HHS Public Access

Author manuscript

Kidney Int. Author manuscript; available in PMC 2017 October 01.

Published in final edited form as:

Kidney Int. 2016 October ; 90(4): 878–887. doi:10.1016/j.kint.2016.06.029.

Twenty years of evolving trends in racial disparities for adult kidney transplant recipients

David J Taber, PharmD, MS[1,2], **Mulugeta Gebregziabher, PhD**[3], **Kelly J Hunt, PhD**[3], **Titte Srinivas, MD**[4], **Kenneth D Chavin, MD, PhD**[1], **Prabhakar K Baliga, MD**[1], and **Leonard E Egede, MD, MS**[5]

[1]Division of Transplant Surgery, College of Medicine, Medical University of South Carolina, Charleston, SC

[2]Department of Pharmacy Services, Ralph H Johnson VAMC, Charleston, SC

[3]Department of Public Health Sciences, College of Medicine, Medical University of South Carolina, Charleston, SC

[4]Division of Transplant Nephrology, College of Medicine, Medical University of South Carolina, Charleston, SC

[5]Veteran Affairs HSR&D Health Equity and Rural Outreach Innovation Center (HEROIC), Ralph H Johnson VAMC, Charleston, SC

Abstract

Disparities in outcomes for African-American (AA) kidney transplant recipients have persisted for 40 years without a comprehensive analysis of evolving trends in risks associated with this disparity. Here we analyzed United States transplant registry data, which included adult Caucasian or AA solitary kidney recipients transplanted between 1990 and 2009 encompassing 202,085 transplants. Over this 20 year period, the estimated rate of 5 year graft loss decreased from 27.6% to 12.8%. Notable trends in baseline characteristics that significantly differed by race over time included: increased prevalence of diabetes from 2001–09 in AAs (5 year slope difference: 3.4%), longer time on the waiting list (76.5 more days per 5 years in AAs), fewer living donors in AAs from 2003–09 (5 year slope difference: −3.36%), more circulatory death donors in AAs from 2000–09 (5 year slope difference: 1.78%), and a slower decline in delayed graft function in AAs (5 year slope difference: 0.85%). The absolute risk difference between AAs and Caucasians for 5 year graft loss significantly declined over time (−0.92% decrease per 5 years), while the relative risk difference actually significantly increased (3.4% increase per 5 years). These results provide a mixed picture of both promising and concerning trends in disparities for AA kidney transplant recipients. Thus, although the disparity for graft loss has significantly improved, equity is still far off and other disparities, including living donation rates and delayed graft function rates have widened during this time.

Corresponding Author: David J Taber, PharmD, BCPS, Division of Transplant Surgery, Medical University of South Carolina, 96 Jonathan Lucas Street, MSC 611, Charleston, SC 29425, Tele: (843) 792 3368, Fax: (843) 792 8596, taberd@musc.edu.

Disclosure

The authors have no conflicts of interest to disclose as it relates to the content of this manuscript.

Keywords

Kidney transplant; African American; Racial disparities; Graft loss

INTRODUCTION

It is well established that African-Americans (AAs), as compared to Caucasians, are at a significantly increased risk of developing hypertension and diabetes, major risk factors for developing end-stage renal disease.[1–3] As such, the lifetime prevalence of ESRD in AAs is nearly three times higher as compared to non-Hispanic Whites (AAs: 8.5% for men and 7.8% for women vs. non-Hispanic Whites [NHWs]: 3.3% in men and 2.2% in women).[4,5] For those that develop ESRD, kidney transplantation offers the optimal treatment option, as it has demonstrated substantial advantages to dialysis, both in terms of life longevity and quality.[6–9] Over the past 40 years, there have been remarkable enhancements in kidney allograft survival rates. In 1973, the average kidney transplant lasted approximately 1.5 to 2 years,[10] whereas in 2012, the kidney allograft half-life was 11.3 years.[11]

During this same timeframe, it is unclear if racial disparities in allograft survival have significantly changed, both in scope and magnitude. As AAs are dramatically over-represented on the U.S. dialysis and transplant waiting lists, this disparity has enormous public health implications.[5] In 1977, Opelz and colleagues demonstrated that at 3 years post-transplant, AAs had a 10% absolute lower rate of graft survival, as compared to Caucasians (25% in AA, 35% in Caucasians).[12] The most recent Scientific Registry of Transplant Recipients (SRTR) annual report that details racial differences in outcomes, demonstrates a 12% difference in absolute five year graft survival rates.[11] An analysis recently published, using SRTR data, demonstrated a 20–30% reduction in the adjusted risk for 5-year graft loss for both deceased and living donor AA recipients, but did not fully assess change in baseline risk over time and determine the trends in factors associated with this racial disparity, beyond delayed graft function (DGF) and acute rejection.[13]

Racial disparities in transplant have primarily been attributed to immunologic risk factors in AAs which lead to higher acute rejection rates,[14–16] lower socioeconomic status,[17,18] medication non-adherence,[19,20] reduced access to care[21] and more frequent comorbid conditions.[22–25] Recent studies demonstrate gene variants may also account for this disparity, both in the higher prevalence of ESRD in AAs and the increased risk of graft loss after transplant. Polymorphisms within Apolipoprotein L1 (APOL1), which are only present in those of African ancestry, are significantly associated with the risk of developing ESRD in AAs and graft loss in those that receive AA donor organs.[26] To date, there are limited studies that seek to determine if the prevailing etiologies attributed to racial disparities in kidney transplantation have evolved over time.[27] Such an analysis may provide insightful information regarding which factors to focus interventional studies within the contemporary era of kidney transplantation in the hopes of removing racial disparities for AA recipients.

The objective of this study was to utilize national registry data from all adult kidney transplant recipients accumulated over a 20 year time period to determine which baseline

and follow up variables that are implicated in racial disparities have significantly evolved over time.

RESULTS

Between Oct 1, 1987 and Sept 30, 2014, there were 394,359 kidney transplants identified in the UNOS dataset. Of these, 19,313 were excluded for age <18 years, 37,810 were excluded for receiving non-renal transplants, 62,813 were excluded for non-AA or Caucasian race/ethnicity and 72,338 were excluded for being outside the study time period (Jan 1, 1990 to Dec 31, 2009); leaving 202,085 transplant events included in the final analysis. Supplemental Figure 1 displays the study flowchart and number of transplants per year, stratified by race. Of the 202,085 transplants, 144,081 (71%) were Caucasian, while 58,004 (29%) were AA recipients. The proportion of kidney transplants performed in AAs substantially increased over the 20 year time period, starting at 24% in 1990 and increasing to 33% in 2009 (2.11% increase per five years, see top left chart in Supplemental Figure 2 and top of Table 2). The mean follow-up for the entire cohort was 7.0±4.9 years.

Table 1 displays the baseline sociodemographics, comorbidities, donor characteristics, immunologic risks and immunosuppression for the entire cohort, stratified by race. During the 20 year period, AAs were significantly younger, had a higher BMI, were less likely to have graduated college, were more likely to be receiving public insurance and more likely to have hypertension or diabetes. For donor characteristics, AAs were less likely to receive a living donor, but more likely to receive an expanded criteria donor (ECD), donor after circulatory death (DCD) and substantially more likely to receive an AA donor organ. AAs also had significantly higher immunologic risks, including more HLA mismatches, higher PRA levels above 20% and 80% and longer cold ischemic times. Finally, AAs were more likely to receive potent immunosuppression regimens, as compared to Caucasians, including cytolytic induction therapy, tacrolimus, mycophenolate and corticosteroids at discharge.

Over the 20 year study, there were significant evolutions in these variables, a number of which differed substantially by race. Recipient age in Caucasians significantly increased at a faster rate over time, as compared to AAs (3.54 vs. 2.69 years of age per 5 year study period, $p<0.0001$). Other trajectories that differed by race include female gender (faster increase in AAs), hypertension (increased faster in Caucasians from 1990–2002), diabetes (increased faster in AAs from 2001–2009), receiving dialysis at the time of transplant (decreased faster in Caucasians), waiting list time (increased faster in AAs), receiving an organ from a Caucasian donor (decreased faster in AAs), living donors (decreased more in AAs from 2003 to 2009), circulatory death donors (increased faster in AAs from 2000 to 2009), HLA Type A and B mismatches (increased faster in AAs), PRA >80% (increased faster in AAs from 1998 to 2009) and previous transplant (decreased faster in AAs from 1990–94, then increased in AAs from 1995–2009); see Table 2 for slope estimates, Figure 1 and Supplemental Figure 2 to visualize temporal trends and knots in slopes (dotted vertical lines).

Post-transplant clinical outcomes compared by race are displayed in Table 3; the prevalence of all events were significantly higher in AA recipients ($p<0.001$). The trajectories of these

events over time and compared by race are displayed in Table 4 and Figure 2. The rate of decline in delayed graft function was significantly faster in Caucasians; while graft loss, death and overall graft loss rates all declined at a faster rate in AAs. The rate of decline in 5-year graft loss rates was 0.92% faster in AAs, as compared to Caucasians (p=0.0066), while the rate in decline in 5-year mortality rates was 0.87% faster in AAs (p=0.0172). Post-transplant outcomes, stratified by donor type (living and deceased) and compared by race are presented in Supplementary Table 2. The estimated decrease in disparities for graft loss and death were all significantly higher in magnitude within deceased donor recipients, although all estimates were statistically significant in both living and deceased donor recipients.

The absolute risk difference between AAs and Caucasians for 5 year graft loss significantly declined over time (−0.92% decrease per 5 years, p<0.001, see Figure 3), while the relative risk difference increased (3.4% increase per 5 years, p<0.001, see Figure 3). Figure 4 displays the unadjusted and adjusted hazard-ratios for AA race (Caucasians are the referent group) for graft loss between 1994 and 2009. The unadjusted hazard-ratios for AAs significantly increased during the entire time period (0.10 increase in hazard-ratio per 5 years, p=0.0008), while the adjusted hazard-ratios increased from 1994–2001 (0.26 increase per 5 years, p=0.0165) then reversed and decreased from 2002–2009 (0.16 decrease per 5 years, p=0.0052).

DISCUSSION

This study provides a detailed assessment of 20 years of evolving trends in racial disparities in kidney transplantation, demonstrating a number of interesting findings. Most importantly, although there is still a long way to go to achieve equity, the disparity in AAs for graft loss has significantly improved over the past 20 years, with an ***absolute*** risk difference decrease of 0.9% per 5 years, when compared to Caucasians. Yet, the ***relative*** risk difference between AAs and Caucasians has actually increased (3.4% increase per 5 year time period). Thus, depending on your viewpoint, the conclusions with regards to trends in racial disparities over time in kidney transplantation are paradoxical. Further, when the risk of graft loss in AAs is fully adjusted using explanatory variables, the hazard-ratios after 2001 significantly decrease (−0.16 per 5 years), suggesting more of the inherent risk in AA recipients is captured in measured covariates during recent transplant years. These results, in terms of graft loss disparities, are similar to those reported in a recently published analysis.[13]

With regards to other post-transplant outcomes, these results present a mixed message of both significant improvements and areas of concern. Five year graft loss and mortality rates have decreased significantly faster in AAs, as compared to Caucasians (~0.9% difference per 5 years, p<0.02). Additionally, acute rejection rates have dramatically decreased since 1996 (~70% per 5 years), which was similar in magnitude in AAs and Caucasians. However, the difference in delayed graft function rates between AA and Caucasians has widened over time, which is a strong risk factor for acute rejection and graft loss.[28,29] This is a concerning trend, and one that may be a function of donor type.[28,30] Between 2003 and 2009, the disparity between AAs and Caucasians in living donor rates has also significantly widened, and this likely represents an important disparities driving outcome differences.[31] Further, AA recipients had an increased utilization of circulatory death donors between 2000 and

2009, likely a compensatory effect of the decrease in living donor rates. While this probably contributed to the increase in transplant rates within AAs, it may also be influencing post-transplant outcomes, including delayed graft function and graft function.[28,30] These results demonstrate that living donation rates have decreased recently in the U.S.; while other international data indicates continued increased rates across the EU and Scandinavia. However, living donation rates per million are still very high in the U.S, only surpassed by the Netherlands, U.K., Turkey, Iceland and Macedonia.[32] It is clear from this data that future interventions in racial disparities need to focus on improving living donation rates, particularly within the AA community.

At the time of transplant, there were a number of interesting trends in baseline variables that significantly differed by race over time. Between 2001 and 2009, the proportion of AAs that were females and those that had pre-existing diabetes significantly increased, as did time on the waiting list; conversely, the number of preemptive transplants decreased more so in AAs. Some of these issues are likely to be related, as it is well known that AAs are referred for transplant evaluation later in their course, usually after chronic renal replacement therapy has already been initiated. Thus, earlier referral and listing, coupled with more living donors in AAs will likely improve these growing disparities.[33]

It is interesting that the proportion of AA donors increased within AA recipients, as compared to Caucasians (with a statistically significant compensatory decrease in Caucasian donors in AAs). This is likely an unintentional effect of significant changes in U.S. organ allocation policies that occurred during this time period. AAs have markedly different HLA polymorphisms, and thus, are less likely to have unacceptable HLA antibodies (negative virtual cross-match) with AA donors. This trend is further exaggerated by the increasing rates of HLA mismatches and PRA levels that are seen in AAs over this time period.[34,35] There may be significant clinical implications of this, as it relates to racial disparities. Recent data demonstrates that APOL1 gene variants, which are only present in those of African ancestry, are strongly associated with increased risk of graft loss.[26] Thus, as the proportion of AA donors allocated to AA recipients has grown, so has the potential impact of the APOL1 gene variant on graft outcomes and disparity gaps. There were major changes made to the U.S. organ allocation policy for kidneys in December of 2014. It will be interesting to determine what impact these have on donor race trends. Without widespread donor genotyping for APOL1, we can only speculate the impact these trends have on graft outcomes and racial disparities.[36]

The use of potent immunosuppressive regimens, which includes cytolytic induction therapy, tacrolimus and mycophenolate, dramatically increased during this study period for the entire cohort, particularly since the mid to late 1990s. Concurrently, there was a compensatory drop in acute rejection rates, starting in 1996. Overall, this occurred at a similar rate in both AAs and Caucasians; but in the most recent years (2006–2009), the absolute difference in rejection rate was only 1.7% between AAs and Caucasians (vs. 4.7% in years prior). This decrease in disparities for acute rejection is likely due to the known immunologic risk factors common in AA recipients, including HLA mismatches, higher PRAs, immune hyper-responsiveness and genetic polymorphisms in cytokine production and immunosuppressant metabolism.[37, 38] Steroid utilization at discharge substantially decreased between 2002 and

2005, with a levelling off starting in 2006. Yet, steroids continue to be used more often in AA recipients. This is perhaps because there continues to be controversy regarding the safety of steroid withdrawal in AA recipients.[39–41]

Globally, outside of the U.S., there is controversy whether disparities in outcomes for those of African descent are of significant magnitude. Large studies from both France and Canada failed to demonstrate a significant difference in outcomes between those of African descent, as compared to those of European ancestry.[42,43] Both countries have universal healthcare access and there is conjecture that this is a major factor driving U.S. disparities. However, there are significant disparities in those of African descent within both the U.K. and Brazil, which have universal healthcare access.[44,45] There are likely other more complex issues driving these differences in outcomes as it relates to racial disparities across global regions. Migratory patterns and etiologies for migration are vastly different based on country of destination. Thus, the constitutions of those of African descent substantially differ across the U.S., Canada, Brazil, France and the U.K. Comorbidities, such as hypertension and diabetes are significantly more common in AAs and those of African descent in Brazil. Gene variants associated with outcomes, including APOL1, cytochrome P450, and MDR1 also likely differ across these heterogeneous populations. Healthcare access and socio, cultural and economic disparities also differ substantially across these global regions. Thus, the reasons for differences in racial disparities across the Americas and Europe are likely a complex convergence of different populations, socioeconomics and culture.[46] The results from this analysis demonstrate that the risk factors likely driving these disparities do evolve over time, with improvements juxtaposed with increasing challenges. However, there is reason to believe that achieving equity in outcomes across racial groups can be achieved by intensely focusing on these evolving trends.

Although the results of this analysis provide considerable insights into the trends in racial disparities, this study does have several significant limitations. This was a retrospective analysis that relied on registry data input by transplant programs without detailed validation. Additionally, the level of missingness and definitions of a number of variables evolved over time.

Although data were available back to 1987, we chose to start the analysis in 1990 because of missingness issues (with Cox regression adjusted models starting in 1994 for this issue). The number of patients with missing data decreased over time and the definitions of important variables, included diabetes, panel reactive antibody, functional status and expanded criteria donor changed as well. Also, using regressed slopes to define and compare trends assumes linearity, and clearly, a number of these trends were not linear across the entire 20 year period. To account for this, we utilized spline and knot analysis, which improved model fit (see Supplemental Table 1). Because of these issues and the inherent flaws embedded within retrospective analyses, including being prone to residual confounding and misclassification of variables that have evolved over time, these results should not be misconstrued as cause and effect. Rather, they provide associations that can be utilized to guide future prospective observational and interventional studies and allow the transplant community to focus on the pertinent mutable variables that are likely driving racial disparities in the contemporary era of kidney transplantation.

In conclusion, although equity is still far off, over the past 20 years, there has been a significant improvement in racial disparities in graft loss rates for AA kidney transplant recipients. However, there are a number of concerning trends for AA recipients, as compared to Caucasians, including a decrease in living donation rates, coupled with higher rates of delayed graft function, diabetes, longer waiting times, and less preemptive transplants. Disparity research endeavors should focus on reducing these growing differences or mitigating their influence on outcomes, as a mechanism to move closer to equitable outcomes.

METHODS

Study design

This was an analysis of the United Network of Organ Sharing (UNOS) Transplant Registry database, which was implemented in 1987 to track baseline and follow up data for all patients awaiting and undergoing solid organ transplants within the United States. These data were merged with the Social Security Death Master File (SSDMF) to obtain accurate patient death dates. After local IRB approval and a data use agreement (DUA) with UNOS, we obtained national Standard Transplant Analysis and Research (STAR) de-identified datasets, which were pre-linked to the SSDMF data. This study focused on patients transplanted between January 1, 1990 and December 31, 2009 (20 years), with follow up through December 31, 2014. This time period was chosen because of the large amount of missing data prior to 1990 and to ensure all patients had at least 5 years of potential follow up. Inclusion criteria were adult (≥18 years of age at the time of transplant) recipients of solitary kidney transplants. Those that were not either AA or Caucasian were excluded for ease of comparison and reporting of results.

Primary Outcome

The primary outcome for this study was graft loss, with death analyzed as a competing risk event, which was defined as a composite of returning to chronic dialysis or undergoing preemptive retransplant. We also assessed mortality and overall graft loss, which was defined as a composite of either graft loss or death.

Risk Factors

We assessed for a large number of risk factors that have been previously identified as potential explanatory variables for racial disparities in kidney transplantation. These included recipient sociodemographics (age, gender, body mass index [BMI], functional status, education and insurance), recipient comorbidities (reason for ESRD, cardiovascular disease [CVD] comorbid conditions and time on waitlist), donor characteristics (age, gender, race, and donor type), transplant characteristics/immunologic risks (HLA mismatches, PRA, cold ischemic time, previous kidney transplant) and finally, baseline immunosuppression (induction and maintenance therapy). The definitions of these risk factors can be found in the Supplemental Methodology.

Statistical Analysis

First, we assessed baseline variables aggregated for the 20-year cohort and compared by recipient race (Caucasian vs. AA). This was done using standard descriptive and univariate statistics. Continuous variables are reported as medians with interquartile ranges (IQR), with comparisons made using the Mann Whitney U test. Categorical variables are presented as percentages with comparisons made using the Chi square test. One, three, and five year event rates for graft loss, death and overall graft loss were analyzed using Cox regression to estimate survival and cumulative incidence functions, with death events accounted for as a competing risk in the graft loss models (Fine and Gray method).[47] Repeated patients were accounted for within a given year through the use of a marginal model (COVS(aggregate) option).

Next, we assessed the temporal trends in these variables by transplant year and whether these differed by race. This was done by plotting the frequency or median of the variable on the y-axis and the transplant year on the x-axis, stratified by race. We utilized linear regression for frequencies and quantile regression for medians (PROC QUANTREG) to estimate the slope change per year; visualization of the data was used in conjunction with formal spline and knot analysis to determine if significant changes in the direction or magnitude of slopes were present (PROC TRANSREG and PBSSPLINE). If so, dummy terms were created from the time variable to account for the knots; goodness of fit (R^2) was used to assess optimal knots and data transformations through comparison of iterative models. Interaction terms (race*time) were utilized to assess if the variable slope significant differed by race over time. The number of knots and transformations utilized for each variable can be found in Supplementary Table 1. For non-categorical variables, we conducted analyses using both means and medians and linear and quantile regression; based on model fit and variable distribution, chose to report medians with quantile regression in the final results. Results using means were comparable, with differences noted for functional status, BMI, PRA, HLA subtypes and cold time.

Finally, we determined if the absolute and relative risk of 5-year graft loss by recipient race (Caucasian set as referent group) changed over time. We calculated the graft loss relative risk difference (AA − Caucasian / AA), absolute risk difference (AA − Caucasian), unadjusted and adjusted hazard-ratios for each transplant year and assessed the temporal trends in these using linear regression with spline analysis (same methodology detailed above). To estimate the hazard-ratios for each year, we utilized Cox regression, with death treated as a competing risk (Fine and Gray method).[47] Repeated patients were accounted for within a given year through the use of a marginal model; with retransplant entered as a covariate to adjust for between years retransplant status. The following were included in the model for adjustment: delayed graft function, acute rejection, re-transplant, primary insurance, recipient gender, recipient BMI, education, diabetes, hypertension, pre-emptive transplant, cold ischemic time, HLA mismatches, PRA, living donor, ECD, DCD, induction therapy, tacrolimus, cyclosporine, mycophenolate, azathioprine, mTOR inhibitors and steroids. Statistical significance was based on a two-sided p-value of less than 0.05. Statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC).

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Source of Support: Research reported in this publication was supported by the National Institute of Diabetes and Digestive and Kidney Diseases of the National Institutes of Health under Award Number K23DK099440. Running Headline: Trends in racial disparities in kidney transplantation

References

1. Harris MI, Flegal KM, Cowie CC, et al. Prevalence of diabetes, impaired fasting glucose, and impaired glucose tolerance in U.S. adults. The third national health and nutrition examination survey, 1988–1994. Diabetes Care. 1998; 21(4):518–524. [PubMed: 9571335]
2. Kato N. Ethnic differences in genetic predisposition to hypertension. Hypertension Research. 2012; 35(6):574–581. [PubMed: 22476227]
3. Carson AP, Howard G, Burke GL, Shea S, Levitan EB, Muntner P. Ethnic differences in hypertension incidence among middle-aged and older adults: The multi-ethnic study of atherosclerosis. Hypertension. 2011; 57(6):1101–1107. [PubMed: 21502561]
4. Coresh J, Selvin E, Stevens LA, et al. Prevalence of chronic kidney disease in the United States. J Am Med Assoc. 2007; 298(17):2038–2047.
5. U S Renal Data System. USRDS 2011 annual data report: Atlas of chronic kidney disease and end-stage renal disease in the United States. National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases; Bethesda, MD: 2011.
6. Griva K, Davenport A, Harrison M, Newman SP. The impact of treatment transitions between dialysis and transplantation on illness cognitions and quality of life–A prospective study. British Journal of Health Psychology. 2012; 17(4):812–27. [PubMed: 22536819]
7. Landreneau K, Lee K, Landreneau MD. Quality of life in patients undergoing hemodialysis and renal transplantation--a meta-analytic review. Nephrol Nurs J. 2010; 37(1):37–44. [PubMed: 20333902]
8. Rana A, Gruessner A, Agopian VG, et al. Survival benefit of solid-organ transplant in the united states. JAMA Surgery. 2015; 150(3):252–259. [PubMed: 25629390]
9. Tonelli M, Wiebe N, Knoll G, et al. Systematic review: Kidney transplantation compared with dialysis in clinically relevant outcomes. Am J Transplant. 2011; 11(10):2093–2109. [PubMed: 21883901]
10. Opelz G, Sengar DP, Mickey MR, Terasaki PI. Effect of blood transfusions on subsequent kidney transplants. Transplant Proc. 1973; 5(1):253–259. [PubMed: 4572098]
11. Matas A, Smith J, Skeans M, et al. OPTN/SRTR 2012 annual data report: Kidney. Am J Transplant. 2014; 14(S1):11–44. [PubMed: 24373166]
12. Opelz G, Mickey MR, Terasaki PI. Influence of race on kidney transplant survival. Transplant Proc. 1977; 9(1):137–142. [PubMed: 325754]
13. Purnell, TS.; Luo, X.; Kucirka, LM.; Cooper, LA.; Crews, DC., et al. Reduced racial disparity in kidney transplant outcomes in the United States from 1990 to 2012. J Am Soc Nephrol. 2016. epub ahead of print Feb 4, 2016
14. Ciancio G, Burke GW, Suzart K, et al. The use of daclizumab, tacrolimus and mycophenolate mofetil in African-American and hispanic first renal transplant recipients. Am J Transplant. 2003; 3(8):1010–1016. [PubMed: 12859538]
15. Neylan JF. Racial differences in renal transplantation after immunosuppression with tacrolimus versus cyclosporine. FK506 kidney transplant study group. Transplantation. 1998; 65(4):515–523. [PubMed: 9500626]
16. Podder H, Podbielski J, Hussein I, Katz S, Buren C, Kahan BD. Sirolimus improves the two-year outcome of renal allografts in African-American patients. Transplant Int. 2001; 14(3):135–142.

17. Butkus DE, Meydrech EF, Raju SS. Racial differences in the survival of cadaveric renal allografts. overriding effects of HLA matching and socioeconomic factors. N Engl J Med. 1992; 327(12): 840–845. [PubMed: 1508243]
18. Curtis JJ. Kidney transplantation: Racial or socioeconomic disparities? Am J Kidney Dis. 1999; 34(4):756–758. [PubMed: 10516360]
19. Kalil R, Heim-Duthoy K, Kasiske B. Patients with a low income have reduced renal allograft survival. American journal of kidney diseases: the official journal of the National Kidney Foundation. 1992; 20(1):63. [PubMed: 1621680]
20. Schweizer RT, Rovelli M, Palmeri D, Vossler E, Hull D, Bartus S. Noncompliance in organ transplant recipients. Transplantation. 1990; 49(2):374–377. [PubMed: 2305467]
21. Young CJ, Kew C. Health disparities in transplantation: Focus on the complexity and challenge of renal transplantation in African Americans. Med Clin N Am. 2005; 89:1003–1031. [PubMed: 16129109]
22. Cosio FG, Dillon JJ, Falkenhain ME, et al. Racial differences in renal allograft survival: The role of systemic hypertension. Kidney Int. 1995; 47(4):1136–1141. [PubMed: 7783411]
23. Cosio FG, Pesavento TE, Kim S, Osei K, Henry M, Ferguson RM. Patient survival after renal transplantation: IV. impact of post-transplant diabetes. Kidney Int. 2002; 62(4):1440–1446. [PubMed: 12234317]
24. Cosio FG, Hickson LJ, Griffin MD, Stegall MD, Kudva Y. Patient survival and cardiovascular risk after kidney transplantation: The challenge of diabetes. Am J Transplant. 2008; 8(3):593–599. [PubMed: 18294155]
25. Taber DJ, Meadows HB, Pilch NA, Egede LE. The impact of diabetes on ethnic disparities in kidney transplantation. Ethnicity and Disease. 2013; 23:238–44. [PubMed: 23530307]
26. Freedman BI, Julian BA, Pastan SO, Israni AK, Schladt D, et al. Apolipoprotein L1 gene variants in deceased organ donors are associated with renal allograft failure. Am J Transplant. 2015; 15:1615–22. [PubMed: 25809272]
27. Young CJ, Gaston RS. African Americans and renal transplantation: Disproportionate need, limited access, and impaired outcomes. Am J Med Sci. 2002; 323(2):94–9. [PubMed: 11863086]
28. Siedlecki A, Irish W, Brennan DC. Delayed graft function in the kidney transplant. Am J Tansplant. 2011; 11(11):2279–2296.
29. Yarlagadda SG, Coca SG, Formica RN Jr, Poggio ED, Parikh CR. Association between delayed graft function and allograft and patient survival: A systematic review and meta-analysis. Nephrol Dial Transplant. 2009; 24(3):1039–1047. [PubMed: 19103734]
30. Siedlecki A, Irish W, Brennan DC. Delayed graft function in the kidney transplant. Am J Tansplant. 2011; 11(11):2279–2296.
31. Gore JL, Danovitch G, Litwin M, Pham P, Singer JS. Disparities in the utilization of live donor renal transplantation. Am J Transplant. 2009; 9(5):1124–1133. [PubMed: 19422338]
32. [Accessed May 14, 2016] 2014 Nov. http://ec.europa.eu/health/blood_tissues_organs/docs/ev_20141126_factsfigures_en.pdf
33. Patzer RE, Plantinga LC, Paul S, et al. Variation in dialysis facility referral for kidney transplantation among patients with end-stage renal disease in Georgia. J Am Med Assoc. 2015; 314(6):582–594.
34. Roberts JP, Wolfe RA, Bragg-Gresham JL, Rush SH, Wynn JJ, et al. Effect of changing the priority of HLA matching on the rates and outcomes of kidney transplantation in minority groups. New Eng J Med. 2004; 350:545–51. [PubMed: 14762181]
35. Baxter-Lowe, LA. [Accessed May 16, 2016] 2014 Oct. http://2014.ashi-hla.org/sites/default/files/docs/2014/Baxter-Lowe2.pdf
36. Stewart DE, Kucheryavaya AY, Klassen KD, Turgeon NA, Formica RN, Aeder MI. Changes in deceased donor kidney transplantation one year after KAS implementation. Am J Transplant. 2016; epub ahead of print. doi: 10.1111/ajt.13770
37. Padiyar A, Hricik DE. Immune factors influencing ethnic disparities in kidney transplantation outcomes. Expert Review of Clinical Immunology. 2011; 7(6):769–778. [PubMed: 22014018]

38. Malat GE, Culkin C, Palya A, Ranganna K, Kumar MS. African American kidney transplantation survival: The ability of immunosuppression to balance the inherent pre- and post-transplant risk factors. Drugs. 2009; 69(15):2045–2062. [PubMed: 19791826]

39. Hricik DE, Knauss TC, Bodziak KA, et al. Withdrawal of steroid therapy in African American kidney transplant recipients receiving sirolimus and tacrolimus. Transplantation. 2003; 76(6):938–942. [PubMed: 14508357]

40. Hricik DE, Augustine JJ, Knauss TC, et al. Long-term graft outcomes after steroid withdrawal in African American kidney transplant recipients receiving sirolimus and tacrolimus. Transplantation. 2007; 83(3):277–281. [PubMed: 17297401]

41. Kumar M, Khan S, Ranganna K, Malat G, Sustento-Reodica N, Meyers W. Long-Term outcome of early steroid withdrawal after kidney transplantation in African American recipients monitored by surveillance biopsy. Am J Transplant. 2008; 8(3):574–585. [PubMed: 18294153]

42. Pallet N, Thervet E, Alberti C, Emal-Algae V, Bedrossian J, et al. Kidney transplant in black recipients: are African Europeans different from African Americans? Am J Transplant. 2005; 5:2682–7. [PubMed: 16212627]

43. Yeates K, Wiebe N, Gill J, Sima C, Schaubel D, et al. Similar outcomes among Black and White renal allograft recipients. J Am Soc Nephrol. 2009; 20:172–9. [PubMed: 18971374]

44. Medina-Pestana, JO. Clinical Transplants 2010. Chapter 9: Renal transplant – Sao Paulo, Brazil. Terasaki Foundation Laboratory; Los Angeles, CA: p. 107-26.

45. Medcalf JF, Andrews PA, Bankart J, Bradley C, Carr S, et al. Poorer graft survival in ethnic minorities: results from a multi-centre UK study of kidney transplant outcomes. Clin Nephrol. 2044; 75:294–301. [PubMed: 21426883]

46. Malek SK, Keys BJ, Kumar S, Milford E, Tullius SG. Racial and ethnic disparities in kidney transplantation. Transplant Int. 2011; 24:419–24.

47. Fine JP, Gray RJ. A proportional hazards model for the subdistribution of a competing risk. J Am Stat Assoc. 1999; 94(446):496–509.

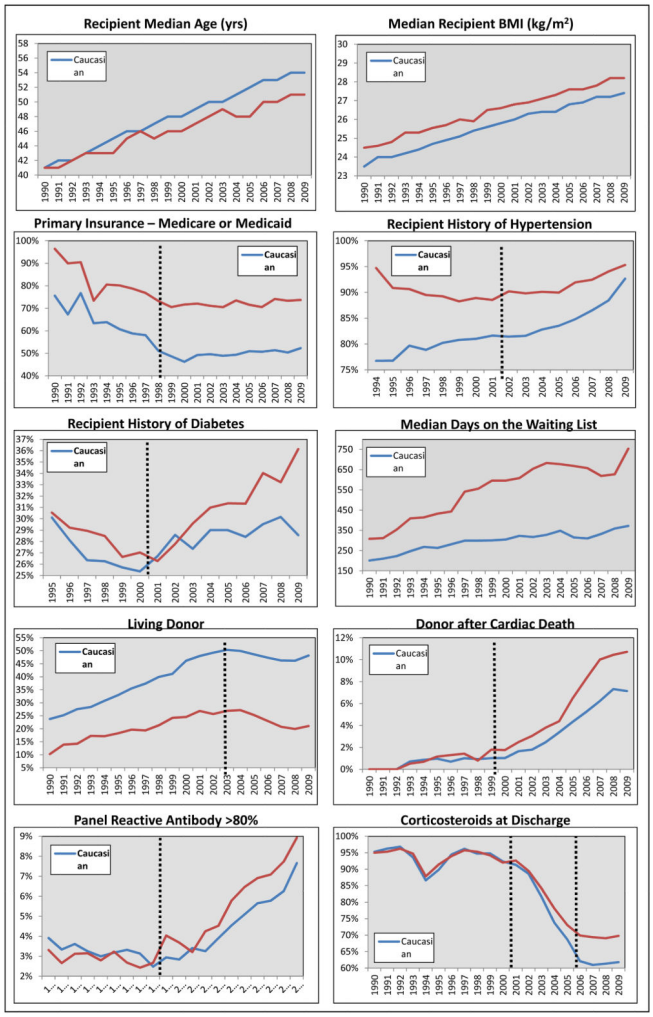

Figure 1.

Annual trends in baseline variables for adult kidney transplant recipients transplanted between 1990 and 2009, stratified and compared based on recipient race. Dotted vertical lines represent knots in the trends over time.

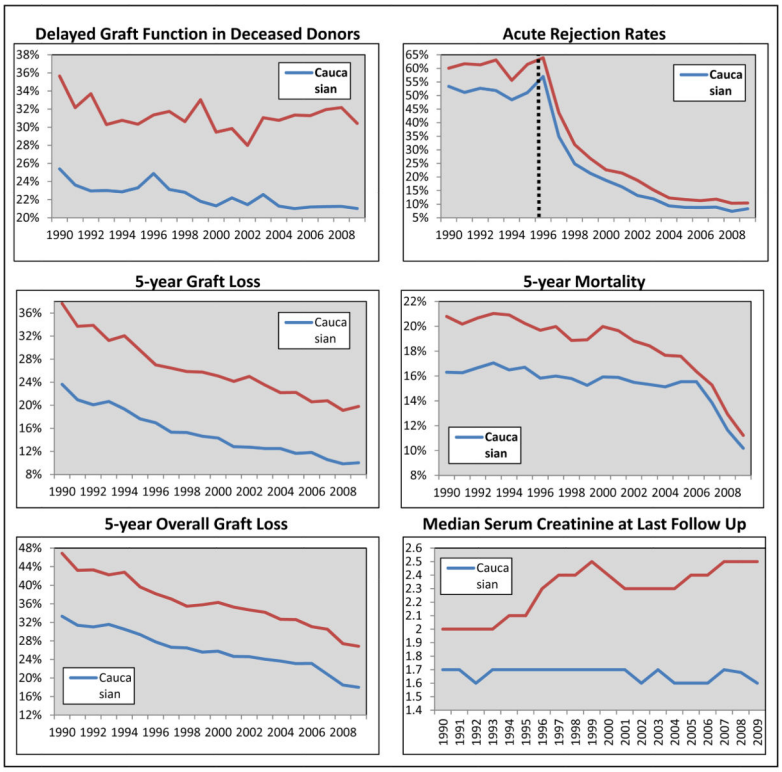

Figure 2.

Annual trends in post-transplant clinical outcomes for adult kidney transplant recipients transplanted between 1990 and 2009, stratified and compared based on recipient race. Dotted vertical lines represent knots in the trends over time.

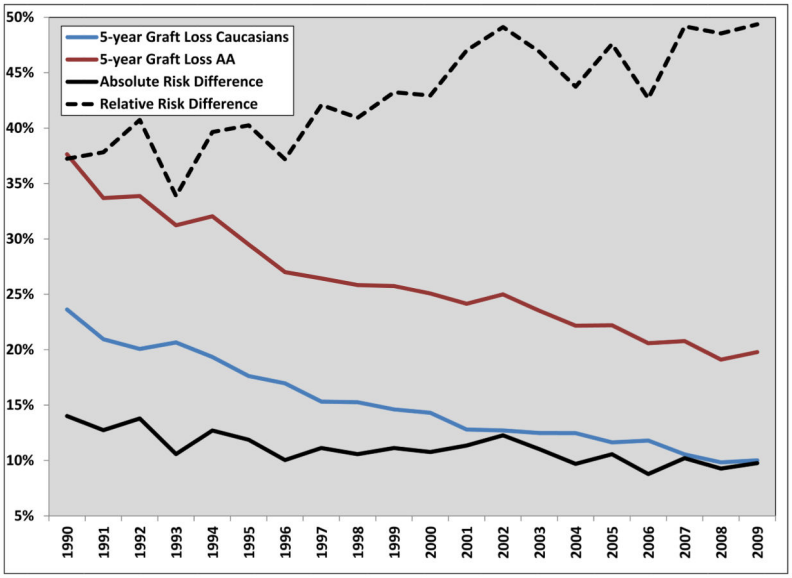

Figure 3.

Annual five-year death-censored graft loss rates and absolute and relative risk differences for adult kidney transplant recipients transplanted between 1990 and 2009, compared based on recipient race

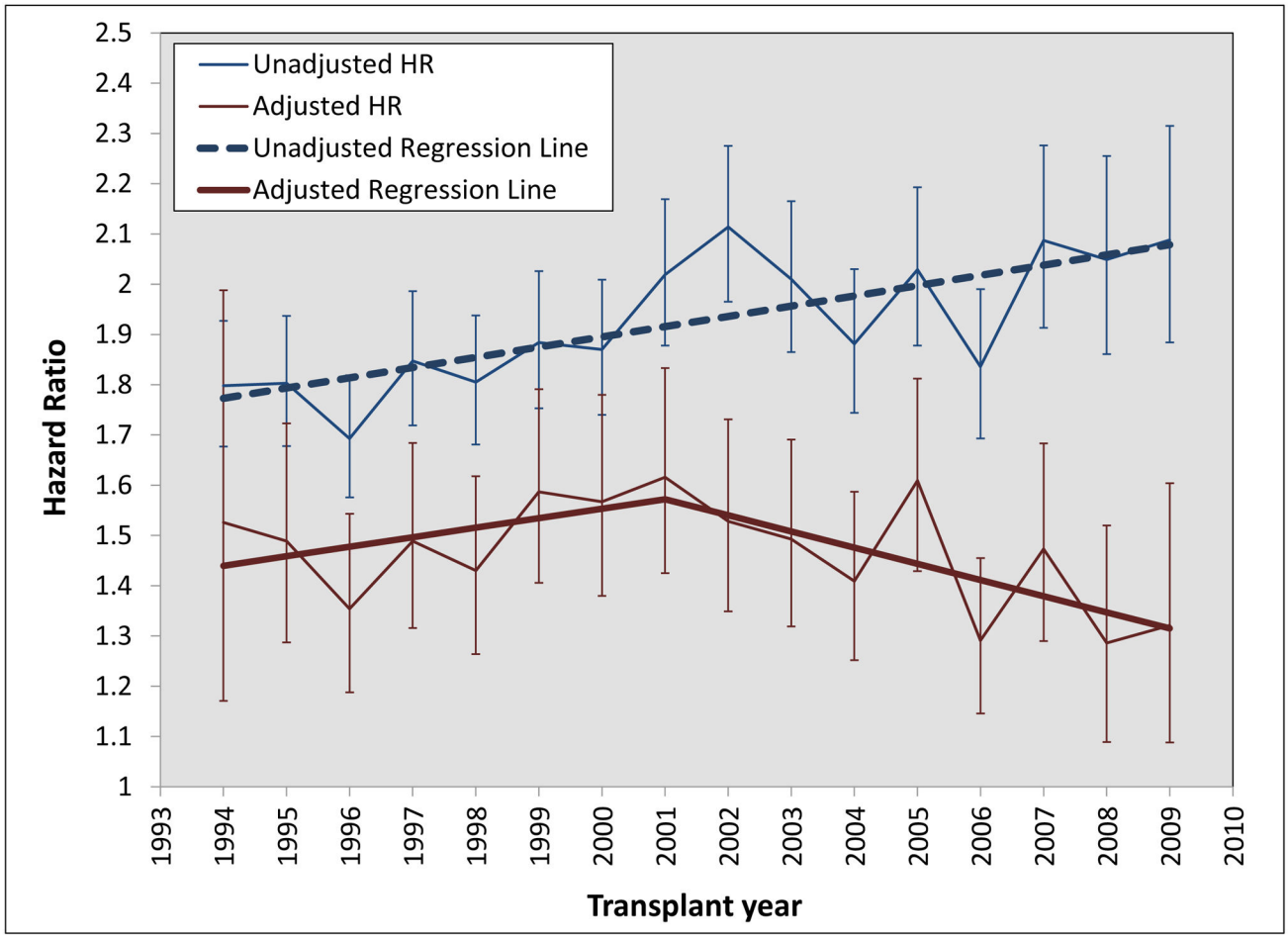

Figure 4.

Annual trends in unadjusted and adjusted hazard ratios in African-Americans for the outcome of graft loss (death as a competing risk event) in adult kidney transplant recipients transplanted between 1940 and 2009

Table 1

Baseline recipient sociodemographics, donor information and transplant characteristics for adult kidney transplant recipients transplanted between 1990 and 2009, stratified by recipient race

Variable	Caucasian	African-American
Number of Patients	144,081 (71%)	58,004 (29%)
Median Age (IQR)	48 (37, 58)	47 (37, 56)
Female Gender	39.1%	40.9%
Median BMI (IQR)	25.7 (22.6, 29.7)	26.7 (23.2, 30.9)
Median Karnofsky Functional Status (IQR)	100% (80, 100%)	100% (80, 100%)
Some College or College Graduate	52.3%	43.1%
Primary Insurance - Medicare or Medicaid	52.0%	73.4%
Primary Diagnosis for ESRD		
Hypertension	12.3%	40.0%
Diabetes	21.8%	20.0%
Other	65.9%	40.0%
Comorbidities		
Hypertension	82.5%	91.3%
Diabetes	31.7%	32.6%
Angina	11.9%	8.1%
Cerebrovascular Accident	2.5%	2.5%
Peripheral Vascular Disease	4.5%	2.8%
Receiving Dialysis at Time of Transplant	81.8%	93.2%
Median Days on Wait List (IQR)	295 (119, 647)	553 (221, 1093)
Median Donor Age (IQR)	40 (27, 50)	37 (24, 49)
Donor Female Gender	48.0%	43.4%
Donor Race		
Caucasian	88.8%	55.0%
African-American	4.5%	35.3%
Other	6.7%	9.7%
Living Donor	41.3%	21.6%
Expanded Criteria Donor	10.3%	12.2%
Donor after Cardiac Death	2.6%	4.3%
Median HLA Mismatches (IQR)	3 (2–4)	4 (3–5)
A Mismatches (IQR)	1 (0–2)	1 (1–2)

Variable	Caucasian	African-American
B Mismatches (IQR)	1 (1–2)	2 (1–2)
DR Mismatches (IQR)	1 (0–1)	1 (1–2)
Median Peak PRA (IQR)	0% (0, 11%)	0% (0, 21%)
Median Current PRA (IQR)	0% (0, 4%)	0% (0, 7%)
Current PRA >20%	13.3%	15.9%
Current PRA >80%	4.1%	4.9%
Median Cold Ischemic Time (hrs±SD)	15.0 (2.0, 23.0)	17.0 (10.0, 24.0)
Previous Kidney Transplant	13.4%	9.9%
Induction Therapy		
IL-2 Receptor Antagonist	20.1%	18.8%
Cytolytic Therapy	36.8%	42.2%
Immunosuppression at Discharge		
Tacrolimus	44.3%	51.1%
Cyclosporine	48.5%	41.7%
Mycophenolate	60.7%	64.9%
Azathioprine	26.3%	22.2%
mTOR Inhibitor	6.5%	6.7%
Corticosteroids	82.7%	84.1%

Table 2

Five-year trajectories of baseline characteristics for adult kidney transplant recipients transplanted between 1990 and 2009, stratified by recipient race

Baseline Characteristic	Slope in Caucasians	Slope in African Americans	Difference in Slopes by Race	p-value difference in slopes
Population Proportion	−2.11%	2.11%	4.22%	<0.0001
Median Age (years)	3.57	2.71	−0.87	0.0002
Female Gender	−0.59%	0.44%	1.02%	0.0007
Median BMI (kg/m^2)	1.05	1.00	−0.05	0.4198
Median Functional Status	−1.98%	−3.30%	−1.48%	0.7405
Some College or College Graduate	2.97%	2.16%	−0.81%	0.0841
Medicare or Medicaid 1990–1998	−16.3%	−13.4%	3.0%	0.3531
Medicare or Medicaid 1999–2009	2.7%	2.6%	−0.07%	0.9717
Primary Diagnosis for ESRD				
Hypertension	2.45%	1.56%	−0.90%	0.0541
Diabetes	−0.17%	2.16%	2.33%	<0.0001
Other	−2.28%	−3.72%	−1.44%	0.0144
Comorbidities				
Angina	0.21%	−0.34%	−0.55%	0.5237
Diabetes 1990–2000	−3.8 %	−8.6%	−4.8%	0.0108
Diabetes 2001–2009	2.3%	5.7%	3.4%	0.0004
Cerebrovascular Accident	0.21%	0.49%	0.29%	0.3405
Hypertension 1990–2002	−5.1%	−7.5%	−2.4%	<0.0001
Hypertension 2003–2009	7.3%	5.6%	−1.7%	0.2144
Peripheral Vascular Disease	0.33%	−0.01%	−0.37%	0.1906
Receiving Dialysis at Time of Transplant	−5.18%	−2.45%	2.73%	<0.0001
Median Days on Wait List (days)	38.9	115.5	76.5	<0.0001
Median Donor Age (yrs)	2.73	3.15	0.43	0.3083
Median Donor BMI (kg/m^2)	1.01	1.02	0.01	0.8609
Donor Female	2.23%	1.62%	−0.61%	0.2278
Donor Race				
Caucasian	−0.76%	−2.70%	−1.95%	0.0052
African-American	0.10%	1.22%	1.12%	0.0668
Other	0.65%	1.46%	0.81%	<0.0001
Living Donor 1990–2002	14.3%	12.9%	−1.33%	0.3244

Baseline Characteristic	Slope in Caucasians	Slope in African Americans	Difference in Slopes by Race	p-value difference in slopes
Living Donor 2003–2009	−3.67%	−7.00%	−3.36%	0.0030
Expanded Criteria Donor 1990–1995	3.9%	6.00%	2.1%	0.0959
Expanded Criteria Donor 1996–2009	0.83%	1.10%	0.27%	0.5082
Donor after Cardiac Death 1990–1999	−3.02%	−4.43%	−1.42%	0.0175
Donor after Cardiac Death 2000–2009	3.51%	5.30%	1.78%	<0.0001
Median HLA Mismatches	0.28	0.00	−0.28	0.2077
A Mismatches	0.00	>0.00	>0.00	0.0017
B Mismatches	0.00	0.36	0.36	<0.0001
DR Mismatches	0.00	0.00	0.00	N/A
Median Current PRA	<0.00%	0.00%	<0.00 %	0.0023
Median Peak PRA	−1.07%	−1.23%	−0.15%	0.6265
Current PRA >20% 1990–1997	−7.5%	−7.20%	0.32%	0.3159
Current PRA >20% 1998–2009	4.7%	5.60%	0.95%	0.1267
Current PRA >80% 1990–1997	−2.8%	−2.90%	−0.08%	0.8674
Current PRA >80% 1998–2009	2.0%	2.60%	0.65%	0.0056
Median Cold Time Deceased Donor (hrs)	−1.67	−1.55	0.11	0.6875
Median Cold Time Living Donor (hrs)	0.00	0.00	0.00	N/A
Previous Kidney Transplant 1990–1994	−5.00%	−8.60%	−3.70%	0.0007
Previous Kidney Transplant 1995–2009	−0.13%	0.44%	0.57%	0.0344
Induction Therapy				
IL-2 Receptor Antagonist 1990–1997	9.70%	10.1%	0.44%	0.9323
IL-2 Receptor Antagonist 1998–2000	39.3%	38.1%	−1.19%	0.9404
IL-2 Receptor Antagonist 2001–2009	60.0%	−64.7%	−4.67%	0.7396
Cytolytic Therapy 1990–1993	20.4%	23.4%	3.0%	0.8291
Cytolytic Therapy 1994–1995	−24.1%	−18.6%	5.6%	0.8726
Cytolytic Therapy 1996–1999	−20.8%	−36.6%	−15.8%	0.6301
Cytolytic Therapy 2000–2009	52.6%	62.0%	9.40%	0.5133
Immunosuppression at Discharge				
Tacrolimus 1990–1995	−16.8%	−21.1%	6.30%	0.3674
Tacrolimus 1996–2009	31.8%	31.6%	−0.19%	0.9341
Cyclosporine 1990–1995	19.4%	14.6%	−3.3%	0.5629
Cyclosporine 1996–2009	−32.3%	−32.4%	−0.09%	0.9724
Mycophenolate 1990–1998	43.9%	45.0%	1.11%	0.9231
Mycophenolate 1999–2009	8.42%	7.64%	−0.78%	0.8990
Azathioprine 1990–1994 *	41.3%	41.4%	0.08%	0.9977
Azathioprine 1995–2009 *	−77.9%	−87.5	−9.7%	0.1994
mTOR Inhibitor 1990–1995	−0.29%	0.12%	0.41%	0.8545

Baseline Characteristic	Slope in Caucasians[/]	Slope in African Americans[/]	Difference in Slopes by Race[/]	p-value difference in slopes
mTOR Inhibitor 1996–2001	14.4%	14.6%	0.15%	0.9684
mTOR Inhibitor 2002–2009	−24.2%	−26.7%	−2.54%	0.4527
Corticosteroids 1990–2001	−1.89%	−1.61%	0.29%	0.8133
Corticosteroids 2002–2005	−35.4%	−27.1%	8.29%	0.0853
Corticosteroids 2006–2009	38.6%	31.2%	−7.44%	0.4489

[/] slope is estimated in 5 year increments

[*] log transformed slope difference

Table 3

Graft and patient outcomes for adult kidney transplant recipients transplanted between 1990 and 2009, stratified by race

Outcome	Caucasian	African American
Delayed Graft Function		
Overall	15.0%	25.8%
Deceased Donor	22.4%	31.2%
Living Donor	4.4%	6.4%
Acute Rejection		
6 month	15.0%	16.2%
1 year	15.9%	17.4%
Overall	25.5%	28.8%
Graft Loss		
1 year	5.60%	9.96%
3 year	10.10%	17.61%
5 year	14.68%	25.07%
Death		
1 year	3.96%	4.84%
3 year	8.93%	10.85%
5 year	15.17%	18.28%
Overall Graft Loss		
1 year	8.84%	12.72%
3 year	16.85%	23.77%
5 year	25.52%	35.16%
Median SrCr at Last Follow Up (mg/dL [IQR])	1.7 (1.2–2.7)	2.3 (1.5–4.5)

Table 4

Five-year trajectories of clinical outcomes for adult kidney transplant recipients transplanted between 1990 and 2009, stratified and compared by recipient race

Post-Transplant Outcome	Slope in Caucasians[/]	Slope in African Americans[/]	Difference in Slopes by Race[/]	p-value for difference in slopes
Delayed Graft Function	−2.06%	−1.22%	0.85%	0.0433
Acute Rejection 1990–1996[*]	20.5%	22.7%	2.19%	0.9215
Acute Rejection 1997–2009[*]	−71.16%	−67.6%	3.61%	0.6813
Graft Loss				
1 year	−2.09%	−3.16%	−1.07%	0.0035
3 year	−2.80%	−3.72%	−0.93%	0.0401
5 year	−3.34%	−4.26%	−0.92%	0.0066
Death				
1 year	−0.39%	−0.67%	−0.28%	0.0014
3 year	−0.52%	−1.05%	−0.54%	0.0002
5 year	−1.08%	−1.95%	−0.87%	0.0172
Overall Graft Loss				
1 year	−2.23%	−3.16%	−0.93%	0.0053
3 year	−2.84%	−3.82%	−0.98%	0.0046
5 year	−3.56%	−4.52%	−0.96%	0.0018
Median Last SrCr (mg/dL)	−0.01	0.14	0.14	<0.0001

[/] slope is estimated in 5 year increments

[*] log transformed slope difference