American Journal of Transplantation 2014; 14: 178–183
Wiley Periodicals Inc.

doi: 10.1111/ajt.12547

Brief Communication

The Equitable Allocation of Deceased Donor Lungs for Transplant in Children in the United States

J. J. Snyder[1,2], N. Salkowski[1], M. Skeans[1], T. Leighton[1], M. Valapour[1,3], A. K. Israni[1,2,4], M. I. Hertz[1,2] and B. L. Kasiske[1,4,*]

[1]*The Scientific Registry of Transplant Recipients, Minneapolis Medical Research Foundation, Minneapolis, MN*
[2]*Division of Epidemiology and Community Health, School of Public Health, University of Minnesota, Minneapolis, MN*
[3]*Department of Medicine, University of Minnesota, Minneapolis, MN*
[4]*Department of Medicine, Hennepin County Medical Center, Minneapolis, MN*
[*]*Corresponding author: Bertram L. Kasiske, kasis001@umn.edu*

On June 5, 2013, a US Federal Court ordered a temporary restraining order to allow two children within the court's jurisdiction to be registered on the adolescent lung transplant waiting list. On June 10, 2013, the Organ Procurement and Transplantation Network's Executive Committee altered lung allocation policy to offer candidates aged younger than 12 years greater access to adult lungs at the discretion of the national Lung Review Board. The Scientific Registry of Transplant Recipients reviewed trends over time in deceased donor lung transplant waitlist mortality and transplant rates, comparing children and adults. Mortality rates of candidates active on the waiting list have been higher for children aged 0–5 years, but have not differed for children aged 6–11 years compared with adolescents aged 12–17 years or adults aged 18 years or older. Transplant rates among active waitlist candidates have been comparable across all age groups. Thus, there is little evidence that the allocation system led to differences in waitlist mortality or transplant rates for children compared with adults. However, these comparisons are difficult to interpret given that current policies likely led to unaccounted differences in the severity of illness at the time of listing.

Keywords: Adolescents, lung allocation score, mortality, waiting list

Abbreviations: HHS, US Department of Health and Human Services; LAS, lung allocation score; NOTA, National Organ Transplantation Act; OPTN, Organ Procurement and Transplantation Network; SRTR, Scientific Registry of Transplant Recipients; SSADMF, Social Security Administration Death Master File; UNOS, United Network for Organ Sharing

Received 21 June 2013, revised 21 August 2013 and accepted for publication 12 September 2013

Introduction

For the first time in the history of the US Organ Procurement and Transplantation Network (OPTN), allocation for transplant of a deceased donor organ was altered following a temporary restraining order issued by a Federal Court (1). The order directed the Secretary of Health and Human Services to allow a 10-year-old patient to be considered alongside older candidates for lung offers from adolescent and adult donors without consideration of her age. As a result of this court action, the Scientific Registry of Transplant Recipients (SRTR) independently undertook a review of deceased donor lung allocation and how it affects children. On June 10, 2013, the OPTN Executive Committee adopted a temporary policy allowing US lung transplant programs to submit requests to the Lung Review Board for candidates aged younger than 12 years to be also listed as adolescent candidates. These candidates would then receive a calculated lung allocation score (LAS) if the Lung Review Board approved the request. After this adolescent listing is in effect, it is treated as any other adolescent listing (2). The LAS is a measure of illness severity and projected posttransplant survival that gives priority to the sickest candidates with the best chance of survival. This policy change effectively gives candidates aged 0–11 years greater access to donors of all ages.

Before 1995, lungs were allocated to transplant candidates on the basis of waiting time, blood type and geography (3). In March 2000, the US Department of Health and Human Services (HHS) Final Rule mandated that organ allocation be based on medical necessity (4), and in May 2005, OPTN implemented the LAS. Adoption of the LAS for candidates aged 12 years or older reduced their incentive for early listing. Lungs from adolescent donors (aged 12–17 years) are preferentially offered to adolescent candidates. If there are no suitable adolescent candidates in the local donation service area, the organ is offered to a local candidate aged 0–11 years.

When the LAS-based allocation policy was implemented in 2005, organs were not allocated by LAS to candidates aged 0–11 years due to differences in diagnoses that made the LAS inappropriate as a measure of medical urgency for them. Between May 4, 2005, and September 11, 2010, candidates aged 0–11 years were ranked based on waiting time. Beginning on September 12, 2010, candidates aged 0–11 years are ranked by disease severity as priority 1 or priority 2, and then by waiting time. Thoracic size is an important determinate of which donor lungs are suitable for which candidates. Therefore, when lungs become available from a donor aged 0–11 years, they are preferentially offered to candidates aged 0–11 years, due to the difficulty in finding a size match (2).

We examined trends in waitlist mortality and transplant rates over the past several years, comparing lung transplant candidates aged 0–11, 12–17 and 18 years or older. Our goal was to assess whether disparities exist in death rates and transplant rates for candidates aged 0–11 years compared with adolescent and adult candidates.

Methods

Patient population

We used SRTR data, which include data on all donors, waitlisted candidates and transplant recipients in the United States, submitted by the members of OPTN, and have been described elsewhere (5). The Health Resources and Services Administration provides oversight of the activities of the OPTN and SRTR contractors.

Analytical approach

We examined mortality rates by age for candidates registered on the lung transplant waiting list between January 1, 1999, and December 31, 2011. Deaths were ascertained from OPTN data supplied by transplant centers and from the Social Security Administration Death Master File (SSADMF); starting in November 2011, approximately 40% of deaths in the SSADMF were removed from the publicly available file. However, given the timeframe included in this analysis, this change likely had minimal impact.

Mortality rates were calculated as the number of deaths on the deceased donor waiting list divided by the active patient-years on the waiting list. Mortality rates are shown only for active waitlist time, given the incentive for patients aged 0–11 years to list early to accumulate waiting time (used in allocation) and the concern that inactive time on the list could distort differences in rates between these candidates and candidates aged 12 years or older who have no incentive to accumulate waiting time. Transplant rates were calculated as the number of patients who underwent transplant divided by the active patient-years on the waiting list. The analyses of transplant rates were limited to active time on the waiting list, since patients who are inactive are not ''at risk'' for undergoing transplant.

Each annual rate was calculated using candidates on the waiting list on the first of the year or added during the year. We excluded candidates listed for a heart–lung transplant, as these candidates sometimes list for a lung-only transplant in order to ensure offers for all thoracic matches. Candidates removed from the waiting list as being ''too sick for transplant'' and candidates who died within 2 weeks of becoming inactive were included as deaths for this analysis.

For both mortality and transplant, we also performed a Poisson regression analysis by age group. Age was determined at the later of listing date or the first of the calendar year. Relative risks were estimated by exponentiating the difference in least-square means derived from the model, with 95% confidence intervals derived using the standard error of the least-square mean difference.

Results

Deaths on the waiting list

The death rate on the waiting list was higher for candidates aged younger than 12 years than for candidates aged 12 years or older (Table 1). However, this difference can be entirely explained by increased mortality rates for candidates aged 0–5 years when listed (Figure 1). Mortality rates for candidates aged 6–11 years were similar to rates for

Table 1: Waitlist death rates by age of active lung transplant candidates

	Active candidates aged ≥12 years				Active candidates aged <12 years			
Year	Active, n	Years at risk	Deaths, n	Death rate[1]	Active, n	Years at risk	Deaths, n	Death rate[1]
1999	4128	2273.4	484	21.3	99	37.1	16	43.1
2000	4321	2400.1	434	18.1	87	42.6	11	25.8
2001	4416	2350.7	424	18.0	89	42.1	12	28.5
2002	4243	2281.7	405	17.7	80	33.7	14	41.5
2003	4213	2214.3	397	17.9	71	37.4	4	10.7
2004	4266	2191.1	422	19.3	87	46.4	9	19.4
2005	3621	1490.8	283	19.0	84	42.1	7	16.6
2006	2855	931.3	187	20.1	74	27.9	2	7.2
2007	2974	983.8	235	23.9	60	23.0	9	39.1
2008	3016	1010.3	212	21.0	58	24.1	10	41.5
2009	3373	1113.9	259	23.3	50	13.1	4	30.6
2010	3660	1265.5	266	21.0	50	14.6	5	34.3
2011	3798	1325.8	328	24.7	42	9.3	9	97.0

[1]Deaths per 100 patient-years.

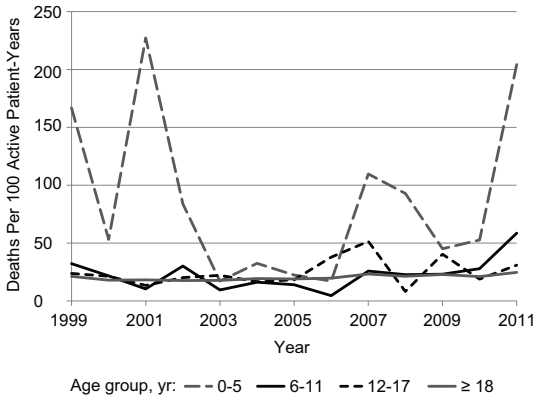

Figure 1: Active death rates by candidate age. Deaths include removals from the waiting list due to being too sick for transplant and deaths that occurred within 2 weeks of inactivation.

candidates aged 12 years or older (Figure 2). Due to the small numbers of candidates in the 6–11 year age range, confidence intervals for the relative risk estimates were wide; nonetheless, no systematic pattern of elevated mortality is evident, either before or after the 2005 implementation of the LAS-based lung allocation system for candidates aged 12 years or older.

Transplant rates

We limited the calculation of transplant rates to active time on the waiting list, since patients who are inactive will not undergo transplant. Transplant rates for pediatric candidates (aged less than 12 years) were lower than rates for adult candidates (aged 12 years or older) after the LAS was implemented in 2005 (Figure 3). However, more recently, the rates have been similar (Table 2). The relative risk of transplant by year and age group shows a lower transplant rate for candidates aged 6–11 years than for candidates aged 12–17 and 18–34 years immediately after implementation of LAS-based allocation, but more recently rates by age have been similar (Figure 4).

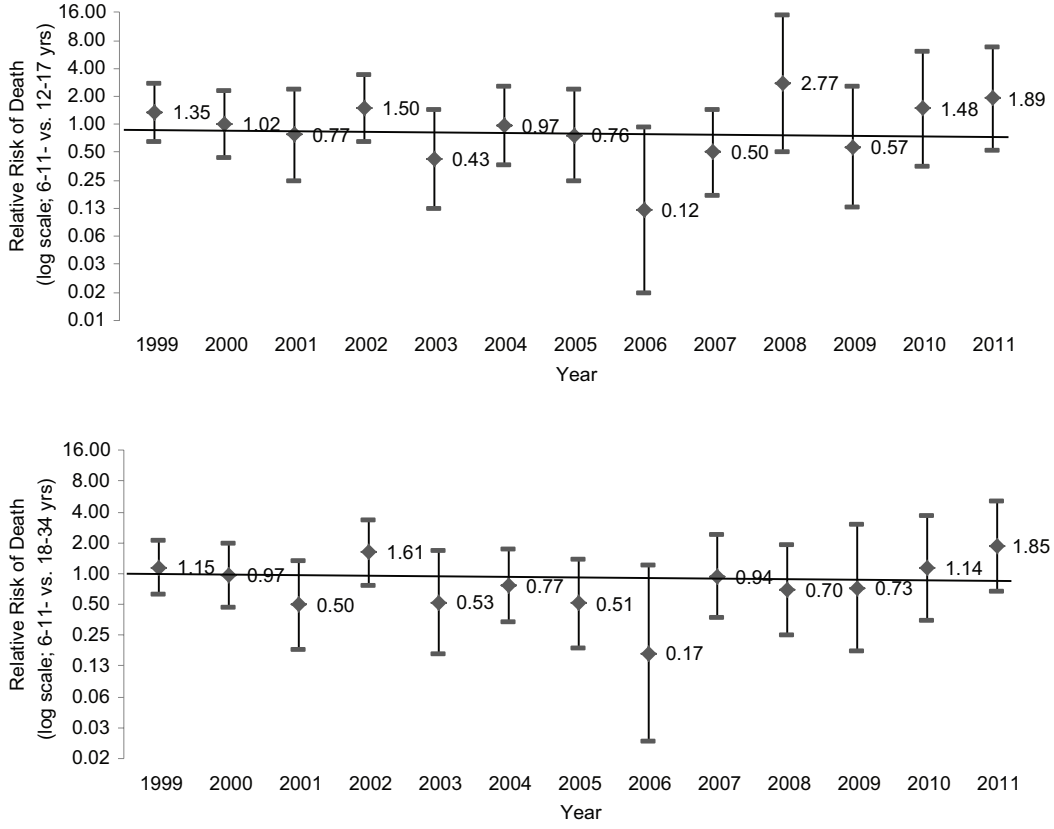

Figure 2: Trends in the relative risk of death on the active waiting list by age at listing. Deaths include removals from the waiting list due to being too sick for transplant and deaths that occurred within 2 weeks of inactivation. Points above and below 1.0 indicate increased and decreased risk, respectively. Inclusion of 1.0 in the 95% intervals (bars) indicates differences that are not statistically significant. Results are those of Poisson regression analysis comparing age at listing 6–11 years with 12–17 years (upper panel) and 6–11 years with 18–34 years (lower panel). Age was computed within each calendar year as the latter of the listing date (if listed within the year), or age on the first of the year.

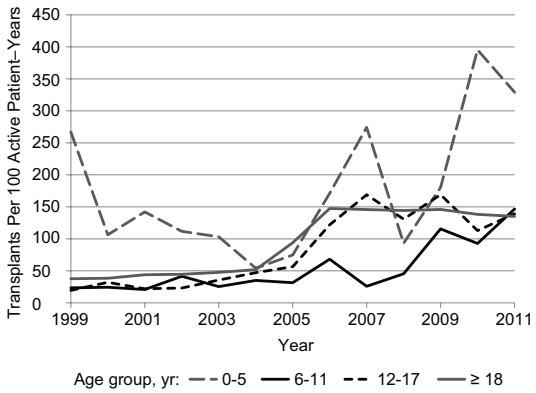

Figure 3: Trends in transplant rates by age at listing among active patients.

As a crude index of equity of access in lung allocation, we compared the percentages of new additions to the waiting list in 2011 with the percentages of transplants in the same year (Table 3). These percentages were very similar within age categories.

Discussion

The results of this study indicate that waitlist mortality and transplant rates are similar for children aged 6–11 years, adolescents (aged 12–17 years) and adults (aged 18 years or older) who are active on the lung transplant waiting list. For children aged 0–5 years, waitlist mortality is higher compared with older children and adults, but transplant rates are not lower compared with other age groups.

The plaintiffs' filing to the US District Court, Eastern District of Pennsylvania, on June 5, 2013, included data from the SRTR/OPTN Annual Data Report, which showed that death rates for patients active on the waiting list were higher for children (aged younger than 12 years) than for adolescents and adults (aged 12 years or older). For example, the 2011 death rate for children active on the waiting list was reported to be 62% versus 26% for adults. However, these death rates were calculated incorrectly; deaths within the calendar year were divided by the number of candidates on the waiting list at a single point in time (December 31) of the prior year. Another major problem with the waitlist death data presented in the brief to the Court resulted when children aged 5 years or younger were included in the group aged younger than 12 years. In fact, mortality rates for candidates aged 6–11 years are similar to rates for candidates aged 12 years or older (Figure 1).

Similarly, in data submitted to the Court by the plaintiffs, the ''success rate'' (number of transplants divided by number of candidates on the list at any time during the year) was reported to be higher for adults than for children who were active on the waiting list. For example, in 2011, 51% of adults underwent transplant and only 30% of children. However, this transplant ''success rate'' did not take into account the length of time candidates were active on the waiting list and therefore eligible to undergo transplant. In 2011, transplant rates were 195 per 100 patient-years for active candidates aged younger than 12 years and 135 per 100 patient-years for candidates aged 12 years or older (Table 2).

Comparing waitlist mortality rates and transplant rates between candidates aged younger than 12 years and candidates aged 12 years or older is difficult, given the different policies that govern the distribution of organs among these age groups and how these differences may motivate listing behaviors. Candidates aged younger than 12 years are incentivized to register on the waiting list early to accumulate waiting time, but this incentive is absent for candidates aged 12 years or older, who receive lung offers determined by the LAS-based allocation system. Therefore,

Table 2: Transplant rates by age of active lung transplant candidates

	Active candidates aged ≥12 years				Active candidates aged <12 years			
Year	Active, n	Years at risk	Transplants, n	Transplant rate[1]	Active, n	Years at risk	Transplants, n	Transplant rate[1]
1999	4128	2272.9	840	36.95696	99	37.1	16	43.1
2000	4321	2399.6	917	38.21526	87	42.6	15	35.2
2001	4416	2350.3	1012	43.05869	89	42.1	13	30.9
2002	4243	2281.1	995	43.61835	80	33.7	19	56.4
2003	4213	2213.6	1043	47.11702	71	37.4	14	37.4
2004	4266	2190.3	1133	51.72763	87	46.4	18	38.8
2005	3621	1490.0	1378	92.48535	84	42.1	19	45.2
2006	2855	930.3	1365	146.7221	74	27.9	25	89.7
2007	2974	982.8	1437	146.2152	60	23.0	15	65.2
2008	3016	1009.4	1453	143.9509	58	24.1	14	58.1
2009	3373	1112.8	1630	146.4738	50	13.1	18	137.5
2010	3660	1264.4	1741	137.6911	50	14.6	25	171.6
2011	3798	1324.8	1790	135.119	42	9.2	18	194.6

Deaths include removals from the waiting list due to being too sick for transplant and deaths that occurred within 2 weeks of inactivation.
[1]Transplants per 100 patient-years.

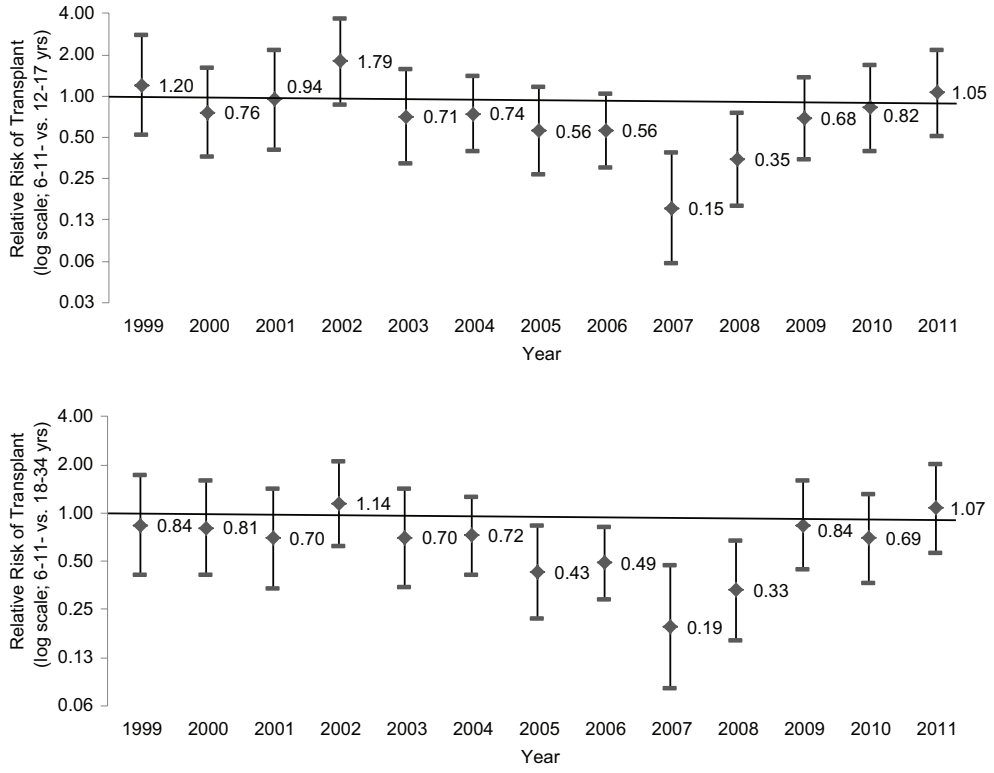

Figure 4: Trends in the relative risk of transplant by age at listing among active patients. Points above and below 1.0 indicate increased and decreased risk, respectively. Inclusion of 1.0 in the 95% intervals (bars) indicates differences that are not statistically significant. Results are those of Poisson regression analysis comparing age at listing 6–11 years with 12–17 years (upper panel) and 6–11 years with 18–34 years (lower panel).

time on the waiting list is not comparable with respect to disease severity for candidates aged older and younger than 12 years. We limited our comparisons to candidates who are active on the waiting list, but even this approach assumes that disease severity is comparable for all active time on the waiting list for children and adults.

For this analysis, we counted as ''deaths'' removals due to being ''too sick for transplant,'' and we looked for deaths within 2 weeks of inactivation in order to identify as many death events as possible. As a sensitivity analysis, we modified this definition to consider only deaths or removals due to being ''too sick'' while active on the waiting list, and conclusions remained consistent (see Figure S1). Although data are available for 2012, we limited this analysis to transplants in 2011 or earlier to compare our results with results in the Court filing, which included only patients listed through the end of 2011.

Table 3: Proportions of additions to the waiting list and transplants in 2011

Age in years	Candidates added	Transplants
n	2406	1816
0–5	0.8%	0.4%
6–11	0.5%	0.6%
12–17	1.3%	1.5%
18–34	12.1%	11.8%
35–49	13.2%	12.3%
50–64	49.5%	48.2%
≥65	22.7%	25.2%

In summary, we could find no evidence that children aged 6–11 years seeking a deceased donor lung transplant are disadvantaged in the current lung allocation system. However, the data are sparse and the analytical comparisons are challenged by the inherent differences in allocation for candidates aged less than 12 years compared with those aged 12 years or older. These differences in allocation likely cause listing at different levels of disease severity, making comparisons of waitlist mortality and transplant rates problematic. The OPTN Executive Committee action of June 10, 2013, expires on July 1, 2014. In the meantime, OPTN will consider whether permanent changes in the lung allocation policy should be made.

Acknowledgments

This work was conducted under the auspices of the Minneapolis Medical Research Foundation, contractor for SRTR, as a deliverable under contract

no. HHSH250201000018C (US Department of Health and Human Services, Health Resources and Services Administration, Healthcare Systems Bureau, Division of Transplantation) and United Network for Organ Sharing (UNOS), contractor for OPTN, under contract no. 234-2005-370011C. As a US Government-sponsored work, there are no restrictions on its use. The views expressed herein are those of the authors and not necessarily those of the US Government, UNOS, or OPTN. The authors thank SRTR colleagues Delaney Berrini, BS, for manuscript preparation, and Nan Booth, MSW, MPH, ELS, for manuscript editing. We also thank Wida Cherikh, PhD, and Leah B. Edwards, PhD, of UNOS, for their many helpful comments and suggestions.

Disclosure

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

References

1. *Janet and Francis Murnaghan, Plaintiff v. United States Department of Health & Human Services*, Kathleen Sebelius, in her official capacity as Secretary of the U.S. Department of Health & Human Services, Defendant; of the House Comm. on Case 2:13-cv-03083-MMB Document 5 Filed 06/05/13, Michael M. Baylson USDJ (Jun 5, 2013).
2. Organ Procurement and Transplantation Network. Policy Management. Policies. Available at: http://optn.transplant.hrsa.gov/policiesAndBylaws/policies.asp. Accessed July 22, 2013.
3. Colvin-Adams M, Valapour M, Hertz M, et al. Lung and heart allocation in the United States. Am J Transplant 2012; 12: 3213–3234.
4. US Department of Health and Human Services (HHS). Final Rule. Available at: http://www.ecfr.gov/cgi-bin/text-idx?c=ecfr&tpl=/ecfrbrowse/Title42/42cfr121_main_02.tpl. 2013. Accessed July 23, 2013.
5. Leppke S, Leighton T, Zaun D, et al. Scientific Registry of Transplant Recipients: Collecting, analyzing, and reporting data on transplantation in the United States. Transplant Rev (Orlando) 2013; 27: 50–56.

Supporting Information

Additional Supporting Information may be found in the online version of this article.

Figure S1: Active death rates by candidate age, excluding deaths that occurred within 2 weeks of inactivation.