

Research

Original Investigation

Age-Related Kidney Transplant Outcomes Health Disparities Amplified in Adolescence

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IMPORTANCE The transition from pediatric to adult health care is a vulnerable time for patients with chronic conditions. We need to better understand the factors affecting the health of kidney transplant recipients during this transition.

OBJECTIVE To determine the age at which renal transplant recipients are at greatest risk for graft loss.

DESIGN, SETTING, AND PARTICIPANTS We performed a retrospective analysis of 168 809 first kidney-only transplant events from October 1987 through October 2010, in recipients up to age 55 years as reported by the Organ Procurement Transplantation Network Standard Transplant Analysis and Research Database. Recipient age at transplant was the primary predictor studied. Confounder and effect modifier covariates were identified and studied using Cox proportional hazard models.

EXPOSURE Kidney-only transplant.

MAIN OUTCOMES AND MEASURES Patient and renal graft survival, along with death-censored and non-death-censored information.

RESULTS A total of 168 809 renal transplant events met the inclusion criteria. Recipients who received their first kidney transplant at age 14 to 16 years were at the highest risk of graft loss, with inferior outcomes starting at 1 and amplifying at 3, 5, and 10 years after transplant. Black adolescents were at disproportionately high risk of graft failure. The variables that had significant interaction with recipient age were donor type (deceased vs living) and insurance type (government vs private). Among 14-year-old recipients, the risk of death was 175% greater in the deceased donor-government insurance group vs the living donor-private insurance group (hazard ratio, 0.92 [95% CI, 0.90-0.94] vs 0.34 [95% CI, 0.33-0.36]), whereas patient survival rates in the living donor-government insurance and deceased donor-private insurance groups were nearly identical (hazard ratio, 0.61 [95% CI, 0.58-0.63] vs 0.54 [95% CI, 0.51-0.56]).

CONCLUSIONS AND RELEVANCE Recipients aged 14 to 16 years have the greatest risk of kidney allograft failure. Black adolescents and those with government insurance are at even higher risk. Private insurance reduces risk of death across all ages. Comprehensive programs are needed for adolescents, especially for those at greater risk, to reduce graft loss during the transition from adolescence to adulthood.

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Renal failure is the most common end-stage organ disease in children and adolescents. With advances in medical and surgical care, the 10-year survival for adolescent-onset end-stage renal disease is 80%.¹ Investigators have reported that compared with younger recipients, adolescents have better graft survival at 1 year but have greater graft losses within a decade of transplant. Graft losses by adolescents are partly due to physiologic and/or immunologic alterations with age, but psychological and sociological factors play a large role, especially in affecting adherence to medication.²⁻⁴ These challenges intensify as adolescents transfer to adult-centered medical care.⁵

The existing literature does not adequately describe the risks of graft failure among renal transplant recipients by age at the time of transplant. Studies have used various arbitrary age groupings with differing results.^{6,7} For example, the Organ Procurement and Transplantation Network (OPTN) data, as evaluated in the Scientific Registry for Transplant Recipients (SRTR) Annual Report, stratifies graft and patient survival outcomes by the following age range categories: less than 1, 1 to 5, 6 to 11, 12 to 17, 18 to 34, 35 to 49, 50 to 64, and older than 65 years.⁸ Thus, the average outcomes within the large age spans of these groups, especially in the pediatric recipients, may be concealing important information that could define particularly high-risk populations. We used this OPTN database to define relative risks of graft and patient survival by age at transplant, adjusted for recipient and donor characteristics.

Methods

Study Population

The OPTN-SRTR contains data on the kidney transplant recipient and donor information from all living and deceased donors in the United States. We investigated all recipients who were not older than 55 years of age, with no transplant history, who received a primary renal graft from a living or standard criteria deceased donor during the period October 1987 through October 2010. Race was indicated by self-report. Recipients were excluded if the transplant date was missing or if they had received organs labeled as coming from donation after cardiac death and extended criteria donors, hepatitis C-positive donors, or non-US citizen donors.

A total of 168 809 renal transplant events met the inclusion criteria for analysis (eFigure 1 in Supplement). Time-to-event analysis was conducted for death-censored and non-death-censored graft failure and for patient death. Graft survival was estimated for both death-censored and non-death-censored graft failure. Patients who died with a functioning graft were considered a graft loss in the latter group. Death-censored results favor outcomes in older recipients, who tend to die with a functioning graft, compared with non-death-censored outcomes, which favor younger recipients because of the larger number of deaths in the older group. The study was approved by the University of Florida institutional review board.

Statistical Analysis

Categorical data are reported as frequencies and percentages, and continuous variables are reported with mean and

standard deviation. The primary analyses consisted of an adjusted Cox proportional hazard regression for all 3 end points (death-censored and non-death-censored graft failure and patient death). All variables in the data set with plausible effect on outcome were evaluated. Continuous variables entered into the model were checked to determine whether they were linear in the log-hazard, using the methods of fractional polynomials. The proportional hazard assumption was tested in the final model by determining whether the graph of the scaled Schoenfeld residuals over event time was horizontal. Age at transplant was entered into the model as a quartic expression (ie, age, age², age³, age⁴) because we expect that the outcomes when graphed over age at transplant would have 3 changes in concavity. Age at transplant for the relative hazard graphs was centered at 18 years. Graft half-life and median graft survival were estimated from the Cox proportional hazard regression model. The final curves of graft half-life were smoothed using fractional polynomials. The 95% confidence intervals were omitted from the figures because they only thicken the graphed line as a result of large sample size.

Because the study's goal was to identify the role of age at transplant in graft and/or patient survival, we used a risk factor modeling approach to determine which covariates to add to the Cox proportional hazard regression model. We included only those covariates that acted either as a confounder or as an effect modifier. A confounder was identified when its addition to the model changed the hazard ratio (HR) associated with the age at transplant by more than 10% in either direction. A covariate that had a statistically significant interaction ($P < .05$) with age at transplant was considered an effect modifier. The figures across age at transplant are produced from the adjusted Cox proportional hazard models, where the covariates held at either their median (if a continuous variable) or at their most prevalent level (if a categorical variable). Analyses were run using Stata, version 11.2 (StataCorp).

Results

The study population characteristics depicted in the **Table** include the recipients' sex, race, and insurance type and the donors' living vs deceased status, sex, and health, and their combined HLA match information. Of the 168 809 first kidney transplants evaluated, there were 46 854 graft failures prior to patient death (27.8%) and 17 826 deaths with a functioning graft (10.6%), for a total of 46 854 death-censored graft failures and 64 680 non-death-censored graft failures. During the follow-up period, 15.2% of the recipients died, and 69.3% had a functioning graft at the time of death. The Kaplan-Meier median patient survival time was 21.2 years. More patients received transplants toward the later years of the study period; therefore, the median (mean) follow-up time was 5.0 (6.0) years.

Two variables had significant interaction with age at transplant: donor type (living vs deceased donor) and the recipient's insurance type at the time of transplant (private vs government). From these 2 variables, it is possible to construct 4 unique groups. The proportional distribution of the 4 groups in the sample is as follows: living donor-government insur-

Table. Recipient and Donor Characteristics

Characteristics and Events	Summary Statistics (n = 168 809)
Recipients	
Male sex, No. (%)	100 031 (59.3)
Age at transplant, mean (SD), y	37.7 (12.6)
Race, No. (%)	
White	95 433 (56.5)
Black	40 363 (23.9)
Hispanic	22 758 (13.5)
Other	10 255 (6.1)
Insurance at transplant, No. (%)	
Government	111 047 (65.8)
Private	57 762 (34.2)
Diabetes mellitus, No. (%)	26 240 (15.5)
Hypertension, No. (%)	88 032 (52.1)
PRA at transplant, median (IQR)	
Current	0.0 (0.0-2.0)
Peak	1.0 (0.0-8.0)
Non-death-censored events (graft failure or death), No. (%)	64 680 (38.2)
Graft survival, median (95% CI), y	10.6 (10.5-10.7)
Deaths, No. (%)	25 714 (15.2)
Survival, median (95% CI), y	21.2 (21.0-21.8)
Death with a functioning graft, No. (%)	17 826 (10.6)
Death-censored events (graft failure prior to death), No. (%)	46 854 (27.8)
Graft survival, median (95% CI), y	13.6 (13.5-13.8)
Donors	
Male sex, No. (%)	90 632 (53.7)
Type, No. (%)	
Living	72 731 (43.1)
Deceased	96 078 (56.9)
Diabetes mellitus, No. (%)	2104 (1.2)
Age, mean (SD), y	34.4 (14.0)
Serum creatinine level, median (IQR)	0.9 (0.7-1.1)
Hypertension, No. (%)	8784 (5.2)
Recipient and donor HLA information	
HLA mismatch level ^a	
0	17 533 (10.5)
1	8838 (5.3)
2	21 369 (12.8)
3	37 859 (22.7)
4	33 175 (19.9)
5	32 277 (19.4)
6	15 717 (9.4)

Abbreviations: IQR, interquartile range; PRA, panel reactive antibody.

^a HLA mismatch level ranges from 0 (6-antigen match) to 6 (complete mismatch). Mismatch level data were missing for 2041 patients (n = 168 809).

ance, 21.0%; living donor-private insurance, 22.1%; deceased donor-government insurance, 44.8%; and deceased donor-private insurance, 12.1%. See eFigure 2 in the Supplement for a complete list of variables. Unless otherwise specified, the “recipient age at transplant” graphs were produced using the following covariate pattern: recipient’s race was white, recipi-

ent’s sex was male, recipient’s and donor’s histories were negative for diabetes mellitus and hypertension, HLA mismatch level was 3, and donor age was 36 years.

Graft Survival Confounders and Effect Modifiers

In the Supplement, eTables 1A and 1B illustrate our 4 effect modifiers in the Cox proportional hazard model, as well as the other potential confounder variables (recipient and donor characteristics) that were candidates for the regression model. Because donor and insurance type significantly interact with age, the HRs for the 4 groups created by these 2 variables are different for each age and are presented graphically (Figure 1). Age was a strong predictor of death-censored and non-death-censored graft failure for all 4 groups. Being a black recipient conveyed the greatest risk of graft failure (HR, 1.72 death censored [95% CI, 1.68-1.75]; HR, 1.43 non-death censored [95% CI, 1.41-1.45] vs white recipients; both $P < .001$). Diabetes mellitus in the recipient was associated with the next highest risk for non-death-censored graft failure, with donor diabetes mellitus hastening both death-censored and non-death-censored graft failure.

The degree of HLA mismatch resulted in increased risk of graft failure in both death-censored and non-death-censored models (HR, 1.08 [95% CI, 1.07-1.08] and HR, 1.05 [95% CI, 1.05-1.06], respectively; both $P < .001$) per unit increase in the degree of mismatch (eFigure 3 in Supplement). Increasing age of the donor predicted increased risk of graft loss in the death-censored and non-death-censored models. Donor hypertension was associated with increased graft failure in the death-censored model (HR, 1.05 [95% CI, 1.01-1.09]; $P < .001$).

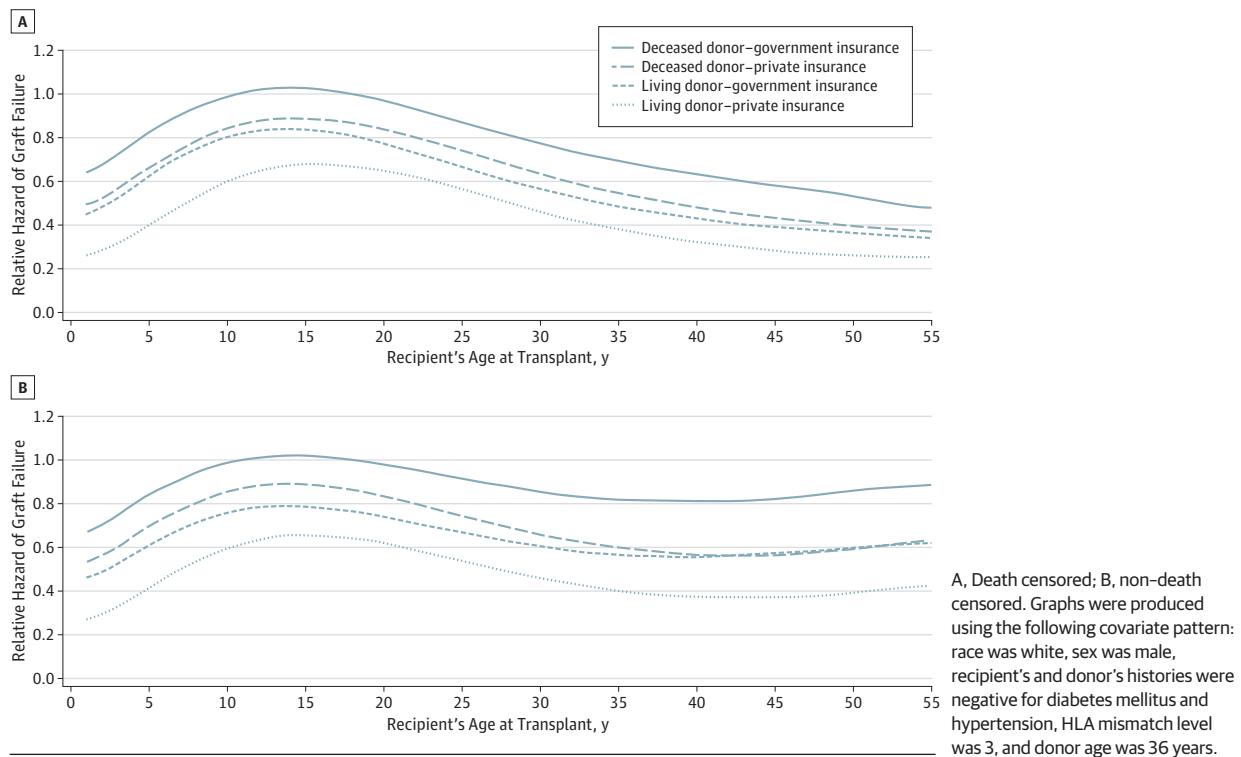
Using age at transplant as the risk factor, we determined a decreasing relative hazard of graft failure, finding the highest risk in the deceased donor-government insurance group, second highest risk in the deceased donor-private insurance group, third in the living donor-government insurance group, and the lowest risk in the living donor-private insurance group. In the death-censored analysis, this order was consistent from infancy to age 55 years. In the non-death-censored analysis, the deceased donor-private insurance group and the living donor-government insurance groups merged at approximately age 40 through 55 years.

Patient Survival Confounders

In the Supplement, eTable 1C illustrates the Cox proportional hazard model of time to patient death. There were no effect modifiers of age, and thus the HR of each confounder is independent of age. Age of the recipient at transplant was strongly predictive of death in the quartic expression. Using deceased donor-government insurance as the reference group, all other groups had improved patient survival, with living donor-government insurance second worst (HR, 0.66 [95% CI, 0.64-0.68]; $P < .001$), deceased donor-private insurance next (HR, 0.63 [95% CI, 0.62-0.66]; $P < .001$), and living donor-private insurance best (HR, 0.42 [95% CI, 0.40-0.43]; $P < .001$). The risk for patient death in the deceased donor-government insurance group increased greatly above the other groups as recipient age exceeded 25 years.

With white race as reference, black recipients had lower rates of posttransplant survival (HR, 1.06 [95% CI, 1.04-1.09];

Figure 1. Graft Failure Relative Hazard According to Age at Transplant, Centered at 18 Years



$P < .001$), whereas recipients of Hispanic and other races had greater survival than white recipients (HR, 0.72 [95% CI, 0.69-0.74] and HR, 0.72 [95% CI, 0.68-0.75]; $P < .001$ for each). Recipient characteristics associated with lower survival included male sex (HR, 1.11 [95% CI, 1.09-1.13]), having diabetes mellitus (HR, 1.69 [95% CI, 1.65-1.73]), increasing HLA mismatch (HR, 1.03 for 1 unit increase [95% CI, 1.02-1.04]), and age of donor (HR, 1.01 for 1 year increase [95% CI, 1.00-1.01]) (all $P < .001$). Recipient hypertension (HR, 0.85 [95% CI, 0.83-0.86]) and donor hypertension (HR, 0.94 [95% CI, 0.90-0.98]) each correlated with lower recipient risk of death.

Graft and Patient Survival by Recipient Age at Transplant

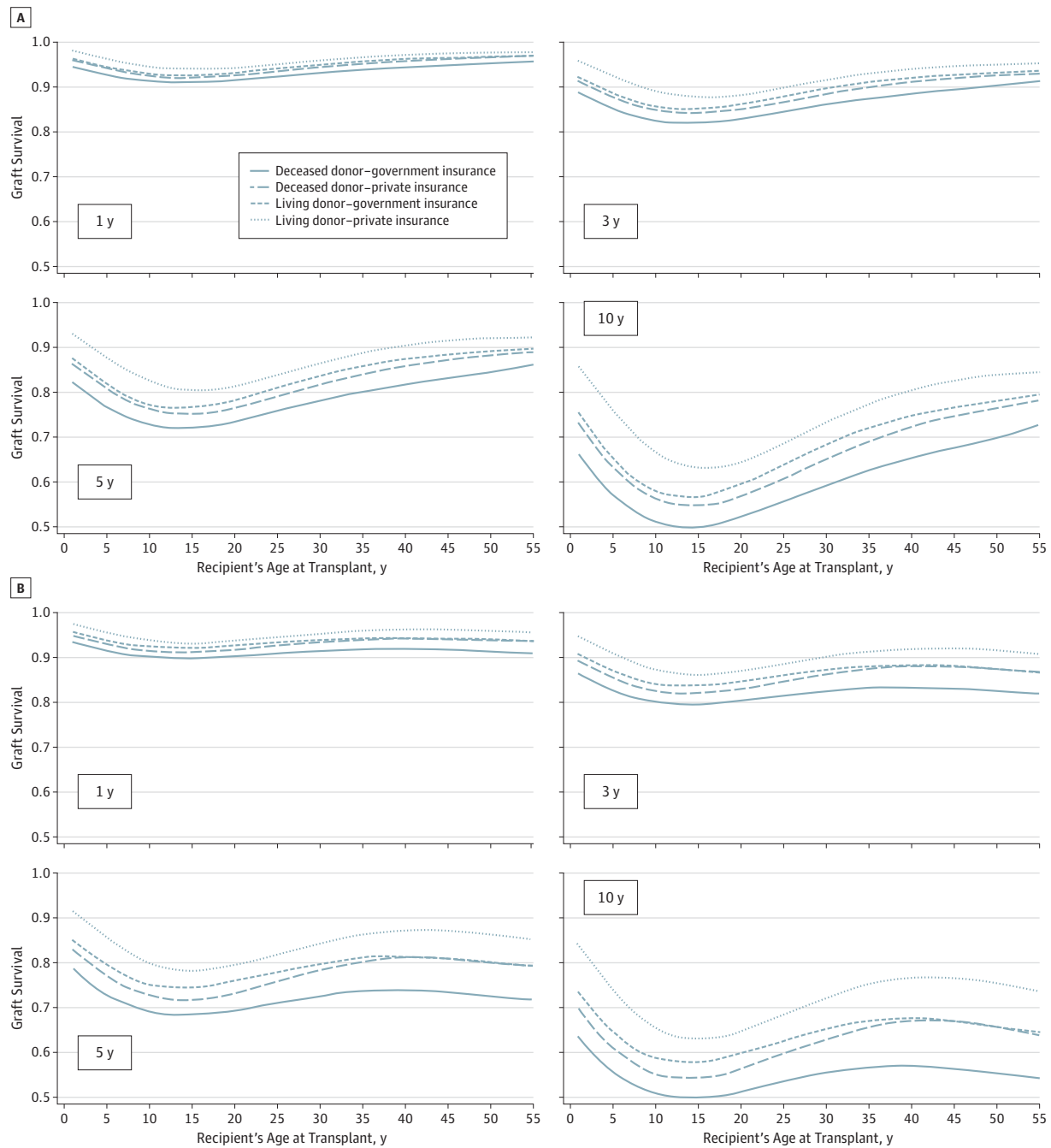
Adolescent recipients aged 14 to 16 years had the highest risk of any age group of graft loss (death censored and non-death censored) starting at 1 year after transplant, and amplifying at 3, 5, and 10 years after transplant (Figure 2). This is despite having the best patient survival (Figure 3). Black adolescents are at a disproportionate risk of graft failure at these time points compared with nonblack adolescents (Figure 4). Black adolescents 14 to 16 years of age had lower rates of graft survival in their highest performing group, living donor-private insurance (0.43 [reported as a proportion] death censored [95% CI, 0.36-0.49], 0.42 non-death censored [95% CI, 0.36-0.48]), than the lowest performing nonblack group, deceased donor-government insurance (0.49 death censored [95% CI, 0.42-0.55], 0.42 non-death censored [95% CI, 0.36-0.48]). The 10-year graft survival for 14-year-old nonblack recipients in the living donor-private insurance group (0.62 death censored [95% CI, 0.57-0.67], 0.58 non-death censored [95% CI, 0.52-0.64])

was more than twice that for black recipients the same age in the deceased donor-government insurance group (0.28 death censored [95% CI, 0.21-0.34], 0.26 non-death censored [95% CI, 0.21-0.32]; data not shown).

At 10 years after transplant, black recipients in the deceased donor-government insurance group who received a transplant when they were 10 years old displayed a 0.28 (95% CI, 0.21-0.34) death-censored graft survival rate and 0.26 (95% CI, 0.21-0.32) non-death-censored graft survival rate, compared with the nonblack recipients at 0.49 (95% CI, 0.42-0.55) and 0.42 (95% CI, 0.36-0.48), respectively. This difference was 75% and 65% between the racial groups. The same comparisons at recipient age 40 years had smaller differences of 39% and 19% between the racial groups.

Although living donor recipients had better rates of graft survival than deceased donor recipients within insurance groups, there were surprisingly similar outcomes between the living donor-government insurance and the deceased donor-private insurance groups. This can be most easily appreciated in Figure 1, which shows the overall HR of death-censored and non-death-censored graft failure. Graft loss in the living donor-private insurance adolescent group was approximately 50% lower than in the deceased donor-government insurance group over all transplant ages. Among 14-year-old recipients, the risk of death was 175% greater in the deceased donor-government insurance group vs the living donor-private insurance group (HR, 0.92 [95% CI, 0.90-0.94] vs 0.34 [95% CI, 0.33-0.36]), whereas the risk of death was similar between the living donor-government insurance and deceased donor-private insurance groups (HR, 0.61 [95% CI, 0.58-

Figure 2. Graft Survival According to Age at Transplant



Comparison of death-censored (A) and non-death-censored (B) graft survival across the 4 categories of recipients at 1, 3, 5, and 10 years after transplant. Death-censored analysis results favor graft outcomes in older recipients, who tend to die with a functioning graft, compared with non-death-censored outcomes, which favor younger recipients because of the larger number of

deaths in the older group. Graphs were produced using the following covariate pattern: race was white, sex was male, recipient's and donor's histories were negative for diabetes mellitus and hypertension, HLA mismatch level was 3, and donor age was 36 years.

0.63] vs 0.54 [95% CI, 0.51-0.56]) (Figure 3). Recipients with private insurance in all age groups had a lower relative hazard risk of death (for both living and deceased donors) compared with those with government insurance (Figure 3).

Graft Half-life

Figure 5 illustrates the graft half-life, in which the death-censored results show similar half-lives for the living donor-government insurance vs the deceased donor-private insur-

ance groups. For children between 5 and 10 years of age, these outcomes are nearly identical. Recipients in the living donor-private insurance group have approximately a 4-year increase in graft half-life compared with those in the living donor-government insurance group and more than 8 years greater than that of a 40-year-old recipient in the deceased donor-government insurance group. For the non-death-censored curve, the most noticeable difference is the merging of the living donor-government insurance and the deceased donor-private insurance curves at just over age 40 years.

Discussion

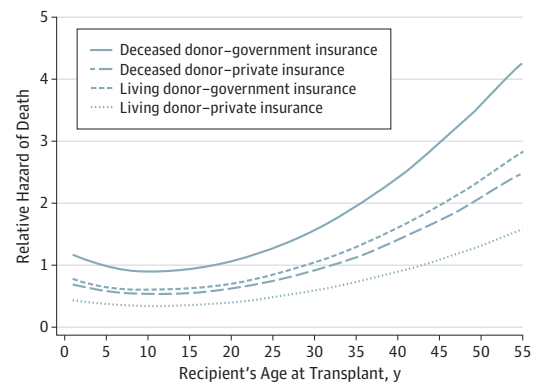
This study uses the OPTN database to determine longitudinal outcomes of recipients based on their age at transplant in 1-year increments. Adolescents between 14 and 16 years of age have worse longitudinal outcomes during a 10-year period than other age cohorts. The realization that this age group is at an increased risk of graft loss as they are becoming young adults should prompt providers to give specialized care and attention to these adolescents in the transition from pediatric to adult-focused care. Implementing a structured health care transition preparation program from pediatric to adult-centered care in transplant centers may improve outcomes.

Our study revealed better outcomes for recipients of transplants from living donors over those who received deceased donor grafts and private over government insurance coverage. However, patients with private insurance at the time of a deceased donor transplant did almost as well as those who received a graft from a living donor but had government insurance. Black adolescents had disproportionately worse outcomes compared with nonblack recipients across all donor and insurance groups. These outcomes may be related to immunological, cultural, educational, learning, and/or economic differences that translate into substantial effects on short-term and long-term graft and/or patient survival. Importantly, others have found that whereas dialysis survival for older black patients is superior to that for white patients, black patients younger than 50 years have a higher mortality than white patients when both dialysis survival and renal transplant outcomes are considered in a competing risk model.⁹

Foster et al¹⁰ performed a recent review of the OPTN database looking at recipients up to age 40 years. These investigators concentrated on the age at which recipients lost their renal grafts, with early failures excluded; they found the highest rate of graft loss in the 19-year-old recipients. They performed the age-at-transplant analysis in varying age groups: 0 to 4, 5 to 9, 10 to 12, 13 to 16, 17 to 20, 21 to 24, 25 to 29, 30 to 34, and 35 to 39 years. They did not present the age-at-transplant data as an overall risk of graft failure but examined graft failure rate per year after transplant by age groups; thus, we cannot easily compare their results to ours.

Levine et al⁷ used OPTN data and divided the recipients into age groups of 0 to 14, 15 to 18, 19 to 25, 26 to 40, 41 to 55, 56 to 70, and older than 70 years. These investigators showed that the adolescent recipients in the 15- to 18-year-old age group had the worst survival of allografts from “ideal deceased do-

Figure 3. Relative Hazard of Death According to Age at Transplant, Centered at 18 Years



Graphs were produced using the following covariate pattern: race was white, sex was male, recipient's and donor's histories were negative for diabetes mellitus and hypertension, HLA mismatch level was 3, and donor age was 36 years.

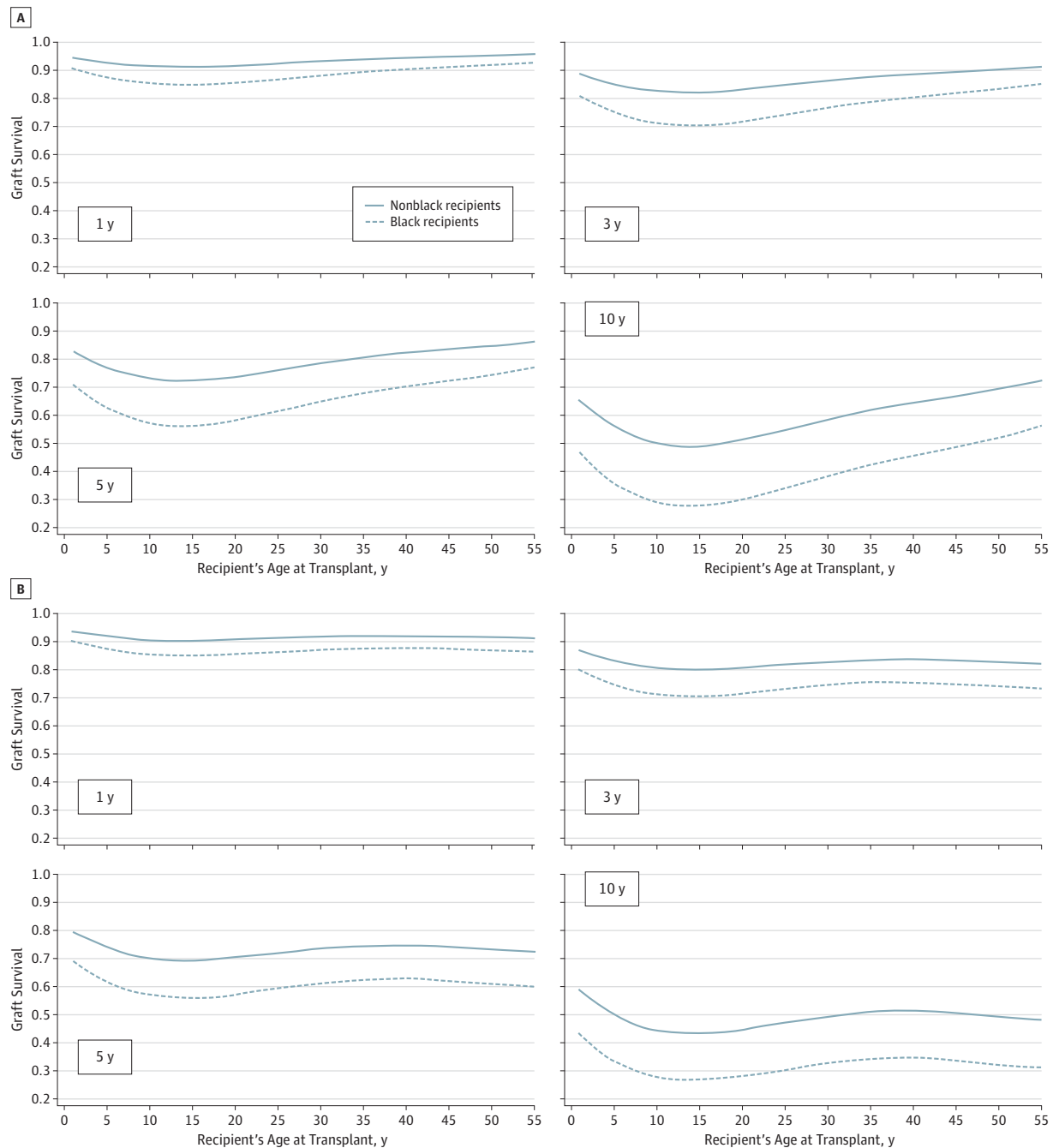
nors” (age <35 years, serum creatinine level <1.5 mg/dL [to convert to micromoles per liter, multiply by 88.4], and no hypertension, diabetes mellitus, or hepatitis C) compared with most age groups, except for those older than 70 years. Ekstrand et al¹¹ examined those who received a renal transplant before age 18 years but were now older than 18 years, a group they termed *transitional recipients*. These authors showed that transitional recipients had increased allograft failure compared with those who were younger than 18 years or those who received a transplant when they were older than 18 years. This difference was present 3 years after transplant (21% graft failure vs 18% in adults and 11% in children). Keith et al¹² also demonstrated that the 10- to 19-year-old age group in the United Network for Organ Sharing database had the worst long-term allograft survival, equivalent to those older than 60 years when all recipients were grouped by decade of life. In our study, year of transplant was neither an effect modifier nor a confounder of the relationship between age at transplant and graft failure or age at transplant and patient survival; therefore, the OPTN kidney allocation policy change to “Pediatric Share 35” in September 2005, in which organs from donors younger than 35 years are preferentially offered to pediatric recipients, did not change the relationships developed in the overall model.

Preparation for the health care transition from pediatric to adult-focused care is gaining interest as a target for improvement in health outcomes. The American Academy of Pediatrics states,^{13(p1304)}

The goal of transition in health care for young adults with special health care needs is to maximize lifelong functioning and potential through the provision of high-quality developmentally appropriate health care services that continue uninterrupted as the individual moves from adolescence to adulthood.

Despite published medical societies' consensus statements since 2002 stating the importance of facilitating health care transition preparation for youth with special health care needs, little improvement has been realized.¹³⁻¹⁵ The effects of the 2011

Figure 4. Graft Survival for a Recipient With a Deceased Donor and Government Insurance According to Age at Transplant



A, Death censored; B, non-death censored. Graphs were produced using the following covariate pattern: race was white, sex was male, recipient's and

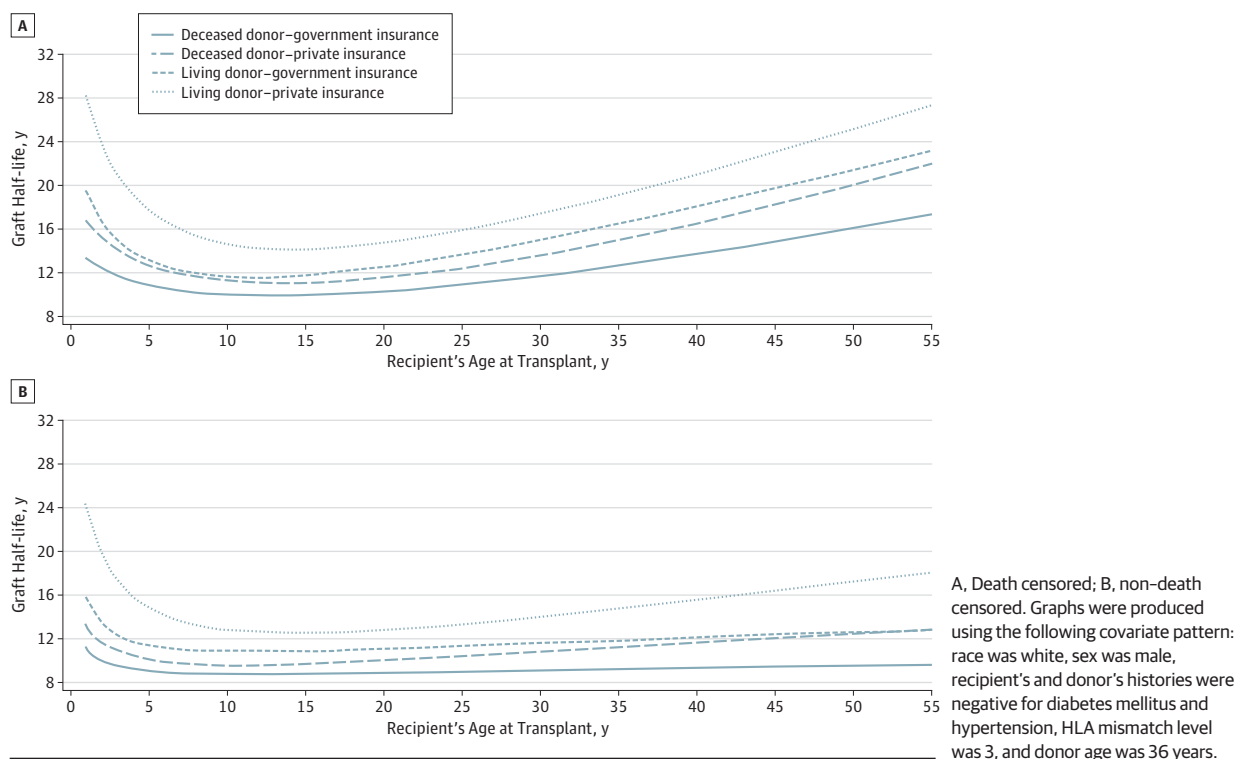
donor's histories were negative for diabetes mellitus and hypertension, HLA mismatch level was 3, and donor age was 36 years.

consensus statements by the International Society of Nephrology and International Pediatric Nephrology Association¹⁶ remain to be seen.

In transplantation, 18 years of age is usually the distinction between adolescence and adulthood. It has been suggested that those undergoing transplant before age 18 years are usually in a pediatric-oriented environment whereas those in their twenties begin in an environment where most patients

are significantly older. Certainly, maturation and complete brain development occur after the age of 18 years, and the concept of emerging adulthood suggests that in modern society, adulthood is often delayed until the late twenties. This is mirrored in our outcomes, in which 12-month mortality steadily decreases as patients age from 20 to 30 years. For this reason, there has been a movement by pediatric specialists including cardiologists,¹⁷ nephrologists,¹⁴ pulmonologists,¹⁸ and gas-

Figure 5. Graft Half-life (Median Survival) According to Age at Transplant



troenterologists and hepatologists^{19,20} to design organized and effective programs that allow patients to optimize transition from pediatric to adult-centered care in an effort to avoid the increased morbidity and mortality associated with young adulthood.

There is no current consensus on how to implement or measure this health care transition preparation or what successful outcomes of this process would be; however, some centers have published methods and are currently validating strategies to improve outcomes as patients with chronic kidney disease transition to adulthood.²¹ The transition process involves the patients, families, pediatric and adult-focused health care providers, and interdisciplinary collaboration. There is a growing literature in asthma, rheumatoid arthritis, and diabetes mellitus that notes that chronic care models that incorporate and promote disease self-management have improved outcomes compared with those lacking such self-management.²² The University of North Carolina STARx (Self-management and Transition to Adulthood With Treatment) Program has designed tools to measure transition and developed culturally appropriate and literacy-appropriate interventions, while determining self-management, adherence, and graft and patient survival, in collaboration with other institutions.²³

Our study clearly displays an increased risk of graft loss for recipients aged 14 to 16 years and a poor 10-year graft survival in this US cohort. This health care disparity is amplified among black adolescents, particularly among those with government insurance. In the United States, an estimated 4000 kidney transplant recipients and 2000 patients receiving di-

alysis are in this critical transition age range with health-related challenges that include not only medical but also cognitive, developmental, psychological, and socioeconomic factors. In this country, dialysis care is covered by Medicare for adults and minors with end-stage renal disease as long as the adult—or the parent of a minor patient—contributed to Medicare payroll tax for 40 work quarters, or the patient has reached 65 years of age or is disabled. Medicare coverage continues for up to 36 months after transplant in regard to immunosuppressive medications for patients younger than 65 years who are no longer considered disabled. The loss of Medicare coverage for immunosuppressive medications may play a role in the morbidity and mortality described, but the impact of this coverage loss was not available for our investigation. The living donor recipient advantage that we noted may be in part related to (1) pretransplant events such as the selection of better immunological matches from family members and the higher quality of the donor organ, (2) peritransplant events such as shorter ischemia times or optimal condition of the recipient at the time of surgery, and (3) posttransplant events such as better immunological tolerance and possibly stronger family support.

The timing of a patient's transfer to adult-focused care should be flexible and personalized on the basis of the readiness of the patient.²⁴ Preparation for health care transition may help offset some of the disparities demonstrated by the adolescent transplant recipients. Implementing health care transition preparation programs in both the pediatric and adult internal medicine settings could be a cost-effective solution to this urgent, unmet need.

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Study concept and design: All authors.

Analysis and interpretation of data: Phillips, Stewart, Ferris.

Drafting of the manuscript: All authors.

Critical revision of the manuscript for important intellectual content: K. A. Andreoni, R. M. Andreoni, Stewart, Ferris.

Statistical analysis: Forbes, Phillips, Ferris.

Administrative, technical, or material support: K. A. Andreoni, R. M. Andreoni.

Study supervision: K. A. Andreoni.

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