# Solid Organ Transplantation Overview and Selection Criteria

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## Abstract

The field of solid organ transplantation has seen significant advances in surgical techniques, medical diagnosis, selection process, and pharmacotherapy over the past 6 decades. Despite these advances, however, there remains a significant imbalance between the supply of organs available for transplant and the number of patients registered on transplant waiting lists. Notably, the past decade has shown gradual increases in the number of candidates waiting for a kidney, while the number of transplants performed in the United States has declined every year for the past 3 years. The waiting list for heart transplants has been the most rapidly growing list. Fortunately, policies designed to improve procurement, screening, and distribution are helping to make transplantation more efficient and organs more accessible, allowing sicker patients to undergo transplants more quickly. This article presents an overview of the most common solid organ transplantations performed (kidney, liver, heart, and lung), along with the requirements, risks, and complications associated with them.


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For author information and disclosures, see end of text.

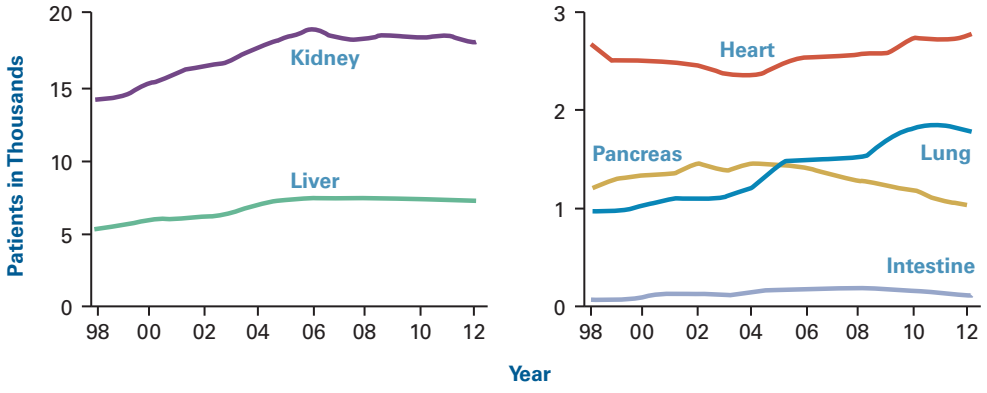
Over the past 6 decades, solid organ transplantation has evolved from an experimental procedure to a standard-of-care, lifesaving procedure, and survival rates have improved in a relatively short time frame. The field has come a long way since the first documented successful kidney transplantation was performed between living identical twins by Joseph Murray, MD, and John Merrill, MD, in 1954.[1,2] Unfortunately, similar operations in nonmatched pairs did not yield similar success. The field of transplantation continued in this manner, hindered by rejection and multiple complications, resulting in only minor success and limited 1-year survivals in nonmatched recipients. Subsequent failures and successes demonstrated a need for refined, targeted, and titratable immunosuppression, as well as recognition, management, and prophylaxis of secondary infection complications to propel the field forward. It was not until cyclosporine was introduced in the 1980s that the modern era of solid organ transplantation began.



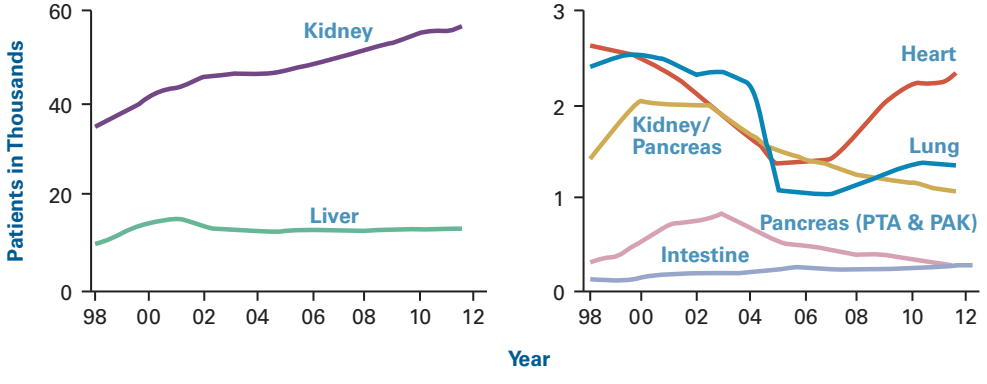
Over the past 3 decades, success in the refinement of antimicrobial agents, development of preemptive and prophylaxis strategies, enhancement in monitoring methods, and advancement of immunosuppressive induction have significantly improved the success rates of solid organ transplantation.[1,2] A confluence of legal parameters facilitating ethical organ donation, procurement, and allocation; advances in organ preservation; and surgical, medical, and pharmacological advances in the management of infections have left cultural acceptance and supply, demand, and distribution as the biggest hurdles to overcome in the field.[1-11]

Solid organ transplantations are now near-routine surgical procedures in hospitals across the United States. There were 18,048 kidney transplants alone performed in the United States in 2012 (**Figure 1**).[12] Other types of solid organ transplants include liver (6781), heart (2407), lung (1795), pancreas (1043), and intestine (106).[12] Unfortunately, challenges continue with the procurement and distribution of organs and post opera-

■ **Figure 1.** Adult and Pediatric Transplants Performed per Year[12]




■ **Figure 2.** Number of Patients on Waiting Lists for Donor Organs (on December 31 of each respective year, active listings only)[12]




Kidney: patients receiving a kidney alone or simultaneous kidney-pancreas transplant. Lung: patients receiving a lung alone or simultaneous heart-lung transplant. Other organs: patients receiving a transplant. Retransplants are counted.
PAK indicates pancreas and kidney transplant; PTA, pancreas transplant alone.

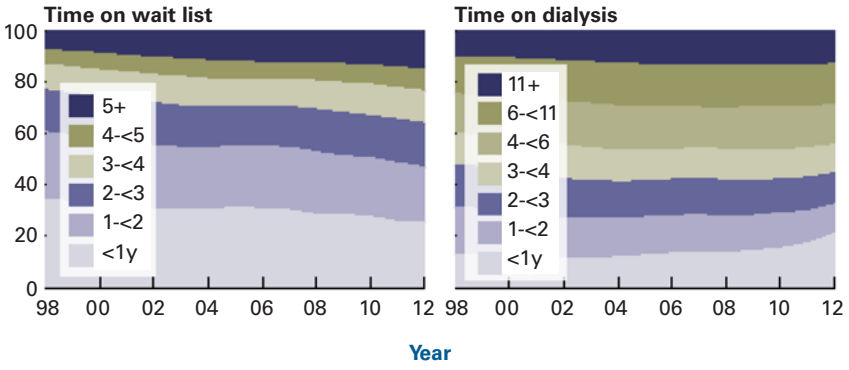
tive management: in 2012, almost 58,000 active candidates were on the kidney transplant waiting list, a 3.5% increase from 2011 (Figure 2).[12] Also, the number of heart transplants performed increased by 2.0% between 2011 and 2012, but the number of patients on the waiting list increased by 10.4%. And although the numbers of patients on the wait lists for liver and lung transplants decreased by 1.8% and 2.9%, respectively, this still resulted in a disparity with the number of transplants performed (declines of 3.9% and 6.2% for lung and liver transplants, respectively). Overall, a shortage of deceased donor organs for transplantation has led to the disparity between patients in need and organs available.[12] This section provides an overview of the most common solid organ transplantations performed (kidney, liver, heart, and lung) and describes changes in waiting list and allocation requirements that will make the process more effective, improve outcomes, and reduce complications.

## Kidney Transplantation: Overview and Selection

### *Overview*

Kidney transplant is one of the most cost-effective surgical interventions and, by far, the most common type of transplant procedure performed. Consequently, it is encountered more often in clinical practice than other solid organ transplantations and is the most researched solid organ transplant (Figure 1).[12] Compared with dialysis, successful kidney transplantation improves long-term survival and quality of life for most end-stage renal disease patients. And for patients under 70 years of age, post transplant outcomes are better when the transplant is performed prior to initiation of dialysis (as outcomes decline with each additional year of pre-transplant dialysis).[12] Despite this successful track record, The Organ Procurement and Transplantation Network (OPTN) database shows that the number of candidates added to the wait list for a kidney transplant has increased every

■ **Figure 3.** Kidney Transplant Waiting List: Trends Over Time (in years)[12]




year for the past decade, while the number of transplants performed each year has declined.

In 2011, approximately 40% of adult patients on the kidney transplant wait list were aged between 50 and 64 years, 34% between 35 and 49 years, and 14% between 18 and 34 years. About one-third of the patients remained on the list for less than a year, and more than 42% remained on the list for more than 2 years (**Figure 3**).[12] The median time to transplant for the adult patients on the wait list was 4.2 years in 2008, an increase from 2.7 years in 1998.[12] Of the 26,263 adult patients taken off the transplant list in 2012, 20% died prior to receiving a transplant and 8% were removed because they were too sick to undergo a transplant. Between 2010 and 2012, more than 21,000 adult patients were taken off the wait list due to death or being too sick to undergo a transplant. Unfortunately, despite the need for kidney donation, the rate of discarded kidneys has increased over the past decade, and the rate of living donor transplants has decreased from 6674 in 2004 to 5622 in 2012.[12]

In 2013, this continued disparity led the OPTN to introduce a new kidney allocation system, which is expected to assist in the allocation of organs to broaden patient access, limit discard rates, and improve survival—although it will not be able to solve the problem of a shortage in the supply of donor kidneys.[12] Despite these limitations and the challenges of immunosuppressive therapy and related complications such as infection, cardiovascular disease, and neoplasia, kidney transplant remains the treatment of choice for end-stage renal disease and offers significant survival benefits compared with other renal replacement therapies (eg, dialysis). In 2012, the 5-year graft survival rate was 73% for deceased donor transplants and 84% for living donor transplants. The overall effectiveness of kidney transplants, including their cost savings for the healthcare system, make effective procurement and distribution of organs equally critical in optimizing the transplant system from both a patient and a managed care perspective.[12]

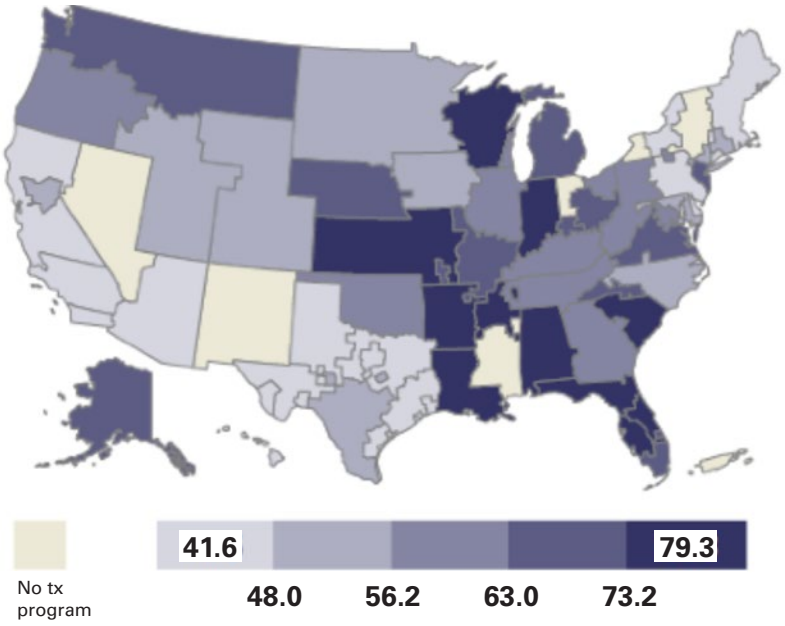
### *Selection Criteria*

Kidney transplant candidates have irreversible chronic kidney disease with estimated glomerular filtration rates less than 30 mL/min per 1.73 $m^2$ without known contraindications such as active infection, active neoplastic disease, significant systemic illnesses with limited survival, and active substance abuse. The majority of kidney transplants in the United States come from deceased donors; however, a sizable number of kidney transplants are conducted using living donors, related or unrelated to the recipient.[12]

Organ supply is the primary rate-limiting factor affecting the number of transplant procedures that can be performed. Therefore, limiting the discard rate and optimizing the longevity of the organ is critically important to the individual patient, particularly those on the waiting list, as well as the overall population.[12] The changes in the kidney allocation system should further decrease access variability by candidate blood type, sensitization level, and geographic location.[12]

A point system will be used to assign donor kidneys and candidates a score[12]: donor kidneys will be assigned a Kidney Donor Profile Index (KDPI) score, ranging from 0% to 100%, that is associated with the functionality of the kidney relative to other kidneys. The receiving candidate will be assigned an Estimated Post Transplant Survival (EPTS) score, also ranging from 0% to 100%, that is associated with the length of time the candidate will need the kidney to function. Together, the KDPI and EPTS scores are expected to efficiently match graft years needed and potentially incorporate more dona-

■ **Figure 4.** DSA Distribution of Percent of Adult Wait Listed Patients in 2007 Who Received a Deceased Donor Liver Transplant Within 5 Years[12]




DSA indicates donation service area; tx, treatment.
Patients with concurrent listings in a single DSA are counted once in that DSA, and those listed in multiple DSAs are counted separately per DSA.

tions from older donors. Priority will be given to children and teenagers, those with blood type B, and those who are highly sensitized. Although waiting time will be calculated based on initiation of dialysis, physicians are encouraged to list patients upon or just before initiating dialysis or reaching end-stage kidney failure.[13]

## Liver Transplantation: Overview and Selection

### *Overview*

For patients with irreversible liver disease or acute or chronic liver failure from any cause, liver transplants are a life-saving procedure. The unadjusted 5-year survival rate was 70.5% for patients receiving a deceased donor transplant in 2007. Typical indications for liver transplant include cirrhosis with complications, acute liver failure, selected liver neoplasia, and liver-related metabolic disorders with systemic manifestations. In 2012, there were 6256 adult liver transplants performed across 132 US transplant centers, and more than 10 times that number were living with a transplanted liver.[12] The distribution of liver disease etiology in 2012 remained mostly unchanged from 2002: Hepatitis C (HCV) remained the primary cause of disease (30.1%), but the number of cases attributed to malignancy jumped from 289 (1.9%) in 2002 to 1052 (6.9%) in 2012.[12]

In 2012, 10,143 candidates were added to the liver transplant wait list, a 2.1% decline from 2011 due to a gradually worsening donor shortage. Unfortunately, the median wait time on the list and the number of candidates removed from the list because they were too sick to undergo transplant have continued to increase. A total of 10,281 adult patients were removed from the wait list in 2012: of these, 2187 patients (21%) died while on the list and 815 (8%) were removed because they were too sick to undergo transplant. In addition to the issue of procurement, distribution and access also proved to be challenges. The overall deceased donor transplant rate varied geographically from 18.9 to 228.0 per 100 patient-years, and the proportion of adults receiving deceased donor organs within 5 years of being registered on the waiting list ranged from 30.5% in the New York donation service area (DSA) to 86.1% in the Arkansas DSA (**Figure 4**).[12]

As of June 30, 2012, there were 56,900 adult liver transplant recipients still alive, almost double the number from 10 years before (28,500 in 2002), a testament to the success of liver transplantation in the United States. Also in 2012, 5468 deceased donor liver transplants and 192 living donor transplants were performed. The overall 90-day graft survival for all deceased donor livers has consistently improved over the past decade. Conversely, living donor

graft survival has abruptly worsened since 2010, as have other short-term outcomes in living donor transplants, such as biliary and vascular complications. Among graft survivors with living or deceased donor liver transplants, the leading causes of death were alcoholic liver disease, cholestatic disease, and HCV, while the development of post transplant diabetes was a major comorbidity.[12]

Average Medicare reimbursement for liver recipients from transplant through 1 year after transplant totals $250,000, including reimbursement to hospitals for the transplant portion of the Medicare Cost Report and Medicare Part D; this is approximately $50,000 more than reimbursement for a kidney transplant recipient. Rehospitalization rates are relatively high in the first year after liver transplant, as well. However, after the first year, annual costs dramatically decrease, so that when all reimbursements issued to hospitals are accounted for, the total cost estimate for subsequent years is approximately $35,000 per year, similar to cost estimates for kidney transplant.[12]

### *Selection Criteria*

Candidates for liver transplants are assigned a score that assesses their chance of death within 3 months. For candidates 18 years and older, this score is based on the Model for End-Stage Liver Disease (MELD) scoring system.[14] This scoring system was originally used to predict survival in patients undergoing the transjugular intrahepatic portosystemic shunt procedure.[15] However, for patients undergoing liver transplants, the MELD score uses objective and stable values (ie, test results for creatinine, bilirubin, and international normalized ratio for prothrombin time) to predict survivability of a patient 3 months after transplant.[15,16] Furthermore, candidates are assigned a medical urgency status: 1A, 1B, priority based on MELD score, or medical exceptions. The adult status 1A is assigned if the candidate has a life expectancy of less than 7 days without a liver transplant. Exceptions are made and additional points allotted based on time on the list, blood type, certain medical circumstances, and medical urgency.[14] Patients with hepatocellular carcinoma nodules larger than 1 cm in size may be eligible for automatic priority.[14]

## Heart Transplantation: Overview and Selection

### *Overview*

Heart transplants, including related medical coverage through the first year after transplant, cost Medicare $298,628 per patient, similar to the cost of lung or intestine transplants but about 3 to 4 times the expenditure for a kidney or liver transplant.[12] Transplant complications and infections, which cost approximately $38,139 (Medicare Part A and B) per year after the first year, are the most common causes of post transplant rehospitalization.[12] The total cost of heart transplantation is more expensive than implantation of a ventricular assist device (VAD); however, in the long run, transplant is considered to be the most cost-effective option in terms of cost per quality-adjusted life-year gained.[17]

As with all other solid organ transplantations, donor organ supply is the primary impediment to heart transplantation. Since 2004, the number of heart transplants performed and the number of adult candidates on the waiting list have increased by 17.1% and 25%, respectively. The issue of available organs notwithstanding, the prognosis for heart transplantation is good: the proportion of candidates awaiting heart transplant for 4 or more years has been cut in half, from 18.7% in 2002 to 9.2% in 2012, and among patients listed for transplant in 2009, 55.9% underwent transplant within 12 months of listing, and 66.7% within 36 months.[12]

Allocation policy changes, along with the evolving management of heart failure over the past few years, may be responsible for the conflicting trends seen in heart transplantation in 2012.[12] For example, centers may defer the early listing of patients on the transplant list because they recognize that a transplant for a patient listed as status 2 is unlikely. This has resulted in a shift in the number of patients listed in the most urgent category (status 1A) compared with those listed as status 2.[12] The greater number of heart transplant patients may reflect a sharing policy initiated in 2006 by the OPTN aimed at increasing heart donation rates, reducing waiting times, and ensuring equitable access to a heart transplant without geographic variances.[12]

Preoperative management of patients with end-stage heart failure, particularly in terms of advances in VADs, as well as policies to improve patient selection and waitlist management, has resulted in successful outcomes for patients undergoing heart transplants. The median survival for candidates who received a transplant is 11.6 years, and the prevalence of living heart transplant recipients continues to increase. The most common causes of mortality in 5-year post transplant survival data were cardiovascular/cerebrovascular events and infection, followed by graft failure, malignancy, and respiratory complications.[12]

*Selection Criteria*

Heart transplant candidates are assigned medical urgency status 1A, 1B, 2, or inactive. Priority status (1A) is assigned if the candidate is admitted to the registering transplant hospital and has a mechanical circulatory support device in place, requires continuous mechanical ventilation, or requires continuous inotrope infusion and hemodynamic monitoring. Candidates may also qualify as 1A if they have a VAD or demonstrate medical evidence of significant device-related complications. Candidates may qualify as 1B if they have a VAD in place or require continuous inotrope infusion. Status 2 is reserved for candidates suitable for transplant but ineligible for status 1A or 1B.[18]

**Table.** Variables Used to Calculate the Lung Allocation Score[19]

| |
|---|
| Age |
| Height and weight |
| Lung diagnosis code |
| Functional status (level of assistance required to perform activities of daily living) |
| Diabetes status |
| Assisted ventilation |
| Supplemental oxygen requirement |
| Amount and percent |
| Percent predicted FVC |
| Pulmonary artery systolic pressure |
| Mean pulmonary artery pressure |
| Pulmonary capillary wedge mean |
| $PCO_2$ |
| Current, highest, lowest, and change |
| Six-minute walk distance |
| Serum creatinine |

FVC indicates forced vital capacity; $PCO_2$, partial pressure of carbon dioxide.

Most of the demographics and distribution of qualifying candidates on the wait list has remained consistent over the past decade; however, there has been a rise in status 1A patients on the wait list (2.5% in 2002 vs 8.9% in 2012) and as transplant recipients (34.8% in 2002 vs 58.5% in 2012). The trend of candidates on the wait list may correlate with the substantial increase in the percent of candidates using VAD implants at listing (3.4% vs 21.7%), which subsequently changes their listing status from 2 to 1B. Heart transplants among status 2 candidates are becoming very rare. As a result of advances in management and the lag in time to transplant for status 2 candidates, the majority of candidates placed on the wait list are either being placed in higher medical urgency categories or centers are deferring listing candidates until they can be listed as status 1B or 1A.[12]

## Lung Transplantation: Overview and Selection

*Overview*

Lung transplants are an option for patients with end-stage lung diseases that are not amenable to further medical and/or surgical therapies. Compared with other solid organ transplant recipients, lung transplant recipients experienced a higher rate of rehospitalization for transplant-related complications (43% in the first year, 36% in the second year). This is likely due to complications from the long-term use of immunosuppressive medications. For patients who have undergone a lung transplant, the unadjusted median survival is 5.3 years, the conditional median survival is 6.7 years, and an impressive 86.5% require no assistance in their activities of daily living 5 years after transplant. Longer-term data may not represent stable trends, as they do not reflect implementation of the Lung Allocation Score (LAS).[12]

As of June 30, 2012, more than 10,000 recipients were living with a transplanted lung. The number of new patients added to the list and the number of patients waiting for a transplant declined in both 2011 and 2012. Nonetheless, more new candidates were added to the list than were removed. The overall median wait time for a transplant was 4 months, and 65.3% of candidates underwent transplant within 1 year of listing. As with other solid organ transplantations, there was significant geographical disparity in the percent of patients who received deceased donor lung transplants within 1 year (range, 43.5%-89.8%).[12]

*Selection Criteria*

Lung transplant allocation is based on use of the LAS (see **Table**[19]), geographic location, and blood type compatibility.[12,18,19] The LAS system, which is based on survival probability and the pathophysiology of the underlying disease, categorizes candidates for lung transplant into 4 main groups: obstructive lung disease, pulmonary vascular disease, cystic fibrosis and immunodeficiency disorders, and restrictive lung disease. The LAS calculation is used to predict the risk of wait list mortality and

probability of post transplant survival, thereby avoiding transplant candidates who have very poor likelihood of survival. Unlike the point system utilized in kidney allocations, the LAS methodology was implemented to de-emphasize time on the wait list and remove incentives for early listing, so as to minimize wait list mortality and reduce wait time.[12]

Since implementation of the LAS, there has been a steady decrease in inactive candidacy, and candidates on the list tend to be older, sicker, and have more restrictive lung disease. In 2012, 53% of patients on the wait list were between the ages of 50 and 63 years. Interestingly, although 58.5% of the candidates in 2012 were female, they represented only 42% of lung transplant recipients.[12]

## Outcomes and Complications

Transplant outcomes are most commonly measured in terms of acute rejection, graft survival, and patient survival.[12] Graft failure and acute rejection are the most common reasons for transplant failure and death among solid organ transplant patients.[12] Risk factors which may affect transplant longevity include hypertension, diabetes, dyslipidemia, cardiovascular disease, malignancy, and infection.[20,21]

Immunosuppressant agents used in patients undergoing solid organ transplants can exacerbate preexisting conditions or contribute to post transplant complications.[20,21] For example, renal dysfunction, a common complication that results in significant morbidity and increases the risk of mortality in all types of solid organ transplants, is associated with certain immunosuppressant agents.[22,23] In general, as immunosuppressive strategies have improved, rejection rates have declined and graft survival has improved. And although graft failure continues to be the leading cause of death in kidney transplant patients, rates of death-censored graft failure in the first 90 days have steadily decreased for both living and deceased donor transplants.[12]

## Conclusion

An ongoing concern in the field of solid organ transplantation is the increasing disparity among supply, demand, and distribution. The increase in donor organ demand is a testament to the overall success in the field of solid organ transplantation. The growth in the field of solid organ transplantation over the past 60 years is remarkable. It is the result of a multidisciplinary collaboration between healthcare practitioners, researchers, and policy makers, as well as the culmination of advances in surgical techniques, medical diagnosis, pharmacotherapy, and screening and distribution policies. Continued innovations in immunosuppressive therapy and screening and distribution policies will further improve outcomes and reduce complications.

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