



# OPEN Assessing health care disparities in US organ procurement organizations

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There is extensive system-wide evidence of disparities in access to organ transplantation in the US based on race, ethnicity, and socioeconomic status. However, little information is available regarding care disparities among US organ procurement organizations (OPOs). Commissioned by the US Centers for Medicare and Medicaid Services (CMS), we studied racial/ethnic disparities in organ donation and transplantation across and within OPOs. Based on the 2020 CMS final rule, we calculated OPO donation and organ transplantation rates with 95% confidence intervals for racial (Black, White, and Asian American and Pacific Islander, AAPI) and ethnic (Hispanic and non-Hispanic) groups. OPOs were ranked with national rates as references and classified according to the CMS 3-tier system. Of the 58 OPOs, 8 and 4 had donation rates lower for Black and AAPI donors than for White donors; 21 and 18 had organ transplantation rates lower for Black and AAPI donors than for White donors; 1 and 1 had a donation rate or organ transplantation rate lower for Hispanic donors than for non-Hispanic donors. Significant racial/ethnic disparities in organ donation and transplantation exist among many OPOs, whereas the overall OPO performance is dominated by White and non-Hispanic donors. These disparities may be influenced by variations and structural barriers in resource access, donor identification, transplantation referral, and waitlisting processes—some of which lie partially outside the direct control of OPOs and disproportionately affect disadvantaged populations. Results support equitable organ donation and allocation through enhanced awareness of health care disparities, increased accountability of OPOs, and informed policies and interventions.

**Keywords** Caterpillar plot, Provider profiling, Organ donation and transplantation, Racial and ethnic disparities

In the US, OPOs are frontline organizations responsible for recovering and delivering organs from deceased donors with authorization, and monitoring donor hospitals in their respective donation service areas (DSAs)<sup>1–4</sup>. As a central component of the national organ transplantation system, OPOs have been routinely evaluated by the US Centers for Medicare and Medicaid Services (CMS)<sup>5,6</sup>. Currently, the evaluation is based on two revised outcome measures, the OPO donation and organ transplantation rates. OPOs failing to meet performance requirements will be de-certified as legal organ procurers and their DSAs will be opened for competition among other incumbent OPOs<sup>7</sup>.

Despite being highly robust and efficient, health care disparities remain significant in the US organ transplantation system. On the demand side, disproportionately many individuals from minority and underrepresented populations are at a disadvantage in being referred, evaluated, and added to the waiting list for organ transplantation<sup>8–10</sup>; on the supply side, despite a number of educational interventions such as culturally appropriate messaging and storytelling<sup>11,12</sup>, organ donation among all racial/ethnic minority populations

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is lower than that of White individuals<sup>13</sup>, although recent evidence suggests that racial/ethnic differences in organ donation have been ameliorating over the past two decades<sup>14</sup>. While these disparities are evident at the population level, data are still lacking regarding the potential variability of performance in potential donor identification and organ procurement stratified by race and ethnicity<sup>15</sup>, nor have racial/ethnic differences been systematically accounted for in current OPO performance evaluation metrics<sup>7</sup>.

Drawing on the revised CMS outcome measures effective in 2021<sup>7</sup>, we were commissioned by CMS to study racial/ethnic differences in organ donation and transplantation across OPOs and set forth a graphical representation of OPO-level disparities via caterpillar plots, commonly used in quality improvement programs<sup>16–18</sup>. OPO assessment based on this graphical tool can enhance the awareness of racial/ethnic disparities in organ donation and transplantation, leading to increased resources and targeted interventions aiming at addressing these disparities at the OPO level. Quality improvement guidelines and policies can be developed to promote evidence-based OPO accountability for significant disparities in organ donation and transplantation. Unlike existing studies on OPO performance evaluation and metrics assessment based on individual-level data<sup>19–21</sup>, the proposed approach only leverages summary information at the OPO level, thereby serving as a proof of concept regarding privacy-preserving evaluation of health care disparities in OPO performance<sup>22</sup>.

## Methods

We conducted a retrospective cross-sectional analysis of OPO donation and organ transplantation in line with the effective CMS definitions of outcome measures and the 3-tier system<sup>7</sup>. This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline.

### Data sources

The construction of OPO performance metrics required the calculation of OPO-specific donor potential (i.e., the number of inpatient deaths among patients aged 75 and younger with the primary cause of death consistent with organ donation), number of donors, and number of organs transplanted in each age and racial/ethnic group. Donor potential is a quantity that aims to reflect the maximum amount of organ donation possible based on the frequency of deaths with causes that have the potential to qualify for organ donation. To calculate the donor potential in each age and racial/ethnic group (Black/African Americans, White Americans, and Asian Americans and Pacific Islanders, AAPIs), we used 2019 county-level national mortality data from the National Center for Health Statistics Multiple Cause of Death (MCOB) database. The following International Classification of Diseases, Tenth Revision (ICD-10) codes were used to identify potential donor deaths: I20–I25 for ischemic heart disease, I60–I69 for cerebrovascular disease, and V01–Y89 for external causes of morbidity and mortality including blunt trauma, gunshot wound, drug overdose, suicide, drowning, and asphyxiation<sup>23</sup>. Potential donors were assigned to an OPO if the county of the hospital where death occurred falls into the OPO's associated DSA. If a county has a hospital with a CMS approved waiver, the donor potential was split between the OPO having the county as part of its DSA and the OPO serving the hospital with a CMS waiver, prorated according to the Medicare inpatient deaths at hospitals with a waiver and at other hospitals. This definition is consistent with the CMS final rule for OPO evaluations<sup>7</sup>.

The OPO-specific number of donors in each racial/ethnic group was calculated as the number of deceased individuals from whom at least one vascularized organ (heart, liver, lung, kidney, pancreas, or intestine) was transplanted according to the 2019 Scientific Registry of Transplant Recipients (SRTR) database; donors with pancreatic or islet cells recovered either for research, or for transplantation but submitted for research, were included per the CMS methodology. While only donors aged 75 and younger were counted in the donor potential, there was no restriction on the age of donors, as OPOs are allowed to procure organs from donors of all ages.

The OPO-specific number of organs transplanted in each age and racial/ethnic group was also determined using SRTR data; pancreatic and islet cells recovered either for research, or for transplantation but submitted for research, were included. Since a deceased donor could donate more than one organ for transplantation, it is possible that the age-adjusted OPO organ transplantation rate in a racial/ethnic group exceeds 100% (the maximum count of each organ type available in Supplemental Table 1).

### Race-/ethnicity-specific OPO donation and organ transplantation rates

Following the CMS final rule<sup>7</sup>, we first define OPO donation and organ transplantation rates specific to a racial/ethnic group, indexed by  $j$ . The OPO donation rate of racial/ethnic group  $j$  is the number of donors as a percentage of the donor potential within racial/ethnic group  $j$ . The OPO organ transplantation rate of racial/ethnic group  $j$  is the ratio of the OPO's observed transplantation rate to the expected, multiplied by the national transplantation rate, i.e.,  $\frac{\text{observed rate}}{\text{expected rate}} \cdot \text{national rate}$ , where the observed rate is the number of organs transplanted from donors within the DSA as a percentage of the donor potential; the expected rate is the expected number of organs transplanted as a percentage of the donor potential; and the national rate is the number of organs transplanted from donors across all OPOs as a percentage of the national donor potential, with all three quantities specific to racial/ethnic group  $j$ . This OPO organ transplantation rate is deemed favorable if it is greater than the national transplantation rate, and unfavorable if less than the national rate.<sup>24</sup> Unlike the OPO donation rate with no risk adjustment, the CMS final rule stipulates that the OPO organ transplantation rate should be risk-adjusted for age with the following 15 groups: < 1, 1–5, 6–11, 12–17, 18–24, 25–29, 30–34, 35–39, 40–44, 45–49, 50–54, 55–59, 60–64, 65–69, and 70–75. Consequently, the expected organ transplantation rate of racial/ethnic group  $j$  for the  $i$ th OPO is calculated as  $\sum_{g=1}^{15} d_{ijg} R_{jg} / \sum_{g=1}^{15} d_{ijg}$ , where  $d_{ijg}$  is the donor potential in age group  $g$  and racial/ethnic group  $j$  for the  $i$ th OPO, and  $R_{jg}$  is the national organ transplantation rate in age group  $g$  and racial/ethnic group  $j$ .

### Confidence intervals and 3-tier system

We constructed two-sided 95% confidence intervals for race-/ethnicity-specific OPO donation and organ transplantation rates to measure their variation. If  $p$  is the OPO donation rate as a fraction of 1 and  $n$  is the donor potential, the corresponding 95% lower and upper confidence limits  $L$  and  $U$  can be expressed as

$$L = 100 \cdot \min \left\{ 0, \frac{2np + z^2 - 1 - z\sqrt{z^2 - 1/n + 4np(1-p) + 4p - 2}}{2(n + z^2)} \right\},$$

$$U = 100 \cdot \max \left\{ 0, \frac{2np + z^2 + 1 + z\sqrt{z^2 - 1/n + 4np(1-p) - 4p + 2}}{2(n + z^2)} \right\},$$

where  $z$  denotes the 97.5th percentile of the standard normal distribution (approximately equal to 1.96)<sup>25</sup>. Let  $O$ ,  $E$ , and  $P$  denote the observed, expected, and national organ transplantation rates as a fraction of 1, respectively. The 95% lower and upper confidence limits  $L$  and  $U$  of the OPO organ transplantation rate can be written as

$$L = 100 \cdot \min \left\{ 0, PO/E - z\sqrt{P^2O/(nE^2)} \right\},$$

$$U = 100 \cdot \left\{ PO/E + z\sqrt{P^2O/(nE^2)} \right\},$$

where  $n$  is the donor potential, and  $z$  is the 97.5th percentile of the standard normal distribution.

Likewise, we can construct one-sided upper 95% confidence limits for OPO donation and organ transplantation rates without race/ethnicity stratification, with  $z$  in  $U$  changed to the 95th percentile of the standard normal distribution. These unstratified metrics and their one-sided upper 95% confidence limits are crucial in defining a competitive 3-tier system for performance-based OPO re-certification<sup>26</sup>. Each OPO is placed into one of the following three tiers: (1) Tier-1 OPOs each have their upper 95% confidence limits lying within the top 25% of all OPOs for both unstratified metrics in the preceding year; (2) Tier-2 OPOs each have their upper 95% confidence limits lying within the top 50% of all OPOs for both unstratified metrics in the preceding year, but unqualified as Tier-1 OPOs; (3) Tier-3 OPOs each have their at least one upper 95% confidence limit lying outside the top 50% of all OPOs for both unstratified metrics in the preceding year. In the CMS final rule, Tier-1 OPOs are considered top performers and will be re-certified; Tier-2 OPOs are considered to have met the outcome requirements under §486.318 of the Code of Federal Regulations, but will not be automatically re-certified; Tier-3 OPOs are considered as failing the outcome requirements and will be de-certified. To ensure that DSAs are entrusted to the highest performing OPOs, at the end of each re-certification cycle, DSAs for Tier-2 and Tier-3 OPOs will be opened for competition from Tier-1 and Tier-2 OPOs.

### Caterpillar plots

Caterpillar plots were used to compare race-/ethnicity-specific OPO donation and organ transplantation rates<sup>17,18</sup>. Each OPO in a caterpillar plot is represented as a point surrounded by a horizontal bar indicating the value of a metric (donation or organ transplantation rate) and its corresponding 95% confidence intervals, respectively. Points and confidence intervals are colored to indicate tier status. Along the vertical axis, OPOs are arranged in a descending order of the metric in question. As a reference level, the dashed vertical line in each plot indicates either the race-/ethnicity-specific national donation or organ transplantation rate. To ease the assessment of racial/ethnic disparities, OPO donation and organ transplantation ratios along with 95% confidence intervals were also visualized as caterpillar plots (with reference lines at 1). OPO name abbreviations were anonymized due to privacy considerations.

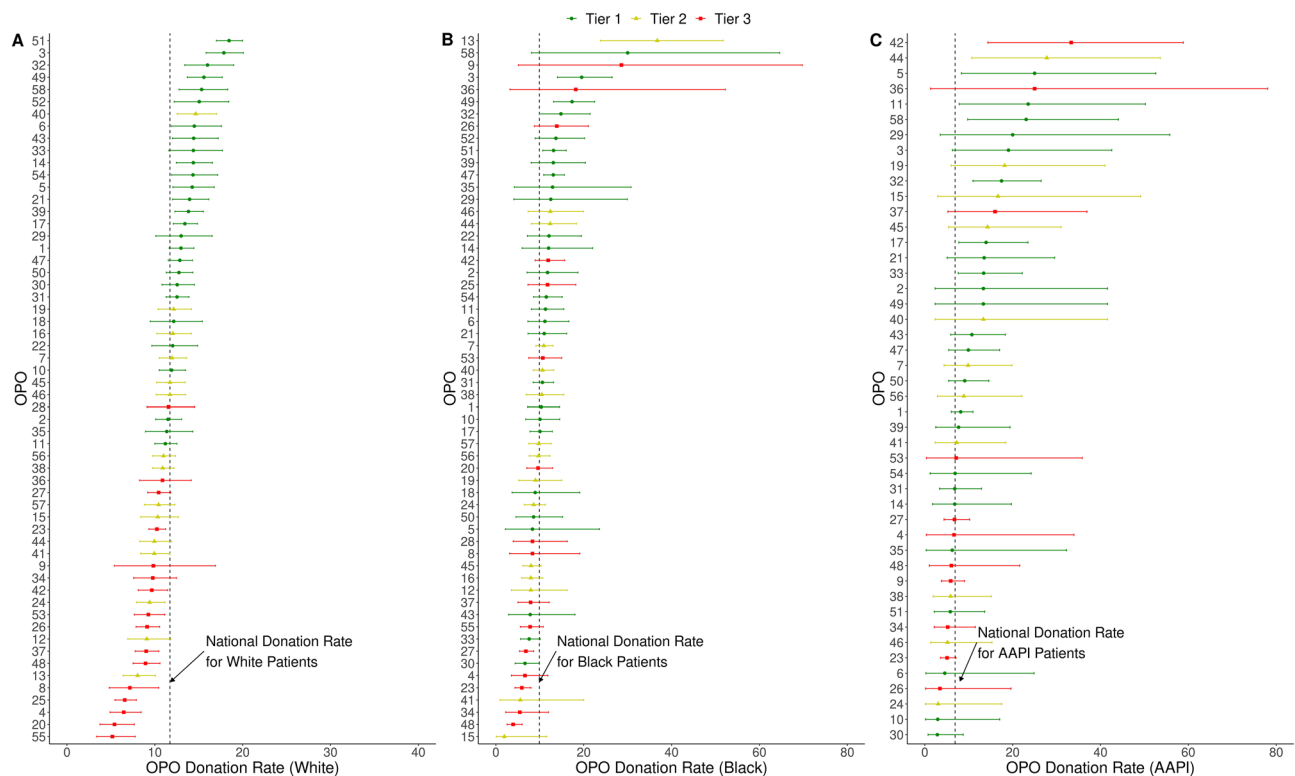
All analyses were conducted using R version 3.4.3. The study was exempted from approval by the University of Michigan Institutional Review Board. Informed consent was waived by the ethics committee as per the national legislation. All methods were carried out in accordance with relevant guidelines and regulations by the CMS.

## Results

### Race-/ethnicity-specific OPO donation rates

OPO donation rates for White, Black, and AAPI individuals are shown in Fig. 1, with race-specific national donation rates as reference. For White donors, the ranking of OPOs is largely consistent with their tier status: 15 top-ranked OPOs had donation rates significantly higher than the national donation rate, 14 of which were classified as best performing OPOs in Tier 1; 13 bottom-ranked OPOs had donation rates significantly lower than the national donation rate, 11 of which were classified as Tier 3 OPOs. In contrast, the rate-based OPO ranking for Black or AAPI groups does not always reflect the overall performance of OPOs: only 5 OPOs had their donation rates for Blacks significantly higher than the national rate, while 3 had their donation rates significantly lower than the national rate. Among AAPI individuals, there were 8 OPOs with donation rates significantly higher than the national rate, but no OPO had a donation rate significantly lower than the national rate.

Similar to the ranking in the White group, the ranking of OPOs based on non-Hispanic OPO donation rates is mostly aligned with the tier status: 12 of 13 top-ranked OPOs were Tier 1 OPOs, while 10 of 13 bottom-ranked OPOs were Tier 3 OPOs (Fig. 2B). Within the Hispanic population, 10 OPOs had their donation rates greater than the national rate, 7 of which were Tier 1 OPOs; only 3 OPOs had their donation rates less than the national rate, 2 of which were Tier 3 OPOs.



**Fig. 1.** OPO donation rate for Whites, Blacks, and Asian Americans and Pacific Islanders (AAPIs).

In addition to intra-race/-ethnicity comparisons, Figs. 1, 2, and 3 facilitate an in-depth assessment of OPO performance in terms of racial/ethnic differences in organ donation. For example, OPO 13, a satisfactory performer in Tier 2, had a Black donation rate significantly higher than the corresponding national rate, but a White donation rate significantly lower. As a result, its OPO donation ratio (Black versus White) was much greater than 1 and the highest among all OPOs (Fig. 3). OPO 30, a Tier 1 organization with outstanding overall performance, had its Black-White and AAPI-White donation ratios significantly lower than 1, a compelling indication of racially inequitable organ donation. OPO 23, an underperforming (Tier 3) OPO with a non-Hispanic donation rate significantly lower than the corresponding national rate and a Hispanic donation rate consistent with national expectations, had its Hispanic-non-Hispanic donation ratio significantly higher than 1.

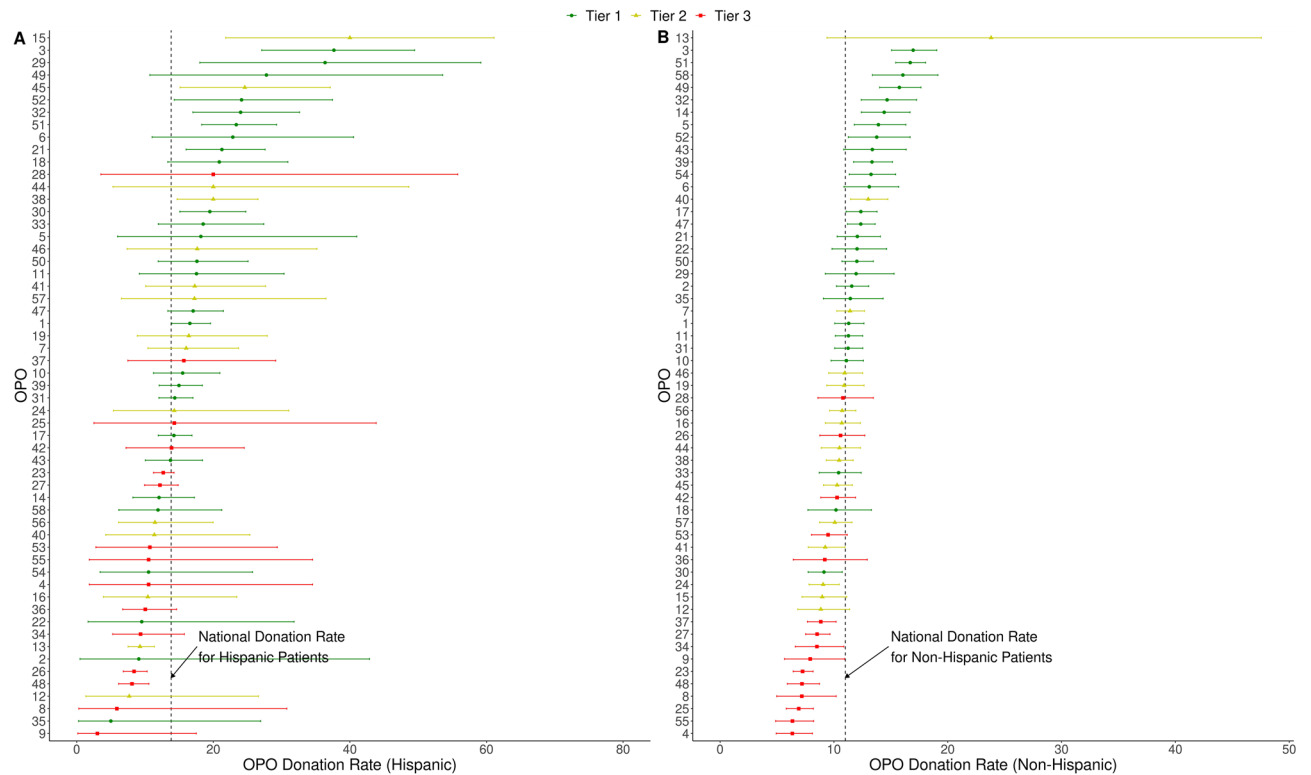
### Race-/ethnicity-specific OPO organ transplantation rates

Figures 4 and 5 display race-/ethnicity-specific OPO organ transplant rates along with 95% confidence intervals. With the ranking being largely consistent with the tier status in the White and non-Hispanic groups, many OPOs were identified as significantly different from the national organ transplantation rate (more than those identified as significantly different from the national organ donation rate), 14 higher and 18 lower than the national rate in the White population, and 18 higher and 21 lower than the national rate in the non-Hispanic population. Rankings in Black, AAPI, and Hispanic groups are generally not in line with tier designations. In the Black group, there were 10 OPOs with organ transplantation rates significantly higher and 14 OPOs with organ transplantation rates significantly lower than the national organ transplantation rate; in the AAPI population, 11 and 9 OPOs had their organ transplantation rates significantly higher than and lower than the national rate, respectively; in the Hispanic population, 14 and 17 OPOs had organ transplantation rates significantly higher and lower than the national reference rate, respectively.

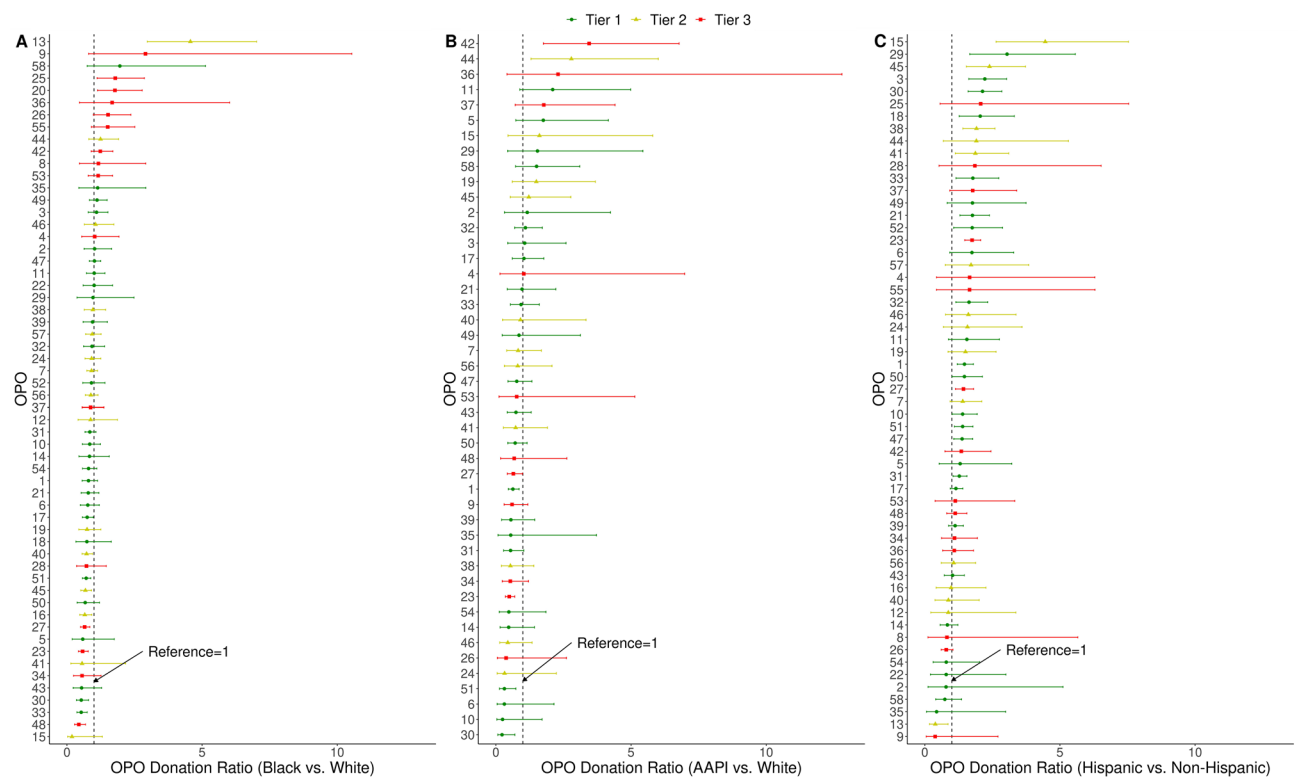
Compared with organ donation, racial disparities against Blacks and AAPIs were more prevalent among OPOs in terms of organ transplantation (Fig. 6). There were 20 OPOs with Black-White organ transplantation ratios significantly less than 1, whereas only 7 OPOs had Black-White organ donation ratios significantly less than 1; 17 OPOs had their AAPI-White organ transplantation ratios less than 1, whereas only 4 OPOs had their AAPI-White organ donation ratios less than 1. Similar as in organ donation, ethnic differences in organ transplantation were mostly in favor of Hispanics: 23 OPOs had their Hispanic-non-Hispanic organ transplantation ratios significantly higher than 1, whereas only 1 OPO had its ratio significantly lower than 1.

### Discussion

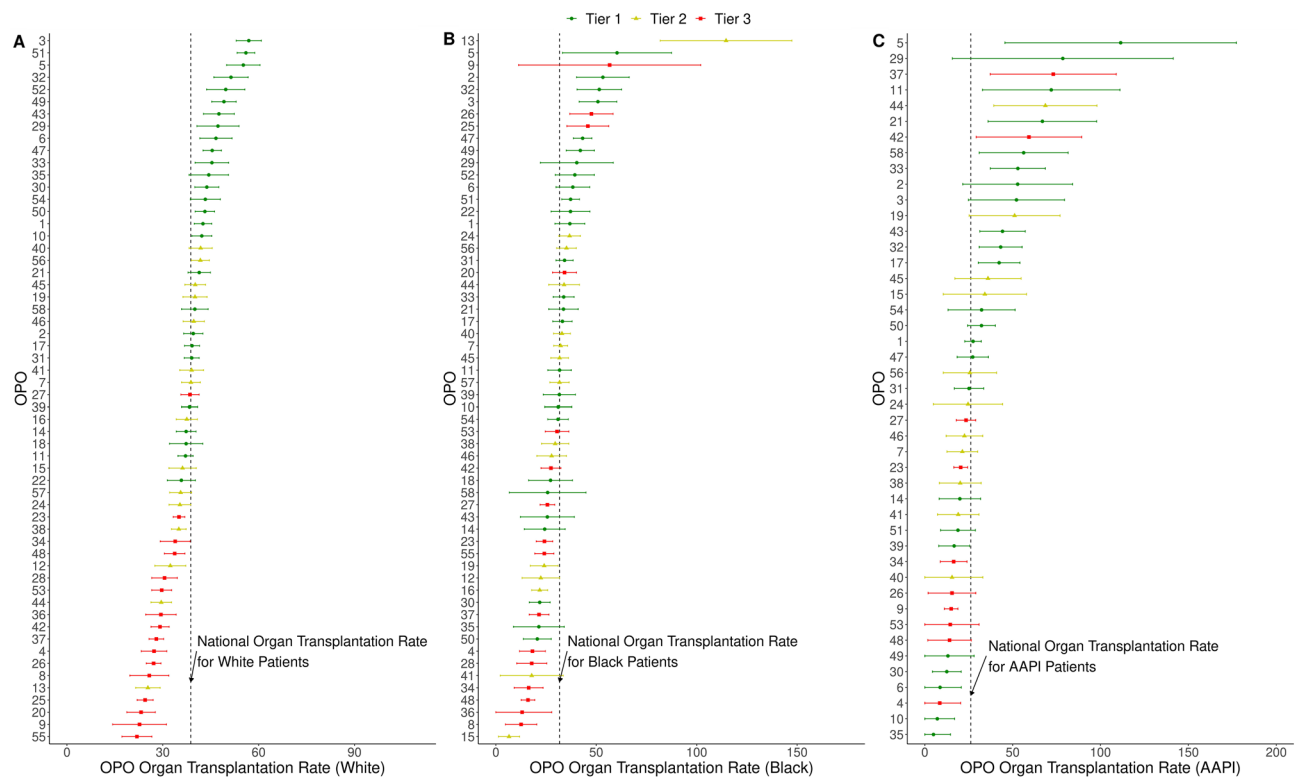
Limited organ donation and access to organ transplantation among minority populations have been well documented<sup>27–33</sup>. To promote an equitable organ transplantation system, it is crucial that the assessment of OPO performance should account for the performance variation in organ donation and transplantation within and across OPOs.



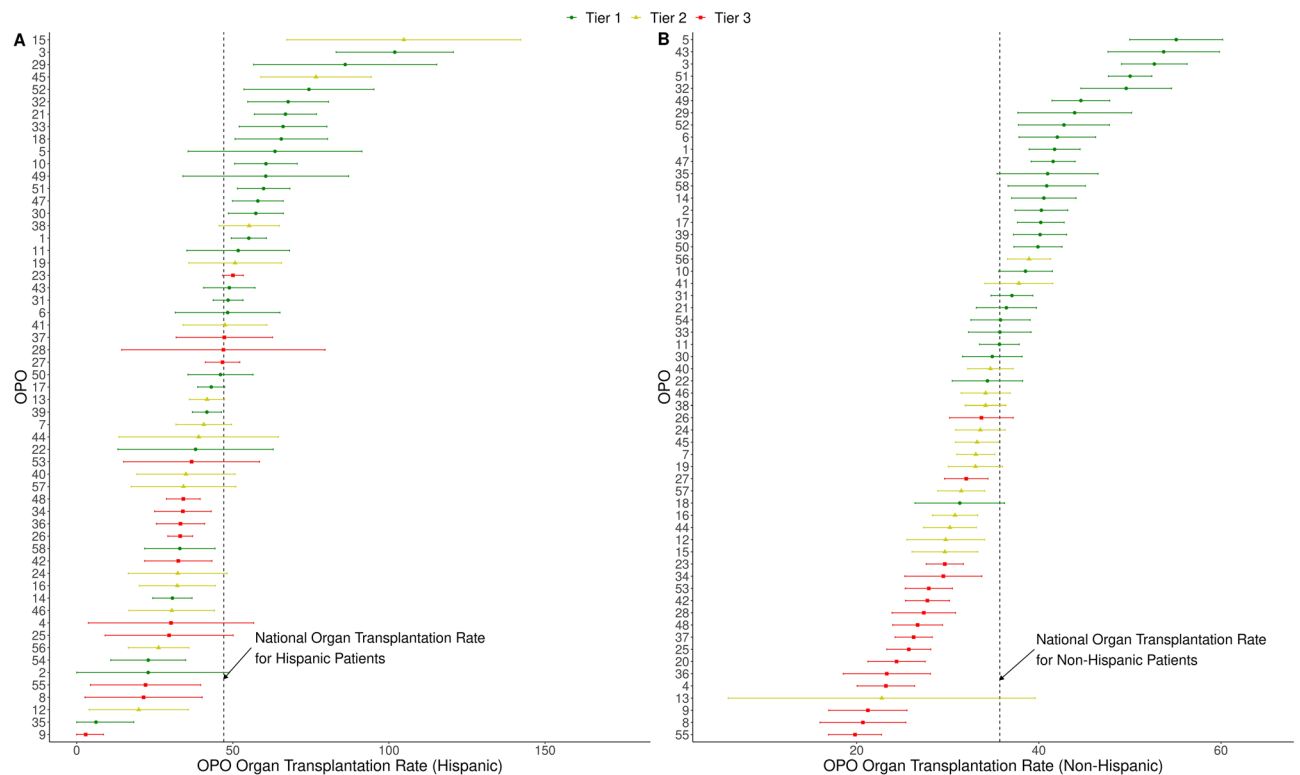
**Fig. 2.** OPO donation rate for Hispanics and non-Hispanics.



**Fig. 3.** OPO donation ratio: Black vs. White, Asian American and Pacific Islander (AAPI) vs. White, and Hispanic vs. non-Hispanic.

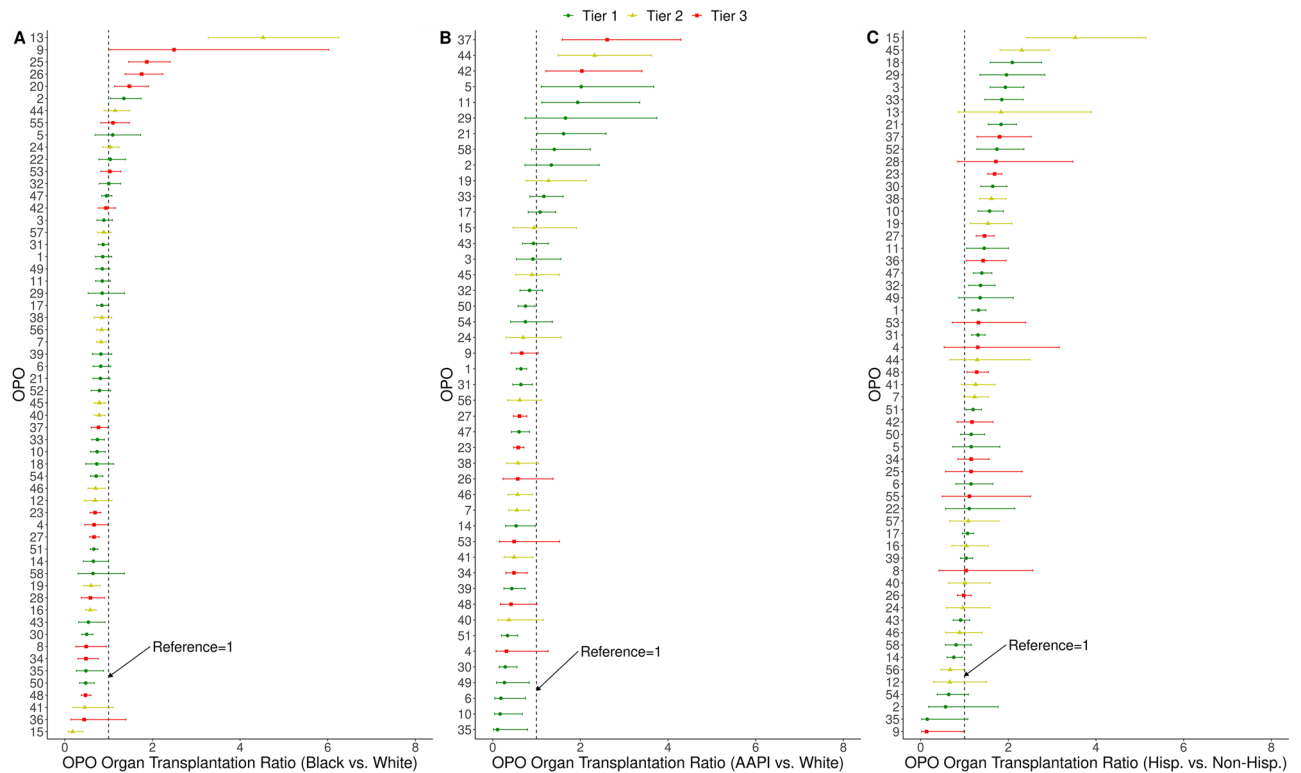


**Fig. 4.** OPO organ transplantation rate for Whites, Blacks, Asian Americans and Pacific Islanders (AAPIs).



**Fig. 5.** OPO organ transplantation rate for Hispanics and non-Hispanics.





**Fig. 6.** OPO organ transplantation ratio: Black vs. White, Asian American and Pacific Islander (AAPI) vs. White, and Hispanic vs. non-Hispanic.

Motivated by population-level racial/ethnic disparities in organ transplantation (Supplemental Fig. 1), this study sheds light on the current status of racial/ethnic disparities in organ supply and efficiency of organ utilization at the OPO level, provides an analytical framework for implementing equity-focused OPO performance assessment based on CMS-endorsed metrics, and catalyzes targeted strategies to alleviate health care disparities in organ donation and to enhance equitable efficiency in organ utilization. While there remain various challenges that preclude sustainable progress, it is important that efforts to identify disparities as noted in this study will enhance the accountability for inequitable organ procurement and distribution among OPOs so that equitable organ access can be better incentivized.

The 3-tier system and metrics were designed to introduce elevated competition among OPOs<sup>7</sup>. To avoid over-penalizing small OPOs which tend to have wider confidence intervals, lower confidence limits are not used to determine tiers. Under this evaluation system, OPOs would have to optimize the number of donors and organs transplanted within their DSAs to preserve their certification status<sup>34</sup>. Nonetheless, OPO performance ranking under the 3-tier system is dominated by White and non-Hispanic donors as reflected in Figs. 1A and 4A and Figs. 2B and 5B. Relying solely on the overall performance of OPOs without considering the variation in performance across racial/ethnic groups may disincentivize efforts to achieve equity, or at least obscure the fact that racial/ethnic disparities exist in organ donation and transplantation<sup>31,35</sup>. Our analytical efforts here, aimed at unveiling inequities in organ donation and transplantation efficiency among OPOs, serve as a timely remedy that increases the awareness of the problem. Figures 3 and 6 provide a means to evaluate OPOs regarding equitable organ donation and transplantation. If the 95% confidence interval of an OPO donation or organ transplantation ratio lies to the left of the reference line at 1, it indicates potential racial/ethnic disparities against the minority population in question. Otherwise, there is no significant evidence of disparities. These plots can be used by CMS for evidence-driven OPO assessment in equitable care, complementing the existing 3-tier system. For example, OPOs with significantly low organ donation and transplantation rates in minority racial/ethnic groups may be required to implement strategies to address disparities, such as diversifying and educating their staff to promote culturally competent and transparent communication with donor families and transplant centers, combating implicit biases against minority donors and their families, advocating for organ donation in socioeconomically disadvantaged communities, and ensuring equitable access to resources, services, and technology throughout the procurement process. Future research that draws from the expertise of clinicians and policymakers is needed to propose incentive structures for OPOs to identify the sources of racial and ethnic disparities among their patient populations and implement solutions to address these issues. This type of incentivization has been successfully applied to improve overall healthcare quality and reduce disparities in other contexts such as hospital readmissions<sup>38</sup>. Admittedly, organ transplantation rates depend on a wide range of factors that are not entirely within the control of OPOs; thus, disparities in transplantation rates among minority donor groups may also reflect the impact of organ transplant centers or other structural factors within

the transplant network. These additional factors should be considered and addressed simultaneously through separate evaluations and incentives to improve quality of care.

Importantly, our analysis highlights issues of inequitable organ donation and transplantation efficiency not captured by the 3-tier system. For instance, OPO 30 is of Tier-1 with excellent overall performance in organ donation and transplantation rates. However, it has much lower OPO donation rates for Blacks and AAPIs than a donation rate for Whites; it also has OPO organ transplantation rates for Blacks and AAPIs significantly lower than the corresponding national rate and an OPO organ transplantation rate for Whites significantly higher than the national rate. Consequently, OPO 30 has Black-White and AAPI-White donation and organ transplantation ratios significantly lower than one, suggesting striking disparities against Blacks and AAPIs. While racial/ethnic segregation and geography might have played a role in the variable performance of OPO organ donation and transplantation<sup>14,36,37</sup>, the proposed approach, complementing the current OPO performance metrics, can still be harnessed to identify profound health equity issues and opportunities for improvement in organ allocation. Additionally, the graphical representation based on caterpillar plots can inform equity-oriented policies and guidelines beyond existing methods.

Our findings provide novel insights over other studies that have assessed racial and ethnic disparities in the context of organ donation and transplantation. Since the revised final rule was announced by CMS in 2020, several studies have evaluated the impact of adjusting for age, race/ethnicity, and area deprivation in outcome measures on OPO tier status change<sup>39–41</sup>. While their reasons for comprehensive risk adjustment in OPO performance metrics are justifiable, their focus remains on overall OPO performance rather than on OPO-level racial/ethnic disparities, especially given the fact that adjusting for race may mask racial disparities<sup>42</sup>. Using radar charts, another study considered a graphical approach to OPO assessment in 8 domains, two of which are equity-related<sup>43</sup>. This approach allows exploration of inter-OPO performance differences, but does not support intra-OPO comparison. By contrast, our approach of visualizing OPO performance from an equity perspective allows both across- and within-OPO performance evaluation under the current CMS framework, which closely aligns with the CMS Disparity Methods applied to the Hospital-Wide Readmission measure<sup>38</sup>. In addition, several studies of European transplant systems have uncovered racial and ethnic disparities in organ donation and transplantation at a national level, which is consistent with the findings of our U.S.-based study<sup>44–46</sup>. However, our study adds to these national assessments by examining racial and ethnic disparities at the level of the OPO, a healthcare entity that is a unique and pivotal component of the U.S. transplant network. Thus, our study is supportive of previous findings that have recognized disparities in organ donation and transplantation, but it allows for the detection of more actionable opportunities within specific OPOs to improve equity in donation and transplant rates. This work is important because successful organ donation and transplantation depends on a wide range of factors, such as patient and family attitudes towards donation, clinician and OPO interactions with patients, and structural factors or policies under the broader transplant network<sup>47,48</sup>. Further research is needed to detect sources of disparities in donation and transplant rates at a more granular level both within and beyond OPO control.

Our study should be considered with the following limitations: First, compared with the large White and non-Hispanic populations, the number of potential donors, donors, and transplanted organs from Black, AAPI, and Hispanic groups was limited. As a consequence, more OPOs with extreme donation and organ transplantation rates for minority groups were associated with wider confidence intervals than OPOs with extreme rates in White and non-Hispanic groups, making it difficult to affirm the significance of disparities in small-sized OPOs<sup>49</sup>. Second, due to the use of summary-level data, comprehensive risk adjustment was not incorporated in the construction of race/ethnicity-specific OPO performance metrics. In line with the revised CMS final rule, only age was adjusted for in OPO organ transplantation rates, while no risk-adjusted standardization was implemented in the calculation of OPO organ donation rates. Despite the aim of assessing health care disparities in OPOs following the CMS methodology, individual- or hospital-level effects may not be fully separated from OPO-level effects, possibly leading to excess cross-race/ethnicity variation in the performance of OPOs<sup>50,51</sup>. Finally, while the national evaluation system for OPOs currently does not distinguish between different donor types, future studies may seek additional data that allows for calculation of donation and transplant rates stratified by donor type (donor after circulatory death versus brain death) or other factors to determine if OPOs need to improve certain types of organ recovery more than others.

In conclusion, this study identified significant racial/ethnic disparities within many OPOs as well as discrepancies between race/ethnicity-stratified performance rankings and the overall tier rankings. Since these findings would otherwise be obscured in a race/ethnicity-unstratified analysis, it is recommended that racial/ethnic-specific outcome measures are implemented along with existing metrics to facilitate a more comprehensive OPO performance assessment. OPOs with significantly inequitable organ donation and transplantation should focus on improving their performance among minority racial/ethnic groups.

### Data availability

The data that support the findings of this study are available from the U.S. Centers for Medicare and Medicaid Services (CMS) but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the corresponding author upon reasonable request and with permission of CMS.

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## Author contributions

WW, JMM, RSS, TS, JCM, and KH participated in research idea and design. JMM, JS, and KH participated in data acquisition. WW, JMM, NH, LB, RSS, and KH participated in data analysis. WW, JMM, RSS, TS, AN, JCM, JS, CD, RP, AE, YC, JS, and KH participated in data interpretation. WW, JMM, NH, LB, and KH participated in statistical analysis. JMM and KH participated in supervision and mentorship. All authors have reviewed and approved the final version of this manuscript and have agreed to the decision to submit it for publication.

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## Declarations

## Competing interests

The authors declare no competing interests.

## Additional information

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