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List of abbreviations:
COVID-19, coronavirus disease 2019; PRISMA, Preferred Reporting Items for Systematic reviews and Meta-Analyses; RCT, randomized controlled trial; US, United States.
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To the Editor: In the context of racial and ethnic disproportionalities throughout the coronavirus disease 2019 (COVID-19) pandemic, one would expect that clinical trials testing therapeutic agents against SARS-CoV-2 would have fair or overrepresentation of minorities. However, that appears not to be the case.1

We performed a brief scoping review to evaluate the representativeness of racial and ethnic groups in COVID-19 outpatient randomized trials enrolling patients in the United States (US). We followed the Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR).2 Three large reference databases were searched by a medical librarian and 467 citations were reviewed in duplicate. Searches were run in March 2021 in Ovid Cochrane Central Register of Controlled Trials (1991+), Ovid Embase (1974+), and Ovid Medline (1946+ including epub ahead of print, in-process & other non-indexed citations). Search strategies are provided in the Supplementary Appendix S1. We included studies of outpatients (non-hospitalized patients) infected with SARS-CoV-2 in which a therapeutic agent was tested using a randomized controlled trial (RCT) design. Non-published studies and pre-prints were not considered. We restricted our eligibility to outpatient trials published in English and in which enrollment occurred in the US territory. For studies that met the eligibility criteria, we extracted data on the type of trial (single center versus multicenter), total number of participants who reported race/ethnicity, and number of participants from each race and ethnicity as it appears in the US census bureau (White, Black or African American, American Indian and Alaska Native, Asian, Native Hawaiian or other Pacific Islander, and Hispanic or Latino). We calculated the proportion of each group by dividing the total number of participants with each race and ethnicity by the
total number of participants who were enrolled in the trial and self-reported their race and ethnicity. Median proportion across studies was also calculated.

We found 5 studies$^{3-7}$ published in high-impact journals including a total of 1,678 participants that met our eligibility criteria. PRISMA study flowchart is available in Supplementary Appendix S2. Among these 5 trials, the proportion of White participants ranged from 47.9%$^5$ to 89.4%$^3$ (median 74.1%). While proportionately less affected by COVID-19 in the US, White people were overrepresented. (Figure) The proportion of Black or African American participants ranged from 3.1%$^5$ to 25.2%$^4$ (median 13.3%). The proportion of Hispanic or Latino participants ranged from 3.4%$^4$ to 42.5%$^3$ (median 5.7%). Despite being significantly affected by COVID-19, Hispanic or Latino people were greatly underrepresented in these trials and are likely the minority group most affected by enrollment disparities. Other groups (Asian, American Indian, and Native Hawaiian) were also underrepresented. (Table, Figure)

By systematically reviewing the published literature, we noted potential disproportionalities in racial and ethnic distributions among participants enrolled in COVID-19 outpatient randomized trials. When the trial enrollments are combined, White people are overrepresented in these trials, whereas Hispanic and Latinos and other minorities are underrepresented. Although the median percent of Black people across these trials was close to the percent of Black in the US population, (Figure) two trials had less than 6% of enrolled participants in this race category, highlighting its likely underrepresentation. In aggregate, these results raise concern about the applicability of outpatient COVID-19 trial findings in minorities.

Several limitations need to be acknowledged in our scoping review. First, we included trials enrolling participants in the US only, so the results are not applicable to research in other countries. Second, only trials involving non-hospitalized patients (ie, outpatient trials)
were considered and if we were to consider a larger body of trials without restriction to the outpatient setting, results might have been different. Third, we used published trial’s data, and reports of race/ethnicity were missing in some studies. Lastly, although 4 of 5 trials were multicenter, different trial geographies may have skewed the distribution of certain races and we did not take that into account in our analysis.

It is evident that a concerted effort to actively engage minority communities is necessary when designing COVID-19 clinical trials and beyond. Potential solutions are the development of guidelines driving organizations to place further and more robust emphasis on integration of racial and ethnic minorities in clinical research of all kinds. Second, better access to interpreter services and research personnel from minority groups that can approach the communities. Third, increase funding for investigators from underrepresented groups, as representation matters. Fourth, mandatory reporting of race and ethnicity in clinical trials, including reach for enrollment to underserved and minority communities while planning the study. Fifth, efforts to address bias amongst health care workers and increase community trust in healthcare. Racial and ethnic disproportionalities in enrollment affect the generalizability of clinical trial results and may limit the appropriate application of interventions.

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Legends

Table. Racial and ethnic distributions of patients in COVID-19 outpatient trials in the US.

Figure. Racial and ethnic distributions in patients enrolled in COVID-19 outpatient trials in the US as compared to distributions in overall US population and US COVID-19 cases.
## Table. Racial and ethnic distributions of patients in COVID-19 outpatient trials in the US.

<table>
<thead>
<tr>
<th>Study Author, Year of Publication</th>
<th>Single or multicenter</th>
<th>White, n/N (%)</th>
<th>Black or African American, n/N (%)</th>
<th>Asian, n/N (%)</th>
<th>American Indian or Alaska Native, n/N (%)</th>
<th>Native Hawaiian or other Pacific Islander, n/N (%)</th>
<th>Hispanic or Latino, n/N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gottlieb³, 2021</td>
<td>Multi</td>
<td>507/567 (89.4%)</td>
<td>33/567 (5.8%)</td>
<td>19/567 (3.4%)</td>
<td>3/567 (0.5%)</td>
<td>1/567 (0.2%)</td>
<td>245/577 (42.5%)</td>
</tr>
<tr>
<td>Lenze⁴, 2020</td>
<td>Single*</td>
<td>106/151 (70.2%)</td>
<td>38/151 (25.2%)</td>
<td>4/151 (2.6%)</td>
<td>1/151 (0.7%)</td>
<td>0/151 (0.0%)</td>
<td>5/146 (3.4%)</td>
</tr>
<tr>
<td>Skipper³, 2020</td>
<td>Multi</td>
<td>235/491 (47.9%)</td>
<td>15/491 (3.1%)</td>
<td>196/491 (39.9%)</td>
<td>3/491 (0.6%)</td>
<td>5/491 (1.0%)</td>
<td>28/491 (5.7%)</td>
</tr>
<tr>
<td>Thomas⁶, 2021</td>
<td>Multi</td>
<td>152/205 (74.1%)</td>
<td>51/205 (24.9%)</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Weinreich⁷, 2021</td>
<td>Multi</td>
<td>224/264 (84.8%)</td>
<td>35/264 (13.3%)</td>
<td>3/264 (1.1%)</td>
<td>2/264 (0.8%)</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td><strong>Median (range)</strong></td>
<td>-</td>
<td>74.1% (47.9% - 89.4%)</td>
<td>13.3% (3.1% - 25.2%)</td>
<td>3.0% (1.1% - 39.9%)</td>
<td>0.7% (0.5% - 0.8%)</td>
<td>0.2% (0.0% - 1.0%)</td>
<td>5.7% (3.4% - 42.5%)</td>
</tr>
</tbody>
</table>

NR, Not Reported.  
*This trial enrolled patients from Saint Louis (Missouri) only.
**Figure.** Racial and ethnic distributions in patients enrolled in COVID-19 outpatient trials in the US as compared to distributions in overall US population and US COVID-19 cases.

AA, African American; AI, American Indian; AN, Alaska Native; NH, Native Hawaiian; OPI, Other Pacific Islander. Data on the percent of US population was extracted from the 2019 US census bureau (estimated sample of 328,239,523). This represents the share of each race if they were present alone or in combination with one or more races. Percent of US Covid-19 cases were extracted from the CDC Covid Data Tracker on May 3rd, 2021 (n=15,890,631 Covid-19 cases in which Race/Ethnicity was available). For this data, all categories except for Hispanic/Latino includes non-Hispanic people only (eg, Black, Non-Hispanic).
Author contributions: Lucas: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Writing- Original draft preparation. Danielle: Data curation. Nathan: Conceptualization, Investigation, Writing- Reviewing and Editing. Aditya: Conceptualization, Investigation, Writing- Reviewing and Editing. Fernanda: Conceptualization, Investigation, Methodology, Supervision, Writing- Reviewing and Editing.