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Broader Geographic Sharing of Pediatric Donor Lungs Improves Pediatric Access to Transplant

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US pediatric transplant candidates have limited access to lung transplant due to the small number of donors within current geographic boundaries, leading to assertions that the current lung allocation system does not adequately serve pediatric patients. We hypothesized that broader geographic sharing of pediatric (adolescent, 12–17 years; child, <12 years) donor lungs would increase pediatric candidate access to transplant. We used the thoracic simulated allocation model to simulate broader geographic sharing. Simulation 1 used current allocation rules. Simulation 2 offered adolescent donor lungs across a wider geographic area to adolescents. Simulation 3 offered child donor lungs across a wider geographic area to adolescents. Simulation 4 combined simulations 2 and 3. Simulation 5 prioritized adolescent donor lungs to children across a wider geographic area. Simulation 4 resulted in 461 adolescent transplants per 100 patient-years on the waiting list (range 417–542), compared with 206 (range 180–228) under current rules. Simulation 5 resulted in 388 adolescent transplants per 100 patient-years on the waiting list (range 348–418) and likely increased transplant rates for children. Adult transplant rates, waitlist mortality, and 1-year posttransplant mortality were not adversely affected. Broader geographic sharing of pediatric donor lungs may increase pediatric candidate access to lung transplant.

Abbreviations: DSA, donation service area; LAS, lung allocation score; OPTN, Organ Procurement and Transplantation Network; SRTR, Scientific Registry of Transplant Recipients; TSAM, thoracic simulated allocation model

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Introduction

Lung transplant has grown into a definitive treatment of end-stage lung disease, reaching an all-time high of 1923 transplants in the United States in 2013; 38 of these were performed in adolescents (aged 12–17 years) and 24 in children (aged <12 years) (1). The US organ allocation system is focused on early transplant for pediatric candidates (aged <18 years) to minimize the impact of end-stage organ disease on lifespan and quality of life; however, a recent national controversy concerned whether the lung allocation system gave pediatric candidates adequate access to transplant (2–5). A federal judicial injunction contributed to lung allocation policy changes for pediatric patients, but it has not led to improved transplant rates (6). The Organ Procurement and Transplantation Network (OPTN) Thoracic Transplantation Committee and the Scientific Registry of Transplant Recipients (SRTR) have been studying alternative allocation schemes to improve pediatric access to lung transplant.

In pediatric lung transplantation, allocation of donor lungs is limited by small donor pools within the current geographic parameters. Geographic boundaries take precedence over the priority- and waiting-time–based system for candidates aged younger than 12 years, and over the lung allocation score (LAS) priority system for candidates aged 12 years or older. We hypothesized that broader geographic sharing of pediatric donor lungs would increase pediatric candidate access to transplant.

Methods

This study used data from SRTR. This data system includes data on all donors, waitlisted candidates, and transplant recipients in the United States, submitted by the members of OPTN, and has been described elsewhere (7).

The Health Resources and Services Administration, US Department of Health and Human Services, provides oversight of the activities of the OPTN and SRTR contractors.

Our study population included all US lung and heart–lung transplant candidates and donors from July 1, 2009, through June 30, 2011. The thoracic simulated allocation model (TSAM), a computer allocation simulation program developed by SRTR, uses actual candidates and donors to create recipients of simulated offers as follows: (1) Arrival of deceased donor lungs into the system and new candidates on the waiting list from July 1, 2009, through June 30, 2011. (2) Confirmation of compatibility between donor lungs and candidates. (3) Simulation of candidate acceptance or refusal of donor lung offers using a logistic regression model based on donor lung acceptance behavior. (4) Projection of posttransplant survival using linear approximations to Cox proportional hazard models. Each simulation was repeated 10 times using actual donors in random order. Since the same donors and candidates were used in each of the simulations and were not independent samples, statistical tests of comparisons were not possible. Instead, the average and the minimum–maximum range of results for the 10 iterations were described for the allocation simulations. This range reflected the variability of simulation modeling. Simulated allocation models have been used by SRTR since 2001 to simulate allocation schemes for liver, kidney, and heart transplants (8–12).

Pediatric donors and candidates were defined as aged younger than 18 years (adolescents, 12–17 years; children, <12 years), following the convention of the current US allocation system. Adults were defined as aged 18 years or older.

We performed five allocation simulations using current rules (simulation 1), broader geographic sharing of adolescent donor lungs (simulation 2), broader geographic sharing of child donor lungs (simulation 3), combined broader geographic sharing of adolescent and child donor lungs (simulation 4), and priority child allocation with broader geographic sharing (simulation 5) (Figure 1). The primary outcome was transplant rate. Secondary outcomes were waitlist mortality and 1-year posttransplant mortality.

Simulation 1: Current allocation rules

Simulation 1 used current allocation rules (13). Donors and candidates were first matched based on geographic region and age. Priority status and waiting time were used to prioritize access to transplant for child candidates, and the LAS, which reflects the net benefit of transplant, for adolescent candidates.

Under current rules, adult donor lungs were first offered to local adolescent or adult candidates, then to local child candidates. Local was defined as within the donation service area (DSA) administered by an organ procurement organization (14). If no local candidates were identified, the donor lungs were offered beyond the local DSA in 500-mile radius increments from the donor's location. This sequence was repeated until the organ was accepted or discarded.

Adolescent donor lungs were first offered to local adolescent candidates. If no suitable local adolescent candidate was identified, local child candidates were considered, then local adult candidates. The sequence of adolescent, child, and adult allocation in 500-mile radius increments from the donor was repeated until the organ was accepted or discarded.

Child donor lungs were first offered to child candidates within a 1000-mile radius of the donor. If no suitable candidate was identified, adolescent candidates within a 500-mile radius of the donor were considered, then local adult candidates, then adult candidates within a 500-mile radius. The allocation sequence was continued until the organ was accepted or discarded.

Our proposals for wider geographic sharing of donor lungs to pediatric candidates (simulations 2–5) were compared with simulation 1.

Simulation 2: Broader geographic sharing of adolescent (ages 12–17 years) donor lungs

Simulation 2 changed the allocation rules by broadening access to adolescent donor lungs for adolescent, then for child, candidates from the local DSA up to a 1000-mile radius. Current rules for the allocation of child and adult donor lungs were used.

Simulation 3: Broader geographic sharing of child (aged <12 years) donor lungs

Simulation 3 broadened access to child donor lungs for adolescent candidates within a 500- to 1000-mile radius. Current rules for the allocation of adolescent and adult donor lungs were used.

Simulation 4: Combined simulations 2 and 3

Simulation 4 combined broader geographic sharing of adolescent donor lungs from simulation 2 and broader geographic sharing of child donor lungs from simulation 3. Current rules for the allocation of adult donor lungs were used.

Simulation 5: Priority child for all pediatric donors (aged <18 years) with broader geographic sharing

Simulation 5 prioritized child candidates over adolescent candidates for adolescent donor lungs, and broadened child access to adolescent donor lungs from the local DSA to a 1000-mile radius. Child donor lungs were allocated first to child candidates within a 1000-mile radius, then to adolescent candidates within the same 1000-mile radius. Current rules for the allocation of adult donor lungs were used.

Results

Study cohort

Our study cohort included 5907 lung and 141 heart–lung candidates listed for transplant for at least 1 day from July 1, 2009, through June 30, 2011; 5808 (96.0%) were adults, 131 (2.2%) were adolescents, 56 (0.9%) were children aged 6–11 years, and 53 (0.9%) were children aged 0–5 years. Candidates who underwent transplant and were listed for retransplant (<4%) during the study period were included in the simulations only for the first listing. Of the cohort, 49.1% were female and 81.1% white; pulmonary fibrosis was the most common indication for listing (43.4%). Among observed transplant recipients, most candidate/donor matches occurred in the local DSA (54%) or within a 500-mile radius of the donor (39%).

Transplant rates

Figure 2 shows transplant rates by age and simulation. The most pronounced increase in transplant rates occurred for adolescents. Broader geographic sharing of adolescent donor lungs (simulation 2) led to 443 adolescent transplants per 100 patient-years on the waiting list (range 387–488), and in combination with broader sharing of child donor lungs (simulation 4) led to 461 adolescent transplants per 100 patient-years on the waiting list (range 417–542), double the

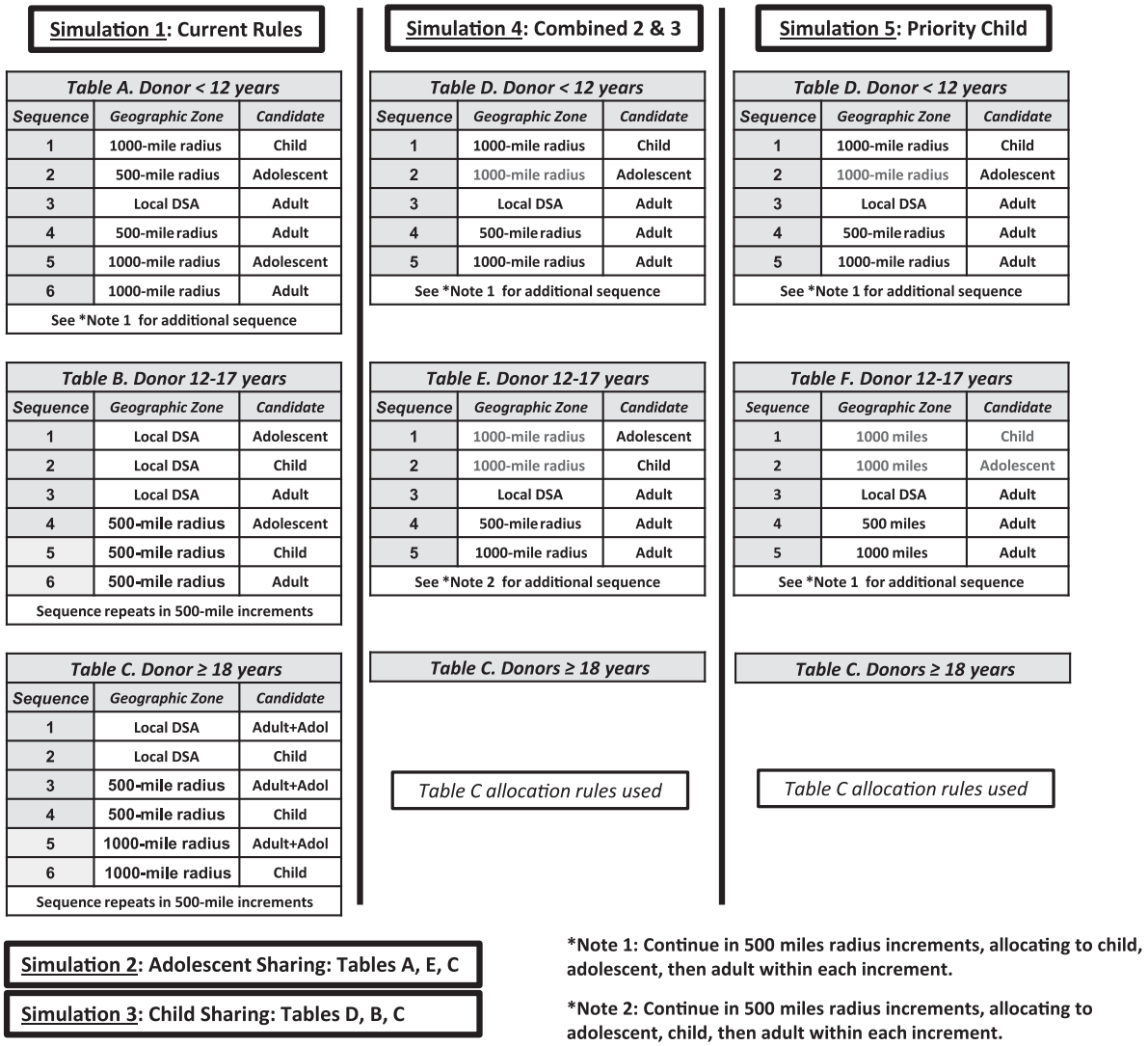

Figure 1: TSAM simulations. DSA, donation service area; TSAM, thoracic simulated allocation model.

simulated transplant rate using current allocation rules (simulation 1, 206, range 180–228) and broader sharing of child donor lungs alone (simulation 3, 206, range 177–233). In addition, priority child allocation (simulation 5) led to 388 adolescent transplants per 100 patient-years on the waiting list (range 348–418) and likely increased transplant rates among candidates aged 6–11 years (310, range 268–359), though the range overlapped with the range for these candidates under current allocation rules (simulation 1, 210, range 177–271). Transplant rates among younger children (0–5 years) were unaffected. Adolescent transplant rates increased without decreasing rates of adult transplants.

Waitlist and 1-year posttransplant mortality

To ensure that our proposed allocation changes for pediatric patients did not adversely affect the transplant population, we simulated waitlist and 1-year posttransplant mortality. All simulations showed similar rates of waitlist (Figure 3) and 1-year posttransplant (Figure 4) mortality within each age group compared with current allocation rules (simulation 1).

Recipient age distribution by donor age and simulation

To determine how donor age contributed to increased transplant rates, we examined recipient age distributions by donor age (Figure 5). Nearly all adult donor lungs were allocated to adult candidates. Percentages of adolescents receiving adolescent donor lungs increased as expected in simulations 2, 4, and 5 compared with current rules (simulation 1). However, simulations 2, 4, and 5 increased allocations of lungs from donors aged 6–11 years to adult candidates compared with current rules (simulation 1). Most lungs from donors aged 0–5 years were allocated to candidates aged 0–11 years.

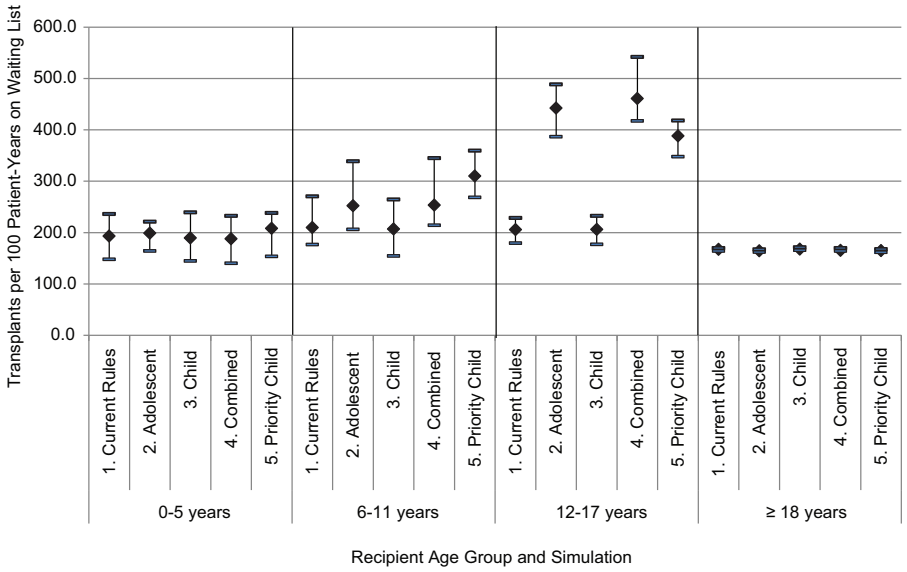

Figure 2: Transplant rates by age group and simulation. Simulation 1, current allocation rules; simulation 2, broader sharing of adolescent (aged 12–17 years) donor lungs; simulation 3, broader sharing of child (aged <12 years) donor lungs; simulation 4, combined simulations 2 and 3; simulation 5, priority child for all pediatric donors (aged <18 years) with broader geographic sharing.

Discussion

We have shown that broader geographic sharing of US pediatric donor lungs would likely increase pediatric candidate access to lung transplant. Specifically, broader sharing of adolescent donor lungs (simulation 2), or in combination with broader sharing of child donor lungs (simulation 4), would more than double adolescent transplant rates. Prioritizing children for all pediatric donor lungs with broader geographic sharing (simulation 5) would increase transplant rates for adolescents and likely for children aged 6–11 years. Transplant rates, waitlist mortality, and 1-year posttransplant

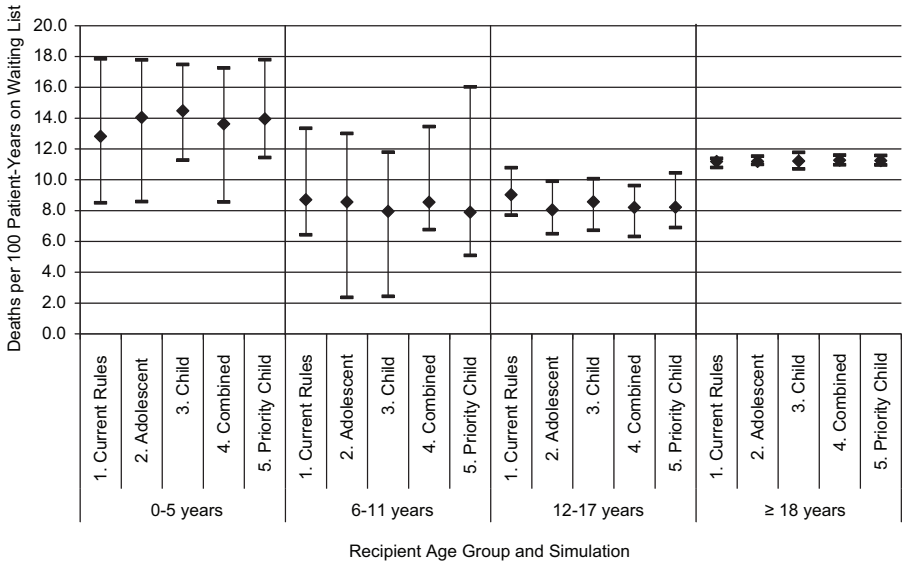

Figure 3: Waitlist mortality rates by age group and simulation. Simulation 1, current allocation rules; simulation 2, broader sharing of adolescent (aged 12–17 years) donor lungs; simulation 3, broader sharing of child (aged <12 years) donor lungs; simulation 4, combined simulations 2 and 3; simulation 5, priority child for all pediatric donors (aged <18 years) with broader geographic sharing.

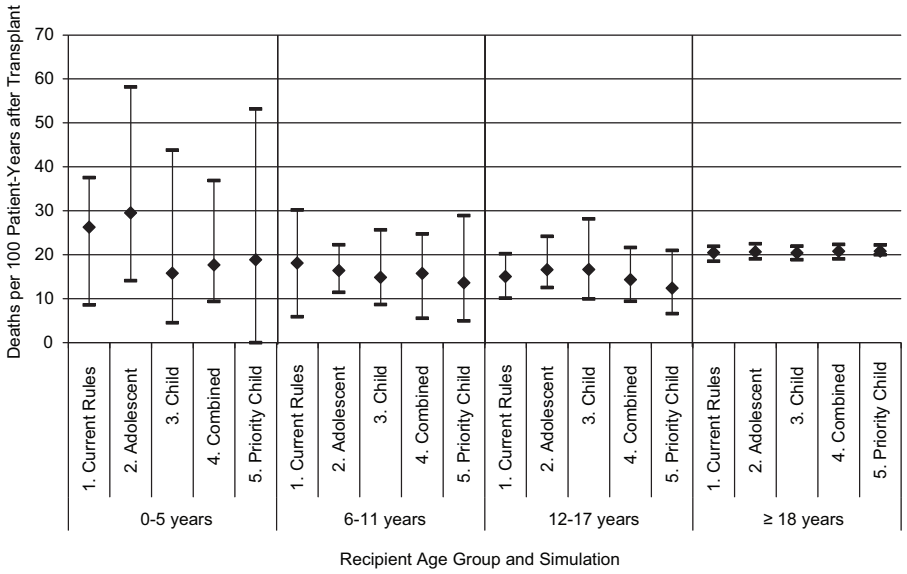

Figure 4: One-year posttransplant mortality by age group and simulation. Simulation 1, current allocation rules; simulation 2, broader sharing of adolescent (aged 12–17 years) donor lungs; simulation 3, broader sharing of child (aged <12 years) donor lungs; simulation 4, combined simulations 2 and 3; simulation 5, priority child for all pediatric donors (aged <18 years) with broader geographic sharing.

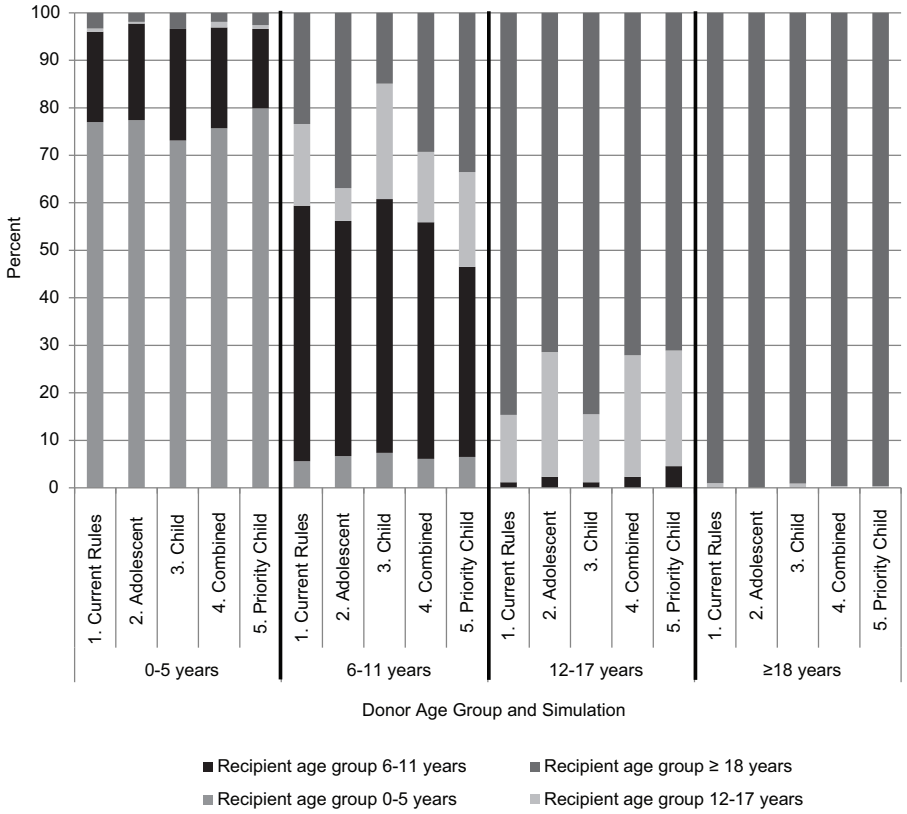

Figure 5: Recipient age distributions by donor age and simulation. Simulation 1, current allocation rules; simulation 2, broader sharing of adolescent (aged 12–17 years) donor lungs; simulation 3, broader sharing of child (aged <12 years) donor lungs; simulation 4, combined simulations 2 and 3; simulation 5, priority child for all pediatric donors (aged <18 years) with broader geographic sharing.

mortality for adults were not adversely affected by any of the broader sharing allocation schemes.

Clinical issues for pediatric lung transplant candidates are unique and separate from issues for adults, and have presented challenges in organ allocation that deserve special consideration. First, the potential donor age range is limited for child candidates because of their small thoracic size. Next, while native lung diseases for adolescents and adults fit in one of four broad categories for LAS calculation, children present with a wider range of rare lung diseases that are difficult to categorize. Finally, data are limited on which to model outcomes, given fewer pediatric than adult transplants. Thus, children aged younger than 12 years were excluded from the LAS system because clinical variables used in the LAS were not reproducible or valid in this population and because of the diversity in their native lung diseases (15–17).

Posttransplant survival for pediatric lung transplant recipients is similar to adult median survival; 5-year mortality is 43% for ages younger than 12 years and 45.6% for ages 12 years or older (18). A recent analysis of US data showed similar waitlist mortality and transplant rates in pediatric and adult populations (19); however, these results must be interpreted cautiously because adolescents and adults are allocated donor lungs through the LAS, and children through the waiting time priority system. Despite these findings, social norms and ethical principles have served as catalysts to prioritize and improve pediatric access to donor organs.

Differing ethical paradigms have been used to justify preferential pediatric access to organ transplant. Most notably, the ''prudential lifespan account'' gives increased value to earlier life stages. It supports the notion that the health of a pediatric patient should be given preferential priority because of a limited time window for growth and development into productive adulthood (20). Other principles include ''fair innings,'' which draws on an individual's right to experience a full life, and the ''max–min principle,'' which refers to tolerating inequalities in the allocation of scarce resources (in our case donor lungs), as long as there is greatest benefit to the least advantaged members of society (20). In acknowledgement of these ethical principles, our work advances US lung allocation toward increased pediatric access to transplant. The international community has used the same ethical paradigms for pediatric populations. For example, in 2014 Germany implemented an allocation system that automatically provides all candidates aged younger than 12 years a LAS of 100, the highest possible score, regardless of clinical acuity (21).

Our study builds on prior discussions regarding the negative impact of US geographic boundaries on access to transplant (22,23). Some researchers have argued that the need to size-match donors and candidates within a local geographic area encourages the flow of organs to adults in the local area due to small numbers of pediatric candidates, and that pediatric access to transplant is limited not by lack of pediatric donors but by lack of appropriately sized donors (3,4). Russo et al (24) showed that with the current geographic boundaries, donor lungs can be allocated to a local low-priority candidate when a matched higher-priority candidate is nearby but outside the local area, resulting in avoidable waitlist deaths of high-priority candidates. We accept this notion that geographic boundaries artificially limit the preferred allocation of organs to sicker nearby candidates, and we studied models of wider geographic sharing of pediatric donor lungs to increase pediatric access to transplant.

Despite our use of a large modern cohort of transplant recipients, our study has limitations. First, the proportion of pediatric transplants (4.0%) was small compared with the proportion of adult transplants (96.0%), limiting our ability to detect differences in pediatric transplant rates, waitlist mortality, and 1-year posttransplant survival. TSAM models become more robust with larger sample sizes. Despite this, our simulations showed that broader geographic sharing improved transplant rates for adolescent candidates, and possibly for candidates aged 6–11 years. The small pediatric cohort size likely explains two other observations. The increase in adolescent transplant rates did not correspond to a reduction in adolescent waitlist mortality. This finding may be attributed to the LAS system, which reduces waitlist time and mortality by prioritizing the sickest patients for transplant. Also, the smaller pediatric cohort size resulted in wider variability in the simulations and may have prevented TSAM from detecting changes in waitlist mortality. Next, when more adolescent transplants occurred, we noted that more lungs from donors aged 6–11 years were allocated to adult candidates; this likely reflects the small number of candidates aged 6–11 years. Even if we increased our overall study population number, the proportion of pediatric patients would remain small relative to the adult population, and the ability to detect changes in the pediatric population would not appreciably increase. Finally, TSAM cannot predict changes in the listing or organ acceptance practices of transplant centers with a new allocation scheme, as models are based on historical behavior.

The most recent attempt in the United States to improve children's access to lung transplant was an appeals process to increase children's access to adolescent and adult donors. The appeals process was quickly implemented in response to a court injunction resulting from a complaint brought by the family of a waitlisted child candidate (2). Subsequently, from June 2013 to June 2014, there were 12 approvals on behalf of 12 candidates for increased access to adolescent and adult donors; one candidate received adult donor lungs and one received adolescent donor lungs (6). The low rate of transplants in children that resulted from appeals was attributed to children's small

thoracic size and indicated that the appeals process, while now a permanent policy (25), is not a practical solution to the problem of access. Also, it may not be an equitable solution because exception requests may be inconsistently applied based on transplant physician advocacy. We propose that changes to geographic boundaries in allocation will more efficiently improve pediatric access to transplant; the simulations presented here will serve as options for actual US policy considerations to be implemented. While our two most promising simulations (broader sharing of adolescent and child donor lungs and prioritizing children for all pediatric donor lungs with broader geographic sharing) increased transplant rates for adolescents, we found that prioritizing children for all pediatric donor lungs also showed the highest likelihood of increasing child transplant rates. However, there is a possible but small risk that prioritizing children for all pediatric donor lungs may disadvantage smaller-sized adolescents, as they would be prioritized behind children for adolescent donor lungs.

Despite the small differences in improved transplant rates achieved by the described algorithms (broader sharing of adolescent and child donor lungs and prioritizing children for all pediatric donor lungs with broader geographic sharing), both meet the stated US organ allocation goal of maximizing access to transplant for all pediatric candidates. Each is likely a superior alternative to the current allocation scheme for pediatric candidates. Our findings show that broader geographic sharing of pediatric donor lungs may be an important strategy to increase US pediatric candidate access to lung transplant.

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Drs. Tsuang and Valapour had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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Disclosure

The authors of this manuscript have no conflicts of interest to disclose as described by the *American Journal of Transplantation*.

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