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Expanded criteria donors for kidney transplantation

Robert A. Metzger[a], Francis L. Delmonico[b], Sandy Feng[c], Friedrich K. Port[d]*, James J. Wynn[e] and Robert M. Merion[f]

[a]*TransLife-Florida Hospital Medical Center, Orlando, FL*
[b]*Massachusetts General Hospital, Boston, MA*
[c]*University of California San Francisco, San Francisco, CA*
[d]*Scientific Registry of Transplant Recipients (SRTR)/ University Renal Research and Education Association (URREA), Ann Arbor, MI*
[e]*Medical College of Georgia, Augusta, GA*
[f]*SRTR/University of Michigan, Ann Arbor, MI*
**Corresponding author: Friedrich K. Port, fport@urrea.org*

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Characteristics of Expanded and Standard Donors, and Differences between Them

The ideal deceased organ donor is a younger person who dies from traumatic head injury that is isolated to the brain and leaves the thoracic and abdominal organ function intact. Such a deceased donor provides excellent transplantable organs with an opportunity to achieve immediate allograft function and long-term patient survival. As the size of the recipient waiting list and the number of waiting list deaths increase, older donors and donors with characteristics once thought to preclude organ donation are being used more and more frequently (1). The clinical characteristics that differentiate 'marginal' renal allografts are derived from the social and medical history of the donor (age, history of hypertension or diabetes, the risk of transmitting infectious disease and/or malignancy), the cause of donor death (trauma vs. cerebrovascular accident), the mechanism of donor death (brain death vs. cardiac death), the anatomy of the allograft (vessel abnormalities), the morphology on biopsy (glomerulosclerosis, interstitial nephritis and/or fibrosis), and the functional profile (serum creatinine or calculated glomerular filtration rate) prior to transplantation (2,3). Kauffman suggests that the term 'expanded' be used to refer to the donor whose organs may be associated with poorer outcome because the term 'marginal' may be considered pejorative by the patients who receive them, as well as by the programs that transplant them (1).

Kidneys transplanted from older donors are considered to be from the expanded pool because these allografts have a higher rate of delayed graft function, more acute rejection episodes, and decreased long-term graft function. Several factors, including prolonged cold ischemia time (CIT), increased immunogenicity, impaired ability to repair tissue, and impaired function with decreased nephron mass may contribute to this (4). But recently, Ojo et al. have demonstrated that the recipients of expanded kidneys receive the benefit of extra life-years when compared to wait-listed dialysis patients (5). Still, placement of these organs is often difficult and delayed, and some centers continue to prefer not to utilize them (6).

The crisis in organ supply presents a compelling responsibility for the transplant community to maximize the use of organs procured from all deceased donors. In March, 2001, representatives of the transplant community convened in Crystal City, VA, in order to develop guidelines that would improve the recovery and transplantation of organs from the deceased donor. This meeting, sponsored by The American Society of Transplantation and The American Society of Transplant Surgeons, produced the 'Report of the Crystal City Meeting to Maximize the Use of Organs Recovered from the Cadaver Donor', published in the *American Journal of Transplantation* (7). At the meeting, five work groups were assembled that focussed upon increasing the use of hearts, lungs, livers, and kidneys, from deceased donors with a history of malignancy or serology testing positive for hepatitis B or C.

The Kidney Work Group (7) noted that in recent years the discard rate of kidneys from deceased donors has increased substantially and approaches 50% for kidneys recovered from donors over age 60. They estimated a potential increase of 38% in the rate of donors per million population if the United States could match Spain's rate of recovery of kidneys from donors over age 45. The work group recommended, and the conference participants endorsed, expedited placement of kidneys from all donors over age 60, based upon waiting time only, to a list of preselected and preinformed recipients who would accept these kidneys. Expanded criteria kidneys are expected to

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increase overall kidney utilization by stimulating higher procurement rates and lower discard rates. Under the work group's proposed plan, the Organ Procurement and Transplantation Network (OPTN), through its contract with the United Network for Organ Sharing (UNOS) would be asked to develop a standard policy whereby a local organ procurement organization (OPO) could adopt the policy upon notification to OPTN/UNOS of local OPO approval. Finally, allocation would occur primarily at the level of the OPO or the region, except for the identification of zero antigen mismatched recipients, which would be allocated nationally.

Another objective of the work group was to evaluate the use of biopsies in the decision to transplant a kidney from an older donor. Currently, biopsies at the time of recovery assume a high importance in kidney distribution; however, available evidence remains controversial (see below). The work group recommended assessing the glomerular filtration rate (GFR) using the Cockcroft–Gault formula or creatinine clearance and to compare the GFR value to biopsy findings to determine the utility of either or both in predicting immediate and long-term function of the older donor's kidney.

At the same time, the OPTN/UNOS Organ Availability and Kidney/Pancreas Committees were each seeking to better define the expanded criteria donor (ECD) in order to provide the transplant community with a more objective basis for decision-making for utilization of these organs for transplantation. The Crystal City kidney proposal was subsequently modified by a collaboration of the OPTN/UNOS Organ Availability Committee, OPTN/UNOS Kidney/Pancreas Committee, and the Scientific Registry of Transplant Recipients (SRTR) contracted to University Renal Research and Education Association (URREA). The result of their interaction with the Crystal City Kidney Group was to define the ECD based upon not only age but also using other statistically significant risk factors determined by the SRTR analyses. Three additional significant donor medical risk factors were identified: history of hypertension, cerebrovascular accident as a cause of death, and final preprocurement creatinine >1.5 mg/dL. Donor kidneys were characterized according to combinations of these four parameters, and a relative risk of graft loss was determined for each donor profile. The ECD kidney was then precisely defined as any kidney whose relative risk of graft failure exceeded 1.7 when compared to a reference group of ideal donor kidneys: those from donors of age 10–39 years, who were without hypertension, who did not die of a cerebrovascular accident, and whose terminal predonation creatinine level was <1.5 mg/dL (Table 1). Using this definition based on the relative risk of graft loss, all donors over age 60 and donors aged 50–59 with at least two of the three medical criteria are identified as ECDs (Table 2) (8). Since the number of donors under age 10 was very small they were not included in the ECD definition in order to keep the defined matrix less complicated.

Table 1: Relative Risk (RR) of graft loss by four donor characteristics

	RR			
	Normal creatinine		High creatinine	
Age (years)	No HTN	HTN	No HTN	HTN
Cause of death was not cerebrovascular accident				
0–9	1.40**	1.59**	1.52**	–
10–39	1.00	1.14**	1.09*	1.24**
40–49	1.17**	1.33**	1.28**	1.45**
50–59	1.41**	1.60**	1.53**	**1.74****
60+	**1.90****	**2.16****	**2.07****	**2.36****
Cause of death was cerebrovascular accident				
0–9	1.60**	**1.82****	**1.74****	**1.98****
10–39	1.14**	1.30**	1.24**	1.41**
40–49	1.34**	1.52**	1.46**	1.66**
50–59	1.61**	**1.83****	**1.75****	**1.99****
60+	**2.17****	**2.47****	**2.37****	**2.69****

Source: SRTR data analyses as of August 1, 2002.
HTN = donor hypertension. Numbers in boldface indicate RR > 1.7.
*p <0.05, **p <0.0005.

Table 2: The expanded criteria for kidney donors. The decision matrix using relative risk of graft failure >1.7 (see Table 1) for donors older than 10 years of age, shown below, are now the OPTN-approved expanded criteria by which kidney donors are defined as expanded and placed into the expedited system

	Donor age categories (years)				
Donor condition	<10	10–39	40–49	50–59	≥60
CVA + HTN + Creat >1.5				X	X
CVA + HTN				X	X
CVA + Creat >1.5				X	X
HTN + Creat >1.5				X	X
CVA					X
HTN					X
Creatinine >1.5					X
None of the above					X

Source: OPTN.
CVA = cerebrovascular accident was cause of death.
HTN = history of hypertension.
Creat >1.5 = creatinine >1.5 mg/dL.

This consistent definition of an ECD was adopted by the OPTN/UNOS Board of Directors in November, 2001, and allocation of ECD became operative within the current allocation policy (UNOS Policy 3.5, Allocation of Cadaveric Kidneys) in October, 2002. The policy states, 'Kidneys procured from the ECD will be allocated to patients determined to be suitable candidates: first, for zero antigen mismatched patients among this group of patients with time limitations; and next, for all other eligible patients locally, regionally, and nationally, based upon time waiting and not HLA matching. The UNOS Organ Center will attempt to place expanded criteria donor organs for the zero antigen mismatched patients, according to the national list of patients waiting for expanded criteria kidneys for

a period of two hours, after which time the UNOS Organ Center will notify the Host OPO that it may allocate the expanded criteria kidneys by the standard geographical sequence of local, regional, and national allocation. OPOs are required to identify potential recipients (i.e. perform a match run and start the process for notifying the appropriate transplant program(s) regarding the organ offer) for kidneys they procure from expanded criteria donors within six hours post cross-clamp or offer the organs for eligible patients listed regionally and then nationally' (7). UNOS Policy 3.5.1 defines standard donors as all other (non-ECD) donors, and notes that potential recipients electing to join the waiting list for the ECD kidneys would also be eligible to receive standard kidneys.

Comparison of the Reasons for Discard of Expanded vs. Standard Donor Kidneys

Given the clear definition of an ECD, there are important issues that must be addressed about the use of organs recovered from such donors. The foremost is deciding whether to transplant kidneys from the ECD or, by not accepting them, permit them to be discarded. The discard of kidneys after recovery from the deceased donor has been increasing at an alarming rate in the United States. During the past 5 years, the discard rate has increased from 12% to 15%—mostly because of the increase in the number of donors older than 50, who now represent over 30% of the national donor population. In the SRTR analysis, roughly 40% of kidneys defined as ECD with >1.7 relative risk of graft failure were discarded in 2001. In contrast, only 8% of standard kidneys were discarded the same year (Tables 3 and 4). The reason for the high rate of kidney discard is often attributed to poor organ function and quality; 47% of ECD kidneys were discarded because of biopsy findings in 2001 (see Table 5).

Should Biopsies Play such an Important Role?

The correlation of kidney biopsy findings with immediate and long-term function remains both controversial and influential. The seminal paper (9) in the field, by Gaber et al., has been criticized for not providing sufficient data to support its conclusion that a biopsy revealing >20% glomerulosclerosis renders a donor kidney generally unacceptable for transplantation (3). This study included only a small number of allografts with poor function 6 months following transplantation and a mean glomerulosclerosis of 20% at the time of implantation; 13 had a serum creatinine >2.5 mg/dL and four had undergone nephrectomy. Only eight of these 17 kidneys had glomerulosclerosis ≥20%. Nevertheless, the determinant of >20% glomerulosclerosis has become a common reason for a transplant physician not to accept a kidney for transplantation. Gaber et al. concluded by advocating the use of routine biopsies of kidneys from older (>50 year) donors and those donors with nontraumatic, cerebrovascular accidents, even those with seemingly normal preprocurement serum creatinine levels (9).

Subsequently, Pokorna and colleagues reported a prospective series of 387 biopsies of deceased donor kidneys, and showed that kidneys whose biopsies demonstrated 25% or more glomerulosclerosis had an acceptable 3-year graft survival rate of 75% (10). However, only 27% of these donors were older than 50. Pokorna et al. concluded that procurement biopsies provide only limited information for the decision whether or not to accept a donor kidney for transplantation.

A definitive, prospective study of kidneys recovered from the ECD that analyzes donor kidney function and pretransplant histology along with post-transplant kidney function and outcome remains to be accomplished. Such a study could significantly affect the transplantation rate of kidneys from older donors. The New England Organ Bank, in collaboration with Life Choice Donor Services, the Transplantation Society of Michigan, and URREA, has received grant funding from the Division of Transplantation (DoT) of the Health Resources and Services Administration (HRSA) to systematically carry out such a study. Others are encouraged to explore this also.

Who Has Received Expanded Criteria Kidneys?

Analyses by the SRTR show that there are significant differences ($p = 0.001$) between the demographic profiles of ECD kidney recipients and standard kidney recipients in 2001, in the areas of recipient age, history of a previous kidney or kidney–pancreas transplant, HLA match, and cause of end-stage renal disease (ESRD) (Table 6). Recipients over the age of 50 (18%) were more likely to receive an ECD kidney than patients under the age of 50 (7%), while recipients who had had a prior kidney or kidney–pancreas transplant were less likely to receive an ECD kidney (8% and 13%, respectively). ECD transplants were less likely to have a 0 HLA mismatch than non-ECD transplants (8% and 13%). Recipients with ESRD due to diabetes or hypertension were more likely to receive an ECD kidney compared to those whose ESRD was caused by glomerulonephritis (14%, 14%, and 10%, respectively). Gender, race, blood type, and PRA at transplant were not associated with significant differences in the use of ECD kidneys.

When Port et al. used multivariate logistic regression to examine the odds of receiving an ECD kidney for the years 1995–2000, more significant differences appeared (8). Characteristics that differed significantly ($p < 0.05$) in the odds (OR) of receiving an ECD rather than a non-ECD kidney included the following: age (OR = 1.03 per year), years of

Table 3: Disposition of kidneys from nonexpanded criteria donors, 1992–2001

	Year									
Organ disposition	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001
Total	7837	8356	8206	8341	8272	8198	8544	8520	8717	8864
Local transplant	5111	5681	5594	5172	5212	5210	5372	5370	5561	5727
Shared transplant	2173	2071	2034	2581	2420	2432	2603	2543	2454	2399
Local not used	314	311	324	349	364	355	367	438	433	440
Shared not used	86	83	63	79	122	80	101	110	194	209
Research	152	207	183	152	151	120	100	58	71	87
Export	1	3	8	4	–	1	–	–	4	2
Unknown	–	–	–	4	3	–	1	1	–	–
Total (%)	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
Local transplant (%)	65.2	68.0	68.2	62.0	63.0	63.6	62.9	63.0	63.8	64.6
Shared transplant (%)	27.7	24.8	24.8	30.9	29.3	29.7	30.5	29.8	28.2	27.1
Not transplanted (%)	7.0	7.2	7.0	6.9	7.7	6.8	6.7	7.1	8.0	8.4

Source: OPTN/SRTR data as of August 1, 2002.
(%) = Percentages are based on totals including missing and unknown.
(–) = None in category.

Table 4: Disposition of kidneys from expanded criteria donors, 1992–2001

	Year									
Organ disposition	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001
Total	664	807	1323	1596	1748	1890	2051	2182	2192	2123
Local transplant	357	377	647	731	804	839	896	868	904	901
Shared transplant	133	162	232	306	350	371	418	440	365	380
Local not used	109	133	224	324	389	440	502	593	554	519
Shared not used	18	39	41	46	66	74	98	152	241	212
Research	47	96	176	184	139	164	137	129	128	109
Export	–	–	3	5	–	–	–	–	–	2
Unknown	–	–	–	–	–	2	–	–	–	–
Total (%)	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
Local transplant (%)	53.8	46.7	48.9	45.8	46.0	44.4	43.7	39.8	41.2	42.4
Shared transplant (%)	20.0	20.1	17.5	19.2	20.0	19.6	20.4	20.2	16.7	17.9
Not transplanted (%)	26.2	33.2	33.5	35.0	34.1	36.0	36.0	40.1	42.1	39.6

Source: OPTN/SRTR data as of August 1, 2002.
(%) = Percentages are based on totals including missing and unknown.
(–) = None in category.
Includes organs recovered for transplant but not transplanted, as well as organs transplanted.

dialysis (OR = 1.03 per year), African American race (OR = 0.92 vs. white), Hispanic/Latino ethnicity (OR = 0.89), male (OR = 0.93), glomerulonephritis as cause of ESRD (OR = 0.68 vs. diabetes), PRA of 10–79% (OR = 0.84 vs. <10%), and PRA of 80% or higher (OR = 0.65 vs. <10%).

Common practice in the United States is to place older donor kidneys in older patients. This practice has been formally implemented in Europe through the Eurotransplant Senior Program (11,12), and has been advocated in the United States as well (13). Kasiske and Snyder, in an analysis of first kidney transplants from 1988 to 1998 using the United States Renal Data System (USRDS), demonstrated that giving older kidneys to older recipients did not improve overall graft survival (14). However, they noted that there may be ethical reasons to do so even if outcomes are not improved. A recent French study, although defining the ECD differently, noted that these older donor kidneys transplanted into significantly older recipients had similar 2-year patient and graft survival as the control donor-recipient group (15). Ongoing analyses following implementation of the expedited ECD kidney allocation policy should clarify which subsets of candidates may be most appropriate for ECD kidneys.

How Well Have the ECD Kidneys Worked?

Graft survival of ECD kidney transplants is by definition inferior to that of standard kidney transplants. Unadjusted (Kaplan–Meier) graft survival estimates at 3 months and 1 year for 1958 ECD kidney transplants performed in 1999

Table 5: Reasons for nonuse of recovered expanded criteria donor kidneys, 1992–2001

Reason for nonuse of recovered organs	Year									
	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001
Total (%)	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
Extended ischemia time (%)	–	–	1.5	2.4	1.1	0.8	2.3	1.9	1.6	2.3
Organ unsatisfactory (%)[1]	–	–	13.2	11.4	11.9	9.7	8.3	11.1	10.7	8.9
Poor organ function/infection (%)	–	–	–	3.8	15.6	9.7	13.2	11.1	16.7	17.0
Donor medical/social history (%)	–	–	11.3	5.4	4.6	7.0	4.7	4.3	2.8	4.2
Biopsy findings (%)	–	–	29.1	52.7	44.6	48.6	47.2	41.2	47.2	46.5
Positive hepatitis/CMV/HIV (%)	–	–	0.8	3.2	1.8	2.3	1.5	1.7	0.8	1.8
No recipient found (%)[2]	–	–	0.8	1.6	7.0	6.8	7.3	6.7	5.2	4.2
Other (%)	–	–	21.9	16.8	13.0	14.4	14.8	12.3	9.4	5.7
Unknown (%)	–	–	–	2.7	0.4	0.6	0.7	9.5	5.7	9.3
Not collected prior to 4/94 (%)	100.0	100.0	21.5	–	–	–	–	–	–	–

Source: OPTN/SRTR data as of August 1, 2002.
(%) = Percentages are based on totals including missing and unknown.
(–) = None in category.
[1]Organ unsatisfactory: organ damage or anatomic abnormalities.
[2]No recipient found: recipient not located or list exhausted.
Reasons for nonuse not collected prior to April 1, 1994.
Includes organs recovered for transplant but not transplanted, as well as organs transplanted.

Table 6: Recipients of expanded criteria donor kidneys, 2001

Variable	ECD transplants*	p-value**
Age under 50	6.6%	≤ 0.001
Age over 50	17.5%	
No previous transplant	12.6%	≤ 0.001
Previous transplant	8.1%	
0 HLA mismatch	8.1%	≤ 0.001
>0 HLA mismatch	12.6%	
ESRD due to diabetes mellitus	14.1%	≤ 0.001
ESRD due to hypertension	13.6%	≤ 0.001
ESRD due to glomerulonephritis	9.9%	Ref.

Source: SRTR Data Analysis, August, 2002.
*As percent of all kidney transplants.
**Analysis of proportions by chi square.

and 2000 are 90% and 82%, respectively (Table 7). These compare to graft survival rates of 94% and 89%, respectively, for 13 892 standard kidney transplants performed during the same years (Table 8). Graft survival estimates show an absolute difference of 15% and 16% at 3 and 5 years, respectively (80% vs. 65% at 3 years for 1997–98 transplants; 65% vs. 49% at 5 years for 1995–96 transplants). Multivariate analysis that adjusts for differences in recipient characteristics indicates that the relative risk of graft failure for ECD recipients is 69% higher than for all standard organ recipients (8).

Very few ECD kidneys have been utilized for pediatric recipients, so graft survival in this subgroup cannot be easily estimated. No clear age-related pattern of graft survival is evident among different groups of adults. Patients of Asian race had higher graft survival than whites or African Americans at all time points, while Hispanic/Latino recipients fared better than non-Hispanic/non-Latino recipients (Table 7). These patterns are similar among recipients of standard kidneys (Table 8).

Prior sensitization, assessed by level of panel reactive antibody (PRA), appeared to influence the results of ECD kidney transplantation. Unsensitized recipients (PRA $<$ 20%) had a 1-year graft survival rate of 82%, compared to 70% for highly sensitized recipients (PRA $\geq$ 80%) (Table 7). The difference in graft survival was much less marked among standard kidney recipients, where unsensitized and highly sensitized recipients had graft survival estimates of 89% and 86%, respectively (Table 8). This suggests that recipient immunologic factors (PRA) may combine with donor quality factors (ECD) to result in more inferior outcomes than either set of characteristics alone. It should be noted, however, that only 3% of ECD kidneys were transplanted into highly sensitized recipients, so these observations must be regarded as somewhat speculative until larger numbers of such cases have been accumulated and analyzed.

Early post-transplant function was associated with better short-term and long-term graft outcomes. At 3 months, ECD kidney graft survival was 89% if dialysis was required within the first week after transplant, whereas among those with immediate graft function, 96% were functioning at 3 months (Table 7). The effects of post-transplant dialysis need on late graft survival differences were quite dramatic. At 5 years, graft survival was 58% for those who had immediate function and 39% for those who did not. For both early and late graft survival, absolute differences between immediately functioning and delayed functioning grafts were similar in ECD and standard grafts, although

Table 7: Graft survival for expanded criteria donor kidney transplants at 3 months, 1 year, 3 years, and 5 years

		3 months		1 year		3 years		5 years	
Categories		n	%	n	%	n	%	n	%
Total	All	1958	90.4	1958	81.7	1909	65.1	1698	48.6
Age (years) at Tx	< 1 year	0	–	0	–	0	–	0	–
	1–5 years	1	*	1	*	1	*	2	*
	6–10 years	2	*	2	*	2	*	4	*
	11–17 years	7	*	7	*	11	80.8	9	*
	18–34 years	177	88.0	177	79.9	186	68.2	219	44.7
	35–49 years	464	92.7	464	84.3	519	70.7	564	52.4
	50–64 years	927	91.2	927	82.6	891	64.8	678	47.8
	65 + years	380	87.4	380	77.5	299	53.9	222	45.2
Recipient race	White	1232	90.5	1232	82.4	1246	67.2	1139	50.5
	Asian	110	94.4	110	88.6	95	72.8	70	63.7
	African American	576	89.8	576	79.5	541	59.4	465	42.0
	Other/multi-race	40	82.1	40	71.0	27	58.2	24	38.4
Recipient ethnicity	Hispanic/Latino	217	94.9	217	89.5	212	75.3	157	51.2
	Non-Hispanic/ Non-Latino	1705	90.1	1705	81.0	1610	63.6	1432	48.4
	Unknown	36	76.8	36	64.5	87	69.0	109	47.5
Recipient gender	Female	786	91.3	786	83.7	755	66.4	651	49.8
	Male	1172	89.7	1172	80.3	1154	64.3	1047	47.9
Previous kidney Tx	No	1772	90.6	1772	82.1	1719	65.6	1523	49.1
	Yes	186	87.8	186	77.9	180	60.0	175	44.4
PRA at transplant	0–19	1594	90.6	1594	82.2	1587	66.4	1454	49.5
	20–79	138	89.6	138	77.2	129	53.2	108	48.4
	80 +	58	84.5	58	69.9	51	59.5	42	23.1
	Unknown	168	90.4	168	84.1	142	63.0	94	47.5
Dialysis needed within	No	1276	95.5	1276	88.4	1183	71.8	1002	57.7
first week after Tx	Yes	557	88.8	557	76.0	621	60.3	609	39.2
	Unknown	39	92.2	39	71.5	23	58.7	15	40.7
Level of HLA	0	240	89.9	240	83.4	231	70.3	218	57.0
mismatch	1	71	92.8	71	83.5	76	67.5	659	42.4
	2	219	92.9	219	83.9	237	64.6	242	44.2
	3	396	92.9	396	85.3	432	67.6	381	49.2
	4	487	89.0	487	78.1	468	63.6	419	44.7
	5	366	90.0	366	81.5	306	60.1	263	52.0
	6	171	85.0	171	77.5	155	64.1	120	47.0
	Unknown	8	*	7	*	4	*	6	*

Source: OPTN/SRTR data as of August 1, 2002.

*Values suppressed due to small numbers (0–9). Cohorts are transplants performed during 1999–2000 for 3 months and 1 year; 1997–1998 for 3 years; and 1995–96 for 5-year survival. Graft survival follows individual transplants until graft failure. Counts for patient and graft survival are different because a patient may have more than one transplant for a type of organ. Multi-organ transplants are excluded.

standard grafts had better overall outcomes, as expected. Although both donor age and prolonged cold ischemia time have been associated with increased risk of delayed graft function, cold ischemia time appears to have little additive effect on 1- and 3-year graft function and survival (16). Most authors suggest that ECD kidneys should be used locally to minimize any detrimental effect of cold ischemia time on graft function and survival. The new OPTN/UNOS algorithm for allocation of ECD kidneys favors reducing cold ischemia time over HLA matching. In an analysis of donor characteristics used in formulating the new ECD definition, Port et al. have shown that the benefits of a shorter cold ischemia time slightly outweigh the benefits of HLA matching (Table 9) (8).

Among ECD kidney recipients, overall patient survival was 96% at 3 months and 91% at 1 year for the 1999–2000 cohort, 79% at 3 years for the 1997–1998 cohort, and 70% at 5 years for the 1995–1996 cohort (Table 10). The differences between ECD and standard patient survival are consistent over time, when viewed as the ratio of percent failures. At 1 year, almost 95% of standard patients were alive, 90% at 3 years and 81% at 5 years (Table 11). These unadjusted results cannot be directly compared, however,

Table 8: Graft survival for nonexpanded criteria donor kidney transplants at 3 months, 1 year, 3 years, and 5 years

		3 months		1 year		3 years		5 years	
Categories		n	%	n	%	n	%	n	%
Total	All	13 892	94.0	13 892	89.3	13 601	80.4	13 488	65.2
Age (years) at Tx	< 1 year	1	*	1	*	0	–	0	–
	1–5 years	81	93.7	81	88.5	80	80.4	89	67.2
	6–10 years	109	89.9	109	87.9	137	89.8	121	71.8
	11–17 years	409	94.5	409	91.3	343	74.7	408	54.8
	18–34 years	2426	94.8	2426	90.4	2498	81.1	2786	63.7
	35–49 years	4810	94.9	4810	91.0	5073	81.8	5128	67.9
	50–64 years	4863	93.1	4863	88.0	4491	79.8	4135	65.7
	65 + years	1193	92.4	1193	85.5	979	74.8	821	54.8
Recipient race	White	9082	94.1	9082	89.9	8985	82.2	9116	68.1
	Asian	632	95.0	632	92.1	629	85.6	530	73.6
	African American	3921	93.5	3921	87.4	3754	74.7	3587	56.0
	Other/multi-race	257	94.4	257	89.6	231	85.6	255	69.5
	Unknown	0	–	0	–	2	*	0	–
Recipient ethnicity	Hispanic/Latino	1688	94.5	1688	91.0	1506	84.9	1535	68.5
	Non-Hispanic/ Non-Latino	11 948	94.0	11 948	89.2	11 528	80.0	11 141	64.7
	Unknown	256	88.8	256	83.4	567	76.3	812	64.9
Recipient gender	Female	5516	93.3	5516	89.1	5386	80.5	5196	66.1
	Male	8376	94.4	8376	89.5	8215	80.3	8292	64.6
Previous kidney Tx	No	11 899	94.3	11 899	89.7	11 671	81.1	11 592	65.9
	Yes	1993	92.2	1993	87.2	1930	76.2	1896	60.3
PRA at transplant	0–19	11 076	94.4	11 076	89.7	11 166	80.9	11 202	66.1
	20–79	1125	90.4	1125	85.2	1041	76.3	999	60.3
	80 +	543	90.7	543	86.0	464	74.9	491	55.8
	Unknown	1148	95.0	1148	91.3	930	81.5	796	63.7
Dialysis needed within	No	10 334	97.4	10 334	93.7	10 171	84.7	10 105	70.5
first week	Yes	2929	91.2	2929	83.0	2972	72.4	2974	53.1
after Tx	Unknown	161	96.2	161	91.1	168	73.3	97	69.1
Level of HLA	0	2427	94.8	2427	91.1	2179	84.6	2104	71.6
mismatch	1	410	95.8	410	92.7	463	84.6	501	65.9
	2	1430	95.4	1430	91.4	1560	83.6	1702	66.6
	3	2889	94.4	2889	89.7	3050	80.9	3103	64.9
	4	3019	93.6	3019	89.0	3081	78.5	3215	64.1
	5	2494	92.3	2494	87.1	2204	77.4	1969	61.4
	6	1205	93.2	1205	86.7	1038	74.9	886	60.0
	Unknown	18	88.9	18	83.3	26	88.3	8	*

Source: OPTN/SRTR Data as of August 1, 2002.

*Values suppressed due to small numbers (0–9). Cohorts are transplants performed during 1999–2000 for 3 months and 1 year; 1997–98 for 3 years; and 1995–96 for 5-year survival. Graft survival follows individual transplants until graft failure. Counts for patient and graft survival are different because a patient may have more than one transplant for a type of organ. Multi-organ transplants are excluded.

since characteristics such as age and comorbidities tend to differ between ECD and standard recipients.

As shown in Figure 1, survival percentages for age groups of adult recipients of ECD kidneys were lower than those of the corresponding age groups who had received standard kidneys. Similar to the results for graft outcome, patient survival was better for Asians than for other races and better for Hispanic/Latino ECD recipients than for non-Hispanic/non-Latino recipients (Table 10). Patient survival after ECD transplant was similar for males and females (Table 10).

Who Should Be Offered the ECD Kidneys?

How to identify the most appropriate candidates for ECD kidneys remains an open question—particularly since, according to SRTR data, essentially all candidates will derive survival benefit from transplantation with an ECD kidney over continued dialysis (17). In considering this question, it is critical to balance this against the reduced graft survival associated with an ECD. Furthermore, in addition to weighing the differential patient and graft outcomes of transplantation with ECD and standard kidneys,

Table 9: Estimated effect of proposed policy for expanded donors (RR > 1.7)

HLA MM, shared or local by CIT	Total n	Number of graft failures	
		Observed	New policy
0MM local, < 24 h CIT	68	14	19
0MM local, > 24 h CIT	7	3	1.1
0MM shared, < 24 h CIT	269	61	71.9
0MM shared, > 24 h CIT	167	44	46.7
1–6MM local, < 24 h CIT	2498	640	640.0
1–6MM local, > 24 h CIT	671	196	170.8
Total	3680	958	949.5

Net effect of no HLA matching and < 24 h CIT: 8.6 fewer failures (0.9%)
Source: SRTR Data Analysis, August 2002.
CIT = cold ischemia time.

the outcomes of ongoing dialysis for various subsets of transplant candidates may also merit consideration. In Philadelphia in March, 2002, a work group entitled 'Expanded Criteria Donor Kidneys: Who Should Get Them?' was convened for 'A National Conference to Analyze the Wait List for Kidney Transplantation'. The group suggested that ECD kidneys should be preferentially directed toward candidates older than 60, diabetic candidates older than 40, candidates with failing vascular access, and candidates whose expected waiting time exceeds their life expectancy on the waiting list without a transplant. The identified candidate groups have the higher risk of mortality on dialysis and are therefore least likely to survive the requisite wait for a standard organ. We acknowledge that regional and local differences in the allocation of standard kidneys and the passing of time may identify different or additional candidate subsets.

The work group also suggested that certain recipients should be discouraged from listing for ECD kidneys in order to avoid logistic and pragmatic issues that might result in delayed allocation or difficulties in post-transplant management. The inclusion of large numbers of patients with elevated PRA levels would result in delays in allocation resulting from a high incidence of a positive crossmatch, obviating the objective to improve outcomes by reducing cold ischemia time. Also, patients at greater immunological risk may face excess disadvantage with an ECD kidney, given that transplants using these organs are associated with a significantly increased risk of delayed graft function as well as lower graft survival.

How Should We Evaluate the Effectiveness of the New Allocation Process for ECD Kidneys?

The participants in the collaborative effort to develop the definition of ECD realize that this is a first step in an attempt to maximize utilization of kidneys from these donors. As the expedited placement of these organs is implemented, ongoing analyses of the effects on utilization and discard rates will be followed by OPTN/UNOS and

Table 10: Patient survival for expanded criteria donor kidney transplants at 3 months, 1 years, 3 years, and 5 years

		3 months		1 year		3 years		5 years	
Categories		n	%	n	%	n	%	n	%
Total	All	1772	96.0	1772	90.6	1729	78.5	1523	69.9
Age (years) at Tx	< 1 year	0	–	0	–	0	–	0	–
	1–5 years	1	*	1	*	0	–	2	*
	6–10 years	1	*	1	*	2	*	2	*
	11–17 years	4	*	4	*	11	100.0	9	*
	18–34 years	129	98.4	129	96.9	144	93.1	172	87.6
	35–49 years	391	98.5	391	95.4	446	86.3	482	77.8
	50–64 years	874	95.4	874	89.5	836	76.7	639	63.5
	65 + years	372	93.8	372	85.8	290	63.8	217	55.5
Recipient race	White	1103	95.9	1103	90.1	1110	77.6	1002	69.0
	Asian	99	98.0	99	92.9	92	85.9	66	80.3
	African American	531	96.0	531	91.7	502	79.3	431	71.7
	Other/multi-race	39	92.3	39	82.1	25	80.0	24	46.7
Recipient ethnicity	Hispanic/Latino	204	97.5	204	95.1	195	82.1	146	70.2
	Non-Hispanic/ Non-Latino	1538	96.0	1538	90.2	1456	78.1	1281	70.6
	Unknown	30	83.3	30	80.0	78	78.2	96	60.0
Recipient gender	Female	708	96.3	708	91.8	677	79.3	586	71.8
	Male	1064	95.8	1064	89.8	1052	78.0	937	68.7

Source: OPTN/SRTR Data as of August 1, 2002.
*Values suppressed due to small numbers (0–9). Cohorts are transplants performed during 1999–2000 for 3 months and 1 year; 1997–98 for 3 years; and 1995–96 for 5-year survival. Patient survival follows patients from first transplant of this type until death. Counts for patient and graft survival are different because a patient may have more than one transplant for a type of organ. Multi-organ transplants are excluded.

Table 11: Patient survival for nonexpanded criteria donor kidney transplants at 3 months, 1 years, 3 years, and 5 years

		3 months		1 year		3 years		5 years	
Categories		n	%	n	%	n	%	n	%
Total	All	11 899	97.5	11 899	94.5	11 671	89.9	11 592	81.2
Age (years) at Tx	< 1 year	1	*	1	*	0	–	0	–
	1–5 years	78	98.7	78	97.4	74	93.2	81	92.6
	6–10 years	86	96.5	86	96.5	116	98.3	98	93.3
	11–17 years	329	99.7	329	99.4	267	97.8	321	95.0
	18–34 years	1928	99.2	1928	97.9	1943	96.3	2202	90.4
	35–49 years	3932	98.5	3932	96.6	4219	92.5	4308	84.8
	50–64 years	4410	96.4	4410	92.3	4113	86.2	3794	74.7
	65 + years	1135	94.6	1135	88.7	939	77.6	788	59.0
Recipient race	White	7599	97.5	7599	94.6	7538	90.0	7618	81.1
	Asian	581	97.6	581	95.4	579	92.6	495	88.0
	African American	3489	97.5	3489	94.3	3342	89.2	3248	80.4
	Other/multi-race	230	98.3	230	95.2	210	90.0	231	81.3
	Unknown	0	–	0	–	2	*	0	–
Recipient ethnicity	Hispanic/Latino	1469	97.3	1469	95.0	1351	93.6	1340	85.1
	Non-Hispanic/ Non-Latino	10 250	97.5	10 250	94.5	9887	89.5	9572	80.8
	Unknown	180	96.1	180	93.9	433	86.8	680	78.8
Recipient gender	Female	4722	97.5	4722	94.8	4632	90.6	4433	82.0
	Male	7177	97.5	7177	94.4	7039	89.4	7159	80.7

Source: OPTN/SRTR Data as of August 1, 2002.

*Values suppressed due to small numbers (0–9). Cohorts are transplants performed during 1999–2000 for 3 months and 1 year; 1997–98 for 3 years; and 1995–96 for 5-year survival. Patient survival follows patients from first transplant of this type until death. Counts for patient and graft survival are different because a patient may have more than one transplant for a type of organ. Multi-organ transplants are excluded.

the SRTR. Appropriate OPTN/UNOS committees (Kidney/Pancreas and Organ Availability) are expected to monitor the implementation and the results of this allocation algorithm on a regular basis and report to the transplant community. Data regarding graft function and patient and graft survival should be readily reported and available so that the OPTN and SRTR can easily monitor the effects of this allocation policy. Such a system could examine the policy's impact on reducing the CIT of ECD kidneys and whether the duration of CIT influences the rate of immediate function of ECD kidneys following transplantation (when compared to standard donor kidneys transplanted within the same OPO). Resolving the question on the importance of organ morphology will be more difficult and will require the design of single-center, multicenter, and/or OPO wide studies to address this issue. Additionally, the SRTR will pursue comparative studies on ECD transplantation regarding implementation and adjusted outcomes by various factors, including OPOs.

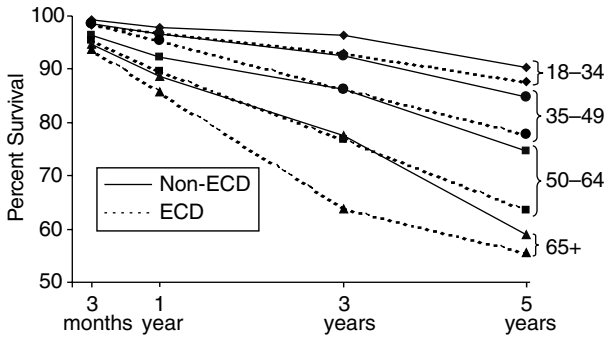

Figure 1: Patient survival after ECD or non-ECD transplant, by recipient age. Source: OPTN/SRTR Data as of August 1, 2002, Tables 10 and 11.

It is possible that certain subgroups of donors can be identified whose predicted graft failure risk is substantially higher than for the average ECD organ. Such identification would have important implications, since it may argue against transplanting such organs. Further stratification of the relative risk data may define ECDs whose kidneys should be offered only for dual placement into a single recipient.

It is likely that additional donor categories will be added to the definition of the ECD. At the time of the initial analysis for 1995–2000, the number of nonheartbeating donors (donors after cardiac death) in the database accounted for only 1.5% of kidney transplants. For this selected group, the relative risk of graft failure was significantly elevated but appeared to be less than 1.7. By contrast, the odds of delayed graft function exceeded 2.0 for kidneys from nonheartbeating donors (F. Port, personal

communication). As the use of nonheartbeating donors increases over time, these analyses will need to be repeated.

Conclusion

The special provisions for the distribution of kidneys procured from the ECD signals a new era for OPTN/UNOS allocation policy. While previous allocation policies have tried to address issues of medical urgency, equity, and outcome, the ECD policy was truly born of a new mission: to increase organ utilization. The genesis of the allocation policy, as outlined above, was the identification and subsequent definition of a subset of deceased donor organs that had a high discard rate after procurement. For these organs of suboptimal quality, data analysis showed that the placement process was often arduous and prolonged, frequently resulting in discard. Since the inefficient allocation of these organs may contribute to both increased organ dysfunction and increased organ discard, the impetus for an expedited allocation policy became clear.

The expedited allocation of ECD kidneys depends strongly upon two elements of the new policy. First, the substantial de-emphasis of immunologic matching concomitant with the primacy of waiting time results in a more predictable lineup of potential recipients. Transplant centers can then ensure that candidates listed for ECD kidneys with the longest waiting time for each blood group are fully evaluated and thereby ready to proceed with transplantation. Second, and perhaps more controversial, is the requested assurance of prior informed consent for every candidate listed for an ECD kidney. Specific informed consent appears wise since the transplantation of an ECD kidney implies additional graft failure risk, which exceeds standard expectations. It is generally agreed that a situation where the outcome may not meet standard expectations merits additional informed consent (18). Persson et al. recently reported that most patients on the waiting list accept information on donor-related risk factors and want to be involved in the decision concerning transplantation with a kidney from expanded donors (19).

Although the definition of an ECD kidney using a relative risk cutoff of 1.7 is arbitrary, it is nevertheless clear that the premise of the ECD kidney definition is the increased risk of an inferior outcome when compared to a standard kidney. Prior informed consent will help safeguard the efficiency of the expedited placement process. Currently, ECD kidneys are often refused for transplantation; refusals prolong cold ischemia and often result in organ discard. It is presumed that a common reason for refusal of an ECD kidney is that the transplant physician does not consider it appropriate for the particular candidate to which it has been offered. It is also possible that the candidate, after discussion with his or her transplant physician, has refused the kidney, choosing to wait for a better organ. Prior informed consent aims to substantially reduce the occurrence of the above scenarios and thereby expedite organ placement. Thoughtful consideration and discussion for both the transplant program and the candidate can occur 'in the light of day' and over time, outside of the pressured time frame of a specific organ offer. Therefore, listing of a particular candidate for an ECD kidney would indicate that the transplant center considers that individual appropriate for transplantation with an ECD kidney and that the candidate will accept transplantation with an ECD kidney. Individuals involved in the definition of the ECD and the formulation of the expedited allocation policy have developed a sample consent form which can be modified, as desired, by individual transplant centers. This form appears as an addendum at the end of this article. All these recommendations can be simply summarized as giving greater opportunity to those who currently have limited access to transplantation.

References

1. Kauffman MH, Bennett LE, McBride MA, Ellison MD. The expanded donor. Transplant Rev 1997; 11: 165–190.
2. Becker TY. Use of marginal donors in kidney transplantation. Graft 2000; 3: 216–220.
3. Randhawa P. Role of donor kidney biopsies in renal transplantation. Transplantation 2001; 71: 1361–1365.
4. De Fijter JW, Mallat MJK, Doxiadis IIN et al. Increased immunogenicity and cause of graft loss of old donor kidneys. J Am Soc Nephrol 2001; 12: 1538–1546.
5. Ojo AO, Hanson JA, Meier-Kriesche H et al. Survival in recipients of marginal cadaveric donor kidneys compared with other recipients and wait-listed transplant candidates. J Am Soc Nephrol 2001; 12: 589–597.
6. Lee CM, Scandling JD, Pavlakis M, Markezich AJ, Dafoe DC, Alfrey EJ. A review of kidneys that nobody wanted: determinants of optimal outcome. Transplantation 1998; 65 (2): 213–219.
7. Rosengard BR, Feng S, Alfrey EJ et al. Report of the Crystal City meeting to maximize the use of organs recovered from the cadaver donor. Am J Transplant 2002; 2: 1–10.
8. Port FK, Bragg JL, Metzger RA et al. Donor characteristics associated with reduced graft survival. an approach to expanding the pool of kidney donors. Transplantation 2002; 74: 1281–1286.
9. Gaber LW, Moore LW, Alloway RR, Amiri MH, Vera SR, Gaber AO. Glomerulosclerosis as a determinant of posttransplant function of older donor renal allografts. Transplantation 1995; 60: 334–339.
10. Pokorna E, Vitko S, Chadimova M, Schuck O, Ekberg H. Proportion of glomerulosclerosis in procurement wedge biopsy cannot alone discriminate for acceptance of marginal donors. Transplantation 2000; 69: 36–43.
11. Voiculescu A, Schlieper G, Hetzel GR et al. Kidney transplantation in the elderly: age-matching as compared to HLA-matching: a single center experience. Transplantation 2002; 73: 1356–1359.
12. Smits JM, Persijn GG, van Houwelingen HC, Claas FH, Frei U. Evaluation of the Eurotransplant Senior Program. The results of the first year. Am J Transplant 2002; 2: 664–670.
13. Lee CM, Carter JT, Weinstein RJ et al. Dual kidney transplantation: older donors for older recipients. J Am College Surgeons 1999; 189: 82–91.
14. Kasiske BL, Snyder J. Matching older kidneys with older patients does not improve allograft survival. J Am Soc Nephrol 2002; 13: 1067–1072.

15. Dahmane D, Hiesse C, Pessione F, Cohen S, Lang P. Survival and renal function of kidney transplants refused and finally accepted. Transplantation 2002; 74: 77.
16. Lee CM, Carter JT, Randall HB et al. The effect of age and prolonged cold ischemia times on the national allocation of cadaveric renal allografts. J Surg Res 2000; 91: 83–88.
17. Merion RM, Ashby VB, Wolfe RA et al. Mortality risk for expanded donor kidney recipients compared with waitlisted dialysis patients. J Am Society Nephrol 2002: 13: 47A–48A.
18. Ferguson M. Informed consent by the recipient of an organ from an expanded donor. Graft 1998; 1 (Suppl. 1): 25–26.
19. Persson MO, Persson NH, Källén R, Ekberg H, Hermerén G. Kidneys from marginal donors. views of patients on informed consent. Nephrol Dial Transplant 2002; 17: 1497–1502.

Addendum: Sample Informed Consent for Acceptance of Expanded Criteria Donor Kidneys

Introduction

We invite you to take part in a program to better use kidneys recovered from donors with conditions that make it more difficult to efficiently place them for transplantation. Please take your time to make your decision. Discuss it with your family and friends and feel free to ask us questions also. This program will not be recommended for all of our patients. It is important that you read this document and understand several general principles that apply to all who take part in our expanded criteria donor program.

1 This program has been developed by the Organ Procurement and Transplantation Network, the organization that manages the national patient waiting list.

2 This program does not replace the waiting list already in place; it simply offers a means for some patients to receive a transplant more quickly.

3 Taking part in this program is entirely voluntary.

4 Those participating in this program will still be participating in the regular waiting list program for the kidneys distributed through that listing.

5 You may withdraw from the program at any time without incurring any penalties or loss of waiting time points.

6 You are urged to ask any questions you have about this program with the staff members who explain it to you.

Why is this program being offered?

There is a serious shortage of cadaver kidneys (kidneys recovered from someone who died) while, at the same time, transplantation is beneficial to an increasing number of patients with kidney failure. The waiting list increases by several thousand each year and over 4000 patients will die waiting for a kidney transplant this year. The waiting time for a cadaver kidney is over four years in most parts of the country. Many patients are waiting longer because their transplant markers, that determine the kidney match, may not be very common and keep them from having enough points to get a kidney offer.

One way to increase the number of cadaver kidneys is to use 'expanded criteria' donors; these are donors who are older or who have specific health problems that might affect how well and how long their kidneys will work after they are transplanted. Many of these kidneys are already being transplanted but a large number are discarded when the time to get them transplanted is too long, resulting in too much damage. This new program will allow transplant centers to use them locally without having to go entirely through the national system. We believe this will help those kidneys to perform better and provide adequate function for the recipients to stop dialysis. A study done by the national kidney program showed that patients receiving these kidneys add about five extra years to their life compared to not receiving a transplant and remaining on dialysis.

You are being told about this program because you have kidney failure, you do not have a potential living kidney donor, and, given your age and overall condition, you might receive significant benefit from an expanded criteria donor kidney.

What is involved in the program?

To take part in the program, you will be asked to sign this informed consent document. Kidneys from expanded criteria donors will be offered only to patients who have agreed in advance to be considered for them. They will be offered first to anyone on this list who is a perfect match. If there is no perfect match, then they will be offered to the compatible patient waiting the longest on the list. The kidneys from donors who meet the following criteria will be placed by this program. All donors 60 or older are considered expanded criteria donors and all donors between the ages of 50–59 who have two or more of the following: (1) the donor died from a stoke or cerebrovascular accident; (2) the donor had a medical history of hypertension (high blood pressure); and/or (3) the donor's most recent creatinine was 1.5 mg/dL or greater (creatinine is a measure of how well the kidney works; normal values typically range from 0.6 to 1.2 mg/dL).

You will have all the medical tests and procedures that are part of the regular recipient medical workup if you do or do not enroll in this program. You may require more frequent biopsies of the transplanted kidney to assess for kidney function and potential rejection episodes after the transplant. You may require dialysis for a short period of time after the transplant. Long-term kidney function may be less than that from a nonexpanded criteria donor kidney.

Are there any benefits to taking part in this program?

The main benefit would be to shorten the time you wait for a kidney transplant. Recent analysis of transplant data showed that the longer you wait on dialysis for a transplant, the poorer the transplant outcome.

What other options are there?
Remember, you will still be listed on the regular waiting list for a non expanded donor kidney. You may also decline to enrol in this program. Your other option would be a living donor transplant from a family member, a friend or even a willing stranger.

What are the costs?
You or your insurance company will be charged for the continuing medical care and/or hospitalization that are part of the kidney transplant procedure. There are no additional or special costs that are part of the expanded criteria kidney donor program.

What are my rights as a participant?
Taking part in this program is voluntary. You may choose not to take part in or leave the program at any time. If so, your regular care will not be affected and you will not lose any of the benefits you would normally receive. We will try to keep you informed of any new developments pertaining to this program.

Who do I call if I have any questions or problems?
For questions about the program, contact:
your pretransplant coordinator _____; or
your transplant physician _____.

Signatures
As a representative of this program, I have explained the purpose, the procedures, the benefits and the risks that are involved in this program. Any questions that have been raised have been answered to the individual's satisfaction.

Signature of person obtaining the consent Date

I, the undersigned, have been informed about this program's purpose, procedures, possible benefits and risks, and I have received a copy of this consent document. I have been given the opportunity to ask questions and I have been told I can ask questions in the future. I voluntarily agree _____ or do not agree _____ (initial appropriately) to participate in this program. I am free to withdraw from the program at any time without need to justify my decision. A withdrawal will not in any way affect my future treatment or medical management.

Signature of Patient Date