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# Patient and allograft survival of Indo Asian and East Asian dialysis patients treated in Canada

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**Kidney failure is relatively common among Canadians of Asian origin. However, little is known about the health outcomes after initiation of renal replacement therapy in this population. Our study evaluates differences in the likelihood of renal transplantation and graft loss among Asian and white patients. We studied 21 523 adults of East Asian, Indo Asian or white ethnicity who had initiated dialysis in Canada from 1990–2000. Subjects were followed until death, loss to follow-up or end of study (2004). The proportion of the eligible subjects who were East Asian, Indo Asian, or white was 6, 3, and 91%, respectively. Compared to white patients, East Asian and Indo Asian patients were significantly less likely to receive a renal transplant after adjusting for potential confounding factors. This disparity is greater for transplants from living donors as compared to those from deceased donors. The adjusted death censored graft loss in transplant recipients was not significantly different between ethnic groups. The adjusted risk of death following transplantation, however, was significantly lower in Indo Asian than in white patients. Our findings show that in a Canadian population, patients of East Asian or Indo Asian origin had lower rates of renal transplantation than white patients, especially for living donor transplantation. These findings warrant further study, especially given the good graft outcomes in these individuals.**

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Canada has relatively large and rapidly growing populations of people whose ancestors were from Indo Asia (also referred to as the Indian subcontinent) and East Asia (countries such as China, Japan, and Korea). In Canada, as in other countries, people of Asian origin are at increased risk for renal diseases, leading to a rising prevalence of kidney failure among Indo and East Asian Canadians.<sup>1–3</sup>

American studies of Asian people with kidney failure have tended to focus on East Asians, and have suggested that this population is at reduced risk of graft loss compared with whites.<sup>4</sup> In contrast, British work typically evaluates people of Indo Asian descent and indicates similar or worse graft survival compared with whites.<sup>5,6</sup> Limited data suggest that both these populations have less access to transplantation than whites. Suggested explanation include socioeconomic factors which may influence access to medical care,<sup>7</sup> and higher prevalence of blood group types which are less favorable for transplantation, namely blood type B.<sup>8</sup> Few studies examine access to transplantation or transplantation-related outcomes in Asian patients outside the United States or Great Britain.

We conducted this study to evaluate the likelihood of renal transplantation and risk of graft loss among people of East Asian or Indo Asian origin who recently initiated dialysis in Canada, which offers equal access to universal health care to all residents.

## RESULTS

### Patient characteristics

There were 26 098 incident dialysis patients in the study, of whom 2179 patients were not white, East Asian, or Indo Asian in origin and were therefore excluded. An additional 2396 individuals had missing data on race and were also excluded. Of the remaining 21 523 incident patients, 1243 (6%) were of East Asian and 736 (3%) were of Indo Asian origin. Of these patients, 5424 (25%) received a transplant (1350 (25%) from living donors). The median length of follow-up from time of dialysis initiation until transplant,

**Table 1 | Demographics and clinical characteristics**

	n (%)			P-value
	East Asian	Indo Asian	White	
N	1243 (6)	736 (3)	19 544 (91)	
Age (years) <sup>a</sup>	65 (48, 73)	58 (46, 67)	64 (50, 73)	<0.0001
Male	672 (54)	455 (62)	11 895 (61)	<0.0001
<i>Cause of ESRD</i>				
Diabetic nephropathy	346 (28)	297 (40)	5342 (27)	<0.0001
Glomerulonephritis	325 (26)	131 (18)	3352 (17)	<0.0001
Hypertensive/ischemic renal disease	205 (16)	104 (14)	4038 (21)	<0.0001
Polycystic kidney disease	29 (2)	28 (4)	1169 (6)	<0.0001
Other	338 (27)	176 (24)	5643 (29)	0.007
<i>Comorbidity</i>				
Diabetes mellitus <sup>b</sup>	73 (6)	51 (7)	1322 (7)	0.46
Coronary disease <sup>c</sup>	263 (21)	239 (32)	6514 (33)	<0.0001
Chronic heart failure	282 (23)	265 (36)	5524 (28)	<0.0001
Stroke or TIA	88 (7)	60 (8)	2041 (10)	0.0001
Chronic lung disease	31 (2)	26 (4)	2127 (11)	<0.0001
Peripheral vascular disease	89 (7)	93 (13)	3589 (18)	<0.0001
Malignancy	64 (5)	19 (3)	1852 (9)	<0.0001
Current smoker	54 (4)	39 (5)	2895 (15)	<0.0001
Initial peritoneal dialysis modality	523 (42)	321 (44)	5502 (28)	<0.0001
Lowest quintile of SES	369 (30)	235 (32)	4407 (23)	<0.0001
<i>Year of dialysis initiation</i>				
1990–1992	227 (18)	132 (18)	4017 (21)	0.04
1993–1994	209 (17)	122 (17)	3242 (17)	0.98
1995–1996	241 (19)	120 (16)	3638 (19)	0.22
1997–1998	271 (22)	162 (22)	4170 (21)	0.85
1999–2000	295 (24)	200 (27)	4477 (23)	0.02
Rural	25 (2)	8 (1)	4220 (22)	<0.0001
<i>Blood group type</i>				
O	312 (41)	157 (35)	5948 (45)	<0.0001
A	212 (28)	113 (25)	5405 (41)	<0.0001
B	178 (23)	150 (33)	1436 (11)	<0.0001
AB	58 (8)	35 (8)	536 (4)	<0.0001

ESRD, end-stage renal disease; SES, socioeconomic status; TIA, transient ischemic attack.

East Asian=participants from Indonesia, China, Philippines, Vietnam, Laos, Singapore, Japan, and Korea; Indo Asian=participants from India, Pakistan, Bangladesh, Nepal, Maldives, and Afghanistan.

<sup>a</sup>Median (interquartile range) and P-value from Kruskal-Wallis test otherwise n (%) and P-value from  $\chi^2$  test.

<sup>b</sup>In participants for whom the primary cause of ESRD was not diabetic nephropathy.

<sup>c</sup>Includes angina, prior myocardial infarction or prior coronary revascularization.

death, or end of study was 2.5 years (1 day to 15 years). Furthermore, 250 (1%) patients were lost to follow-up and were censored after a median period of 1.8 years. Demographic characteristics of study participants appear in Table 1.

East Asian patients were more likely to have glomerulonephritis as the cause of kidney failure, and had less comorbidity such as coronary disease and chronic heart failure than either Indo Asian or white subjects (Table 1). Indo Asian patients were younger and more likely to have diabetic nephropathy than either East Asian or white patients. Both East Asian and Indo Asian patients were more likely to live in low income neighborhoods and less likely to have a rural location of residence.

There were also significant differences in blood group type by race, among the 14 540 (68%) participants who had

information on this characteristic. The proportion of Indo Asian participants with type O, A, B, and AB blood group was 35, 25, 33, and 8%, respectively, as compared with 41, 28, 23, and 8% among East Asian and 45, 41, 11, and 4% among white participants. As blood groups A and AB are associated with a higher likelihood of transplantation than groups O and B, and as group A is much more common than group AB, these differences are likely to place East and Indo Asian patients at a relative disadvantage compared with whites.

### Transplantation

Adjusted transplantation rates per 100 patient years during the study period were 4.5 (95% confidence interval (CI) 3.8–5.2), 4.4 (95% CI 3.7–5.2) and 6.3 (95% CI 5.6–7.0) for East Asian, Indo Asian, and white patients, respectively (pairwise comparisons vs white patients; both  $P < 0.0001$ ).

**Table 2 | Transplantation by race**

	Any transplant			Deceased donor transplant only			Living donor transplant only		
	N (%)	Age-adjusted HR (95% CI)	Adjusted <sup>a</sup> HR (95% CI)	N (%)	Age-adjusted HR (95% CI)	Adjusted <sup>a</sup> HR (95% CI)	N (%)	Age-adjusted HR (95% CI)	Adjusted <sup>a</sup> HR (95% CI)
East Asian	380 (31)	0.88 (0.79, 0.97)	0.71 (0.63, 0.79)	335 (27)	1.03 (0.92, 1.15)	0.90 (0.80, 1.01)	45 (3.6)	0.42 (0.31, 0.56)	0.27 (0.20, 0.37)
Indo Asian	203 (28)	0.69 (0.60, 0.80)	0.69 (0.60, 0.80)	163 (22)	0.74 (0.63, 0.87)	0.82 (0.70, 0.97)	40 (5.4)	0.55 (0.40, 0.75)	0.42 (0.31, 0.58)
White	4841 (25)	1.0	1.0	3576 (18)	1.0	1.0	1265 (6.5)	1.0	1.0

CHD, coronary heart disease; CHF, chronic heart failure; CI, confidence interval; DM, diabetes mellitus; ESRD, end-stage renal disease; HR, hazard ratio; HTN, hypertension; SES, socioeconomic status; TIA, transient ischemic attack.

East Asian=participants from Indonesia, China, Philippines, Vietnam, Laos, Singapore, Japan, and Korea; Indo Asian=participants from India, Pakistan, Bangladesh, Nepal, Maldives, and Afghanistan.

The median year of transplant (interquartile range) among those receiving transplants was 1999 (1995, 2001) for East Asians, 1998 (1995, 2001) for South Asians, and 1997 (1994, 2000) for white patients.

<sup>a</sup>Adjusted for age, sex, primary cause of ESRD, year of diagnosis, comorbidities (DM, CHD, HTN, CHF, stroke or TIA, chronic lung disease, serious medical illness, peripheral vascular disease, malignancy), smoking status, initial dialytic modality, SES, rural status, and geographic region.

Among patients receiving a transplant, the proportion originating from a living donor was significantly lower among East Asian recipients (12%) than either Indo Asian (20%) or white (26%) recipients ( $P < 0.0001$ ). The adjusted likelihood of transplantation was substantially lower for both East Asian and Indo Asian patients than for white patients, especially for living donor transplantation ( $P < 0.0001$ , Table 2).

In the subgroup of patients for whom blood group type was available, additional adjustment for this characteristic did not appreciably change the overall likelihood of transplantation associated with East Asian (hazard ratio (HR) 0.67 and 0.71 with and without adjustment for blood group type) or Indo Asian (HR 0.71 and 0.69 with and without adjustment for blood group type, respectively) race. However, there was a significant interaction between Indo Asian race and blood group type on the likelihood of transplantation ( $P = 0.006$ ). Specifically, among those of AB blood group type, transplantation was nonsignificantly more likely in Indo Asians than in white patients (HR 1.35, 95% CI 0.82–2.24). However, Indo Asians were significantly less likely than white patients to receive transplants in strata defined by all other blood group types, with HR of 0.60 (95% CI 0.46–0.78), 0.70 (95% CI 0.54–0.92), 0.69 (95% CI 0.51–0.92) for types O, A, and B, respectively.

There was no evidence that patient age, sex, diabetic status, socioeconomic status, initial dialytic modality or informative censoring influenced the association between race and transplantation. Three additional sensitivity analyses that reclassified the race of all subjects who were of unknown race as white, or as East Asian, or as South Asian (in turn, one at a time) did not affect the findings. Specifically, the rate of transplantation remained significantly lower among East or South Asian patients than in white patients for all three analyses.

Because we did not have information on transplant waitlist status, it is possible that comorbid disease affected eligibility and thus rates of transplantation. Therefore, we performed an additional analysis considering only younger patients with less comorbidity (age  $< 60$  years without

known coronary disease, chronic heart failure, stroke, chronic lung disease, peripheral vascular disease, known malignancy, or other serious medical illness that would be expected to reduce life expectancy). In the remaining 4135 patients, Indo Asian and East Asian race were again independently associated with lower rates of renal transplantation (HR 0.66, 95% CI 0.55–0.80 and HR 0.70, 95% CI 0.61–0.79, respectively).

#### Graft loss and death after transplantation

Adjusted graft failure rates per 100 patient years during the study period were 4.5 (95% CI 3.3–6.3), 3.9 (95% CI 2.7–5.8), and 5.3 (95% CI 4.1–6.8) for East Asian, Indo Asian, and white patients, respectively. The likelihood of graft loss was similar in all three racial groups whether death was considered a cause of graft failure or not (Table 3). There was no significant interaction between older recipient age, male sex, or dialytic modality and the risk of graft loss by race, suggesting that graft survival in Asians and non-Asians was similar regardless of these characteristics. Although the risk of death among transplant recipients did not significantly differ between East Asian and white recipients (HR 0.72, 95% CI 0.49–1.04), Indo Asian transplant recipients were at markedly lower risk of post-transplantation death than white recipients (HR 0.44, 95% CI 0.25–0.79) (Table 3 and Figure 1).

#### DISCUSSION

After statistical adjustment, East and Indo Asian dialysis patients were significantly less likely than white patients to receive a kidney transplant. The disparity was even more pronounced when considering transplants obtained from a living donor, which is important, as this inequity is potentially amenable to intervention. Although East and Indo Asian patients were both less likely than white patients to have relatively favorable blood group types, their likelihood of transplantation remained lower than white patients after adjustment for this characteristic, suggesting that other factors are responsible for the disparity. We also found that the risk of death following transplantation was similar or

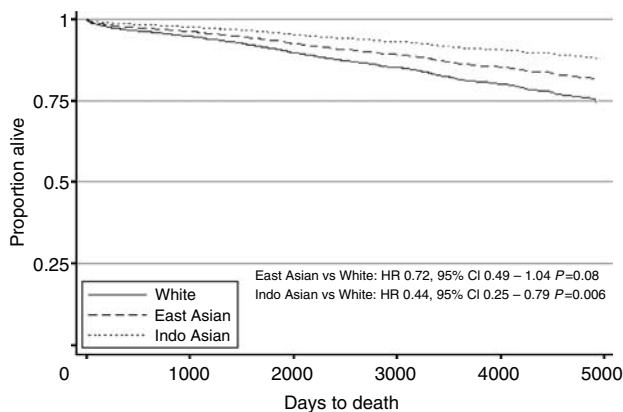
**Table 3 | Graft failure or death by race**

	Graft failure or death			Graft failure			Death		
	N (%)	Age-adjusted HR (95% CI)	Adjusted <sup>a</sup> HR (95% CI)	N (%)	Age-adjusted HR (95% CI)	Adjusted <sup>a</sup> HR (95% CI)	N (%)	Age-adjusted HR (95% CI)	Adjusted <sup>a</sup> HR (95% CI)
East Asian	92 (24)	0.90 (0.73, 1.11)	0.85 (0.68, 1.06)	61 (16)	1.01 (0.78, 1.31)	0.93 (0.71, 1.23)	31 (8.2)	0.74 (0.52, 1.06)	0.72 (0.49, 1.04)
Indo Asian	46 (23)	0.80 (0.60, 1.08)	0.75 (0.55, 1.00)	34 (17)	1.03 (0.73, 1.45)	0.96 (0.67, 1.36)	12 (5.9)	0.50 (0.28, 0.88)	0.44 (0.25, 0.79)
White	1450 (30)	1.0	1.0	821 (17)	1.0	1.0	629 (13)	1.0	1.0

CHD, coronary heart disease; CHF, chronic heart failure; CI, confidence interval; DM, diabetes mellitus; ESRD, end-stage renal disease; HR, hazard ratio; HTN, hypertension; SES, socioeconomic status; TIA, transient ischemic attack.

East Asian=participants from Indonesia, China, Philippines, Vietnam, Laos, Singapore, Japan, and Korea; Indo Asian=participants from India, Pakistan, Bangladesh, Nepal, Maldives, and Afghanistan.

<sup>a</sup>Adjusted for age, sex, primary cause of ESRD, year of diagnosis, comorbidities (DM, CHD, HTN, CHF, stroke or TIA, chronic lung disease, serious medical illness, peripheral vascular disease, malignancy), smoking status, initial dialytic modality, SES, rural status, geographic region, type of donor, and time on dialysis (<1, 1–1.9, ≥2 years).



**Figure 1 | Time to death following kidney transplantation, by race.** Curves have been adjusted for age, sex, primary cause of end-stage renal disease, year of diagnosis, comorbidities (diabetes mellitus, coronary heart disease, hypertension, chronic heart failure, stroke or transient ischemic attack, chronic lung disease, serious medical illness, peripheral vascular disease, malignancy), smoking status, initial dialytic modality, socioeconomic status, rural status, geographic region, type of donor, and time on dialysis (<1, 1–1.9, ≥2 years).

lower in East Asian patients than in white patients, and was lowest among Indo Asian transplant recipients, in whom the risk was approximately 50% lower than in white recipients. This finding is similar to the generally good outcomes reported among incident East and Indo Asian dialysis patients, who have lower mortality rates compared with white patients.<sup>9</sup>

In contrast to earlier studies which showed slightly worse graft survival in Indo Asians as compared with white patients,<sup>5</sup> we found that graft outcomes were similar in patients from all three racial groups. Our findings are similar to a recent study from the United Kingdom, which found equivalent graft outcomes in Indo Asian and white patients.<sup>6</sup> Our findings are slightly different from much larger American studies, which showed that graft survival was better in American people of East Asian descent than in white patients.<sup>4,10</sup> Although our study was substantially smaller, the point estimates for the risk of graft loss among East Asians are close to unity, suggesting that the discrepant findings are

not likely to be due to low statistical power. Given the similarity of our findings to those reported in the United Kingdom (which also has a universal health-care system), we speculate that ethnic minorities in Canada may have more equitable access to transplantation services than those in the United States. However, as our study did not directly compare outcomes between patients treated in different countries, this hypothesis will require confirmation in future studies.

Future studies seeking to determine how to increase transplantation rates among Asian people should focus on three general areas. First, educational programs that target the families and community members of Asian people with kidney disease should be considered. Studies from the United Kingdom indicate that Indo Asian people may be less likely to donate kidneys because of religious beliefs, although other cultural factors (such as the reticence of family members to make a decision about donation on behalf of a deceased relative) may also play a role.<sup>11–13</sup> None of the major Asian religions forbid organ donation, and a 1995 fatwa (edict) from the Muslim Law Council specifically states that organ donation is acceptable.<sup>11,14</sup> However, studies have shown that many UK Muslims are unaware of the fatwa, which (if confirmed in other populations) would suggest that community-based initiatives involving religious leaders may be useful for increasing donation.<sup>15,16</sup> The merit of this approach could be tested in prospective clinical trials, perhaps using a randomized cluster design. In the meantime, transplantation programs should consider targeted educational interventions directed at increasing living and deceased kidney donation for East and Indo Asian patients, especially as graft outcomes appeared favorable in these populations.

Second, as not all Asian immigrants to Canada speak fluent English (especially the elderly), some or all of our findings may be due to a language barrier. Language has been inadequately studied as a potential obstacle to transplantation (and to good quality medical care in general). As this barrier is potentially remediable with the aid of translators, future studies should examine this possibility in detail.

Finally, the explanation for the lower rate of transplantation among Asian patients is probably multifactorial. Therefore,

comprehensive studies that examine all phases of the transplantation workup process would be helpful, as has been done for other ethnic minorities.<sup>17</sup> Such studies should evaluate patient knowledge and preference for transplantation, provider attitudes, transplant referral, transplant wait-listing, and factors which influence time on the waiting list such as intercurrent illness, comorbidity, and immunological characteristics.<sup>7,11,17–23</sup> As the relative importance of such factors might differ among recent immigrants as compared to Canadian-born people of Asian descent, future work should consider these two groups separately. Findings from these studies will be increasingly relevant to clinical care, as the proportion of East and Indo Asian people in the general Canadian population has nearly doubled over the last decade, and further increases are expected in the future.<sup>24,25</sup>

Our study has several limitations. First, Asian patients might be less interested in receiving a kidney transplant than those of white race, which might partially account for the observed disparities. Unfortunately, we did not have data on patient preference for transplantation. Second, bias could have resulted from the exclusion of patients with unknown racial status. However, data are unlikely to have been missing more frequently among East Asian or Indo Asian patients. Information, which was missing or incorrect at random, would bias our results toward the null, suggesting that this limitation is unlikely to have affected our findings. Similarly, racial status was provided by dialysis center personnel, rather than by the subjects themselves, and thus race may have been incorrectly classified in some cases. In addition, the terms we used to define ethnicity may encompass groups of heterogeneous origin – exemplified by people from Guyana and Pakistan – who might both be classified as Indo-Asian although the former would be more likely to also have African ancestors. Although we cannot exclude this possibility, it is unlikely that differential misclassification occurred by race. Again, this suggests that any resulting bias would reduce statistical power rather than result in spurious findings. Third, we did not have data on donor characteristics such as age, sex, or terminal kidney function, or on information relating to the perioperative period such as cold ischemic time or delayed graft function. Although most potentially important recipient characteristics were included in the data set, immunological data (such as panel reactive antibody peak or human leukocyte antigen mismatch), and information on rejection episodes, immunosuppressive therapy, and compliance with medications were not available. Finally, our study is limited by the lack of data on transplant wait-list status, although findings were similar when only subjects who were likely to be good transplant candidates were included.

In conclusion, we found that patients of East or Indo Asian origin receiving dialysis in Canada had lower rates of renal transplantation than white patients, especially for living donor transplantation. Programs aimed at increasing living donation in East and Indo Asian communities may be useful for reducing these disparities.

## MATERIALS AND METHODS

### Study population and data sources

This study was approved by the ethics review board at the University of Alberta and was conducted on a random sample of data from the Canadian Organ Replacement Registry (CORR).<sup>3,26</sup> CORR is a national registry, which collects patient-specific data annually from all Canadian dialysis centers. Patient data are collected by health professionals based on personal knowledge of the patient, chart review, and in some cases, direct inquiry. Using a previously described process that ensured the privacy of subjects,<sup>27</sup> we received a randomly selected subject-level data set from CORR, which included demographic, clinical, treatment, and outcomes data for approximately 73% of all subjects initiating dialysis in Canada between 1 January 1990 and 31 December 2000.

In the CORR registry, patient race is categorized as white, black, Aboriginal, Asian, Indian subcontinent, mideast/Arabian, Pacific Islander, other, and unknown. People of Asian race (East Asian) included those from Indonesia, China, Philippines, Vietnam, Laos, Singapore, Japan, and Korea, whereas people from the Indian subcontinent (Indo Asian) included those from India, Pakistan, Bangladesh, Nepal, Maldives, and Afghanistan. Determination of race is made at the discretion of the health-care professional, as CORR procedure does not require that patients be asked directly about racial status. As the focus of this study was on individuals of Asian origin and as the majority of Canadian dialysis patients are white, individuals who were neither white nor of Asian origin were excluded from this analysis.

### Analyses

The primary outcome was time to receipt of a deceased or living donor kidney transplant. Follow-up time was defined by the period beginning at initiation of dialysis and ending at transplantation, death, loss to follow-up, or end of study (31 December 2004). In secondary analyses, we also considered time to graft loss among transplanted patients from time of transplant. The primary definition of graft loss included death with function; in additional analyses, we considered the outcome of death-censored graft loss.

The independent associations between East Asian or Indo Asian race and time to event outcomes were determined using Cox proportional hazards models, after adjustment for potential confounders, including age, sex, race (white, East Asian, and Indo Asian); cause of end-stage renal disease; year of dialysis initiation; comorbid conditions (diabetes mellitus, coronary disease, previous/current hypertension, chronic heart failure, stroke or transient ischemic attack, chronic lung disease, peripheral vascular disease, malignancy, other serious medical illness); smoking status; initial mode of dialysis; low socioeconomic status (lowest quintile of mean neighborhood income); geographic region of residence (Atlantic Canada, Quebec, Ontario, Manitoba, Saskatchewan, Alberta, British Columbia); rural location of residence (as defined by Statistics Canada<sup>28</sup>); and blood group type (O, A, B, or AB). Models evaluating outcomes after transplantation also adjusted for donor source (deceased vs living donor) and time on dialysis before transplantation (<1, 1–1.9, and  $\geq 2$  years). In order to determine whether the association between race and outcomes differed in participants with certain clinical characteristics, we explored two-way interactions between race and age, sex, socioeconomic status, and initial dialytic modality on the likelihood of the clinical outcomes. We determined that the proportional hazard assumption was satisfied by examining plots of the log-negative-log of the within-group survivorship probabilities vs log-time.

Missing data were dealt with by assuming that the characteristic was absent (10% had missing data on one or more comorbid conditions) or representing the missing data with an indicator variable (9% had missing data on race and 32% had missing data on blood group type). Additionally, participants with unknown races were reclassified as East Asian, Indo Asian, and white in separate analyses. Results did not differ when analyses were repeated after deleting or reclassifying all subjects with missing data, so we have reported results assuming missing comorbid conditions were absent and excluding subjects of unknown race. The primary analysis did not include blood group type, given the large number of subjects for whom this information was unavailable. However, to evaluate whether our findings were influenced by racial differences in blood group type, we performed additional analyses, which evaluated the independent association between race and the likelihood of transplantation or graft loss after adjustment for blood group type and the other variables in the final model.

To deal with other methodological uncertainties, the following sensitivity analyses were conducted. To determine if the relations between race and the clinical outcomes were influenced by donor source, we repeated analyses considering only transplants from deceased donors by censoring follow-up at the time of living donor transplantation. Additionally, we repeated analyses considering only transplants from living donors. Because we did not have information on transplant wait-list status, it is possible that comorbidity affected eligibility and thus rates of transplantation. We addressed this with an additional analysis considering only non-diabetic subjects aged <60 years without known coronary disease, chronic heart failure, stroke, chronic lung disease, peripheral vascular disease, known malignancy, or other serious medical illness that might reduce the likelihood of wait-listing for transplantation. Finally, we assessed the potential for informative censoring (as those who die early are less likely to have received a kidney transplant) by assuming that those who died would not have received a transplant if they had survived until the end of the study (i.e. patients who died were assigned a date of last follow-up of December 31, 2004).

Rates and survival curves were calculated with adjustment for the mean age and the most frequent levels of the categorical covariates in the sample. Statistical analyses were performed using Stata SE 9.0 (College Station, TX, USA) and SAS 9.1 (Cary, NC, USA). Statistical significance was set at  $P < 0.05$ .

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