, transplant with HCV-infected kidney, and hemodialysis, would gain 1.10 QALYs by accepting transplantation with an HCV-infected kidney compared with waiting longer to receive an HCV-uninfected kidney.
Abbreviations: QALYs, quality-adjusted life years; HCV, hepatitis C virus.

in the decision regarding whether to accept an HCV-viremic kidney is predicted waiting time for an organ. This can vary widely based on both patient-specific and transplant center-specific factors. Thus, the KTDST also would integrate predictions of waiting time based on factors such as age, sex, blood type, dialysis vintage, calculated panel reactive antibodies (cPRA), comorbidities, and the region in which the transplant is being done. Such a tool could either be freestanding and require clinicians to enter the necessary clinical information, or it could be integrated with the electronic health record to automatically populate the clinical and demographic information needed for the individualized decision analysis. We have been successful using a similar approach to develop an Atrial Fibrillation Shared Decision-Making Tool (AFSDM) that uses patient-specific information for the electronic health record to calculate stroke risk, bleeding risk on anticoagulant therapy, age, sex, and other comorbidities to generate personalized anticoagulation treatment recommendations.[20] This is available as an online tool and does not require any special computing equipment beyond a standard desktop or tablet. As with the AFSDM, our experience is that the most effective approach is to use the tool during a patient visit to facilitate a shared decision-making discussion.[20]

While we presented results of probabilistic sensitivity analyses for two prototypical patients in order to provide a sense of the uncertainty in model results due to uncertainty in parameter inputs, performing such analyses in real time for a decision support tool is impractical. Ten thousand second-order Monte Carlo simulations of our Markov state transition model takes several hours to run on current desktop or tablet computers. If computational time were no longer a constraint in the future, one could imagine incorporating results of a probabilistic sensitivity analysis into the personalized KTDST report, by replacing the thin line representing the benefit from transplantation with an HCV-infected kidney in Figure 6 with a thin line (representing the mean result) surrounded by a fuzzy haze above and below, representing the 95%

confidence interval. However, this introduces yet one more layer in the complexity of personalized results, making the interpretation potentially more challenging and confusing for both clinician and patient.

We were successful in being able to conduct utility assessments in the field while patients were undergoing hemodialysis, taking advantage of the 3- to 4-hour-long dialysis sessions during which they are tethered to a dialysis machine. Most patients actually appreciated being engaged in a meaningful and mentally stimulating experience during this time. Our next step will be to construct and then test the KTDST on a cohort of patients who are waitlisted for transplantation, and measure the impact of such a shared decision-making discussion on various measures of decisional quality, such as decreases in decisional conflict,[21] satisfaction with decision,[22] self-efficacy, and therapeutic alliance with health care team.[23]

Our study has demonstrated wide variation in individual patient values and preferences, or utilities, for health states relevant to the decision to accept an HCV-viremic kidney transplant, as well as the impact of this variation on the optimal decision for any individual patient. While one study has reported that >80% of patients with kidney failure stated that they would be willing to accept transplantation with an HCV-viremic kidney,[24] our assessment of the values and preferences of 63 ESKD patients undergoing intermittent hemodialysis show 46 (73%) of the patients in our study were willing to take some risk of death (ranging between 1% and 90%) to avoid receiving an HCV-viremic kidney rather than an HCV-unexposed kidney. In our small convenience sample of 63 ESKD patients receiving hemodialysis, patient-level decision analyses indicated that slightly more than a third of patients interested in receiving a transplant would gain more QALYs by waiting longer and receiving an HCV-unexposed kidney rather than accepting an HCV-viremic kidney.

Patients' values and preferences for health states is a significant component of decision making. As an example, prior studies have reported an average utility score of 0.53 for dialysis, on a zero to one scale in which zero represents death and one represents the best possible health state.[25,26] However, in several meta-analyses and systematic reviews examining health utilities in patients with ESKD, utility weights are dependent on the assessment method. Typical utility assessment methods include the visual analog scale (VAS), the time tradeoff, and the standard reference gamble.[27] The VAS requires nothing more than for participants to indicate where each health state should be placed on a linear scale (i.e., feeling thermometer) with anchors at the top and bottom for best and worst possible states of health. The time tradeoff involves trading off some number of years of life in the less than perfect state of health being assessed in exchange for a shorter duration of life in the best possible state of health. The standard gamble assesses how much of a risk of a bad outcome (frequently death) participants are willing to take to avoid the intermediate state of health being evaluated. Standard gamble assessments tend to result in higher utility weights than the other methods described above, since this technique also incorporates risk attitude, and most people are somewhat risk averse.[28,29] Thus, in studies using the standard gamble, utility weights for hemodialysis range between 0.53 and 0.86, closer to what we found in our study.[29] Health utilities following transplantation are generally much higher, 0.84 in some studies.[30] It is interesting to note that in our cohort of patients who have been receiving hemodialysis for an average of roughly 6 years, the mean utility score for dialysis was higher, 0.83, than that reported in some other studies. The utility for kidney transplantation, 0.89, was similar to that reported in other studies. However, to our knowledge, no studies have examined patients' utilities following transplantation with an HCV-viremic kidney. In our study, the average utility for transplantation with an HCV-viremic kidney was 0.76 (SD: 0.28), lower than the average utility for dialysis. That being said, among the 63 patients, 30 rated transplantation with an HCV-viremic kidney higher than dialysis. Since the utility for hemodialysis in our population of dialysis-experienced patients was much higher than published reports, estimated gains in quality of life from transplantation may have been reduced.

Prior analyses at a population level have demonstrated the benefit of using HCV-viremic kidneys as a way to shorten waiting times for patients on dialysis awaiting kidney transplantation, thereby decreasing overall mortality due to the significant survival benefit associated with kidney transplantation.[6,31,32] While use of HCV-viremic kidneys may result in net benefit for the average ESKD patient awaiting transplantation, patients may have widely different values for health states, in particular, life following transplantation with either an HCV-unexposed or an HCV-viremic kidney. Concerns about cure or complications from HCV infection, or the stigma of HCV infection may diminish anticipated quality of life following transplantation with an HCV-viremic kidney. In addition, while our analysis focused primarily on variations in individual patient's utilities for these three key health states, other important parameters that may vary from patient to patient include waiting times for a kidney and competing mortality risks from comorbid diseases over and above ESKD. Thus, the best decision for any

individual may be different depending upon the balance of these factors.

Reports from the Standardized Outcomes in Nephrology-Transplant Initiative (SONG-TX Initiative) highlight the discrepancies between patients, caregivers, and health professionals regarding posttransplant outcomes.[33] Our study identifies another potential discrepancy related to HCV-viremic transplants. As transplantation with HCV-viremic organs becomes standard of care, transplant health professionals should recognize the potential negative impact on transplant recipients' quality of life associated with receiving an HCV-viremic organ. Methods to abrogate these concerns could include increased pre- and posttransplant education surrounding the sustained virologic response rates of direct acting antiviral agents, associated HCV cure rates, and impact on posttransplant outcomes.

Our study has limitations. Given the demographics of our Cincinnati metropolitan dialysis clinics, we had a higher proportion of African American patients (70%) in our sample. To the extent that race may impact assessments of health state utilities or perceptions about receiving HCV-viremic kidneys, our results may not be generalizable to a more racially diverse population. In addition, the average dialysis vintage in our sample was almost 6 years. Thus, accommodation to this treatment and health state may have resulted in higher assessed values of this health state. We modeled outcomes following successful transplantation at a summative level and did not simulate more granular events such as graft failure and possible re-transplantation. As a result, we were not able to consider variability in the quality of organs being transplanted, as measured by the Kidney Donor Profile Index (KDPI).[34] The impact this may have on the decision model results is hard to predict as, on one hand, this may underestimate the benefit of transplantation with organs from donors who died from drug overdoses, as these kidneys tend to come from younger and healthier donors who do not have diabetes mellitus, hypertension, or kidney disease. On the other hand, HCV status is an important component of the KDPI, increasing the chances of graft failure among patients receiving HCV-viremic kidneys.

Finally, although our ultimate goal is to develop decision support tools that can be used to facilitate discussions between clinicians and their patients about transplantation with HCV-viremic kidneys, at the time we performed utility assessments patients were not being faced with imminent decisions about accepting such organs.

In conclusion, if the medical care system is to best utilize the available kidneys from this hopefully self-limited epidemic of opioid deaths, there is an urgent need to quickly develop decision-making tools that incorporate the key decision variables. While our study focused on demonstrating the important impact of patient-to-patient variation in health state utilities, one can imagine the development of an even more comprehensive decision support tool that can aid patients and their physicians in making the best choice, based on individual patient values and preferences for health states, waiting time, and mortality estimates for both HCV-unexposed and HCV-viremic kidneys, along with patient-specific clinical, demographic, and center-specific information.

ORCID iDs

Mark H. Eckman https://orcid.org/0000-0001-8253-269X
Adeboye A. Adejare https://orcid.org/0000-0003-4378-3626

Supplemental Material

Supplemental material for this article is available on the *Medical Decision Making Policy & Practice* website at https://journals.sagepub.com/home/mpp.

References

1. Hart A, Lentine KL, Smith JM, et al. OPTN/SRTR 2019 annual data report: kidney. *Am J Transplant*. 2021; 21(Suppl 2):21–137.
2. Maghen A, Mone TD, Veale J. The kidney-transplant waiting list and the opioid crisis. *N Engl J Med*. 2019;380(23): 2273–4.
3. Durand CM, Bowring MG, Thomas AG, et al. The drug overdose epidemic and deceased-donor transplantation in the United States: a national registry study. *Ann Intern Med*. 2018;168(10):702–11.
4. Wang JH, Gustafson SK, Skeans MA, et al. OPTN/SRTR 2018 annual data report: hepatitis C. *Am J Transplant*. 2020;20(Suppl 1):542–68.
5. Sise ME, Goldberg DS, Kort JJ, et al. Multicenter study to transplant hepatitis C-infected kidneys (MYTHIC): an open-label study of combined glecaprevir and pibrentasvir to treat recipients of transplanted kidneys from deceased donors with hepatitis C virus infection. *J Am Soc Nephrol*. 2020;31(11):2678–87.
6. Eckman MH, Woodle ES, Thakar CV, Alloway RR, Sherman KE. Cost-effectiveness of using kidneys from HCV-viremic donors for transplantation into HCV-uninfected recipients. *Am J Kidney Dis*. 2020;75(6):857–67.
7. Bowring MG, Shaffer AA, Massie AB, et al. Center-level trends in utilization of HCV-exposed donors for HCV-uninfected kidney and liver transplant recipients in the United States. *Am J Transplant*. 2019;19(8):2329–41.
8. United States Renal Data System. United States Renal Data System— 2018 Annual date report. Available from: https://adr.usrds.org/2018

9. Saran R, Robinson B, Abbott KC, et al. US Renal Data System 2019 annual data report: epidemiology of kidney disease in the United States. *Am J Kidney Dis*. 2020;75 (1 Suppl 1):A6–A7.
10. Wolfe RA, Ashby VB, Milford EL, et al. Comparison of mortality in all patients on dialysis, patients on dialysis awaiting transplantation, and recipients of a first cadaveric transplant. *N Engl J Med*. 1999;341(23):1725–30.
11. Arias E, Xu J. National Vital Statistics Reports: United States life tables, 2017 [cited October 16, 2021]. Available from: https://www.cdc.gov/nchs/data/nvsr/nvsr68/nvsr68_07-508.pdf
12. Chong CA, Gulamhussein A, Heathcote EJ, et al. Health-state utilities and quality of life in hepatitis C patients. *Am J Gastroenterol*. 2003;98(3):630–8.
13. Liu S, Cipriano LE, Holodniy M, Owens DK, Goldhaber-Fiebert JD. New protease inhibitors for the treatment of chronic hepatitis C: a cost-effectiveness analysis. *Ann Intern Med*. 2012;156(4):279–90.
14. McLernon DJ, Dillon J, Donnan PT. Health-state utilities in liver disease: a systematic review. *Med Decis Making*. 2008;28(4):582–92.
15. Sherman KE, Sherman SN, Chenier T, Tsevat J. Health values of patients with chronic hepatitis C infection. *Arch Intern Med*. 2004;164(21):2377–82.
16. Younossi ZM, Stepanova M, Esteban R, et al. Superiority of interferon-free regimens for chronic hepatitis C: the effect on health-related quality of life and work productivity. *Medicine (Baltimore)*. 2017;96(7):e5914.
17. Sanders GD, Neumann PJ, Basu A, et al. Recommendations for conduct, methodological practices, and reporting of cost-effectiveness analyses: second panel on cost-effectiveness in health and medicine. *JAMA*. 2016;316(10):1093–103.
18. Adejare AA Jr, Eckman MH. Automated tool for health utility assessments: the Gambler II. *MDM Policy Pract*. 2020;5(1):2381468320914307.
19. Gafni A. The standard gamble method: what is being measured and how it is interpreted. *Health Serv Res*. 1994; 29(2):207–24.
20. Eckman MH, Costea A, Attari M, et al. Shared decision-making tool for thromboprophylaxis in atrial fibrillation—a feasibility study. *Am Heart J*. 2018;199:13–21.
21. O'Connor AM. Validation of a decisional conflict scale. *Med Decis Making*. 1995;15(1):25–30.
22. Holmes-Rovner M, Kroll J, Schmitt N, et al. Patient satisfaction with health care decisions: the satisfaction with decision scale. *Med Decis Making*. 1996;16(1):58–64.
23. Kim SC, Boren D, Solem SL. The Kim Alliance Scale: development and preliminary testing. *Clin Nurs Res*. 2001; 10(3):314–31.
24. McCauley M, Mussell A, Goldberg D, et al. Race, risk, and willingness of end-stage renal disease patients without hepatitis C virus to accept an HCV-infected kidney transplant. *Transplantation*. 2018;102(4):e163–e170.
25. Gorodetskaya I, Zenios S, McCulloch CE, et al. Health-related quality of life and estimates of utility in chronic kidney disease. *Kidney Int*. 2005;68(6):2801–8.
26. Hogan TJ, Elliott WJ, Seto AH, Bakris GL. Antihypertensive treatment with and without benazepril in patients with chronic renal insufficiency: a US economic evaluation. *Pharmacoeconomics*. 2002;20(1):37–47.
27. Chapman GB, Elstein AS. Utility assessment: methods and research. In: Bennett CL, Stinson TJ, eds. *Cancer Policy: Research and Methods*. Boston: Kluwer; 1998. p 13–23.
28. Liem YS, Bosch JL, Hunink MG. Preference-based quality of life of patients on renal replacement therapy: a systematic review and meta-analysis. *Value Health*. 2008;11(4): 733–41.
29. Wyld M, Morton RL, Hayen A, Howard K, Webster AC. A systematic review and meta-analysis of utility-based quality of life in chronic kidney disease treatments. *PLoS Med*. 2012;9(9):e1001307.
30. Elbasha E, Greaves W, Roth D, Nwankwo C. Cost-effectiveness of elbasvir/grazoprevir use in treatment-naive and treatment-experienced patients with hepatitis C virus genotype 1 infection and chronic kidney disease in the United States. *J Viral Hepat*. 2017;24(4):268–79.
31. Gupta G, Zhang Y, Carroll NV, Sterling RK. Cost-effectiveness of hepatitis C-positive donor kidney transplantation for hepatitis C-negative recipients with concomitant direct-acting antiviral therapy. *Am J Transplant*. 2018; 18(10):2496–505.
32. Kadatz M, Klarenbach S, Gill J, Gill JS. Cost-effectiveness of using kidneys from hepatitis C nucleic acid test-positive donors for transplantation in hepatitis C-negative recipients. *Am J Transplant*. 2018;18(10):2457–64.
33. Sautenet B, Tong A, Manera KE, et al. Developing consensus-based priority outcome domains for trials in kidney transplantation: a multinational Delphi survey with patients, caregivers, and health professionals. *Transplantation*. 2017;101(8):1875–86.
34. Organ Procurement and Transplantation Network. A guide to calculating and interpreting the Kidney Donor Profile Index (KDPI) [cited August 27, 2021]. Available from: https://optn.transplant.hrsa.gov/media/1512/guide_to_calculating_interpreting_kdpi.pdf
35. Kucirka LM, Peters TG, Segev DL. Impact of donor hepatitis C virus infection status on death and need for liver transplant in hepatitis C virus-positive kidney transplant recipients. *Am J Kidney Dis*. 2012;60(1):112–20.
36. Gane E, Lawitz E, Pugatch D, et al. Glecaprevir and pibrentasvir in patients with HCV and severe renal impairment. *N Engl J Med*. 2017;377(15):1448–55.
37. Gane E, Lawitz EJ, Pugatch D, et al. Expedition-4: efficacy and safety of glecaprevir/pibrentasvir (ABT-493/ABT-530) in patients with renal impairment and chronic hepatitis C virus genotype 1-6 infection. Paper presented at: AASLD—The Liver Meeting; November 11-15, 2016; Boston, MA.