ORIGINAL RESEARCH

Heart Transplantation in Children With Down Syndrome

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BACKGROUND: Children with Down syndrome (DS) have a high risk of cardiac disease that may prompt consideration for heart transplantation (HTx). However, transplantation in patients with DS is rarely reported. This project aimed to collect and describe waitlist and post–HTx outcomes in children with DS.

METHODS AND RESULTS: This is a retrospective case series of children with DS listed for HTx. Pediatric HTx centers were identified by their participation in 2 international registries with centers reporting HTx in a patient with DS providing detailed demographic, medical, surgical, and posttransplant outcome data for analysis. A total of 26 patients with DS were listed for HTx from 1992 to 2020 (median age, 8.5 years; 46% male). High-risk or failed repair of congenital heart disease was the most common indication for transplant (N=18, 69%). A total of 23 (88%) patients survived to transplant. All transplanted patients survived to hospital discharge with a median posttransplant length of stay of 22 days. At a median posttransplant follow-up of 2.8 years, 20 (87%) patients were alive, 2 (9%) developed posttransplant lymphoproliferative disorder, and 8 (35%) were hospitalized for infection within the first year. Waitlist and posttransplant outcomes were similar in patients with and without DS (P=non-significant for all).

CONCLUSIONS: Waitlist and post-HTx outcomes in children with DS selected for transplant listing are comparable to pediatric HTx recipients overall. Given acceptable outcomes, the presence of DS alone should not be considered an absolute contraindication to HTx.

Key Words: Down syndrome ■ health disparities ■ heart transplantation ■ outcomes

See Editorial by Schumacher et al.
outcomes, including pulmonary hypertension, immunologic dysfunction with an increased risk for infections and autoimmunity disorders, obesity, and an increased risk of acute leukemia. Whether these potential risk factors impact waitlist or posttransplant outcomes, however, remains unclear. There are currently no large-scale studies to suggest that HTx is contraindicated in patients with DS, and the limited available studies suggest that acceptable outcomes can be achieved. A better understanding of how patients with DS fare with HTx is critical to assess the feasibility of this procedure in this population and to allow for equitable access to this life-saving therapy.

The aim of this study is to describe waitlist and post-HTx outcomes of children with DS across a multicenter cohort. We hypothesized that children with DS would have acceptable waitlist and post-HTx outcomes without increased risks of posttransplant infection, posttransplant lymphoproliferative disorder (PTLD), or posttransplant mortality.

METHODS

Study Cohort and Data Source

This is a retrospective case series of children with DS who were listed for HTx. Pediatric HTx centers belonging to the International Society of Heart and Lung Transplantation or Pediatric Heart Transplant Society listservs were contacted to identify patients with DS who were listed for HTx at their center at any timepoint. Centers reporting a patient with DS listed for HTx were then asked to participate in detailed retrospective data collection.

Study data were collected and managed using REDCap (Research Electronic Data Capture) electronic data capture tools hosted at Vanderbilt University Medical Center. REDCap is a secure, web-based software platform designed to support data capture for research studies. Data were collected pertaining to cardiac diagnosis, comorbidities, pretransplant support, the transplant procedure, and patient outcomes. Outcomes assessed included waitlist and posttransplant survival, rejection, posttransplant malignancy, and hospitalization for infection in the first year after transplant. Rejection was defined by each center as a clinical event, with or without biopsy confirmation, that prompted augmentation of the immunosuppression regimen. Detailed data collection forms are provided in Data S1.

Data from the Organ Procurement and Transplantation Network (OPTN) were used to generate matched control groups. Controls were randomly selected (4:1) after matching for age (±2 years), sex, diagnosis (CHD with prior surgery, CHD without prior surgery, anthracycline cardiomyopathy, dilated cardiomyopathy, or myocarditis), year of transplant, and the need for ventricular assist device, extracorporeal membrane oxygenation, or mechanical ventilatory support. Separate control groups were generated for waitlist and posttransplant outcomes. Because of limitations of OPTN data, an analysis of hospitalization for infection in the first year after transplant was not possible for the matched control group.

Statistical Analysis

Data are presented using summary statistics and reported as frequency (percentage) for categorical and median (interquartile range [IQR]) for continuous data. The Kaplan–Meier method was used to assess posttransplant graft survival, freedom from rejection, freedom from posttransplant malignancy, and freedom from hospitalization for infection in the first year after transplant. The log-rank test was used to compare outcomes between patients with DS and the matched control groups.

Institutional review board approval or exemption was obtained at each participating institution with a waiver of informed consent. The corresponding author had full access to all the data in the study and takes responsibility for its integrity and the data analysis. A subset of deidentified data that support the findings of this study may be made available upon reasonable request from the corresponding author.

RESULTS

A total of 17 centers across 4 different countries (Canada, Sweden, the United Kingdom, and the United States) reported 28 patients with DS who were
listed for HTx. Of this group, 15 (88%) centers agreed to participate in detailed retrospective data collection, accounting for 26 (93%) of the 28 identified patients. The earliest reported HTx listing was in 1992. The timeline of HTx listings in patients with DS is shown in Figure S1. Most patients were listed for HTx only, with 1 patient listed for combined heart–kidney transplantation.

**Baseline Demographics and Clinical Characteristics**

Demographic data for the 26 included patients are presented in Table 1. The median age at listing was 8.5 years (IQR, 2.6–12.5 years), 62% were White, and 46% were male. Of this group, 6 (23%) were aged <1 year at the time of listing (Figure S2). A total of 21 (81%) patients had a history of CHD, with atrioventricular septal defects being the most common lesion. Failed repair of CHD was the most frequent indication for HTx (N=16, 62%) followed by cardiomyopathy secondary to anthracycline administration (N=5, 19%). Most patients were inpatient at the time of listing, with 18/20 (90%) requiring intensive care. A total of 9 (35%) patients were supported with a ventricular assist device, and 3 required biventricular support. Of the listed patients, 19 (73%) underwent a diagnostic catherization in the pretransplant period. The median pretransplant indexed pulmonary vascular resistance (PVR) was 3.3 Woods units (WU)xm² (IQR, 2.5–5.7 WU)xm². The maximum pretransplant PVR in this cohort was 11.3 WU)xm². Detailed data regarding pretransplant PVR is presented in Figure S3. Data pertaining to the reactivity of PVR were not collected.

**Transplant Hospitalization Outcomes**

A total of 23 (88%) patients survived to transplantation (including 1 concomitant heart–kidney multiorgan transplant), with a median waitlist time of 105 days (IQR, 27–189 days). Waitlist survival was similar when comparing patients with DS to controls (P=0.433; Figure 1). Causes of waitlist death were not collected as part of the study protocol. Demographics of patients who survived to HTx are shown in Table 2. The median donor-to-recipient weight ratio was 1.3 (IQR, 1.1–1.6), and the median donor ischemic time was 3.6 hours (IQR, 2.9–4.2 hours). Of those who survived to transplant, 1 (4%) required extracorporeal membrane oxygenation in the posttransplant period, and 1 (4%) required dialysis (heart-only transplant). No centers reported alterations in their standard immunosuppression protocols. Induction therapy was used in 13 (57%) patients with 10 (43%) receiving antithymocyte globulin and 3 (13%) receiving interleukin-2 receptor antagonists. All patients who underwent transplantation survived to hospital discharge with a median posttransplant length of stay of 22 days (IQR, 13–32 days). A total of 17 (74%) (Continued)
patients received maintenance steroids at the time of hospital discharge. The most common maintenance immunosuppression at hospital discharge was tacrolimus and mycophenolate mofetil (N=12) followed by cyclosporine and azathioprine (N=6).

**Posttransplant Outcomes**

The median posttransplant follow-up time was 2.8 years (IQR, 1.4–15.5 years). A total of 3 (13%) patients have died as of the last data collection in August 2021. The causes of death were (1) coronary allograft vasculopathy at 22.6 years posttransplant, (2) multiple episodes of rejection and PTLD at 1.6 years posttransplant, and (3) respiratory arrest at 1.4 years posttransplant. Posttransplant survival was similar between patients with DS and controls (P=0.423; Figure 2).

A total of 10 (43%) patients experienced at least 1 episode of acute rejection, with a median time to first rejection of 30 days posttransplant. Of this group, 7 patients had an isolated episode of rejection (80% cellular rejection), and 3 patients demonstrated recurrent rejection events with episodes of cellular, antibody-mediated, and mixed forms of rejection. Hemodynamic compromise occurred in 2 patients. Overall freedom from rejection is presented in Figure 3. There was no difference in the incidence of rejection between patients with DS and controls (P=0.773).

A total of 8 (35%) patients were rehospitalized for infection in the first year after transplant. Of this group, 5 patients had a single hospitalization, whereas the remaining 3 had multiple readmission encounters. Freedom from rehospitalization for infection is shown in Figure 4. The median time to first readmission was 175 days (IQR, 94–279 days) posttransplant. Documented infections were predominantly viral and included viral upper respiratory tract infection (N=5) and cytomegalovirus viremia (N=2) as well as norovirus, human herpesvirus 6, adenovirus, and BK viremia (N=1 each). Bacterial infections included bacterial sinusitis, methicillin-resistant *Staphylococcus aureus* tracheitis, *Clostridium difficile*, and disseminated...
Table 2. Patient Demographics at the Time of Transplant (N=23)

|                          |     |
|--------------------------|-----|
| Age, y                   | 10.4 (3–13.8) |
| Male sex                 | 10 (43.5) |
| Prior CHD surgery         | 16 (69.6) |

Support at transplant

|                          |     |
|--------------------------|-----|
| Ventilator               | 3 (13) |
| ECMO                     | 0 (0) |
| Inotropes                | 12 (52.2) |
| Inhaled nitric oxide     | 2 (8.7) |
| Prostacyclin             | 1 (4.3) |
| Ventricular assist device| 9 (39.1) |
| Donor ischemic time, h   | 3.6 (2.9–4.2) |
| Donor-to-recipient weight ratio | 1.3 (1.1–1.6) |
| Required ECMO posttransplant | 1 (4.3) |
| Required dialysis posttransplant | 1 (4.3) |
| Survived to hospital discharge | 23 (100) |
| Posttransplant length of stay, d | 22 (13–32) |
| Maintenance steroids     | 17 (73.9) |

Maintenance immunosuppression at discharge

|                          |     |
|--------------------------|-----|
| Tacrolimus/mycophenolate | 12 (64.5) |
| Cyclosporine/azathioprine| 6 (27.3) |
| Cyclosporine/mycophenolate| 2 (9.1) |
| Tacrolimus monotherapy   | 1 (4.5) |
| Sirolimus/mycophenolate  | 1 (4.5) |

Data are reported as frequency (percentage) for categorical and median (interquartile range) for continuous variables. CHD indicates congenital heart disease, and ECMO, extracorporeal membrane oxygenation.

Pseudomonas. One patient was admitted with oral candidiasis and feeding intolerance.

A total of 5 (19%) patients had histories of pretransplant malignancy. Each of these patients survived to HTx, and at a median follow-up of 7.4 years, all remained cancer free. Across the entire cohort, 2 (9%) patients were diagnosed with PTLD in the posttransplant period, including 1 patient with monomorphic diffuse large B cell lymphoma and 1 with polymorphic Epstein-Barr virus–positive PTLD presenting at 5 and 7 months after transplant, respectively. Freedom from posttransplant malignancy is shown in Figure 5, with no statistical difference between patients with DS and controls (P=0.883).

Functional Status

The majority of patients continue to be followed by pediatric providers. A total of 5 (22%) patients have been transitioned to adult practices. At last known follow-up, 5/22 (23%) patients require assistance for all activities, 14/22 (64%) perform age-appropriate activities with some assistance, and 3/22 (14%) perform most age-appropriate activities without assistance.

DISCUSSION

We present the largest report of HTx in patients with DS to date. We found that children with DS who are listed for HTx have waitlist and posttransplant survival similar to their non-DS counterparts.26,29 Moreover, patients with DS have comparable rates of posttransplant infection requiring hospitalization, rejection, and PTLD as other pediatric HTx recipients.28,30–35 Based on these data, despite historical concerns about transplant candidacy in this population, a diagnosis of DS alone does not appear to lead to inferior posttransplant outcomes and therefore should not be considered an a priori contraindication to HTx.

There are limited prior reports of HTx in individuals with DS. Broda and colleagues used administrative data from the Pediatric Health Information System (PHIS) to analyze HTx outcomes in children with chromosomal anomalies.13 There were 5 patients with DS in their cohort with a reported 20% mortality before hospital discharge. This is in contrast to our data where all patients survived to hospital discharge. This difference highlights potential limitations of administrative data in identification of in-hospital mortality or identification of patients with DS using International Classification of Diseases, Ninth Revision (ICD-9) codes as 22 of the patients from our cohort are from centers that participate in PHIS and likely overlap with the patients reported by Broda et al. Consistent with our data, 2 previous single-center reports demonstrate acceptable posttransplant outcomes in patients with DS.8,14

One important consequence of DS is dysfunction of the innate as well as adaptive immune system, which likely plays a critical role in the heightened risk of hematologic malignancies, autoimmune disorders, and infectious complications in this population.21–25,36–38 Although it would have been reasonable to consider alterations in induction and/or posttransplant immunosuppression for patients with DS undergoing HTx, no centers in our study reported doing so. Although a number of patients were hospitalized for posttransplant infections, the frequency was not out of proportion to published reports in pediatric HTx, where >60% of patients are readmitted in the first year and infection accounts for up to 25% of these admissions.30,31 Importantly, the risk of rejection is similar in patients with DS. This finding further supports that a standard immunosuppression strategy is likely warranted in patients with DS undergoing HTx.
Patients with DS have a 20-fold increased risk of acute leukemia. The risk is highest between the ages of 1 and 4 years but persists well into adulthood. However, with the exception of testicular cancer, there is a low incidence of solid tumors in this population, and the overall risk of cancer is similar to matched controls.
the general population. Importantly, no patients in our cohort with anthracycline-induced cardiomyopathy experienced recurrence of their primary malignancy or any secondary malignancies, and only 2 patients in our cohort developed PTLD. Although the potential for malignancy remains a concern in patients with DS and expert oncology consultation may be warranted, our data suggest that posttransplant malignancy is not exaggerated in those with DS.

Intellectual disability is nearly universal in patients with DS, with a high degree of variability among individuals and a wide spectrum of cognitive capabilities. Although the presence of cognitive delay may inappropriately influence consideration of HTx listing, a number of studies have demonstrated that the presence of cognitive delay does not negatively impact solid organ transplant outcomes in the pediatric population and should not discourage programs from offering HTx to a patient with sufficient social support. Ensuring a strong social support structure likely represents a critical step to ensure long-term success in patients with DS undergoing HTx. This is underscored by our data showing that the majority of patients in our cohort required at least some degree of assistance for activities of daily living at the time of last known follow-up.

Children with DS are at higher risk for the development of pulmonary hypertension, which is more common with coexisting cardiac disease. Fixed and significantly elevated PVR has traditionally been regarded as a contraindication to HTx given concerns for acute right ventricular failure in the graft. Although this may have been the basis by which patients with DS were excluded from transplant consideration previously, a number of patients in our cohort were successfully transplanted in the face of elevated PVR. Evolution of mechanical circulatory support strategies, donor selection, and posttransplant management has helped to mitigate some of the risks associated with elevated PVR. Therefore, although elevated PVR may identify higher risk patients, it may not be prohibitive to HTx in the current era.

Although the lower than expected rates of referral for transplantation in patients with DS likely suggests an underlying systematic bias, parental decision making and potential misconceptions about transplant candidacy may also play a role. There are limited data addressing the reasons for the lack of transplant consideration in this population, representing an important area for future research to ensure equitable access to potentially life-saving therapies. Importantly, our data highlight that acceptable outcomes can be achieved following HTx in patients with DS, providing critical insights for both...
providers and families when considering transplant candidacy.

There are a number of limitations to our analysis. We only queried pediatric HTx centers and therefore may have missed adults with DS who have undergone HTx. However, given the lack of published reports of HTx in adults with DS and the fact that pediatric providers are less likely to view DS as a contraindication to transplantation,55 we believe that we have captured a large extent of the worldwide experience in this population. Although this represents the largest report of HTx in DS to date, the numbers remain small. Therefore, the study is largely descriptive. There is almost certainly a selection bias encompassed in our data. Centers are less likely to pursue transplantation in a patient with DS who has multiple comorbidities, and therefore our data may contain only the most ideal candidates. Despite this, there were patients in our cohort with high-risk features, including the need for biventricular mechanical support, multiorgan transplant, and elevated PVR. Our results should also be interpreted with caution because of the potential for survivorship bias. Centers may be less likely to report patients who did not survive to transplantation or who experienced posttransplant mortality, potentially biasing our results toward improved patient outcomes. Lastly, event definitions within the OPTN data used as our comparison group may differ from the definitions used in our study, representing a potential source of error.

Despite the noted limitations, patients with DS transplanted in this multicenter cohort appear to have acceptable posttransplant outcomes. Therefore, the presence of DS alone should not serve as an absolute contraindication to HTx.

ARTICLE INFORMATION

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Disclosures
None.
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SUPPLEMENTAL MATERIAL
## Demographics

| Record ID |
|-----------|
| __________|

| Center |
|--------|
| Ann & Robert H. Lurie Children's Hospital of Chicago |
| Arkansas Children's Hospital |
| Children's Hospital of Philadelphia |
| Children's Hospital of Pittsburgh of UPMC |
| Cincinnati Children's Hospital Medical Center |
| Columbia University - Morgan Stanley Children's Hospital of New York Presbyterian |
| Freeman Hospital, Newcastle upon Tyne |
| Le Bonheur Children's Hospital |
| Lucile Packard Children's Hospital at Stanford |
| Monroe Carell Jr. Children's Hospital at Vanderbilt |
| Primary Children's Hospital |
| St. Louis Children's Hospital |
| Texas Children's Hospital |
| University of Alberta |
| University of Minnesota Masonic Children's Hospital |
| Other |

| Transplant center |
|-------------------|
| __________|

| Patient Date of Birth |
|-----------------------|
| __________|

| Gender |
|--------|
| Male |
| Female |

| Blood type |
|-----------|
| O |
| A |
| B |
| AB |

| Race |
|------|
| Caucasian |
| African American |
| Asian |
| Hispanic |
| Other |

| Congenital heart disease? |
|---------------------------|
| Yes |
| No |

| Details of congenital heart defect |
|-----------------------------------|
| __________|
Indication for transplantation?

Date of initial transplant listing

Listed for multi-organ transplant?  
- Yes
- No

In addition to the heart, what other organs was the patient listed for?
- Liver
- Lung
- Kidney
- Other

What other organ was the patient listed for?

Weight at listing  (kg)

Height at listing  (cm)

Initial Listing Status  
- 1A
- 1B
- 2

Initial Listing Status

Location at the time of listing  
- In ICU
- Hospitalized, not in ICU
- Outpatient

Support at the time of listing (Check all that apply)
- Ventilator
- ECMO
- Inotropes
- VAD
- Inhaled nitric oxide
- Other
- None of the above

Other support details

VAD type

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### Biventricular support?
- Yes
- No

### Functional status at the time of listing?
- Performs most age-appropriate activities independently
- Performs age-appropriate activities with some assistance
- Required assistance for all activities
- n/a patient < 1 year of age

### Events preceding transplant listing

| Event                                      | Response |
|--------------------------------------------|----------|
| Prior cardiac surgery?                     | Yes      |
|                                           | No       |
| Number of prior cardiac surgeries          |          |
| Most recent preceding cardiac surgery date |          |
| Prior malignancy                          | Yes      |
|                                           | No       |
| Malignancy type                            |          |
| Date of malignancy diagnosis               |          |
| Catheterization performed pre-transplant?  | Yes      |
|                                           | No       |
| Date of most recent catheterization preceding listing |          |

| Hemodynamics: PVR                         | (wU)     |
| Hemodynamics: Cardiac Index               | (mL/kg/m²) |
| Hemodynamics: Wedge pressure (mean)       | (mmHg)   |

### Other events or other patient comorbidities preceding transplantation
-
# Transplant

| Waitlist outcome | ☐ Underwent transplant  |
|------------------|------------------------|
|                  | ☐ Died or delisted due to clinical deterioration |
|                  | ☐ Delisted due to clinical improvement |
|                  | ☐ Other |

| Date of waitlist death | ____________________________ |
|------------------------|-----------------------------|

| Delisting date | ____________________________ |
|----------------|-----------------------------|

| Other outcome | ____________________________________________ |
|---------------|-----------------------------------------------|

| Date of transplant | ____________________________ |
|--------------------|-----------------------------|

| Multi-organ transplant? | ☐ Yes |
|-------------------------|------|
|                         | ☐ No |

| In addition to the heart, what other organs were transplanted? (Check all that apply) | ☐ Liver |
|-----------------------------------------------------------------------------|------|
|                                                                             | ☐ Lung |
|                                                                             | ☐ Kidney |
|                                                                             | ☐ Other |

| What other organ was transplanted? | ____________________________________________ |
|-----------------------------------|-----------------------------------------------|

| Weight at transplant | ____________________________ (kg) |
|----------------------|----------------------------------|

| Height at transplant | ____________________________ (cm) |
|----------------------|----------------------------------|

| Donor weight | ____________________________ (kg) |
|--------------|----------------------------------|

| Donor height | ____________________________ (cm) |
|--------------|----------------------------------|
| Support at the time of transplantation (Check all that apply) | □ Ventilator  
□ ECMO  
□ Inotropes  
□ VAD  
□ Inhaled nitric oxide  
□ Other  
□ None of the above |
|----------------------------------------------------------|
| Donor ischemic time                                       | (min) |
| Required ECMO post-transplant                             | □ Yes  
□ No |
| Required dialysis post-transplant?                       | □ Yes  
□ No |
| Survived to hospital discharge?                          | □ Yes  
□ No |
| Date of initial hospital discharge (post-transplant)     | ____________________________________ |
| Induction immunosuppression used (check all that apply)  | □ Steroids  
□ Thymoglobulin  
□ Basiliximab  
□ IVIG  
□ Other |
| Other induction immunosuppression detail                 | ____________________________________ |
| Maintenance immunosuppression at the time of discharge (check all that apply) | □ Steroids  
□ Tacrolimus  
□ Mycophenolate  
□ Azathioprine  
□ Cyclosporine  
□ Sirolimus  
□ Everolimus  
□ Other |
| Other maintenance immunosuppression detail               | ____________________________________ |
| Did you alter your standard immunosuppression strategy due to the presence of Down syndrome? | □ Yes  
□ No |
| How was immunosuppression altered for this patient compared to your standard practice? | ____________________________________ |
| Treated infection prior to hospital discharge            | □ Yes  
□ No |
Details of infection prior to hospital discharge
### Follow-up

| Field                              | Description |
|------------------------------------|-------------|
| Date of last known follow-up       | ____________ |
| Last known patient status          | Alive, Deceased, Retransplanted |
| Retransplant date                  | ____________ |
| Indication for retransplantation   | ____________ |
| Cause of death                     | ____________ |
| Has the patient been transitioned to an adult practice? | Yes, No |
| Last known functional status       | Performs most age-appropriate activities independently, Performs age-appropriate activities with some assistance, Required assistance for all activities, n/a patient < 1 year of age |

### Rejection Events

| Field                              | Description |
|------------------------------------|-------------|
| Has the patient had any episodes of treated rejection? | Yes, No |
| How many episodes of treated rejection has the patient had? | 1, 2, 3, 4 or more |
| Date of rejection episode #1       | ____________ |
| Hemodynamic compromise with rejection episode #1? | Yes, No |
| Type of rejection event #1         | Cellular, Antibody mediated, Mixed, No biopsy performed / empiric therapy |
### Date of rejection episode #2

**Hemodynamic compromise with rejection episode #2?**
- Yes
- No

**Type of rejection event #2**
- Cellular
- Antibody mediated
- Mixed
- No biopsy performed / empiric therapy

### Date of rejection episode #3

**Hemodynamic compromise with rejection episode #3?**
- Yes
- No

**Type of rejection event #3**
- Cellular
- Antibody mediated
- Mixed
- No biopsy performed / empiric therapy

### Date of rejection episode #4

**Hemodynamic compromise with rejection episode #4?**
- Yes
- No

**Type of rejection event #4**
- Cellular
- Antibody mediated
- Mixed
- No biopsy performed / empiric therapy

### Post-transplant malignancy

**Has the patient had malignancy post-transplant?**
- Yes
- No

**Date of post-transplant malignancy diagnosis**

**Type of post-transplant malignancy?**
| Post-transplant infection |
|---------------------------|
| **Hospitalized for infection in the first year post-transplant?** |
| Yes | No |
| **Number of hospitalizations for infection in the first year post-transplant?** |
| 1 | 2 | 3 | 4 or more |
| **Date of infection #1** |
| ____________________________ |
| **Type of infection: Episode #1** |
| ____________________________ |
| **Date of infection #2** |
| ____________________________ |
| **Type of infection: Episode #2** |
| ____________________________ |
| **Date of infection #3** |
| ____________________________ |
| **Type of infection: Episode #3** |
| ____________________________ |
| **Date of infection #4** |
| ____________________________ |
| **Type of infection: Episode #4** |
| ____________________________ |
Figure S1. Number of patients with Down syndrome listed for transplant by year. Dashed line demonstrates the linear trend over time.
Figure S2. Age distribution of listed patients and associated indications for listing.
Figure S3. Distribution of indexed pulmonary vascular resistance for patients who underwent a pre-transplant catheterization.