Chapter 6: Transplantation

Introduction

During calendar year 2012, 17,305 kidney transplants, including kidney-alone and kidney plus at least one additional organ, were performed in the United States. Of these kidney transplants, 5,617 were identified as coming from living donors and 11,535 from deceased donors. Overall, there were 340 fewer kidney transplants in 2012 than in 2011. Although the number of kidney transplants has in general remained stable since 2005, ranging from a high of 18,072 in 2006, to a low of 17,305 in 2012, the cumulative number of recipients living with a functioning kidney transplant continues to grow, reaching 186,303 in 2012, a 3.6 percent increase over 2011.

The kidney transplant waiting list continues to increase, with a seven percent increase from 2011 to 2012, reaching 81,981 candidates on December 31, 2012, of which 83 percent were awaiting their first kidney transplant and 17 percent were listed for repeat kidney transplantation. On December 31, 2012, 35,288 (43 percent) candidates were wait-listed in Status 7 (inactive status) and 46,693 (57 percent) candidates were active. With fewer than 18,000 transplants performed in 2012, the active waiting list is 2.7 times larger than the supply of donor kidneys, representing a continuing challenge.

Sixteen percent of new candidates in 2011 were added to the waiting list or received a deceased or living donor transplant within one year of ESRD initiation. Among candidates newly wait-listed for either a first or repeat kidney-alone transplant in 2009, the median waiting time to transplant was 3.6 years.

The probability of first-year all-cause graft failure (return to dialysis, repeat transplantation, or death with a functioning transplant) for deceased donor kidney transplant recipients in 2011 was 7.7 percent, which improved from 9.1 percent in 2000. When graft failure is looked at as its separate components, the probability of either returning to dialysis or undergoing repeat transplantation was 4.7 percent, while that of death was 3.7 percent. These probabilities were substantially lower in living donor transplant recipients, at 3.3 percent for all-cause graft failure, 1.8 percent for returning to dialysis or repeat transplantation, and 1.3 percent for death. For recipients of a deceased donor transplant in 2007, the probability of five-year all-cause graft failure fell to 29 percent compared to 30 percent in the prior year. Corresponding five-year graft failure rates remained the same as the previous year for living donor transplant recipients, at 17 percent.

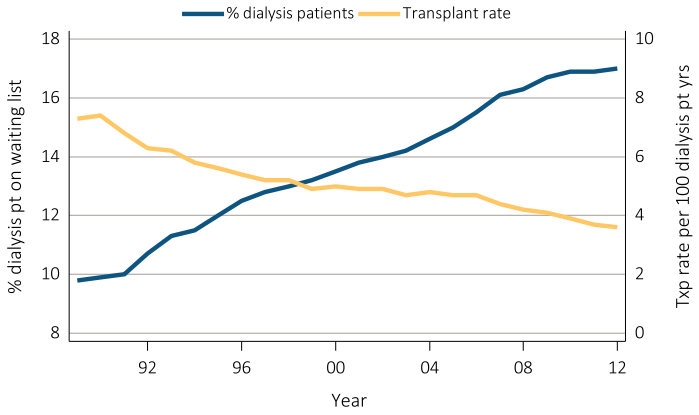
The percent of acute rejection during the first year was highest in 1996 among both deceased (51 percent) and living (52 percent) donor recipients. It declined over the next decade, and stabilized in 2006 at 12 and 10 percent for deceased and living donor recipients, respectively. Since 2004, the percent of reported biopsy-proven rejection during the first year post-transplant has been 7-9 percent for both deceased and living donor recipients.

The unadjusted transplant rate per 100 dialysis patient years is falling while the percent of prevalent dialysis patients wait-listed for a kidney has been rising (Figure 6.1.a). Probable contributing causes include a higher prevalent dialysis population; longer survival of ESRD patients on dialysis; initiation of older and perhaps more ill dialysis patients who are not suitable candidates for transplantation; and the growing mismatch between donor supply and demand, which in turn leads to longer kidney transplant waiting times. Waiting list counts and median waiting time to transplantation for both first and repeat kidney transplant candidates continue to grow (Figure 6.1.b). Many candidates waiting for repeat kidney transplantation were sensitized against a portion of the potential kidney donor pool as a consequence of their initial transplant. Thus, as expected, waiting times for those seeking a repeat kidney transplant are longer than those observed for candidates wait-listed

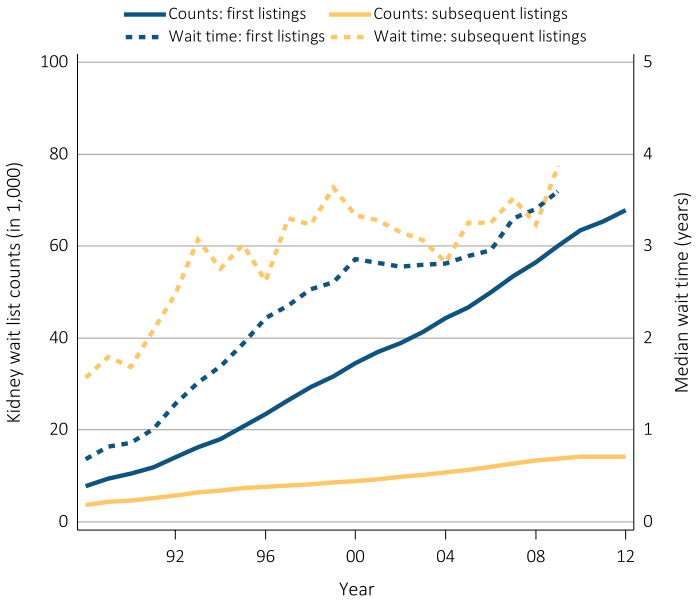
for a first kidney transplant. The total number of kidney transplants has leveled off over the past decade (Figure 6.1.c). During this period, a small overall increase in deceased donation has balanced a small decrease in living donation. The latter is driven in part by changes in pediatric allocation policy that direct deceased donor kidneys from donors under the age of 35 years to children. Introduction of this policy was associated with a decrease in living donation to children. As noted above, the total number of recipients with functioning living and deceased donor kidney transplants continues to grow (Figure 6.1.d).

vol 2 Figure 6.1 Trends in transplantation: unadjusted rates, waiting list counts, waiting time, counts of transplants per year, & total functioning transplants

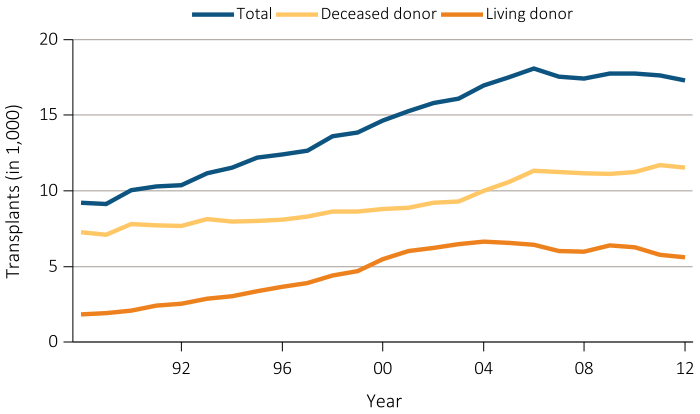
(a) Percent of dialysis patients wait-listed and unadjusted transplant rates



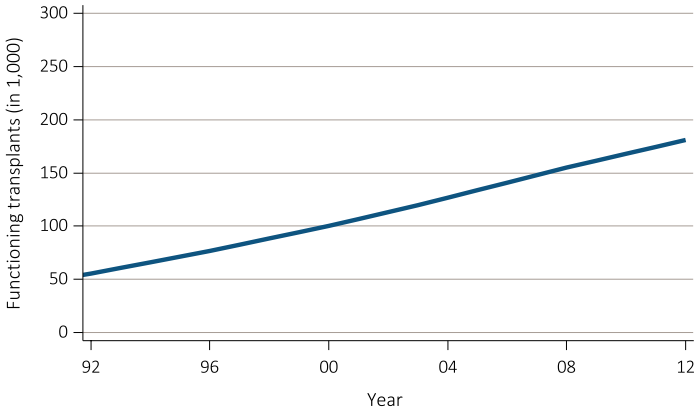
(b) Kidney waiting list counts and waiting time



(c) Counts of transplants



(d) Counts of total functioning transplants

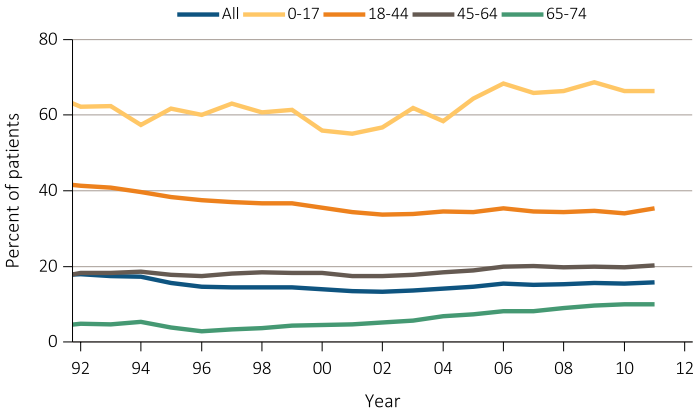


Data Source: Reference Tables E4, E9; E2, E3; E8, E8(2), E8(3); D9. Percent of dialysis patients on the kidney waiting list is for all dialysis patients. Unadjusted transplant rates are for all dialysis patients. Waiting list counts include all candidates listed for a kidney transplant on December 31 of each year. Waiting time is calculated for all candidates enrolled on the waiting list in a given year. Functioning transplant is the annual status on December 31 of each year of all patients who received a kidney transplant, regardless of transplant date.

Waiting List

Kidney transplant rates are lower with increasing candidate age. As an indicator of access to transplantation, the percent of patients wait-listed or receiving a transplant in their first ESRD-year has declined for those between the ages of 18 and 44 and increased slightly in recent years for those age 44 and above (Figure 6.2).

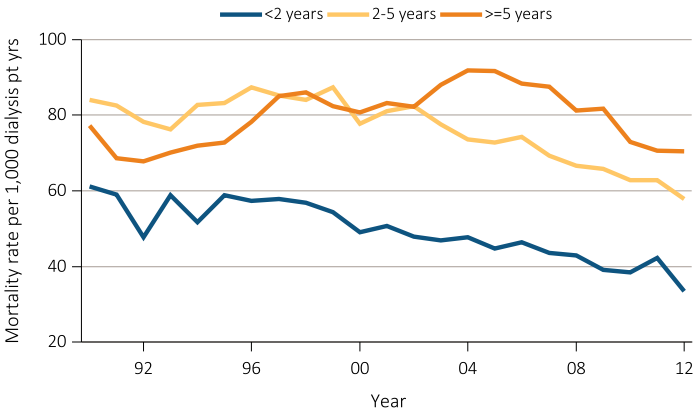
vol 2 Figure 6.2 Percent of incident patients being wait-listed or receiving a kidney transplant within one year of ESRD initiation, by age



Data Source: Reference Table E5(2). Waiting list or transplantation among incident ESRD patients by age (0-74 years).

The annual mortality rates of dialysis patients on the kidney transplant waiting list have declined in recent years (Figure 6.3).

vol 2 Figure 6.3 Annual mortality rates while on the waiting list for dialysis patients from time of placement on the kidney transplant waiting list



Data Source: Reference Table H6. Annual mortality rates of dialysis patients on the kidney transplant waiting list per 1,000 dialysis patient years at risk, by patient vintage.

Transplant Events

Counts of Deceased Donor Transplants

The overall number of deceased donor transplants has leveled off since 2007 (Figure 6.1.c). We review here trends by age, sex, race and primary diagnosis (cause of ESRD) (Figure 6.4). In addition to considering transplant counts, it is important to also examine transplant rates which are based on the number of dialysis patients for each category (Figure 6.5).

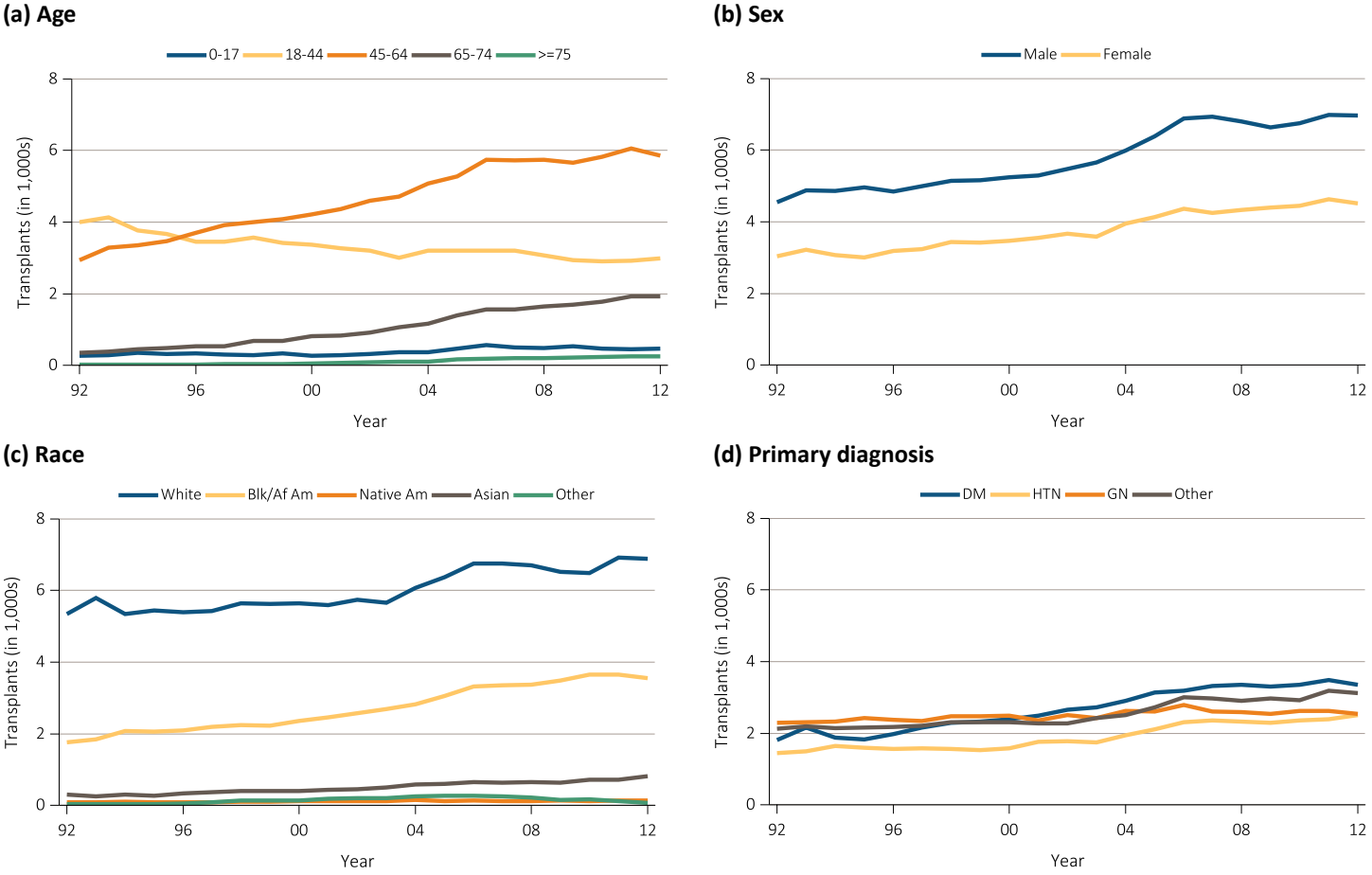
For the age groups 45-64 and 65-74, the number of deceased donor transplants has continued to increase throughout the past two decades, although less steeply since 2006. The counts were highest for recipients in the 45-64 age group, reaching 5,851 in 2012 (Figure 6.4.a, Age). In contrast, during this same time period, the number of transplants has decreased steadily in the cohort aged 18-44 years to 2,997, while it remained fairly stable for children and for the small group of deceased donor kidney recipients older than 75 years.

The trends for counts of deceased donor transplants by year are similar for males and females, rising over the past decade with some leveling off after 2006 (Figure 6.4.b, Sex). Males received substantially more transplants than females. This difference seems to be largely explained by the observation that males account for more than 58 percent (females less than 42 percent) of wait-listed candidates.

Among Whites and African Americans, the number of deceased donor transplants has grown substantially over the past decade, with smaller increases for Asians and Native Americans and small decreases for the other races (Figure 6.4.c, Race).

The largest growth in deceased donor transplant numbers has been among recipients with diabetes or hypertension, and these recipient diagnoses were the most common among the major causes of ESRD (Figure 6.4.d, Primary diagnosis).

vol 2 Figure 6.4 Deceased donor transplant counts and trends, by recipient age, sex, race, & primary diagnosis



Data Source: Reference Table E8(2). Deceased donor kidney transplant counts by recipient age, sex, race and primary diagnosis. Abbreviations: Blk/Af Am, Black/African American; DM, Diabetes Mellitus; GN, glomerulonephritis; HTN, hypertension; Native Am, Native American.

Deceased Donor Transplant Rates

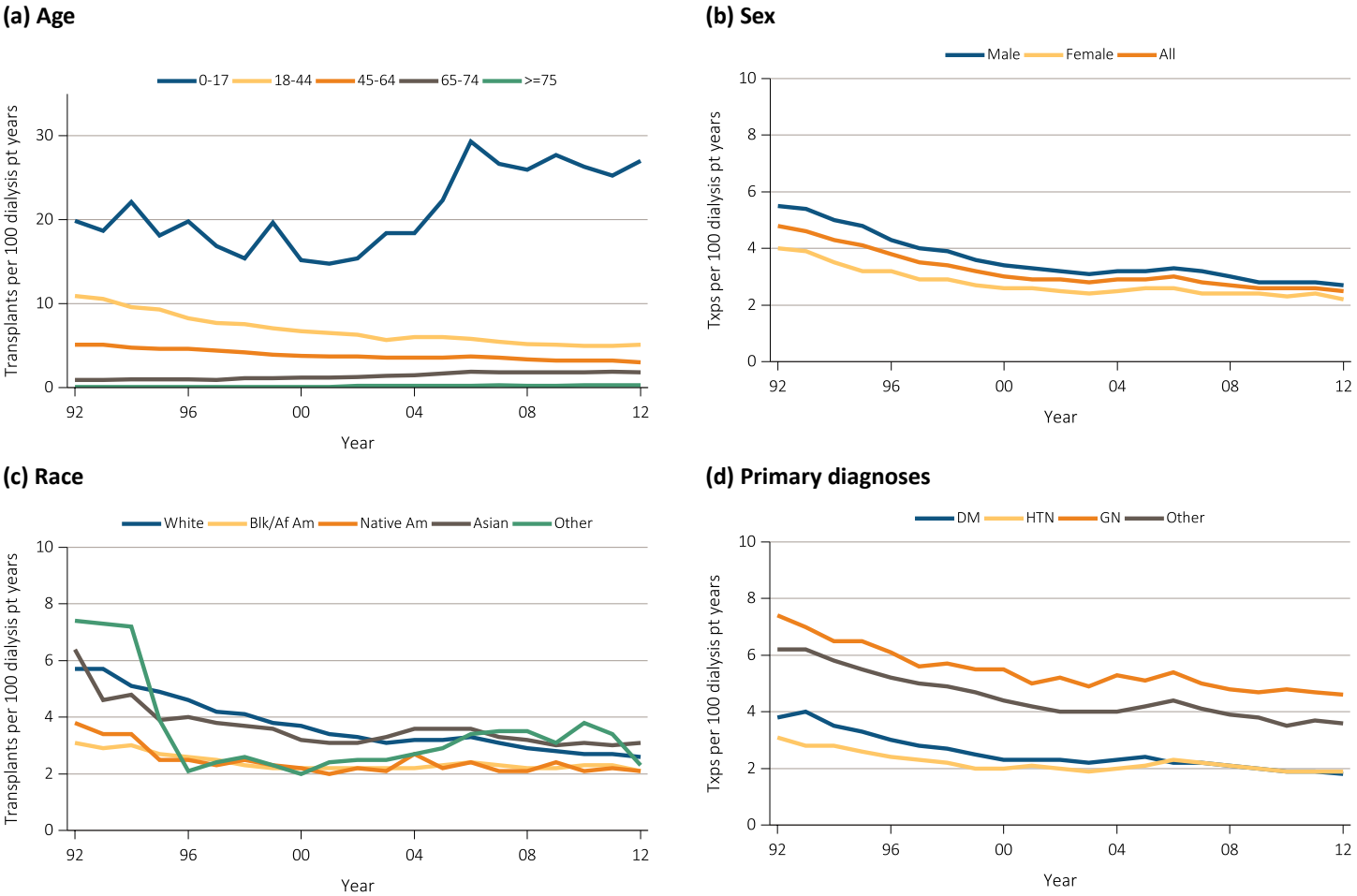
Rates of deceased donor transplantation per 100 dialysis patient years are presented by demographic categories without statistical adjustment. As shown in Figure 6.5.a (Age), the patterns look very different than that seen for deceased donor transplant counts in Figure 6.4.a (Age) because the number of dialysis patients varies and increases markedly with age. Due to the small denominator for children on dialysis and pediatric allocation priority for kidneys from deceased donors under the age of 35 years, deceased donor transplant rates are highest in children (<18 years old) and their rates increased in 2005-2007, stabilizing thereafter. While there has been a reduction in deceased donor kidney transplantation rates for those aged 18-44 and 45-64 years, the rates for those aged 65-74 years and 75 and over have stabilized at low levels.

The rates of deceased donor kidney transplantation declined for both male and female dialysis patients (Figure 6.5.b, Sex). This is explained partly by the increasing number of dialysis patients. The difference in transplantation rates between males and females has been narrowing in recent years.

Since 1992, the deceased donor transplant rates for White dialysis patients have declined, and since 2003, the transplant rates for Asians have been higher than for Whites (Figure 6.5.c, Race). The rates of deceased donor transplants for African Americans and Native Americans have remained low although their deficit compared to Whites has persisted.

The rates of deceased donor transplants for all diagnosis groups have been declining since 2006 (Figure 6.5.d, Primary diagnosis). Transplant rates among dialysis patients with glomerular disease by far exceeded that for any other diagnoses, followed by the category of other causes. Deceased donor transplant rates for candidates with ESRD attributed to hypertension and diabetes are similar to each other, but lower than that observed for the other two categories. This rank order likely is partly explained by differences in the average age of patients with these primary diagnoses.

vol 2 **Figure 6.5 Unadjusted transplant rates among deceased donors, by age, sex, race, & primary diagnosis**



Data Source: Reference Table E9(2). Unadjusted decease donor kidney transplant rates by age, sex, race, primary diagnosis. Abbreviations: Blk/Af Am, Black/ African American; DM, Diabetes Mellitus; GN, glomerulonephritis; HTN, hypertension; Native Am, Native American.

Counts of Living Donor Transplants

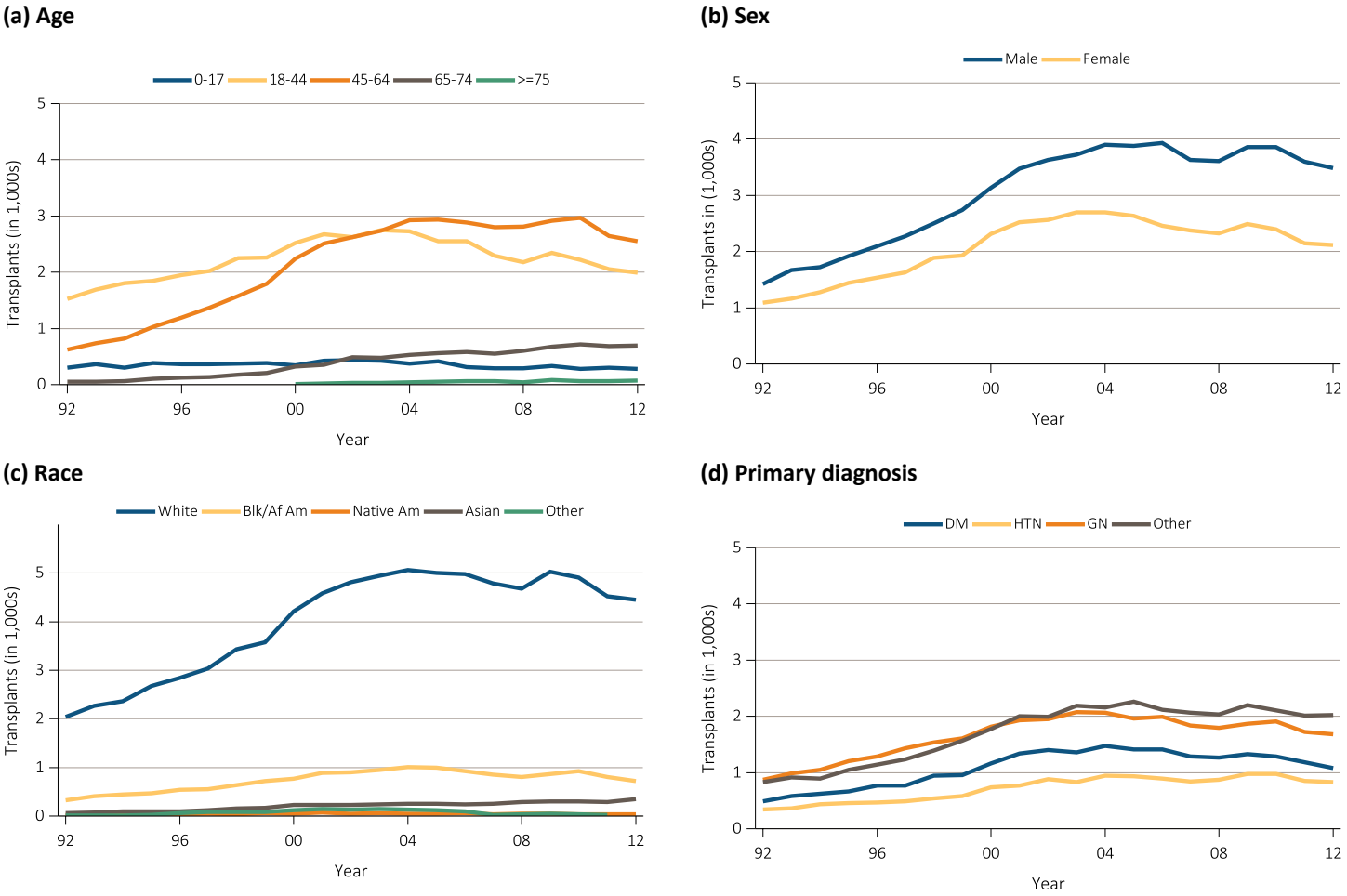
Live donor kidney transplants counts rose steadily for adult recipients between 1992 and 2004. Since 2004, the annual number of living donor transplants has declined. Counts for living donor transplants for those aged 18-44 years fell from 2,726 in 2004 to 1,991 in 2012, while the number of living donor transplants for the age group 45-64 years has shown a more recent decline, falling from 2,963 in 2010 to 2,549 in 2012 (Figure 6.6.a, Age). While transplant counts for those over 65 years old have shown an increase, more recently they have remained stable at close to 800 per year from 2010 to 2012.

The annual counts of live donor kidney transplantation show consistently higher numbers of male compared to female recipients (Figure 6.6.b, Sex). Since 2009, live donor kidney transplant counts have decreased for both males and females.

The overall live donor kidney transplant counts had been steadily increasing until 2004 for all races (Figure 6.6.c, Race). Since then, the number of live donor kidney transplants has decreased for Whites and African Americans while the counts for Asians have shown a small increase.

The ranking of living donor kidney transplantation counts by primary cause of ESRD (other, glomerulonephritis, diabetes, and hypertension) has remained the same over the past decade (Figure 6.6.d, Primary diagnosis). This is in contrast to the pattern seen in deceased donor recipients where the number with ESRD from diabetes mellitus has grown steadily in comparison to other diagnoses.

vol 2 Figure 6.6 Living donor transplant counts and trends by recipient age, sex, race, & primary diagnosis



Data Source: Reference Table E8(3). Live donor kidney transplant counts and trends by age, sex, race, and primary diagnosis. Abbreviations: Blk/Af Am, Black/African American; DM, Diabetes Mellitus; GN, glomerulonephritis; HTN, hypertension; Native Am, Native American.

Living Donor Transplant Rates

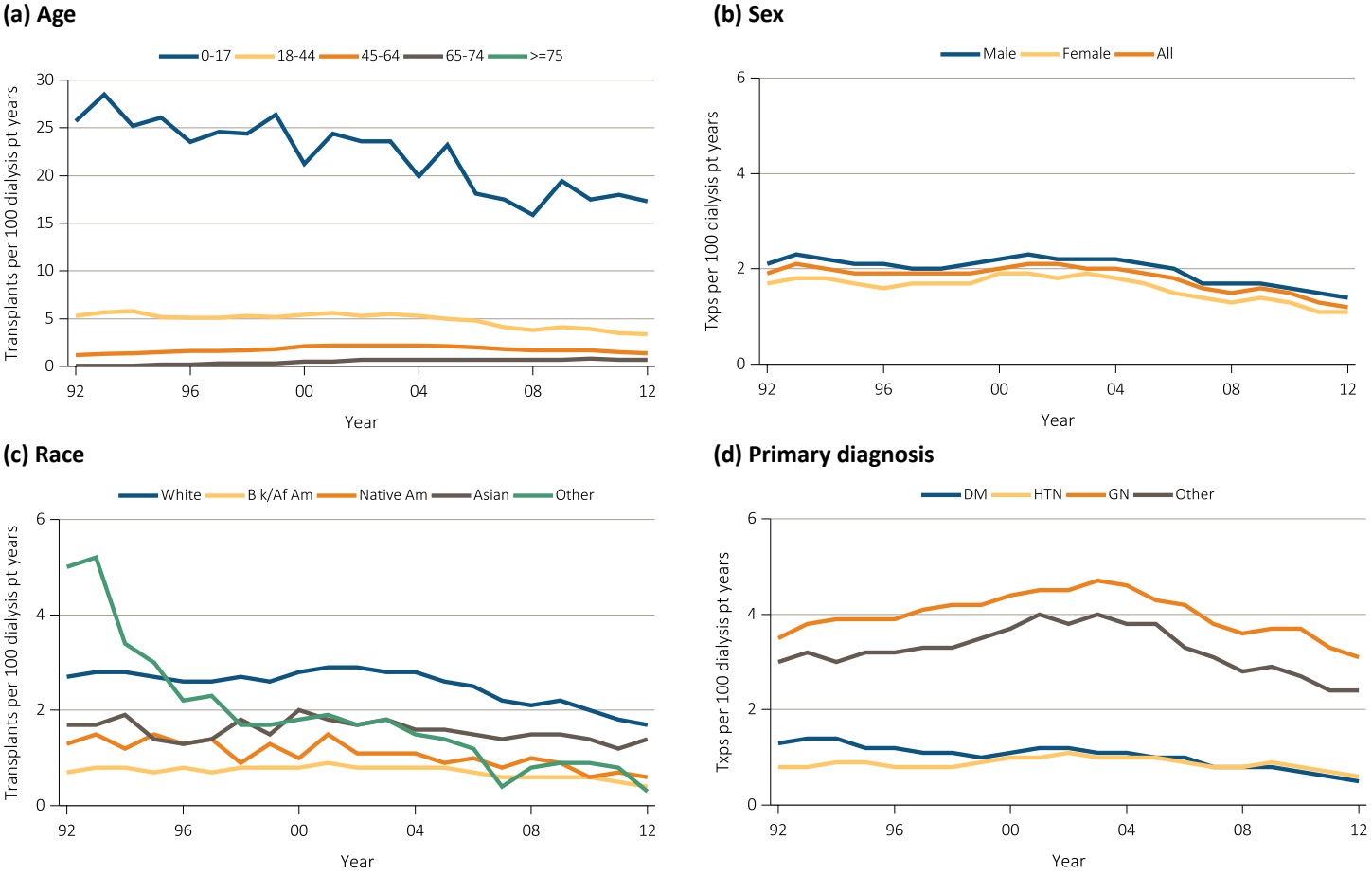
Similar to the observations for deceased donors, the patterns of living donor transplant counts (Figure 6.6) are markedly different from the unadjusted live donor transplantation rates shown in Figure 6.7, largely because the size of the dialysis patient denominator varies by patient group.

Kidney transplant rates from living donors per 100 dialysis patient years show that younger age groups have substantially higher annual transplant rates and also a steeper decline in these rates since about 1999 (Figure 6.7.a, Age). Among adults, the rates are declining slightly, but have remained highest for the 18-34 age group. Only the very low rates for ages 65-74 years have remained stable over the past decade.

The live donor transplant rates are higher for males than for females but the difference is relatively small (Figure 6.7.b, Sex). Live donor transplant rates for Whites are the highest among all racial groups while rates among Other are the lowest (Figure 6.7.c, Race). A decline since 2008 has been observed for all racial groups.

The rates of live donor transplantation for all diagnosis groups have been declining over the past decade (Figure 6.7.d, Primary diagnosis). The rate among patients with glomerular disease by far exceeds that for any other diagnoses, followed by other causes including cystic disease, and is lowest for hypertension and diabetes.

vol 2 **Figure 6.7 Unadjusted transplant rates among living donors, by age, sex, race, & primary diagnosis**



Data Source: Reference Table E9(3). Unadjusted live donor kidney transplant rates by age, sex, race, primary diagnosis. Abbreviations: Blk/Af Am, Black/African American; DM, Diabetes Mellitus; GN, glomerulonephritis; HTN, hypertension; Native Am, Native American.

Outcomes and Follow-up Care

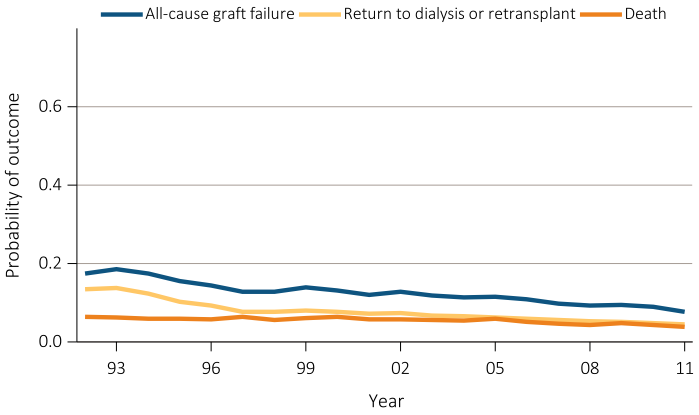
Among recipients of a deceased donor kidney transplant in 2011, the probability of all-cause graft failure (including death with a functioning graft) in the first year following transplant was 0.08 (Figure 6.8.a, One-year), compared to 0.03 in those receiving a transplant from a living donor (Figure 6.9.a, One-year). The probability of death among the recipients who received a deceased donor kidney transplant in the first year post-transplant was 0.04 (Figure 6.8.a, One-year), compared to 0.01 (Figure 6.9.a, One-year) in those receiving a living donor transplant.

The one-year graft survival and patient survival advantage experienced by living donor transplant recipients persists at five and ten years post-transplant, with probabilities of all-cause graft failure of 0.17 (Figure 6.9.b, Five-year) and 0.41 (Figure 6.9.c, Ten-year), compared to 0.29 (Figure 6.8.b, Five-year) and 0.54 (Figure 6.8.c, Ten-year), respectively, for those receiving a deceased donor transplant.

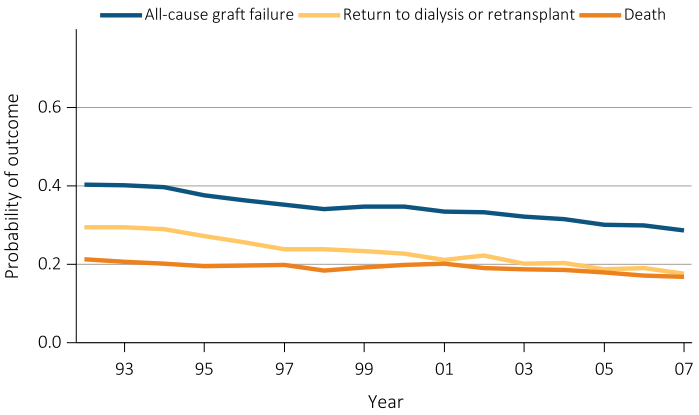
From 1991 to 2002, the probability of returning to dialysis or repeat transplantation by the tenth year post-transplant fell 10 and seven percent for deceased and living donor first-time kidney transplant recipients, respectively. The probability of death at 10 years post-transplant remained fairly stable for both deceased and living donor first-time kidney transplant recipients. The probability of death at one, five, and 10 years post-transplant is substantially higher for deceased donor transplant recipients than living donor transplant recipients.

vol 2 Figure 6.8 Outcomes: deceased donor transplants

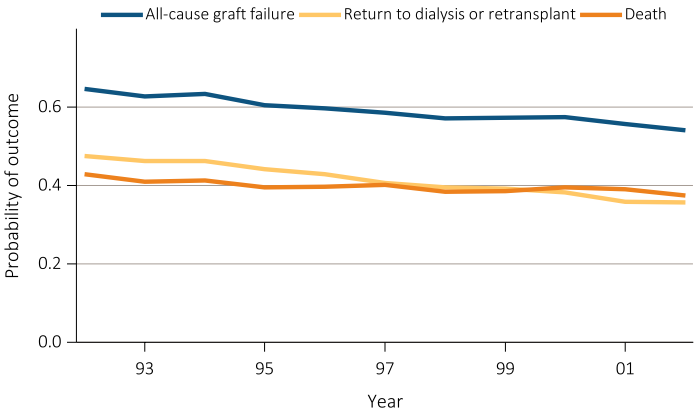
(a) One-year



(b) Five-year



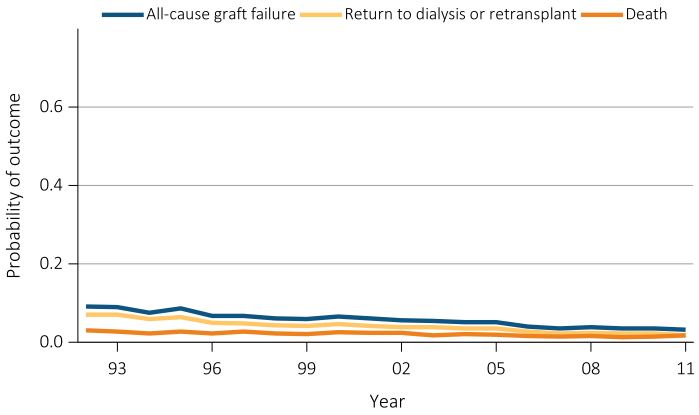
(c) Ten-year



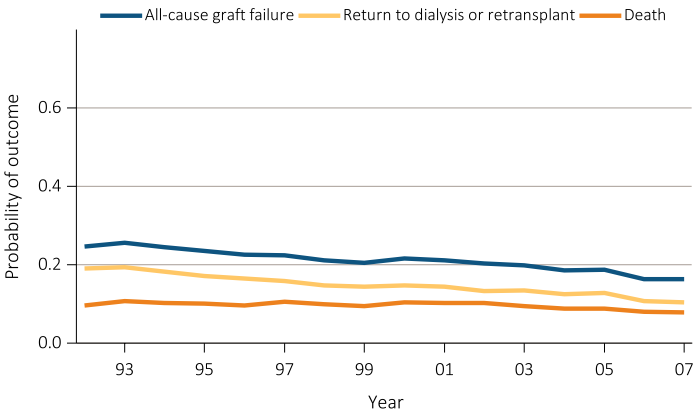
Data Source: Reference Tables F2, F14, I26; F5, F17, I29; F6, F18, I30. Outcomes among recipients of a first-time deceased donor kidney transplant; unadjusted.

vol 2 Figure 6.9 Outcomes: living donor transplants

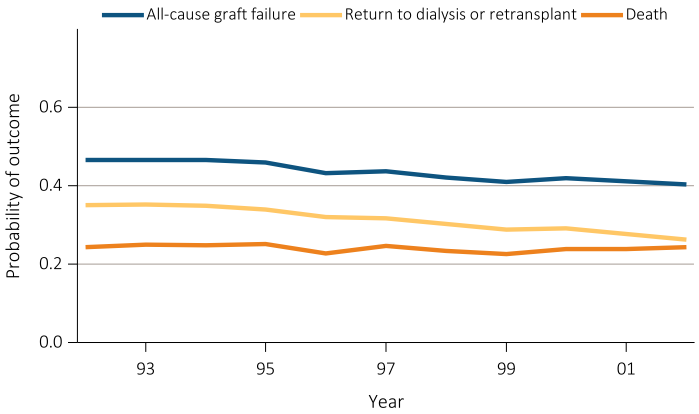
(a) One-year



(b) Five-year



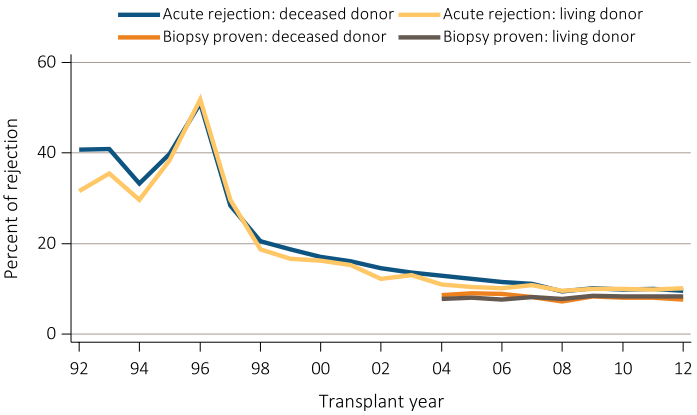
(c) Ten-year



Data Source: Reference Tables F8, F20, I32; F11, F23, I35; F12, F24, I36. Outcomes among recipients of a first-time live donor kidney transplant; unadjusted.

The percentage of kidney transplant recipients experiencing an acute rejection during the first year post-transplant has declined steadily since 1996 and stabilized in recent years (Figure 6.10). The risk of rejection is similar for living donor and deceased donor kidney transplants.

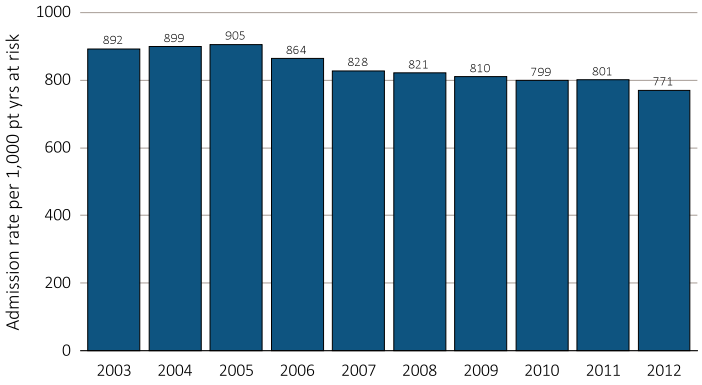
vol 2 Figure 6.10 Acute rejection within the first year post-transplant



Data Source: Special analyses, USRDS ESRD Database. Acute rejection rates during the first year post-transplant for recipients age 18 and older with a functioning graft at discharge.

The hospitalization rate for all kidney transplant recipients has declined steadily since 2005 (Figure 6.11).

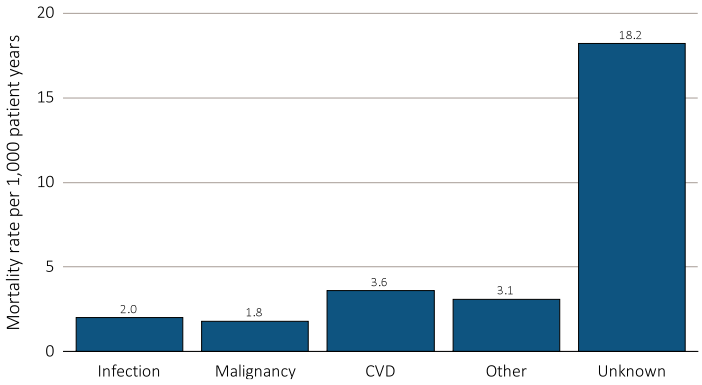
vol 2 Figure 6.11 Post-transplant total hospital admission rates



Data Source: Reference Table G5. All kidney transplant recipients.

Figure 6.12 displays post-transplant mortality rate by primary causes of death for patients who received a deceased or live donor kidney-alone or kidney plus an additional organ transplant during 2010–2012. The death rate from cardiovascular disease is nearly twice that observed for infection or malignancy.

vol 2 Figure 6.12 Mortality rate by causes of death



Data Source: Reference Table H12. Kidney transplant recipients who died.

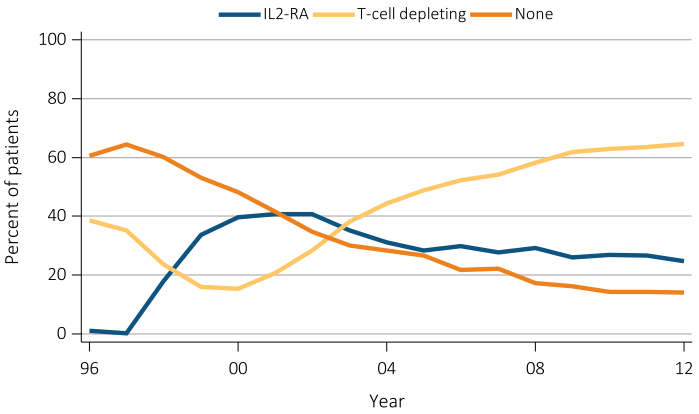
The majority (90 percent in 2012) of kidney transplant recipients received antibody induction. While the use of anti-IL2-RA (interleukin-2 receptor) antagonists has fallen from a peak of 41 percent in 2002, the use of T-cell depleting agents continues to increase, reaching 65 percent in 2012 (Figure 6.13.a, Induction agents).

Nearly all transplant recipients in 2012 received a calcineurin inhibitor (Figure 6.13.b, Calcineurin inhibitor at transplant) and an anti-metabolite (Figure 6.13.c, Anti-metabolites at transplant) as components of their initial immunosuppressive regimen. Ninety-two percent of these patients were prescribed tacrolimus as their first-line calcineurin inhibitor, and mycophenolate has almost completely replaced azathioprine as the anti-metabolite of choice. Use of mTOR inhibitors, both initially and at one year following transplantation, has declined to 2 and 4 percent, respectively, in 2012 (Figure 6.13.d, mTOR inhibitors), while steroid use seems to be stabilizing at about 67 percent (Figure 6.13.e, Steroids).

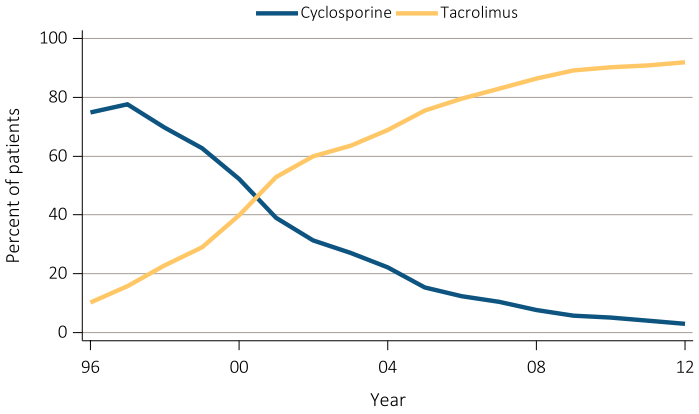
The trends in donation, access to transplantation, treatment and outcomes observed in kidney transplantation over the past 15 years deserve future monitoring.

vol 2 Figure 6.13 Immunosuppression use at transplantation (and one year post-transplant)

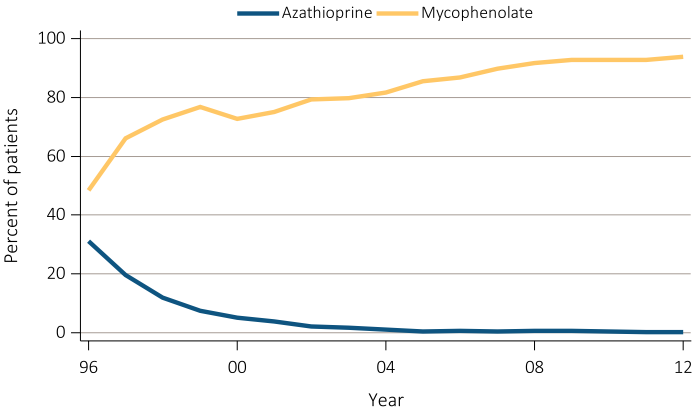
(a) Induction agents



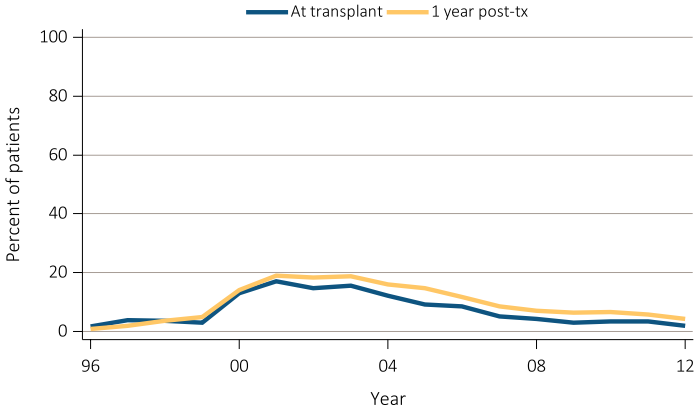
(b) Calcineurin inhibitors at transplant



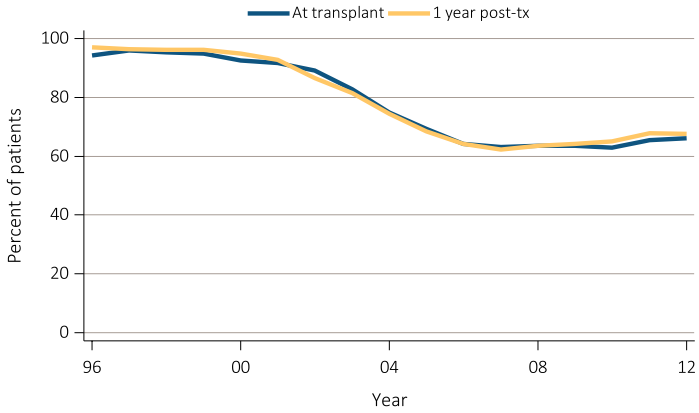
(c) Anti-metabolites at transplant



(d) mTOR inhibitors



(e) Steroids



Data Source: Special analyses, USRDS ESRD Database. All adult kidney transplant recipients. Abbreviations: IL2-RA, interleukin 2 receptor antagonist.