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An economic assessment of contemporary kidney transplant practice

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Kidney transplantation is the optimal therapy for end-stage renal disease, prolonging survival and reducing spending. Prior economic analyses of kidney transplantation, using Markov models, have generally assumed compatible, low-risk donors. The economic implications of transplantation with high Kidney Donor Profile Index (KDPI) deceased donors, ABO incompatible living donors, and HLA incompatible living donors have not been assessed. The costs of transplantation and dialysis were compared with the use of discrete event simulation over a 10-year period, with data from the United States Renal Data System, University HealthSystem Consortium, and literature review. Graft failure rates and expenditures were adjusted for donor characteristics. All transplantation options were associated with improved survival compared with dialysis (transplantation: 5.20-6.34 quality-adjusted life-years [QALYs] vs dialysis: 4.03 QALYs). Living donor and low-KDPI deceased donor transplantations were cost-saving compared with dialysis, while transplantations using high-KDPI deceased donor, ABO-incompatible or HLA-incompatible living donors were cost-effective (<$100 000 per QALY). Predicted costs per QALY range from $39 939 for HLA-compatible living donor transplantation to $80 486 for HLA-incompatible donors compared with $72 476 for dialysis. In conclusion, kidney transplantation is cost-effective across all donor types despite higher costs for marginal organs and innovative living donor practices.

KEYWORDS
business/management, cost-effectiveness, economics, health services and outcomes research, kidney transplantation/nephrology, kidney transplantation/living donor, organ transplantation, simulation

1 | INTRODUCTION

The survival benefit of kidney transplantation in the management of patients with end-stage renal disease (ESRD) has been well established during the past 50 years. Wolfe and colleagues demonstrated superior patient survival after renal transplantation compared with long-term dialysis, particularly for patients with diabetes.[1,2] Subsequently, Whiting and associates demonstrated that deceased donor renal transplantation was cost-saving, with a breakeven cost occurring at 3 to 14 years depending on organ quality.[3] Living donor

Abbreviations: ABOi, ABO-incompatible; DDKT, deceased donor kidney transplantation; DES, discrete event simulation; DRG, diagnosis-related group; ESRD, end-stage renal disease; ICER, incremental cost-effectiveness ratio; ILDKT, incompatible living donor kidney transplantation; KDPI, Kidney Donor Profile Index; LDKT, living donor kidney transplantation; PHS, US Public Health Service; QALY, quality-adjusted life-year; SRTR, Scientific Registry of Transplant Recipients; USRDS, United States Renal Data System.

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kidney transplantation (LDKT) has been shown to be more economically beneficial, given the prolonged survival of the allografts and the potential to avoid dialysis treatments completely. [4,5]

To meet the growing demand for kidney allografts, transplant professionals have expanded use of higher-risk deceased donor organs. Organ quality is influenced by donor age, comorbidity, and allograft function at the time of donation. The expected risk of graft failure is now quantified in allocation policy by the Kidney Donor Profile Index (KDPI). Higher KDPI is correlated with a greater risk of allograft failure.[6,7] Despite shorter half-lives, organs with KDPI scores > 85 have been shown to benefit patients aged > 50 years at transplantation at programs with a median waiting time > 33 months compared with long-term dialysis.[6] Among the perceived barriers to use of high-risk organs are data demonstrating a higher rate of delayed graft function, incidence of readmission, and cost of transplantation care, leading to projected economic losses for transplant programs.[8] Similarly, deceased donor organs deemed to be at increased risk of viral disease transmission by the US Public Health Service (PHS) have been demonstrated to improve survival compared with dialysis, despite the small risk of disease transmission.[9] Broader use of these kidneys may reduce organ discard and increase access to transplantation.

Living donor kidney transplantation has been repeatedly associated with improved survival, reduced expenses, and enhanced quality of life for patients with ESRD. The economic benefit of a single LDKT has been calculated at $250 000 to $1.45 million per transplantation, including resumption of employment income.[5] However, these calculations presume transplantation with an HLA- and ABO-compatible allograft. Fortunately, patients unable to identify an immunologically compatible donor through either their social network or kidney paired donation programs still successfully undergo transplantation with the use of strategies to reduce ABO or donor-specific HLA antibody titers. However, recent analyses demonstrate that ABO-incompatible (ABOi) transplantation was associated with $33 041 in higher costs, compared with compatible transplantation.[10] Similarly, HLA-incompatible LDKT (ILDKT) was $44 388 more expensive than compatible LDTs.[11] Moreover, ILDKTs incur higher rate of graft failure, return to dialysis, and posttransplantation expenses.

To better quantify the economic implications of an increasingly complex organ supply, we evaluated the cost-effectiveness of kidney transplantation in contemporary practice using discrete event simulation (DES) to examine the impact of donor factors on economic and clinical outcomes.

2 | METHODS

A decision analytic model was constructed to assess the cost-effectiveness of kidney transplant using various deceased donor (standard criteria, high-KPDI, and PHS increased-risk) and living donor (HLA HLA-compatible 0-3 mismatches, HLA-compatible 4-6 mismatches, ABOi, ILDKT) organs was compared with maintenance dialysis treatment for a hypothetical cohort of 20,000 patients with ESRD.

2.1 | Structure of the model

In brief, the model compares maintenance dialysis with each transplantation option to determine cost per quality-adjusted life-year (QALY) gained. Two models were constructed for ease of analysis: a living donor model and a deceased donor model. In the living donor model, 4 types of LDKT were compared with dialysis (compatible transplant with 0-3 HLA mismatches, compatible transplant with 4-6 HLA mismatches, ABOi, and ILDKT [Figure 1]). In the deceased donor kidney transplant model (DDKT), 3 types of deceased donor transplants (KDPI ≤, KPDI >85, and PHS high risk) were compared with maintenance dialysis (Figure 2). Transplant recipients may experience ≥ 1 of the following 5 health states: alive with a functioning graft, primary nonfunction, maintenance dialysis, death with function, or death after graft failure while on dialysis. Patients whose grafts fail are assumed to remain on dialysis until the end of the model or death. Frequency of primary nonfunction and distribution of time to graft failure and death varied by graft type and were derived from the Scientific Registry of Transplant Recipients (SRTR) data and retrospective cohort studies (ILDKT). Patients who do not undergo kidney transplantation continue with maintenance dialysis until death. A 10-year time horizon was chosen for the model, with 1-month intervals used to accrue cost and survival. A secondary analysis was conducted using a 20-year time horizon.

2.2 | Data sources

2.2.1 | Clinical data

Deidentified registry data in the United States Renal Data System (USRDS) and patient-level data from the SRTR (kidney transplantations between January 1, 2005, and December 31, 2015) were used to estimate the time to primary nonfunction, graft failure, and posttransplantation mortality based on donor characteristics, as well as mortality on dialysis in the simulation cohort (Table 1). These data were supplemented with survival data from a large clinical cohort of ILDKT recipients. To address uncertainty, Weibull distributions were assumed for these time-to-event variables by using SRTR data as well as published data for ABOi LDKT and ILDKT.[10,12] The distribution for death on dialysis was assumed to be the same for patients who were waitlisted and those who returned to dialysis at the time of graft failure. Because these distributions are non-Gaussian, we present scale factors and shape rather than mean and SD values. Mean 5-year death and graft failure rates using these distributions were compared with observed data and presented as Table 1 in the supplemental digital content. Health state utility scores were drawn from a comprehensive literature review of dialysis and kidney transplantation and modeled as distributions.[13]

2.2.2 | Economic data

Two sources were combined to estimate the healthcare resource use associated with transplantation in this analysis, which, in general,

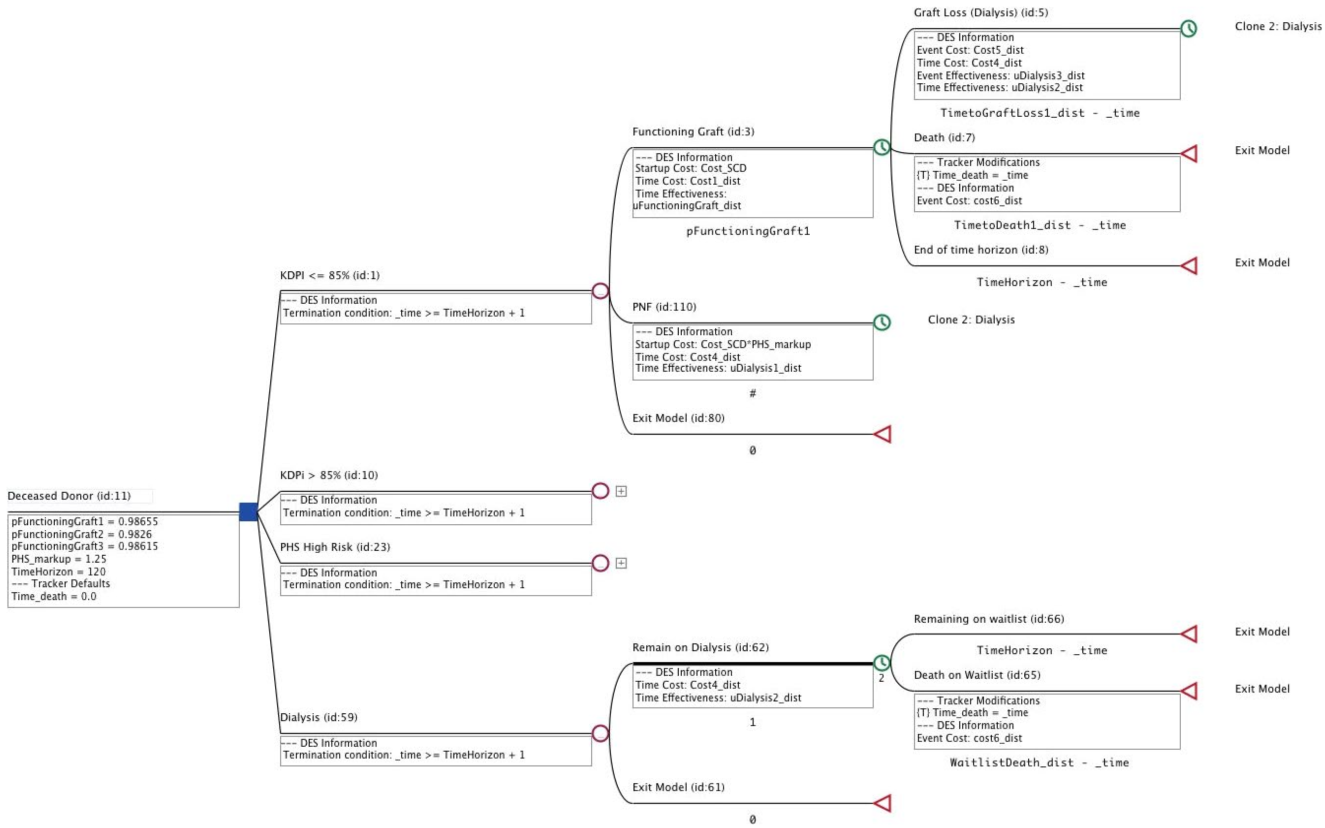

FIGURE 1 Discrete event simulation model for living donor transplantation [Color figure can be viewed at wileyonlinelibrary.com]

assumes a payer perspective. Medicare claims data were obtained from the USRDS, which includes payment data for all patients receiving maintenance renal replacement therapy with Medicare as their primary insurance, including professional charges and payments for hospitalizations.[14] Medicare claims data (between January 1, 2003, and December 31, 2012) were queried to determine expected monthly costs after transplantation stratified by donor type (deceased/living), KDPI, and immunologic/blood group compatibility. Medicare payments were chosen to measure pretransplantation costs including maintenance dialysis and death on dialysis. Multivariate risk-adjusted models were developed to estimate the cost of posttransplantation care, graft failure, and death after transplantation, as a function of organ quality for transplant recipients for those grafts.

Because Medicare diagnosis-related group (DRG)-based payments are poorly correlated with the actual cost of the transplantation procedure, we used estimates from a novel data set linking national registry data and hospital cost-accounting data from the University HealthSystem Consortium corporation, as per previous methods.[14] These data were queried to determine the cost of hospitalization for the transplantation procedure, stratified by donor source, organ quality, and the need for additional therapy. Cost ranges are shown in Table 2 and include estimates for low-KDPI (<85) and high-KDPI (>85) DDKT, compatible LDKT and incompatible LKDT. The cost of PHS increased-risk DDKT was assumed to be equivalent to the transplantation cost of a low-KDPI organ with additional cost for posttransplantation monitoring and treatment of hepatitis C virus or HIV infection based on standard treatment regimens.[15,16] All dollar values are presented in US dollars at 2016 price levels, based on the medical component of the United States Consumer Price Index.

2.3 | Simulation

DES was used to model patients' progression.[17-19] In DES modeling, occurrence of clinical events is defined as time to event, as drawn from distributions based on population data. Time to event distributions for key clinical events varied by donor type and organ characteristics (Table 1). Both QALYs and costs were discounted to present values by using an annual rate of 3%. Model results were obtained by using 20 000 simulations, which produced stable results. Given the nature of DES simulation analysis, no measures of statistical significance can be reported. Cost per QALY and the incremental cost-effectiveness ratio (ICER) were calculated by comparing each transplantation option with dialysis.

2.4 | Ethics

Analyses of national registry and linked data sets were covered by the Saint Louis University Institutional Review Board. The data reported here have been supplied by the USRDS. The interpretation and reporting of these data are the responsibility of the author(s)

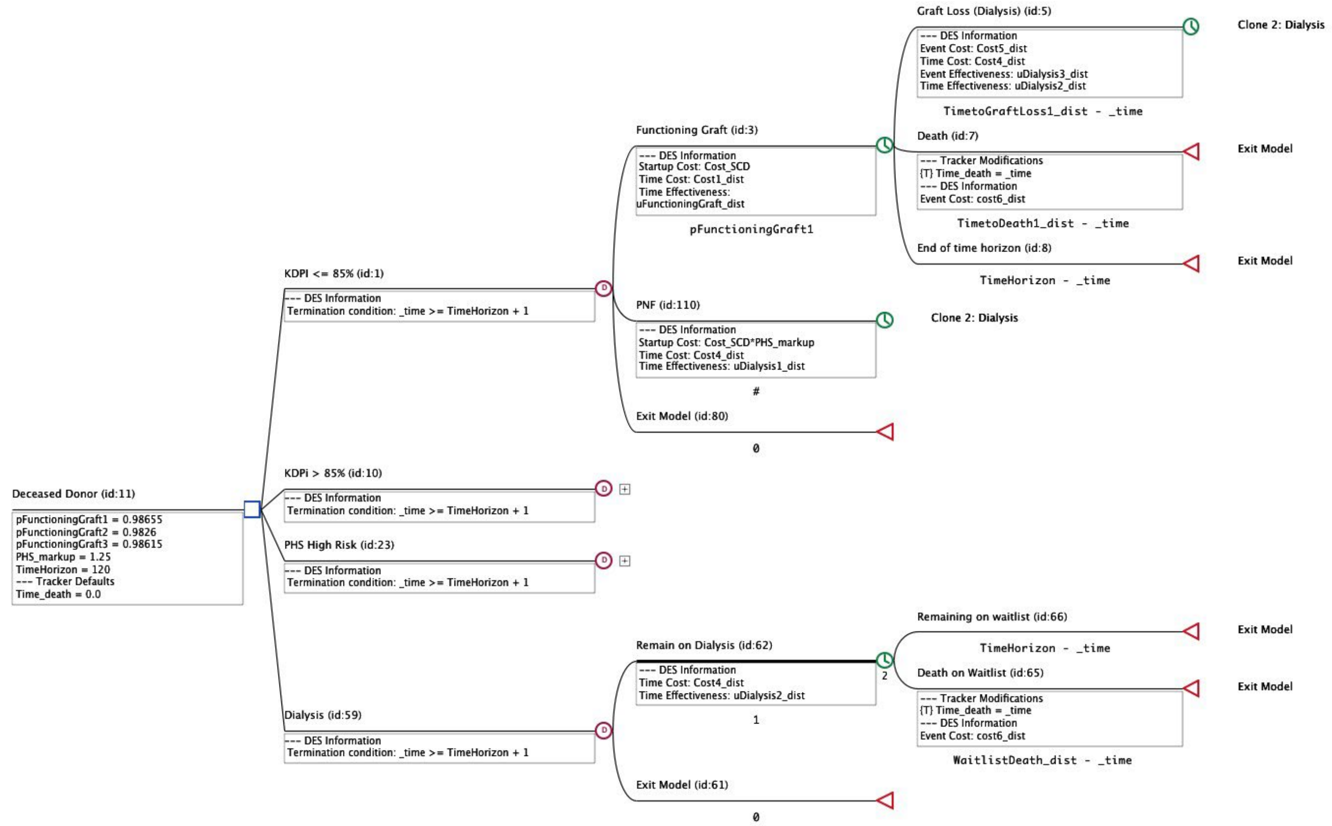

FIGURE 2 Discrete event simulation model for deceased donor transplantation [Color figure can be viewed at wileyonlinelibrary.com]

and in no way should be seen as an official policy or interpretation of the US government.

3 | RESULTS

During the 10-year study period, transplantation was associated with a significant improvement in expected survival (Figure 3). After adjustment for the difference in quality of life among patients on dialysis, maintenance dialysis therapy results in 4.03 QALYs over 10 years (Table 3). In comparison, deceased donor transplantation was associated with significant increases in quality-adjusted survival. Transplantation with low-KDPI and PHS increased-risk kidneys was predicted to increase average survival by 50% (6.07 and 5.91 QALYs, respectively). High-KDPI DDKT was associated with a survival gain of approximately 29% (5.20 QALYs). LDKT yielded greater increases in predicted survival. Compatible, well-matched living donor transplants increased survival over dialysis by 57%, to 6.34 QALYs. ABOi LDKT was associated with a 51% (6.12 QALYs) greater survival. ILDKT transplantation improved mean survival by 35% (5.47 QALYs).

The economic advantage of transplantation over dialysis varied by donor type. Patients on dialysis are expected to incur medical expenses of $292 117 over 10 years. Among DDKT recipients, we estimated that the cost of transplantation (including the cost of performing the procedure and subsequent care) with low-KDPI organs was essentially cost equivalent with dialysis ($297 286 at 10 years) as survival is extended with transplantation. Care after transplantation with organs from PHS increased-risk donors was marginally more expensive than transplantation from non–PHS increased-risk donors, given the predicted cost of rare hepatitis C virus and HIV transmissions ($307 052). Transplantation with high-KDPI organs was more expensive than maintenance dialysis over 10 years ($330 576). LDKT was cost-saving at 10 years, reducing expected expenditures for ESRD therapy by 13% ($253 119) compared with dialysis. ABOi LDKT ($364 755) and HLA ILDKT ($440 234) were more expensive than maintenance dialysis treatments.

Compared with maintenance dialysis therapy, transplantation, in general, was found to be highly cost-effective, resulting in a substantially lower cost per QALY (Table 3; Figure 4). Maintenance dialysis costs were estimated at $72 476 per QALY over 10 years. HLA-compatible, well-matched LDKT provided the most cost-effective form of renal replacement therapy. LDKTs were predicted to be 45% less expensive than dialysis ($39 939 per QALY). Despite being more expensive initially, ABOi transplantation was associated with a lower mean cost per QALY than dialysis ($59 564). ILDKT, however, was associated with a slightly higher cost per QALY ($80 486 per QALY) than dialysis over 10 years.

Deceased donor transplantation with a low-KDPI organ was estimated to be more cost-effective than dialysis ($49 017 vs $72 376 per QALY) but 23% more costly than LDKT. Despite higher initial expenses and shorter survival, transplantation with high-KPDI DDKT

TABLE 1 Clinical variables

Variable	Distribution	Characteristics	Reference
Time death with functioning graft (0-3 mismatch LDKT)	Weibull	scale factor: 0.000677820, shape: 1.1797	(30)
Time death with functioning graft (4-6 mismatch LDKT)	Weibull	scale factor: 0.002897632, shape: 0.8626	(30)
Time to death with functioning graft (ABOi LDKT)	Weibull	scale factor: 0.000710302, shape: 1.1792	(30)
Time to death with functioning graft (ILDKT)	Weibull	scale factor: 0.003978024, shape: 0.88932	(30)
Time to death with functioning graft (KDPI ≤85 DDKT)	Weibull	scale factor: 0.001829, shape 1.0632	(30)
Time death with functioning graft (KDPI >85 DDKT)	Weibull	scale factor: 0.003948, shape 1.0176	(30)
Time to death with functioning graft (PHS increased risk DDKT)	Weibull	scale factor: 0.0019966, shape 1.0543	(30)
Time to death-censored graft loss (0-3 mismatch LDKT)	Weibull	scale factor: 0.0009327, shape: 1.1474	(30)
Time to death-censored graft loss (4-6 mismatch LDKT)	Weibull	scale factor: 0.000876736, shape: 1.2719	(30)
Time to death-censored graft loss (ABOi LDKT)	Weibull	scale factor: 0.008061012, shape: 0.7018	(30)
Time to death-censored graft loss (ILDKT)	Weibull	scale factor: 0.017126085, shape: 0.7018	(31)
Time to death-censored graft loss (KDPI ≤85 DDKT)	Weibull	scale factor: 0.002616, shape 0.9934	(30)
Time to death-censored graft loss (KDPI >85 DDKT)	Weibull	scale factor: 0.00836027, shape 0.8666	(30)
Time to death-censored graft loss (PHS increased risk DDKT)	Weibull	scale factor: 0.00185948, shape 1.0776	(30)
Utility functioning graft distribution	β	α: (((0.84)^2)*(1-(0.84))/((0.037)^2)-(0.84)), β: ((1 -(0.84))*(((1-(0.84))*(0.84))/((0.037)^2)-1)) (	(13)
Utility of Primary non-function	β	α: (((.44)^2)*(1-(.44))/((.037)^2)-(.44)), β: ((1-(.44))*(((1-(.44))*(.44))/((.037)^2)-1))	(13)
Utility of graft loss event (mo)	β	subtype: 2, α: (((0.2)^2)*(1-(0.2))/((0.037)^2)-(0.2)), β: ((1-(0.2))*(((1-(0.2))*(0.2))/((0.037)^2)-1))	(13)
Utility of dialysis distribution	β	subtype: 2, α: (((0.69)^2)*(1-(0.69))/((0.037)^2)-(0.69)), β: ((1-(0.69))*(((1-(0.69))*(0.69))/((0.037)^2)-1))	(13)

ABOi, ABO-incompatible; DDKT, deceased donor kidney transplant; ILDKT, incompatible living donor kidney transplantation; KDPI, Kidney Donor Profile Index; LDKT, living donor kidney transplant; PHS, US Public Health Service.

($63 531 per QALY) costs 12.2% less per QALY than dialysis. These analyses were repeated using a 20-year time horizon and the patterns were consistent, with all transplantation options resulting in cost-effectiveness ratios less than a willingness-to-pay threshold of $100 000 per QALY (Table S2).

4 | DISCUSSION

Kidney transplantation is widely cited as a unique example of a medical therapy that is both cost-saving and life extending. Our study demonstrates a more complex relationship between cost and outcomes by using DES analysis. LDKT is cost-saving, as recipients of these transplants live longer and incur fewer costs. Low-KPDI DDKT is cost equivalent; however, it is highly cost-effective as patient survival is improved by 50%. High-KDPI DDKT and immunologically complex LDKT are slightly more expensive than dialysis. However, the survival advantage of kidney transplantation over dialysis is so substantial that all options including ILDKT are cost-effective, as expenditures per QALY are less than the current willingness to pay threshold of $100 000 per QALY.[20]

The economic and clinical benefits of LDKT have been demonstrated in multiple studies in the United States and abroad. The survival benefit of LDKT, both compatible and incompatible, is well established.[12,21] In 2003, Schnitzler and Matas estimated that compared with maintenance dialysis, LDKT was associated with a cost-savings of $94 579 and added 3.5 QALYs over 20 years.[4] This estimate assumed a cost per transplantation of only $44 201 (including the cost of hospitalization and organ acquisition). This is far less that the average cost of $106 636 for a compatible LDKT reported by transplant centers in a contemporary study.[14] More recently, Held and colleagues suggested that the value of a donated living donor kidney was up to $1.45 million. The authors included an estimate of $200 000 per QALY lost due to premature mortality

TABLE 2 Economic data

Costs	Distribution	Mean	SD	Reference
ABOi LDKT	Normal	$130 000	$10 000	(10)
Compatible LDKT	Normal	$94 000	$10 000	(14)
Death after transplantation	Normal	$64 494	$10 000	(30)
Death on the waiting list	Normal	$64 494	$10 000	(30)
Death with function	Normal	$24 228	$5000	(30)
Graft failure	Normal	$94 508	$9000	(30)
ILDKT	Normal	$150 000	$10 000	(11)
KDPI ≤85 DDKT	Normal	$92 575	$10 000	(14)
KDPI >85 DDKT	Normal	$98 589	$10 000	(14)
PHS increased risk DDKT	Normal	$98 286	$10 000	(14), (32)
ABOi LDKT posttransplantation per month	Normal	$2156	$220	(30)
Dialysis per month	Normal	$3639	$300	(30)
HLA 0-3 mismatch LDKT posttransplantation per month	Normal	$1334	$130	(30)
HLA 4-6 mismatch LDKT posttransplantation per month	Normal	$1345	$130	(30)
ILDKT posttransplantation per month	Normal	$2809	$300	(30)
KDPI ≤85 DDKT posttransplantation per month	Normal	$1691	$180	(30)
KDPI >85 DDKT posttransplantation per month	Normal	$2019	$200	(30)
PHS increased risk DDKT posttransplantation per month	Normal	$1795	$200	(30)

ABOi, ABO-incompatible; DDKT, deceased donor kidney transplantation; ILDKT, incompatible living donor kidney transplantation; KDPI, Kidney Donor Profile Index; PHS, US Public Health Service.

as well as estimated economic value of return to work after transplantation, despite data suggesting that few patients actually return to employment after kidney transplantation.[22] Our current analysis suggests that although the absolute economic benefit is less than estimated in some studies, compatible LDKT is indeed the dominant strategy for patients with advanced kidney disease. ABOi transplantation, while more expensive, is cost-effective and should be strongly considered as an option for appropriate candidates. Currently, ILDKT offers substantial survival benefits, with a cost per QALY that is higher than dialysis but remains below $100 000 per QALY.

The clinical benefit of deceased donor transplantation was demonstrated initially by Wolfe and colleagues and confirmed in multiple subsequent studies.[2] However, at the time of the landmark study, donor selection was conservative, waiting times were shorter, and recipients were generally younger than in contemporary practices. The use of older, higher-risk, deceased donors has clear benefits in appropriate populations. Merion et al. demonstrated a benefit of expanded criteria donor kidneys for patients with diabetes, extended waiting times, and older age.[23] Massie and colleagues reported similar results using the newer KDPI scoring system.[6] While they are beneficial, the economic impact of these organs on patients and payers has not been well studied. Englesbe reported that expanded criteria donor kidneys were associated with net financial loss for the transplant program.[8] Similarly, we previously reported that higher-risk deceased donor organs were associated with higher costs and that Medicare payments did not compensate for these expenditures.[14] The higher costs were due to longer length of stay, higher rates of delayed graft function, and greater pharmaceutical costs. This cost differential may be contributing to rising discard rates for high-risk donor organs.[24-26]

These data confirm an economic benefit for DDKT. Low-KDPI organs were demonstrated to yield a significantly lower cost per QALY than maintenance dialysis. Total costs over 10 years were nearly equivalent; however, median survival at 10 years was estimated to be 30% higher after DDKT and quality of life is improved after transplantation. Thus, kidney transplantation results in a more favorable cost per year of survival ratio and a cost per QALY well below the $100 000 threshold. High-KDPI DDKT remained cost-effective, despite higher costs resulting from increased incidence of primary nonfunction, initial transplantation cost, and rate of return to dialysis.

While it is widely believed that kidney transplantation is cost-saving compared with dialysis, these data reflect transplantation in an era of restrictive donor and recipient selection.[27] Wong et al. recently reported a contemporary evaluation of the benefits of listing for

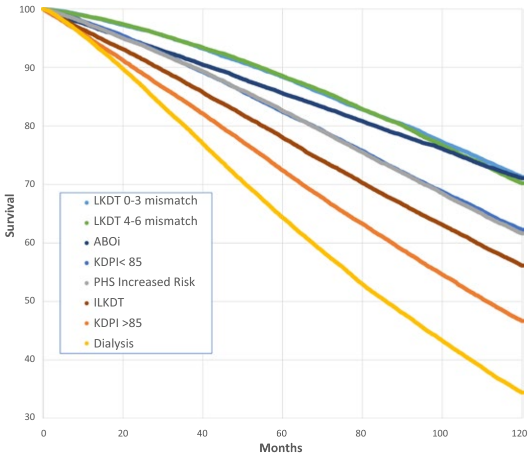

FIGURE 3 Kaplan–Meier survival estimates for posttransplantation survival by donor type [Color figure can be viewed at wileyonlinelibrary.com]

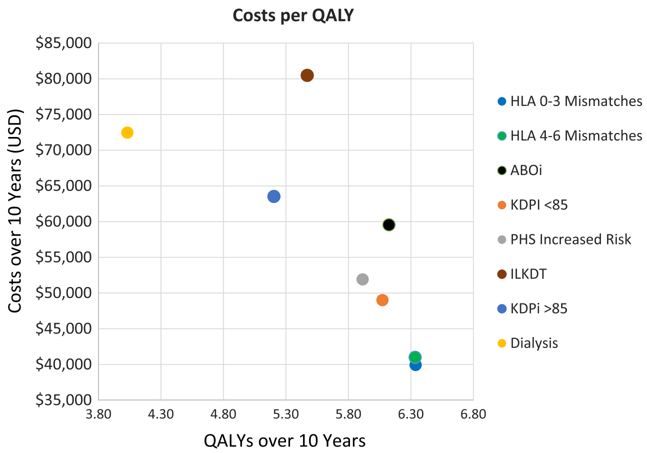

FIGURE 4 Mean cost and effectiveness kidney transplant of various donor characteristics over 10 years [Color figure can be viewed at wileyonlinelibrary.com]

TABLE 3 Survival, cost, and cost-effectiveness results for discrete event simulation analysis of kidney transplantation

	KDPI ≤85 DDKT	KDPI >85 DDKT	PHS increased risk DDKT	Dialysis	HLA 0-3 mismatch LDKT	HLA 4-6 mismatch LDKT	ABOi LDKT	ILDKT
Cost over 10 y								
Mean	$292 286	$330 576	$307 052	$292 117	$253 119	$259 771	$364 755	$440 234
10%	$220 641	$211 611	$231 365	$131 037	$196 129	$200 125	$288 000	$289 993
Median	$273 835	$314 843	$290 808	$324 534	$234 935	$238 051	$356 059	$445 569
90%	$407 856	$476 886	$420 533	$407 548	$354 417	$366 870	$480 380	$569 605
Average QALY over 10 years								
Mean	6.07	5.20	5.91	4.03	6.34	6.33	6.12	5.47
10%	2.68	1.49	2.41	1.10	3.40	3.44	2.59	1.76
Median	6.95	6.15	6.91	4.45	7.07	7.06	7.05	6.53
90%	7.56	7.47	7.57	6.16	7.59	7.60	7.59	7.52
Cost per QALY over 10 years								
Mean	$49 017	$63 531	$51 922	$72 476	$39 939	$41 016	$59 564	$80 486
Median	$39 437	$51 206	$42 103	$72 926	$33 226	$33 704	$50 534	$68 219

ABOi, ABO-incompatible; ILDKT, incompatible living donor kidney transplantation; KPDI, Kidney Donor Profile Index; PHS, US Public Health Service; QALY, quality-adjusted life-year.

kidney transplantation in higher-risk populations in Australia. Except for transplantation in a 25-year-old without comorbid conditions, all renal transplantation options were associated with incremental cost compared with maintenance dialysis, albeit with demonstrable improvement in life expectancy. For example, the additional cost of listing and transplantation for a 60-year-old man with cardiovascular disease was $30 359 and incremental life expectancy was only 0.88 year, resulting in an incremental cost per life-year of $34 489. In this study, only ILDKT and deceased donor transplantation with low-KDPI kidneys were at least cost equivalent at 10 years. In the current era of decreasing reimbursement for dialysis, increasing cost of transplantation, and growing donor complexity, it is likely that the economic benefits of kidney transplantation will be more limited.

These data demonstrate the benefit of increased overall rates of transplantation, which can best be achieved by increasing living donation and reducing deceased donor discard rates. Clearly, the economic benefits of LDKT would justify an economic incentive for living donation, should there be an ethically acceptable vehicle for this to be delivered. Similarly, efforts to increase the use of high-KDPI kidneys appear warranted as they appear to be both clinically and economically beneficial. Despite this observation, the discard rate of deceased donor kidneys has increased recently from 12.9% to 15.7%.[24] Factors associated with higher rates of discard include age, biopsy, donation after cardiac death, serology results (eg, hepatitis C virus infection), blood group, and terminal creatinine. Pulsatile perfusion was demonstrated to reduce discard rates. These factors also correlated with a higher cost of transplantation due to increased risk of delayed graft function, need for expensive immunosuppressive agents, and longer hospital stays.[8,14] For example, prior assessment of the medical center's cost of kidney transplantation is increased with organs from donors with diabetes ($3370) or hypertension ($665) and, markedly, with donation after cardiac death ($6182), while there is no corresponding increase in payments for use of these organs.[14] However, the current analysis suggests that despite this early expense, which is borne by the transplant program, patients and the health system benefit from these transplantations economically. Therefore, potential strategies to reduce organ discard include increasing reimbursement to transplant programs that use these organs or reducing the cost of acquiring the organs through differential pricing based on organ quality. Additional action is needed in the United States to overcome physicians' concerns that using these organs will result in adverse regulatory action based on poor outcomes, improve patient education, and reduce logistical complexity resulting from the new US kidney allocation system.[26,28]

Our study has several potential limitations. First, the economic data are drawn from 2 sources: Medicare payments and hospital cost-accounting data. We combined these data as Medicare payments provide reliable estimates of the cost of pretransplantation and post-transplantation care. The cost of the transplantation procedure itself, however, is poorly reflected in standard Medicare payments.[14] This is due to the nature of the DRG payment system, which is not adjusted for donor or recipient characteristics and the large payment that is received via the Medicare cost report. Thus, the true "cost" of the procedure is better captured using inpatient cost-accounting data, which include both medical care and organ acquisition costs, as per previous methods.[14] Second, the survival data are based on average survival among patients who received organs of differential quality. These survival data were not directly adjusted for patient characteristics, as organs are used in the most clinically acceptable recipient (eg, older patients receive high-KDPI organs). However, we use survival estimates from actual recipients of the organs who are most likely to benefit, including older patients and those with diabetes. Third, we assume a 10-year time horizon despite longer expected survival for many recipients. However, this time frame was chosen to provide clinically and economically relevant assessments in light of current outcome data, which are difficult to predict beyond 10 years.[29] We provide additional data in the supplemental digital content on 20-year outcomes, which are generally similar. Fourth, we did not consider repeat transplantation as an option here, although these patients could be assumed to derive less benefit than patients receiving initial transplantations given higher costs and shorter half-lives.

In conclusion, kidney transplantation remains the most cost-effective therapy for patients with advanced kidney failure. LDKT is clearly cost-saving and efforts should be directed toward interventions that increase willingness to donate though education and, potentially, economic incentives. Deceased donor transplantation using high-KDPI organs is cost-effective over the lifetime of the organ, emphasizing the need to develop strategies to reduce economic disincentives to use of these organs. Finally, use of desensitization for patients with willing but HLA-incompatible living donors appears clinically reasonable and economically feasible should kidney paired donation not be possible.

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DISCLOSURE

The authors of this manuscript have no conflicts of interest to disclose as described by the *American Journal of Transplantation*.

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REFERENCES

1. Wolfe RA, McCullough KP, Leichtman AB. Predictability of survival models for waiting list and transplant patients: calculating LYFT. *Am J Transplant*. 2009;9(7):1523-1527.
2. 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):1725-1730.
3. Whiting JF, Woodward RS, Zavala EY, et al. Economic cost of expanded criteria donors in cadaveric renal transplantation: analysis of Medicare payments. *Transplantation*. 2000;70(5):755-760.
4. Matas AJ, Schnitzler M. Payment for living donor (vendor) kidneys: a cost-effectiveness analysis. *Am J Transplant*. 2004;4(2):216-221.
5. Held PJ, McCormick F, Ojo A, Roberts JP. A cost-benefit analysis of government compensation of kidney donors. *Am J Transplant*. 2015;16:877-885.
6. Massie AB, Luo X, Chow EK, Alejo JL, Desai NM, Segev DL. Survival benefit of primary deceased donor transplantation with high-KDPI kidneys. *Am J Transplant*. 2014;14(10):2310-2316.
7. Rao PS, Schaubel DE, Guidinger MK, et al. A comprehensive risk quantification score for deceased donor kidneys: the kidney donor risk index. *Transplantation*. 2009;88(2):231-236.
8. Englesbe MJ, Ads Y, Cohn JA, et al. The effects of donor and recipient practices on transplant center finances. *Am J Transplant*. 2008;8(3):586-592.
9. Chow EK, Massie AB, Muzaale AD, et al. Identifying appropriate recipients for CDC infectious risk donor kidneys. *Am J Transplant*. 2013;13(5):1227-1234.

10. Axelrod D, Segev DL, Xiao H, et al. Economic impacts of ABO-incompatible live donor kidney transplantation: a national study of Medicare-insured recipients. *Am J Transplant*. 2016;16(5):1465-1473.
11. Axelrod D, Lentine KL, Schnitzler MA, et al. The incremental cost of incompatible living donor kidney transplantation: a national cohort analysis. *Am J Transplant*. 2017;17:3123-3130.
12. Orandi BJ, Luo X, Massie AB, et al. Survival benefit with kidney transplants from HLA-incompatible live donors. *N Engl J Med*. 2016;374(10):940-950.
13. 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.
14. Axelrod DA, Schnitzler MA, Xiao H, et al. The changing financial landscape of renal transplant practice: a national cohort analysis. *Am J Transplant*. 2017;17(2):377-389.
15. Ison MG. Nucleic acid testing of organ donors: is the glass half empty or half full? *Am J Transplant*. 2015;15(7):1743-1745.
16. Smith-Palmer J, Cerri K, Valentine W. Achieving sustained virologic response in hepatitis C: a systematic review of the clinical, economic and quality of life benefits. *BMC Infect Dis*. 2015;15:19.
17. Salleh S, Thokala P, Brennan A, Hughes R, Dixon S. Discrete event simulation-based resource modelling in health technology assessment. *Pharmacoeconomics*. 2017;35:989-1006.
18. Rejeb O, Pilet C, Hamana S, et al. Performance and cost evaluation of health information systems using micro-costing and discrete-event simulation [published online ahead of print 2017]. *Health Care Manag Sci*. https://doi.org/10.1007/s10729-017-9402-x
19. Desai VC, Ferrand Y, Cavanaugh TM, et al. Comparative effectiveness of tacrolimus-based steroid sparing versus steroid maintenance regimens in kidney transplantation: results from discrete event simulation. *Med Decis Making*. 2017;37:827-843.
20. Neumann PJ, Cohen JT, Weinstein MC. Updating cost-effectiveness – the curious resilience of the $50 000-per-QALY threshold. *N Engl J Med*. 2014;371(9):796-797.
21. Abecassis M, Bartlett ST, Collins AJ, et al. Kidney transplantation as primary therapy for end-stage renal disease: a National Kidney Foundation/Kidney Disease Outcomes Quality Initiative (NKF/KDOQITM) conference. *Clin J Am Soc Nephrol*. 2008;3(2):471-480.
22. Tzvetanov I, D'Amico G, Walczak D, et al. High rate of unemployment after kidney transplantation: analysis of the United Network for Organ Sharing database. *Transpl Proc*. 2014;46(5):1290-1294.
23. Merion RM, Ashby VB, Wolfe RA, et al. Deceased-donor characteristics and the survival benefit of kidney transplantation. *JAMA* 2005;294(21):2726-2733.
24. Wey A, Salkowski N, Kasiske BL, Israni AK, Snyder JJ. Influence of kidney offer acceptance behavior on metrics of allocation efficiency. *Clin Transplant*. 2017;31(9):e13057.
25. Hart A, Smith JM, Skeans MA, et al. OPTN/SRTR 2015 annual data report: kidney. *Am J Transplant*. 2017;17(Suppl 1):21-116.
26. Hart A, Gustafson SK, Skeans MA, et al. OPTN/SRTR 2015 annual data report: early effects of the new kidney allocation system. *Am J Transplant*. 2017;17(Suppl 1):543-564.
27. Karlberg I, Nyberg G. Cost-effectiveness studies of renal transplantation. *Int J Technol Assess Health Care*. 1995;11(3):611-622.
28. Schold JD, Arrington CJ, Levine G. Significant alterations in reported clinical practice associated with increased oversight of organ transplant center performance. *Prog Transplant*. 2010;20(3):279-287.
29. Benbassat J, Baumal R. The time horizons of formal decision analyses. *QJM*. 2007;100(6):383-388.
30. United States Renal Data System. 2015 USRDS annual data report: epidemiology of kidney disease in the United States. Bethesda, MD: National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases; 2015. https://www.usrds.org/2015/view/. Accessed March 14, 2018.
31. Orandi BJ, Garonzik-Wang JM, Massie AB, et al. Quantifying the risk of incompatible kidney transplantation: a multicenter study. *Am J Transplant*. 2014;14(7):1573-1580.
32. Ison MG, Grossi P, AST Infectious Diseases Community of Practice. Donor-derived infections in solid organ transplantation. *Am J Transplant*. 2013;13(Suppl 4):22-30.

SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

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