Final Report

OPTN Thoracic Transplantation Committee | Descriptive Data Request

Monitoring of the Lung Allocation Change, 6 Month Report
Removal of DSA as a Unit of Allocation

Task 1.s, Item 25
DHHS Contract No. 234-2005-370011C
Submitted: June 29, 2018

Prepared for:
Thoracic Transplantation Committee
Committee Meeting
June 29, 2018

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Purpose

On November 24, 2017 an emergency action change to lung allocation policy removed the donor service area (DSA) level of allocation for deceased donor lungs (first unit of allocation) and replaced it with a 250 nautical mile (NM) circle around the donor hospital. The OPTN/UNOS monitored allocation directly following the changes. An out-of-the-gate monitoring report was completed for the OPTN/UNOS Thoracic Transplantation Committee (Thoracic Committee) approximately 10 weeks after the change to ensure there were no unexpected consequences. The out-of-the-gate report was a weekly behavior report. A second report that focused on examining cohort level changes was published to the OPTN site approximately 4 months after the change. This report will also focus on cohort levels changes with a larger 6 month cohort. Specifically, this report will focus on the geographic distribution of lungs. These metrics should aid in determining whether this policy achieves the goals being developed by the Thoracic Committee and Ad-hoc Committee on Geography on geographic distribution of organs.

As more data and time is accumulated, more extensive analyses will be performed on behalf of the Thoracic Committee. The OPTN will respond to further requests by the Thoracic Committee as well as relay appropriate requests to the SRTR related to these changes.

Executive Summary

Monitoring began upon implementation of the emergency action lung policy change on November 24, 2017. The primary goal of the policy was to address concerns over compliance with the final rule.
Based on the first 6 months of data collection post policy:

- An expected change was seen in the distribution of match LAS at transplant for recipients. As predicted there was an increase in the mean match LAS at transplant. This change and it's magnitude varied across OPTN region.
- An increase was seen in the median distance between donor hospital and transplant center and a decrease in the number of local lung transplants. However, the majority of lungs are allocated within the first unit of allocation (250 NM radius from the donor hospital).
- There was a decrease in deceased donor utilization nationally, but the impact varied by OPTN region.
- The national discard rate increased, but varied by OPTN region.
- Nationally there was an increase in ischemic time and time from first electronic offer to cross clamp.
- The number of additions to the lung waiting list increased. However, the cohort does not show evidence of change with respect to diagnosis group, match LAS at listing, or removals due to too sick to transplant or death.
- Nationally there was an increase in the number of lung alone transplants, but this varied by OPTN region.
- Nationally there was an increase in the number of DCD donors.
- The recipient cohorts do not show evidence of a difference across eras with respect to diagnosis group, procedure type, or ABO.

The conclusions from the 6 month report predominantly align with those from the earlier 4 month report. However, it is still early post-implementation. Changes such as those to behavior or clinical practice may have an impact on the system. The implications of the policy change will continue to be monitored closely with regular reports to the Thoracic Committee.

Monitoring Plan

Six months of data has been collected since the November emergency action lung policy change. A pre versus post analysis will be performed on metrics for which sufficient data has been collected on the waiting list, transplants, and deceased donor utilization. Specifically the analysis will include:

- Waiting List
  - Number of additions stratified by OPTN region and diagnosis group
  - Distribution of removals stratified by OPTN region and diagnosis group
  - Distribution of lung allocation score (LAS) at listing nationally and by OPTN region
- Transplants
  - National volume stratified by recipient characteristics: diagnosis group, ABO, de-identified center, and OPTN region
  - National volume stratified by transplant characteristics: procedure type
  - National volume stratified by donor characteristics: donor type
  - Distribution of LAS at transplant nationally and by OPTN region
  - Geographic distribution of lungs
  - Summary of match process time and offer number of the final acceptor
  - Summary of ischemic time
- Deceased Donor Utilization
  - Number of deceased donor lungs by de-identified organ procurement organization (OPO)
  - Discard Rate
  - Utilization Rate

Cohorts

1. Adults (age $\geq$ 12) added to the waiting list, removed from the waiting list, or ever waiting for a lung alone transplant from November 25, 2016 through May 24, 2017 (pre) and November 25, 2017 through May 24, 2018 (post)
2. Adults (age $\geq$ 12) that received a lung alone transplant from November 25, 2016 through May 24, 2017 (pre) and November 25, 2017 through May 24, 2018 (post)
3. All lung donors, donors from which at least 1 lung was recovered and transplanted, from November 25, 2016 through May 24, 2017 (pre) and November 25, 2017 through May 24, 2018 (post)
4. All lungs for which an allocation match is run from November 25, 2016 through May 24, 2017 (pre) and November 25, 2017 through May 24, 2018 (post)

The pre and post era cohorts were collected exactly 1 year apart. This will hopefully mitigate some of the seasonal and external factors that may impact the waiting list, transplants, and utilization. Only candidates and recipients (age $\geq$ 12) who are allocated based on LAS are included in the analysis. This analysis is restricted to data elements known at the time of transplant. **This analysis is based on OPTN data as of Jun 22, 2018 and is subject to change based on future data submission or correction.**

Results

Waiting List

Candidates added to the waiting list during the two eras (pre: November 25, 2016 - May 24, 2017 and post: November 25, 2017 - May 24, 2018) were compared using various clinical and geographic metrics. Summarized in Figure 1 and Table 1 are the number of candidates added to the waiting list in each era by diagnosis group defined as A- candidates with obstructive lung disease, B- candidates with pulmonary vascular disease, C- candidates with cystic fibrosis and immunodeficiency disorder, and D- candidates with restrictive lung disease.

Figure 1. Candidates Added to the Waiting List by Diagnosis Group

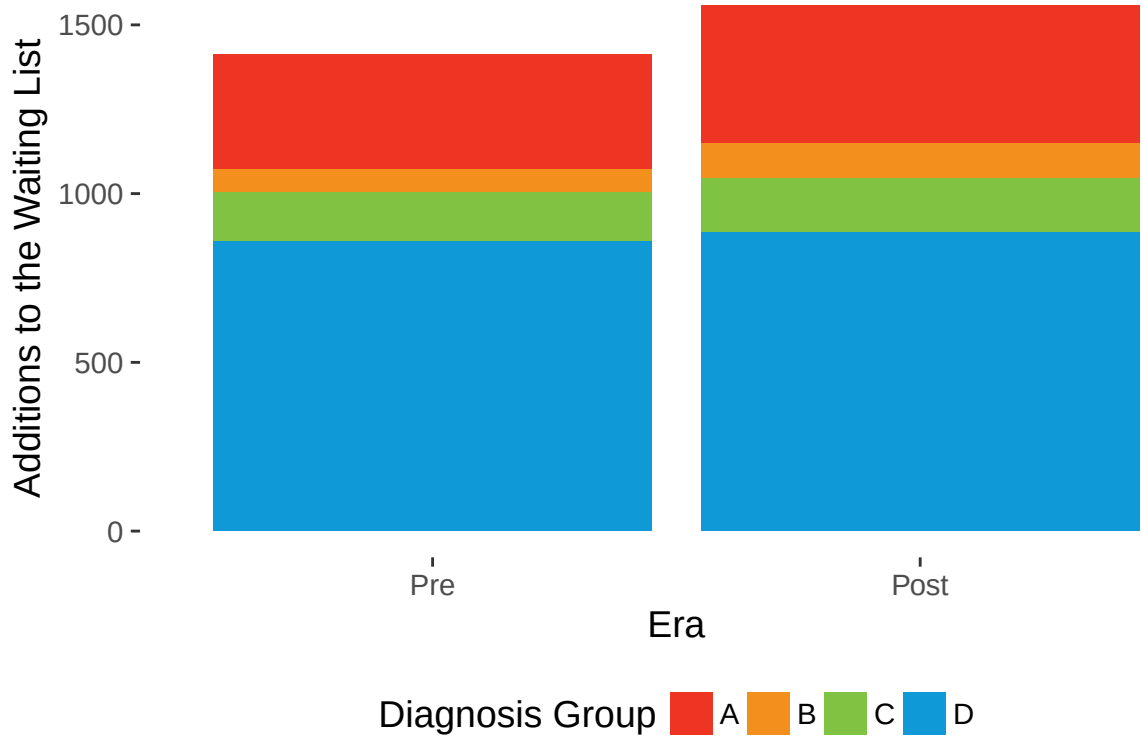


Table 1. Candidates Added to the Waiting List by Diagnosis Group

	Diagnosis Group				
Era	A	B	C	D	Total
Pre	340	68	144	861	1413
Post	407	102	162	886	1557

Following the same general trend as the overall OPTN waiting list, there has been an increase over time in the number of additions to the lung waiting list. There have been more additions to the lung waiting list in the post era than in the pre era. There is not a statistically significant difference between the diagnosis groups of the two cohorts ($\chi^2_3 = 7.26$, p-value $= 0.064$). To analyze the geographic distribution of additions to the waiting list, they are summarized by OPTN region in Figure 2 and Table 2.

Figure 2. Candidates Added to the Waiting List by OPTN Region

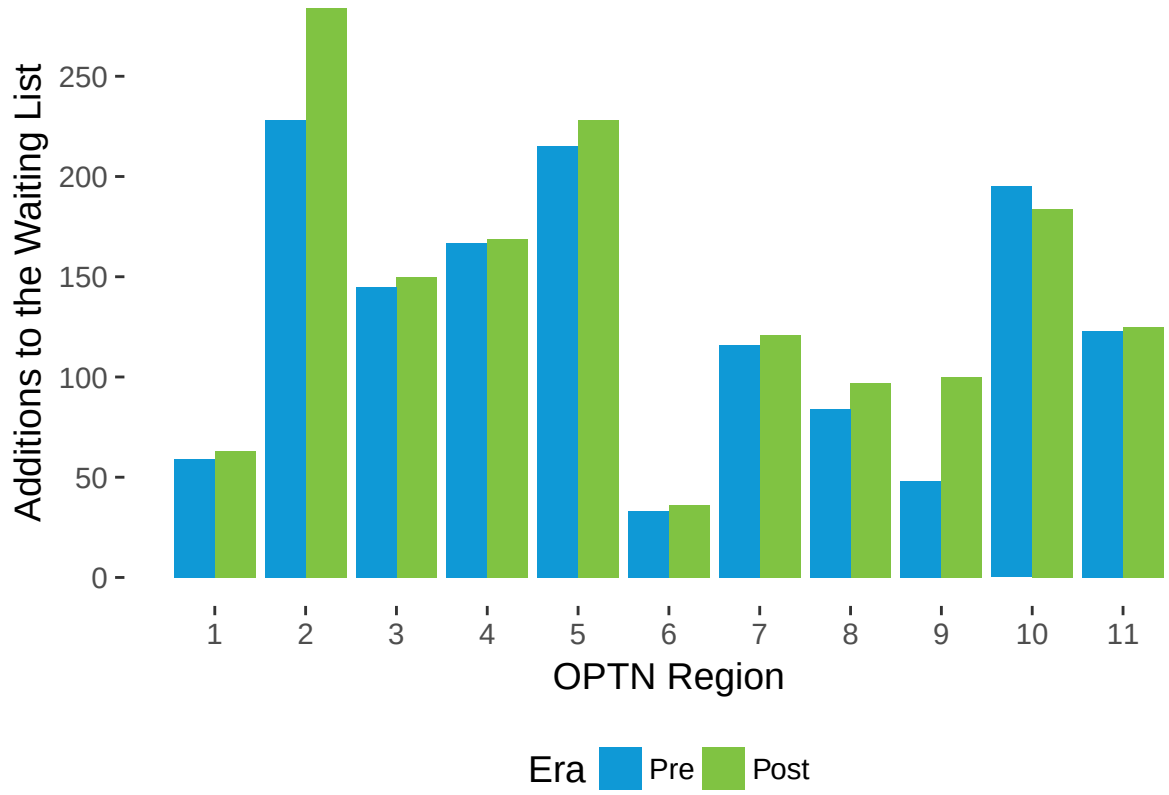


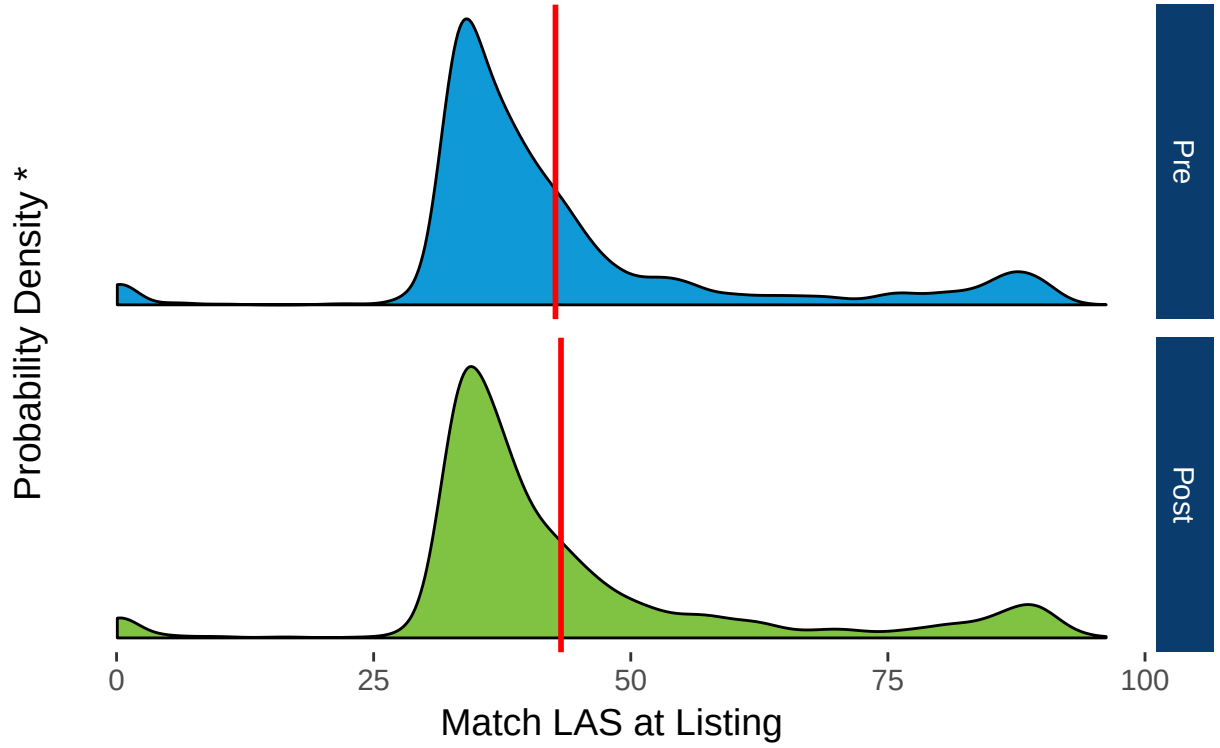
Table 2. Candidates Added to the Waiting List by OPTN Region

	OPTN Region											
Era	1	2	3	4	5	6	7	8	9	10	11	National
Pre	59	228	145	167	215	33	116	84	48	195	123	1413
Post	63	284	150	169	228	36	121	97	100	184	125	1557

Nationally there has been an increase in the number of candidates added to the lung waiting list in the post era compared to the pre era. The increase is seen in all OPTN regions except 10 which saw a decrease in the number of additions to the waiting list.

Adults (age ≥ 12) are allocated lungs according to their lung allocation score (LAS). Figure 3 depicts the distribution of the LAS at listing for the two eras.

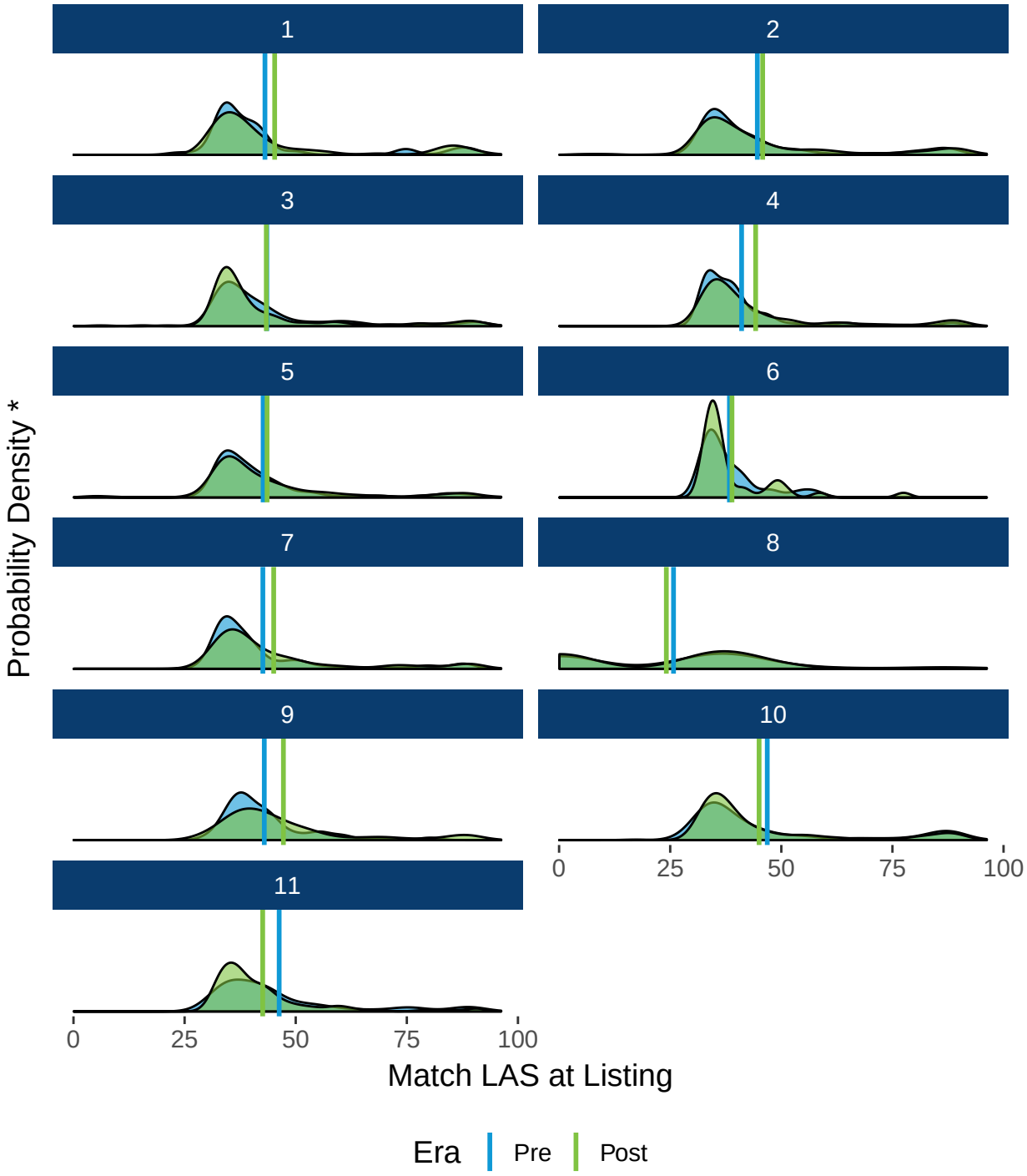
Figure 3. Distribution of LAS at Listing for Candidates Added to the Waiting List



* High probability density values mean that a high percentage of the population lies at or around the corresponding x−axis value, and vice versa. Red line indicates the mean in each corresponding era.

The mean match LAS at listing for the pre era is 42.68 and 43.22 for the post era. There is not a statistically significant difference between the mean LAS for the two eras (p-value=0.387), implying that the average severity of illness doesn't greatly vary across eras. To further examine the LAS for additions to the waiting list, Figure 4 summarizes the LAS at listing by OPTN region.

Figure 4. Summary of LAS at Listing by OPTN Region for Candidates Added to the Waiting List



* High probability density values mean that a high percentage of the population lies at or around the corresponding x−axis value, and vice versa. Vertical line indicates the mean in each corresponding era.

The variation in LAS at listing by OPTN region can be seen in Figure 4. Region 8 has the lowest average LAS at listing in both eras. The majority of OPTN regions have a mean LAS at listing in the pre and post era of approximately 45.

When examining candidates that were ever waiting in either era, there were a total of 169 removals due to death or too sick to transplant in the pre era and 190 in the post era. In Figure 5 and Table 3 below, the number of removals due to death or too sick to transplant are summarized by OPTN region.

Figure 5. Candidates Removed Due To Death or Too Sick to Transplant by OPTN Region

Table 3. Candidates Removed Due To Death or Too Sick to Transplant by OPTN Region

	OPTN Region											
Era	1	2	3	4	5	6	7	8	9	10	11	National
Pre	8	39	19	16	20	5	12	9	7	29	5	169
Post	7	38	27	13	23	8	12	12	15	29	6	190

There was an increase in the total number of removals due to death or too sick to transplant. However, to appropriately assess the difference between the eras, the changes in the waiting list from the pre to post era must be accounted for. In the pre era there were 24.78 deaths or removals for too sick to transplant per 100 patient years while waiting and in the post era there were 27.90 deaths or removals for too sick to transplant per 100 patient years while waiting. Comparing the waiting list mortality rates between the two eras, there was no evidence of a statistically significant increase from the pre to the post era (rate ratio = 1.12, 95 % credible limits = (0.97, 1.29)). The diagnosis group of candidates removed due to death or too sick to transplant are summarized in Table 4.

Table 4. Candidates Removed Due To Death or Too Sick to Transplant by Diagnosis Group

Diagnosis Group	Pre	Post
A	32 (18.9 %)	28 (14.7 %)
B	7 (4.1 %)	16 (8.4 %)
C	7 (4.1 %)	6 (3.2 %)
D	123 (72.8 %)	140 (73.7 %)

In the pre and post era, the majority of removals are for candidates in diagnosis group D- restrictive lung disease. The smallest diagnosis groups removed for too sick to transplant or death are groups B- pulmonary vascular disease and C- cystic fibrosis and immunodeficiency disorders.

Transplant

There were a total of 1181 deceased donor lung transplants for recipients (age $\geq$ 12) in the pre (November 25, 2016 - May 24, 2017) era and a total of 1207 deceased donor lung transplants for recipients (age $\geq$ 12) in the post (November 25, 2017 - May 24, 2018) era. There were 6 pediatric (age <12) lung transplants in the pre era and 5 in the post era that are not included in the analysis cohort. Figure 6 and Table 5 summarize deceased donor lung transplants by recipient diagnosis group and era.

Figure 6. Deceased Donor Lung Transplants by Diagnosis Group

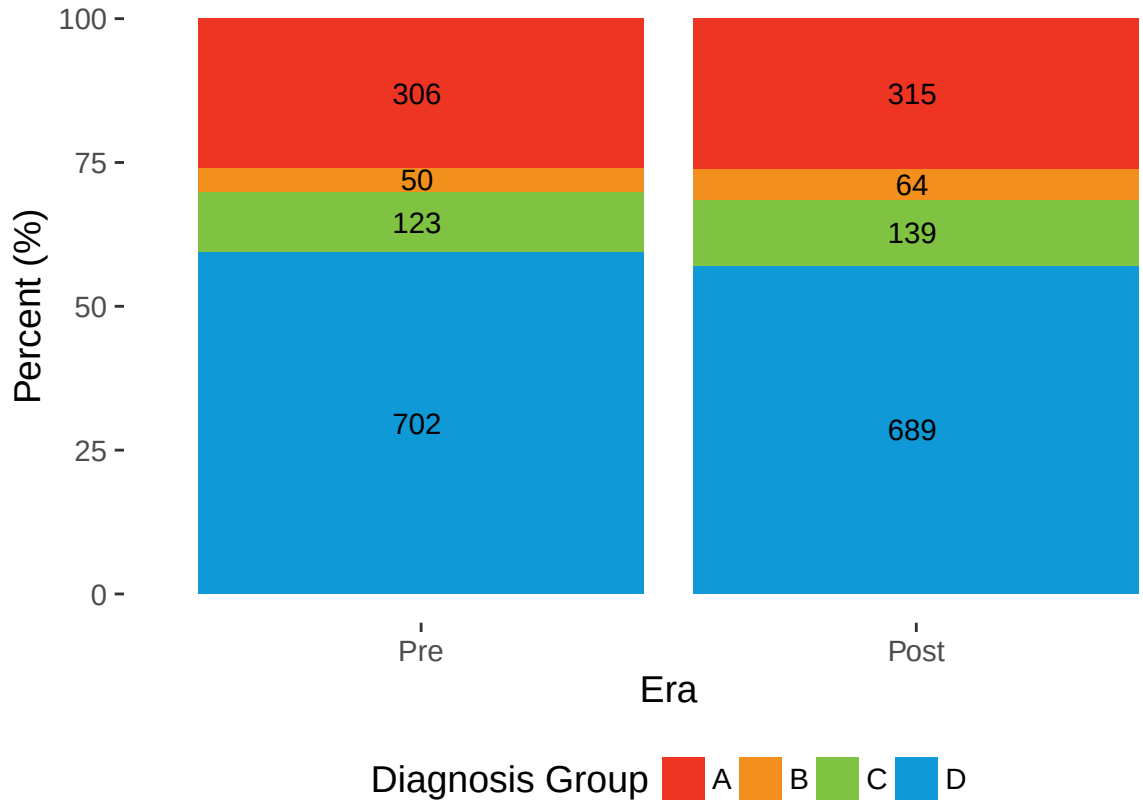


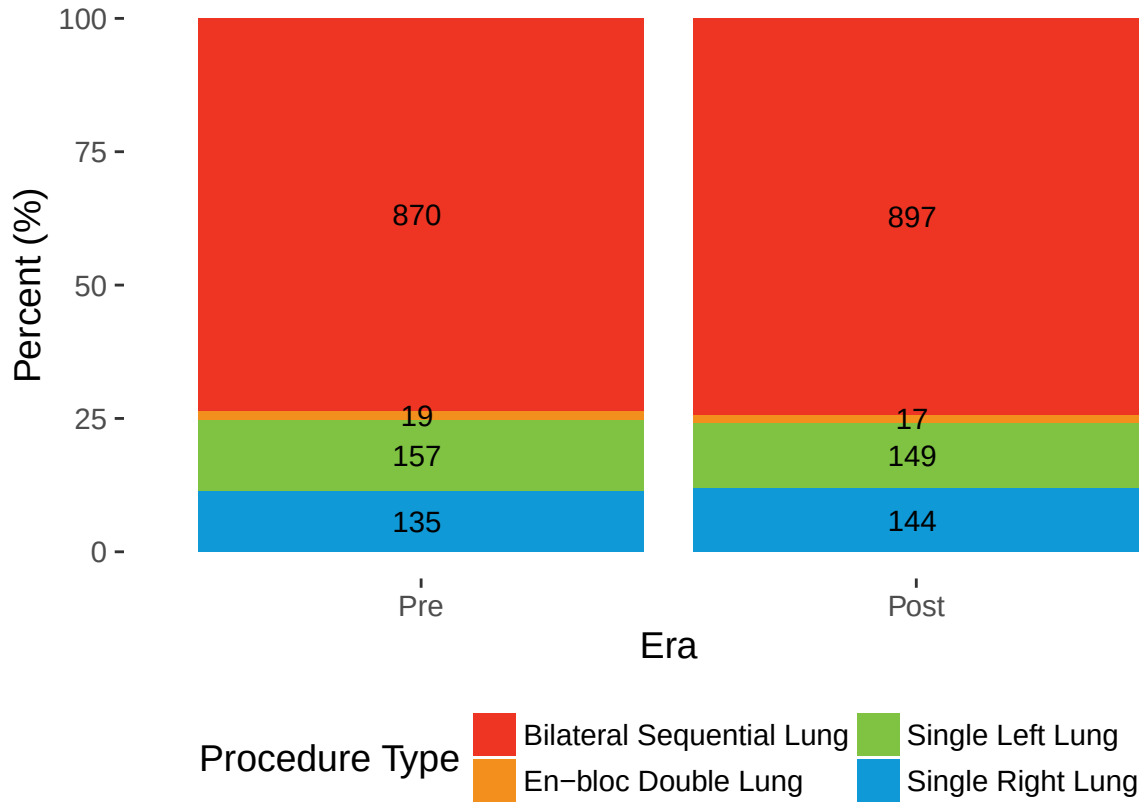
Table 5. Deceased Donor Lung Transplants by Diagnosis Group

	Diagnosis Group				
Era	A	B	C	D	Total
Pre	306	50	123	702	1181
Post	315	64	139	689	1207

There is not a statistically significant difference in the diagnosis group of recipients of deceased donor lung transplants between the two eras ($\chi^2_3 = 2.67$, p-value $= 0.446$). The majority of lung transplant recipients in both eras were in diagnosis group D- restrictive lung disease. There were approximately twice as many transplants for recipients in diagnosis group D than there were in the second largest diagnosis group, A- obstructive lung disease. The smallest transplant recipient diagnosis group in both eras is B- pulmonary vascular disease.

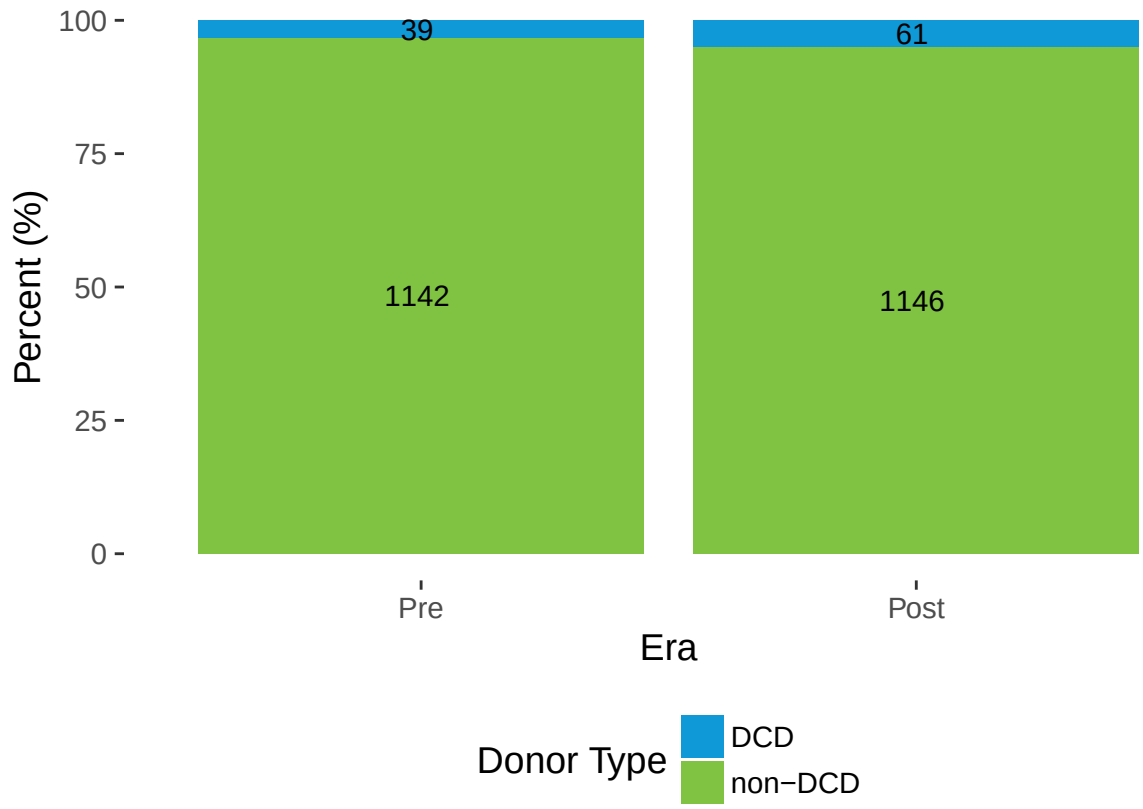
To thoroughly examine any impact the policy had on lung transplants, lungs transplants were examine by procedure type (single left lung, single right lung, en-bloc double lung, and bilateral sequential lung).

Figure 7. Deceased Donor Lung Transplants by Procedure Type



From Figure 7, there is not a statistically significant difference in the procedure type of recipients of deceased donor lung transplants between the two eras ($\chi^2_3 = 0.74$, p-value $= 0.864$). Figure 8 shows the number of deceased donor lung transplants by donor type (DCD vs. non-DCD).

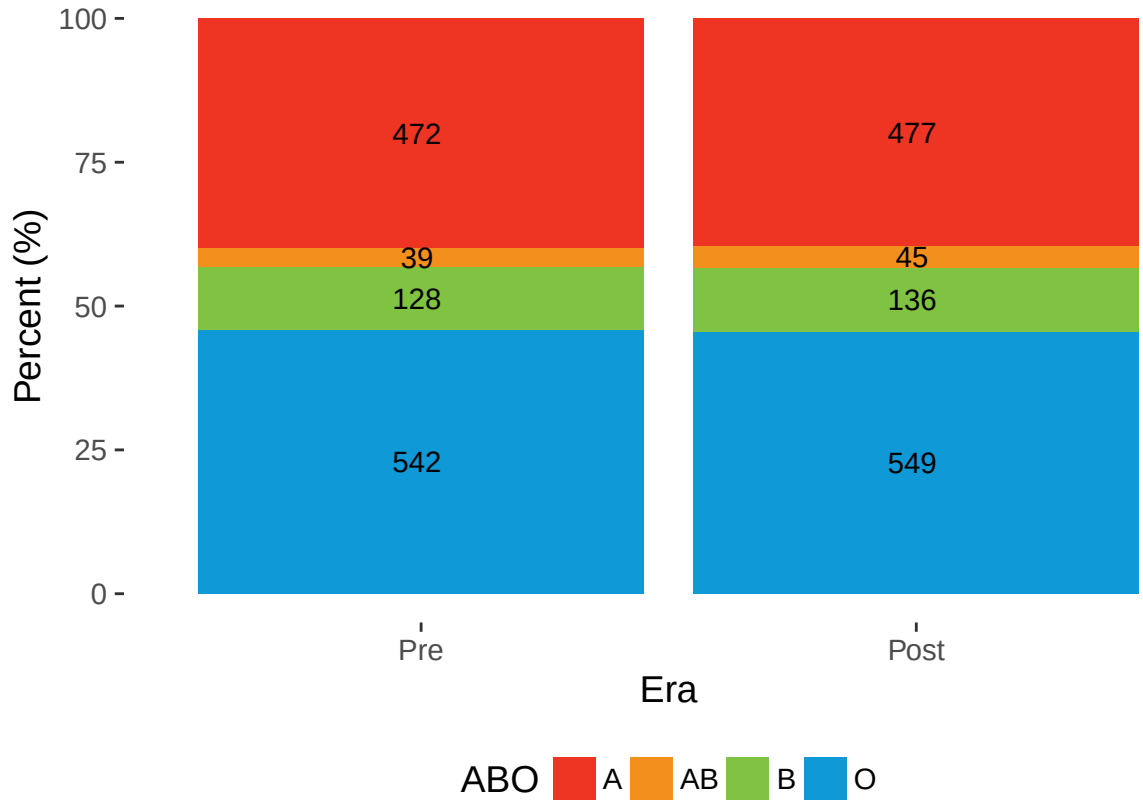
Figure 8. Deceased Donor Lung Transplants by Donor Type



In the pre era there were only 39 DCD donors compared to 61 in the post era. There is a statistically significant difference in the proportion of DCD donors between the two eras ($\chi^2_1 = 4.14$, p-value $= 0.042$). This aligns with the general trend of increasing use of DCD lung donors over the past couple of years.

Since deceased donor lungs are first allocated to ABO identical before compatible, it was of interest to determine whether there was a change in the ABO of transplant recipients.

Figure 9. Transplant Recipients by ABO



There is not a statistically significant difference in the blood type of transplant recipients between the two eras ($\chi^2_1 = 0.22$, p-value $= 0.640$).

Since the November policy change removed DSA as the first unit of allocation for lungs and replaced it with a 250 NM radius around the donor hospital, it was of interest to determine whether there was an impact on the number of lung transplants in each OPTN region. Figure 10 and Table 6 summarize the number of lung transplants by OPTN region.

Figure 10. Deceased Donor Lung Transplants by OPTN Region

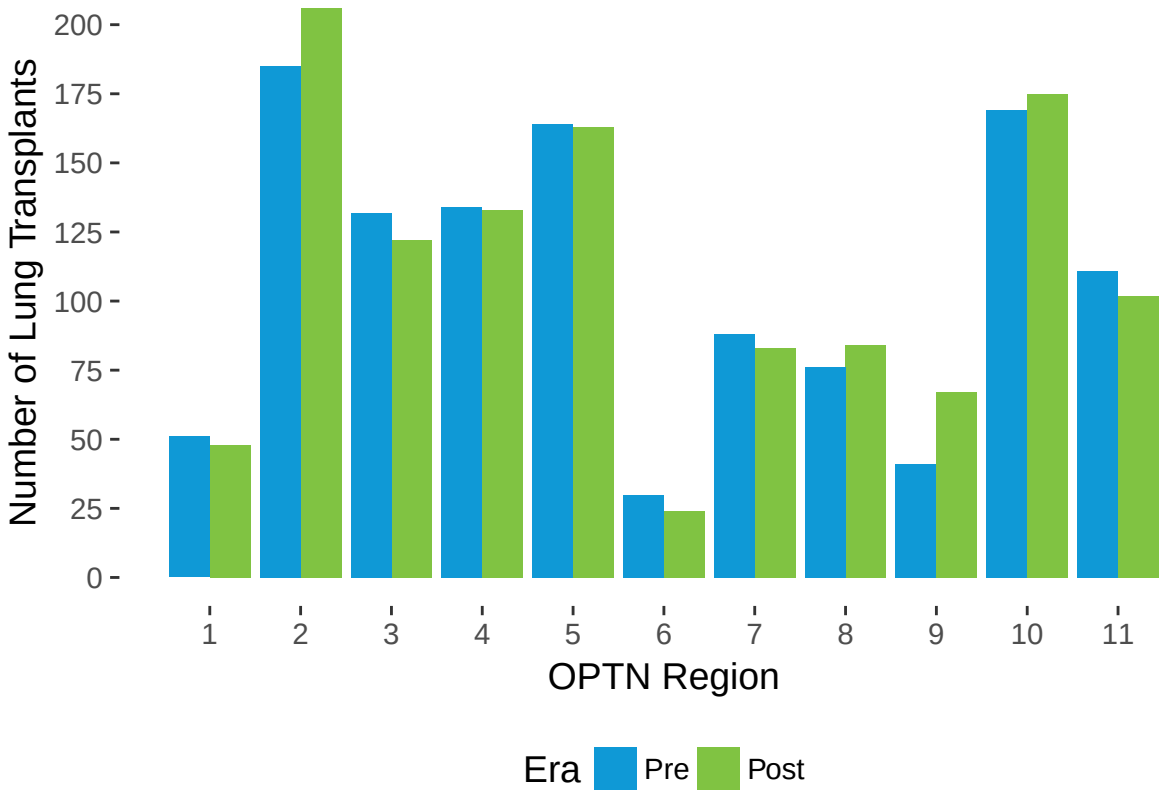


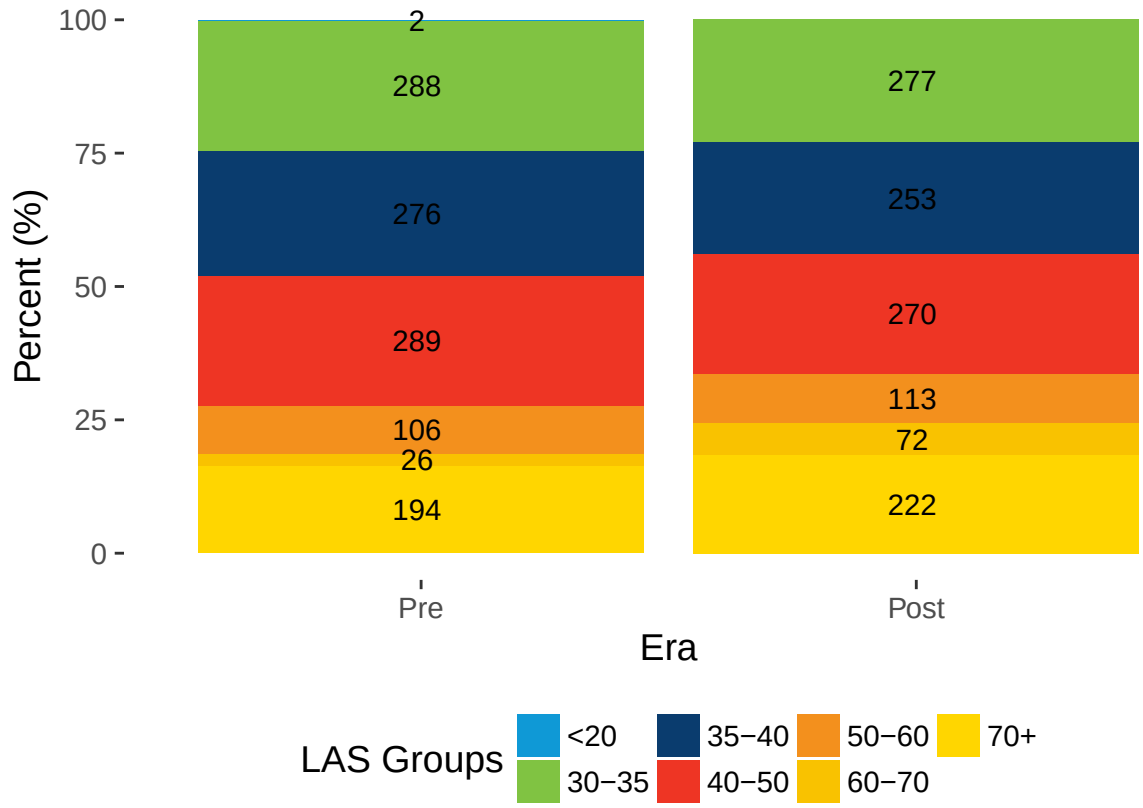
Table 6. Transplant Recipients by OPTN Region

	Era		
Region	Pre	Post	Difference (Post-Pre)
1	51	48	-3
2	185	206	21
3	132	122	-10
4	134	133	-1
5	164	163	-1
6	30	24	-6
7	88	83	-5
8	76	84	8
9	41	67	26
10	169	175	6
11	111	102	-9

The impact of the policy change varied by OPTN region with some seeing an increase in the number of lung transplants and some seeing a decrease in the number of lung transplants.

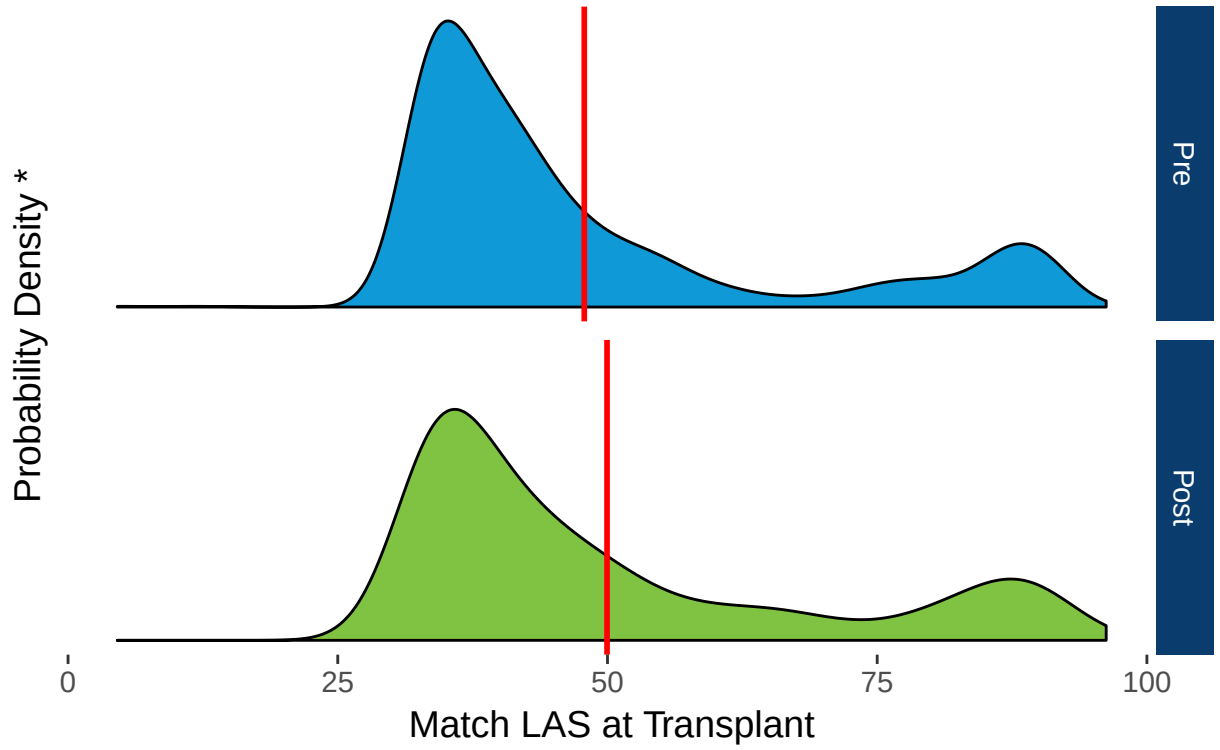
The November 2017 emergency action lung policy change allowed for the majority of candidates to appear within the first unit of allocation (250 NM radius from the donor hospital) for a larger geographic area. Only candidates located within a DSA larger than a 250 NM radius might have seen a decrease in the geographic size of their first unit of allocation. It was hypothesized there would be an increase in the average LAS at transplant as a result from transplanting more high LAS candidates. In Figure 11, deceased donor lung transplant recipients are summarized by LAS group. The LAS groups were defined as follows: <20, 20-30, 30-35, 35-40, 40-50, 50-60, 60-70, 70<, where higher LAS score represent clinically sicker patients.

Figure 11. Deceased Donor Lung Transplants by LAS Group



There was an increase in the number of lung recipients with LAS in the three highest categories (50-60, 60-70, and 70+). Similarly, the distribution of match LAS at transplant is depicted in Figure 12.

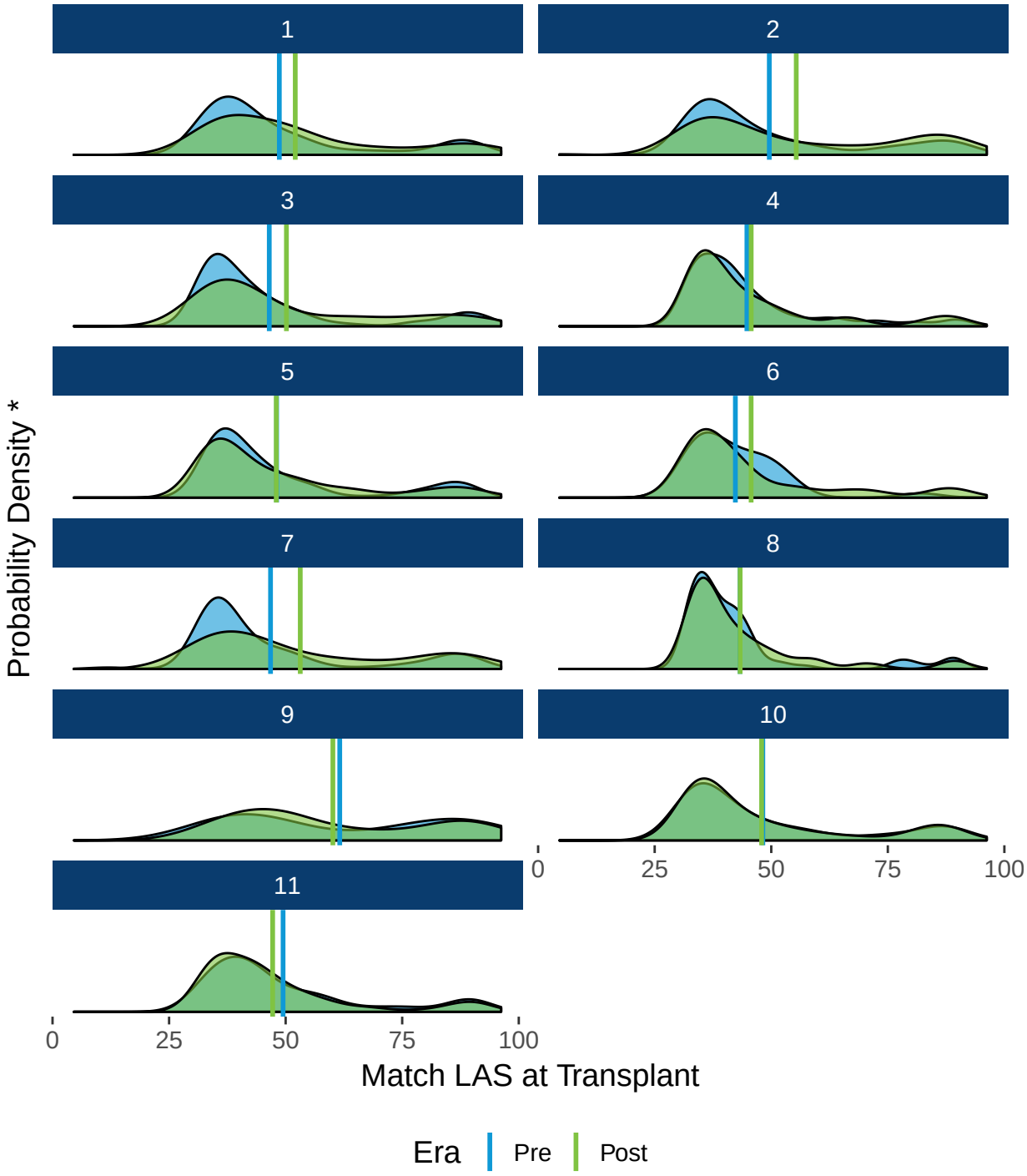
Figure 12. Transplant Recipients by LAS



* High probability density values mean that a high percentage of the population lies at or around the corresponding x−axis value, and vice versa. Red line indicates the mean in each corresponding era.

The average match LAS at time of transplant for the pre era is 47.85 and 49.96 for the post era. There is a statistically significant difference between the mean LAS in the pre era compared to the post era (p-value=0.005). While this is statistically significant, it has yet to be concluded whether there has been a clinically meaningful increase in the LAS at transplant. Additionally, there were 176 recipients with a LAS of at least 75 in the pre era and 204 in the post era. Before the November policy change, it was known that the average LAS at transplant varied by OPTN region. Figure 13 examines the impact on each OPTN region.

Figure 13. Transplant Recipients by LAS and OPTN Region

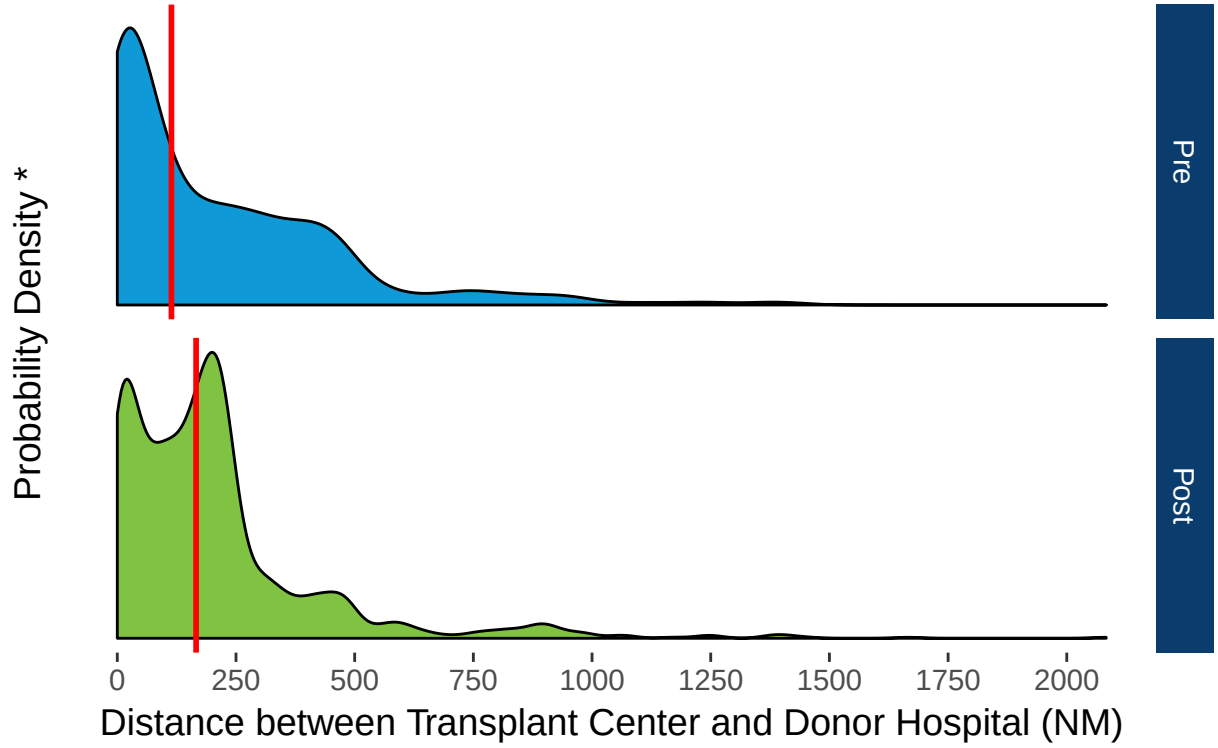


* High probability density values mean that a high percentage of the population lies at or around the corresponding x−axis value, and vice versa. Vertical line indicates the mean in each corresponding era.

There are noticeable differences in the distribution of match LAS across all OPTN regions. However, this observed difference varies by OPTN region.

The emergency policy changed how lungs were distributed across the United States. A concern within the community was related to the distance that lungs would be travelling or the distance from donor hospital to transplant center. The distribution of the distance lungs traveled within both eras is shown in Figure 14.

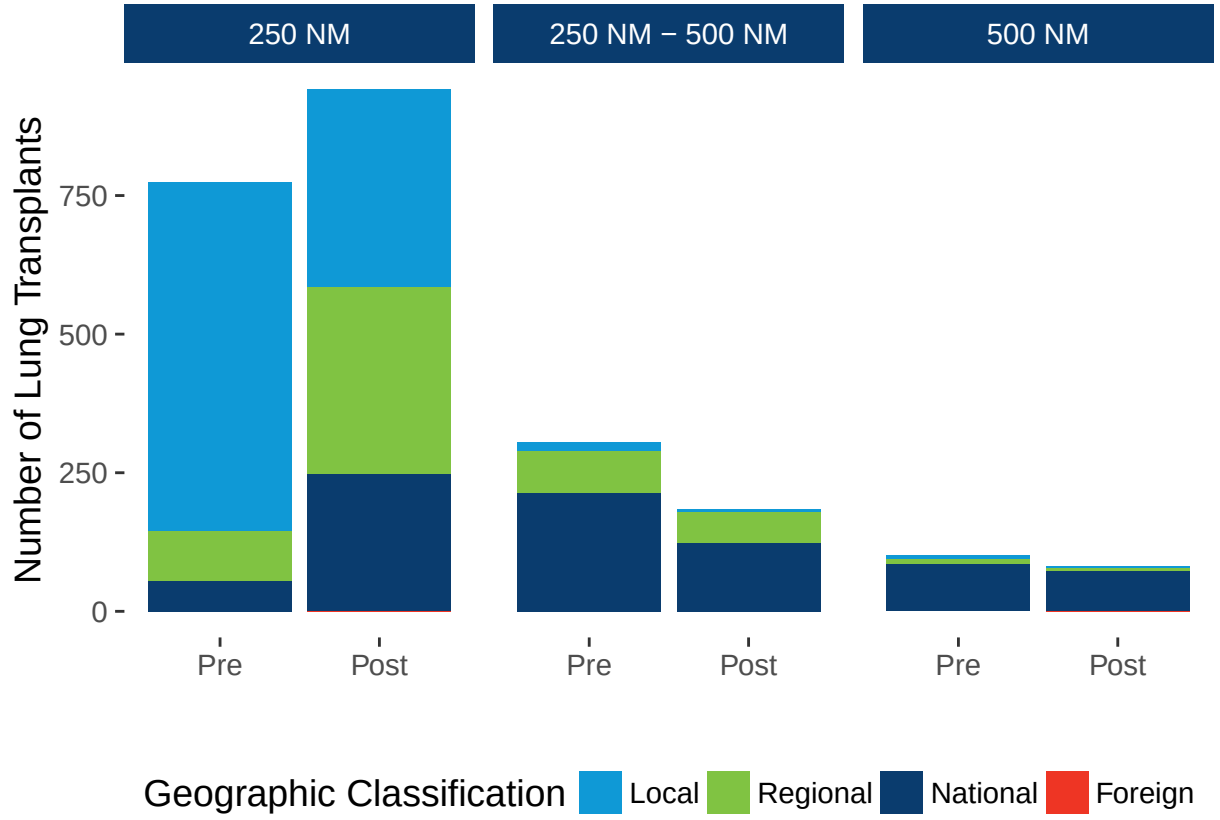
Figure 14. Distance between Transplant Center and Donor Hospital



* High probability density values mean that a high percentage of the population lies at or around the corresponding x−axis value, and vice versa. Red line indicates the median in each corresponding era.

The median distance in the pre era is 114NM and 166NM in the post era. A Wilcoxon rank sum test showed a statistically significant difference between the median distance between donor hospital and transplant center in the pre and post era (p-value = 0.013). It can be seen that the median distance a lung travels has increased in the post era. However, the majority of lungs travel under 250 NM for transplant. In Figure 15, the distance between donor hospital and transplant center is categorized as within 250 NM (new first unit of allocation), between 250 NM and 500 NM (new second unit of allocation), and over 500 NM and summarized by geographic classification (local, regional, national, and foreign).

Figure 15. Transplants by Geographic Classification and Distance (NM)



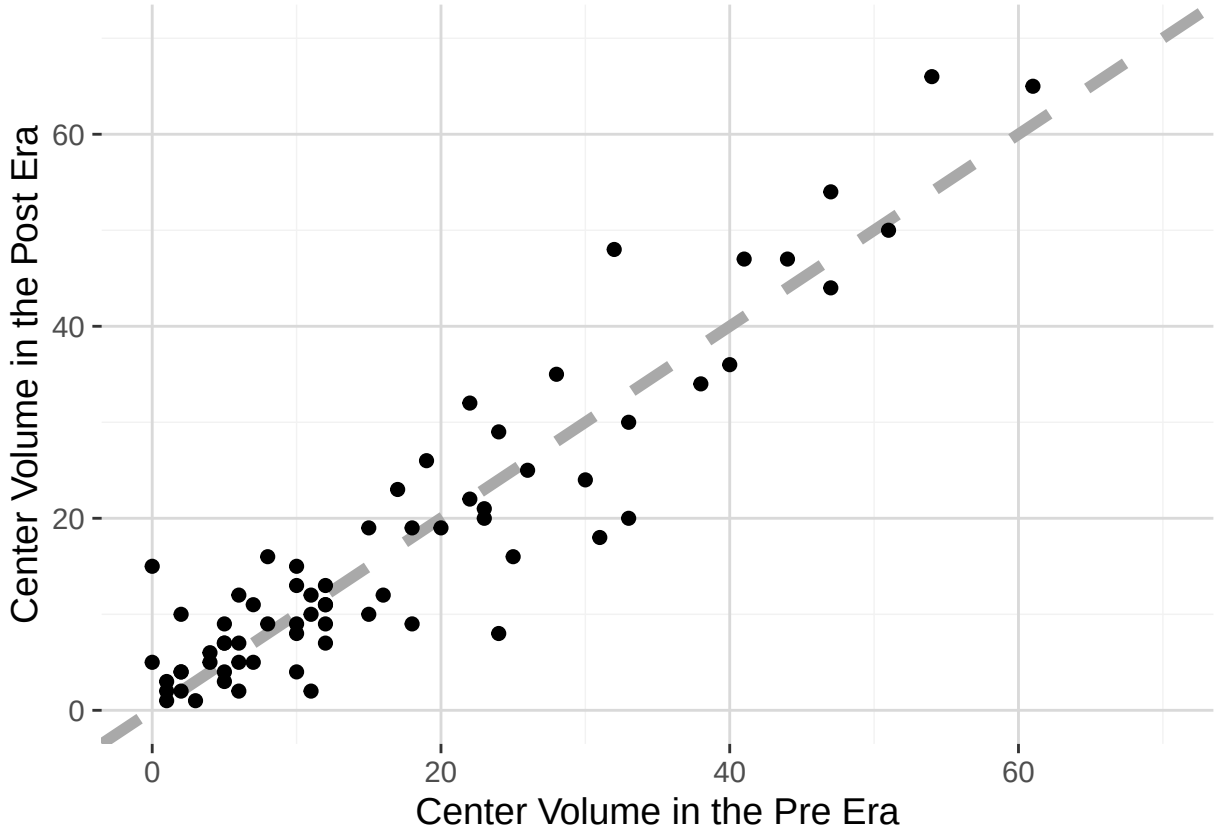
There is a 55.5% decrease in the number of local transplants. There is an increase in the number of regional transplants with the majority of that increase within the first unit of allocation (250 NM). There is also an overall increase in the number of nationally allocated lung transplants. Figure 15 shows that 65.5% of lung transplants happen within the first unit of allocation (250 NM) in the post era. Table 7 shows the number of transplants by categorized distance and geographic classification.

Table 7. Transplants by Geographic Classification and Distance (NM)

	250 NM		250 NM - 500 NM		500 NM	
Geographic Classification	Pre	Post	Pre	Post	Pre	Post
Local	629	356	16	4	7	2
Regional	89	339	76	57	8	6
National	56	247	214	123	86	71
Foreign	0	0	0	0	0	2

There was concern within the community regarding the impact the policy change would have on smaller lung transplant centers. The transplant center level impact can be seen in Figure 16, a scatter plot of center volume in the two eras.

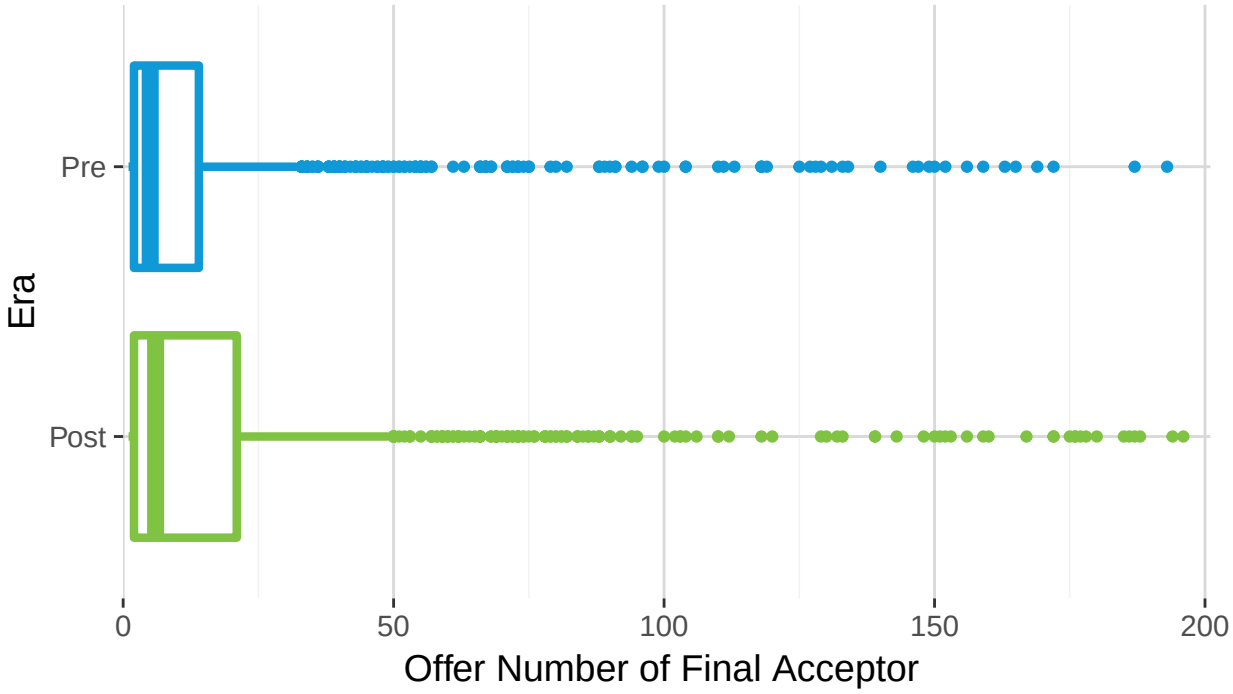
Figure 16. Scatter Plot of Center Volume



Dots that fall below the gray dashed line indicate transplant centers that have seen a decrease in the number of lung transplants from the pre to the post era. Conversely, those above the gray dashed line have seen an increase in the number of lung transplants. Smaller transplant centers who do fewer lung transplants are represented by dots in the bottom left corner. There were 69 transplant centers that performed at least one lung transplant in either era. Of those, 37 performed equal or more lung transplants in the post era compared to the pre era.

To examine the impact on the match process, Figure 17 and Table 8 summarize the sequence number of the final acceptor for all lung donors.

Figure 17. Boxplot of the Sequence Number of the Final Acceptor for Lung Donors



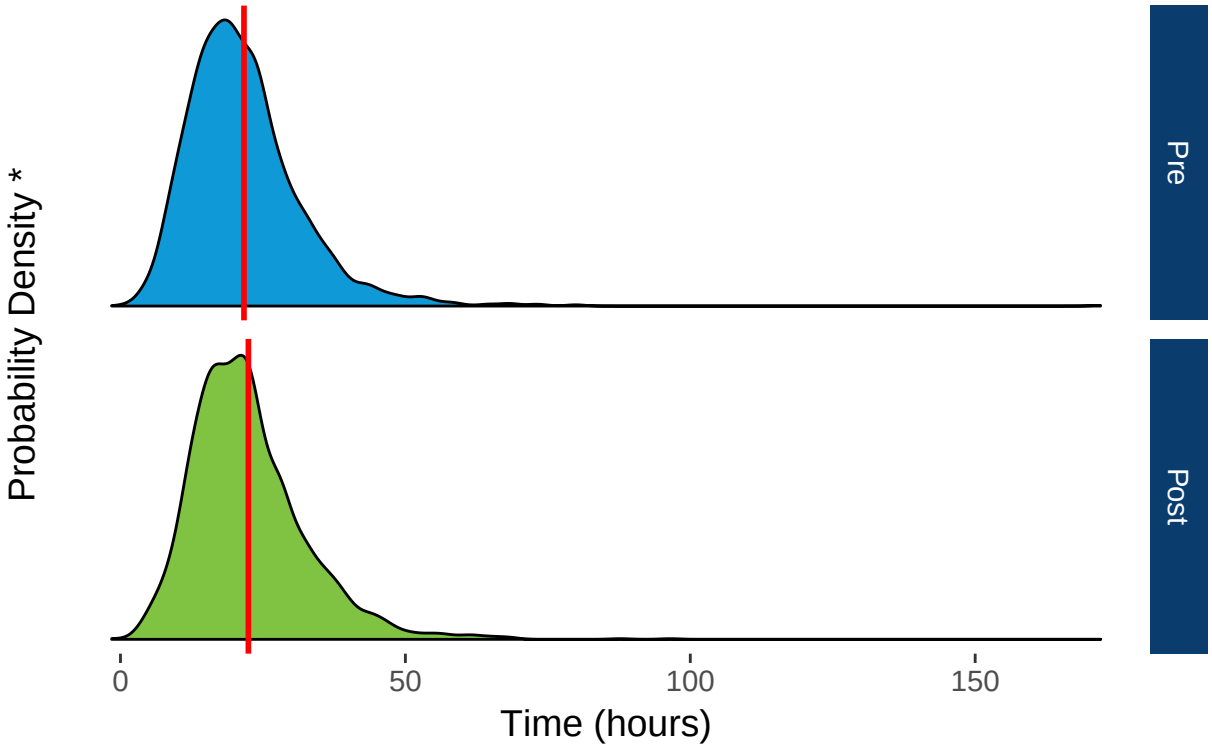
There were 15 final acceptances with an offer number over 200 in the pre era and 13 in the post era.

Table 8. Summary of the Sequence Number of the Final Acceptor for Lung Donors

Era	Median	10th Percentile	90th Percentile
Pre	5	1	43
Post	6	1	59

There is some indication that the offer number of the final acceptor is higher in the post era than in the pre era. Further data collection will be needed to examine the true difference. This could stabilize over time as OPOs and transplant centers adapt to the change. To measure match time, the time from first electronic offer to cross clamp for deceased donors who donated at least 1 lung is shown in Figure 18.

Figure 18. Time from First Electronic Offer to Cross Clamp for Deceased Donors

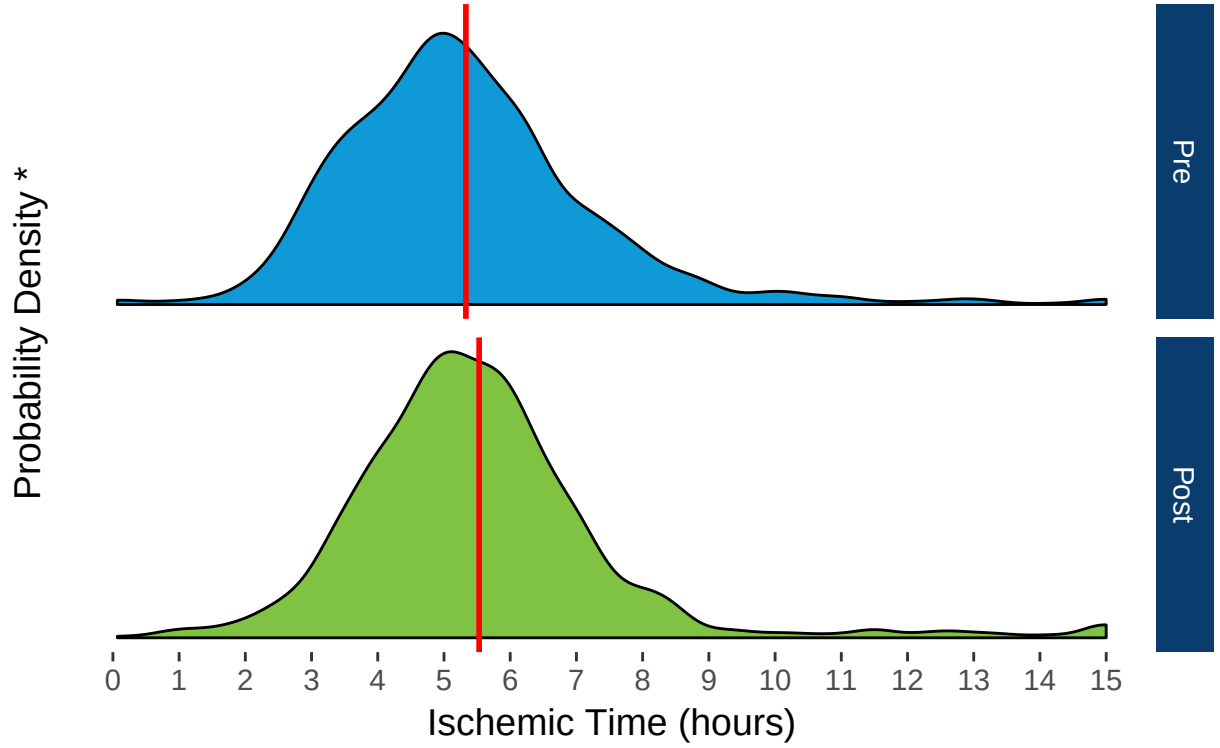


* High probability density values mean that a high percentage of the population lies at or around the corresponding x−axis value, and vice versa. Red line indicates the mean in each corresponding era.

The mean time in the pre era is 21.67 hours and 22.45 hours in the post era. There is a statistically significant difference between the pre and post era mean time from first electronic offer to cross clamp (p-value=0.008). However, other OPO and allocation factors, such as Figure 14 which showed an increase in the distance lungs are traveling, should be considered when determining whether this difference is clinically meaningful.

Figure 19 shows the distribution of ischemic time in hours for the pre and the post era.

Figure 19. Ischemic Time (Cold, Warm, and Anastomotic Time)



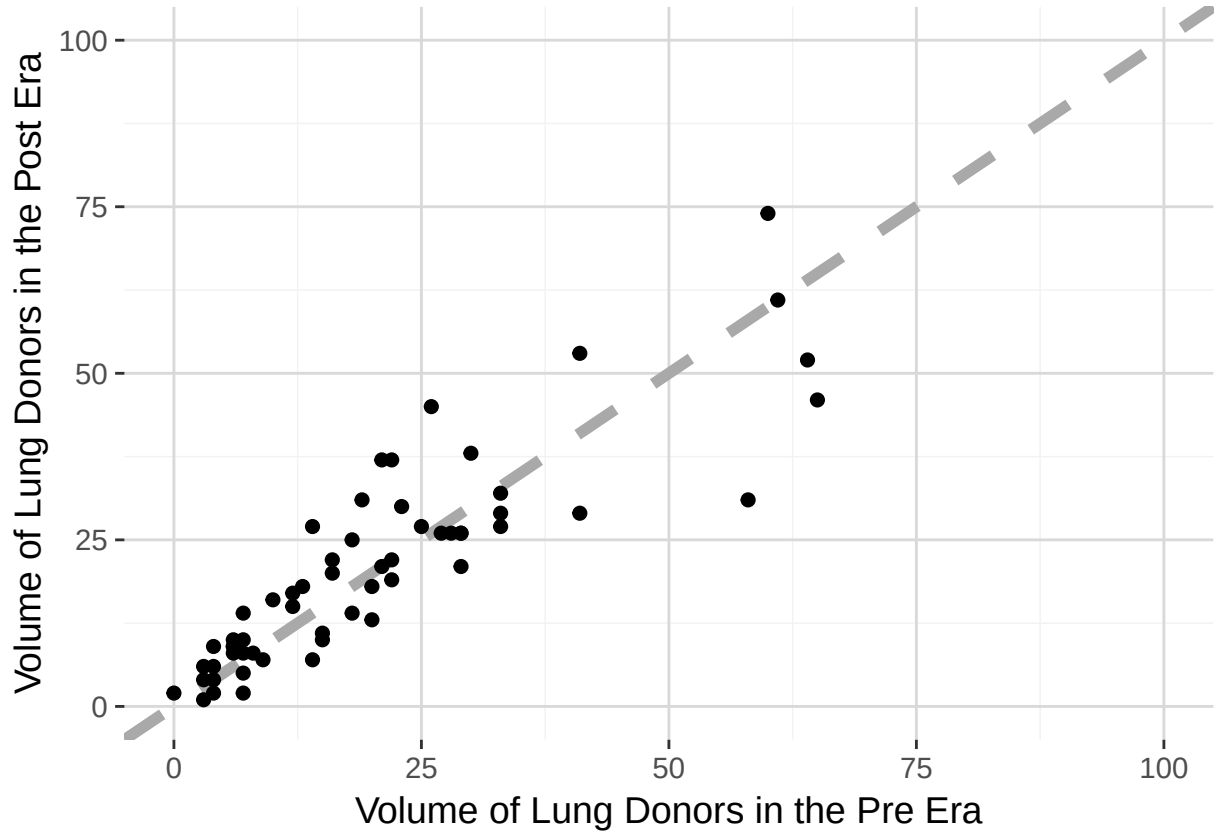
* High probability density values mean that a high percentage of the population lies at or around the corresponding x−axis value, and vice versa. Red line indicates the mean in each corresponding era.

The mean ischemic time in the pre era is 5.33 and 5.53 for the post era. There is a statistically significant difference between the pre and post mean ischemic time (p-value=0.016). A clinical assessment should be considered of the impact of a mean increase of approximately 12 minutes of ischemic time in the post era. Future analyses may examine the outcomes related to a change in ischemic time.

Utilization

The utilization of lung transplantation within the United States was compared between the pre (November 25, 2016 - May 24, 2017) and post (November 25, 2017 - May 24, 2018) era. First, the number of deceased lung donors by de-identified OPO are graphically shown in Figure 20. The x-axis represents the number of deceased lung donors in the pre era and the y-axis represented the number of deceased lung donors in the post era for each de-identified OPO.

Figure 20. Scatter Plot of OPO Volume



Dots that fall below the gray dashed line indicate OPOs that have seen a decrease in the number of deceased lung donors from the pre to the post era. Conversely, those above the gray dashed line have seen an increase in the number of deceased lung donors. There were 58 OPOs from which at least 1 deceased donor donated lungs. Of those, 34 recovered equal or more deceased donors that had lungs transplanted in the post era compared to the pre era. The discard rate, the rate at which lungs that are recovered for transplant but not transplanted, is summarized by OPTN region and nationally (Figure 21 and Table 9).

Figure 21. Discard Rate by OPTN Region

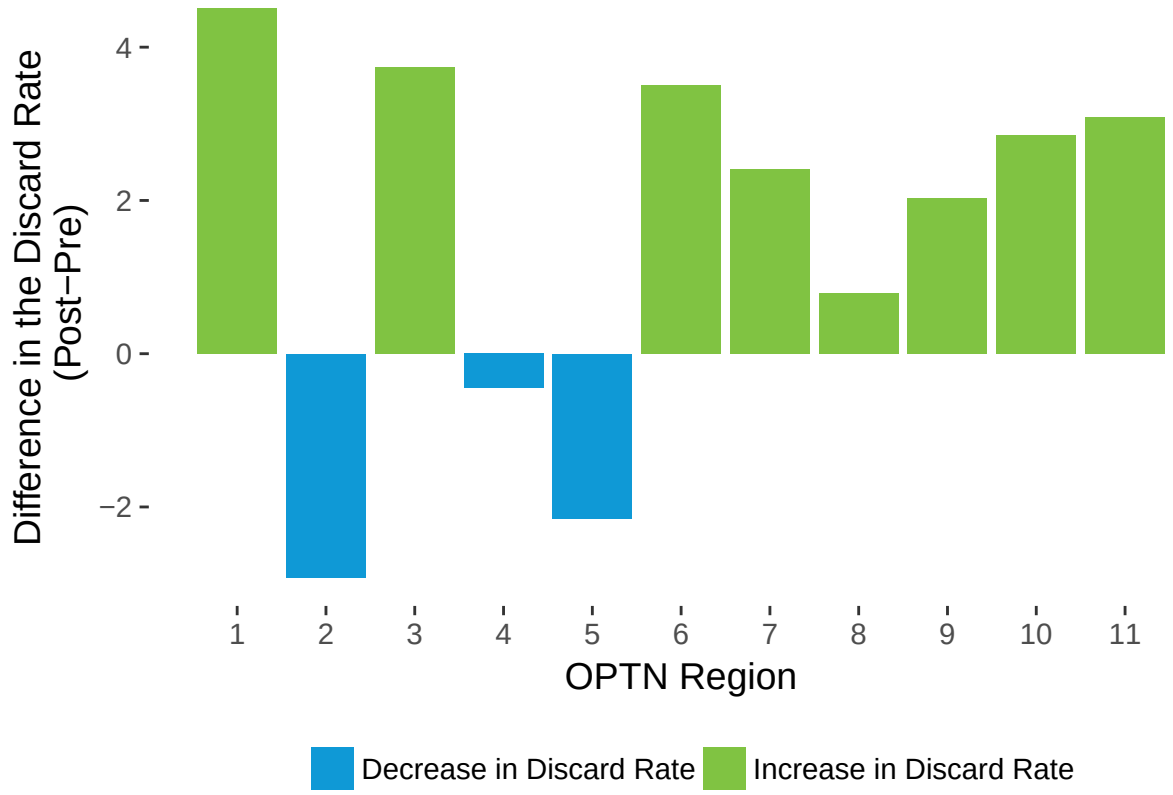


Table 9. Discard Rate by OPTN Region

	Era	
OPTN Region	Pre	Post
1	2.74	7.25
2	13.69	10.77
3	6.17	9.91
4	1.77	1.32
5	3.72	1.57
6	0.00	3.51
7	2.00	4.41
8	1.28	2.07
9	6.67	8.70
10	5.36	8.21
11	3.36	6.45
National	4.74	6.13

Nationally we see an increase in the discard rate for deceased donor lungs. However, when discard rate is examine by OPTN region, it can be seen that some regions have seen an increase and some a decrease in the discard rate. Traditionally lungs have a low discard rate; therefore, it was of interest to examine the utilization rate or the rate at which lungs are transplanted from all deceased donors. Figure 22 and Table 10 summarize the utilization rate by OPTN region and nationally for both eras.

Figure 22. Utilization Rate by OPTN Region

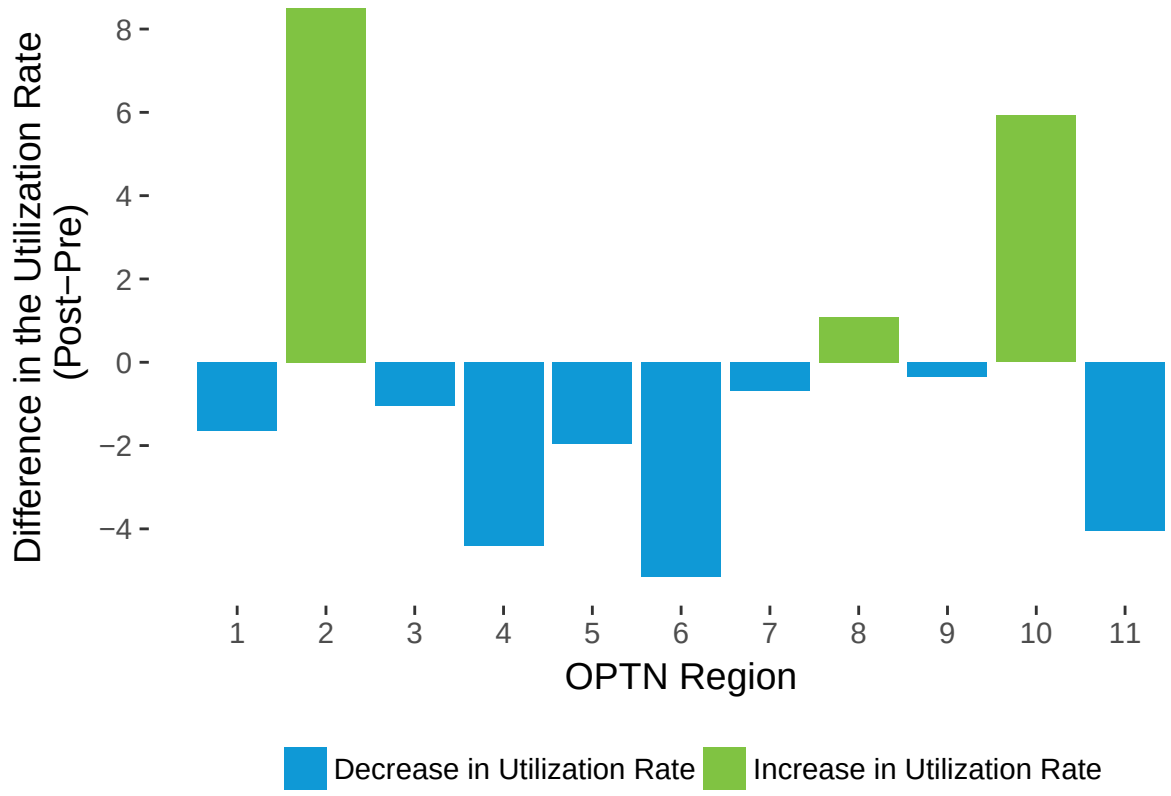


Table 10. Utilization Rate by OPTN Region

	Era	
OPTN Region	Pre	Post
1	20.86	19.21
2	18.51	27.02
3	20.92	19.88
4	25.83	21.43
5	21.90	19.95
6	18.75	13.59
7	26.49	25.81
8	24.04	25.13
9	14.16	13.81
10	23.12	29.05
11	25.70	21.66
National	22.25	22.19

Nationally, the utilization rate decreased in the post era. However, much like discard rate, there is variability in the utilization rate by OPTN region. Just in the post era, the utilization rate varies from as low as 13.59 in OPTN region 6 to as high as 29.05 in OPTN region 10.

Since it was hypothesized that lungs would have to travel further (on average) post- policy change, it was of interest to monitor the use of ex vivo lung perfusion (EVLP). Table 11 summarizes the use of EVLP by OPTN region and era.

Table 11. Number of Lungs with Machine Perfusion Intended or Performed by OPTN Region

	Era	
OPTN Region	Pre	Post
1	0	4
2	8	21
3	16	24
4	0	6
5	0	6
6	0	2
7	6	8
8	2	2
9	0	4
10	10	34
11	0	8
National	42	119

There has been an increase in the number of deceased donor lungs with machine perfusion intended or performed. Interestingly, OPTN region 10 has the highest use of EVLP and the highest utilization rate.

Conclusion

This report provides a 6-month evaluation of the emergency action lung policy implemented on November 24, 2017. It examines waiting list additions, transplant recipient population, deceased donor population, and lung deceased donor utilization. While statistically significant differences were found between the pre to post era on some metrics, clinical relevance still needs to be established. When analyzing additions to the waiting list, there were not statistically significant differences between pre and post era candidates' diagnosis group, match LAS at listing, or removals due to too sick to transplant or death. These metrics were also summarized with more granularity by OPTN region.

The transplant cohorts do not differ across eras with respect to diagnosis group, procedure type, or ABO. The post era transplant cohort did show an increase in the number of DCD donors when compared to the pre era cohort. Some OPTN regions saw a decrease in the number of transplants between pre and post era; however, the majority saw an increase. The distribution of LAS at transplant for the recipient population has changed- there has been an increase in the mean match LAS at transplant. This is considered an expected change as it was predicted that more high LAS candidates would receive transplants. The mean match LAS at transplant still varies across OPTN region. The distance that lungs travel (distance between donor hospital and transplant center) has changed with an increase in the median distance. There has also been a decrease in the number of local lung transplants and increase in the number of regional and national lung transplants. The mean time between first electronic offer and cross clamp and the mean ischemic time have increased in the post era.

The last metric examined was deceased donor utilization. The majority of OPOs recovered equal or more lungs that were eventually transplanted in the post era compared the pre era. The discard rate for lungs remained low; notably, the OPTN regional variability of discard rate remains present in both eras. The same may be said for the utilization rate of lungs. Generally, the utilization rate for lungs is lower than other organs. While it remains low, there is clear variability across the OPTN regions. There has been an increase in the use of EVLP; however, this is presumably not entirely due to the policy change, but also due to the progression of this technology.

The changes to lung allocation will continue to be monitored regularly. In future reports, once adequate data has been collected, outcome analyses will be performed. These will specifically include metrics such as changes in transplant rate and 1-year post-transplant survival.