Abstract

IMPORTANCE Representativeness of populations within neonatal clinical trials is crucial to moving the field forward. Although racial and ethnic disparities in research inclusion are well documented in other fields, they are poorly described within neonatology.

OBJECTIVE To describe the race and ethnicity of infants included in a sample of recent US neonatal clinical trials and the variability in this reporting.

EVIDENCE REVIEW A systematic search of US neonatal clinical trials entered into Cochrane CENTRAL 2017 to 2021 was conducted. Two individuals performed inclusion determination, data extraction, and quality assessment independently with discrepancies adjudicated by consensus.

FINDINGS Of 120 studies with 14,479 participants that met the inclusion criteria, 75 (62.5%) included any participant race or ethnicity data. In the studies that reported race and ethnicity, the median (IQR) percentage of participants of each background were 0% (0%-1%) Asian, 26% (9%-42%) Black, 3% (0%-12%) Hispanic, 0% (0%-0%) Indigenous (eg, Alaska Native, American Indian, and Native Hawaiian), 0% (0%-0%) multiple races, 57% (30%-68%) White, and 7% (1%-21%) other race or ethnicity. Asian, Black, Hispanic, and Indigenous participants were underrepresented, while White participants were overrepresented compared with a reference sample of the US clinical neonatal intensive care unit (NICU) population from the Vermont Oxford Network. Many participants were labeled as other race or ethnicity without adequate description. There was substantial variability in terms and methods of reporting race and ethnicity data. Geographic representation was heavily skewed toward the Northeast, with nearly one-quarter of states unrepresented.

CONCLUSIONS AND RELEVANCE These findings suggest that neonatal research may perpetuate inequities by underrepresenting Asian, Black, Hispanic, and Indigenous neonates in clinical trials. Studies varied in documentation of race and ethnicity, and there was regional variation in the sites included. Based on these findings, funders and clinical trialists are advised to consider a 3-point targeted approach to address these issues: prioritize identifying ways to increase diversity in neonatal clinical trial participation, agree on a standardized method to report race and ethnicity among neonatal clinical trial participants, and prioritize the inclusion of participants from all regions of the US in neonatal clinical trials.
Introduction

Neonatal research is the key mechanism to advance medical knowledge, improve treatment options, and optimize outcomes within neonatology. Including a diverse population in research studies is critical to improving patient outcomes. Difficulty recruiting from marginalized populations, such as Black communities, is a prevalent and long-standing problem in adult medical research. Underrepresentation of Black and Hispanic children has been documented in pediatric critical care and oncology research. Although data from neonatal research are limited, those available suggest similar underrepresentation. Within neonatal research, Black infants were less likely to enroll in Neonatal Research Network studies compared with Hispanic or White infants. Parents on Medicaid, those reporting lower income, and those identifying as Black were less likely to enroll their infant in a multicenter neonatal clinical trial.

Failure to include minoritized racial and ethnic populations in neonatal clinical trials is particularly problematic because these populations have significantly worse clinical outcomes. Black mothers and birthing parents have higher preterm birth rates than their White counterparts, a gap that has increased over time. There are significant disparities in outcomes for minoritized infants, including both for term newborns and for preterm infants, resulting in increased morbidity, cost, and long-term disability. We must note that race is a social construct, and these disparities are due to systemic racism, not biological differences. Nonetheless, because of these documented worse outcomes, including minoritized infants in neonatal research is critical, as the underrepresentation of these populations in neonatal research threatens to exacerbate existing health disparities.

We sought to quantify the race and ethnicity of neonatal research participants and describe how race and ethnicity are reported. We included only clinical trials as they are the most fundamental contributors to the knowledge base. The primary objective was to identify the race and ethnicity of participants in neonatal clinical trials and compare with a reference population. We hypothesized that non-Hispanic and White infants would be overrepresented and that Hispanic infants and those with races other than White would be underrepresented. We compared these data with both US census data and data from the Vermont Oxford Network (VON) as the best estimates of available recent race and ethnicity data of the US neonatal intensive care unit (NICU) population. As a secondary objective, we aimed to describe the geographic location of sites participating in included studies.

Methods

For this systematic review, we performed a systematic search of Cochrane CENTRAL in February 2022 with assistance from a research librarian (Table 1) following the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) reporting guidelines. We limited the search to full-length English-language articles on neonatal human studies conducted exclusively in the US and entered into Cochrane CENTRAL from 2017 to 2021. We included only peer-reviewed neonatal

<table>
<thead>
<tr>
<th>Table 1. Search Criteria for Studies</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Criterion</strong></td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>2</td>
</tr>
<tr>
<td>3</td>
</tr>
<tr>
<td>4</td>
</tr>
<tr>
<td>5</td>
</tr>
<tr>
<td>6</td>
</tr>
</tbody>
</table>

Abbreviations: ICU, intensive care unit; mh, medical subject heading; NICU, neonatal intensive care unit.
studies that met the National Institutes of Health definition of a clinical trial with at least 20 neonates. We excluded fetal studies, placental tissue studies, cord blood studies, well newborns, and infants not born in the US. To avoid the potential of participants in a study being represented multiple times, only the first published report from a clinical trial was eligible. Our planned methods were published on PROSPERO (record No. 240234).

Our ideal comparison group would be all patients admitted to US NICUs. As no nationally available data on NICU admissions contain race and ethnicity data, we used a large VON publication on very preterm infants for this comparison. The major disadvantage of this data set was its focus solely on preterm infants. Its advantages were that it was recent (infants born 2014-2016) and captured 743 NICUs and 122,269 infants across all US regions. The VON data set included the percentages of preterm infants by race and ethnicity, including 4.8% Asian neonates, 29.7% Black neonates, 17.8% Hispanic neonates, 0.7% Indigenous (eg, Alaska Native, American Indian, and Native Hawaiian), 44.1% White neonates, and 2.8% neonates with race and ethnicity reported as other or unknown. US National Vital Statistics data on race and ethnicity were also reviewed and showed the racial composition of all live births in the US during 2018 to 2020 as 7% Asian neonates, 15% Black neonates, 24% Hispanic neonates, 0.8% Indigenous neonates, and 52% White neonates. The discrepancy between the race and ethnicity of preterm infants and all live-born infants is likely due to the disproportionate number of Black infants born preterm. Given the discrepancies in these 2 potential reference samples, we included both as comparisons to establish our best estimate of the US clinical NICU population.

Two researchers (including A.N.J.L., H.S., or E.O.) independently screened the abstracts and titles of articles for potential inclusion. The full text of the remaining articles was obtained and evaluated against the same inclusion and exclusion criteria. Disagreement on which articles met inclusion criteria was settled by consensus of 3 team members (including A.N.J.L., H.S., E.O., and E.M.W.). Data extraction included any available race and ethnicity data of participants and geographic locations of participating sites. Two team members (including A.N.J.L., H.S., or E.O.) performed data extraction independently. Discrepancies were settled by group consensus with at least 3 authors (A.N.J.L., H.S., E.O., and E.M.W.). The University of Washington REDCap database was used for data collection and management. Two independent researchers assessed the quality and potential for bias of each article using the scoring system for methodological rigor developed by Hawker et al, which prompts users to rank different domains and aspects of study reporting (eg, abstract and title, implications and usefulness) on a 4-point Likert scale, ranging from 4, indicating good to 1, very poor. Scores were then added up to determine the overall study quality, as others have done previously.

**Statistical Analysis**

Data were analyzed with Stata version 18 (StataCorp), and graphics were created using Tableau software version 2022 (Tableau Software). Descriptive statistics were used to tabulate counts and percentages. Percentages were reported for both percentages of individuals with a stated race or ethnicity per study and for the percentage of the whole pooled study sample. The comparison of reporting of race and ethnicity data over time was evaluated with 2-sided Fisher exact testing with significance set at $P = .05$. Data were analyzed in March 2023, with additional confirmatory analyses performed in October 2023.

**Results**

We identified 120 studies that were entered into Cochrane CENTRAL 2017 to 2021 and met our inclusion criteria (eFigure 1 in Supplement 1). There was a range in the articles’ availability via electronic publication (2016-2021) and publication year (2017-2023). In total, 14,479 participants from study sites with 174 unique zip codes spanning 38 states and the District of Columbia were represented in these studies. The studies evaluated a wide range of interventions within...
neonatology, including procedural (eg, delayed cord clamping), pharmacologic (eg, antithrombin), feeding (eg, protein supplementation), and diagnostic (eg, genome sequencing) (eTable in Supplement 1).23-142 There were 75 studies25-27,30,32-34,37-44,47-49,51,53,57,58,61,62,64,68,70,72-75,77,78,81-83,87,88,90-92,94-98,100,104,105,107-110,115,116,119-126,128-138,141 (62.5%) that included participant race and ethnicity data of any kind (eTable in Supplement 1). Most studies reported race and ethnicity as a single combined variable (eg, non-Hispanic White), while some reported them as separate variables (eg, non-Hispanic and White).

Among the 75 studies,25-27,30,32-34,37-44,47-49,51,53,57,58,61,62,64,68,70,72-75,77,78,81-83,87,88,90-92,94-98,100,104,105,107-110,115,116,119-126,128-138,141 that reported race and ethnicity, there was a pooled sample of 10,650 participants. This pooled sample was classified as 1.2% Asian participants, 33.0% Black participants, 11.2% Hispanic participants, 0.2% Indigenous, 0.8% participants identifying as multiple races, 49.3% White participants, and 10.3% participants identifying as other race or ethnicity (eFigure 2 in Supplement 1).

The median (IQR) percentage of participants of each background were 0% (0%-1%) Asian participants, 26% (9%-42%) Black participants, 3% (0%-12%) Hispanic participants, 0% (0%-0%) Indigenous participants, 0% (0%-0%) participants identifying as multiple races, 57% (30%-68%) White participants, and 7% (1%-21%) participants identifying as other race or ethnicity. The difference between aggregate and median percentage was particularly notable among Black participants, because 10 studies38,49,77,97,110,120-122,131,133 had very high percentages of Black participants. Among these studies with more than half of the sample reported as Black participants, 9 studies38,49,97,110,120-122,131,133 were single-centered trials in cities with a predominantly Black population and 1 study77 had Black race as an inclusion criterion.

We evaluated study methods to identify where race and ethnicity information originated and whom it described. A few studies specified the source of race and ethnicity information: 8 studies32,77,82,88,90,91,96 reported that it was from parental report and 1 study92 reported that it was from the medical record; the other 66 studies did not specify. Of studies that specified whose race was reported, 31 studies26,30,37,47-49,51,53,57,58,61,68,75,78,91,92,100,104,107,108,110,121,123,129,131,133-135,137,138,141 reported the infant’s information, 13 studies32,39,42,43,81-83,88,96,115,125,126,128 reported the mother’s information (using the label mother specifically), and 1 study77 reported the mother’s, father’s (using the label father specifically), and infant’s information.

The number of included studies each year was too low to meaningfully compare trends in reporting race and ethnicity data over time. However, exploring the binary outcome of reporting vs not reporting race and ethnicity data was valuable. Figure 1 shows that the distribution of reporting vs not reporting race and ethnicity data in NICU clinical studies over the 5 years evaluated. We
assessed reporting by NIH funding: of the 52 studies funded by the NIH, 35 (67%) included race and ethnicity data. Among 68 studies not funded by the NIH, 40 studies (58%) reported race and ethnicity data; the difference between NIH-funded and non-NIH–funded studies was not statistically significant by Pearson χ².

We compared median percentages of reported race and ethnicity with the best available published clinical data on race and ethnicity in patients admitted to the NICU and with National Vital Statistics Data on US births. In our research population of 10,650 infants from 75 publications for whom any race and/or ethnicity data were available, Asian, Hispanic, and Indigenous participants were underrepresented compared with both comparator groups. Black infants (26% in our sample) were overrepresented compared with US birth statistics (15%) but underrepresented compared with the clinical NICU population (30%) (Figure 2). White participants were overrepresented (57%) compared with both comparator groups (52% of US live births, 44% of US clinical NICU population).

We evaluated the labels used by studies to describe the race and ethnicity of included infants. Studies used a range of labels to describe the race and ethnicity of participants (Table 2). For example, 8 labels were used by studies that reported any Black participants. In addition, there were many labels, typically poorly defined, to signify other, unknown, or not specified race and ethnicity (Table 2).

Finally, we also extracted data regarding the geographic location of every clinical site in each study, including hospital name, city, state, and zip code. In this set of 120 studies, there was regional variation in the study sites included: 38 states and the District of Columbia were represented (Figure 3). There was a skew to the Northeast US (40 studies [33.3%]). Study sites on the East Coast were more likely to contribute to multiple research studies.

Figure 2. Race and Ethnicity of Participants Compared With the Best Estimate of the US Clinical Neonatal Intensive Care Unit (NICU) Population

Dots indicate each individual trial’s proportion of participants in each racial and ethnic category; bars, medians; boxes, IQRs; whiskers, ranges.
**Discussion**

The findings of this systematic review of data from 120 studies including a large sample of US neonatal clinical trial participants (14,479 participants) support 3 important conclusions. First, Asian, Black, Hispanic, and Indigenous infants were underrepresented in these studies compared with our

**Table 2. Label Used to Describe Race and Ethnicity of Participants**

<table>
<thead>
<tr>
<th>Category</th>
<th>Label used*</th>
<th>No. Studies using label</th>
<th>Infants categorized as label</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asian</td>
<td>Asian</td>
<td>19</td>
<td>102</td>
</tr>
<tr>
<td></td>
<td>Asian American</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Asian or Pacific Islander</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Asian/Pacific Islander</td>
<td>1</td>
<td>17</td>
</tr>
<tr>
<td>Black</td>
<td>African American</td>
<td>21</td>
<td>672</td>
</tr>
<tr>
<td></td>
<td>African American/Black</td>
<td>2</td>
<td>43</td>
</tr>
<tr>
<td></td>
<td>African, African American</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Black</td>
<td>33</td>
<td>2439</td>
</tr>
<tr>
<td></td>
<td>Black non-Hispanic</td>
<td>1</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td>Black or African American</td>
<td>3</td>
<td>76</td>
</tr>
<tr>
<td></td>
<td>Non-Hispanic African American</td>
<td>1</td>
<td>34</td>
</tr>
<tr>
<td></td>
<td>Non-Hispanic Black</td>
<td>1</td>
<td>232</td>
</tr>
<tr>
<td>Hispanic</td>
<td>Hispanic</td>
<td>32</td>
<td>1010</td>
</tr>
<tr>
<td></td>
<td>Hispanic or Latino</td>
<td>6</td>
<td>112</td>
</tr>
<tr>
<td></td>
<td>Hispanic/Latino</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>Hispanic/Mexican</td>
<td>1</td>
<td>13</td>
</tr>
<tr>
<td></td>
<td>Hispanic-Latino</td>
<td>1</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>Latino</td>
<td>1</td>
<td>46</td>
</tr>
<tr>
<td>Indigenous</td>
<td>American Indian or Alaska Native</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>American Indian/Alaskan Native</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Native American</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Native Hawaiian or other Pacific Islander</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>Native Hawaiian or other Pacific Islander or other</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Non-Hispanic</td>
<td>Non-Hispanic</td>
<td>2</td>
<td>144</td>
</tr>
<tr>
<td></td>
<td>Non-Hispanic or Latino</td>
<td>1</td>
<td>71</td>
</tr>
<tr>
<td></td>
<td>Not Hispanic</td>
<td>1</td>
<td>23</td>
</tr>
<tr>
<td>Multiple</td>
<td>Biracial</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>More than 1</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>Multiracial</td>
<td>3</td>
<td>64</td>
</tr>
<tr>
<td></td>
<td>Multiple/biracial</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>White</td>
<td>Caucasian</td>
<td>14</td>
<td>498</td>
</tr>
<tr>
<td></td>
<td>Non-Hispanic White</td>
<td>2</td>
<td>270</td>
</tr>
<tr>
<td></td>
<td>White</td>
<td>46</td>
<td>4449</td>
</tr>
<tr>
<td></td>
<td>White non-Hispanic</td>
<td>2</td>
<td>31</td>
</tr>
<tr>
<td>Other</td>
<td>Missing</td>
<td>2</td>
<td>32</td>
</tr>
<tr>
<td></td>
<td>Non-White</td>
<td>1</td>
<td>14</td>
</tr>
<tr>
<td></td>
<td>Not reported</td>
<td>1</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>Not specified</td>
<td>1</td>
<td>23</td>
</tr>
<tr>
<td></td>
<td>Other</td>
<td>27</td>
<td>365</td>
</tr>
<tr>
<td></td>
<td>Other/unknown</td>
<td>2</td>
<td>42</td>
</tr>
<tr>
<td></td>
<td>Unknown</td>
<td>6</td>
<td>56</td>
</tr>
<tr>
<td></td>
<td>Unknown ethnicity</td>
<td>2</td>
<td>16</td>
</tr>
<tr>
<td></td>
<td>Unknown, not reported</td>
<td>2</td>
<td>86</td>
</tr>
<tr>
<td></td>
<td>Unknown/undetermined ethnicity</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Unreported</td>
<td>1</td>
<td>6</td>
</tr>
</tbody>
</table>

* The exact label used by each article is presented.
proxy for the US clinical NICU population. Second, there was substantial variation in the
documentation of race and ethnicity, which complicates the accurate interpretation of sampling and
trial findings. Third, there was substantial regional variation in participation in neonatal clinical trials.

Neonatal research risks perpetuating inequities by underrepresenting non-White neonates in
clinical trials. A recent American Academy of Pediatrics policy statement affirms that “Race is not a
biological category that produces disparities due to genetic differences; rather, it is a social category
that can have devastating biological consequences.” While reporting race and ethnicity has the
potential for benefit, it can also worsen health disparities if used to support spurious connections of
race and ethnicity with medical outcomes.

Underrepresentation of Minoritized Racial and Ethnic Populations

Clinical trials must strive to mirror the populations impacted by the studied conditions to ensure they
align with the ethical principles of beneficence and justice. Failing to include a diverse
population in neonatal clinical trials deprives neonatal research of valuable information and threatens
to exacerbate existing disparities in care. Our finding that Asian, Black, Hispanic, and
Indigenous infants were underrepresented compared with our best estimate of the national NICU
clinical population is consistent with the limited available data from the neonatal literature. The
proportions of these 4 minoritized groups in our review were higher than a review of pediatric
trials, which may be due to the sample (published articles vs ClinicalTrials.gov) or discipline
(neonatology vs pediatrics).

We must prioritize increasing diversity within neonatal clinical trials, as recommended in the
recently proposed 10 steps for increasing representativeness in neonatal clinical trials. Such work
includes upstream issues, such as when certain populations are not approached due to a perceived
disinterest in research or unavailability for follow-up. Language differences may also be a reason
for not approaching certain groups, and processes can be put in place to overcome this barrier, such
as hiring interpreters or multilingual research staff. Parents may differently consider reasons for and
against participation when deciding whether to participate in research. Certain burdens of
participation may be an annoyance for well-resourced individuals but deeply problematic for

Figure 3. Map of Sites Contributing to Included Studies

Map is based on longitude (generated) and latitude (generated). Color shows sum of counts. Details are
shown for state and county. The view is filtered on inclusions (county and state), which includes
97 studies.
individuals with fewer resources.¹⁵² Ways to improve the enrollment processes, support relationship building between researchers and parents of potential participants,¹⁵³ and decrease the burdens of participation should be considered as key targets of future work to decrease disparities in participation.

**Variation in Documentation of Race and Ethnicity Data**

Studies in this systematic review varied in their documentation of race and ethnicity in at least 4 distinct ways: categories included, specific labels used, 1-variable vs 2-variable reporting, and reporting of the data source. Many studies did not report any race and ethnicity data at all, which is consistent with prior reviews.¹⁴⁸,¹⁵⁴ Studies reporting race and/or ethnicity did not consistently use the same categories. For example, not all studies that reported race and ethnicity included a category for Asian participants. Considering this issue on a granular level, among studies with no reported Asian participants, there was rarely a way to differentiate among 4 potential realities: (1) parent was not asked about race; (2) parent declined to answer; (3) parent chose an other race or ethnicity category; and (4) parent did not fit into available choices. If researchers fail to ask race and ethnicity questions in a way that supports meaningful answers from all parents, our data on these issues will remain incomplete and unclear. Research participants may be more reluctant to answer race and ethnicity questions if they are part of certain marginalized groups¹⁵⁵ or if the options presented do not reflect their lived experience.¹⁵⁶

The labels used to describe each race and ethnicity category were inconsistent. The updated *AMA Manual of Style* emphasizes that “terminology, usage, and word choice are critically important, especially when describing people and discussing race and ethnicity.”¹⁵⁷ Heterogeneity of the labels used makes it nearly impossible to compare studies meaningfully. For example, 5 different labels were used to describe Indigenous participants. This variation in labeling is important because respondents may respond differently to the presented labels and because the variation makes it more difficult to compare race and ethnicity data across studies.¹⁵⁶ The heterogeneity of labels used diminishes data quality and decreases the ability of researchers to address disparities in research inclusion.¹⁵⁸,¹⁵⁹

The issue of 1-variable (eg, describing a participant as Hispanic Black) vs 2-variable (eg, describing a participant as Hispanic and as Black) does not have an easy solution. Most studies reported race and ethnicity as a single variable in our sample, consistent with prior work.¹⁴³,¹⁴⁸ However, racial and ethnic identity is deeply complex¹⁶⁰ and seems unlikely to be perceived as 2 independent variables. The US census treats race and ethnicity as separate and independent constructs,¹⁶¹ further complicating comparisons with 1-variable data. Recent *JAMA* guidelines¹⁶² on the reporting of race and ethnicity in medical journals did not address the issue of 1-variable vs 2-variable reporting.

Our findings reflect that, both within medicine and more broadly, there is no consensus on how to query, report, and analyze data from multiracial individuals.¹⁶⁰ None of the included studies explicitly discussed allowing individuals to choose more than 1 race category, and very few offered a multiple races option. Furthermore, the variability in other categories makes it difficult to compare between studies: for example, parents could sometimes select an other option, and sometimes other was used to describe nonrespondents. In the 2020 census, nearly 15% of individuals selected “two or more races,” indicating a growing need to ensure accurate reporting of multiracial individuals in research.¹⁶³

Few studies reported the data source of race and ethnicity; this is important because there can be discrepancies between self-reported race and ethnicity and that documented in the medical record, particularly for the Hispanic population.¹⁶⁴ In updated guidance for the *AMA Manual of Style*,¹⁵⁷ identifying the source of race and ethnicity data (eg, self-report or electronic medical record) is recommended and consistent with recent recommendations for increasing representativeness in neonatal clinical trials.¹⁴⁹
Researchers have increasingly understood that race is a social construct, and there is an evolving appreciation of the potential problems of attributing differences by race to genetics rather than as markers of systemic inequities.\textsuperscript{14,15} It would be deeply disappointing if researchers, being unsure how to work with these data, did not present them at all. A review of pediatric trials from 2008 to 2018 showed an increase in reporting of race and ethnicity over time.\textsuperscript{148}

Researchers, funders, and journal editors must agree on a standard method to ask, report, and analyze the race and ethnicity of neonatal clinical trial participants. Issues to address include separate or combined race and ethnicity variables, data origination, standardization of labels, categorization of multiracial infants, and the use of an other category. The interplay of race and ethnicity is a deeply complicated issue,\textsuperscript{160} and guidelines will need to be changed over time as they are used and as best practices evolve. Starting with established general guidelines\textsuperscript{162} and adjusting to the neonatal clinical trial context could be a good start. Simply requiring that all published neonatal clinical trials report any race and ethnicity data would be a huge step in the right direction.

**Regional Variation in Participation in Neonatal Clinical Trials**

There was geographic variability of included sites, with an overrepresentation of infants from the eastern portion of the US. Large portions of the country with minimal or no representation (eg, the American West and South) in this group of published trials included much of the rural, Asian,\textsuperscript{166} and Indigenous\textsuperscript{165} populations in the US. An Australian study\textsuperscript{167} also has noted the underrepresentation of the rural patient population in clinical research and the need to focus on increasing research capacity in such areas.

Broader geographic inclusion of infants within neonatal clinical trials should be prioritized. US regions with the highest populations of the most underrepresented populations, particularly Asian, Hispanic, and Indigenous infants,\textsuperscript{143,168,169} should be prioritized. Increased inclusion of sites within the western US could be an effective way to narrow the gap between the clinical and research populations.

**Limitations**

This study has some limitations. In an attempt to capture all US-based neonatal clinical trials, we used a variety of search terms, chosen with the assistance of an experienced research librarian; however, it is possible that we missed relevant articles. We excluded articles including infants from both the US and other countries. This was necessary because country-level demographic data were never available, but it limits the generalizability of our findings. If more granular data were available, future work should ideally include clinical trials that include both US and international NICU patients.

**Conclusions**

This systematic review of recently published US neonatal clinical trials found that Asian, Black, Hispanic, and Indigenous infants were underrepresented. Studies varied in whether and how race and ethnicity data were documented. There was regional variation in the sites included. Based on these findings, we propose the following recommendations: (1) prioritize increasing diversity within neonatal clinical trials, including research that aims to identify empirically sound and ethically acceptable ways to do so; (2) agree on a standardized method to ask, report, and analyze race and ethnicity of neonatal clinical trial participants; and (3) prioritize the inclusion of participants from all US regions.
Race and Ethnicity of Infants Enrolled in Neonatal Clinical Trials

Open Access: This is an open access article distributed under the terms of the CC-BY License. © 2023 Lyle ANJ et al. JAMA Network Open.

Corresponding Author: Elliott M. Weiss, MD, MSME, Treuman Katz Center for Pediatric Bioethics, Seattle Children's Hospital & Research Institute, 4800 Sand Point Way NE, M/S FA.2.113 Neonatology, Seattle, WA 98105 (emweiss@uw.edu).

Author Affiliations: Department of Pediatrics, University of Washington School of Medicine, Seattle (Lyle, Shaikh, Gray, Weiss); Treuman Katz Center for Pediatric Bioethics and Palliative Care, Seattle Children's Research Institute, Seattle, Washington (Oslin, Weiss).

Author Contributions: Dr. Weiss had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: Lyle, Shaikh, Weiss.

Acquisition, analysis, or interpretation of data: All authors.

Drafting of the manuscript: Lyle, Oslin, Weiss.

Critical review of the manuscript for important intellectual content: All authors.

Statistical analysis: Lyle, Oslin, Gray.

Obtained funding: Weiss.

Administrative, technical, or material support: Lyle, Shaikh, Gray, Weiss.

Supervision: Weiss.

Conflict of Interest Disclosures: None reported.

Funding/Support: This study was funded in part by the Faculty Research Support Fund from the Center for Clinical & Translational Research at Seattle Children's Research Institute, as well as matching funds from the Treuman Katz Center for Pediatric Bioethics and Palliative Care. This study was also supported in part by the National Institutes of Health through the Eunice Kennedy Shriver National Institute of Child Health and Human Development (grant No. K23HD103872).

Role of the Funder/Sponsor: The funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Data Sharing Statement: See Supplement 2.

Additional Contributions: Amanda Mercer, BA (Seattle Children's Hospital) assisted with the literature review. Peggy Cruse, MA (Seattle Children's Hospital), assisted in performing the systematic review. Nicolas Barat, MD, MSME (University of Pennsylvania), assisted with developing the methods and reviewed earlier drafts. Ben Wilford, MD (University of Washington), reviewed earlier drafts. Kathryn Porter, JD (Treuman Katz Center for Pediatric Bioethics), reviewed earlier drafts. Nicolas J Dundas, MPH (Seattle Children's Research Institute, Treuman Katz Center for Pediatric Bioethics); Jana Ebong, BA (Pennsylvania College of Optometry, Salus University); John B. Feltner, MS (Department of Pediatrics, University of Washington); Devineae C. McNeil, MS (Department of Pediatrics, University of Washington). Alyssa Taíra, BS, Clinical Research Coordinator, Seattle Children's Hospital; Calin White, MHIHIM (Department of Pediatrics, University of Washington) assisted with abstract selection and data extraction processes. They were not compensated outside of their normal salaries for this work.

REFERENCES


SUPPLEMENT 1.
- eTable. Characteristics of Included Studies
- eFigure 1. Flowchart of Included Studies
- eFigure 2. Race and Ethnicity of Participants
- eReferences.

SUPPLEMENT 2.
- Data Sharing Statement