Final Report

OPTN Histocompatibility Meeting | Descriptive Data Request

# Impact of Changing the CPRA Calculation to a Genotype-Based, Stem Cell Donor-Derived Metric

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## Background/Purpose

The OPTN CPRA calculator uses data derived from a cohort of deceased kidney donors recovered from January 1, 2007 – December 31, 2008 and lacks frequencies for many of the unacceptable antigen values that can now be entered for waiting list candidates. The Histocompatibility Committee wishes to revise the CPRA calculator by replacing the existing frequency data with frequencies derived from over two million stem cell donors, replacing the current haplotype frequency calculation with a less computationally-intensive genotype calculation similar to the calculation used by the Canadian CPRA calculator[1], and adding DPB1, DQA1, and DPA1 to the loci used when calculating the CPRA. Additionally, the much larger stem cell donor cohort would allow for the inclusion of ethnic groups with too few representatives in OPTN donor data to calculate accurate donor HLA frequencies. The expansion of the number of ethnic groups used in the CPRA calculation from four to seven is another potential enhancement that could be made during this revision of the CPRA calculator.

After an initial review of data in July 2021, the Committee determined that CPRA metrics based on stem cell donor data collected at the antigen recognition domain (ARD) level would not be sufficient for the Committee's needs. These metrics included many values that can be selected separately in UNet (such as C*02:02 and C*02:10) but could not be distinguished in the stem cell donor data, with the result that they were assigned the same CPRA value. In cases where a common allele and a rare allele could not be distinguished, the two would often share a high CPRA value, sometimes in excess of 40%, even though the rare allele is found in only a small percentage of donors and therefore has a minimal impact on a candidate's access to transplant. In order to address this issue, the Committee requested a reanalysis using a new extract of the stem cell donor data collected at the extracellular domain (ECD) level. This dataset allows many, but not all, of these alleles to be distinguished. Based on their review of the ARD-based CPRA metrics, the Committee determined that a CPRA incorporating seven ethnic groups would be preferable to one incorporating four ethnic groups, and the ECD CPRA was therefore calculated only for seven ethnic groups.

This report investigates how many waiting list candidates would be impacted by a shift from a solid organ donor-derived CPRA to a stem cell donor-derived CPRA and how their allocation priority would change as a result. The Committee also believed that the revised CPRA would more accurately reflect candidates' true level of sensitization by including unacceptable antigen values that lack frequencies under the current calculation, and this report compares the correlation between the existing and proposed CPRA metrics and measures of access to transplant. Finally, this report compares a stem cell donor-derived CPRA incorporating four ethnic groups to one that incorporates seven ethnic groups to determine whether expanding the CPRA calculation to include all ethnic groups collected by the OPTN would be appropriate.

## Strategic Plan Goal or Committee Project Addressed

Change CPRA Calculation

## Committee Request

- Count and percent of candidates in a recent kidney waiting list cohort whose CPRA would change under the proposed calculation
- Distribution of the change in CPRA for a recent kidney waiting list cohort under the proposed calculation
- Count and percent of candidates in a recent kidney waiting list cohort who would change allocation category under the proposed calculation
- The correlation between offer rate and CPRA both under the existing and the proposed CPRA calculation for a recent kidney waiting list cohort
- The correlation between transplant rate and CPRA both under the existing and the proposed CPRA calculation for a recent kidney waiting list cohort

[1]Tinckam, K. J., R. Liwski, D. Pochinco, M. Mousseau, A. Grattan, P. Nickerson, and P. Campbell. "cPRA increases with DQA, DPA, and DPB unacceptable antigens in the Canadian cPRA calculator." *American Journal of Transplantation* 15, no. 12 (2015): 3194-3201.

## Methods

This report compares four CPRA metrics: the current CPRA; two stem cell donor-derived CPRA metrics based on an ARD-level dataset using either four or seven donor ethnic groups, respectively; and a stem cell donor-derived CPRA metric based on ECD-level data. These are referred to as the Current (solid organ donor), 4 Group (stem cell ARD with four ethnic groups), 7 Group (stem cell ARD with seven ethnic groups), and 7 Group Recalc (stem cell ECD with seven ethnic groups) metrics, respectively.

Waiting list analyses were based on a snapshot of the kidney waiting list as of December 31st, 2020. This comprised 98455 kidney registrations, of which 41880 had any unacceptable antigens.

Analyses examining how well the four metrics predict offer and transplant rates were based on unacceptable antigen and offer data for all kidney candidates ever waiting between January 1st, 2018 and December 31st, 2020. Within each kidney CPRA allocation category Poisson models predicting offer rate or transplant rate were fit based on wait time and each of the four metrics. Model fits were evaluated based on the Akaike information criterion (AIC), with lower AIC indicating that the model better described the data.

To determine how well the four metrics predicted the actual proportion of incompatible kidney donors, the unacceptable antigens for 41880 kidney registrations waiting on December 31st, 2020 were compared to a cohort of 23077 deceased kidney donors recovered between January 1st, 2019 and December 31st, 2020. Compatibility of these donors with the registrations in the waiting list cohort was determined based on the OPTN unacceptable antigen equivalency tables as of June 25th, 2021. The "observed" CPRA for each registration was calculated as the number of incompatible donors out of the total number of deceased kidney donors in the cohort. How well each of the three metrics predicted this observed CPRA was determined based on the root mean square error (RMSE) of the calculated metric compared to the observed CPRA on the assumption that a perfect CPRA metric would exactly match the observed proportion of incompatible donors.

For all analyses, the proposed CPRA metrics were calculated by Dr. Loren Gragert based on data from stem cell donors. For the four-group metric, the calculation used frequencies from donors categorized into one of the four ethnic groups included in the current OPTN CPRA calculation: Black, White, Hispanic, or Asian. The seven-group metrics incorporated these four ethnic groups plus stem cell donors classified as one of American Indian/Alaska Native, Native Hawaiian/other Pacific Islander, or Multiracial. All analyses are based on OPTN data as of December 31, 2021 and are subject to change based on future data submission or correction.

**Note:** The 7 Group Recalc metric (stem cell ECD with seven ethnic groups) is the primary candidate for implementation and is still undergoing validation and testing. While it is unlikely that any major errors will be discovered with further analysis, minor changes to the calculation may occur. These are expected to have only very slight impacts on the CPRA metric, but the Committee will be informed of any subsequent updates and may choose not to go forward with this metric if revisions change the conclusions from any of these analyses.

# Results

## Change in CPRA for Waiting List Registrations

Table 1: Count and Percent of Registrations that Change CPRA Under the Proposed Metrics

| | N | CPRA Change, 4 Ethnic Groups | Percent with CPRA Change, 4 Ethnic Groups | CPRA Change, 7 Ethnic Groups | Percent with CPRA Change, 7 Ethnic Groups | CPRA Change, 7 Groups Recalc | Percent with CPRA Change, 7 Groups Recalc |
|---|---|---|---|---|---|---|---|
| Overall | 98455 | 41835 | 42.49% | 41835 | 42.49% | 41880 | 42.54% |
| Registrations w/UAs | 41880 | 41835 | 99.89% | 41835 | 99.89% | 41880 | 100.00% |

Table 1 shows the count and percent of registrations that experienced a change in CPRA under the proposed metrics. Nearly all registrations with any unacceptable antigens on the waiting list on December 31, 2020 experienced some CPRA change under the proposed metrics; under the recalculated stem cell metric, 100% of candidates with unacceptable antigens experienced some change in CPRA. Ultimately, around 40% of all registrations in the cohort experienced a change in CPRA under the proposed metrics.

Tables 2-5 show the count and percent of registrations that changed CPRA under the proposed metrics stratified by ethnicity, pediatric or adult, region, and whether or not the registration had any unacceptable antigens without a frequency under the current CPRA metric, respectively. In all cases, nearly 100% of registrations with any unacceptable antigens changed CPRA under the proposed metrics. There is greater variability in the total proportion of each waiting list group that changed CPRA under the proposed metrics. This reflects how likely different waiting list groups are to be sensitized rather than resulting from the properties of the proposed CPRA metrics. For example, fewer pediatric candidates have unacceptable antigens than adult candidates, and therefore a lower proportion of registrations for pediatric candidates than adult candidates changed CPRA under the proposed metrics.

There was no meaningful difference in the number of registrations to change CPRA under the proposed metric with four ethnic groups relative to the proposed metrics with seven ethnic groups for any condition examined here.

Table 2: Count and Percent of Registrations that Change CPRA Under the Proposed Metrics by Ethnicity

| | | N | CPRA Change, 4 Ethnic Groups | Percent with CPRA Change, 4 Ethnic Groups | CPRA Change, 7 Ethnic Groups | Percent with CPRA Change, 7 Ethnic Groups | CPRA Change, 7 Groups Recalc | Percent with CPRA Change, 7 Groups Recalc |
|---|---|---|---|---|---|---|---|---|
| White | Overall | 34674 | 13047 | 37.63% | 13047 | 37.63% | 13068 | 37.69% |
| | Registrations w/UAs | 13068 | 13047 | 99.84% | 13047 | 99.84% | 13068 | 100.00% |
| Black | Overall | 31351 | 16272 | 51.90% | 16272 | 51.90% | 16286 | 51.95% |
| | Registrations w/UAs | 16286 | 16272 | 99.91% | 16272 | 99.91% | 16286 | 100.00% |
| Hispanic | Overall | 20837 | 7971 | 38.25% | 7971 | 38.25% | 7978 | 38.29% |
| | Registrations w/UAs | 7978 | 7971 | 99.91% | 7971 | 99.91% | 7978 | 100.00% |
| Asian | Overall | 9094 | 3453 | 37.97% | 3453 | 37.97% | 3455 | 37.99% |
| | Registrations w/UAs | 3455 | 3453 | 99.94% | 3453 | 99.94% | 3455 | 100.00% |
| Amer Ind/AK Native | Overall | 842 | 371 | 44.06% | 371 | 44.06% | 371 | 44.06% |
| | Registrations w/UAs | 371 | 371 | 100.00% | 371 | 100.00% | 371 | 100.00% |
| Native HI/other PI | Overall | 584 | 259 | 44.35% | 259 | 44.35% | 259 | 44.35% |
| | Registrations w/UAs | 259 | 259 | 100.00% | 259 | 100.00% | 259 | 100.00% |
| Multiracial | Overall | 1073 | 462 | 43.06% | 462 | 43.06% | 463 | 43.15% |
| | Registrations w/UAs | 463 | 462 | 99.78% | 462 | 99.78% | 463 | 100.00% |

Table 3: Count and Percent of Registrations that Change CPRA Under the Proposed Metrics by Pediatric vs Adult

| | | N | CPRA Change, 4 Ethnic Groups | Percent with CPRA Change, 4 Ethnic Groups | CPRA Change, 7 Ethnic Groups | Percent with CPRA Change, 7 Ethnic Groups | CPRA Change, 7 Groups Recalc | Percent with CPRA Change, 7 Groups Recalc |
|---|---|---|---|---|---|---|---|---|
| Adult | Overall | 97351 | 41446 | 42.57% | 41446 | 42.57% | 41490 | 42.62% |
| | Registrations w/UAs | 41490 | 41446 | 99.89% | 41446 | 99.89% | 41490 | 100.00% |
| Pediatric | Overall | 1104 | 389 | 35.24% | 389 | 35.24% | 390 | 35.33% |
| | Registrations w/UAs | 390 | 389 | 99.74% | 389 | 99.74% | 390 | 100.00% |

Table 4: Count and Percent of Registrations that Change CPRA Under the Proposed Metrics by Region

| | | N | CPRA Change, 4 Ethnic Groups | Percent with CPRA Change, 4 Ethnic Groups | CPRA Change, 7 Ethnic Groups | Percent with CPRA Change, 7 Ethnic Groups | CPRA Change, 7 Groups Recalc | Percent with CPRA Change, 7 Groups Recalc |
|---|---|---|---|---|---|---|---|---|
| 1 | Overall | 4809 | 1177 | 24.47% | 1177 | 24.47% | 1178 | 24.50% |
| | Registrations w/UAs | 1178 | 1177 | 99.92% | 1177 | 99.92% | 1178 | 100.00% |
| 2 | Overall | 12495 | 5566 | 44.55% | 5566 | 44.55% | 5573 | 44.60% |
| | Registrations w/UAs | 5573 | 5566 | 99.87% | 5566 | 99.87% | 5573 | 100.00% |
| 3 | Overall | 12824 | 6904 | 53.84% | 6904 | 53.84% | 6909 | 53.88% |
| | Registrations w/UAs | 6909 | 6904 | 99.93% | 6904 | 99.93% | 6909 | 100.00% |
| 4 | Overall | 10377 | 4789 | 46.15% | 4789 | 46.15% | 4791 | 46.17% |
| | Registrations w/UAs | 4791 | 4789 | 99.96% | 4789 | 99.96% | 4791 | 100.00% |
| 5 | Overall | 22256 | 8690 | 39.05% | 8690 | 39.05% | 8703 | 39.10% |
| | Registrations w/UAs | 8703 | 8690 | 99.85% | 8690 | 99.85% | 8703 | 100.00% |
| 6 | Overall | 2500 | 931 | 37.24% | 931 | 37.24% | 931 | 37.24% |
| | Registrations w/UAs | 931 | 931 | 100.00% | 931 | 100.00% | 931 | 100.00% |
| 7 | Overall | 7104 | 2995 | 42.16% | 2995 | 42.16% | 2998 | 42.20% |
| | Registrations w/UAs | 2998 | 2995 | 99.90% | 2995 | 99.90% | 2998 | 100.00% |
| 8 | Overall | 3736 | 1224 | 32.76% | 1224 | 32.76% | 1226 | 32.82% |
| | Registrations w/UAs | 1226 | 1224 | 99.84% | 1224 | 99.84% | 1226 | 100.00% |
| 9 | Overall | 7640 | 2158 | 28.25% | 2158 | 28.25% | 2159 | 28.26% |
| | Registrations w/UAs | 2159 | 2158 | 99.95% | 2158 | 99.95% | 2159 | 100.00% |
| 10 | Overall | 5292 | 2332 | 44.07% | 2332 | 44.07% | 2334 | 44.10% |
| | Registrations w/UAs | 2334 | 2332 | 99.91% | 2332 | 99.91% | 2334 | 100.00% |
| 11 | Overall | 9422 | 5069 | 53.80% | 5069 | 53.80% | 5078 | 53.90% |
| | Registrations w/UAs | 5078 | 5069 | 99.82% | 5069 | 99.82% | 5078 | 100.00% |

Table 5: Count and Percent of Registrations that Change CPRA Under the Proposed Metrics by Presence or Absence of Unacceptable Antigens without Frequencies

| | | N | CPRA Change, 4 Ethnic Groups | Percent with CPRA Change, 4 Ethnic Groups | CPRA Change, 7 Ethnic Groups | Percent with CPRA Change, 7 Ethnic Groups | CPRA Change, 7 Groups Recalc | Percent with CPRA Change, 7 Groups Recalc |
|---|---|---|---|---|---|---|---|---|
| No UAs w/o Freqs | Overall | 21112 | 21112 | 100.00% | 21112 | 100.00% | 21112 | 100.00% |
| | Registrations w/UAs | 21112 | 21112 | 100.00% | 21112 | 100.00% | 21112 | 100.00% |
| UAs w/o Freqs | Overall | 77343 | 20723 | 26.79% | 20723 | 26.79% | 20768 | 26.85% |
| | Registrations w/UAs | 20768 | 20723 | 99.78% | 20723 | 99.78% | 20768 | 100.00% |

Figure 1: Distribution of Change in CPRA Under the Proposed Metrics

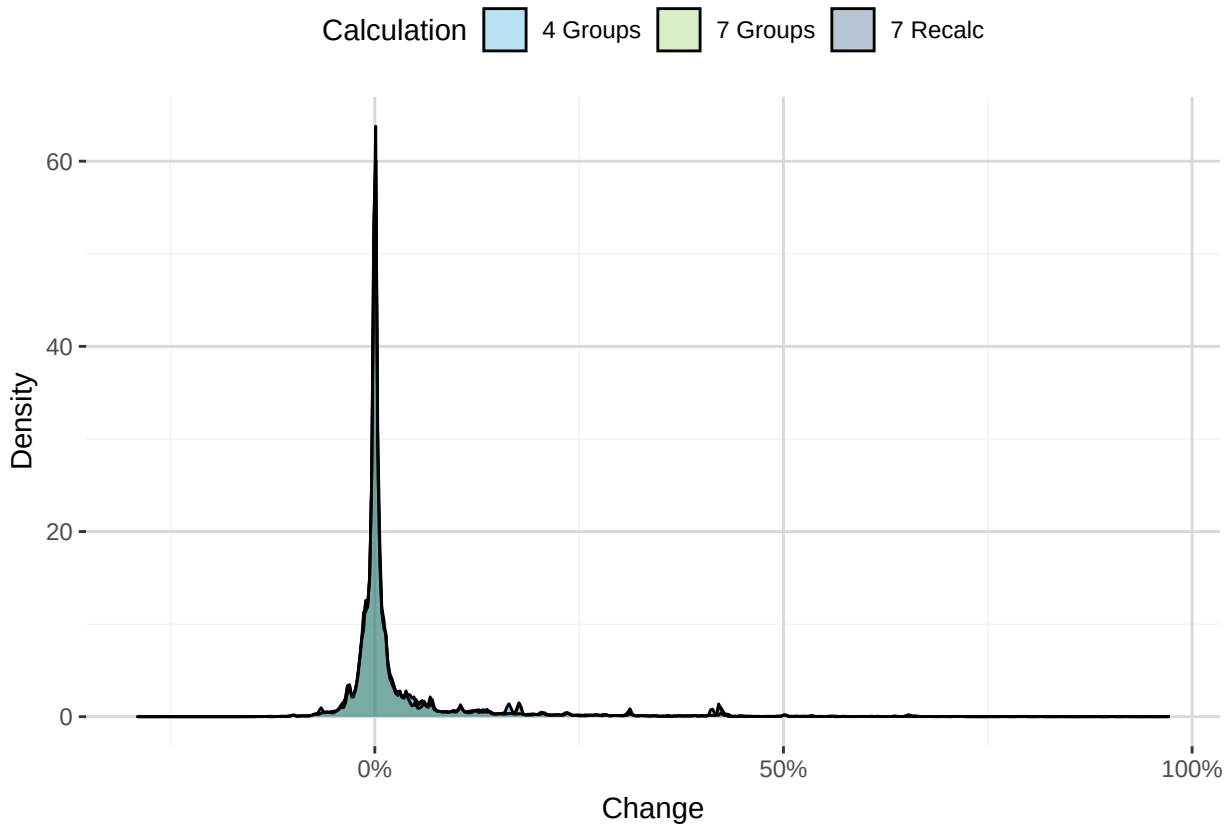


Table 6: Distribution of Change in CPRA Under the Proposed Metrics

| Calculation | N | Min | 25th Percentile | Mean | Median | 75th Percentile | Max |
|---|---|---|---|---|---|---|---|
| 4 Groups | 41880 | -15.47% | -0.34% | 2.80% | 0.04% | 1.36% | 97.12% |
| 7 Groups | 41880 | -15.31% | -0.37% | 2.80% | 0.04% | 1.28% | 97.03% |
| 7 Recalc | 41880 | -29.02% | -0.34% | 2.79% | 0.06% | 1.34% | 94.31% |

Figure 1 and Table 6 show the distribution of the change in CPRA for kidney registrations with any unacceptable antigens waiting on December 31, 2020. The change in CPRA for all registrations without unacceptable antigens was zero.

For the majority of registrations, the change in CPRA was less than 1%. Overall, CPRA tended to increase rather than decrease, which is unsurprising given that the proposed metrics added frequencies for alleles and loci not included in the current CPRA. Registrations with any of these previously-excluded values would therefore usually experience an increase in CPRA under the proposed metrics. Figure 5 and Table 10 demonstrate this; registrations without any unacceptable antigens not included in the current CPRA tended to experience a smaller change in CPRA under the new metrics than registrations with any unacceptable antigens lacking frequencies. For those registrations that had no unacceptable antigens without frequencies under the current calculation, it was actually more common for the CPRA to decrease than it was for the CPRA to increase under the proposed metrics.

Registrations experiencing a large increase in CPRA were usually those with a large number of unacceptable antigens that had no frequencies under the current calculation. These registrations typically had close to 0% CPRA under the current calculation, and in some cases their CPRA increased by over 90% under the new metrics. On the other hand, large decreases in CPRA were usually the result of differences in unacceptable antigen equivalences used under the proposed metrics vs the current metrics. The equivalences used by the new metrics involved the

removal of some broad antigen equivalents, with the result that antigens or alleles previously equivalent to a broad antigen experienced a decrease in CPRA. These changes to equivalences are included in the 2021 approved updates to the HLA equivalency tables in OPTN policy;and since these changes are approved, then these large drops in CPRA would not be seen at the time that a new CPRA metric was implemented, as affected registrations would already have experienced CPRA adjustments as a result of the updates to the OPTN HLA equivalency tables.

Figures 2-4 and tables 7-9 show the distribution of the change in CPRA for kidney registrations with any unacceptable antigens that were waiting on December 31, 2020 stratified by ethnicity, pediatric vs adult, and region. Similar patterns were seen regardless of how registrations were stratified: most registrations saw a slight increase in CPRA, with a few seeing a large increase as the result of the addition of frequencies to alleles and loci not included in the current CPRA and a small number seeing a decrease in CPRA as a result of changes to the equivalency tables. The exception is Region 1 (see Table 9), where the median CPRA decreased slightly rather than increasing. This is likely because Region 1 had the lowest proportion of registrations with any unacceptable antigens without frequencies (14.6%) and the lowest proportion (5.88%) of highly-sensitized (CPRA $>=$ 90%) candidates under the current CPRA metric. Highly-sensitized registrations, usually with a large number of unacceptable antigens, and registrations with large numbers of unacceptable antigens without frequencies in the current CPRA were the most likely to increase CPRA under the proposed metrics, so a low incidence of them could result in more registrations decreasing CPRA than increasing CPRA. The difference between Region 1 and other regions may be explained by listing practices or could reflect a real difference in sensitization levels and the antigens against which candidates in this region tend to become sensitized.

There was little difference between the recalculated seven-ethnicity stem cell metric and the original seven-ethnicity stem cell metric in the majority of cases; however, for some groups, such as pediatric or native Hawaiian/other Pacific islander candidates, the change in CPRA under the recalculated metric could be more than four times as great as the change in CPRA under the seven-ethnicity stem cell ARD metric. The median change in CPRA for these groups remained below 1%, however, and there was overall little difference between the stem cell donor metrics that used seven ethnic groups.

There was no meaningful difference in the distribution of change in CPRA under the proposed metric with four ethnic groups relative to the proposed metrics with seven ethnic groups for any condition examined here. Although Figures 1-5 show the distributions under both of these proposed metrics as well as the recalculated seven-ethnicity stem cell metric, the difference between them is too small to be distinguishable and the distributions appear to completely overlap.

Figure 2: Distribution of Change in CPRA Under the Proposed Metrics by Ethnicity

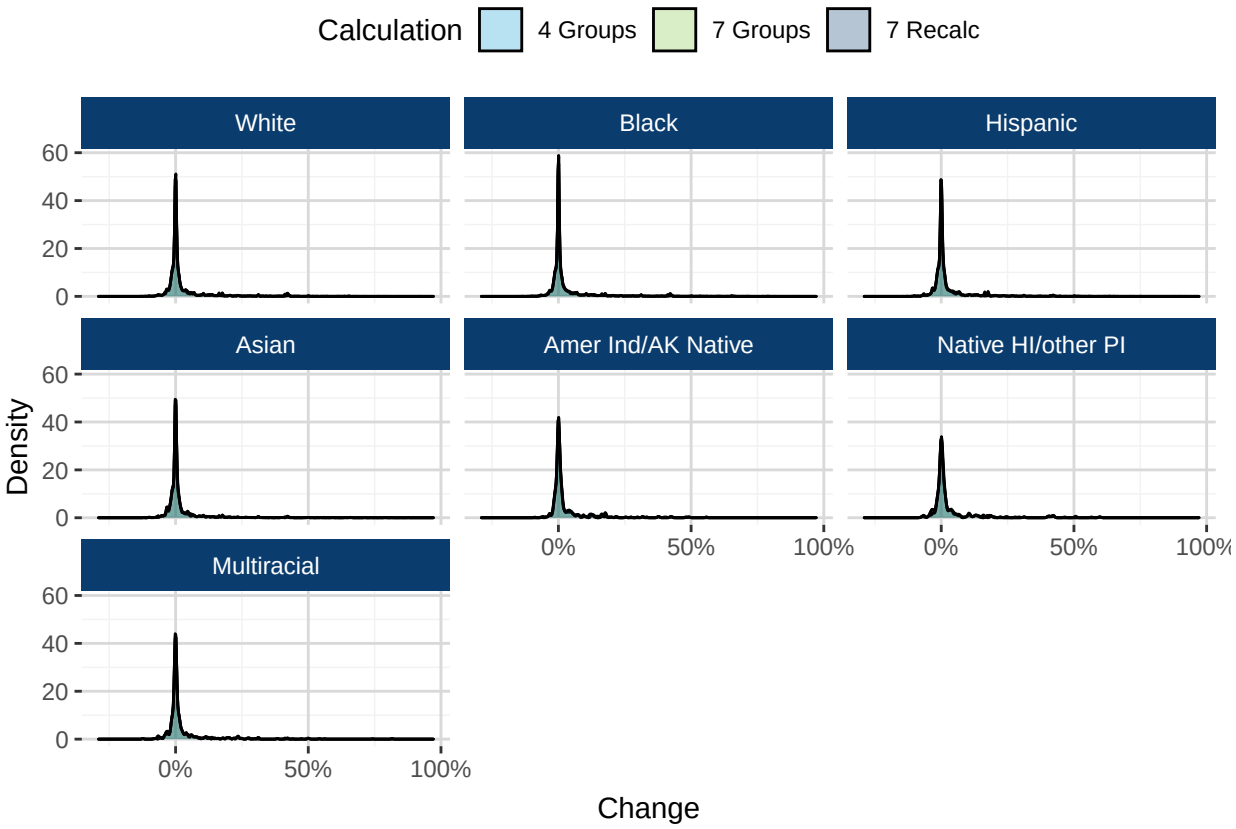

Table 7: Distribution of Change in CPRA Under the Proposed Metrics by Ethnicity

| Ethnicity | Calculation | N | Min | 25th Percentile | Mean | Median | 75th Percentile | Max |
|---|---|---|---|---|---|---|---|---|
| White | 4 Groups | 13068 | -13.71% | -0.39% | 2.86% | 0.04% | 1.36% | 92.29% |
| | 7 Groups | | -13.69% | -0.41% | 2.86% | 0.05% | 1.30% | 92.20% |
| | 7 Recalc | | -13.76% | -0.37% | 2.85% | 0.08% | 1.41% | 90.11% |
| Black | 4 Groups | 16286 | -15.47% | -0.26% | 3.17% | 0.04% | 1.38% | 97.12% |
| | 7 Groups | | -15.31% | -0.31% | 3.16% | 0.04% | 1.37% | 97.03% |
| | 7 Recalc | | -15.41% | -0.30% | 3.06% | 0.06% | 1.43% | 94.31% |
| Hispanic | 4 Groups | 7978 | -14.46% | -0.43% | 2.28% | 0.04% | 1.32% | 91.84% |
| | 7 Groups | | -14.44% | -0.45% | 2.27% | 0.04% | 1.27% | 91.73% |
| | 7 Recalc | | -29.02% | -0.41% | 2.35% | 0.06% | 1.29% | 90.12% |
| Asian | 4 Groups | 3455 | -11.91% | -0.57% | 2.13% | 0.02% | 1.09% | 87.62% |
| | 7 Groups | | -11.80% | -0.54% | 2.12% | 0.02% | 1.09% | 87.61% |
| | 7 Recalc | | -12.01% | -0.45% | 2.22% | 0.04% | 1.11% | 84.96% |
| Amer Ind/AK Native | 4 Groups | 371 | -6.02% | -0.20% | 2.79% | 0.09% | 1.36% | 55.75% |
| | 7 Groups | | -6.16% | -0.24% | 2.77% | 0.09% | 1.28% | 55.81% |
| | 7 Recalc | | -8.90% | -0.17% | 2.76% | 0.27% | 1.58% | 49.18% |
| Native HI/other PI | 4 Groups | 259 | -7.37% | -0.28% | 2.71% | 0.09% | 1.63% | 59.85% |
| | 7 Groups | | -7.28% | -0.37% | 2.70% | 0.08% | 1.62% | 59.80% |
| | 7 Recalc | | -7.47% | -0.19% | 3.47% | 0.30% | 1.75% | 59.53% |
| Multiracial | 4 Groups | 463 | -12.44% | -0.28% | 2.51% | 0.04% | 1.36% | 81.72% |
| | 7 Groups | | -12.37% | -0.37% | 2.49% | 0.04% | 1.36% | 81.44% |
| | 7 Recalc | | -12.14% | -0.28% | 2.52% | 0.05% | 1.41% | 74.26% |

Figure 3: Distribution of Change in CPRA Under the Proposed Metrics by Pediatric vs Adult

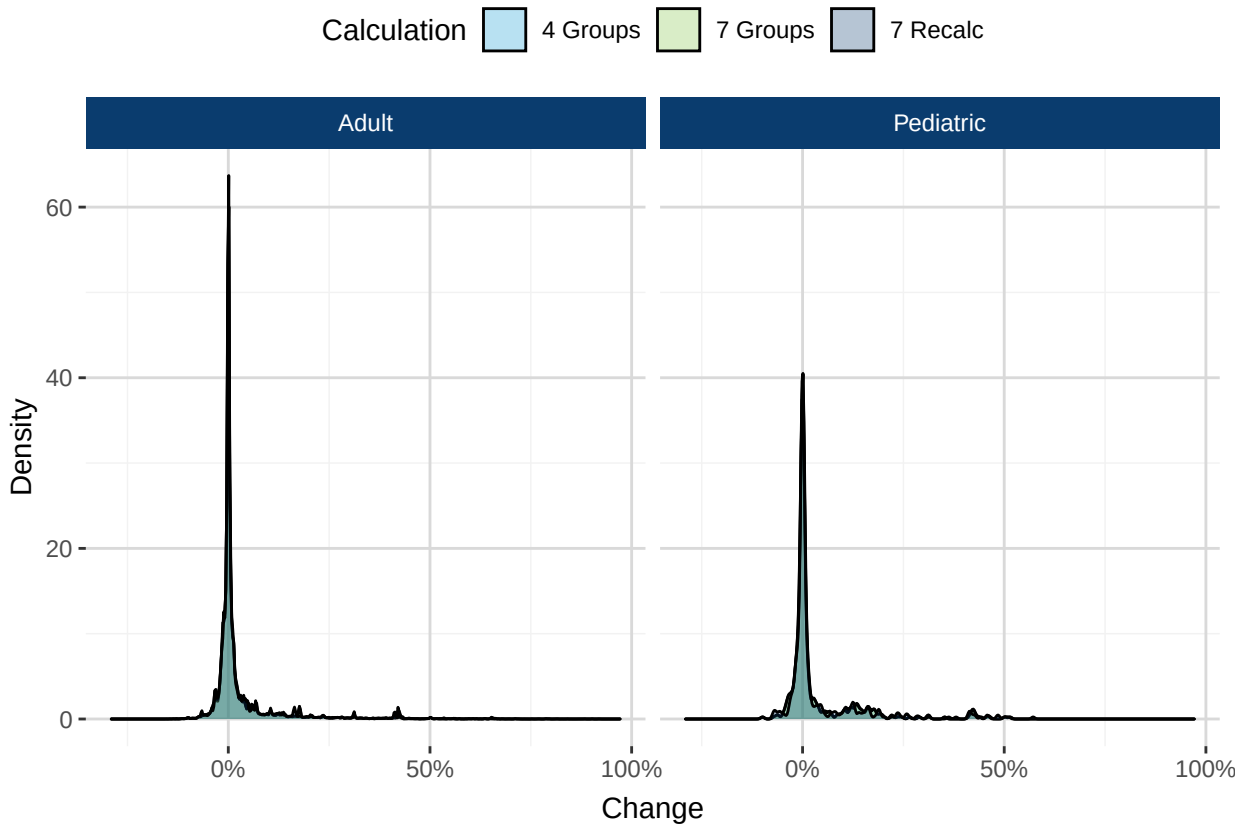


Table 8: Distribution of Change in CPRA Under the Proposed Metrics by Pediatric vs Adult

| Age Group | Calculation | N | Min | 25th Percentile | Mean | Median | 75th Percentile | Max |
|---|---|---|---|---|---|---|---|---|
| Adult | 4 Groups | 41490 | -15.47% | -0.34% | 2.80% | 0.04% | 1.36% | 97.12% |
| | 7 Groups | | -15.31% | -0.37% | 2.79% | 0.04% | 1.28% | 97.03% |
| | 7 Recalc | | -29.02% | -0.34% | 2.77% | 0.06% | 1.33% | 94.31% |
| Pediatric | 4 Groups | 390 | -10.03% | -0.26% | 3.64% | 0.04% | 1.83% | 51.46% |
| | 7 Groups | | -9.90% | -0.28% | 3.63% | 0.05% | 1.64% | 51.47% |
| | 7 Recalc | | -9.89% | -0.28% | 4.02% | 0.12% | 1.65% | 57.16% |

Figure 4: Distribution of Change in CPRA Under the Proposed Metrics by Region

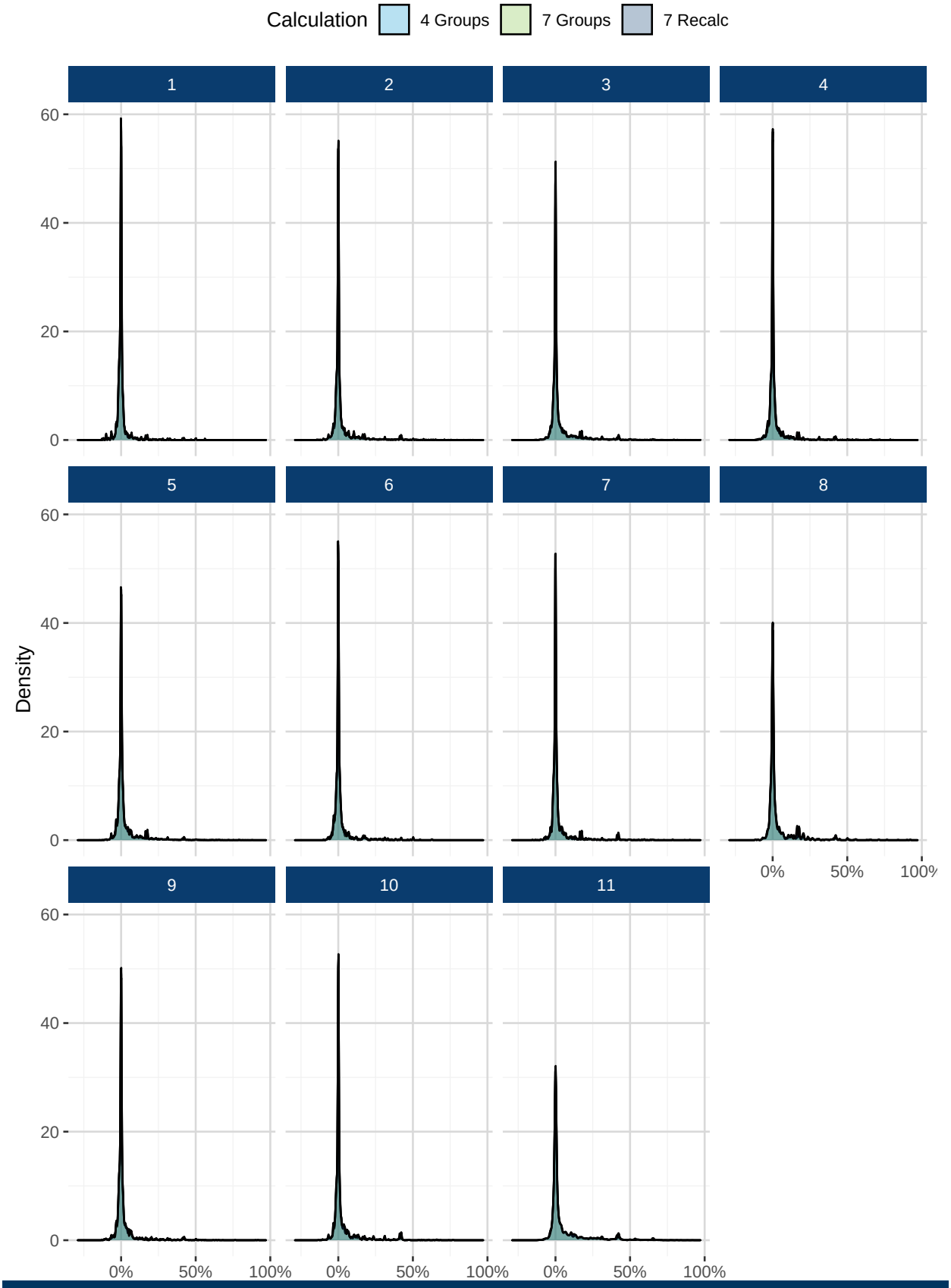

Table 9: Distribution of Change in CPRA Under the Proposed Metrics by Region

| Region | Calculation | N | Min | 25th Percentile | Mean | Median | 75th Percentile | Max |
|---|---|---|---|---|---|---|---|---|
| 1 | 4 Groups | 1178 | -11.91% | -0.78% | 0.56% | -0.05% | 0.32% | 50.13% |
| | 7 Groups | | -11.80% | -0.79% | 0.55% | -0.05% | 0.28% | 50.18% |
| | 7 Recalc | | -12.82% | -0.76% | 0.63% | -0.02% | 0.39% | 56.28% |
| 2 | 4 Groups | 5573 | -14.44% | -0.44% | 2.42% | 0.02% | 1.04% | 90.24% |
| | 7 Groups | | -14.51% | -0.44% | 2.42% | 0.02% | 1.04% | 90.12% |
| | 7 Recalc | | -14.39% | -0.44% | 2.40% | 0.03% | 1.03% | 87.13% |
| 3 | 4 Groups | 6909 | -13.86% | -0.22% | 3.39% | 0.07% | 1.83% | 97.12% |
| | 7 Groups | | -13.72% | -0.27% | 3.38% | 0.07% | 1.77% | 97.03% |
| | 7 Recalc | | -14.86% | -0.28% | 3.29% | 0.08% | 1.95% | 94.31% |
| 4 | 4 Groups | 4791 | -10.78% | -0.38% | 1.92% | 0.02% | 1.02% | 80.79% |
| | 7 Groups | | -10.75% | -0.38% | 1.91% | 0.02% | 1.00% | 80.51% |
| | 7 Recalc | | -29.02% | -0.40% | 1.78% | 0.03% | 0.95% | 71.88% |
| 5 | 4 Groups | 8703 | -14.46% | -0.50% | 2.38% | 0.04% | 1.36% | 88.16% |
| | 7 Groups | | -14.44% | -0.49% | 2.37% | 0.04% | 1.29% | 87.99% |
| | 7 Recalc | | -12.88% | -0.41% | 2.57% | 0.08% | 1.36% | 84.96% |
| 6 | 4 Groups | 931 | -8.01% | -0.38% | 1.61% | 0.01% | 0.91% | 62.78% |
| | 7 Groups | | -8.00% | -0.38% | 1.60% | 0.01% | 0.89% | 62.68% |
| | 7 Recalc | | -9.79% | -0.41% | 1.69% | 0.02% | 0.97% | 62.88% |
| 7 | 4 Groups | 2998 | -15.47% | -0.38% | 2.27% | 0.03% | 0.99% | 90.17% |
| | 7 Groups | | -15.31% | -0.39% | 2.26% | 0.03% | 0.98% | 90.03% |
| | 7 Recalc | | -15.41% | -0.37% | 2.28% | 0.05% | 1.04% | 86.62% |
| 8 | 4 Groups | 1226 | -11.58% | -0.26% | 3.38% | 0.09% | 1.94% | 92.29% |
| | 7 Groups | | -11.52% | -0.30% | 3.38% | 0.08% | 1.94% | 92.20% |
| | 7 Recalc | | -11.33% | -0.28% | 3.42% | 0.12% | 1.99% | 90.11% |
| 9 | 4 Groups | 2159 | -11.58% | -0.63% | 1.66% | 0.01% | 0.84% | 91.84% |
| | 7 Groups | | -11.52% | -0.63% | 1.66% | 0.01% | 0.85% | 91.73% |
| | 7 Recalc | | -12.83% | -0.60% | 1.69% | 0.01% | 0.91% | 90.12% |
| 10 | 4 Groups | 2334 | -13.42% | -0.29% | 2.78% | 0.04% | 1.31% | 76.91% |
| | 7 Groups | | -13.25% | -0.37% | 2.77% | 0.04% | 1.27% | 76.81% |
| | 7 Recalc | | -13.17% | -0.31% | 2.72% | 0.06% | 1.40% | 77.07% |
| 11 | 4 Groups | 5078 | -11.51% | -0.15% | 5.42% | 0.19% | 3.80% | 91.79% |
| | 7 Groups | | -11.49% | -0.12% | 5.41% | 0.18% | 3.81% | 91.81% |
| | 7 Recalc | | -11.50% | -0.09% | 5.18% | 0.29% | 4.07% | 84.11% |

Figure 5: Distribution of Change in CPRA Under the Proposed Metrics by by Presence or Absence of Unacceptable Antigens without Frequencies

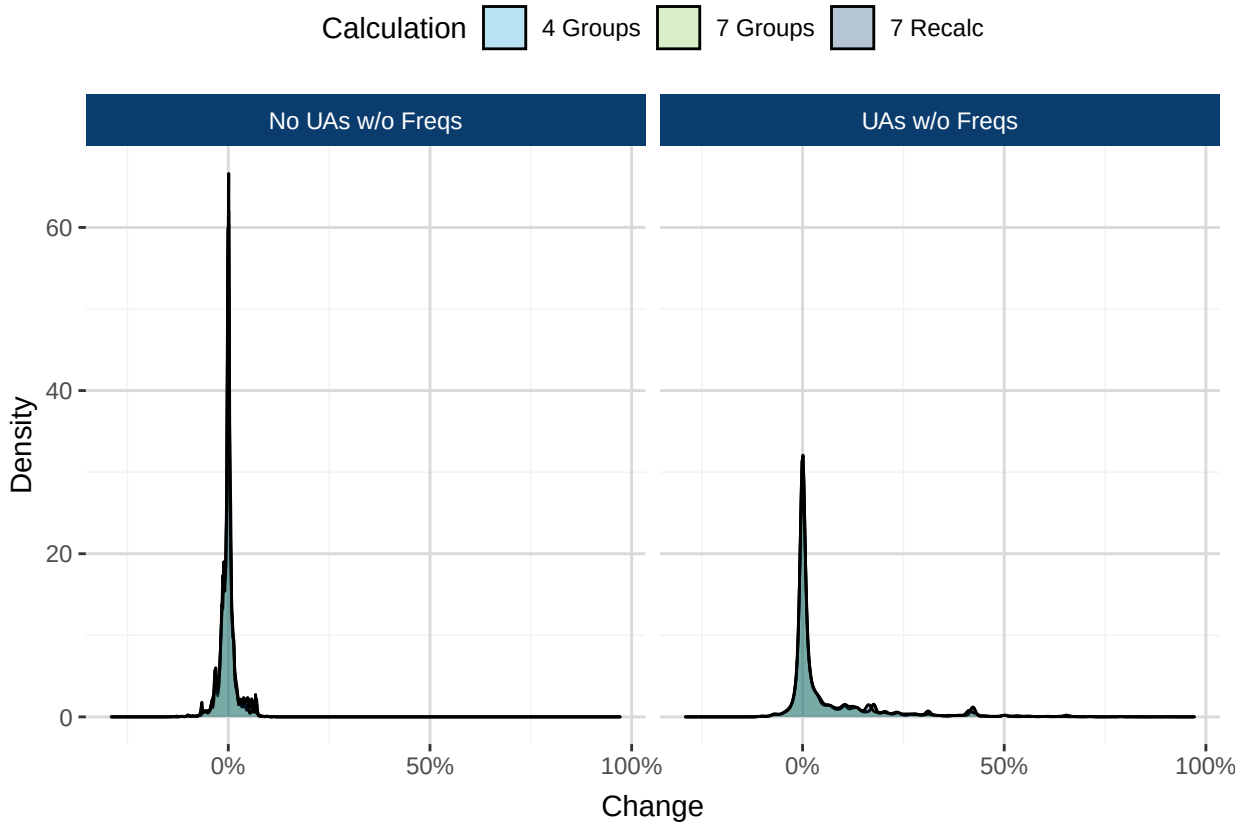


Table 10: Distribution of Change in CPRA for Candidates with Unacceptable Antigens by Presence or Absence of Unacceptable Antigens without Frequencies

| Frequency Status | Calculation | N | Min | 25th Percentile | Mean | Median | 75th Percentile | Max |
|---|---|---|---|---|---|---|---|---|
| No UAs w/o Freqs | 4 Groups | 21112 | -15.47% | -0.95% | -0.09% | -0.06% | 0.43% | 11.36% |
| | 7 Groups | | -15.31% | -0.93% | -0.10% | -0.03% | 0.42% | 11.49% |
| | 7 Recalc | | -15.41% | -0.91% | -0.13% | -0.01% | 0.45% | 11.48% |
| UAs w/o Freqs | 4 Groups | 20768 | -14.44% | -0.04% | 5.74% | 0.27% | 5.45% | 97.12% |
| | 7 Groups | | -14.51% | -0.04% | 5.74% | 0.27% | 5.44% | 97.03% |
| | 7 Recalc | | -29.02% | -0.02% | 5.75% | 0.37% | 6.32% | 94.31% |

Table 11: Count and Percent of Registrations that Change Allocation Priority Under the Proposed Metrics

| | N | Allocation Change, 4 Ethnic Groups | Percent with Allocation Change, 4 Ethnic Groups | Allocation Change, 7 Ethnic Groups | Percent with Allocation Change, 7 Ethnic Groups | Allocation Change, 7 Group Recalc | Percent with Allocation Change, 7 Group Recalc |
|---|---|---|---|---|---|---|---|
| Overall | 98455 | 12173 | 12.36% | 12186 | 12.38% | 12052 | 12.24% |
| Registrations w/UAs | 41880 | 12173 | 29.07% | 12186 | 29.10% | 12052 | 28.78% |

Table 11 shows the count and percent of kidney registrations waiting on December 31, 2020 that changed allocation priority as a result of a change in CPRA under the proposed CPRA metrics. Among registrations with any unacceptable antigens, about 29% changed allocation priority for all of the proposed CPRA metrics. Overall, around 12% of registrations changed allocation priority as a result of a change in CPRA for all of the proposed metrics. Because CPRA was more likely to increase than decrease under the proposed metrics (see Figure 1), the majority of these changes were an increase rather than a decrease in allocation priority.

Tables 12-15 show the count and percent of kidney registrations waiting on December 31 2020 that changed allocation priority as a result of their change in CPRA under the proposed CPRA metrics by ethnicity, adult vs pediatric, region, and whether or not a registration had any unacceptable antigens without a frequency under the current CPRA metric, respectively. Between 13.82% and 44.14% of registrations with unacceptable antigens changed allocation priority, while between 5.09% and 19.33% of of all registrations in any given category changed allocation priority.

There was no meaningful difference in the number of registrations to change allocation priority under the proposed metric with four ethnic groups relative to the proposed metrics with seven ethnic groups for any condition examined here.

Table 12: Count and Percent of Registrations that Change Allocation Priority Under the Proposed Metrics by Ethnicity

| | | N | Allocation Change, 4 Ethnic Groups | Percent with Allocation Change, 4 Ethnic Groups | Allocation Change, 7 Ethnic Groups | Percent with Allocation Change, 7 Ethnic Groups | Allocation Change, 7 Group Recalc | Percent wi Allocation Change, 7 Group Rec |
|---|---|---|---|---|---|---|---|---|
| White | Overall | 34674 | 3866 | 11.15% | 3882 | 11.20% | 3851 | 11.11% |
| | Registrations w/UAs | 13068 | 3866 | 29.58% | 3882 | 29.71% | 3851 | 29.47% |
| Black | Overall | 31351 | 4794 | 15.29% | 4785 | 15.26% | 4740 | 15.12% |
| | Registrations w/UAs | 16286 | 4794 | 29.44% | 4785 | 29.38% | 4740 | 29.10% |
| Hispanic | Overall | 20837 | 2271 | 10.90% | 2274 | 10.91% | 2236 | 10.73% |
| | Registrations w/UAs | 7978 | 2271 | 28.47% | 2274 | 28.50% | 2236 | 28.03% |
| Asian | Overall | 9094 | 922 | 10.14% | 922 | 10.14% | 892 | 9.81% |
| | Registrations w/UAs | 3455 | 922 | 26.69% | 922 | 26.69% | 892 | 25.82% |
| Amer Ind/AK Native | Overall | 842 | 109 | 12.95% | 110 | 13.06% | 113 | 13.42% |
| | Registrations w/UAs | 371 | 109 | 29.38% | 110 | 29.65% | 113 | 30.46% |
| Native HI/other PI | Overall | 584 | 78 | 13.36% | 77 | 13.18% | 79 | 13.53% |
| | Registrations w/UAs | 259 | 78 | 30.12% | 77 | 29.73% | 79 | 30.50% |
| Multiracial | Overall | 1073 | 133 | 12.40% | 136 | 12.67% | 141 | 13.14% |
| | Registrations w/UAs | 463 | 133 | 28.73% | 136 | 29.37% | 141 | 30.45% |

Table 13: Count and Percent of Registrations that Change Allocation Priority Under the Proposed Metrics by Pediatric vs Adult

| | | N | Allocation Change, 4 Ethnic Groups | Percent with Allocation Change, 4 Ethnic Groups | Allocation Change, 7 Ethnic Groups | Percent with Allocation Change, 7 Ethnic Groups | Allocation Change, 7 Group Recalc | Percent with Allocation Change, 7 Group Recalc |
|---|---|---|---|---|---|---|---|---|
| Adult | Overall | 97351 | 12038 | 12.37% | 12049 | 12.38% | 11919 | 12.24% |
| | Registrations w/UAs | 41490 | 12038 | 29.01% | 12049 | 29.04% | 11919 | 28.73% |
| Pediatric | Overall | 1104 | 135 | 12.23% | 137 | 12.41% | 133 | 12.05% |
| | Registrations w/UAs | 390 | 135 | 34.62% | 137 | 35.13% | 133 | 34.10% |

Table 14: Count and Percent of Registrations that Change Allocation Priority Under the Proposed Metrics by Region

| | | N | Allocation Change, 4 Ethnic Groups | Percent with Allocation Change, 4 Ethnic Groups | Allocation Change, 7 Ethnic Groups | Percent with Allocation Change, 7 Ethnic Groups | Allocation Change, 7 Group Recalc | Percent with Allocation Change, 7 Group Recalc |
|---|---|---|---|---|---|---|---|---|
| 1 | Overall | 4809 | 245 | 5.09% | 248 | 5.16% | 251 | 5.22% |
| | Registrations w/UAs | 1178 | 245 | 20.80% | 248 | 21.05% | 251 | 21.31% |
| 2 | Overall | 12495 | 1504 | 12.04% | 1498 | 11.99% | 1498 | 11.99% |
| | Registrations w/UAs | 5573 | 1504 | 26.99% | 1498 | 26.88% | 1498 | 26.88% |
| 3 | Overall | 12824 | 2172 | 16.94% | 2167 | 16.90% | 2151 | 16.77% |
| | Registrations w/UAs | 6909 | 2172 | 31.44% | 2167 | 31.36% | 2151 | 31.13% |
| 4 | Overall | 10377 | 1205 | 11.61% | 1203 | 11.59% | 1156 | 11.14% |
| | Registrations w/UAs | 4791 | 1205 | 25.15% | 1203 | 25.11% | 1156 | 24.13% |
| 5 | Overall | 22256 | 2493 | 11.20% | 2499 | 11.23% | 2465 | 11.08% |
| | Registrations w/UAs | 8703 | 2493 | 28.65% | 2499 | 28.71% | 2465 | 28.32% |
| 6 | Overall | 2500 | 229 | 9.16% | 232 | 9.28% | 231 | 9.24% |
| | Registrations w/UAs | 931 | 229 | 24.60% | 232 | 24.92% | 231 | 24.81% |
| 7 | Overall | 7104 | 786 | 11.06% | 791 | 11.13% | 797 | 11.22% |
| | Registrations w/UAs | 2998 | 786 | 26.22% | 791 | 26.38% | 797 | 26.58% |
| 8 | Overall | 3736 | 424 | 11.35% | 426 | 11.40% | 417 | 11.16% |
| | Registrations w/UAs | 1226 | 424 | 34.58% | 426 | 34.75% | 417 | 34.01% |
| 9 | Overall | 7640 | 593 | 7.76% | 593 | 7.76% | 581 | 7.60% |
| | Registrations w/UAs | 2159 | 593 | 27.47% | 593 | 27.47% | 581 | 26.91% |
| 10 | Overall | 5292 | 708 | 13.38% | 708 | 13.38% | 687 | 12.98% |
| | Registrations w/UAs | 2334 | 708 | 30.33% | 708 | 30.33% | 687 | 29.43% |
| 11 | Overall | 9422 | 1814 | 19.25% | 1821 | 19.33% | 1818 | 19.30% |
| | Registrations w/UAs | 5078 | 1814 | 35.72% | 1821 | 35.86% | 1818 | 35.80% |

Table 15: Count and Percent of Registrations that Change Allocation Priority Under the Proposed Metrics by Presence or Absence of Unacceptable Antigens without Frequencies

| | | N | Allocation Change, 4 Ethnic Groups | Percent with Allocation Change, 4 Ethnic Groups | Allocation Change, 7 Ethnic Groups | Percent with Allocation Change, 7 Ethnic Groups | Allocation Change, 7 Group Recalc | Percent with Allocation Change, 7 Group Recalc |
|---|---|---|---|---|---|---|---|---|
| No UAs w/o Freqs | Overall | 21112 | 3162 | 14.98% | 3189 | 15.11% | 2830 | 13.40% |
| | Registrations w/UAs | 21112 | 3162 | 14.98% | 3189 | 15.11% | 2830 | 13.40% |
| UAs w/o Freqs | Overall | 77343 | 9011 | 11.65% | 8997 | 11.63% | 9222 | 11.92% |
| | Registrations w/UAs | 20768 | 9011 | 43.39% | 8997 | 43.32% | 9222 | 44.40% |

Table 16: Change in Number of Registrations with CPRA >= 95 Under the Proposed Metrics

| | Registrations with CPRA >= 95 | Registrations Increasing to CPRA >= 95 | Registrations Falling Below CPRA 95 | Net Change | Percent Change |
|---|---|---|---|---|---|
| Four Ethnic Groups | 7931 | 650 | 171 | 479 | 6.04% |
| Seven Ethnic Groups | 7931 | 645 | 168 | 477 | 6.01% |
| Seven Groups Recalc | 7931 | 633 | 162 | 471 | 5.94% |

Table 16 shows the count and percent of kidney registrations waiting on December 31, 2020 that would either rise to or fall below 95% CPRA under the proposed metrics. More registrations rose to at least 95% CPRA than fell below that threshold. Overall, the number of registrations with CPRA 95% or greater increased by more than 5% for all of the proposed metrics.

Tables 17-20 show the change in the number of registrations at or above 95% CPRA based on the kidney waiting list as of December 31, 2020 by ethnicity, adult vs pediatric, region, and whether or not a registration had any unacceptable antigens without a frequency under the current CPRA metric, respectively. The number of registrations with CPRA 95% or greater increased by 3-11% for nearly all categories.

As shown in Table 19, the number of registrations with CPRA 95% or greater decreased slightly in Region 1. This is likely due to Region 1's relatively low number of registrations with unacceptable antigens without frequencies and relatively low number of registrations with current CPRA >= 90%, which led to more registrations decreasing CPRA than increasing CPRA under the proposed metrics (Table 9). It is therefore unsurprising that more registrations with CPRA >= 95% under the current metric decreased to a CPRA < 95% under the proposed metrics in Region 1.

There is no meaningful difference in the number of registrations that would have CPRA 95% or above under the proposed metric with four ethnic groups relative to the proposed metrics with seven ethnic groups for any condition examined here.

Table 17: Change in Number of Registrations with CPRA >= 95 Under the Proposed Metrics by Ethnicity

| | | Registrations with CPRA >= 95 | Registrations Increasing to CPRA >= 95 | Registrations Falling Below CPRA 95 | Net Change | Percent Change |
|---|---|---|---|---|---|---|
| White | Four Ethnic Groups | 2118 | 202 | 66 | 136 | 6.42% |
| | Seven Ethnic Groups | 2118 | 200 | 65 | 135 | 6.37% |
| | Seven Groups Recalc | 2118 | 202 | 61 | 141 | 6.66% |
| Black | Four Ethnic Groups | 3747 | 288 | 56 | 232 | 6.19% |
| | Seven Ethnic Groups | 3747 | 286 | 54 | 232 | 6.19% |
| | Seven Groups Recalc | 3747 | 274 | 57 | 217 | 5.79% |
| Hispanic | Four Ethnic Groups | 1265 | 100 | 28 | 72 | 5.69% |
| | Seven Ethnic Groups | 1265 | 98 | 28 | 70 | 5.53% |
| | Seven Groups Recalc | 1265 | 98 | 24 | 74 | 5.85% |
| Asian | Four Ethnic Groups | 586 | 41 | 15 | 26 | 4.44% |
| | Seven Ethnic Groups | 586 | 41 | 15 | 26 | 4.44% |
| | Seven Groups Recalc | 586 | 38 | 14 | 24 | 4.10% |
| Amer Ind/AK Native | Four Ethnic Groups | 70 | 6 | 1 | 5 | 7.14% |
| | Seven Ethnic Groups | 70 | 6 | 1 | 5 | 7.14% |
| | Seven Groups Recalc | 70 | 7 | 1 | 6 | 8.57% |
| Native HI/other PI | Four Ethnic Groups | 47 | 6 | 1 | 5 | 10.64% |
| | Seven Ethnic Groups | 47 | 6 | 1 | 5 | 10.64% |
| | Seven Groups Recalc | 47 | 7 | 1 | 6 | 12.77% |
| Multiracial | Four Ethnic Groups | 98 | 7 | 4 | 3 | 3.06% |
| | Seven Ethnic Groups | 98 | 8 | 4 | 4 | 4.08% |
| | Seven Groups Recalc | 98 | 7 | 4 | 3 | 3.06% |

Table 18: Change in Number of Registrations with CPRA >= 95 Under the Proposed Metrics by Adult vs Pediatric

| | | Registrations with CPRA >= 95 | Registrations Increasing to CPRA >= 95 | Registrations Falling Below CPRA 95 | Net Change | Percent Change |
|---|---|---|---|---|---|---|
| Adult | Four Ethnic Groups | 7860 | 640 | 168 | 472 | 6.01% |
| | Seven Ethnic Groups | 7860 | 635 | 165 | 470 | 5.98% |
| | Seven Groups Recalc | 7860 | 624 | 159 | 465 | 5.92% |
| Pediatric | Four Ethnic Groups | 71 | 10 | 3 | 7 | 9.86% |
| | Seven Ethnic Groups | 71 | 10 | 3 | 7 | 9.86% |
| | Seven Groups Recalc | 71 | 9 | 3 | 6 | 8.45% |

Table 19: Change in Number of Registrations with CPRA >= 95 Under the Proposed Metrics by Region

| | | Registrations with CPRA >= 95 | Registrations Increasing to CPRA >= 95 | Registrations Falling Below CPRA 95 | Net Change | Percent Change |
|---|---|---|---|---|---|---|
| 1 | Four Ethnic Groups | 246 | 5 | 9 | -4 | -1.63% |
| | Seven Ethnic Groups | 246 | 5 | 9 | -4 | -1.63% |
| | Seven Groups Recalc | 246 | 5 | 9 | -4 | -1.63% |
| 2 | Four Ethnic Groups | 1120 | 61 | 24 | 37 | 3.30% |
| | Seven Ethnic Groups | 1120 | 61 | 24 | 37 | 3.30% |
| | Seven Groups Recalc | 1120 | 60 | 23 | 37 | 3.30% |
| 3 | Four Ethnic Groups | 1395 | 128 | 32 | 96 | 6.88% |
| | Seven Ethnic Groups | 1395 | 128 | 31 | 97 | 6.95% |
| | Seven Groups Recalc | 1395 | 128 | 29 | 99 | 7.10% |
| 4 | Four Ethnic Groups | 850 | 53 | 19 | 34 | 4.00% |
| | Seven Ethnic Groups | 850 | 52 | 19 | 33 | 3.88% |
| | Seven Groups Recalc | 850 | 38 | 18 | 20 | 2.35% |
| 5 | Four Ethnic Groups | 1305 | 122 | 34 | 88 | 6.74% |
| | Seven Ethnic Groups | 1305 | 121 | 34 | 87 | 6.67% |
| | Seven Groups Recalc | 1305 | 119 | 32 | 87 | 6.67% |
| 6 | Four Ethnic Groups | 183 | 12 | 0 | 12 | 6.56% |
| | Seven Ethnic Groups | 183 | 12 | 0 | 12 | 6.56% |
| | Seven Groups Recalc | 183 | 14 | 0 | 14 | 7.65% |
| 7 | Four Ethnic Groups | 593 | 42 | 16 | 26 | 4.38% |
| | Seven Ethnic Groups | 593 | 42 | 15 | 27 | 4.55% |
| | Seven Groups Recalc | 593 | 44 | 16 | 28 | 4.72% |
| 8 | Four Ethnic Groups | 281 | 27 | 8 | 19 | 6.76% |
| | Seven Ethnic Groups | 281 | 27 | 8 | 19 | 6.76% |
| | Seven Groups Recalc | 281 | 33 | 9 | 24 | 8.54% |
| 9 | Four Ethnic Groups | 459 | 37 | 9 | 28 | 6.10% |
| | Seven Ethnic Groups | 459 | 36 | 9 | 27 | 5.88% |
| | Seven Groups Recalc | 459 | 37 | 8 | 29 | 6.32% |
| 10 | Four Ethnic Groups | 526 | 46 | 7 | 39 | 7.41% |
| | Seven Ethnic Groups | 526 | 46 | 6 | 40 | 7.60% |
| | Seven Groups Recalc | 526 | 46 | 6 | 40 | 7.60% |
| 11 | Four Ethnic Groups | 973 | 117 | 13 | 104 | 10.69% |
| | Seven Ethnic Groups | 973 | 115 | 13 | 102 | 10.48% |
| | Seven Groups Recalc | 973 | 109 | 12 | 97 | 9.97% |

Table 20: Count and Percent of Registrations with CPRA >= 95 Under the Proposed Metrics by Presence or Absence of Unacceptable Antigens without Frequencies

| | | Registrations with CPRA >= 95 | Registrations Increasing to CPRA >= 95 | Registrations Falling Below CPRA 95 | Net Change | Percent Change |
|---|---|---|---|---|---|---|
| No UAs w/o Freqs | Four Ethnic Groups | 606 | 69 | 41 | 28 | 4.62% |
| | Seven Ethnic Groups | 606 | 69 | 41 | 28 | 4.62% |
| | Seven Groups Recalc | 606 | 66 | 41 | 25 | 4.13% |
| UAs w/o Freqs | Four Ethnic Groups | 7325 | 581 | 130 | 451 | 6.16% |
| | Seven Ethnic Groups | 7325 | 576 | 127 | 449 | 6.13% |
| | Seven Groups Recalc | 7325 | 567 | 121 | 446 | 6.09% |

Table 21: Change in Number of Registrations with CPRA = 100 Under the Proposed Metrics

| | Registrations with CPRA = 100 | Registrations Increasing to CPRA = 100 | Registrations Falling Below CPRA = 100 | Net Change | Percent Change |
|---|---|---|---|---|---|
| Four Ethnic Groups | 4323 | 616 | 192 | 424 | 9.81% |
| Seven Ethnic Groups | 4323 | 609 | 191 | 418 | 9.67% |
| Seven Groups Recalc | 4323 | 601 | 180 | 421 | 9.74% |

Table 21 shows the count and percent of kidney registrations waiting on December 31, 2020 that would either rise to or fall below 100% CPRA under the proposed metrics. More registrations rose to 100% CPRA than fell from 100% to a lower CPRA. Overall, the number of registrations with 100% CPRA increased by over 8% for all of the proposed metrics.

Tables 22-25 show the change in the number of registrations with 100% CPRA based on the kidney waiting list as of December 31, 2020 by ethnicity, adult vs pediatric, region, and whether or not a registration had any unacceptable antigens without a frequency under the current CPRA metric, respectively. The number of registrations with 100% CPRA increased by for nearly all categories.

As shown in Table 24, the number of registrations with 100% CPRA decreased slightly in Region 1. This is likely due to Region 1's relatively low number of registrations with unacceptable antigens without frequencies and relatively low number of registrations with current CPRA $>=$ 90%, which led to more registrations decreasing CPRA than increasing CPRA in under the proposed metrics (Table 9). It is therefore unsurprising that more registrations with 100% CPRA under the current metric decreased to a CPRA $<$ 100% under the proposed metrics in Region 1. The number of registrations with 100% CPRA also decreased slightly for candidates with no unacceptable antigens without frequencies, as shown in Table 25. This is likely because the new metrics add frequencies for a large number of alleles, and as the frequencies can only ever total one, the addition of new frequencies mean that the frequencies for existing antigens must decrease. For registrations without any of the newly-added alleles, the CPRA for the majority of their unacceptable antigens is expected to decrease, and an overall decline in the number of registrations with 100% CPRA is therefore unsurprising.

There was no meaningful difference in the number of registrations that would have 100% CPRA under the proposed metric with four ethnic groups relative to the proposed metrics with seven ethnic groups for any condition examined here.

Table 22: Change in Number of Registrations with CPRA = 100 Under the Proposed Metrics by Ethnicity

| | | Registrations with CPRA >= 100 | Registrations Increasing to CPRA >= 100 | Registrations Falling Below CPRA 100 | Net Change | Percent Change |
|---|---|---|---|---|---|---|
| White | Four Ethnic Groups | 1067 | 132 | 78 | 54 | 5.06% |
| | Seven Ethnic Groups | 1067 | 130 | 76 | 54 | 5.06% |
| | Seven Groups Recalc | 1067 | 147 | 66 | 81 | 7.59% |
| Black | Four Ethnic Groups | 2192 | 315 | 64 | 251 | 11.45% |
| | Seven Ethnic Groups | 2192 | 312 | 65 | 247 | 11.27% |
| | Seven Groups Recalc | 2192 | 292 | 62 | 230 | 10.49% |
| Hispanic | Four Ethnic Groups | 620 | 103 | 38 | 65 | 10.48% |
| | Seven Ethnic Groups | 620 | 102 | 38 | 64 | 10.32% |
| | Seven Groups Recalc | 620 | 95 | 38 | 57 | 9.19% |
| Asian | Four Ethnic Groups | 333 | 45 | 10 | 35 | 10.51% |
| | Seven Ethnic Groups | 333 | 44 | 10 | 34 | 10.21% |
| | Seven Groups Recalc | 333 | 44 | 11 | 33 | 9.91% |
| Amer Ind/AK Native | Four Ethnic Groups | 35 | 4 | 0 | 4 | 11.43% |
| | Seven Ethnic Groups | 35 | 4 | 0 | 4 | 11.43% |
| | Seven Groups Recalc | 35 | 6 | 0 | 6 | 17.14% |
| Native HI/other PI | Four Ethnic Groups | 22 | 6 | 0 | 6 | 27.27% |
| | Seven Ethnic Groups | 22 | 6 | 0 | 6 | 27.27% |
| | Seven Groups Recalc | 22 | 5 | 1 | 4 | 18.18% |
| Multiracial | Four Ethnic Groups | 54 | 11 | 2 | 9 | 16.67% |
| | Seven Ethnic Groups | 54 | 11 | 2 | 9 | 16.67% |
| | Seven Groups Recalc | 54 | 12 | 2 | 10 | 18.52% |

Table 23: Change in Number of Registrations with CPRA = 100 Under the Proposed Metrics by Adult vs Pediatric

| | | Registrations with CPRA >= 100 | Registrations Increasing to CPRA >= 100 | Registrations Falling Below CPRA 100 | Net Change | Percent Change |
|---|---|---|---|---|---|---|
| Adult | Four Ethnic Groups | 4280 | 609 | 187 | 422 | 9.86% |
| | Seven Ethnic Groups | 4280 | 602 | 186 | 416 | 9.72% |
| | Seven Groups Recalc | 4280 | 595 | 176 | 419 | 9.79% |
| Pediatric | Four Ethnic Groups | 43 | 7 | 5 | 2 | 4.65% |
| | Seven Ethnic Groups | 43 | 7 | 5 | 2 | 4.65% |
| | Seven Groups Recalc | 43 | 6 | 4 | 2 | 4.65% |

Table 24: Change in Number of Registrations with CPRA = 100 Under the Proposed Metrics by Region

| | | Registrations with CPRA >= 100 | Registrations Increasing to CPRA >= 100 | Registrations Falling Below CPRA 100 | Net Change | Percent Change |
|---|---|---|---|---|---|---|
| 1 | Four Ethnic Groups | 125 | 8 | 11 | -3 | -2.40% |
| | Seven Ethnic Groups | 125 | 8 | 11 | -3 | -2.40% |
| | Seven Groups Recalc | 125 | 9 | 10 | -1 | -0.80% |
| 2 | Four Ethnic Groups | 657 | 58 | 32 | 26 | 3.96% |
| | Seven Ethnic Groups | 657 | 57 | 31 | 26 | 3.96% |
| | Seven Groups Recalc | 657 | 56 | 31 | 25 | 3.81% |
| 3 | Four Ethnic Groups | 814 | 104 | 26 | 78 | 9.58% |
| | Seven Ethnic Groups | 814 | 102 | 27 | 75 | 9.21% |
| | Seven Groups Recalc | 814 | 101 | 26 | 75 | 9.21% |
| 4 | Four Ethnic Groups | 464 | 79 | 14 | 65 | 14.01% |
| | Seven Ethnic Groups | 464 | 79 | 14 | 65 | 14.01% |
| | Seven Groups Recalc | 464 | 75 | 14 | 61 | 13.15% |
| 5 | Four Ethnic Groups | 678 | 98 | 52 | 46 | 6.78% |
| | Seven Ethnic Groups | 678 | 97 | 51 | 46 | 6.78% |
| | Seven Groups Recalc | 678 | 99 | 47 | 52 | 7.67% |
| 6 | Four Ethnic Groups | 86 | 16 | 4 | 12 | 13.95% |
| | Seven Ethnic Groups | 86 | 15 | 4 | 11 | 12.79% |
| | Seven Groups Recalc | 86 | 15 | 5 | 10 | 11.63% |
| 7 | Four Ethnic Groups | 294 | 48 | 10 | 38 | 12.93% |
| | Seven Ethnic Groups | 294 | 48 | 10 | 38 | 12.93% |
| | Seven Groups Recalc | 294 | 49 | 8 | 41 | 13.95% |
| 8 | Four Ethnic Groups | 141 | 22 | 7 | 15 | 10.64% |
| | Seven Ethnic Groups | 141 | 22 | 7 | 15 | 10.64% |
| | Seven Groups Recalc | 141 | 21 | 6 | 15 | 10.64% |
| 9 | Four Ethnic Groups | 204 | 42 | 12 | 30 | 14.71% |
| | Seven Ethnic Groups | 204 | 41 | 12 | 29 | 14.22% |
| | Seven Groups Recalc | 204 | 46 | 12 | 34 | 16.67% |
| 10 | Four Ethnic Groups | 269 | 46 | 8 | 38 | 14.13% |
| | Seven Ethnic Groups | 269 | 45 | 8 | 37 | 13.75% |
| | Seven Groups Recalc | 269 | 41 | 7 | 34 | 12.64% |
| 11 | Four Ethnic Groups | 591 | 95 | 16 | 79 | 13.37% |
| | Seven Ethnic Groups | 591 | 95 | 16 | 79 | 13.37% |
| | Seven Groups Recalc | 591 | 89 | 14 | 75 | 12.69% |

Table 25: Count and Percent of Registrations with CPRA = 100 Under the Proposed Metrics by Presence or Absence of Unacceptable Antigens without Frequencies

| | | Registrations with CPRA >= 100 | Registrations Increasing to CPRA >= 100 | Registrations Falling Below CPRA 100 | Net Change | Percent Change |
|---|---|---|---|---|---|---|
| No UAs w/o Freqs | Four Ethnic Groups | 128 | 19 | 21 | -2 | -1.56% |
| | Seven Ethnic Groups | 128 | 19 | 21 | -2 | -1.56% |
| | Seven Groups Recalc | 128 | 19 | 20 | -1 | -0.78% |
| UAs w/o Freqs | Four Ethnic Groups | 4195 | 597 | 171 | 426 | 10.15% |
| | Seven Ethnic Groups | 4195 | 590 | 170 | 420 | 10.01% |
| | Seven Groups Recalc | 4195 | 582 | 160 | 422 | 10.06% |

Figure 6: Distribution of Difference between Proposed CPRA Metrics, Four vs Seven Ethnic Groups

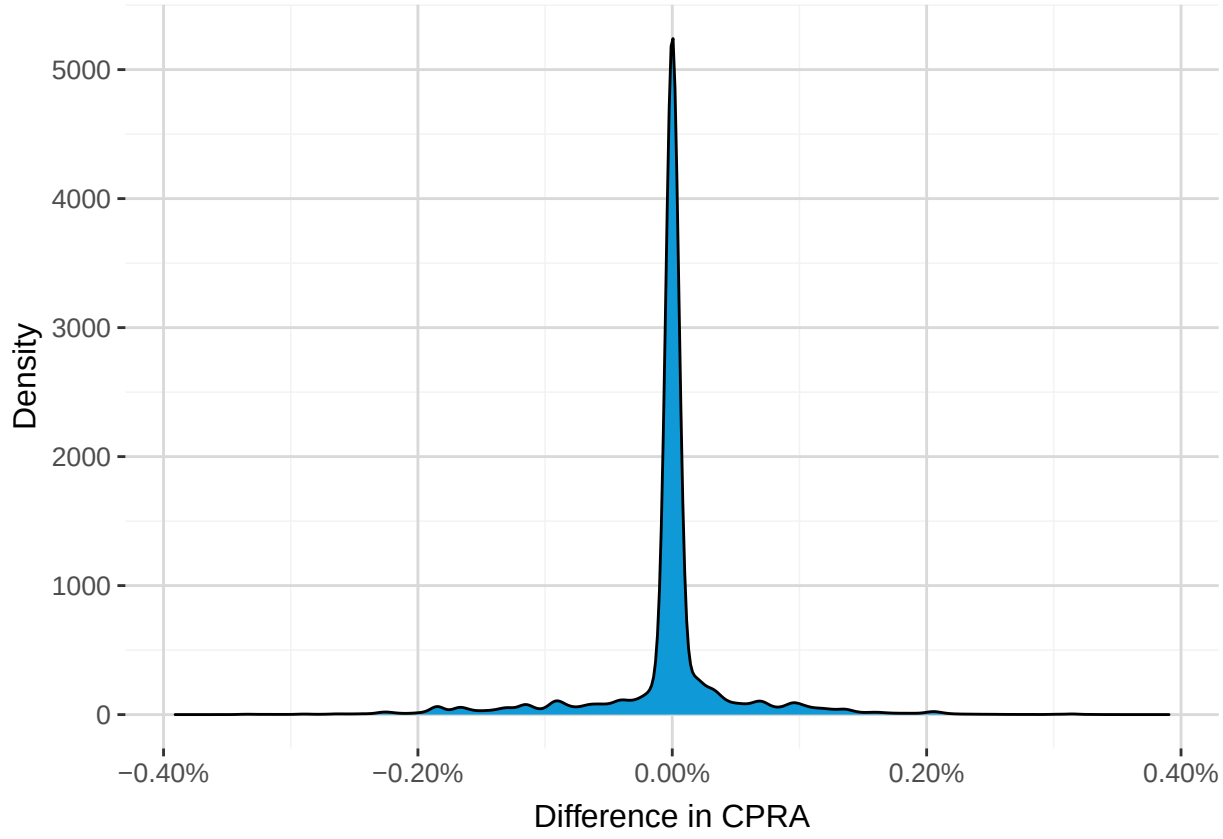


Table 26: Distribution of Difference between Proposed CPRA Metrics, Four vs Seven Ethnic Groups

| Min | 25th Percentile | Mean | Median | 75th Percentile | Max |
|---|---|---|---|---|---|
| -0.39% | 0.00% | -0.00% | 0.00% | 0.00% | 0.39% |

Figure 6 and Table 26 show the distribution of the difference between the proposed stem cell ARD CPRA metric with four ethnic groups and the proposed stem cell ARD metric with seven ethnic groups. The difference between the two metrics was very small, with no candidate seeing a difference of more than 0.39% CPRA between one metric and the other.

## Correlation between Offer and Transplant Rates and CPRA Metrics

Figure 7: Offer Rate Model Fit by Metric and Allocation Category, All Registrations

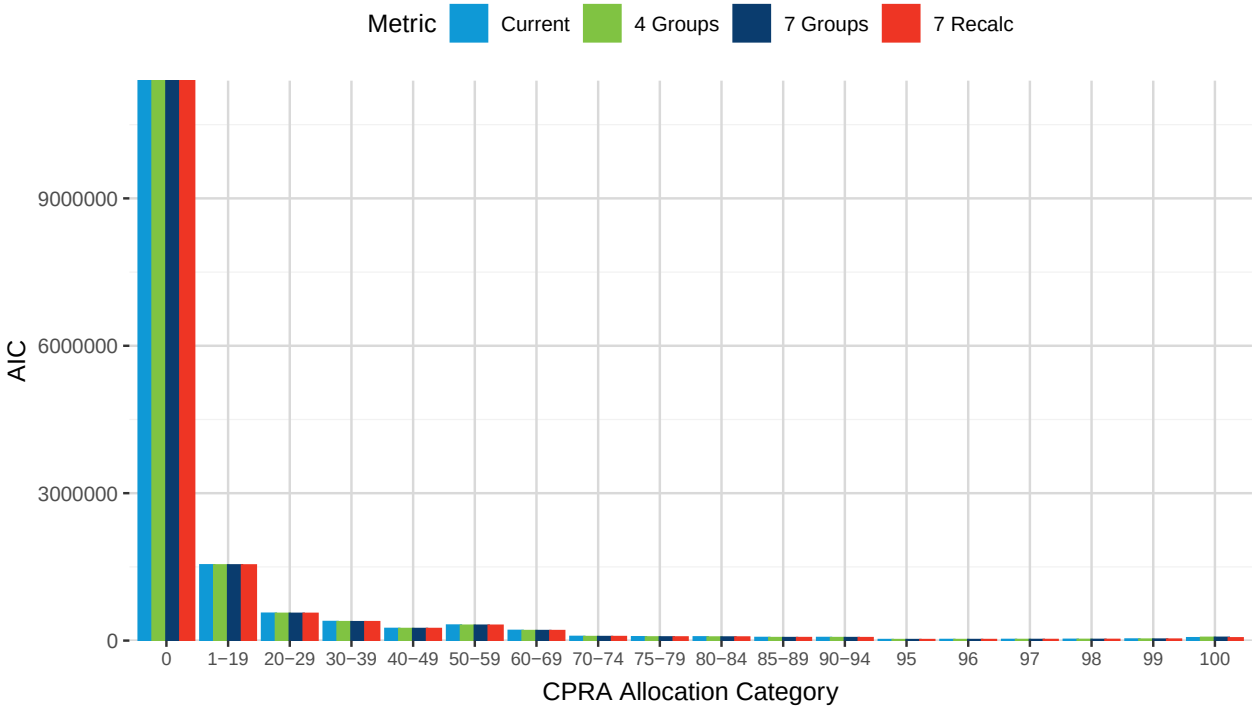


Figure 7 shows how predictive models built based on both the current CPRA metric and the proposed metrics were of the offer rate for registrations ever waiting between January 1st, 2018 and December 31st, 2020. The AIC is a measure of goodness of fit, with a *lower* AIC indicating a better model fit and that the CPRA metric is more predictive of offer rate.

In general, CPRA is more predictive of offer rate at higher levels of sensitization where more donors are are screened and the CPRA therefore has a greater impact on the number of offers received. An offer model based on CPRA is expected to be least predictive when the CPRA is zero because at this level of sensitization no offers are being screened and the candidate receives no allocation priority from CPRA: CPRA has no relationship to the number of offers received. This is reflected in the AICs shown in Figure 7. There was little difference in how predictive the four metrics are of offer rate for any of the CPRA allocation categories. The proposed metrics were slightly more predictive in all allocation categories except 100%, and the recalculated ECD stem cell metric was the most predictive of all in the majority of allocation categories.

There is no meaningful difference in how predictive the proposed stem cell ARD metric with four ethnic group is of the offer rate relative to the proposed stem cell ARD metric with seven ethnic groups in any of the CPRA allocation categories.

Figure 8: Offer Rate Model Fit by Metric and Allocation Category, Registrations with UAs Against Loci Not in Current CPRA

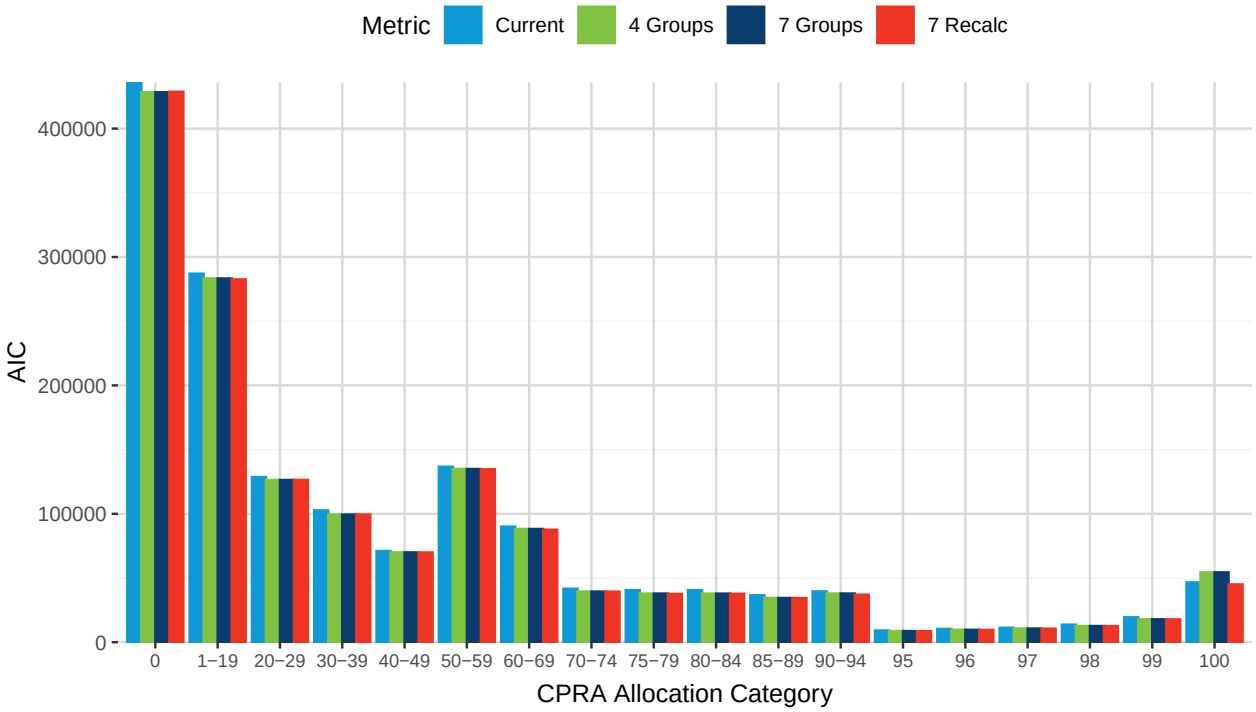


Figure 8 shows how predictive models built based on both the current CPRA metric and the proposed metrics were of the offer rate for registrations with unacceptable antigens not included in the current metric ever waiting between January 1st, 2018 and December 31st, 2020. The AIC is a measure of goodness of fit, with a *lower* AIC indicating a better model fit and that the CPRA metric is more predictive of offer rate.

For candidates with unacceptable antigens not included in the current metric, the proposed CPRA is again more predictive of offer rate than the current CPRA for all allocation categories except 100%, but to a greater degree than when considering all registrations (Figure 7). The recalculated stem cell ECD metric is the most predictive overall in all but five categories; notably, it is more similar to the current CPRA in the 100% category, and therefore the most predictive of the stem cell CPRAs for that category, although the current CPRA is most predictive for this category overall. The difference between the four metrics is not large in any allocation category.

There is no meaningful difference in how predictive the proposed stem cell ARD metric with four ethnic groups is of the offer rate relative to the proposed stem cell ARD metric with seven ethnic groups in any of the CPRA allocation categories.

Figure 9: Transplant Rate Model Fit by Metric and Allocation Category, All Registrations

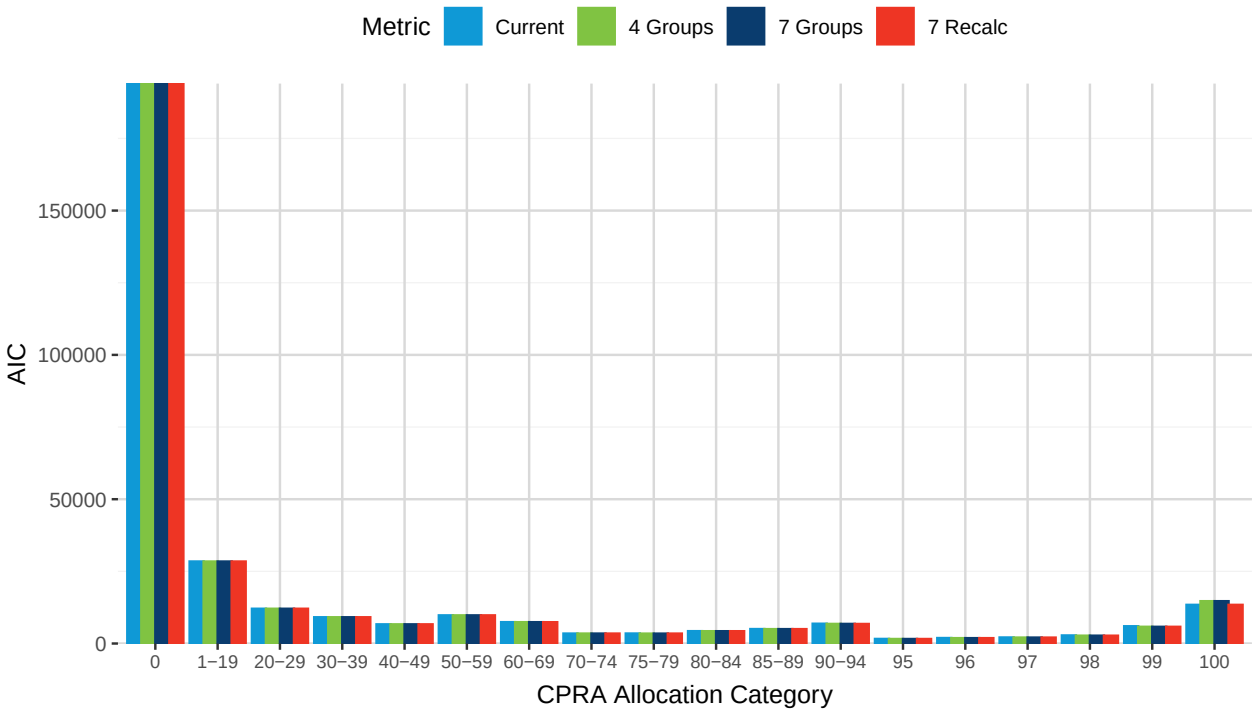


Figure 9 shows how predictive models built based on both the current CPRA metric and the proposed metrics were of the transplant rate for registrations ever waiting between January 1st, 2018 and December 31st, 2020. The AIC is a measure of goodness of fit, with a *lower* AIC indicating a better model fit and that the CPRA metric is more predictive of transplant rate.

The difference in how predictive models based on the four metrics were was small for all allocation categories. However, the proposed metrics were found to be slightly more predictive of transplant rate in all allocation categories except 20-29%, 30-39%, and 100%. The recalculated stem cell ECD metric was the most predictive in the highest number of allocation categories.

There was no meaningful difference in how predictive the proposed metric with four ethnic groups was of the transplant rate relative to the proposed metric with seven ethnic groups in any of the CPRA allocation categories.

Figure 10: Transplant Rate Model Fit by Metric and Allocation Category, Registrations with UAs Against Loci Not in Current CPRA

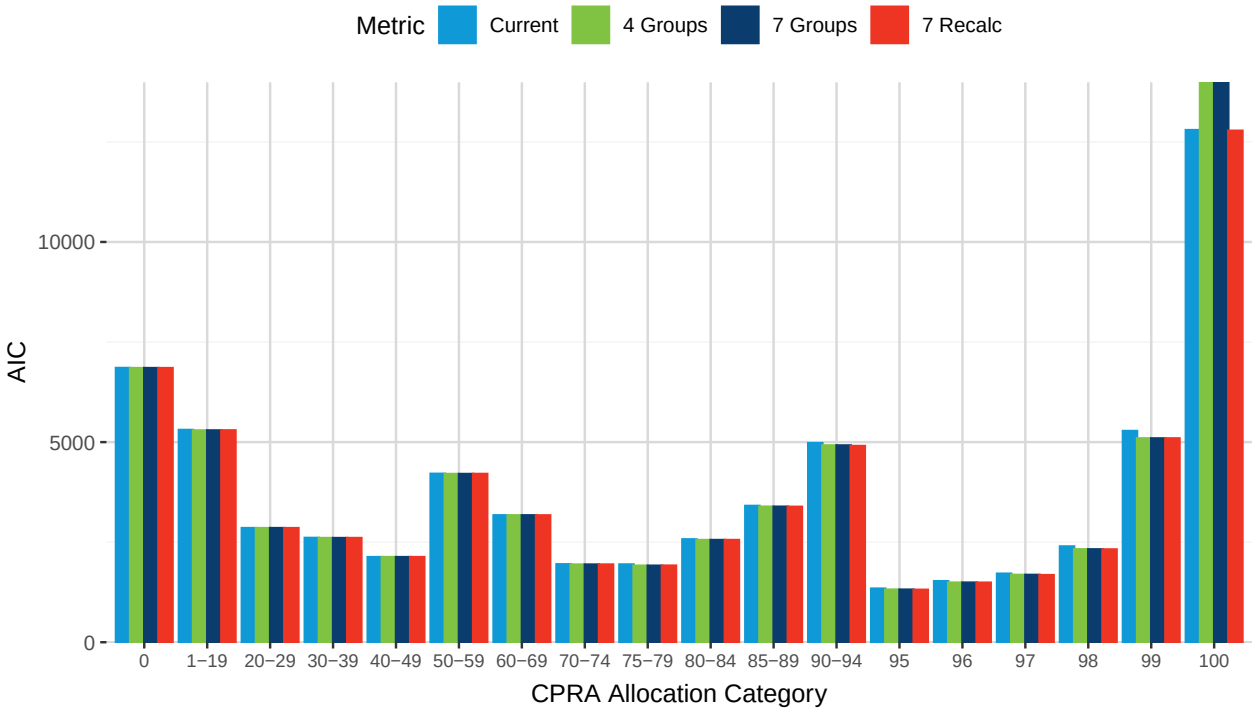


Figure 10 shows how predictive models built based on both the current CPRA metric and the proposed metrics were of the transplant rate for registrations ever waiting between January 1st, 2018 and December 31st, 2020. The AIC is a measure of goodness of fit, with a *lower* AIC indicating a better model fit and that the CPRA metric is more predictive of transplant rate.

The difference in how predictive models based on the four metrics were was small for all allocation categories. The proposed metrics were slightly more predictive than the current CPRA in all allocation categories except 40-49%, and 100%. It is not clear why all metrics were found to be less predictive for the 100% category than the 0% category, but it's possible that while there is a strong link between very high CPRA and offer screening, and therefore offer rate, there are more unanticipated barriers to transplantation at this level of screening, such as unexpected positive crossmatches. This could weaken the relationship between CPRA and transplant rate at very high levels of sensitization and result in the observed poorer transplant rate model fits in the 100% CPRA category.

There was no meaningful difference in how predictive the proposed stem cell ARD metric with four ethnic groups was of the transplant rate relative to the proposed stem cell ARD metric with seven ethnic groups in any of the CPRA allocation categories.

## Similarity between CPRA Metrics and Observed Percent of Incompatible Donors

Figure 11: Distribution of Difference Between Calculated CPRA and Observed Percent Incompatible Donors by CPRA Metric

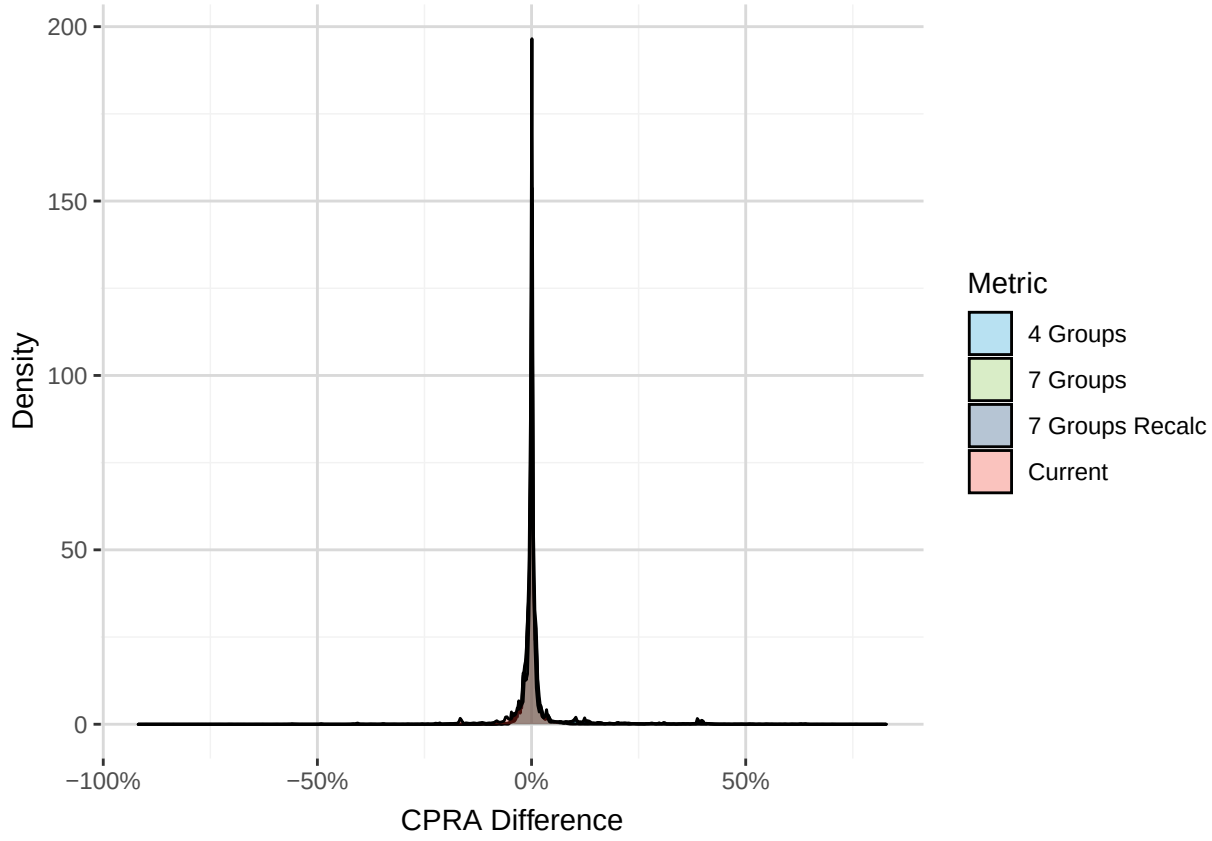


Table 27: Difference Between Calculated CPRA and Observed Percent Incompatible Donors by CPRA Metric

| Metric | Min | 25th Percentile | Mean | Median | 75th Percentile | Max | RMSE |
|---|---|---|---|---|---|---|---|
| Current | -91.84% | -0.94% | -1.52% | -0.05% | 0.29% | 14.00% | 0.065 |
| 4 Groups | -13.93% | -0.50% | 1.29% | 0.05% | 0.46% | 82.77% | 0.068 |
| 7 Groups | -13.91% | -0.49% | 1.28% | 0.04% | 0.43% | 82.79% | 0.068 |
| 7 Groups Recalc | -31.14% | -0.35% | 1.27% | 0.07% | 0.44% | 70.28% | 0.062 |

Figure 11 and Table 27 show the distribution of the difference between the calculated CPRA and the observed percent incompatible donors for all kidney registrations with any unacceptable antigens waiting on December 31, 2020 for the current and proposed CPRA metrics.

As shown in Table 27, the current CPRA metric is more likely to underestimate than overestimate the observed percent of incompatible donors, largely as a result of unacceptable antigens that can be entered but which do not have frequencies. Conversely, the proposed metrics are more likely to overestimate than underestimate the observed percent of incompatible donors. This discrepancy has two primary sources. First, solid organ donor typing is rarely carried out at the allele level, meaning that many donors will not be screened off a match by an allele-level unacceptable antigen, even though they may in truth bear that allele. In these cases, the percent incompatible donors metric *underestimates* the true proportion of donors with an allele in the donor population. The second

reason that the stem cell metrics may overestimate the true percent incompatible donors is the fact that the stem cell datasets cannot distinguish all the values that are currently available to choose as unacceptable antigens in the OPTN system. When a common allele has its frequency combined with that of a rare allele, the CPRA granted to that rare allele can be much higher than the proportion of donors screened by an unacceptable antigen against that allele.

There was no meaningful difference in how closely the stem cell ARD metric with four ethnic groups reflected the observed percent incompatible donors relative to the stem cell ARD metric with seven ethnic groups.

Figure 12: Calculated vs Observed Percent of Incompatible Donors by CPRA Metric

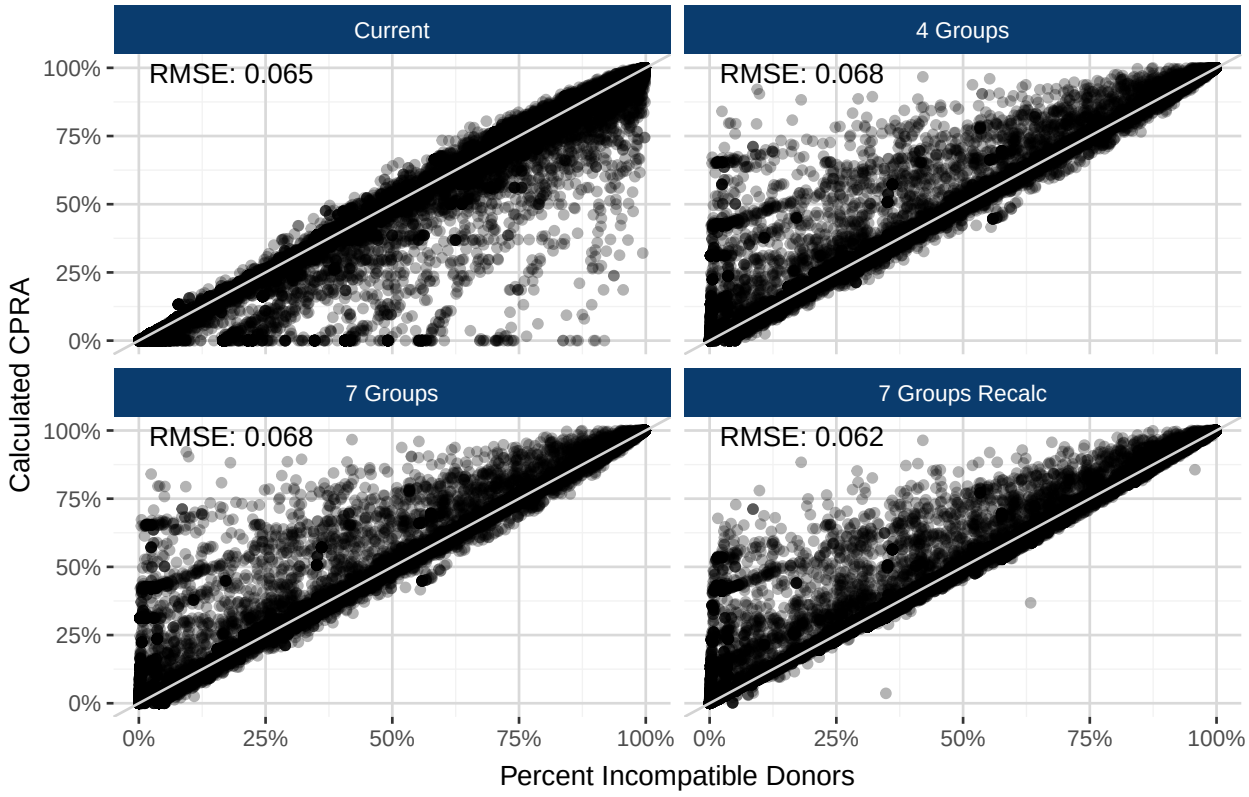


Figure 12 shows the relationship between the observed percent of incompatible donors and the three CPRA metrics for all kidney registrations with any unacceptable antigens waiting on December 31, 2020. For a perfect CPRA metric, which predicted the percent of incompatible deceased kidney donors with 100% accuracy, all points would lie exactly along the diagonal line.

The current CPRA tends to underestimate the true proportion of incompatible donors. Registrations with exclusively unacceptable antigens without frequencies under the current metric lie along the horizontal line at 0%, and the wide spread of these points illustrates the broad range of proportion of incompatible donors currently being represented as 0% CPRA. The proposed CPRAs tend to overestimate rather than underestimate the proportion of incompatible donors, as most points lie above the 1:1 line.

Comparing the four- and seven-group ARD stem cell metrics to the recalculated ECD stem cell metric reveals the impact of the change in dataset. The density of points in the upper left quadrant of the plots, indicating cases where the proposed metric overestimated the percent incompatible donors, is lower for the recalculated metric. Off-diagonal bands at ~70% and ~27% are visible on the ARD stem cell metric plots but have disappeared from the recalculated metric plot. These differences are the result of the recalculated metric's ability to distinguish alleles that the ARD metrics could not; when allele frequencies were combined, they tended to overestimate the true proportion of donors with those alleles to a greater degree than when the allele frequencies could be estimated independently. Ultimately, the RMSE was slightly lower for the recalculated ECD stem cell metric than the current CPRA metric, indicating it agreed slightly better with the observed proportion of incompatible donors.

There was no meaningful difference in how closely the stem cell ARD metric with four ethnic groups reflected the observed percent incompatible donors relative to the stem cell ARD metric with seven ethnic groups.

Figure 13: Calculated vs Observed Percent of Incompatible Donors by CPRA Metric, Registrations with Any UAs without Frequencies

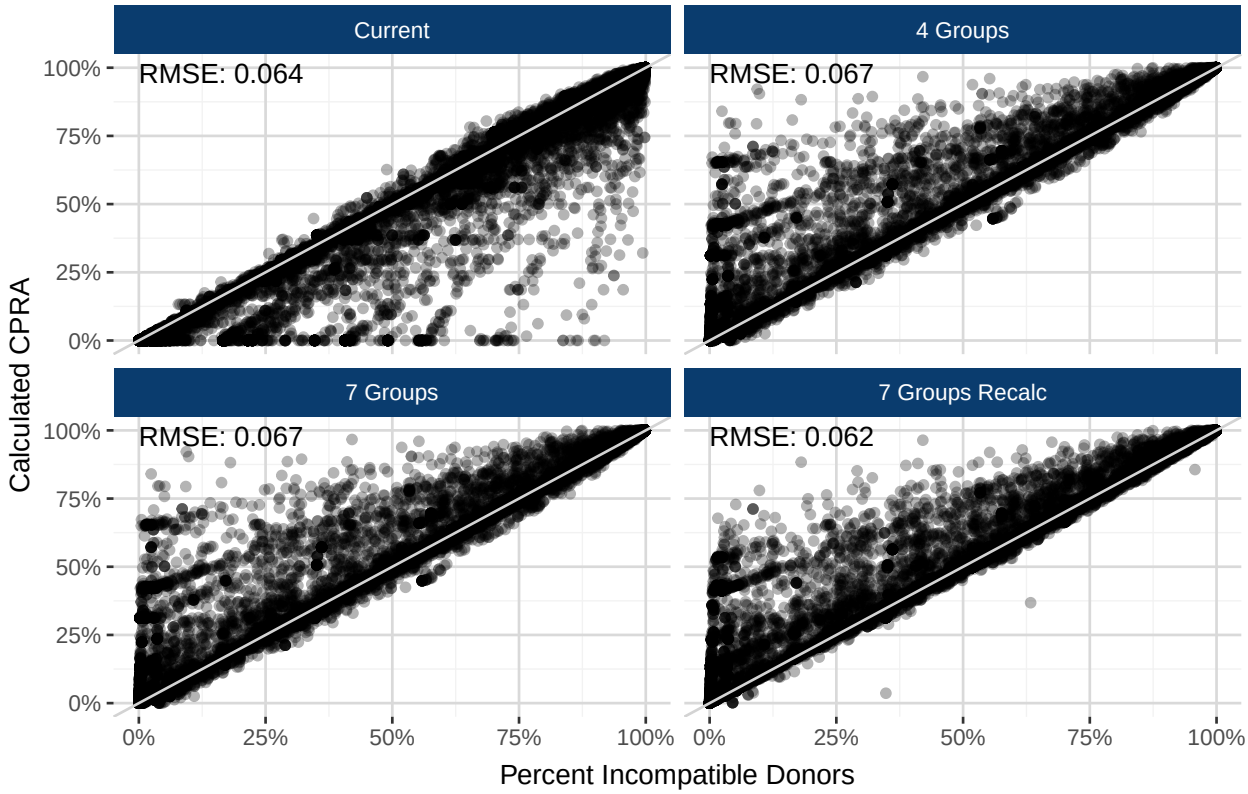


Figure 12 shows the relationship between the observed percent of incompatible donors and the three proposed CPRA metrics for all kidney registrations with any unacceptable antigens without frequencies under the current calculation waiting on December 31, 2020.

This subset of registrations is the one where the CPRA metrics are expected to perform the worst: it includes registrations with allelic unacceptable antigens, where the percent of incompatible donors will be underestimated (at 0%) under the current CPRA and overestimated (due to lack of allelic donor typings) by the stem cell metrics. It also includes the alleles that could not be distinguished in the stem cell datasets. For this subset of "most difficult" registrations, the stem cell ARD metrics were less reflective of the percent incompatible donors than the current CPRA metric, while the recalculated stem cell ECD metric was more reflective of the percent incompatible donors than the current CPRA.

There was no meaningful difference in how closely the stem cell ARD metric with four ethnic groups reflected the observed percent incompatible donors relative to the stem cell ARD metric with seven ethnic groups.

Figure 14: Calculated vs Observed Percent of Incompatible Donors by CPRA Metric, Registrations with No UAs without Frequencies

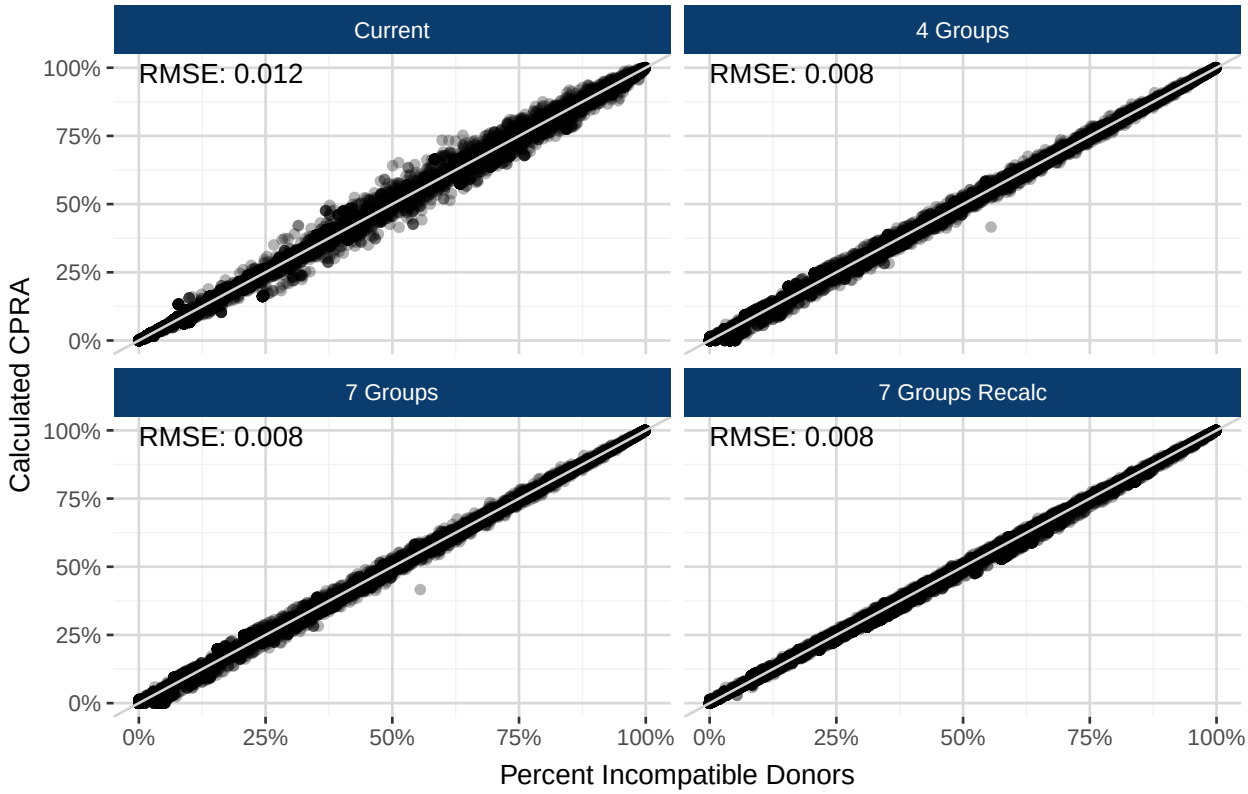


Figure 12 shows the relationship between the observed percent of incompatible donors and the three CPRA metrics for all kidney registrations having only unacceptable antigens with frequencies under the current calculation that were waiting on December 31, 2020.

All CPRA metrics were more reflective of the proportion of incompatible donors for this subset of registrations than overall. The recalculated stem cell ECD metric was slightly less reflective of the percent of incompatible donors than the stem cell ARD metrics for this subset of registrations, but still reflected the percent incompatible donors better than the current CPRA.

There was no meaningful difference in how closely the stem cell ARD metric with four ethnic groups reflected the observed percent incompatible donors relative to the stem cell ARD metric with seven ethnic groups.

## Conclusion

The proposed changes to the CPRA calculation are expected to impact nearly all registrations with any unacceptable antigens entered, although for the majority of registrations the change in CPRA is expected to be very small. More registrations are likely to increase CPRA than decrease CPRA, with the most dramatic increases occurring for registrations with many unacceptable antigens without frequencies under the current calculation. The proposed CPRA metrics are slightly more predictive of offer and transplant rate than the current metric. The recalculated stem cell donor metric is slightly more reflective of the observed percent of incompatible donors than the current metric. There is no meaningful difference between the stem cell ARD metric that used seven ethnic groups relative to the stem cell ARD metric that used four ethnic groups for any of the measures examined here.