Final Report

OPTN Thoracic Transplantation Committee | Descriptive Data Request

Monitoring of the Lung Allocation Change, 2 Year Report
Removal of DSA as a Unit of Allocation

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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 monitored allocation directly following the changes. An out-of-the-gate monitoring report was completed for the OPTN 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 with a similar updated report 6 months, 9 months and 1 year after the change. This report will also focus on cohort levels changes including an analysis of waiting list and post-transplant outcomes with a larger 2 year cohort. This will be the first report to examine post transplant patient survival for lung transplant recipients. All of the metrics in the report 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.

The OPTN and the Scientific Registry of Transplant Recipients(SRTR) will respond to further requests by the Thoracic Committee.

Executive Summary

Monitoring began upon implementation of the emergency action lung policy change on November 24, 2017. The immediate primary goal of the policy was to address concerns over compliance with the OPTN final rule.
Based on the first 2 years 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 its magnitude varied across OPTN region.
- An increase was seen in the median distance between donor hospital and transplant program and a decrease in the number of local (within the same DSA) lung transplants. However, the majority of lungs are allocated within the first unit of allocation (250 NM radius from the donor hospital).
- There was no statistically signficant change in the waiting list mortality rate overall, but some high LAS groups saw a slight decrease in the waiting list mortality rate.
- There was a no statistically signficant change in the transplant rate overall. High LAS groups saw an increase in the transplant rate and some low LAS groups saw a decrease in the transplant rate.
- Nationally there was a minimal change in deceased donor utilization, but the impact varied by OPTN region.
- The national discard rate increased, but varied by OPTN region. When excluding perfused lungs and lungs from DCD donors, which have increased in utilization since the policy change, the discard rate remained stable.
- 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.
- Nationally there was an increase in the number of lung alone transplants, but this varied by OPTN region.
- There was not a statistically significant change in 6-month unadjusted patient survival.

The conclusions from the 2 year report predominantly align with those from the earlier analyses performed for the committee. This report incorporates data on the impact to the waiting list mortality rate, transplant rate, early post-transplant patient survival, and multiorgan transplants. 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

Two years 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 lung allocation score (LAS) at listing nationally and by OPTN region
  - Deaths per 100 patient years by LAS group and diagnosis group
- Transplants
  - National volume stratified by recipient characteristics: diagnosis group, ABO, de-identified program, 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
  - Transplants per 100 active patient years by LAS group and diagnosis group
  - 6-month patient survival
- Deceased Donor Utilization
  - Number of deceased donor lung donors by de-identified organ procurement organization (OPO)
  - Discard Rate
  - Utilization Rate
- Multiorgan
  - Number of multiorgan candidates on the waiting list
  - Deaths per 100 patient years for multiorgan candidates
  - Transplants per 100 patient years for multiorgan candidates

Statistical tests are performed on most of the metrics. It should be noted that statistical significance does not always equate to a clinically meaningful difference.

Methods

Data Sources:

OPTN data were used for this analysis. The OPTN data system includes data on all donor, wait-listed candidates, and transplant recipients in the US, submitted by the members of the Organ Procurement and Transplantation Network (OPTN).**This analysis is based on OPTN data as of Feb 21, 2020 and is subject to change based on future data submission or correction.** The removal of DSA from lung allocation was implemented on November 24, 2017. This report compares metrics for the 2 years before and after the implementation date. The dates for the pre and post era were define such that both eras contained exactly 729 days. All analyses described below compare metrics pre verses post policy change. For categorical variables, counts, frequencies, and p-values from Chi-square tests were reported. For continuous variables, medians and p-values from Kruskal-Wallis tests were reported. Diagnosis groups utilized in this monitoring report align with those outlined in OPTN lung allocation policy: A- obstructive lung disease, B- pulmonary vascular disease, C- cystic fibrosis and immunodeficiency disorder, and D- restrictive lung disease {OPTN Policies, https://optn.transplant.hrsa.gov/media/1200/optn_policies.pdf Accessed 1/28/2020}.

Waiting List

Cohort: Candidates (age $\geq$ 12) added to the waiting list, removed from the waiting list, or ever waiting for a lung alone transplant from November 26, 2015 through November 24, 2017 (pre) and November 25, 2017 through November 24, 2019 (post).

Analysis: Additions to the waiting list are summarized by diagnosis group, OPTN region, and LAS at listing. The waiting list mortality rate for the waiting list cohort was summarized by diagnosis group and LAS group. Candidates have a calculated and a match LAS. These differ when a candidate has an exception request. The match LAS is reflective of the exception value and the calculated LAS is based on the clinical data entered on the waiting list. For analyses by LAS, the match LAS or the LAS that was used for allocation was utilized. Waiting list mortality rates as expressed by deaths per 100 patient-years were calculated by dividing the number of all deaths by the number of years patients spent waiting. Dividing by the number of person-years serves to normalize the rates to account for often drastic differences in the number of candidates and durations of time waited (within each era) by different patient characteristics. The waiting list mortality rates were summarized by the diagnosis group and LAS group at the time of listing.

Transplant

Cohort: Recipients (age $\geq$ 12) that received a lung alone transplant from November 26, 2015 through November 24, 2017 (pre) and November 25, 2017 through November 24, 2019 (post). All lungs for which an allocation match is run from November 26, 2015 through November 24, 2017 (pre) and November 25, 2017 through November 24, 2019 (post).

Analysis: Lung transplant recipients are summarized by diagnosis group, procedure type, donor type, recipient ABO, OPTN region, state of the transplant program, and LAS at transplant. For analyses by LAS, the match LAS or the LAS that was used for allocation was utilized. The lung transplant recipient cohort was also summarized by the distance between the donor hospital and transplant program and geographic classification (local- within the same DSA, region- within the same OPTN region, national, or foreign), and total ischemic time. The change in lung transplant volume was plotted using a scatter plot. Transplant rates as expressed by transplants per 100 active patient-years were calculated by dividing the number of all deceased donor lung transplants by the number of active years patients spent waiting. Dividing by the number of person-years serves to normalize the rates to account for often drastic differences in the number of candidates and durations of time waited (within each era) by different patient characteristics. For each time interval, only active waiting time within the interval analyzed was used for the patient-years calculation. Since some candidates may spend several months or years on the waiting list, a candidate may contribute waiting time to both eras, but a transplant is attributed only to the era in which it occurred. For transplant rates by LAS group, if the LAS changed for a registration during an era, the person-years was divided appropriately among the LAS groups in which the registration spent time. The transplant rates were summarized by the diagnosis group and LAS group at the time of listing.

Using the lung match data the sequence number of the final acceptor and the time from first electronic offer to cross clamp were summarized.

Utilization

Cohort: All lung donors, donors from which at least 1 lung was recovered and transplanted, from November 26, 2015 through November 24, 2017 (pre) and November 25, 2017 through November 24, 2019 (post).

Analysis: The discard rate defined as the number of lungs discarded out of the total number of lungs recovered for the purpose of transplant is summarized by OPTN region. Similarly the discard rate was summarized for a subset of lungs that were not from a DCD donor or perfused. Simiarly, the utilization rate, the number of lung donor out of all donors where a donor is defined as anyone having at least one organ recovered for the purpose of transplant, is summarized by OPTN region and donor type.

Outcomes

Cohort: Recipients (age $\geq$ 12) that received a lung alone transplant from November 26, 2015 through November 24, 2017 (pre) and November 25, 2017 through January 1, 2019 (post).
Analysis: A six-month unadjusted Kaplan Meier patient survival analysis was performed. The cohort was limited to transplants before January 1, 2019 in order to allow sufficient time for complete follow up on all recipients. Patient survival was examined overall and by diagnosis group.

Multiorgan

Cohort: Candidates (age $\geq$ 12) added to the waiting list, removed from the waiting list, or ever waiting for a lung transplant and listed for at least one additional organ at the time of the analysis from November 26, 2015 through November 24, 2017 (pre) and November 25, 2017 through November 24, 2019 (post).

Analysis: The volume of multiorgan registrations is summarized by multiorgan combination. The waiting list mortality rate and transplant rate were calculated by multiorgan group using the same methods descibed above.

Results

Waiting List

Candidates added to the waiting list during the two eras (pre: November 26, 2015 - November 24, 2017 and post: November 25, 2017 - November 24, 2019) 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

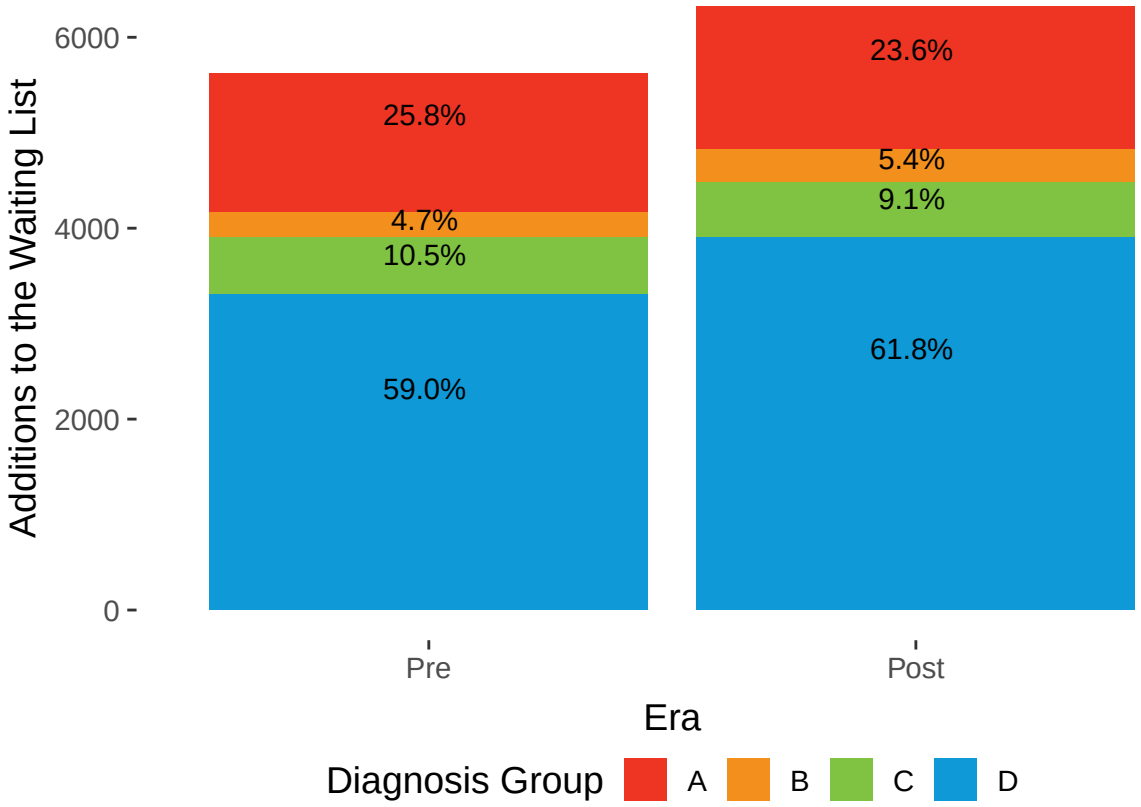


Table 1. Candidates Added to the Waiting List by Diagnosis Group

	Diagnosis Group				
Era	A	B	C	D	Total
Pre	1451	267	588	3318	5624
Post	1495	344	576	3909	6324

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 a statistically significant difference between the diagnosis groups of the two cohorts ($\chi^2_3 = 17.86$, p-value <0.001). In the post era there are more candidates being added to the waiting list in diagnosis groups B and D and fewer in groups A and C. 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

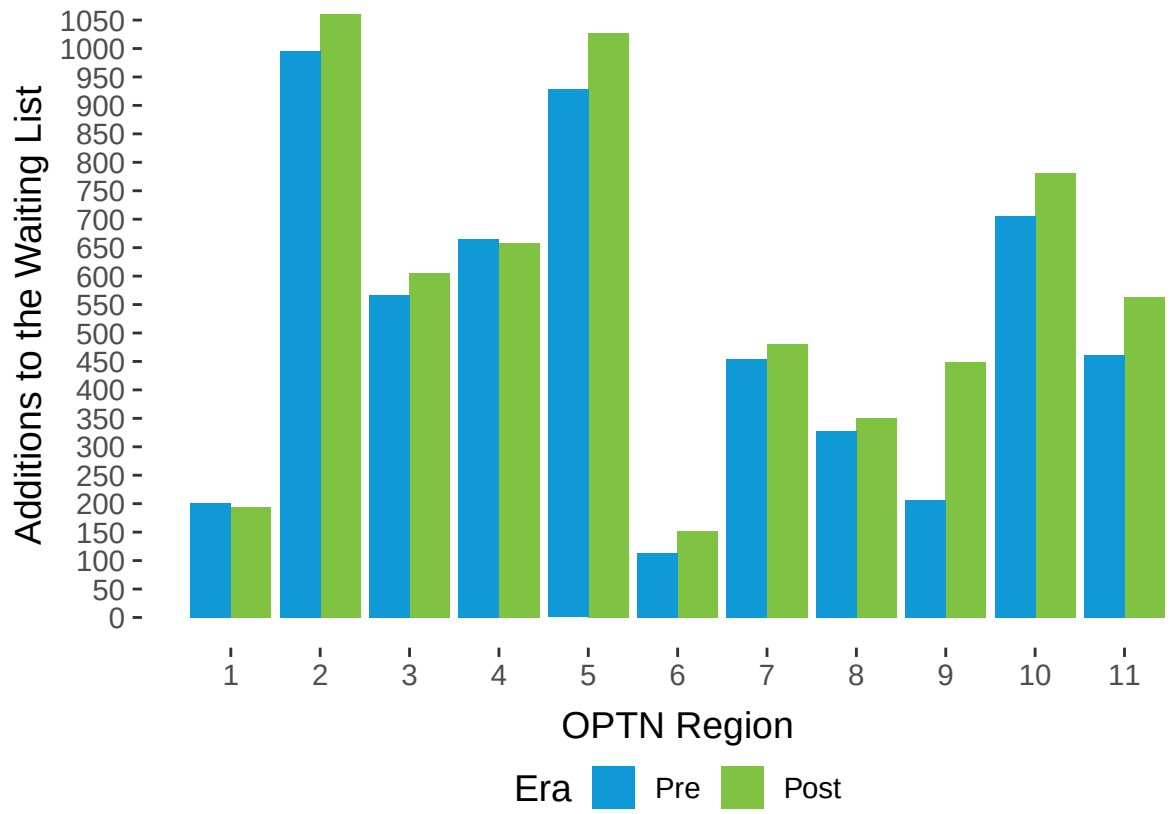


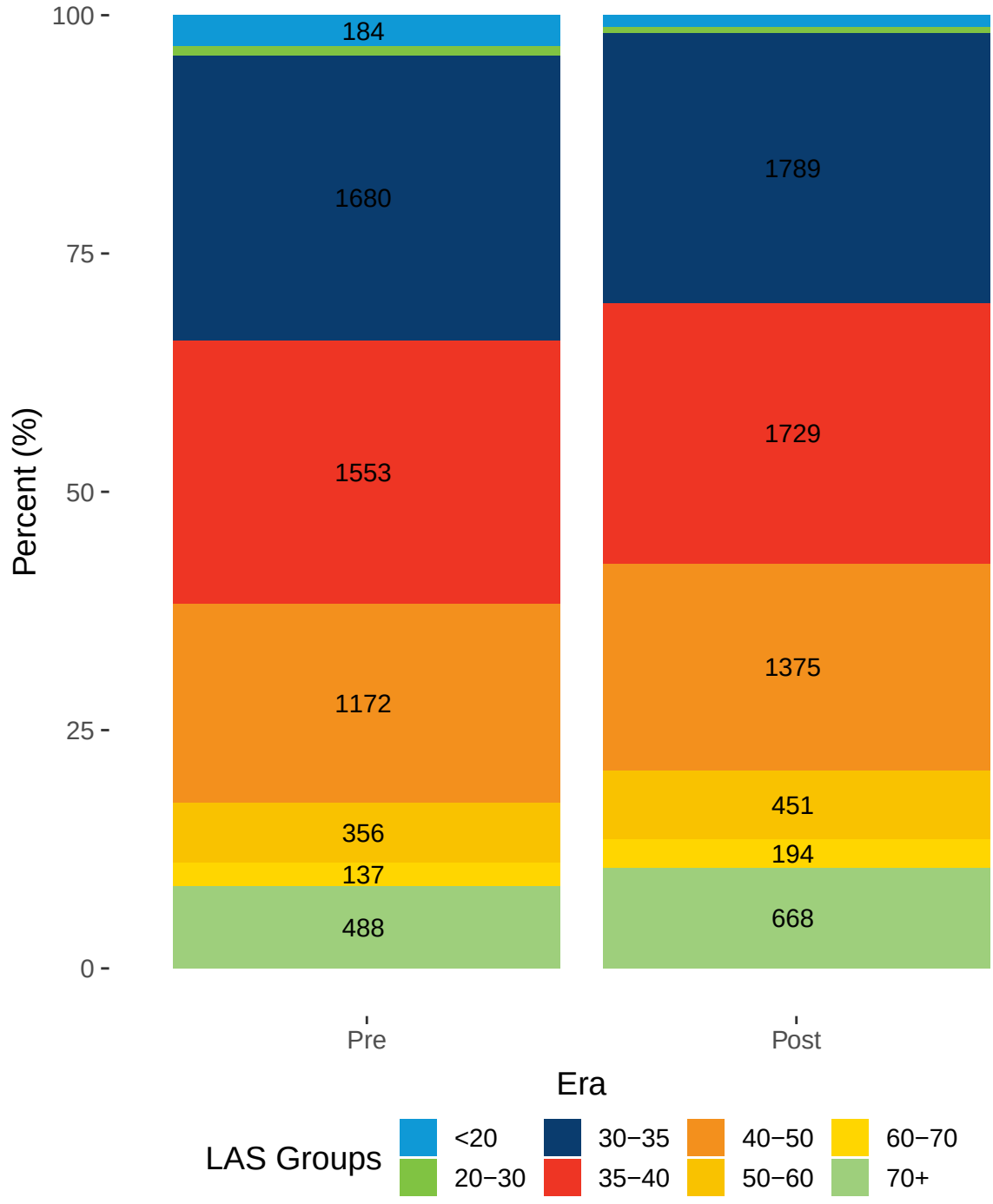
Table 2. Candidates Added to the Waiting List by OPTN Region

	OPTN Region											
Era	1	2	3	4	5	6	7	8	9	10	11	National
Pre	202	995	566	665	928	113	454	327	206	706	462	5624
Post	195	1061	606	658	1028	152	480	351	449	781	563	6324

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 1 and 4 which saw a slight decrease in the number of additions to the waiting list. OPTN region 9 saw the largest increase in the number of candidates being added to the waiting list. This is at least in part due to a new program opening in this region.

Candidates (age $\geq$ 12) are allocated lungs according to their lung allocation score (LAS) as specified by lung allocation policy. In Figure 3, candidates 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 a higher LAS score represents a clinically sicker candidate.

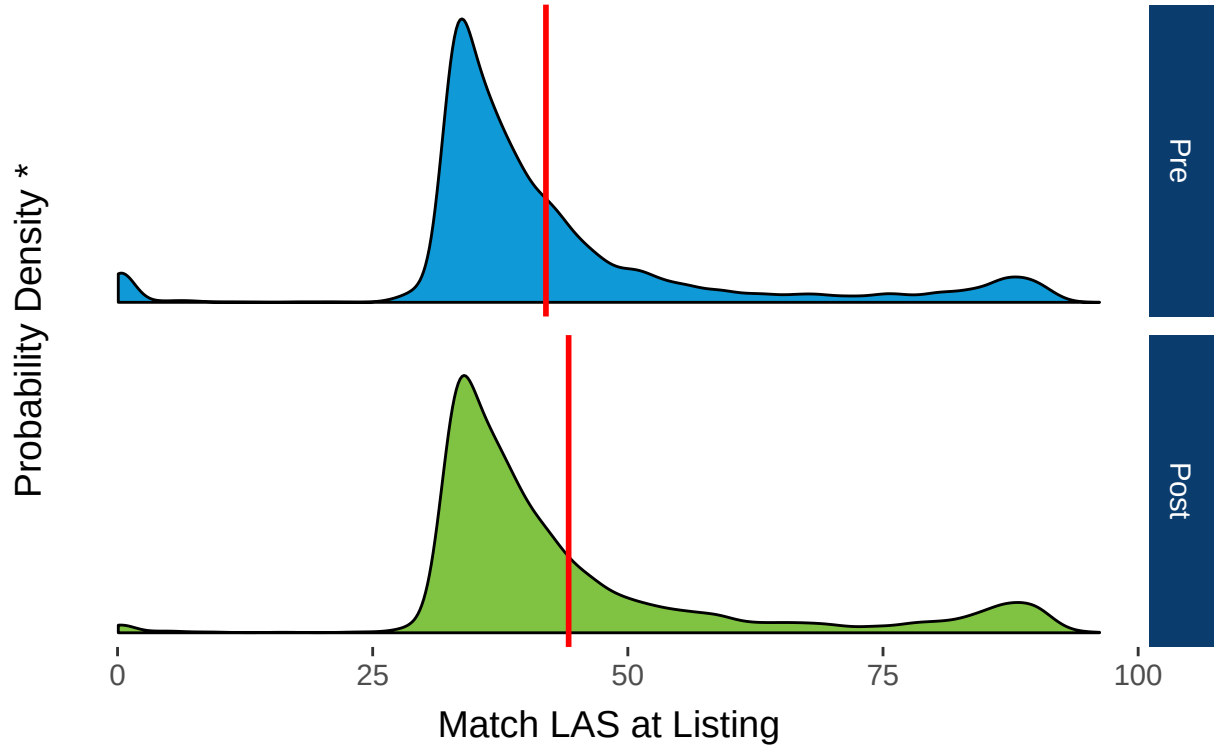
Figure 3. LAS at Listing for Candidates Added to the Waiting List by LAS Group



In the pre era there were 54 in LAS group 20–30. In the post era there were 76 in LAS group <20 and 42 in LAS group 20–30.

Similarly, Figure 4 depicts the distribution of the LAS at listing for the two eras.

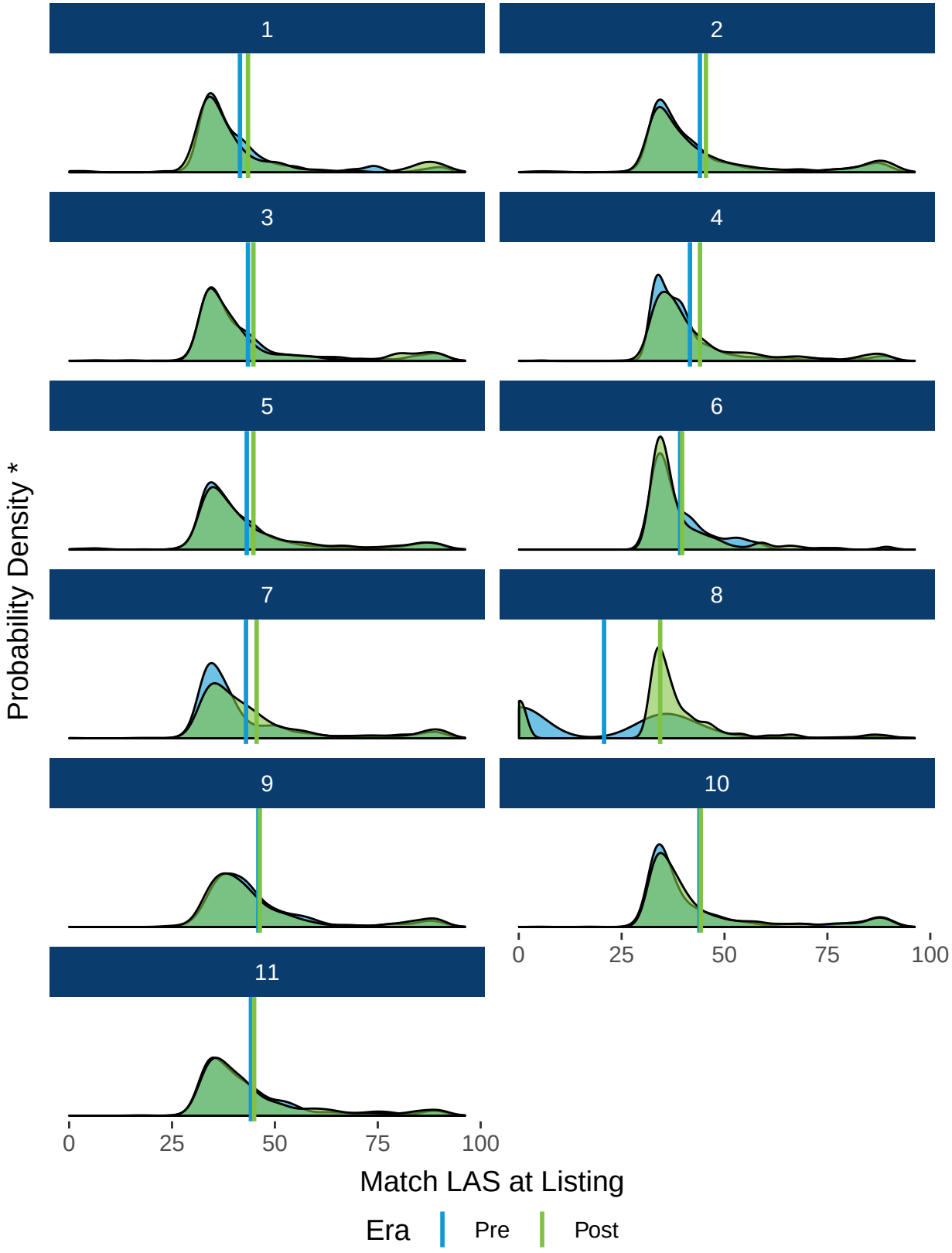
Figure 4. Distribution of LAS at Listing for Candidates Added to the Waiting List



* 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 41.97 and 44.20 for the post era. There is a statistically significant difference between the mean LAS for the two eras (p-value <0.001), implying that the average severity of illness for candidates added has increased from the pre era to the post era. To further examine the LAS for additions to the waiting list, Figure 5 summarizes the LAS at listing by OPTN region.

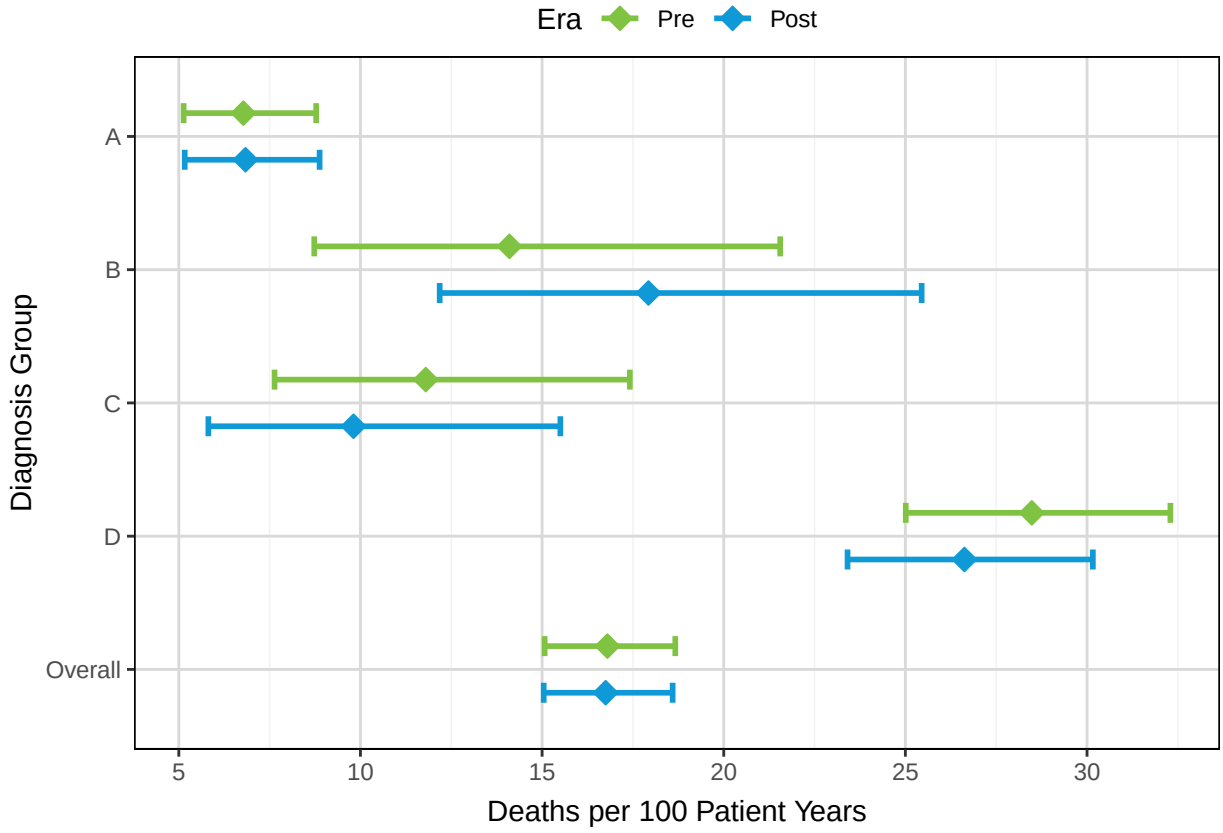
Figure 5. Summary of LAS at Listing by OPTN Region for Candidates Added to the Waiting List



The variation in LAS at listing by OPTN region can be seen in Figure 5. 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.

Early data on the waiting list mortality rate, measured as deaths per 100 patient years while waiting, for lung candidates is summarized below by diagnosis group and LAS group.

Figure 6. Deaths per 100 Patient Years while Waiting by Diagnosis Group



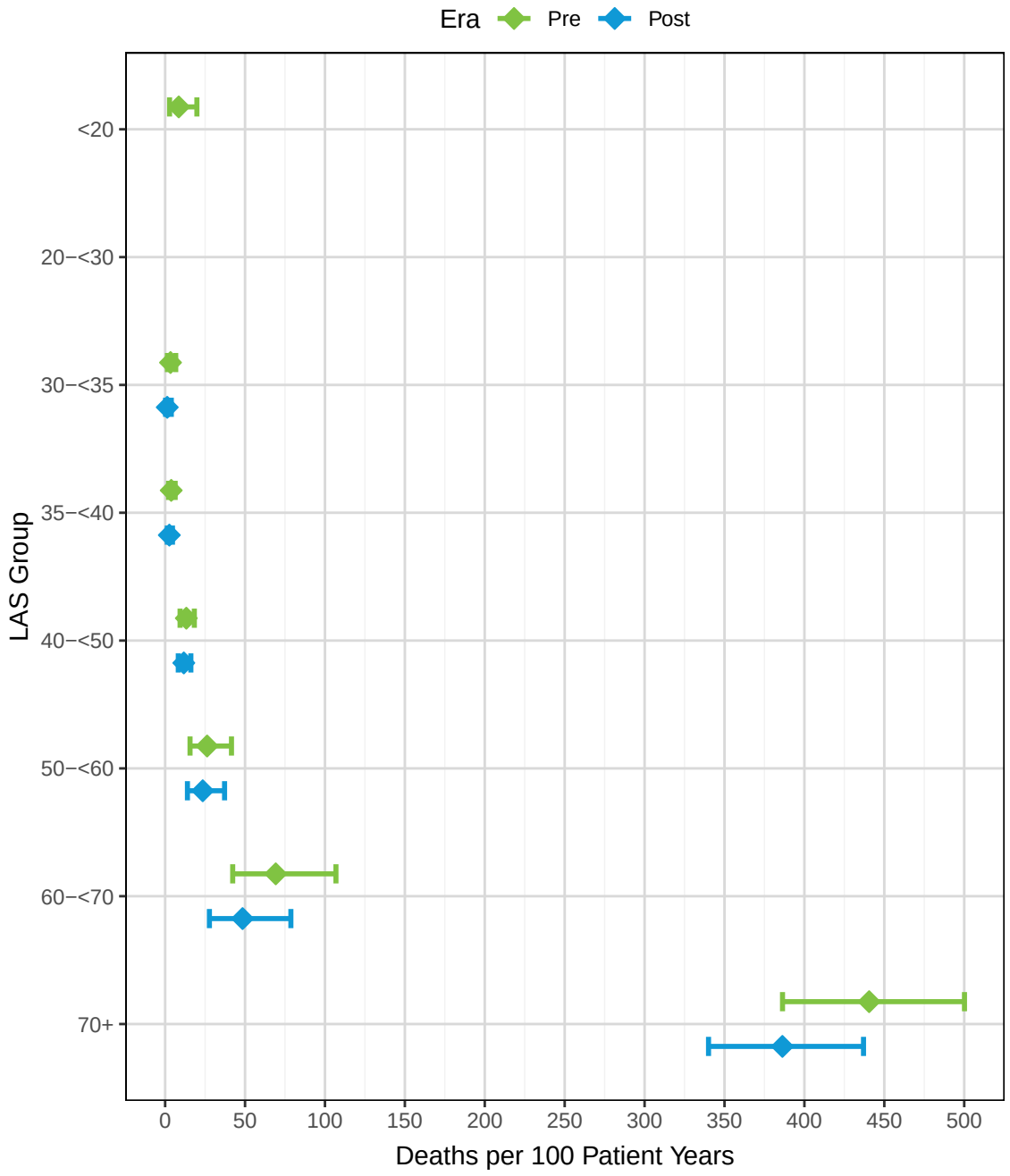
From the figure above it can be seen that there is no change in the overall waiting list mortality rate per 100 patient years. Below is the corresponding table with the number of deaths per 100 patient years and corresponding 95% confidence interval by diagnosis group.

Table 3. Deaths per 100 Patient Years while Waiting by Diagnosis Group

Group	Era	Patients Ever Waiting	Deaths per 100 Patient years	Lower 95% CI	Upper 95% CI
A	Pre	1668	7	5.13	8.78
A	Post	1616	7	5.16	8.88
B	Pre	333	14	8.73	21.55
B	Post	403	18	12.18	25.45
C	Pre	574	12	7.64	17.42
C	Post	550	10	5.81	15.50
D	Pre	3004	28	25.01	32.29
D	Post	3373	27	23.41	30.16
Overall	Pre	5560	17	15.07	18.67
Overall	Post	5927	17	15.04	18.59

While diagnosis group B exhibits the largest change in the deaths per 100 patient years, it is also the smallest cohort. Since the confidence intervals for the waiting list mortality rate for each diagnosis group overlap, the findings are not statistically significant. While the findings are not statistical significance, the waiting list mortality rate will continue to be closely monitored in future reports. In the figure below, deaths per 100 patients years while waiting is shown below by LAS group.

Figure 7. Deaths per 100 Patient Years while Waiting by LAS Group



From the figure above it can be seen that there is a slight decrease in the waiting list mortality rate for candidates in the 60-70 and 70+ LAS groups. Below is the corresponding table with the deaths per 100 patient years and corresponding 95% confidence interval by LAS group. Since there were no deaths in the <20 post group and 20-30 group pre and post the death rate is not calculated.

Table 4. Deaths per 100 Patient Years while Waiting by LAS Group

LAS Group	Era	Patients Ever Waiting	Deaths per 100 Patient years	Lower 95% CI	Upper 95% CI
<20	Pre	273	9	2.76	19.87
<20	Post	207	-	-	-
20-<30	Pre	83	-	-	-
20-<30	Post	72	-	-	-
30-<35	Pre	722	3	1.45	6.63
30-<35	Post	772	1	0.27	3.85
35-<40	Pre	1587	4	2.13	6.27
35-<40	Post	1757	3	1.36	4.58
40-<50	Pre	1583	13	9.33	18.27
40-<50	Post	1882	12	8.22	16.09
50-<60	Pre	731	26	15.57	41.51
50-<60	Post	879	24	13.94	37.18
60-<70	Pre	433	69	42.27	106.88
60-<70	Post	551	48	27.69	78.68
70+	Pre	931	441	386.31	500.17
70+	Post	1199	386	340.02	436.98

Since the confidence interval for the waiting list mortality rate overlap between pre and post within LAS group, the findings are not statistically significant.

Transplant

There were a total of 4709 deceased donor lung transplants for recipients (age $\geq$ 12) in the pre (November 26, 2015 - November 24, 2017) era and a total of 5147 deceased donor lung transplants for recipients (age $\geq$ 12) in the post (November 25, 2017 - November 24, 2019) era. There were 28 pediatric (age <12) lung transplants in the pre era and 30 in the post era that are not included in the analysis cohort. Figure 8 and Table 5 summarize deceased donor lung transplants by recipient diagnosis group and era.

Figure 8. Deceased Donor Lung Transplants by Diagnosis Group

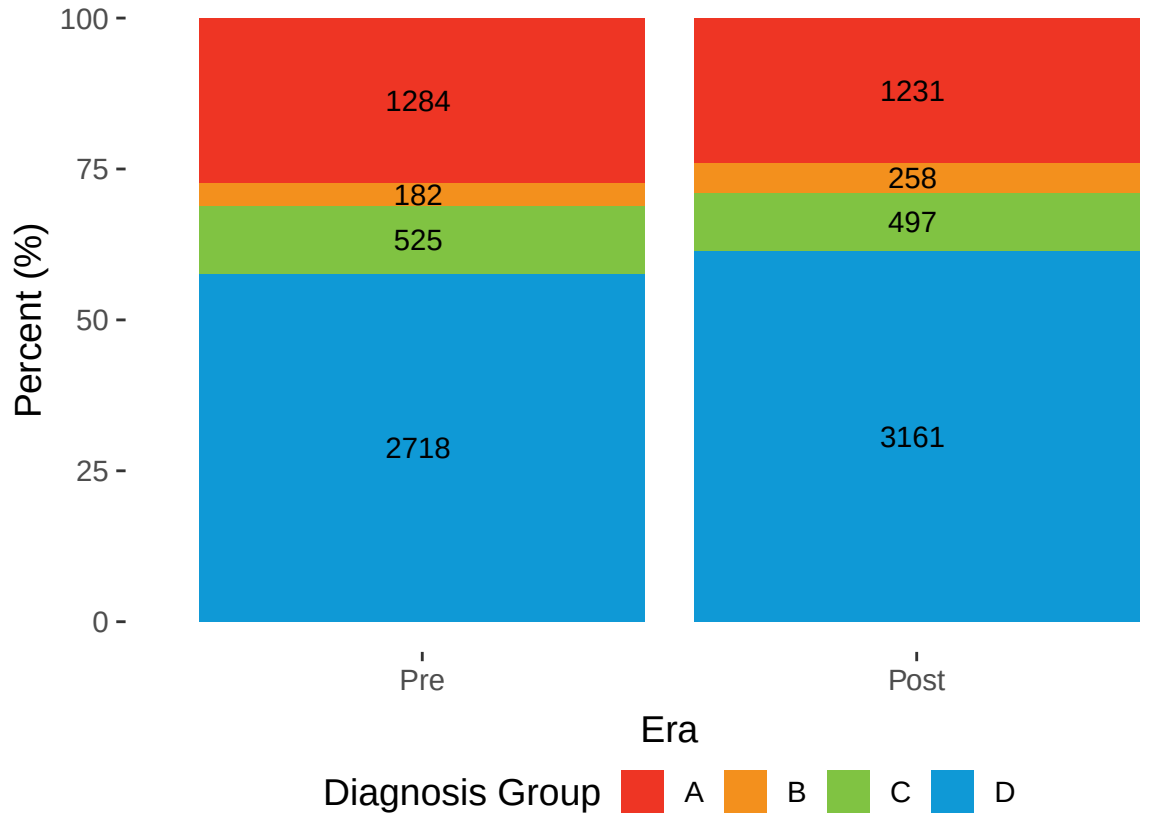


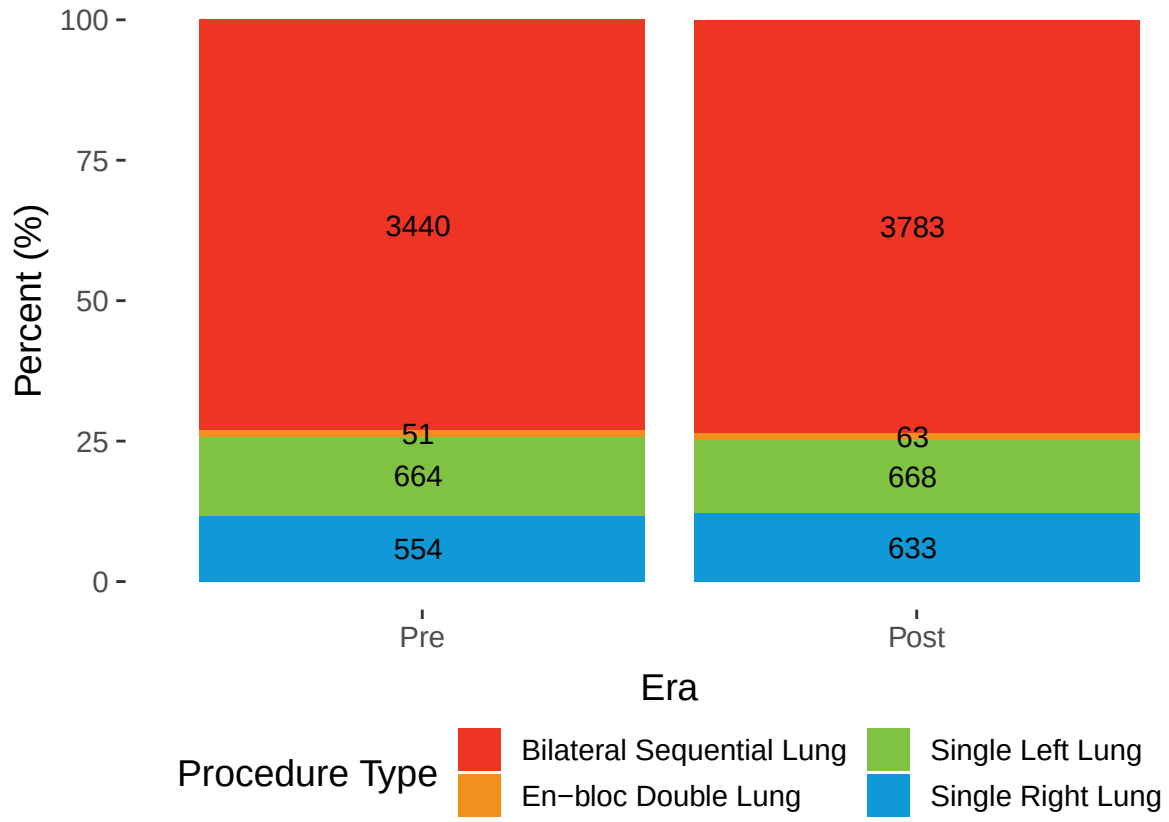
Table 5. Deceased Donor Lung Transplants by Diagnosis Group

	Diagnosis Group				
Era	A	B	C	D	Total
Pre	1284	182	525	2718	4709
Post	1231	258	497	3161	5147

There is a statistically significant difference in the diagnosis group of recipients of deceased donor lung transplants between the two eras ($\chi^2_3 = 17.86$, p-value <0.001). 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.

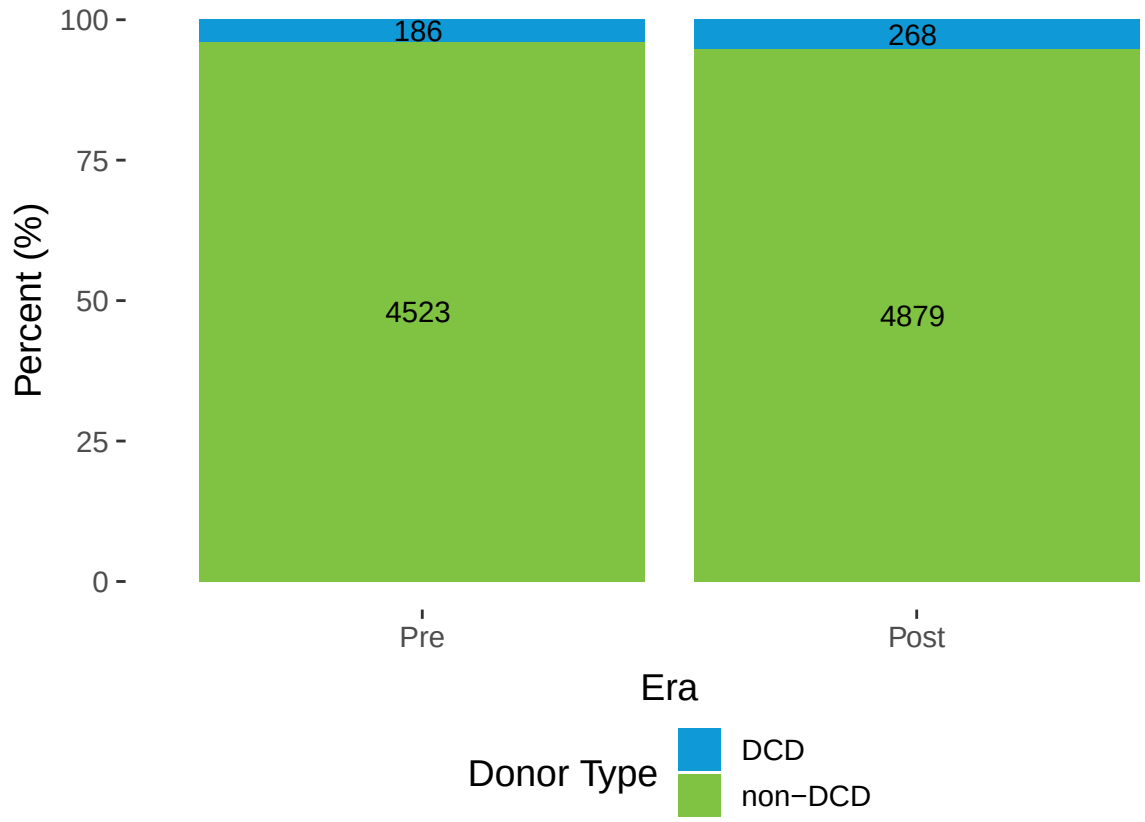
To thoroughly examine any impact the policy had on lung transplants, lungs transplants were examine by procedure type (single left lung, single right lung, en-bloc double lung, and bilateral sequential lung).

Figure 9. Deceased Donor Lung Transplants by Procedure Type



From Figure 9, there is a not statistically significant difference in the procedure type of recipients of deceased donor lung transplants between the two eras ($\chi^2_3 = 3.36$, p-value $= 0.339$). Figure 10 shows the number of deceased donor lung transplants by donor type (DCD vs. non-DCD).

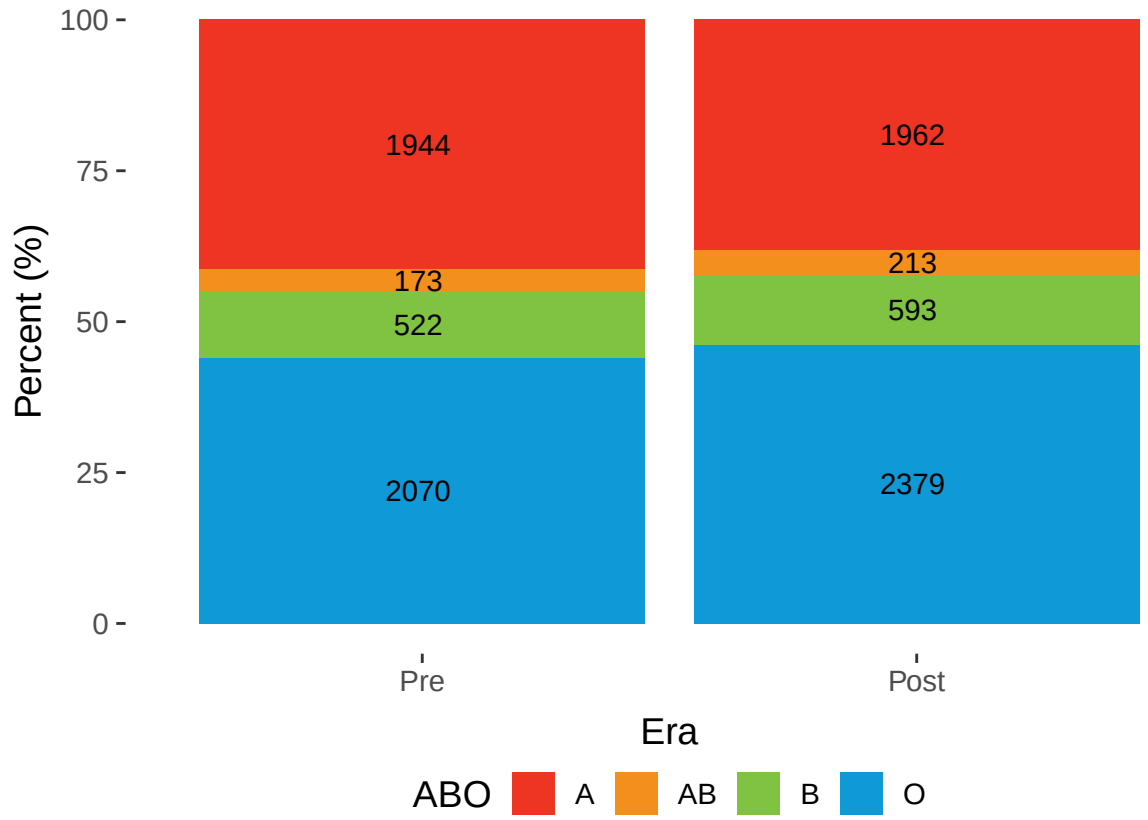
Figure 10. Deceased Donor Lung Transplants by Donor Type



In the pre era there were only 186 DCD donors compared to 268 in the post era. There is a statistically significant difference in the proportion of DCD donors between the two eras ($\chi^2_1 = 8.84$, p-value $= 0.003$). This aligns with the general trend of increasing use of DCD lung donors over the past few 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 11. Transplant Recipients by ABO



There is a statistically significant difference in the blood type of transplant recipients between the two eras ($\chi^2_1 = 10.77$, p-value $= 0.013$). In the post era a larger percentage of transplants are recipients with blood type O.

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 12 and Table 6 summarize the number of lung transplants by OPTN region.

Figure 12. Deceased Donor Lung Transplants by OPTN Region

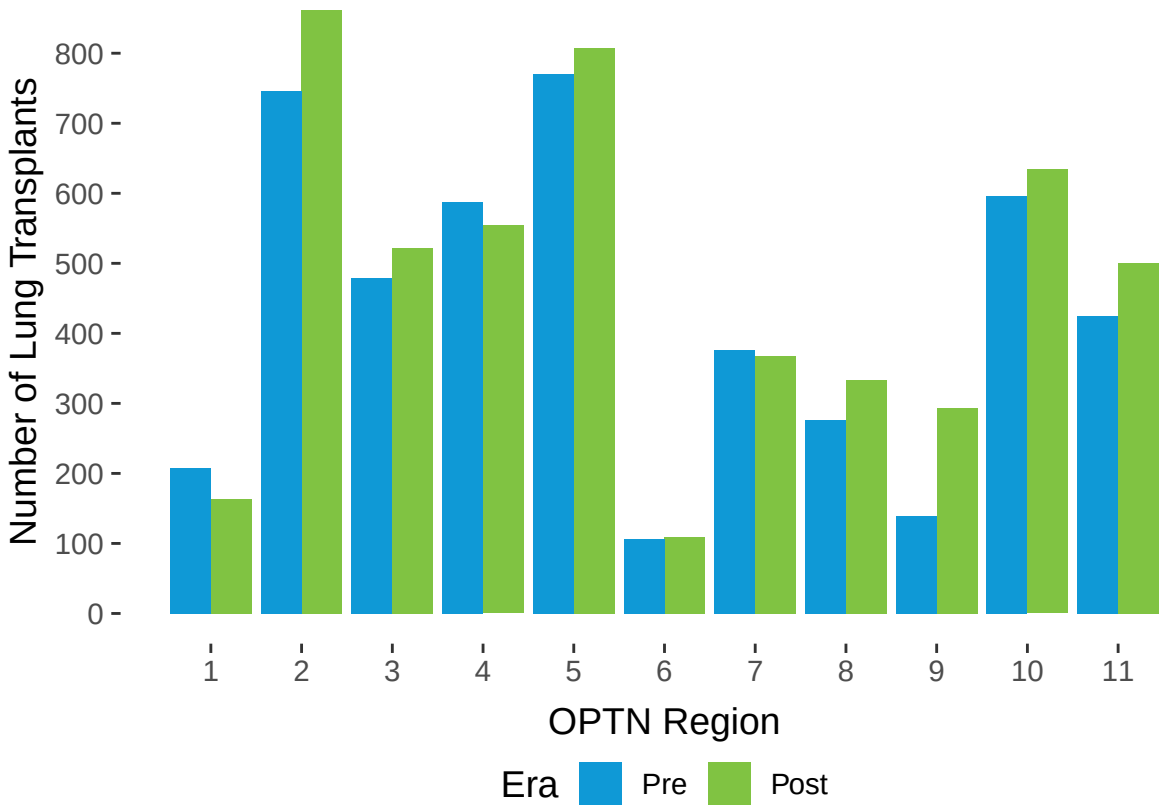
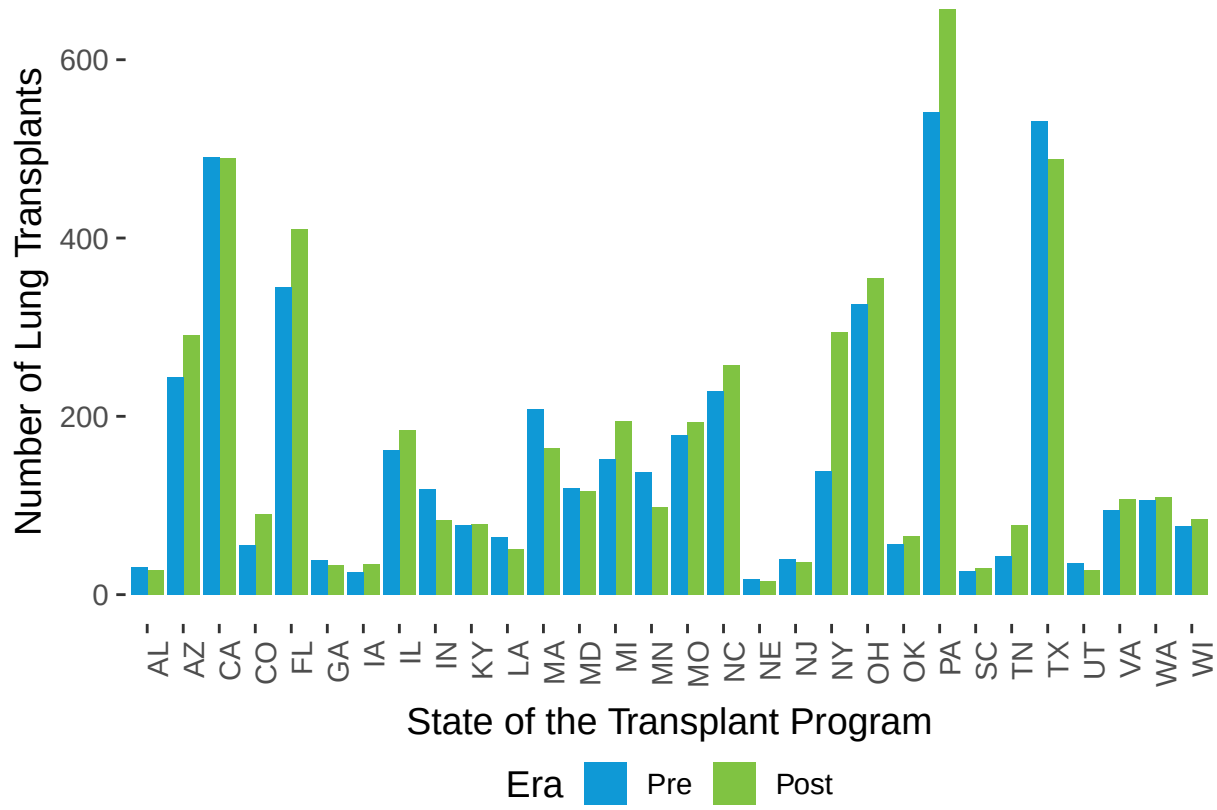


Table 6. Transplant Recipients by OPTN Region

	Era		
Region	Pre	Post	Difference (Post-Pre)
1	208	164	-44
2	746	862	116
3	479	522	43
4	588	554	-34
5	770	808	38
6	106	109	3
7	376	367	-9
8	276	333	57
9	139	294	155
10	596	634	38
11	425	500	75

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 largest impact was seen in OPTN regions 2 and 9. Similarly, summarized in Figure 13 below are the number of transplants by state of the transplant program and era.

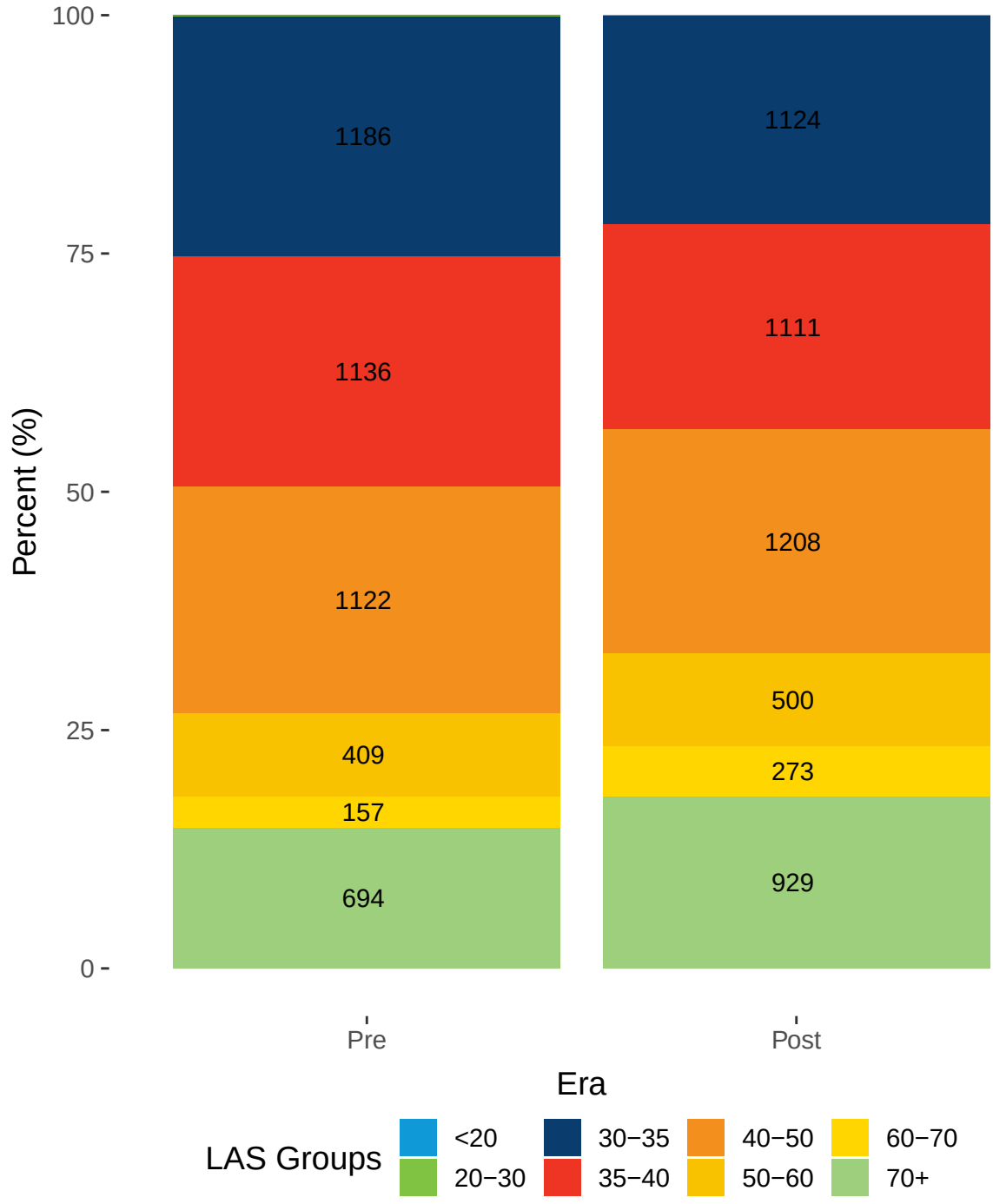
Figure 13. Deceased Donor Lung Transplants by State of Transplant Program



Overall, 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 14, 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 a higher LAS score represents a clinically sicker recipient.

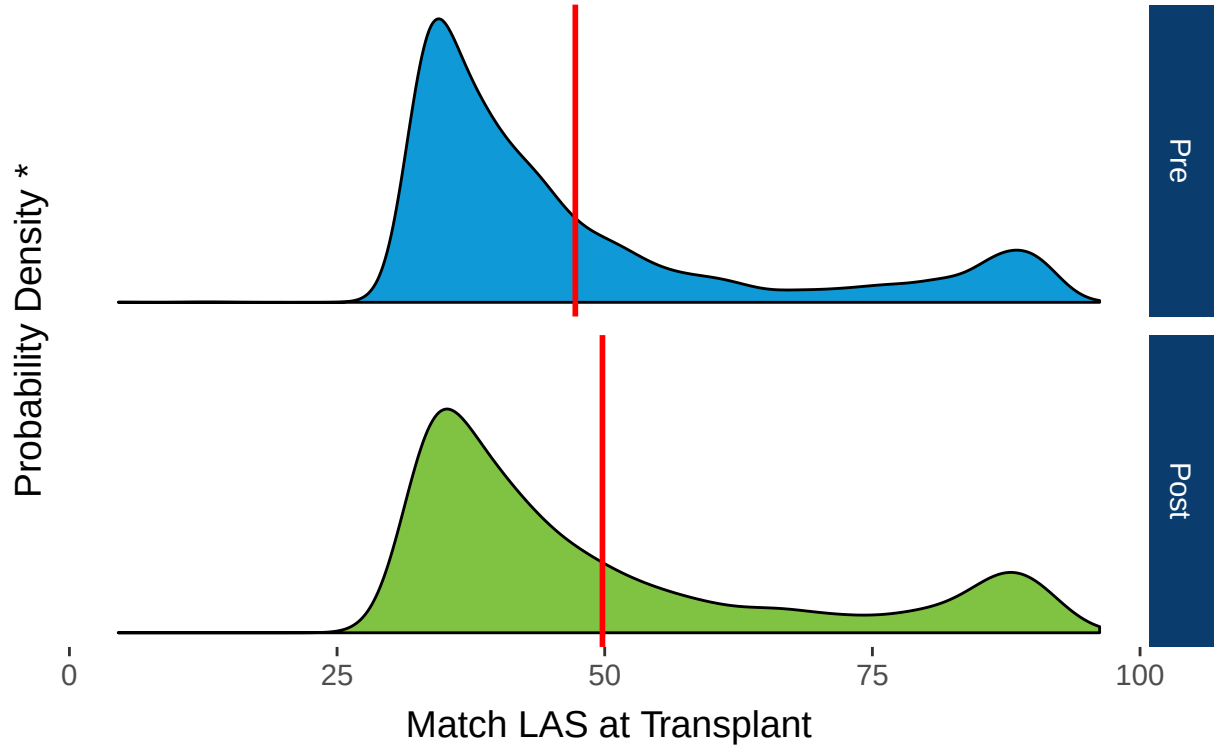
Figure 14. Deceased Donor Lung Transplants by LAS Group



In the pre era there were 3 transplants in LAS group <20 and 2 transplant in LAS group 20−30. In the post era there were 0 transplants in LAS group <20 and 2 transplants in LAS group 20−30.

There was an increase in the number of lung recipients with a LAS in the three highest categories (50-60, 60-70, and 70+). Similarly, the distribution of match LAS at transplant is depicted in Figure 15.

Figure 15. 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 47.25 and 49.79 for the post era. There is a statistically significant increase between the mean LAS in the pre era compared to the post era (p-value <0.001). 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 623 recipients with a LAS of at least 75 in the pre era and 830 in the post era. Before the November policy change, it was known that the average LAS at transplant varied by OPTN region. Figures 16 and 17 examine the impact on each OPTN region.

Figure 16. Deceased Donor Lung Transplants by LAS Group and OPTN Region

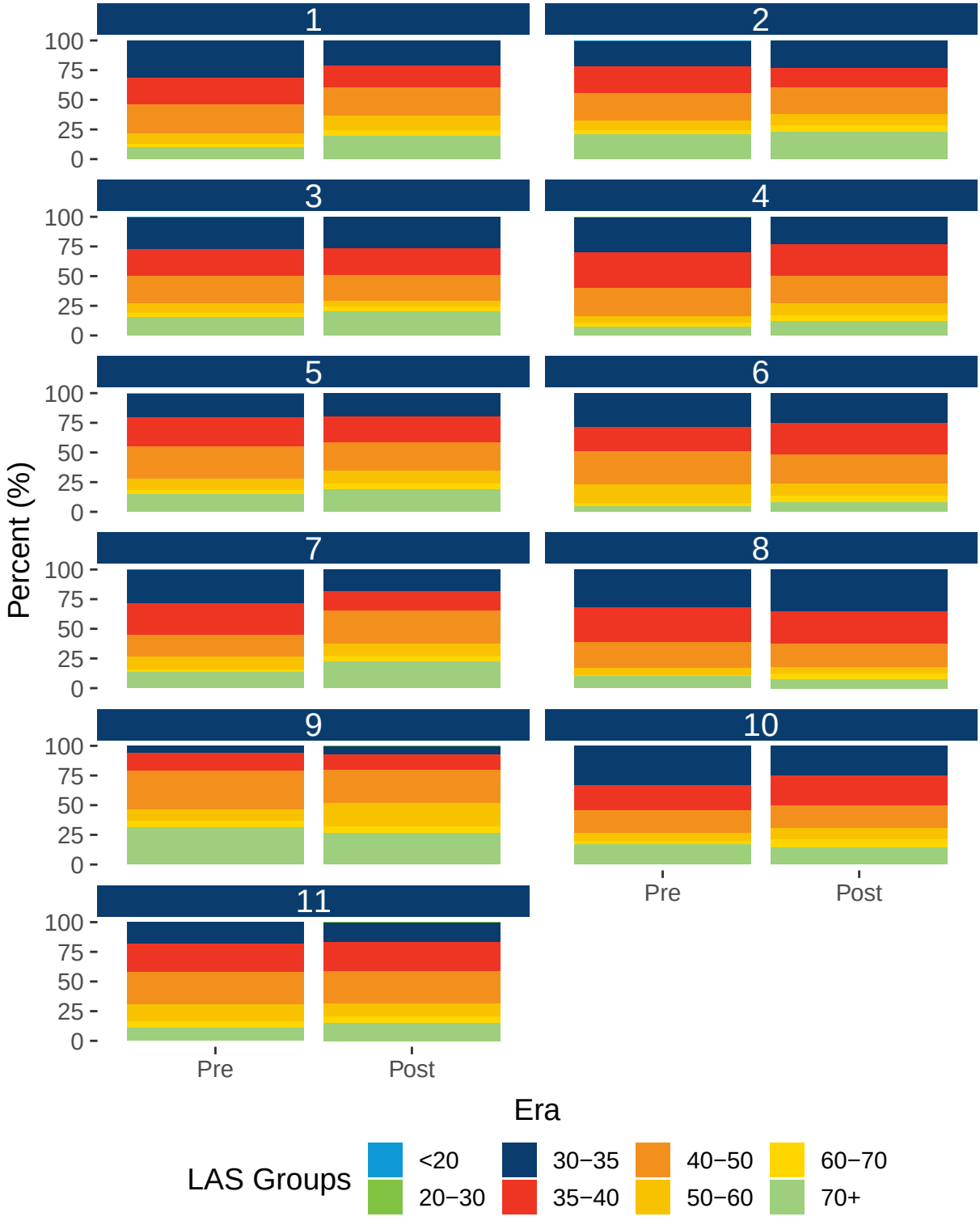
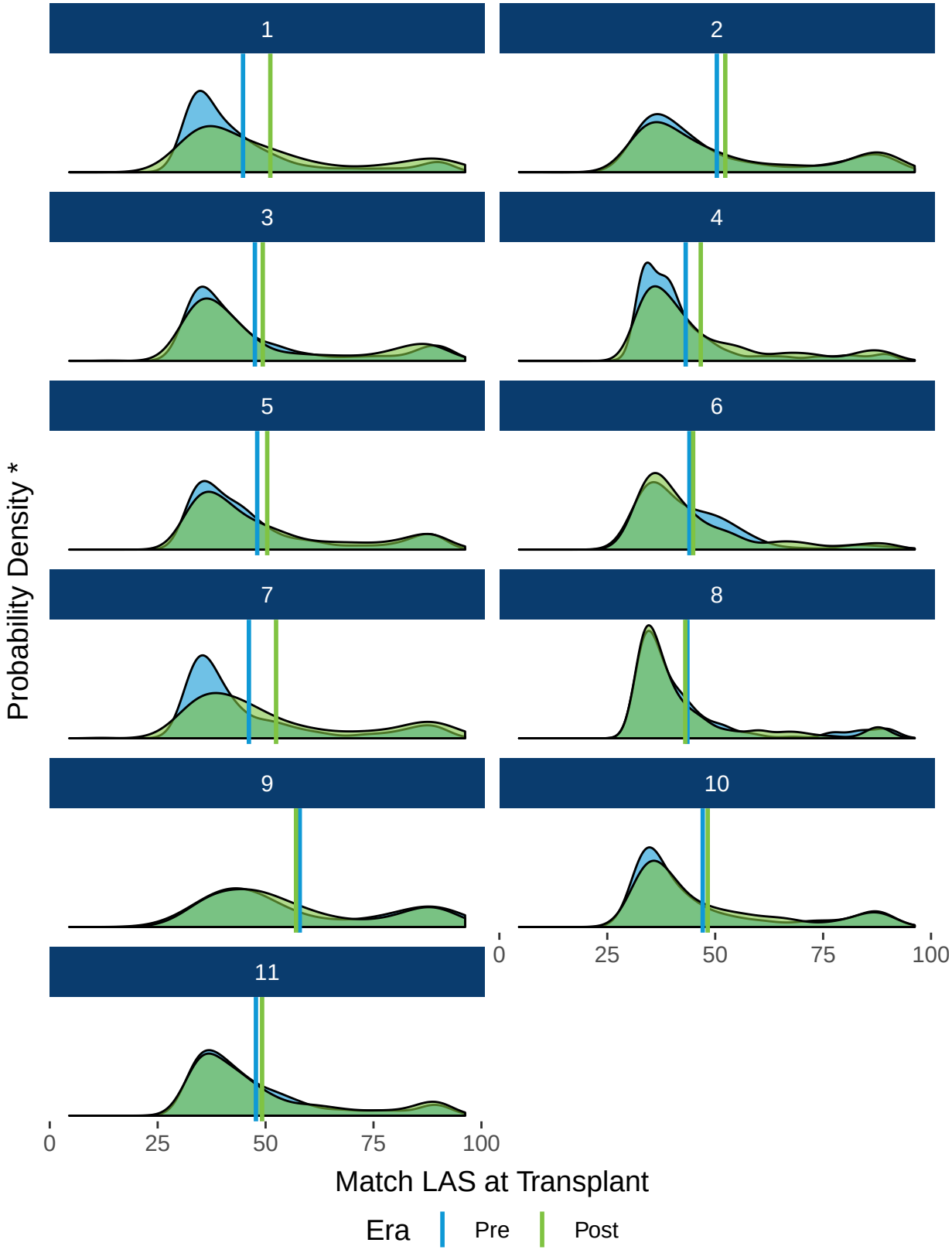


Figure 17. Transplant Recipients by LAS and OPTN Region



There are noticeable differences in the distribution of match LAS across all OPTN regions. However, the magnitude of the 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 program. A bar plot of the categorized distance lungs traveled by era is shown in Figure 18 and the distribution of the distance lungs traveled by era is shown in Figure 19.

Figure 18. Categorized Distance between Transplant Program and Donor Hospital

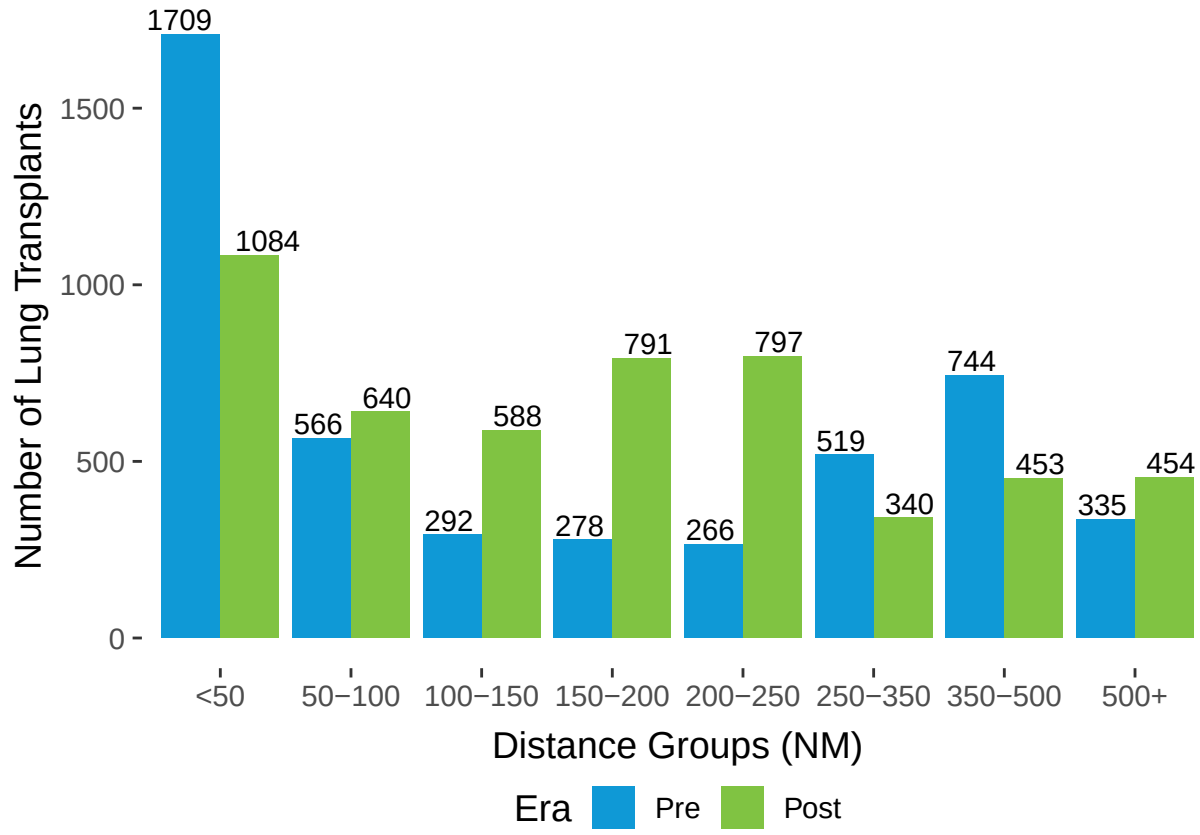
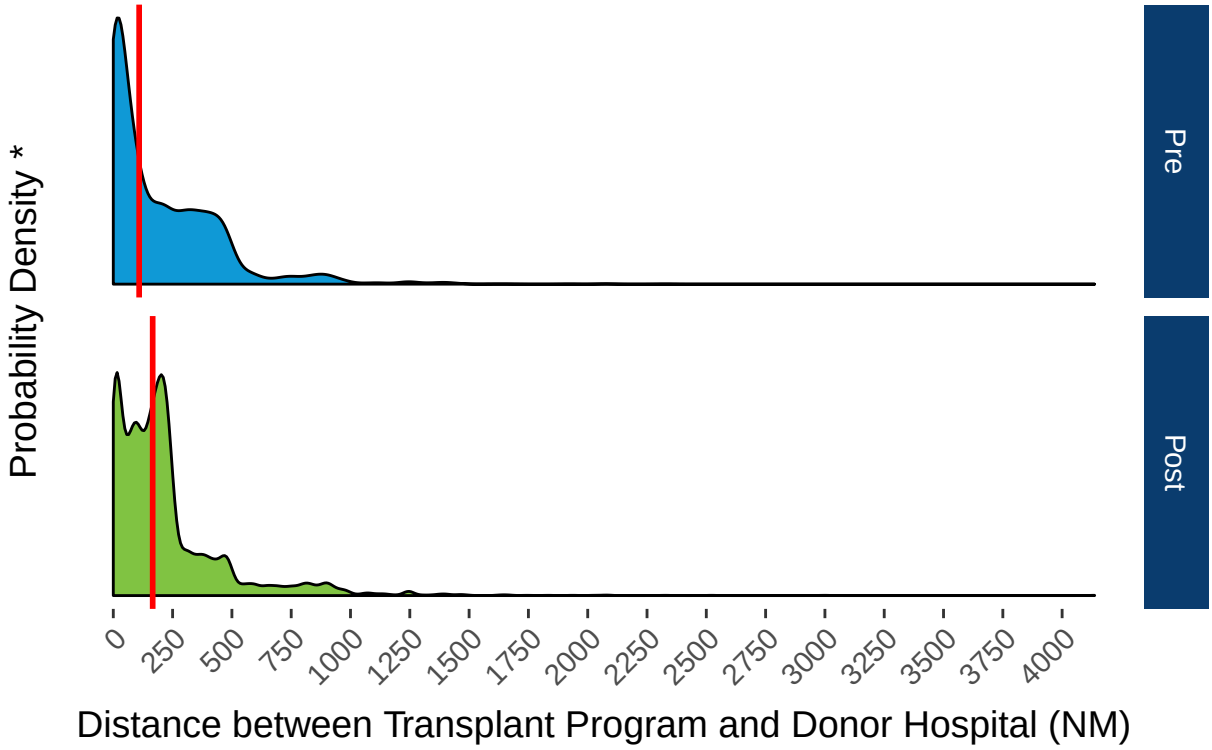


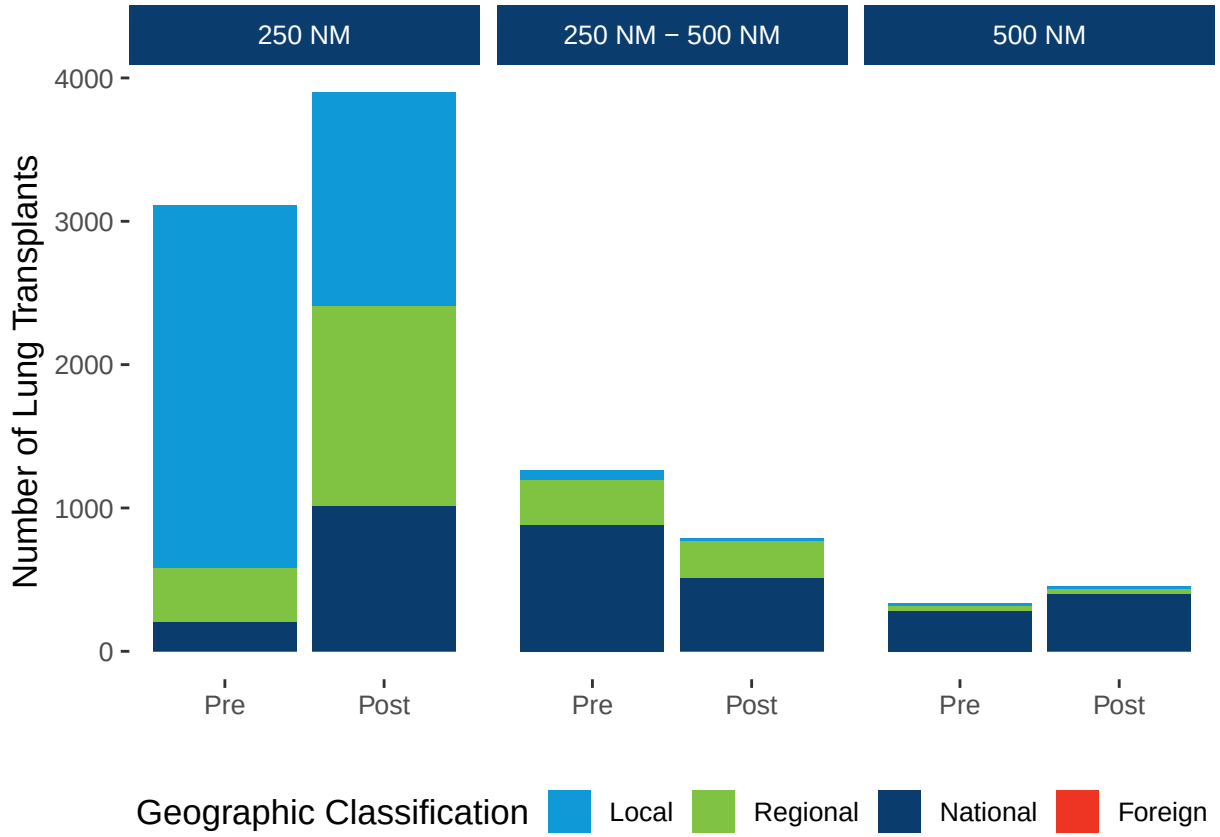
Figure 19. Distance between Transplant Program and Donor Hospital



* 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 109NM 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 program in the pre and post era (p-value <0.001). 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. The maximum distance a lung travelled in the pre era is 2327 NM and the maximum in the post era is 4137 NM. In Figure 20, the distance between donor hospital and transplant program 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 20. Transplants by Geographic Classification and Distance (NM)



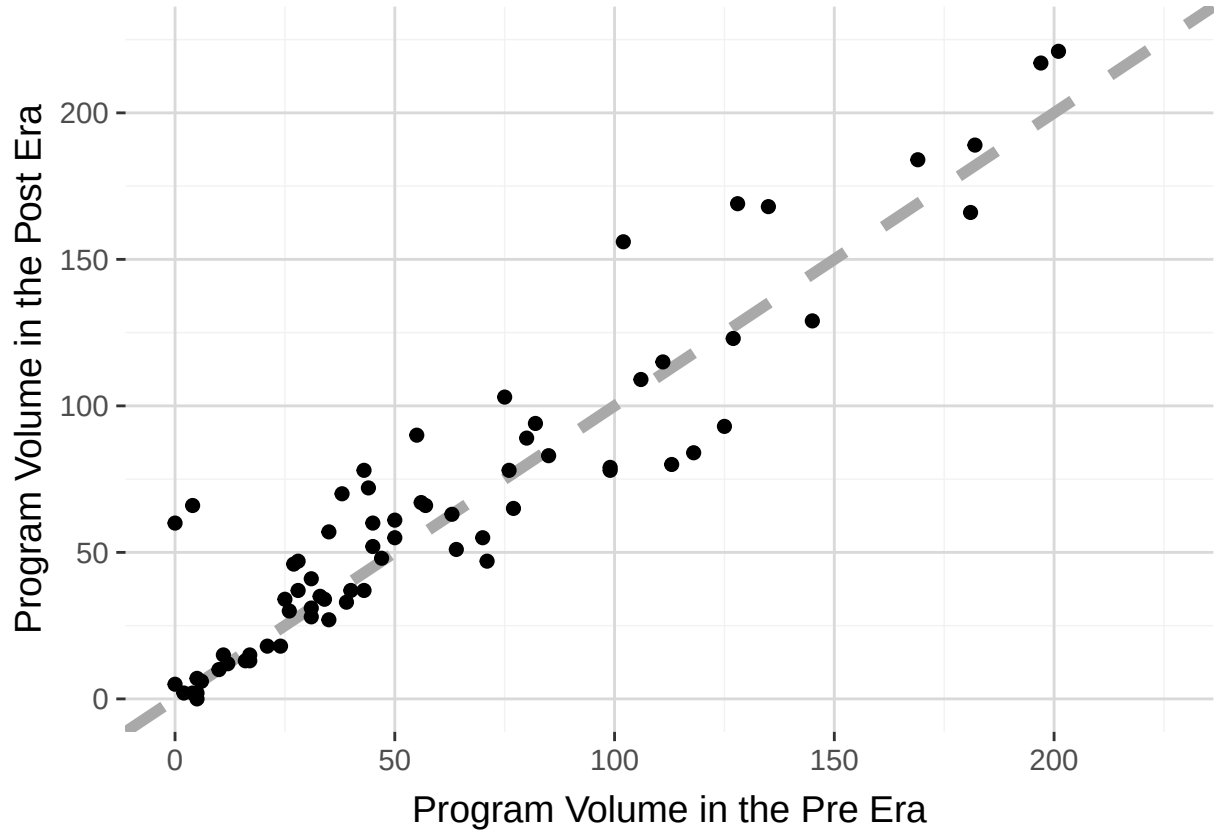
There is a 58.4% decrease in the number of local (within the same DSA) transplants. There is an increase in the number of regional transplants with the majority of that increase within the first unit of allocation (250 NM). There is also an overall increase in the number of nationally allocated lung transplants. Figure 20 shows that 75.8% 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	2532	1491	66	20	16	15
Regional	376	1391	314	265	37	35
National	201	1018	883	507	282	402
Foreign	2	0	0	1	0	2

There was concern within the community regarding the impact the policy change would have on smaller lung transplant programs. The transplant program level impact can be seen in Figure 21, a scatter plot of program volume in the two eras.

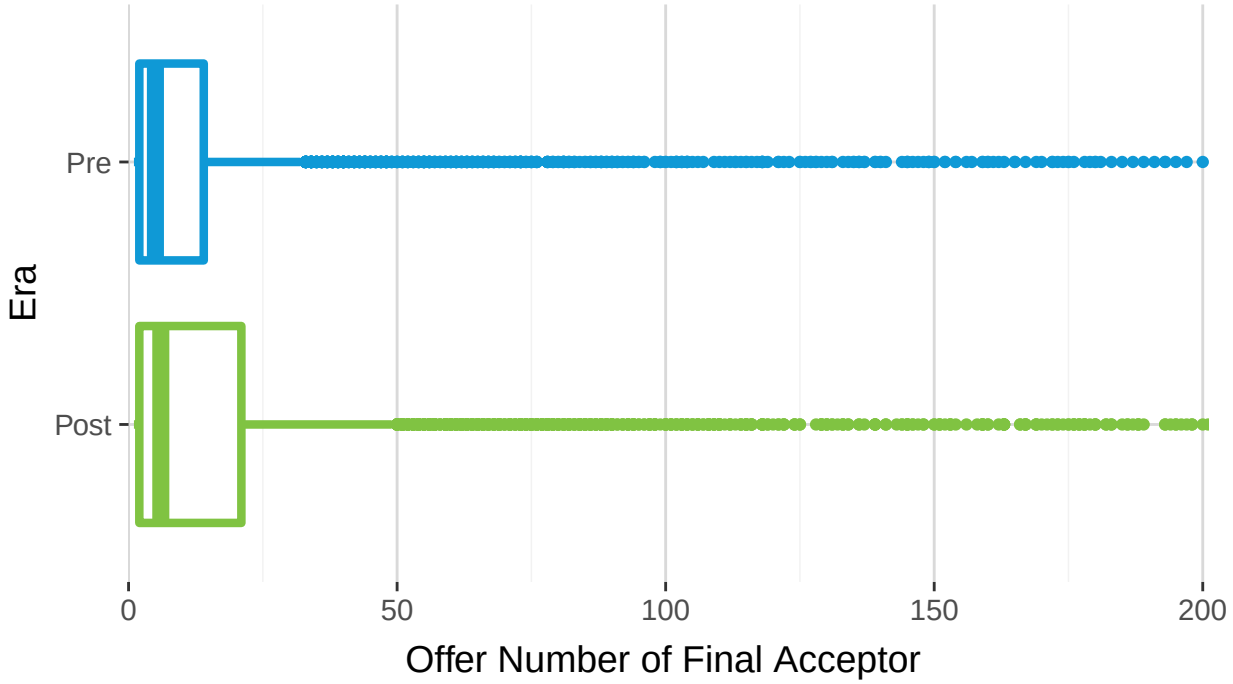
Figure 21. Scatter Plot of Program Volume



Dots that fall below the gray dashed line indicate transplant programs 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 programs who do fewer lung transplants are represented by dots in the bottom left corner. There were 72 transplant programs that performed at least one lung transplant in either era. Of those, 46 of the 72 tranplant programs performed equal or more lung transplants in the post era compared to the pre era.

To examine the impact on the match process, Figure 22 and Table 8 summarize the sequence number of the final acceptor for all lung donors.

Figure 22. Boxplot of the Sequence Number of the Final Acceptor for Lung Donors



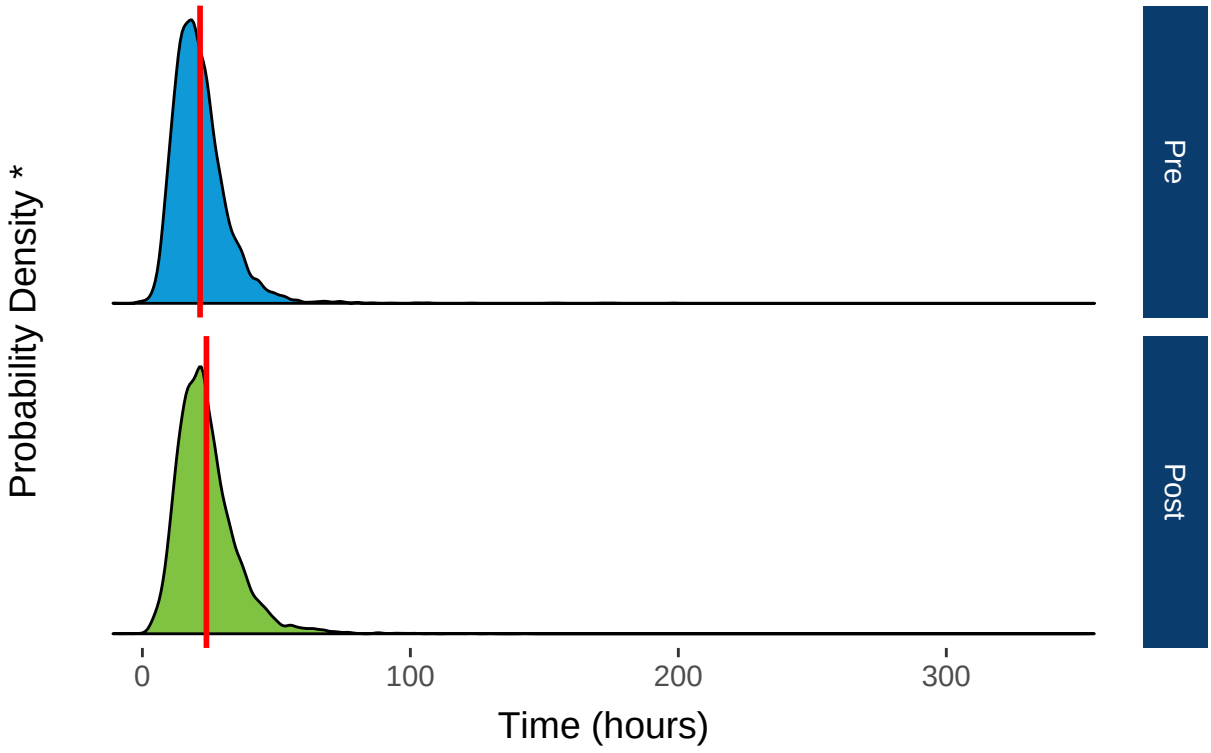
There were 46 final acceptances with an offer number over 200 in the pre era and 68 in the post era.

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

Era	Median	10th Percentile	90th Percentile
Pre	5	1	42
Post	6	1	63

There is some indication that the offer number of the final acceptor is higher in the post era than in the pre era. Further analysis will be needed to examine the true difference. This could stabilize over time as OPOs and transplant programs adapt to the change. To measure match time, a measure of organ placement efficiency, the time from first electronic offer to cross clamp for deceased donors who donated at least one lung is shown in Figure 23.

Figure 23. Time from First Electronic Offer to Cross Clamp for Deceased Donors

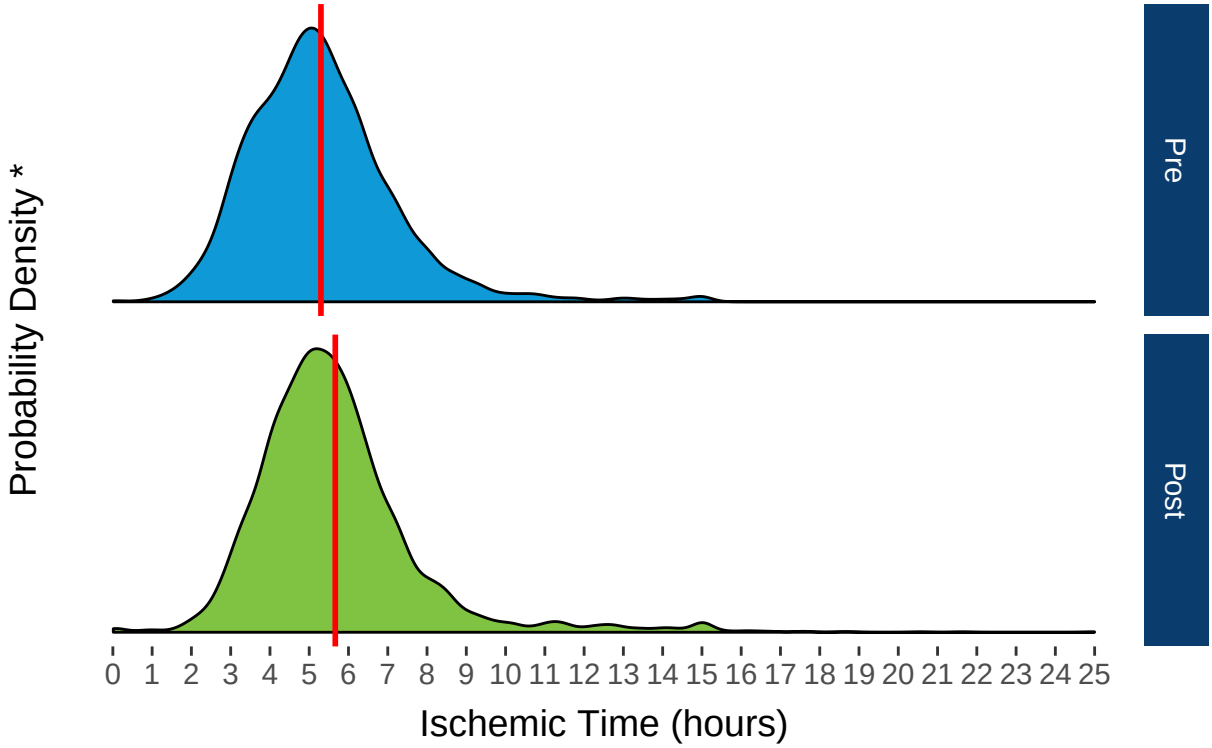


* High probability density values mean that a high percentage of the population lies at or around the corresponding x−axis value, and vice versa. Red line indicates the mean in each corresponding era.

The mean time in the pre era is 21.52 hours and 23.90 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 <0.001). However, other OPO and allocation factors, such as Figure 19 which showed an increase in the distance lungs are traveling, should be considered when determining whether this difference is clinically meaningful.

Figure 24 shows the distribution of ischemic time in hours for the pre and the post era.

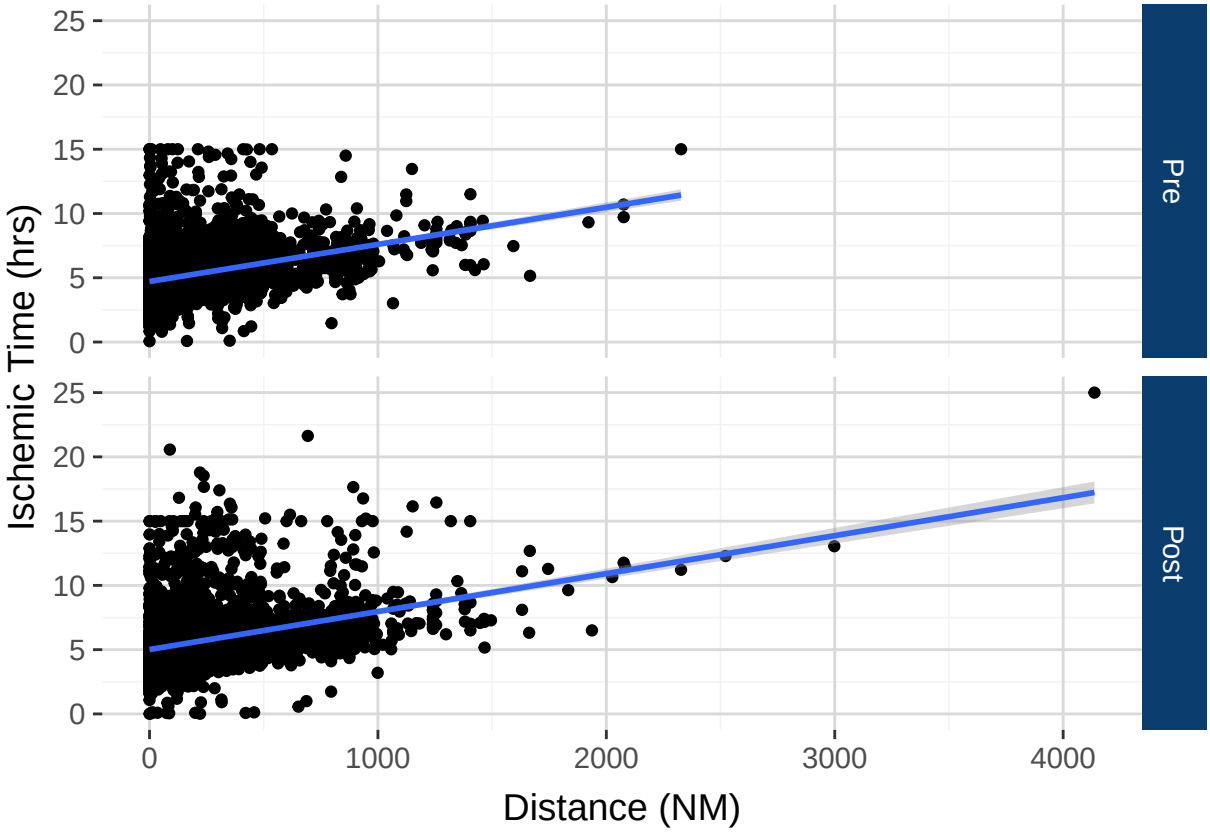
Figure 24. Ischemic Time (Cold, Warm, and Anastomotic Time)



* 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.

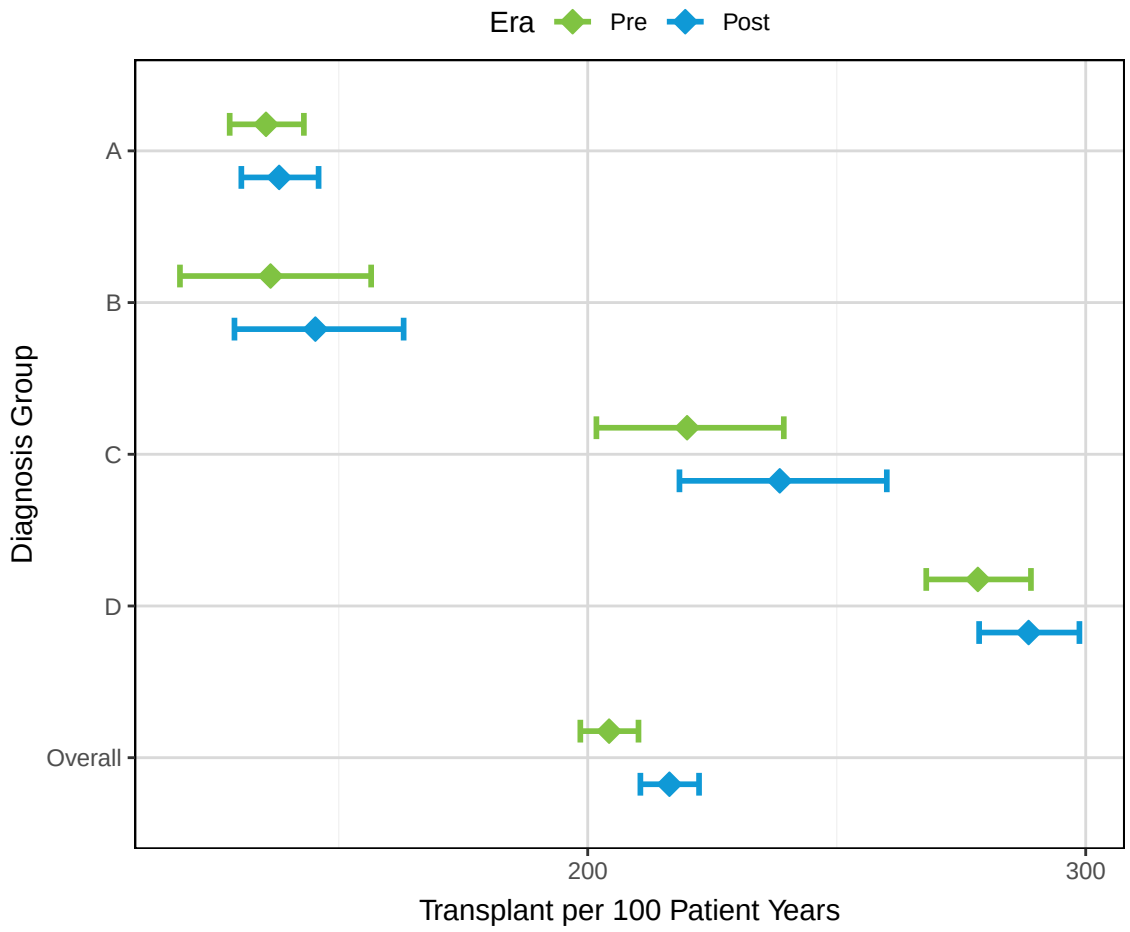
The mean ischemic time in the pre era is 5.30 and 5.66 for the post era. There is a statistically significant difference between the pre and post mean ischemic time (p-value <0.001). Additionally, the increase use of lung perfusion shown later in the report could be contributing to the increase in ischemic time. Future analyses may examine the outcomes related to a change in ischemic time. Figure 25 depicts a scatter plot of distance by ischemic time for each era.

Figure 25. Scatter Plot of Distance by Ischemic Time and Era



It can be seen that the correlation between distance and ischemic time is moderate in both the pre and the post era. The Pearson's correlation estimate in the pre era is 0.371 and 0.35 in the post era. Early data on the transplant rate for lung recipients is summarized below by diagnosis group and LAS group.

Figure 26. Transplants per 100 Active Patient Years while Waiting by Diagnosis Group



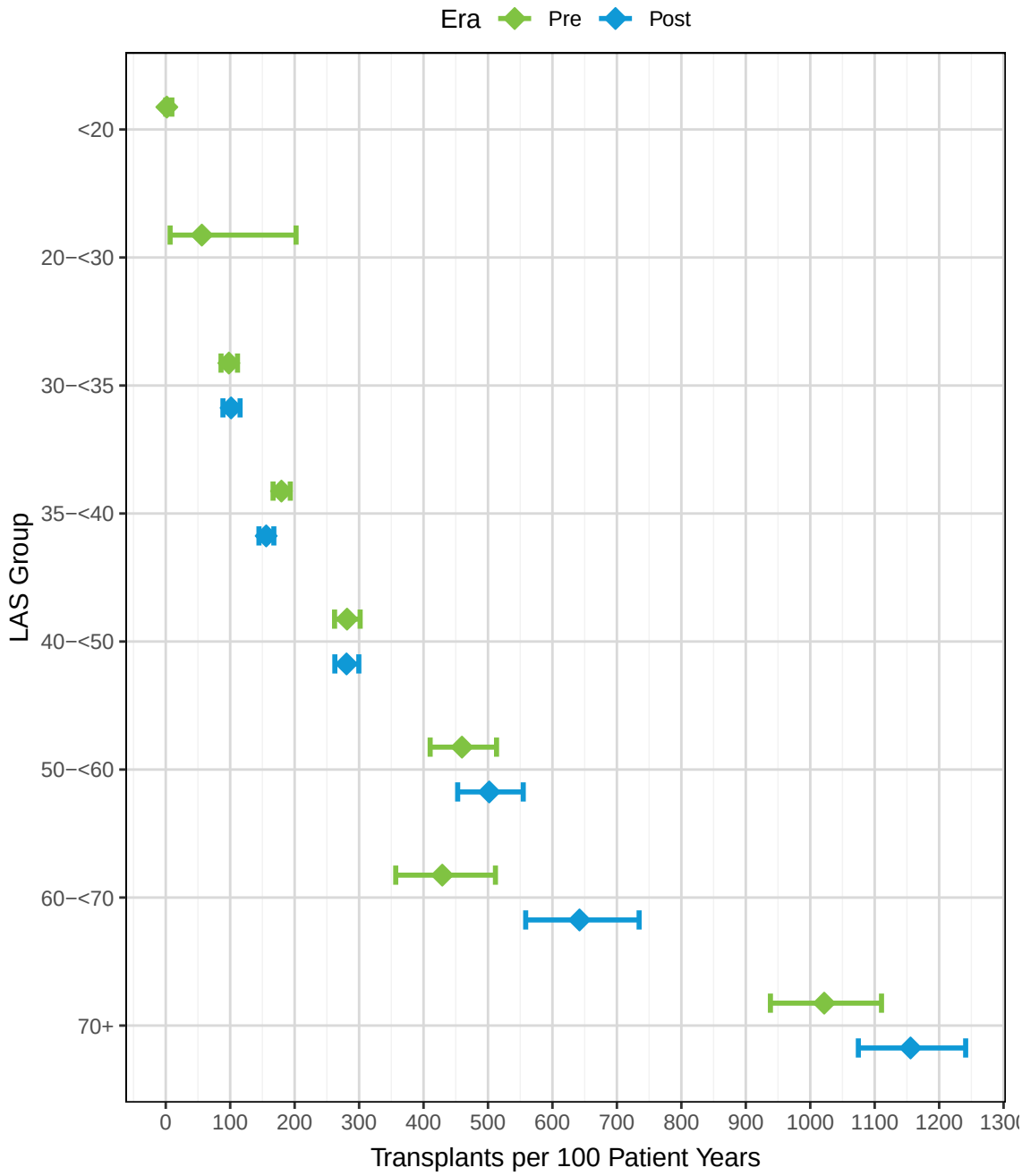
From the figure above it can be seen that there is little change in the transplant rate overall and by diagnosis group. Below is the corresponding table with the transplant rate and 95% confidence interval by diagnosis group.

Table 8. Transplants per 100 Active Patient Years while Waiting by Diagnosis Group

Group	Era	Patients Ever Waiting	Transplants per 100 Patient years	Lower 95% CI	Upper 95% CI
A	Pre	1983	135.40	128.10	143.00
A	Post	1941	138.04	130.45	145.96
B	Pre	368	136.31	118.12	156.51
B	Post	489	145.31	129.06	163.03
C	Pre	715	219.96	201.75	239.37
C	Post	669	238.56	218.42	260.06
D	Pre	3771	278.34	267.98	289.00
D	Post	4363	288.53	278.59	298.73
Overall	Pre	6808	204.29	198.51	210.20
Overall	Post	7444	216.40	210.57	222.36

Since the confidence interval for pre and post within each diagnosis group and overall overlap, the findings are not statistically significant. Similarly, in Figure 27 below is the transplant rate summarized by LAS group.

Figure 27. Transplants per 100 Active Patient Years while Waiting by LAS Group



From the figure above it can be seen that there is an overall little change in the transplant rate per 100 patient years. The only statistically significant change is the increase in the transplant rate for LAS group 60-70. Below is the corresponding table with the transplant rate and 95% confidence interval by LAS group.

Table 9. Transplants per 100 Active Patient Years while Waiting by LAS Group

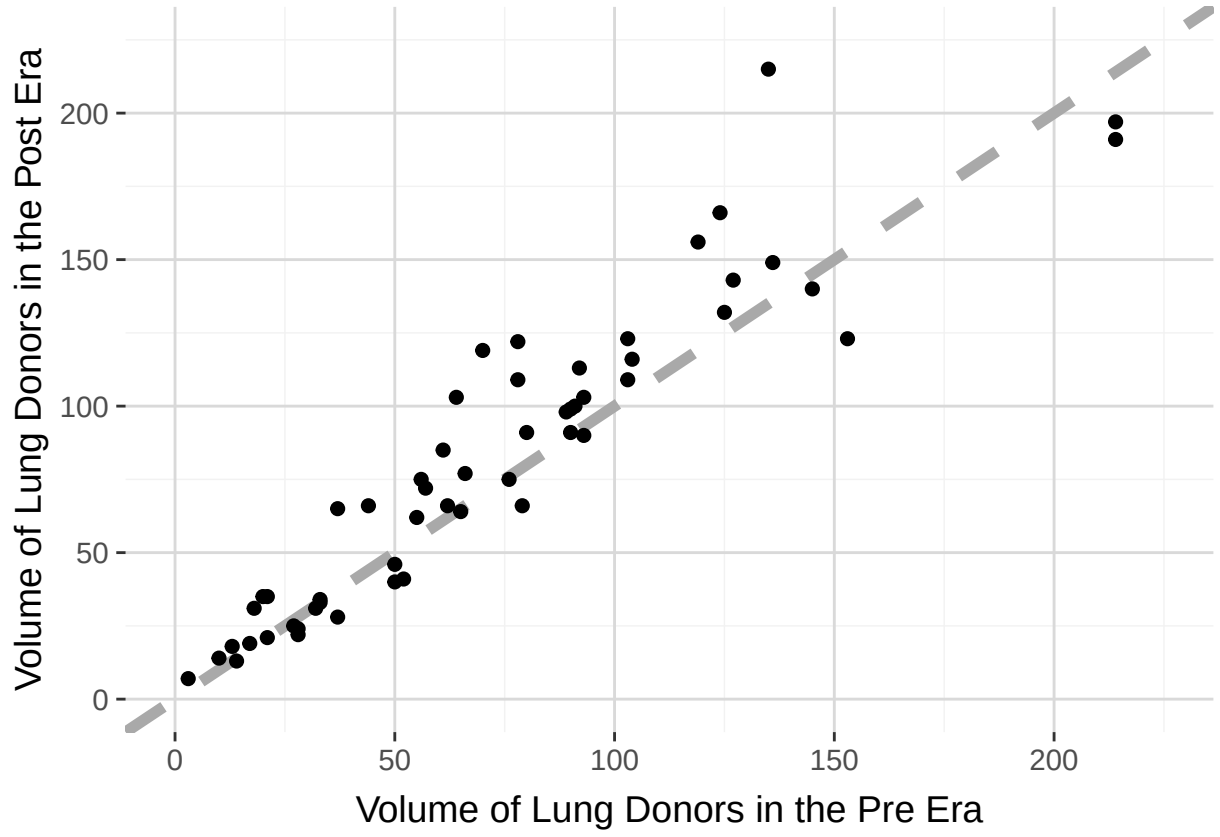
LAS Group	Era	Patients Ever Waiting	Transplants per 100 Patient years	Lower 95% CI	Upper 95% CI
<20	Pre	273	2	0.04	9.49
<20	Post	207	-	-	-
20-<30	Pre	83	56	6.78	202.24
20-<30	Post	72	-	-	-
30-<35	Pre	722	98	85.77	111.36
30-<35	Post	772	101	88.74	115.35
35-<40	Pre	1587	179	166.51	193.21
35-<40	Post	1757	156	144.61	167.71
40-<50	Pre	1583	281	261.93	301.65
40-<50	Post	1882	280	262.36	299.56
50-<60	Pre	731	460	410.25	513.27
50-<60	Post	879	502	452.95	554.70
60-<70	Pre	433	429	356.86	511.55
60-<70	Post	551	642	558.46	734.46
70+	Pre	931	1022	938.21	1110.57
70+	Post	1199	1156	1074.61	1241.15

Since the confidence interval for all LAS groups except 60-70 overlap, the findings are not statistically significant. However, it does appear like some of the lower LAS groups have seen a slight decrease in the transplant rate while the higher LAS groups have seen slight increases in the transplant rate. Since there were no transplants in the <20 post group and 20-30 group post the transplant rate is not calculated.

Utilization

The utilization of lung transplantation within the United States was compared between the pre (November 26, 2015 - November 24, 2017) and post (November 25, 2017 - November 24, 2019) era. First, the number of deceased lung donors with at least one recovered for the purpose of transplant by de-identified OPO are graphically shown in Figure 28. 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 28. 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, 40 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 (Table 10).

Table 10. Discard Rate by OPTN Region

	Era	
OPTN Region	Pre	Post
1	2.75	6.64
2	14.59	14.76
3	6.11	6.64
4	2.53	3.72
5	2.47	2.84
6	1.59	2.30
7	5.51	6.86
8	1.82	5.13
9	8.68	4.66
10	4.55	7.77
11	6.32	5.97
National	5.49	6.54

Nationally we see a statistically significant increase in the discard rate in the post era for deceased donor lungs (p-value =0.002). However, when discard rate is examined by OPTN region, it can be seen that some regions have seen an increase and some a decrease in the discard rate. Reported in Figure 29 and Table 11 is the discard rate for non-DCD lungs with no indication of perfusion.

Figure 29. Discard Rate for non-DCD lungs with no indication of perfusion reported by OPTN Region

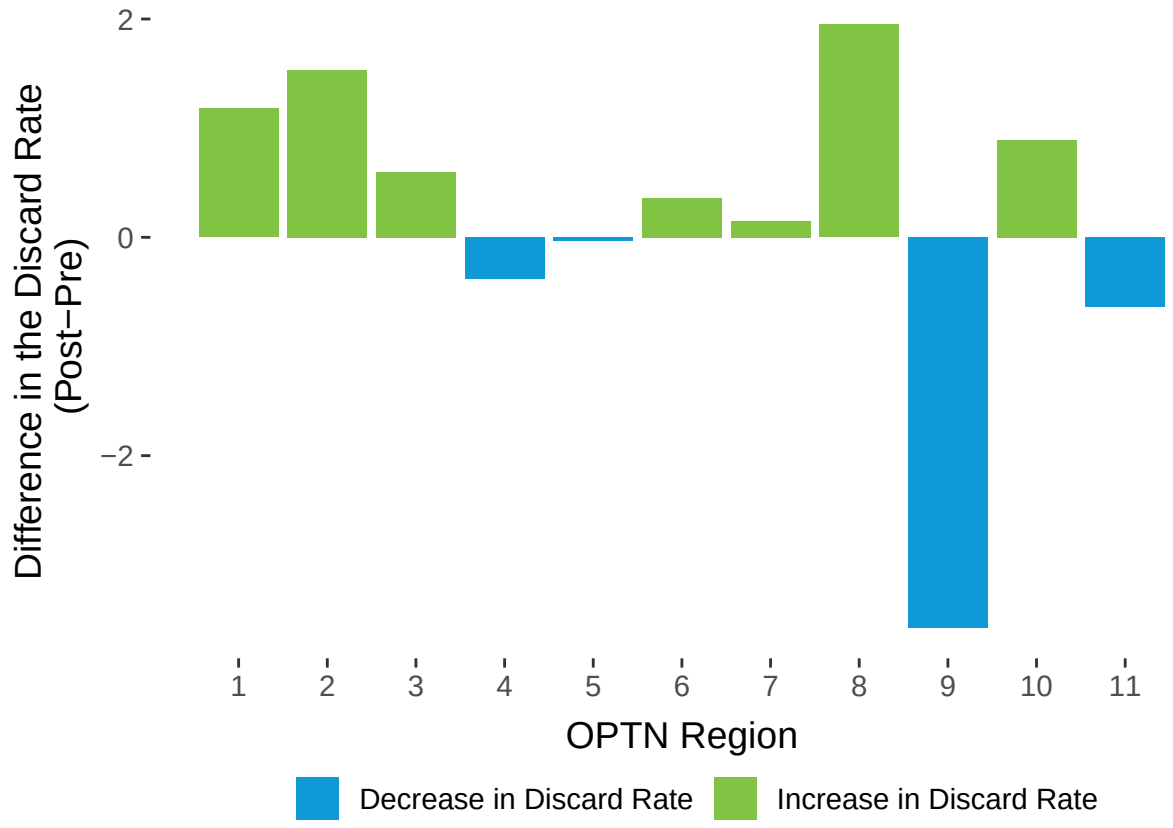


Table 11. Discard Rate for non-DCD lungs with no indication of perfusion reported by OPTN Region

	Era	
OPTN Region	Pre	Post
1	1.08	2.26
2	10.60	12.13
3	3.32	3.92
4	1.31	0.93
5	2.54	2.51
6	0.00	0.36
7	3.17	3.32
8	1.63	3.58
9	6.18	2.60
10	1.31	2.20
11	4.87	4.23
National	3.59	4.02

After removing DCD lungs and lungs with perfusion reports, there is not a statistically significant change in the discard rate (p-value =0.148).

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 30 and Table 12 summarize the utilization rate by OPTN region and nationally for both eras.

Figure 30. Utilization Rate by OPTN Region

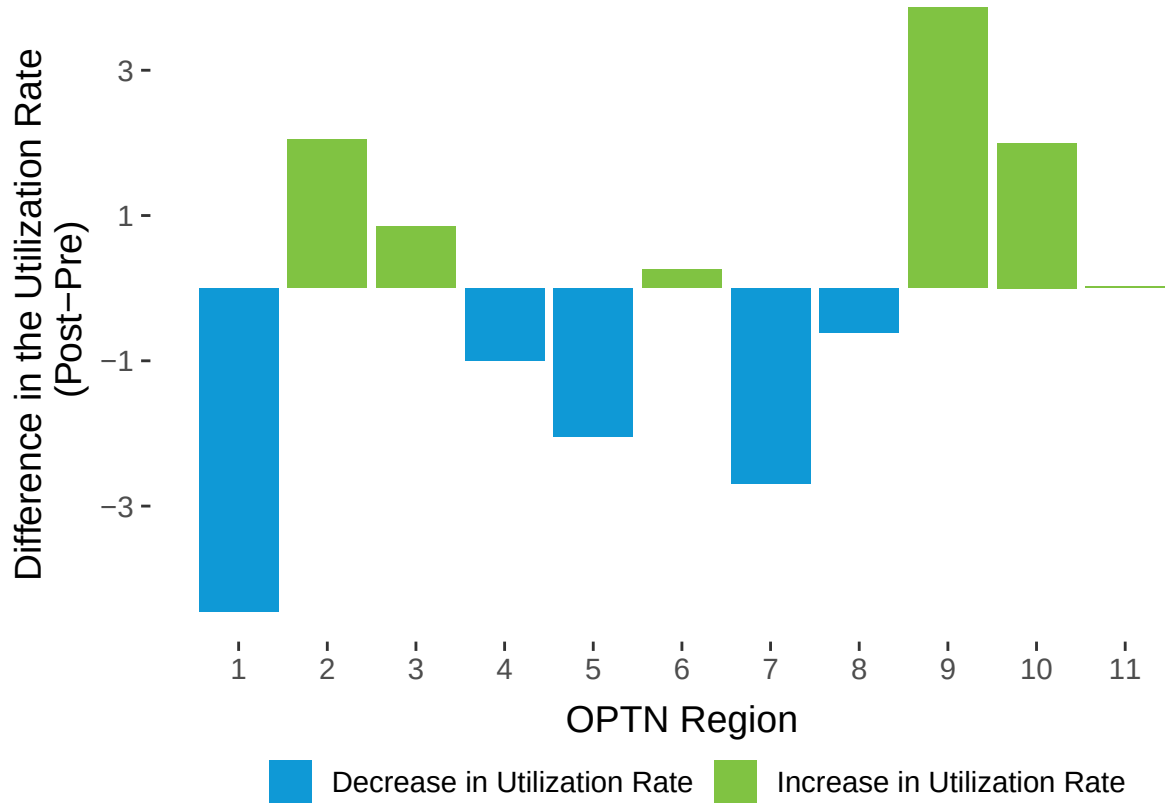


Table 12. Utilization Rate by OPTN Region

	Era	
OPTN Region	Pre	Post
1	22.93	18.48
2	20.57	22.62
3	19.70	20.55
4	25.34	24.34
5	24.66	22.62
6	16.24	16.50
7	24.63	21.94
8	25.09	24.48
9	13.06	16.92
10	24.22	26.22
11	23.72	23.74
National	22.43	22.35

Nationally, there was a not a statistically significant decrease in the utilization rate in the post era compared to the pre era (p-value =0.847). 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 16.50 in OPTN region 6 to as high as 26.22 in OPTN region 10. The utilization rate by OPTN region and donor type are displayed in the table below.

Table 13. Utilization Rate by OPTN Region and Donor Type

	DCD		non-DCD	
OPTN Region	Pre	Post	Pre	Post
1	8.54	5.38	27.05	23.63
2	5.30	6.30	23.73	26.96
3	4.24	6.94	21.50	22.60
4	3.68	4.80	30.26	29.31
5	4.83	5.58	28.84	27.01
6	4.64	2.86	20.10	21.49
7	5.75	7.74	30.10	27.12
8	2.71	2.95	31.16	32.17
9	5.79	4.72	15.01	20.69
10	10.30	9.31	27.51	31.46
11	2.95	3.63	26.81	28.62

The utilization rate for non-DCD donors is higher across all OPTN regions than the utilization rate for DCD donors. OPTN region 1, 2, 7, and 10 have the highest utilization rate in both eras for the use of DCD donors for lung transplantation. 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 14 summarizes the use of EVLP by OPTN region and era.

Table 14. Number of Lungs with Machine Perfusion Intended or Performed by OPTN Region

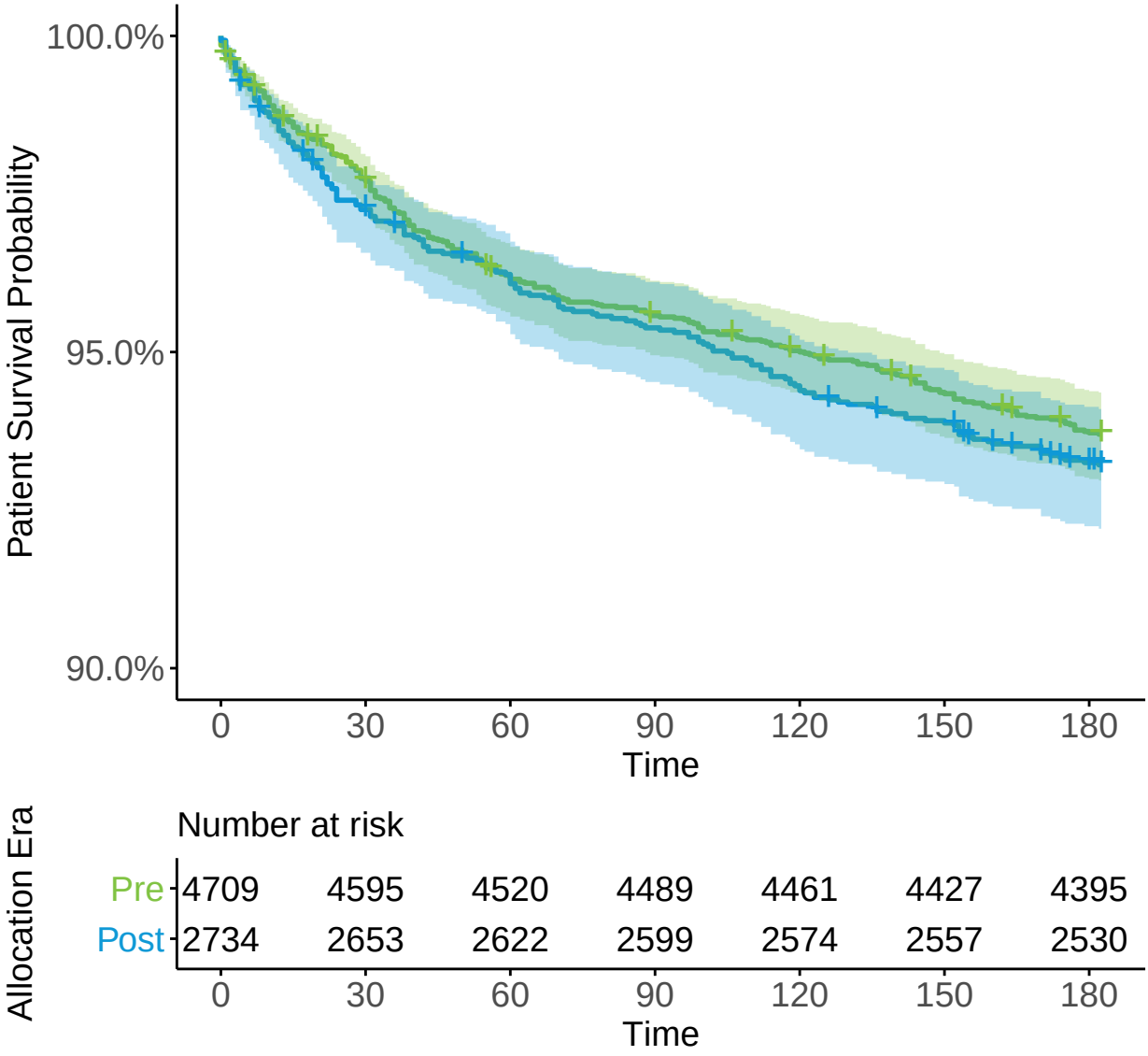
	Era	
OPTN Region	Pre	Post
1	12	23
2	49	69
3	60	136
4	13	101
5	6	42
6	6	15
7	40	61
8	12	48
9	4	20
10	38	121
11	24	44
National	264	680

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.

Outcomes

For a limited cohort of candidates that were transplanted before January 1, 2019 a 6-month unadjusted Kaplan Meier survival analysis was performed. The pre cohort included recipients (age $\geq$ 12) that received a lung alone transplant from November 26, 2015 through November 24, 2017 and the post cohort included recipients from November 25, 2017 through January 1, 2019. The cohort was limited to transplants before January 1, 2019 in order to allow sufficient time for complete follow up.

Figure 31. 6-Month Unadjusted Patient Survival by Era



There is not a statistically significant difference between the 6-month patient survival pre vs. post policy change as shown by the overlapping confidence intervals depicted by the blue and green bands. The 6-month patient survival pre vs. post policy change was also examined by diagnosis group.

Figure 32. 6-Month Unadjusted Patient Survival by Era for Diagnosis Group A- Obstructive Lung Disease

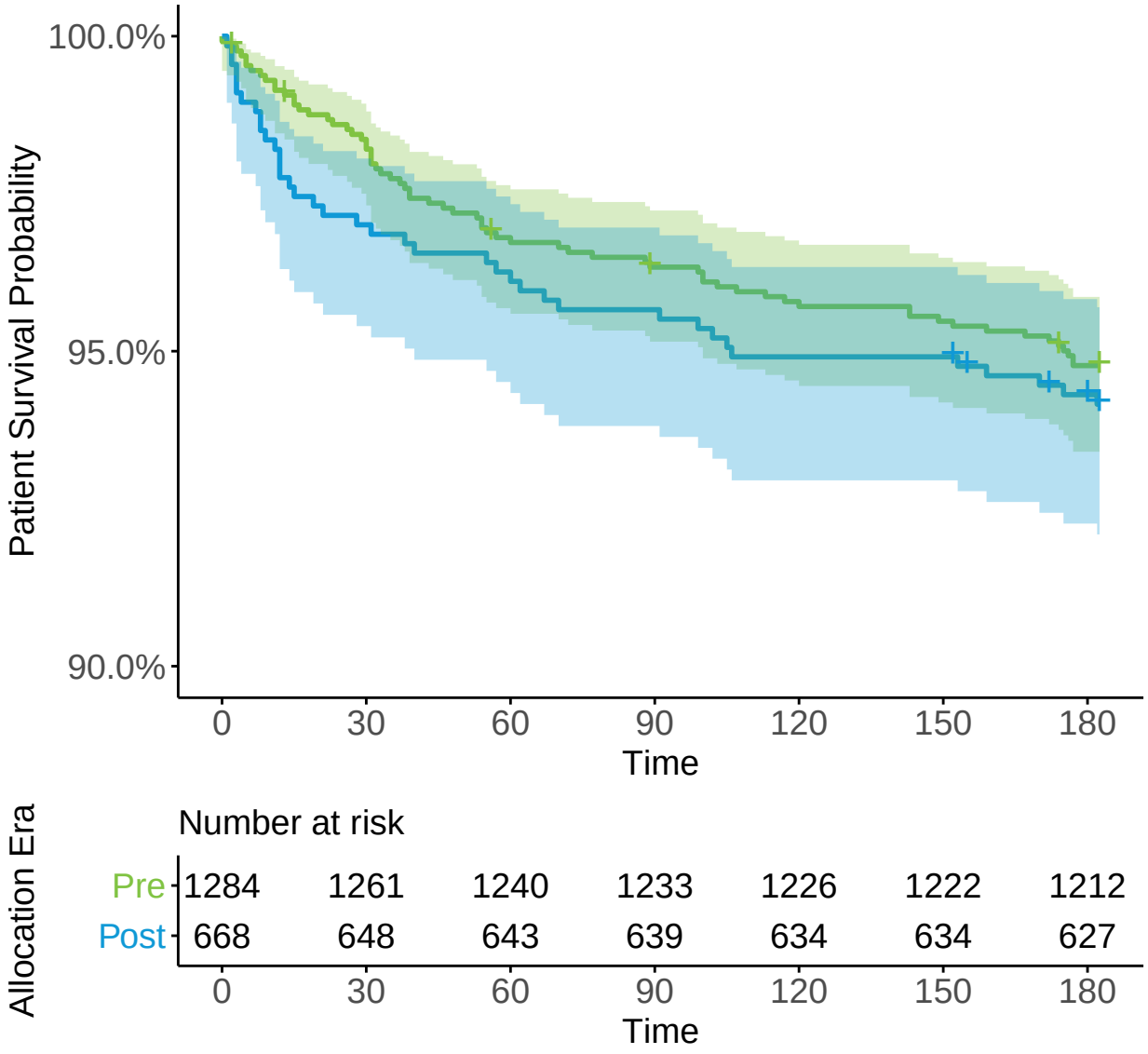


Figure 33. 6-Month Unadjusted Patient Survival by Era for Diagnosis Group B- Pulmonary Vascular Disease

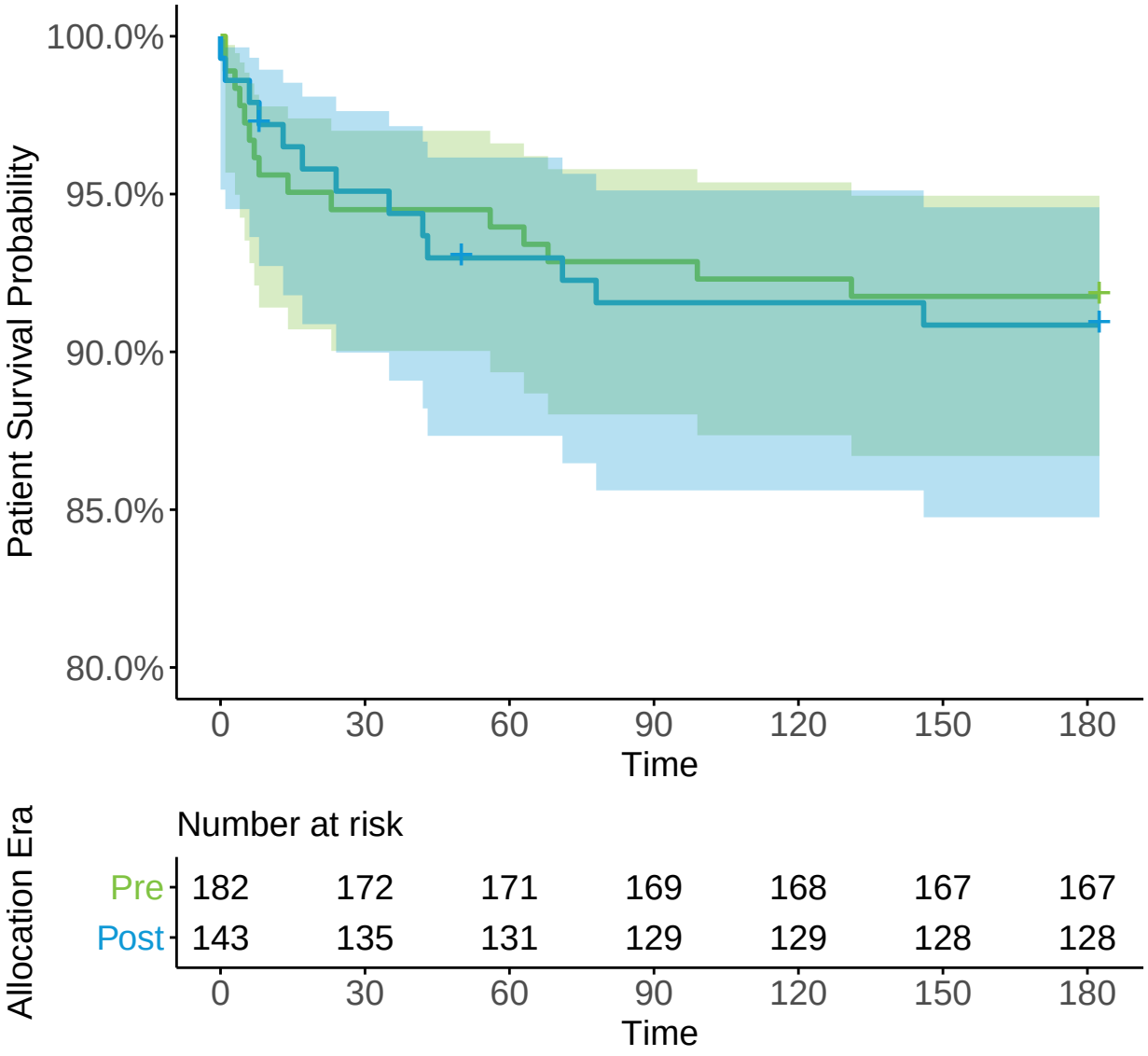


Figure 34. 6-Month Unadjusted Patient Survival by Era for Diagnosis Group C- Cystic Fibrosis and Immunodeficiency Disorder

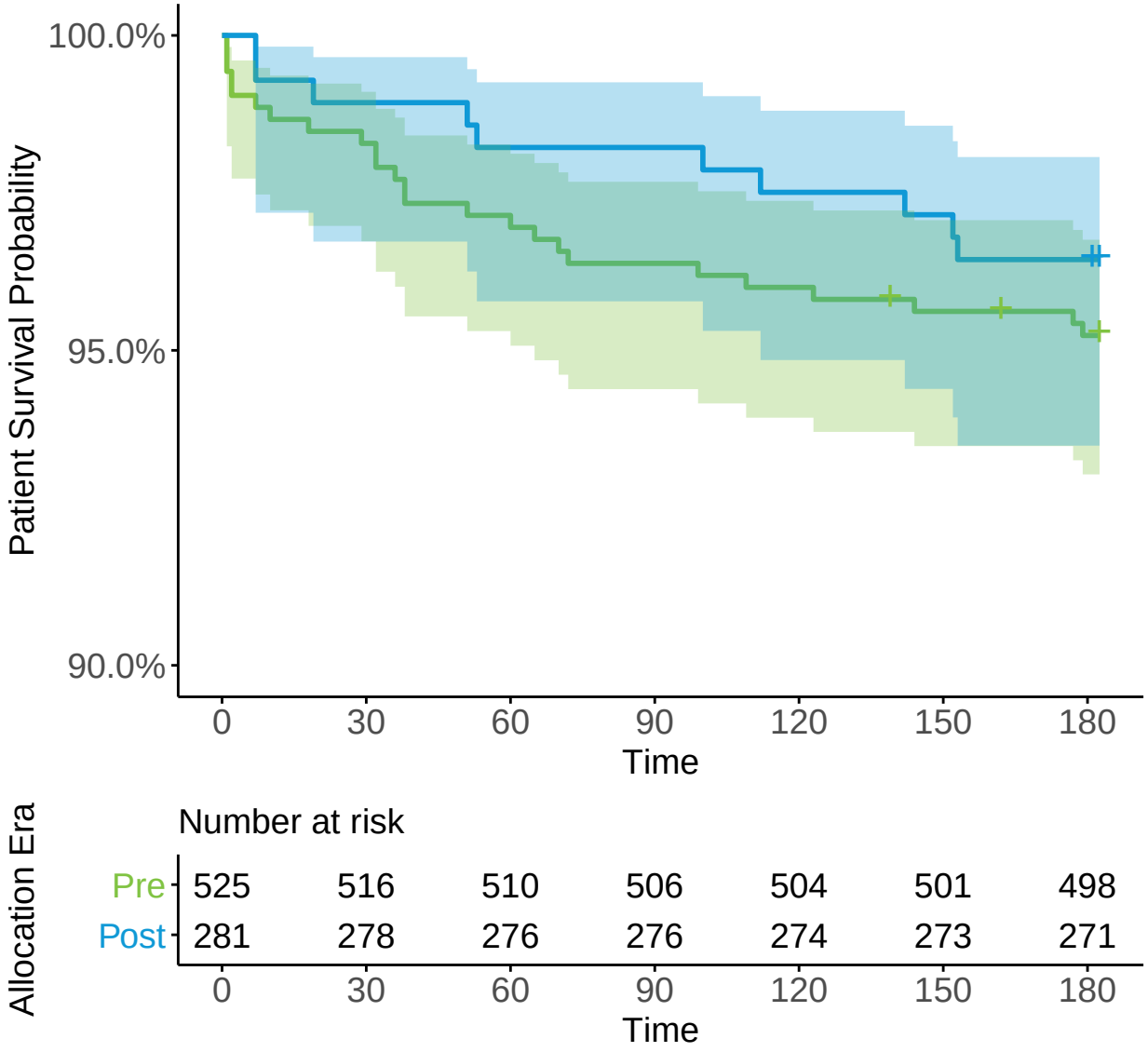
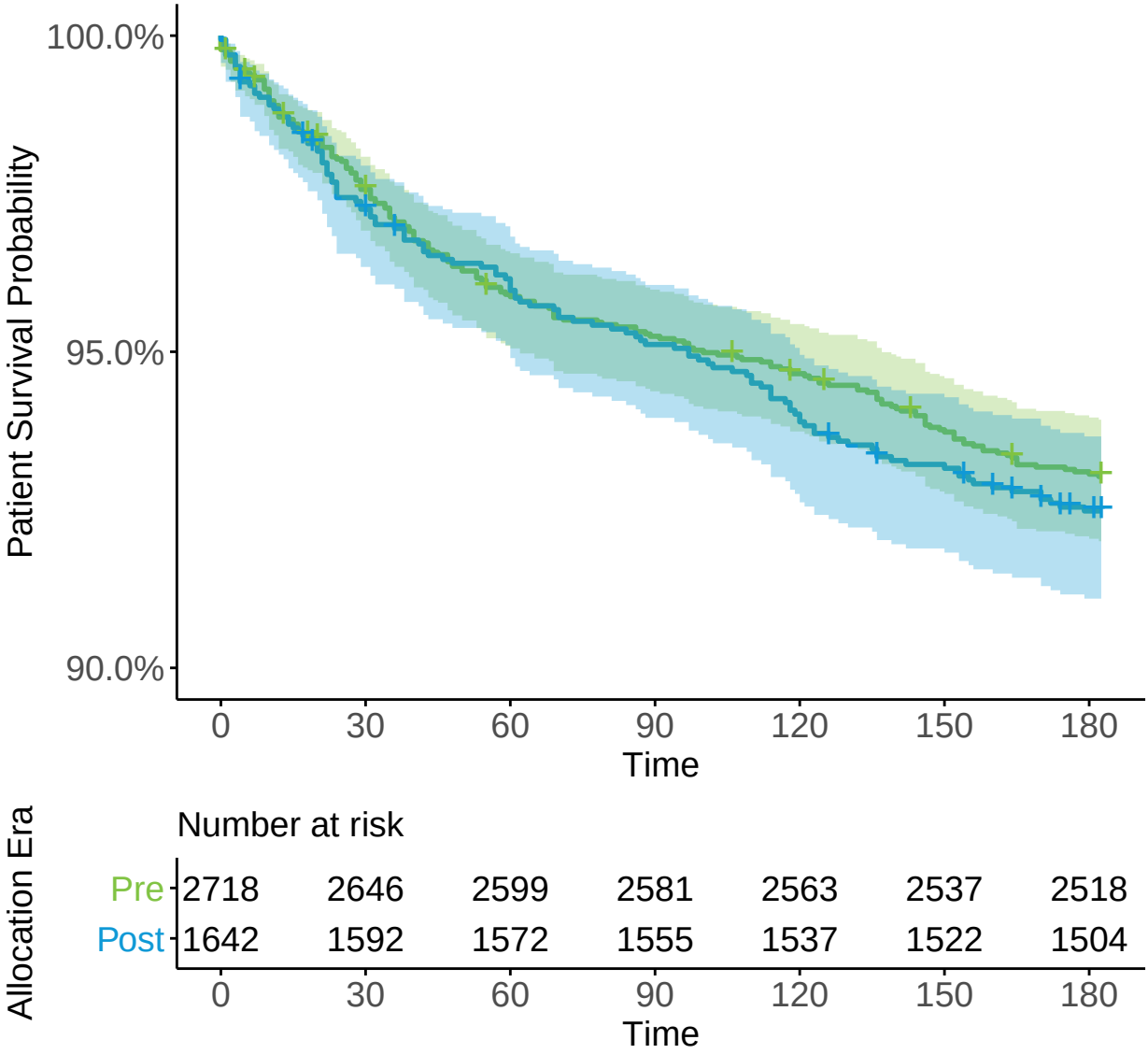


Figure 35. 6-Month Unadjusted Patient Survival by Era for Diagnosis Group D- Restrictive Lung Disease



There are no statistically significant changes in the 6-month patient survival within the four diagnosis groups.

Multiorgan Transplants

It was of interest to the Committee to examine multiorgan candidates ever on the waiting list pre vs. post policy change. Summarized below are the changes in the number of multiorgan listings from pre to post policy change for candidates listed for a lung.

Table 15. Number and Percentage of Lung Registrations also Listed for a Heart by Era

	Pre	Post	Total
No Heart Listing	5632 (99.0%)	6327 (98.4%)	11959 (98.7%)
Heart Listing	57 (1.0%)	102 (1.6%)	159 (1.3%)
Total	5689 (100.0%)	6429 (100.0%)	12118 (100.0%)

Table 16. Number and Percentage of Lung Registrations also Listed for a Heart-Lung by Era

	Pre	Post	Total
No Heart-Lung Listing	5625 (98.9%)	6326 (98.4%)	11951 (98.6%)
Heart-Lung Listing	64 (1.1%)	103 (1.6%)	167 (1.4%)
Total	5689 (100.0%)	6429 (100.0%)	12118 (100.0%)

Table 17. Number and Percentage of Lung Registrations also Listed for a Kidney by Era

	Pre	Post	Total
No Kidney Listing	5668 (99.6%)	6389 (99.4%)	12057 (99.5%)
Kidney Listing	21 (0.4%)	40 (0.6%)	61 (0.5%)
Total	5689 (100.0%)	6429 (100.0%)	12118 (100.0%)

Table 18. Number and Percentage of Lung Registrations also Listed for a Liver by Era

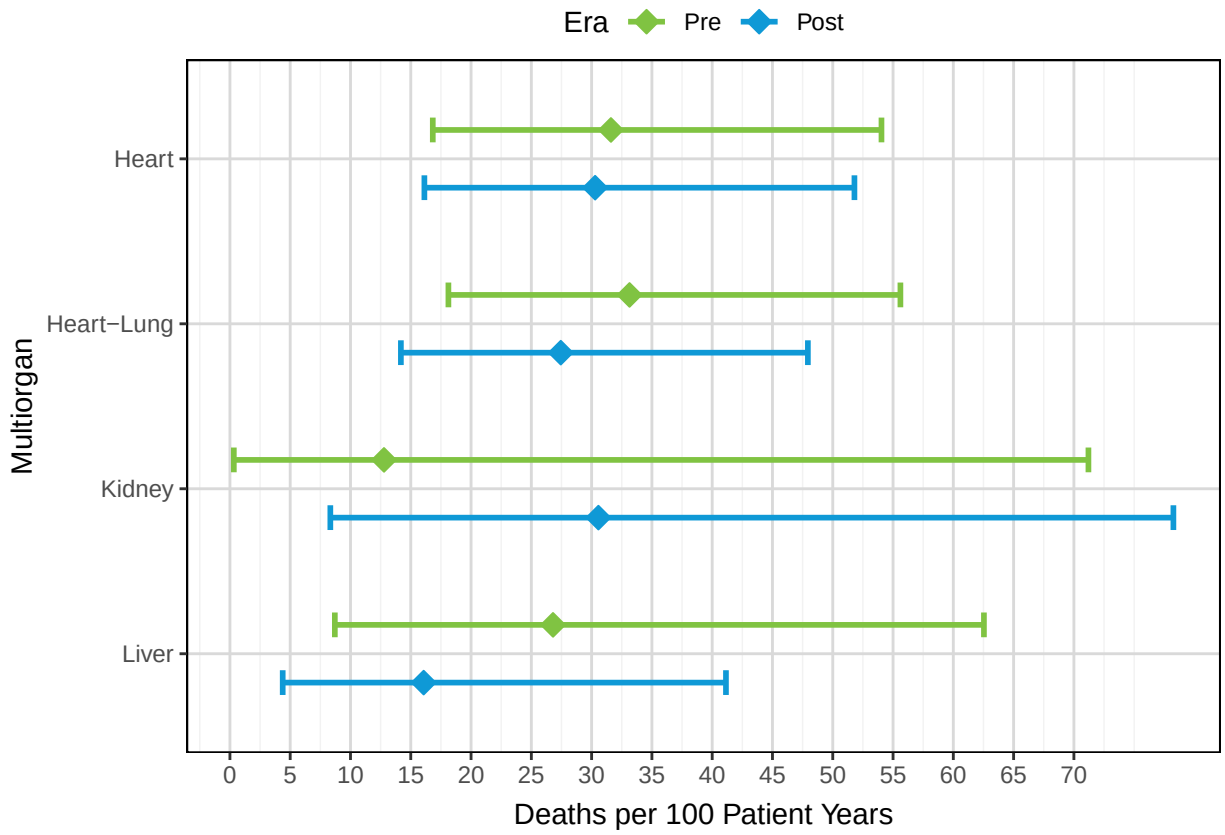
	Pre	Post	Total
No Liver Listing	5652 (99.3%)	6378 (99.2%)	12030 (99.3%)
Liver Listing	37 (0.7%)	51 (0.8%)	88 (0.7%)
Total	5689 (100.0%)	6429 (100.0%)	12118 (100.0%)

Table 19. Number and Percentage of Lung Registrations also Listed for a Pancreas by Era

	Pre	Post	Total
No Pancreas Listing	5688 (100.0%)	6429 (100.0%)	12117 (100.0%)
Pancreas Listing	1 (0.0%)	0 (0.0%)	1 (0.0%)
Total	5689 (100.0%)	6429 (100.0%)	12118 (100.0%)

In both eras,there are no lung registrations that also have a kindey-pancreas, intestine, or pancreas-islet listing. Overall, the volume of lung candidates listed for an additional organ on the waiting list has not changed. Below is the waiting list mortality rate per 100 patient years for each multiorgan group except pancreas due to the the small sample size. Similarly, the results were not stratified by heart status due to the small sample sizes in each multiorgan group.

Figure 36. Deaths per 100 Patient Years while Waiting by Multiorgan Group



From the figure above it can be seen that there are no changes in the waiting list mortality rate for multiorgan lung candidates per 100 patient years. Below is the corresponding table with the number of deaths per 100 patient years and corresponding 95% confidence interval by multiorgan group.

Table 20. Deaths per 100 Patient Years while Waiting by Multiorgan Group

Multiorgan Group	Era	Patients Ever Waiting	Deaths per 100 Patient years	Lower 95% CI	Upper 95% CI
Heart	Pre	76	32	16.83	54.04
Heart	Post	93	30	16.13	51.80
Heart-Lung	Pre	82	33	18.12	55.61
Heart-Lung	Post	94	27	14.18	47.94
Kidney	Pre	21	13	0.32	71.21
Kidney	Post	40	31	8.33	78.25
Liver	Pre	36	27	8.70	62.54
Liver	Post	49	16	4.38	41.14

Below is the transplant rate per 100 patient years for each multiorgan group except pancreas due to the the small sample size. Similarly, the results were not stratified by heart status due to the small sample sizes in each multiorgan group.

Figure 37. Transplant per 100 Patient Years while Waiting by Multiorgan Group

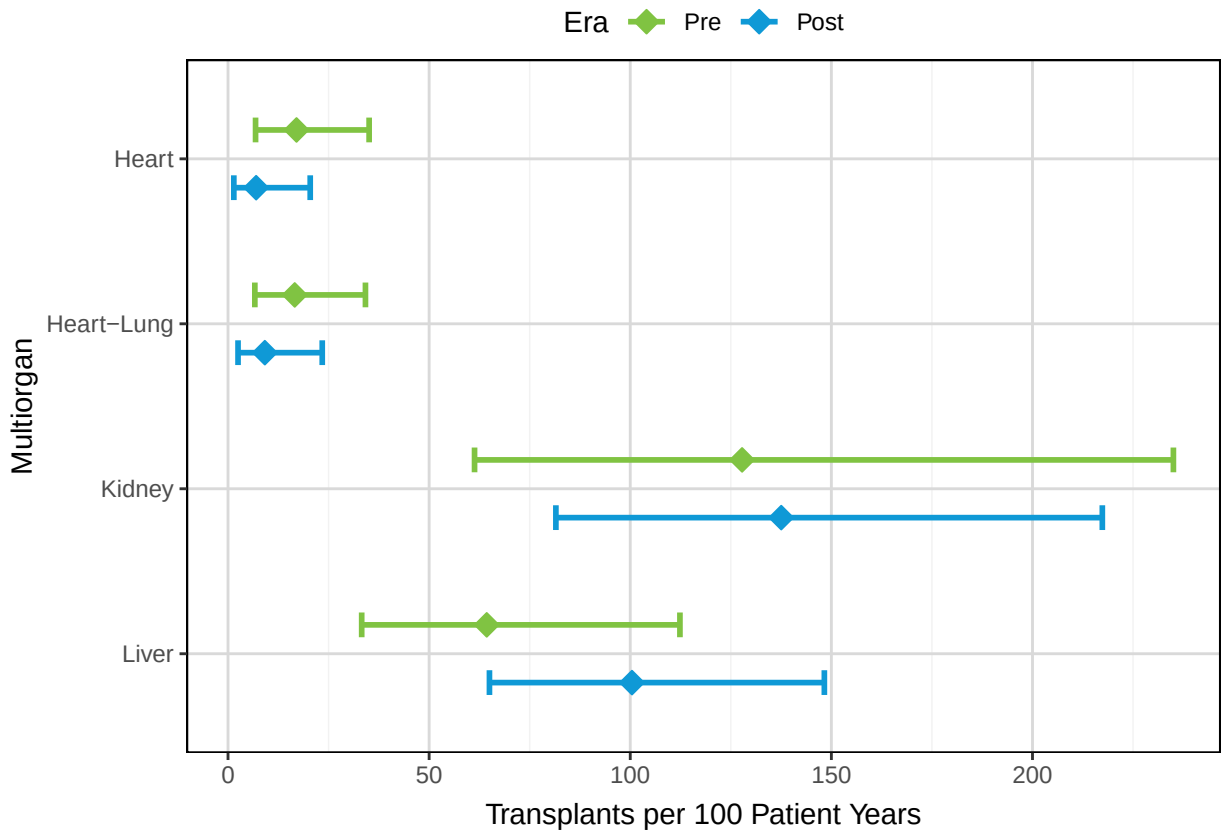


Table 21. Transplants per 100 Patient Years while Waiting by Multiorgan Group

Multiorgan Group	Era	Patients Ever Waiting	Transplants per 100 Patient years	Lower 95% CI	Upper 95% CI
Heart	Pre	76	17	6.85	35.08
Heart	Post	93	7	1.44	20.43
Heart-Lung	Pre	82	17	6.67	34.17
Heart-Lung	Post	94	9	2.49	23.43
Kidney	Pre	21	128	61.29	235.03
Kidney	Post	40	138	81.51	217.36
Liver	Pre	36	64	33.23	112.35
Liver	Post	49	100	64.99	148.25

From the figure and table above it can be seen that there are no changes in the transplant rate for multiorgan lung candidates per 100 patient years.

Conclusion

This report provides a 2 year evaluation of the lung policy implemented on November 24, 2017. Each monitoring report revealed an increase in the mean match LAS at the time of transplant, suggesting that clinically sicker candidates are recieving more lung transplants under the new system. This is also clear from the increase in the number of high LAS transplants defined as candidates with an LAS of at least 75. The magnitude of the increase in LAS has not varied drastically across the reports with the difference in LAS being between 2 and 3 points. Similarly, all reports have shown an increase in the median distance between the donor hospital and transplant program. The median distance under the new allocation system has remained relatively stable in each monitoring report ranging from 160NM to 170NM. Lastly, the utilization of lungs is consistent across the monitoring reports with very little change from pre to post policy. There has however been an increase in the use of perfusion displayed in each monitoring report however this may not be influenced by the policy change but by the FDA approval of various perfusion technologies.

Currently the Lung Subcommittee of the OPTN Thoracic Organ Transplantation Committee is working on transitioning lung allocation to a Continuous Distribution framework. For additional information about future changes to lung allocation policy please read the concept paper on the OPTN public comment website: https://optn.transplant.hrsa.gov/governance/public-comment/.