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EDITORIAL

Equity in ARDS trials: some encouraging findings, and the significant work ahead

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Antiracism, as defined by Ibram X. Kendi, is characterized not by ethics or intentions, but rather by policies that produce or sustain racial equity [1]. To create policies that produce equity, and to evaluate whether those policies have achieved their goals, we need data [2]. Critical care researchers have a particular inquiry gap to fill in the pursuit of equity:

- Are we achieving equity through the inclusion of minoritized patients in trials, in proportions that are reflective of the impact of critical care syndromes on these patients?
- Are we achieving equity as evidenced by equivalent patient-centered outcomes across minoritized and majority groups in trials?
- What can we learn from the answers to the above questions that enables us to pursue policies and practices that increase equity among critically ill patients?

In this issue of Intensive Care Medicine (ICM), Papoutsi and her colleagues analyzed eight acute respiratory distress syndrome (ARDS) Network (ARDSNet) and PETAL Network therapeutic clinical trials published between 2000 and 2019, to evaluate the inclusion and outcomes of racialized participants [3]. Their results are encouraging, though not generalizable to other critical care trials or research consortia. First, only 3% of participants had undocumented race and ethnicity in the five most recent trials (supplementary Table E1 in the original article). This is in contrast to infrequent reporting of race and ethnicity and other important demographic characteristics in other clinical trials [4–6]. Second, the representation of minoritized individuals was good compared to other trials. Representation of racial and ethnic minority participants ranged from 24.9% in ALVEOLI to 38.5% in VIOLET, with a pooled representation of 30.4% across the 8 studies (supplementary Fig. E1 in the original article). Figure 1 of the original article highlights that two trials conducted more than a decade apart, FACTT (2006) and VIOLET (2019) included a higher minoritized participant representation than the population-adjusted disease burden of ARDS. This is in contrast to other studies, in which disadvantaged groups may be intentionally or unintentionally excluded from participation [7, 8]. Third, other than the FACTT trial in which mortality was higher in non-White participants, mortality rates were not statistically different between White and racial minority participants with ARDS of any severity in the seven other trials (supplementary Table E6 in the original article). The authors' findings of similar mortality outcomes in these studies differ from other publications reporting worse outcomes for people who self-identify as Black and other minoritized groups [9–11].

What can we learn from these positive findings of equity in representation and outcomes in this series of ARDS trials? First, in terms of representation, the National Heart, Lung, and Blood Institute (NHLBI) required inclusion of and reporting on minority racial groups from the inception of the ARDS Network [12]. This suggests that inclusiveness and reporting mandates from government agencies that fund large-scale research can be effective in driving equitable representation in research. Second, the finding of similar mortality outcomes in racialized versus white participants is important in its uniqueness. A systematic review of 25 studies performed in intensive care units (ICUs) including more than 751,000 patients reported that Black patients had higher mortality; the authors emphasized the impact of

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structural inequalities on racial differences in mortality in critically ill patients [11]. These contradictory findings across studies raise the question of whether some large interventional trials like those in ARDSNet and PETAL may mask and/or mitigate some of the impacts of structural inequalities that exist in usual clinical care, through the highly protocolized nature of eligibility, enrollment, protocols, and hospital sites in the trials. Other contributory factors could include selective enrollment, such that minoritized patients with the highest social risks were excluded from ARDS trial participation [8], or because participants in interventional trials have better outcomes than similar patients who are not enrolled in a clinical trial. This deserves close scrutiny to understand what is different in this series of ARDSNet and PETAL studies that led to more equitable outcomes by racial groups than has been seen in other trials and in non-research clinical settings.

In addition, what can we learn from this analysis that suggests a need to do better in critical care trials? While reporting of racial groups was high in this series of trials, there was inconsistent reporting of racial and ethnic groups across the eight trials, with three reporting only "White race", three reporting four categories (i.e., White, Black, Hispanic, and other/unknown), and two reporting five categories in the manuscript (White, Black, Hispanic, Asian, and other in one; non-Hispanic White, Black, non-Black Hispanic, other, and NA in the other). A major limitation of pooling racial and ethnic groups is that the pooled categories each represent very heterogeneous groups, particularly the "Other" category. In addition, it is challenging to compare racial and ethnic diversity, and the outcomes of specific racial and ethnic groups across trials. Initiatives to improve the inclusiveness of research and to evaluate critical care outcomes of minoritized groups are limited by the lack of granular and consistently reported demographic data. This underscores the importance of capturing self-reported and standardized social identity data, including race, ethnicity, gender, sexual orientation, ability, socioeconomic status, geographic location, and the intersection of these factors [13]. Trials need to incorporate a practical data collection tool to enhance standardized collection of sociodemographic variables for research participants, and one such tool already exists [14].

The study published in this issue of ICM [3] nicely illustrates the power of critical care networks to produce data on race and ethnicity, which can inform our work toward equity as clinicians, investigators, and advocates. When such studies have inequitable enrollment and/or outcomes, we can use this to push for change toward greater equity within clinical research. In cases like this study, where some successes in equity are demonstrated, we can use this evidence to drive change: what processes within this series of trials have been positive forces for equity, and what can be applied even outside trial settings to increase equity in critical care outcomes?

In addition, the discussion about inclusion and representation in clinical trials extends beyond race and ethnicity. Initiatives to ensure representativeness of the population with the condition of interest must extend to other equity-deserving groups, including but not limited to women, older adults, persons living with disabilities, people of sexual orientation minorities, and people in poorer socioeconomic strata. A major pillar of these initiatives is the reporting of granular, disaggregated, standardized demographic and social determinants of health data [14].

We are encouraged that investigators are increasingly measuring equity, diversity and inclusion in clinical trials, and that funding bodies are effectively mandating inclusion and reporting. We are also reassured to see an example of a series of trials in which minority-race participants' mortality outcomes are similar to white participants. However, important work remains. Next steps include improving the comparability and granularity of reporting of minoritized groups, and rigorous research into what may be contributing to equitable outcomes for minoritized patients in trials, to understand any factors that are transferrable to other trials and to clinical care.

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Conflict of interests
The authors declare that they have no competing interests.

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