

# Half of Kidney Transplant Candidates Who Are Older than 60 Years Now Placed on the Waiting List Will Die before Receiving a Deceased-Donor Transplant

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**Background and objectives:** Waiting times to deceased-donor transplantation (DDTx) have significantly increased in the past decade. This trend particularly affects older candidates given a high mortality rate on dialysis.

**Design, setting, participants, & measurements:** We conducted a retrospective analysis from the national Scientific Registry of Transplant Recipients database that included 54,669 candidates who were older than 60 yr and listed in the United States for a solitary kidney transplant from 1995 through 2007. Using survival models, we estimated time to DDTx and mortality after candidate listing with and without patients initially listed as temporarily inactive (status 7).

**Results:** Almost half (46%) of candidates who were older than 60 yr and listed in 2006 through 2007 are projected to die before receiving a DDTx. This proportion varied by individual characteristics: Diabetes (61%), age  $\geq 70$  yr (52%), black (62%), blood types O (60%) and B (71%), highly sensitized (68%), and on dialysis at listing (53%). Marked variation also existed by United Network for Organ Sharing region (6 to 81%). The overall projected proportion was reduced to 35% excluding patients who initially were listed as status 7.

**Conclusions:** These data highlight the prominent and growing challenge facing the field of kidney transplantation. Older candidates are now at significant risk for not surviving the interval in which a deceased-donor transplant would become available. Importantly, this risk is variable within this population, and specific information should be disseminated to patients and caregivers to facilitate informed decision-making and potential incentives to seek living donors.

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Currently, more than half of a million patients have ESRD in the United States. Among these individuals, approximately one half (48%) are older than 60 yr (1). Rates of ESRD have increased in the past decade in virtually all patient groups, most rapidly in older patients (2). Among patients who have ESRD and are medically cleared for the procedure, kidney transplantation has repeatedly been shown to convey a significant survival advantage as compared with the alternative treatment modality of maintenance dialysis (3). This survival advantage is applicable across age groups including a nearly doubling of life expectancy among patients who are older than 60 yr (3,4); however, one of the greatest challenges facing this population is that the number of available organs from deceased donors has not kept pace with the growing number of transplant candidates. There was a 50% rise in the number of new kidney candidate listings from 1997 through 2006—an increase evident across age groups, race, blood type,

and gender (5). Consequences of this unmet demand are longer waiting periods for transplantation and increased mortality on the waiting list before receiving an organ. Even among patients who meet initial screening criteria, there is a significantly elevated risk among older candidates of health deterioration while awaiting transplantation, rendering many patients ineligible for the procedure (6,7).

Factors that influence patient decisions to list for a deceased-donor transplant are complex, including individual patient preferences, perceived benefit, and the availability and desire to obtain a living donor (8,9). Rates of listing for a deceased-donor transplant and progression on the waiting list vary significantly by race/ethnicity, body mass index, socioeconomic factors, and geographic location (10,11). Numerous reports demonstrated that patients who are proactive and are able to navigate the processes involved to receive a transplant have significantly improved prognoses (12–14). In general, patient prognoses are not the sole determinant of expeditious listing for the procedure. In fact, a sizeable proportion of candidates are listed for renal transplantation and have a relatively poor prognosis, and many patients with substantial life expectancy are never listed (15).

We undertook this study to examine specific considerations for prospective older transplant candidates with the primary

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aim of projecting the likelihood of newly listed older candidates to receive a deceased-donor transplant on the basis of the combination of patient and regional factors. The aim of the study was to provide consolidated information for older candidates concerning individual prognoses, the likelihood to receive a deceased-donor transplant, or alternatively the incentive to consider seeking living donors. In addition, this information may inform policy makers as to the general prognoses for prospective older transplant candidates in the modern era and the potential role and need for organ allocation algorithms based on factors specific to this rapidly growing population.

## Materials and Methods

We examined older (age  $\geq 60$  yr), solitary renal transplant candidates who were listed from 1995 to July 2007 from the national Scientific Registry of Transplant Recipients database. The database contains the census of candidates listed for transplantation in the United States along with specific clinical patient-level data. In addition, (nonidentifiable) center and regional indicators are included in the database. For candidates who were listed multiple times during the study period, only the initial listing was considered for the analysis. For the purpose of the analysis and to present descriptive statistics, candidate race/ethnicity was categorized as white, Asian, black, Hispanic/Latino, and other. Panel reactive antibody (PRA) levels were categorized as 0, 1 to 10, 11 to 30,  $\geq 31$ , and missing. Body mass index (BMI) was categorized as  $< 25$ , 25 to 30, and  $> 30$  kg/m<sup>2</sup> and missing. The 11 regions corresponded to the United Network for Organ Sharing (UNOS) membership structure (16).

Kaplan-Meier and parametric survival models were incorporated to estimate time to receiving a deceased-donor transplant and time to death before transplantation on the basis of known factors that are associated with these events. The specific forms of these parametric models were evaluated on the basis of goodness-of-fit statistics and inspection of graphic diagnostics. Both the models for time to transplantation and candidate mortality assumed a Weibull distributional form. For the model for time to deceased-donor transplantation (DDTx), patients were evaluated from the time of listing, and receipt of a living transplant, time of delisting, last follow-up time, and patient death were censored for the analysis. Multivariate models incorporated age, PRA, race, region, gender, BMI, blood type, and year of listing. Time to candidate death was considered on an intention-to-treat basis, and models were censored for receipt of a transplant and last follow-up only. This was considered appropriate because deaths that occurred after patients' delisting were still of interest for the study. In addition, models were constructed excluding patients who were initially listed with a status indicating that they were temporarily inactive (status 7). Because a portion of candidates who initially are listed as status 7 may not ever become active whereas others may be activated after various durations and still accrue waiting time, it is possible that these patients may significantly alter survival estimates (17). Explanatory variables in these models included candidate age, primary diagnosis, gender, region, race, BMI, and initiation of dialysis at the time of listing. To estimate time to death and receipt of a DDTx from the adjusted survival model, we used the SAS macro %PREDICT (18). As a sensitivity analysis, models were also reconstructed eliminating patients who eventually received living transplants. This analysis was specifically undertaken to investigate the potential for informed censoring to bias estimates (*i.e.*, determining whether patients who received a living transplant and were censored for the analysis were more or less likely

to receive a deceased-donor transplant). The proportion of patients with a shorter expected time to death as compared with time to transplantation was evaluated within patient subgroups. All analyses were performed in SAS 9.1 (SAS Institute, Cary, NC).

## Results

### Study Population

The study included solitary kidney transplant candidates who were newly listed between 1995 and July 2007 who were at least 60 yr of age at the time of listing ( $n = 54,699$ ). Table 1 displays the distribution of patient characteristics during the study period. Half of older candidates were in the age range of 60 to 64, 37% had diabetes as a primary diagnosis, 29% were obese (BMI  $\geq 30$  kg/m<sup>2</sup>), 57% were white, 79% were on dialysis at the time of listing, 69% had PRA levels equal to 0%, and 62% were male. The number of newly listed older candidates nearly tripled during the study period from 2367 in 1995 to 6982 in 2006.

### Time to DDTx

The proportion of patients who received a deceased-donor transplant within 5 yr during the study period is displayed in Table 1. In aggregate, 61% of the population received a transplant within 5 yr; however, this proportion was significantly reduced among patients with diabetes, with nonwhite race/ethnicity, with type B and type O blood, with high PRA and, who were listed in certain UNOS regions. As represented in Figure 1, the time to receiving a deceased-donor transplant increased significantly during the period for older candidates. Among listing years in which median time to DDTx could be calculated, the median months to transplantation ranged from 30 to 49 during the study period.

### Time to Candidate Mortality

Table 1 also displays the proportion of candidates who were estimated to die within 5 yr of after listing and before transplantation. In aggregate during the study period, 52% of patients were estimated to die within 5 yr before transplantation; however, the proportion was notably higher among candidates who were older than 70 yr, had diabetes, were white, and were on dialysis at listing. Mortality rates varied mildly during the study period for older candidates (median survival from the time of listing ranged from 52 mo in 1997 to 59 mo in 2001). Figure 1 also displays an overlay of candidate mortality aggregated during the study period. In particular, Figure 1 represents the narrowing gap between the time to DDTx by year of listing and average older candidate mortality.

### Multivariate Models for Time to Transplantation and Mortality

Statistically significant factors associated with increased time to DDTx from the multivariate model were increasing PRA level, types B and O blood, white race, lower BMI, more proximate year of listing, and certain UNOS regions. Figure 2 displays the projected proportion of patients who were expected to receive a deceased-donor transplant by year of listing. In particular, among patients who were newly listed in 2006

Table 1. Proportion of older candidates who received a deceased-donor transplant and proportion of patient deaths at 5 yr after listing (1995 through 2007)<sup>a</sup>

| Patient Characteristic   | Level (%)            | 5-yr Probability of DDTx (%) <sup>b</sup> | 5-yr Probability of Mortality (%) <sup>c</sup> |
|--------------------------|----------------------|---|--|
| Age                      | 60 to 64 (50)        | 61  | 49   |
|                          | 65 to 69 (34)        | 61  | 53   |
|                          | ≥70 (17)             | 59  | 57   |
| Primary diagnosis        | Diabetes (37)        | 54  | 58   |
|                          | Hypertension (20)    | 60  | 49   |
|                          | Other (43)           | 67  | 40   |
| BMI <sup>†</sup>         | 13 to 25 (29)        | 62  | 54   |
|                          | 25 to 30 (38)        | 62  | 51   |
|                          | ≥30 (29)             | 58  | 51   |
| Race/ethnicity           | White (57)           | 68  | 58   |
|                          | Black (23)           | 51  | 48   |
|                          | Asian (5)            | 55  | 41   |
|                          | Hispanic/Latino (13) | 53  | 47   |
|                          | Other (2)            | 56  | 48   |
| On dialysis at listing   | Yes (79)             | 61  | 54   |
|                          | No (21)              | 61  | 40   |
| Blood type               | A (35)               | 72  | 55   |
|                          | AB (4)               | 81  | 53   |
|                          | B (14)               | 50  | 49   |
|                          | O (47)               | 55  | 52   |
| PRA <sup>d</sup>         | 0 (69)               | 62  | 51   |
|                          | 1 to 30 (15)         | 59  | 52   |
|                          | >30 (7)              | 47  | 52   |
| Gender                   | Male (62)            | 63  | 54   |
|                          | Female (39)          | 58  | 49   |
| OPTN region <sup>e</sup> | 1 (4)                | 66  | 55   |
|                          | 2 (16)               | 63  | 55   |
|                          | 3 (11)               | 66  | 52   |
|                          | 4 (7)                | 71  | 46   |
|                          | 5 (20)               | 49  | 51   |
|                          | 6 (3)                | 77  | 49   |
|                          | 7 (9)                | 67  | 54   |
|                          | 8 (5)                | 73  | 53   |
|                          | 9 (8)                | 44  | 53   |
|                          | 10 (8)               | 68  | 52   |
|                          | 11 (8)               | 61  | 53   |
| Overall                  | <i>n</i> = 54699     | 61  | 52   |

<sup>a</sup>DDTx, deceased-donor transplantation; OPTN, Organ Procurement and Transplantation Network; PRA, panel reactive antibody.

<sup>b</sup>Based on Kaplan-Meier models, censored for end of follow-up, death, removal from waiting list, and receipt of living transplant.

<sup>c</sup>Based on Kaplan-Meier models, censored for transplantation (either deceased donor or living) and end of follow-up period.

<sup>d</sup>Missing levels not displayed.

<sup>e</sup>OPTN regions are defined as follows: Region 1: Connecticut, Maine, Massachusetts, New Hampshire, Rhode Island; region 2: Washington, DC, Delaware, Maryland, New Jersey, Pennsylvania, West Virginia; region 3: Alabama, Arkansas, Florida, Georgia, Louisiana, Mississippi, Puerto Rico; region 4: Oklahoma, Texas; region 5: Arizona, California, Nevada, New Mexico, Utah; region 6: Alaska, Hawaii, Idaho, Montana, Oregon, Washington; region 7: Illinois, Minnesota, North Dakota, South Dakota, Wisconsin; region 8: Colorado, Iowa, Kansas, Missouri, Nebraska, Wyoming; region 9: New York, Vermont; region 10: Indiana, Michigan, OH; region 11: Kentucky, North Carolina, South Carolina, Tennessee, Virginia.

through 2007, approximately half of candidates were expected to receive a deceased-donor transplant within 5 yr. The proportion of patients who were projected to receive a transplant within 1 and 3 yr after listing also significantly declined during

the study period. Neither gender nor age group was statistically significantly associated with time to DDTx in this model. For the model for time to candidate mortality, all included factors were statistically significant: Increasing age, white race,

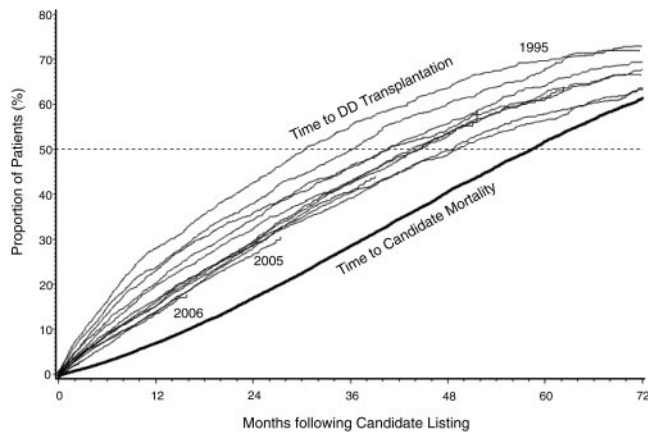


Figure 1. Kaplan-Meier plots of time to deceased donor transplantation (DDTx) by year of listing and time to mortality for older candidates. DD, deceased donor. Time to mortality includes all older candidates listed during the study period.

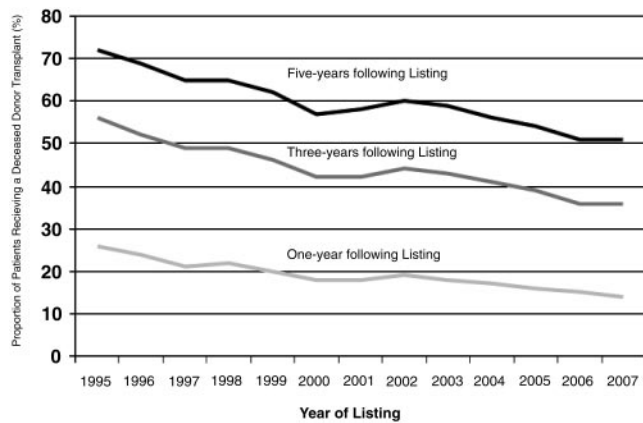


Figure 2. Projected proportion of candidates who were older than 60 yr and receiving a deceased-donor transplant by year of listing (based on Weibull survival model censored at the times of patient death, last follow up, delisting, and receipt of a living transplant).

male gender, lower BMI, certain years of listing, and UNOS regions and primary diagnoses.

Candidates Listed in 2006 through 2007

On the basis of the projected candidate times to transplantation and mortality, Figure 3A displays the proportion of patients who were listed in 2006 through 2007 and had a shorter projected time to death than time to receipt of a deceased-donor transplant. In particular, nonwhite patients, candidates with types B and O blood, highly sensitized candidates, older patients, female patients, patients with low and high BMI levels, and candidates who were on dialysis at listing had increased probability of not reaching the time when a deceased-donor transplant would become available as compared with their respective counterparts. The overall proportion of older candidates who were listed in 2006 through 2007 and were expected to die before transplantation was 46%. This projected propor-

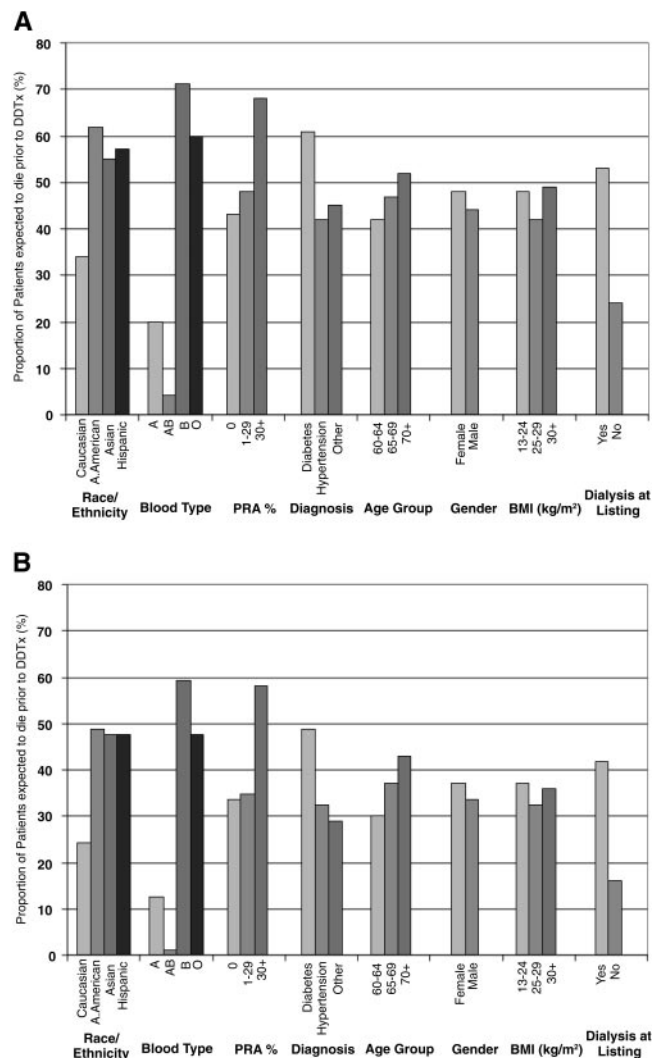


Figure 3. (A) Projected proportion of candidates who were listed in 2006 through 2007 and expected to die before receiving a deceased-donor transplant by patient characteristics (overall 46%). PRA, panel reactive antibody; BMI, body mass index. (B) Projected proportion of candidates who were listed in 2006 through 2007 and expected to die before receiving a deceased-donor transplant by patient characteristics excluding candidates who initially were listed as temporarily inactive (overall 35%).

tion increased steadily during the study period, which was initially 22% of candidates in 1995. This proportion was reduced to 35% when patients who initially were listed as temporarily inactive were excluded (Figure 3B); however, even with these projections, approximately half of minority race groups, type B and type O blood types, highly sensitized patients, and candidates with diabetes as a primary diagnosis were expected to die before DDTx. Figure 4 represents these proportions by UNOS region both with and without including patients who initially were listed status 7. As displayed, estimates for the proportion of candidates who were listed in 2006 through 2007 and expected to die varied widely between regions from 6% (region 6) to 81% (region 5).

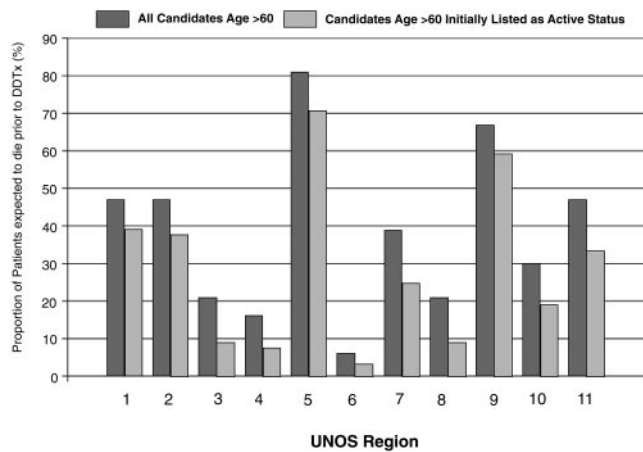


Figure 4. Projected proportion of candidates who were listed in 2006 through 2007 and expected to die before receiving a deceased-donor transplant by United Network for Organ Sharing (UNOS) region. Organ Procurement and Transplantation Network regions are defined as follows: Region 1: Connecticut, Maine, Massachusetts, New Hampshire, Rhode Island; region 2: Washington, DC, Delaware, Maryland, New Jersey, Pennsylvania, West Virginia; region 3: Alabama, Arkansas, Florida, Georgia, Louisiana, Mississippi, Puerto Rico; region 4: Oklahoma, Texas; region 5: Arizona, California, Nevada, New Mexico, Utah; region 6: Alaska, Hawaii, Idaho, Montana, Oregon, Washington; region 7: Illinois, Minnesota, North Dakota, South Dakota, Wisconsin; region 8: Colorado, Iowa, Kansas, Missouri, Nebraska, Wyoming; region 9: New York, Vermont; region 10: Indiana, Michigan, OH; region 11: Kentucky, North Carolina, South Carolina, Tennessee, Virginia.

As a sensitivity analysis, estimates were also recalculated excluding living transplant recipients (rather than censoring at the time of living-donor transplantation) on the basis of the potential for informed censoring. After eliminating these cases, the projected proportion of patients who were expected to die before transplantation and were listed in 2006 through 2007 was similar (47%) to the original analysis. In addition, estimates by region and patient characteristics were relatively consistent with the primary models.

## Discussion

The primary findings from this study detail the impact of expanding waiting times for older kidney transplant candidates. In particular, the study documents the growing proportion of older candidates who are at risk for dying before transplantation associated with increasing waiting periods and rates of candidate listing. Important, however, this risk is widely variable among older candidates on the basis of individual characteristics and the region in which they list. On the basis of these trends, older candidates and their caregivers may want to consider this information in their decision to list for a deceased-donor transplant or, alternatively, the possible incentive to seek a living donor. Regardless, dissemination of these data is important to facilitate informed decision-making among current and prospective kidney transplant candidates in the United States.

The primary results of the study inform a question that many (if not all) renal transplant candidates should consider asking: *If I list for a deceased-donor transplant today, what is my likelihood of surviving to receive the transplant?* Although there are various sources by which candidates may gather data on this subject, there is not any existing consolidated information to answer this important question. Knowledge about this information could potentially influence patients' behavior, most directly by providing information to compare with the possibility and incentive of seeking a living donor. In addition, these data may further substantiate the important incentive for candidates to list as rapidly as possible. It is likely that some candidates who are told that they have a 25% chance of surviving the interval to receiving a deceased-donor transplant *versus* a 90% chance would consider acquiring a living donor differently. For many candidates and their caregivers, there may be a general sense for patients' prognosis on the waiting list but little opportunity to translate this to tangible estimates. Critical in this process is to inform patients on the basis of the most salient information, and as these results demonstrate, a white candidate with type AB blood in region 1 is in a very different circumstance than an black candidate listed with type B blood in region 5.

Expanding waiting times clearly affect all portions of the transplant candidate populations; however, older and frailer patients may be the most directly affected because of rapid mortality rates before receiving a deceased-donor transplant. In other words, the marginal impact of rapid listing, individual characteristics, and region of listing on mortality are elevated relative to their younger and healthier counterparts. As such, it could be argued that rapid decision-making and navigation through steps that are involved in acquiring a transplant are most critical for this subset of the population. There are numerous examples in health care in which decision-making can have an important role in patient prognoses. In most health care paradigms, a significant presence of asymmetric information renders patients dependent on caregivers to disseminate the most salient data to inform these decision-making processes. Unfortunately, for a variety of reasons, including the type of health care provider, patient characteristics, and cultural barriers, the most relevant information does not always reach patients in a coherent manner (13,19,20); therefore, more effective interventional programs and mechanisms to disseminate critical information in a systematic manner are needed. Alternatively, these types of data are likely to be received by proactive (often well-educated or affluent) patients and may in fact exacerbate known disparities in care. Certainly, as caregivers and researchers, we should strive to inform patients in an equitable manner, which may ultimately also be an important component of eliminating disparities in health care.

There are several notable limitations of this study, some of which are consistent with many retrospective and population-based analyses. Many noncodified factors ultimately influence patients' prognoses and propensity to receive a transplant that are not incorporated in the analyses for this study. In this sense, these results provide a general framework that can be used to guide patients and illustrate the importance of various factors but should not be used exclusively ignoring individual circum-

stances. An additional challenge with this retrospective analysis is in defining the population of transplant candidates. This study used two approaches: One by including all first candidate listings included in the database and another by excluding patients who initially were listed as temporarily inactive. The purpose of the latter approach was to provide estimates that were not affected by patients who were technically listed as candidates but may still require additional medical evaluation or clearance before becoming activated; however, because these patients can still accrue waiting time, limiting the analysis period to the time of activation on the waiting list could underestimate the time to events as well. Therefore, the results provide both optimistic and pessimistic estimates that are applicable only to patients who are listed as active and to the entire older candidate population, respectively.

Another important consideration for these study results is that the field of transplantation is rapidly evolving with respect both to the composition of the patient population and to the policies that affect older candidates. In these regards, the results presented in this study may have significantly different implications in the future. For example, the current consideration for a new kidney allocation algorithm may markedly affect (perhaps exacerbate) the estimates presented and the importance and type of decision-making processes described in this study (21). For instance, elements of the newly proposed policy include more rapid access to deceased-donor transplants to younger patients as compared with older candidates; as such, the overall proportion of older candidates who are at risk for death before transplantation could increase even more than continuation of existing allocation policy. In addition, recently enacted policy that has eliminated national sharing of six-antigen matching may reduce the projected disparities by race/ethnicity because white patients were significantly more likely to receive these transplants (22). Another limitation of these results relates to the reporting of data aggregated at the regional level. Regions in this case largely serve as a proxy for variable waiting times in the United States. Although there may be other factors specific to regions (e.g., variants on allocation algorithms), data should be interpreted more specifically at the center level within regions. The impact of center characteristics (primarily waiting time) has a profound effect on candidate outcomes, and this information should be clear to prospective candidates (23). Finally, projected estimates are intrinsically accompanied by increased uncertainty; although it is unlikely that times to transplantation will significantly decline or that candidate mortality will rapidly shift, the particular estimates reported in this study certainly have a degree of variability. Cumulatively, the information presented in this study is only a sample of important information for this population, but these results provide objective data about key factors that are associated with older candidates' prognoses that could be considered crucial to disseminating to prospective and currently listed candidates.

## Conclusions

The study results indicate that nearly half of older candidates are projected to die before receiving a deceased donor trans-

plant nationally but, importantly, that these projections vary substantially within the population. Both regional- and patient-level characteristics are strongly associated with time to transplantation and mortality for older transplant candidates listed in the United States. Caregivers should strive to empower patients with information that can affect potentially life-altering decisions. Dissemination of this information may facilitate informed choices and provide tangible data to prospective older candidates who are considering transplantation as a treatment option.

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## Disclosures

None.

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