

OPTN OPTN Lung Committee

Descriptive Data Request

## **Comparing CPRA with Lung-Specific vs All-Deceased-Donor Ethnic Weights**

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## Background/Purpose

The Lung Committee expects to include CPRA as a factor in the upcoming lung continuous distribution proposal. One element of the CPRA calculation is a set of ethnic weights that adjust the frequencies of different HLA antigens present in the donor pool based on the observed ethnicities of recently-recovered deceased donors. CPRA for lung candidates could be based on the ethnicities of recently-recovered deceased lung donors, but as more organs move to continuous distribution, using CPRAs with organ-specific parameters becomes confusing and difficult to maintain. This is especially true for multi-organ candidates, who might possess different CPRAs for each of the organs for which they had been listed. An alternative would be to use ethnic weights based on all recovered deceased donors, which could be applied to all allocation systems that include CPRA. The Lung Committee wishes to view data on differences between CPRA calculated with ethnic weights based on lung donors and CPRA based on all deceased donors in order to determine whether the all-donor CPRA would be an acceptable substitute for a CPRA using lung-specific values.

For this analysis, Dr. Loren Gragert will calculate the CPRA using both the overall ethnic weights and the lung-specific ethnic weights based on a dataset of lung candidate unacceptable antigens provided by the OPTN contractor. These CPRA values will then be linked to OPTN data using encrypted Waitlist IDs.

## Strategic Plan Goal or Committee Project Addressed

Continuous Distribution of Lungs

## Committee Request

1. Count and percent of a recent lung candidate cohort with any unacceptable antigens entered
2. Count and percent of a recent lung candidate cohort where the CPRA when using lung-specific ethnic weights would differ from the CPRA when using overall deceased donor ethnic weights
3. Distribution of difference in CPRA between the metric using lung-specific ethnic weights and the metric using overall deceased donor ethnic weights
4. Count and percent of lung candidates who would rise to  $\geq 95\%$  CPRA for each of the two metrics
5. Count and percent of lung candidates who would rise to 100% CPRA for each of the two metrics

The above analyses will be provided as overall measures as well as stratified by ethnicity.

## Methods

Analyses were based on the cohort of 31553 lung registrations ever waiting between January 01, 2010 and June 30, 2021. Because CPRA is not currently calculated for lung candidates, the CPRA was determined based on each registration's most recent set of unacceptable antigens. Three CPRA metrics were calculated from these unacceptable antigens: the current CPRA, based on the value returned by the OPTN CPRA calculator API, and two CPRA values based on the OPTN Histocompatibility Committee's proposed revised CPRA calculation. This proposed metric increases the number of HLA loci used in the CPRA calculation and expands the unacceptable antigens assigned a CPRA value. All CPRA metrics use a set of ethnic weights to adjust the frequencies of deceased donor HLA antigens based on the proportion of each ethnicity among deceased donors recovered within a specific time period. The current CPRA uses weights based on deceased kidney donors recovered between January 1, 2007 and December 31, 2008. The CPRA with lung-specific ethnic weights is based on deceased lung donors recovered between January 1, 2018 and December 31, 2020, and the CPRA with ethnic weights based on all deceased donors uses all deceased donors recovered between January 1, 2018 and December 31, 2020. Table 1 shows the ethnic weights used for all of the CPRA metrics presented in this analysis. Note that the current CPRA metric uses weights for four ethnic groups, while the proposed CPRA metric uses weights for seven ethnic groups.

Table 1: Ethnic Weights by CPRA Metric

Ethnicity	Current	Lung Donor Weights	All DD Weights
White	0.687	0.6130	0.6650
Black	0.147	0.1753	0.1565
Hispanic	0.143	0.1639	0.1456
Asian	0.023	0.0327	0.0252
Amer Ind/Alaska Native		0.0057	0.0061
Native Hawaiian/other Pacific Islander		0.0022	0.0028
Multiracial		0.0072	0.0088

Both CPRA values under the proposed CPRA calculation were provided by Dr. Loren Gragert and were generated according to the methodology used in evaluating the proposed CPRA calculation against the current OPTN CPRA. The proposed CPRA metric has not been finalized and is subject to change based on the assessment of the OPTN Histocompatibility Committee and in response to public comment. However, changes to this metric are expected to be minor and have negligible impact on the results of these analyses.

Throughout this report CPRA values were rounded to six decimal places to agree with the proposed precision to be used in lung continuous distribution. This differs from current practice in kidney allocation, where CPRA values are rounded to two decimal places. Analyses referring to 95% or 100% CPRA use the kidney definition because no allocation categories are currently defined for CPRA in lung candidates.

All analyses are based on OPTN data as of November 12, 2021 and are subject to change based on future data submission or correction.

## Results

Table 2: Count and Percent of Lung Candidates Impacted by Use of Lung-Specific vs All Deceased Donor Ethnic Weights

Total Candidates	Candidates with UAs	Candidates with Different Lung and All DD CPRA
31553	5713 (18.11%)	5711 (99.96%)

Table 2 shows the basic characteristics of the lung CPRA dataset. Between January 01, 2010 and June 30, 2021 only about 18% of all lung registrations had any associated unacceptable antigens at their most recent time point. Changing the set of ethnic weights used in the CPRA calculation caused the CPRA to change for all but two registrations.

Table 3 shows the count and percent of lung registrations with unacceptable antigens by ethnicity. The percent of lung registrations with unacceptable antigens varied between 12% and 22% for most ethnic groups. However, there were few American Indian/Alaska Native, Native Hawaiian/other Pacific Islander, and Multiracial lung registrations in the dataset, and even fewer of these had unacceptable antigens entered. This makes the results of analyses for these ethnic groups difficult to assess.

Almost all registrations had different CPRAs under the two sets of ethnic weights; the exception was two White candidates with the same CPRA regardless of whether lung-specific or all-deceased-donor ethnic weights were used.

Table 3: Count and Percent of Lung Candidates Impacted by Use of Lung-Specific vs All Deceased Donor Ethnic Weights

Ethnicity	Total Candidates	Candidates with UAs	Candidates with Different Lung and All DD CPRA
White	24614	4397 (17.86%)	4395 (99.95%)
Black	3085	676 (21.91%)	676 (100%)
Hispanic	2814	463 (16.45%)	463 (100%)
Asian	790	127 (16.08%)	127 (100%)
Amer Ind/Alaska Native	117	26 (22.22%)	26 (100%)
Native Hawaiian/other Pacific Islander	29	11 (37.93%)	11 (100%)
Multiracial	104	13 (12.5%)	13 (100%)

Figure 1: Distribution of Difference between CPRA Using Lung Weights vs All Deceased Donor Weights

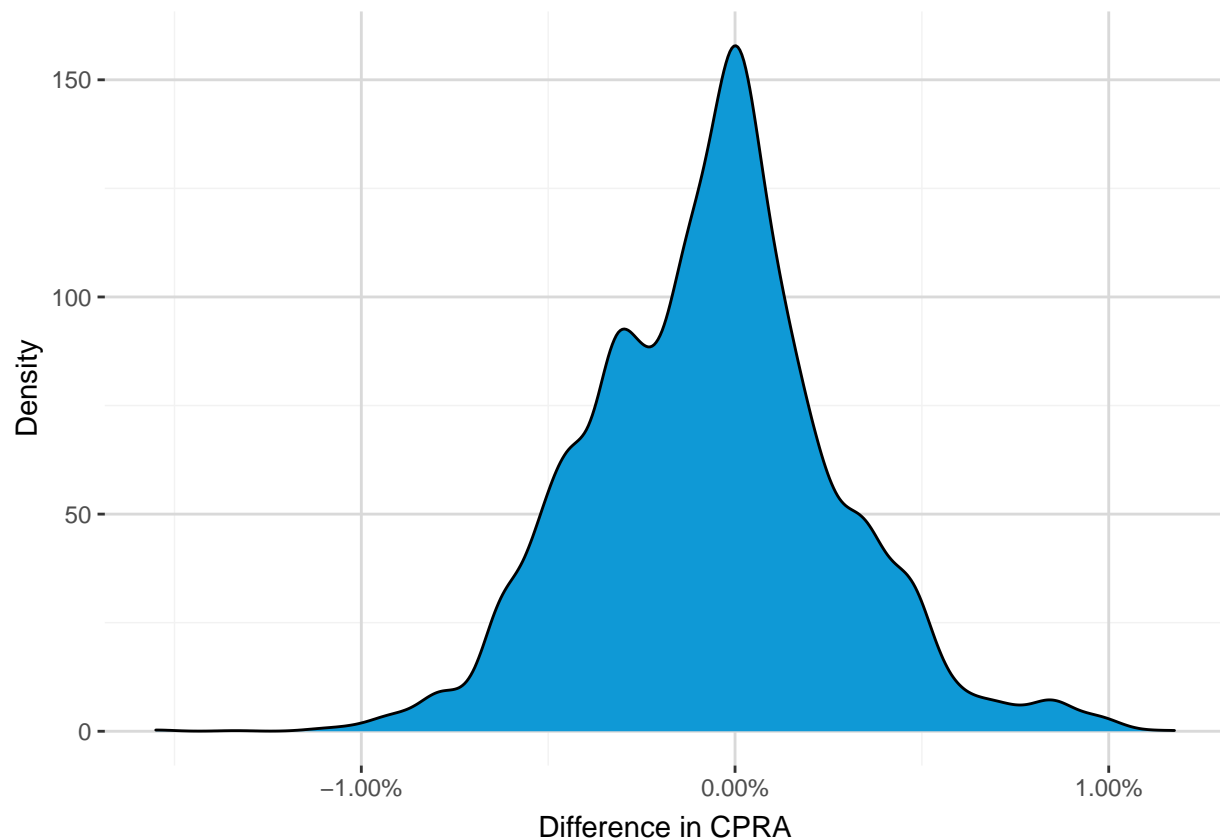


Table 4: Distribution of Difference between CPRA with Lung Donor Ethnic Weights and All Deceased Donor Ethnic Weights

Min	25th Percentile	Mean	Median	75th Percentile	Max
-1.55%	-0.29%	-0.06%	-0.05%	0.12%	1.18%

Figure 1 and Table 4 show the distribution of the difference in CPRA under the two sets of ethnic weights for lung registrations with unacceptable antigens ever waiting between January 01, 2010 and June 30, 2021. The majority of registrations had little change in CPRA, indicated by the high density near zero in Figure 1. A negative change in CPRA indicates that the CPRA using ethnic weights based on all deceased donors is *lower* than the CPRA for a registration when using ethnic weights based only on lung deceased donors. Thus, figure 1 also shows that the CPRA based on ethnic weights from all deceased donors tended to be lower than the CPRA using ethnic weights only from lung deceased donors. Overall the median absolute difference between CPRAs using the two different sets of ethnic weights was 0.5% and the maximum absolute difference for any registration in the dataset was 1.55%.

Figure 2 and Table 5 show the distribution of the difference in CPRA using lung-specific weights vs all-deceased-donor weights stratified by ethnicity. The shapes of the distributions in Figure 2 vary considerably, but much of this is likely due to the low sample size available for some ethnicities. For example, there are only 13 Multiracial registrations with any unacceptable antigens in the dataset (Table 3), leading to peaks in the density curve corresponding to individual registrations. In general, the majority of registrations show close to zero difference in CPRA depending on the ethnic weights used; as shown in Table 5, the CPRA using all deceased donor ethnic weights was lower than the CPRA using lung donor ethnic weights for the majority of all registrations within all ethnic groups. The greatest differences between CPRAs using the two different sets of ethnic weights were seen in

White candidates. The ethnic group with the greatest absolute median difference between CPRAs using the two sets of ethnic weights was Native Hawaiian/other Pacific Islander, with an absolute median difference of 0.17%.

Figure 2: Distribution of Difference between CPRA Using Lung Weights vs All Deceased Donor Weights by Ethnicity

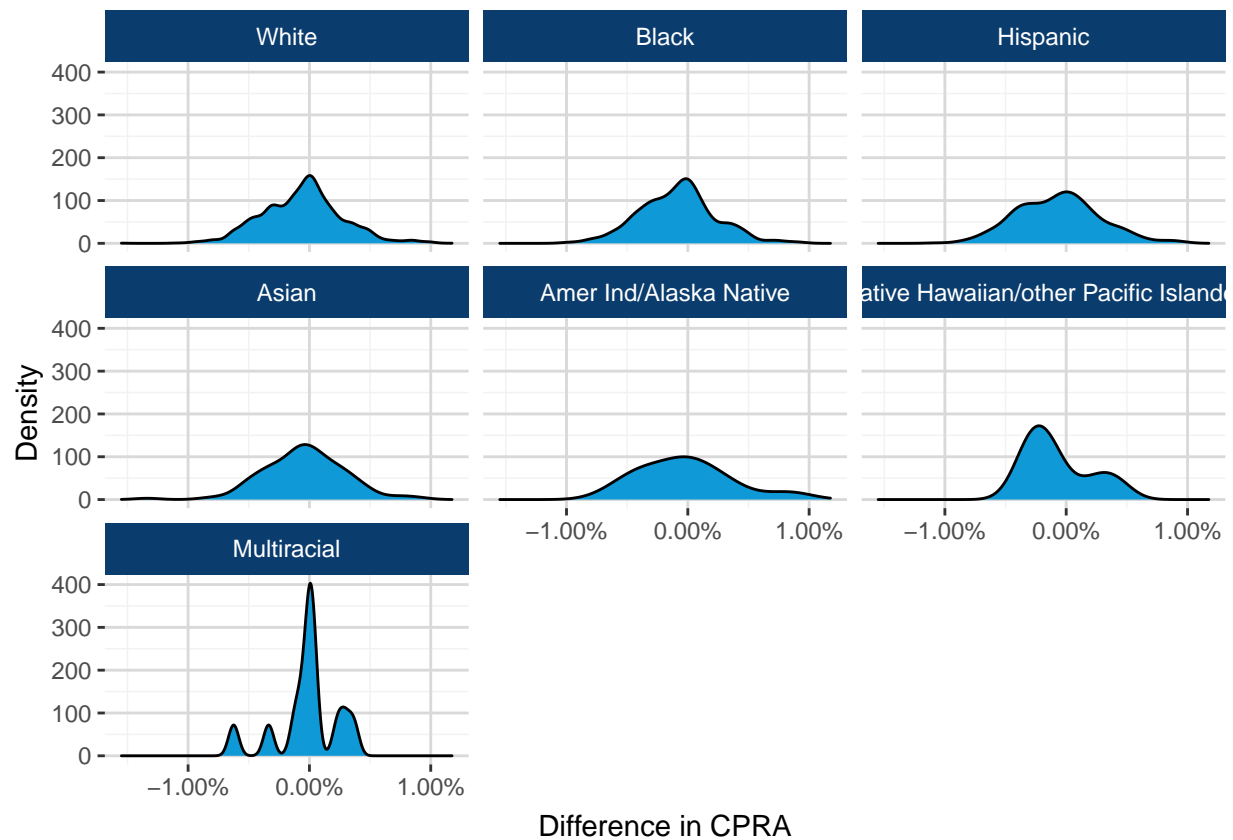


Table 5: Distribution of Difference between CPRA with Lung Donor Weights and All Deceased Donor Weights by Ethnicity

Ethnicity	Min	25th Percentile	Mean	Median	75th Percentile	Max
White	-1.55%	-0.28%	-0.06%	-0.04%	0.13%	1.18%
Black	-1.01%	-0.30%	-0.08%	-0.07%	0.09%	0.93%
Hispanic	-1.07%	-0.33%	-0.07%	-0.05%	0.14%	0.98%
Asian	-1.34%	-0.26%	-0.04%	-0.04%	0.16%	0.91%
Amer Ind/Alaska Native	-0.62%	-0.33%	-0.02%	-0.02%	0.21%	0.88%
Native Hawaiian/other Pacific Islander	-0.36%	-0.27%	-0.08%	-0.17%	0.05%	0.43%
Multiracial	-0.62%	-0.07%	-0.02%	0.00%	0.03%	0.37%

Table 6: Change in Number of Registrations with CPRA  $\geq$  95, Lung Donor Weights vs All Deceased Donor Weights

	<b>Registrations with Current CPRA <math>\geq</math> 95</b>	<b>Registrations Increasing to CPRA <math>\geq</math> 95</b>	<b>Registrations Falling Below CPRA 95</b>	<b>Net Change</b>	<b>Percent Change</b>
All DD CPRA	120	16	13	3	2.50%
Lung CPRA	120	15	13	2	1.67%

Table 6 shows the count and percent of lung registrations that would either rise to or fall below 95% CPRA, based on the current kidney allocation definition of CPRA, under the proposed sets of ethnic weights. For either set of ethnic weights the number of registrations falling below 95% CPRA is nearly equal to the number of registrations rising to at least 95%, resulting in a small increase in the number of registrations with at least 95% CPRA overall.

Table 7 shows the count and percent of lung registrations that would either rise to or fall below 95% CPRA stratified by ethnicity. Only the White, Black, and Multiracial categories showed any net change in the number of registrations with CPRA 95% or greater under either set of ethnic weights. The number of White and Black registrations with CPRA 95% or greater increased slightly under both sets of ethnic weights, while the number of Multiracial registrations decreased slightly under both sets of ethnic weights. The only difference between the lung-specific weights and all-deceased-donor weights was a single White registration that would rise to a CPRA of 95% or greater under the all-deceased-donor weights that would not be assigned that high a level of sensitization under the lung-specific weights.

Table 7: Change in Number of Registrations with CPRA  $\geq 95$ , Lung Donor Weights vs All Deceased Donor Weights by Ethnicity

		Registrations with Current CPRA $\geq 95$	Registrations Increasing to CPRA $\geq 95$	Registrations Falling Below CPRA 95	Net Change	Percent Change
White	All DD CPRA	95	13	11	2	2.11%
	Lung CPRA	95	12	11	1	1.05%
Black	All DD CPRA	16	2	0	2	12.50%
	Lung CPRA	16	2	0	2	12.50%
Hispanic	All DD CPRA	6	1	1	0	0.00%
	Lung CPRA	6	1	1	0	0.00%
Asian	All DD CPRA	2	0	0	0	0.00%
	Lung CPRA	2	0	0	0	0.00%
Amer Ind/Alaska Native	All DD CPRA	0	0	0	0	0.00%
	Lung CPRA	0	0	0	0	0.00%
Native Hawaiian/other Pacific Islander	All DD CPRA	0	0	0	0	0.00%
	Lung CPRA	0	0	0	0	0.00%
Multiracial	All DD CPRA	1	0	1	-1	-100.00%
	Lung CPRA	1	0	1	-1	-100.00%

Table 8: Change in Number of Registrations with CPRA = 100, Lung Donor Weights vs All Deceased Donor Weights

	Registrations with Current CPRA $\geq$ 100	Registrations Increasing to CPRA $\geq$ 100	Registrations Falling Below CPRA 100	Net Change	Percent Change
All DD CPRA	24	4	5	-1	-4.17%
Lung CPRA	24	4	5	-1	-4.17%

Table 8 shows the count and percent of lung registrations that would either rise to or fall below 100% CPRA, based on the current kidney allocation definition of CPRA, under the proposed sets of ethnic weights. There were very few candidates reported with a 100% CPRA between January 01, 2010 and June 30, 2021, and few registrations would see their CPRA increase to 100% under either set of ethnic weights. Ultimately, whichever set of ethnic weights was used, the overall number of lung registrations with a CPRA of 100% would decrease by one under the proposed CPRA calculation.

Table 9 shows the count and percent of lung registrations that would either rise to or fall below 100% CPRA stratified by ethnicity. All registrations with 100% CPRA were either White or Black regardless of which set of ethnic weights was used, and the impact on the number of registrations in this classification was slight under either set of ethnic weights. The number of White candidates with 100% CPRA decreased slightly under the proposed calculation, while the number of Black registrations with 100% CPRA increased slightly.

Table 9: Change in Number of Registrations with CPRA = 100, Lung Donor Weights vs All Deceased Donor Weights by Ethnicity

		Registrations with Current CPRA $\geq 100$	Registrations Increasing to CPRA $\geq 100$	Registrations Falling Below CPRA 100	Net Change	Percent Change
White	All DD CPRA	19	3	5	-2	-10.53%
	Lung CPRA	19	3	5	-2	-10.53%
Black	All DD CPRA	5	1	0	1	20.00%
	Lung CPRA	5	1	0	1	20.00%
Hispanic	All DD CPRA	0	0	0	0	0.00%
	Lung CPRA	0	0	0	0	0.00%
Asian	All DD CPRA	0	0	0	0	0.00%
	Lung CPRA	0	0	0	0	0.00%
Amer Ind/Alaska Native	All DD CPRA	0	0	0	0	0.00%
	Lung CPRA	0	0	0	0	0.00%
Native Hawaiian/other Pacific Islander	All DD CPRA	0	0	0	0	0.00%
	Lung CPRA	0	0	0	0	0.00%
Multiracial	All DD CPRA	0	0	0	0	0.00%
	Lung CPRA	0	0	0	0	0.00%

## Conclusion

There is little difference between a CPRA using lung-specific ethnic weights and a CPRA using ethnic weights based on all deceased donors. The maximum difference in CPRA between metrics using these two different sets of weights was 1.55%, and for the majority of lung registrations the difference was less than 0.1%. The difference between the CPRA metrics was similar across all ethnicities. Even among highly-sensitized lung registrations, there would be little impact as a result of using a CPRA with ethnic weights based on all deceased donors instead of a CPRA with ethnic weights based on deceased lung donors.