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Why Calls to Diversify Trial Populations Fall Short

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Drawing on a SARS-CoV-2 vaccine trial in a Latinx community in San Diego, we show how trial designs fail to redress structural racism and may introduce new harms. While important, trial diversity alone cannot redress entrenched inequities that affect Black, Indigenous, and People of Color (BIPOC) communities.

The highly uneven, racialized impacts of the COVID-19 pandemic in the United States are now well documented. Black and Latinx people are three times more likely to die from COVID-19 than white people, according to federal data. One response from the medical community has been to attend to the racial diversity and makeup of SARS CoV-2 vaccine trial populations to ensure safety and efficacy on people of different races. Research shows that Black people make up only 5% of clinical trial participants (while accounting for 13% of the total population), whereas Latinx people make up only 1% of trial populations (while accounting for 18% of the U.S. population).

While important, the focus on recruiting diverse trial populations is an insufficient response to redress the racialized impacts of SARS Co-V-2. Our concern is that these calls may stand in for the need for permanent structural changes in medicine—needs which Black, Indigenous, and Persons of Color (BIPOC) communities are themselves demanding. Calls to diversify trial populations may obscure how privileged institutions can capitalize on the intersection of health crises and scientific and economic inequality.

Drawing on the example of one ongoing vaccine trial in our community that has prioritized the recruitment of a diverse, historically "underserved" Latinx population, we show how a narrow vision of "diversity" in terms of representation will not only negatively affect trial recruitment, but may exacerbate vulnerabilities faced by such communities. As public health scholars have argued, in contrast to the more passive term "social determinants of health," structural violence explicitly identifies social, economic, and political systems as the *causes of the causes* of poor health. The term is evocative in its framing of health inequities as violence. In the case of clinical trials, we consider how a narrow focus on diversity at the level of trial recruitment may result in vaccine trials becoming unintended vectors of structural violence. We are specifically concerned about the risks of large-scale biodata collection, compromised consent, and the low, patchwork quality of healthcare being offered for trial participants.

Uneven Risk and Experimental Subjects: From Vaccine Trials to Bio Data Mining

In September 2020, the University of California, San Diego (UCSD) announced that it would join a Phase III national AstraZeneca vaccine trial, one of hundreds underway in the U.S. Instead of conducting the trial in white and affluent neighborhoods, as the UCSD Medical System has historically done, the trial aims to recruit 1,600 participants from majority Latinx communities in San Diego county, including National City, a city with a 63.8% Latinx population and one of the highest case rates of COVID-19 in the county (https://www.nbcsandiego.com/news/investigations/which-san-diego-countys-city-had-the-highest-number-of-covid-19-deaths/2373246/). According to the study's lead investigator, "the study bring(s) vaccine trial opportunities to high-burden communities that might otherwise be underserved" (https://health.ucsd.edu/news/releases/Pages/2020-09-02-uc-san-diego-joins-second-major-national-clinical-trial-for-novel-coronavirus.aspx). What, precisely, constitute "trial opportunities"? How might the notion of opportunity be rethought considering the social, political, and economic environment of places like National City? We spotlight this clinical trial, not because it is exceptional, but because most of us live in San Diego county and are attentive to histories of medical and environmental racism in our region. The rationales for the trial's location and recruitment exemplify our broader critique of how claims to diversity and inclusion may remain unfulfilled in other trials underway in other BIPOC communities in the U.S.

What precisely constitutes "opportunity" in the claim that clinical trials bring beneficial opportunities to BIPOC communities? In the race for drug and vaccine development, market concerns have historically trumped community needs. While National City residents were selected for their vulnerability to SARS-CoV-2, what are the long-term costs and benefits of participation? This question was very much on the minds of National City community

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activists, who asked the study's lead investigator Dr. Susan Little questions during a community forum that she was unable to answer. Would people of color be prioritized when an effective vaccine was approved? Would National City residents receive a share of the profits of the vaccine, in exchange for their bodies being tested upon? These questions are important not only because they reflect histories of medical racism, but because they hint at concerns that clinical trials might reproduce new harms if they do not adequately address these concerns.

When assessing the costs and benefits of trial participation, researchers and communities must also recognize that SARS-CoV-2 is the first pandemic in the era of big data, and it's leading to the largest biological data collection haul in history. While government programs like the National Institutes of Health's "All of Us" initiative are not profit driven, they are involved in collecting unprecedented amounts of genetic information.[1] All of this is happening in a context of loosening ethical norms and heightened economic precarity. Under Operation Warp Speed, the FDA has relaxed its standards for lab-developed tests and emergency use authorization (https://www.fda.gov/regulatory-information/search-fda-guidance-documents/policy-coronavirus-disease-2019-tests-during-public-health-emergency-revised). Institutional review boards are being bypassed (https://www.fda.gov/regulatory-information/search-fda-guidance-documents/institutional-review-board-irb-review-individual-patient-expanded-access-requests-investigational). In the process of swabbing people's nasal cavities during COVID-19 diagnostic tests, methods like "SwabSeq" generate genome sequence data.

While this wealth of data is revolutionary for drug or vaccine development, it can be misused.[2] For example, Vertex Pharmaceuticals obtained genome sequence data from cystic fibrosis (CF) patients, developed a targeted drug, and then offered the drug back to CF patients for $300,000 per patient, per year (https://www.nytimes.com/2014/07/19/opinion/joe-nocera-cystic-fibrosis-drug-price.html). Genetics research targeting Indigenous communities within North America has likewise been used to undermine Indigenous sovereignty and identity.[3] Look no further than the example of *Havasupai v. Arizona State University*, in which the Havasupai Nation successfully sued the university for improperly using its members' blood samples. In the long term, access and use of genetic data may lead to the further surveillance, discrimination, and criminalization of BIPOC populations, now deemed "high risk" for disease profiles.

Determining whether or not this trial constitutes an "opportunity" for communities like National City thus demands an accounting of all biological data likely to be extracted during a vaccine trial. Histories of medical research are rife with examples of biological data of untold value being extracted without the consent of colonized and racialized communities—from the now-famous Henrietta Lacks to medical researchers' "cannibalistic" thirst for the genes, cells, or tissues of the Fore people to explain kuru, a fatal brain disease. As in those cases, "opportunities" for participation were disguised forms of dispossession of bodily material that became valuable intellectual property for others. Scientific communities must earn the merit of their assertions not only through standards of methodological validity but by establishing relations of trust with marginalized or disadvantaged communities. One way to do this is to prioritize meeting these communities' pressing needs rather than simply focusing on data extraction.[4]

The Conceit of Consent

Many lay people lack the necessary scientific and technical knowledge to properly consent to or understand the long-term implications of the biological data extraction currently underway. There are also additional conditions that complicate the process of gathering informed consent. As medical anthropologists have argued, consent cannot be reduced to a bureaucratic procedure, but rather, people's capacities to consent must be considered in light of broader social, economic, and political situations.

One of the implicit "opportunities" of trial participation is access to healthcare. Like other trials, the UCSD/AstraZeneca trial promises health care to trial participants for the duration of participation (2 years), which will make it attractive to many. How might the desire for this scarce good—affordable healthcare—reshape capacities to consent and/or drive trial participation? In the case of National City, participating in a clinical trial may render conditions for informed consent difficult. For example, residents of National City disproportionately lack health insurance, are elderly, are essential workers, and have a high proportion of multigenerational households. According to the county's public health data (**see** Figure 1), only about 20% of adults have health insurance (https://www.sandiegocounty.gov/).

Local populations can be pressured to participate in clinical trials as they become one of the only ways to access reliable care in places where health infrastructures are unavailable or have been systematically depleted. This reveals a key paradox in clinical trial participation: those most "in need" are often the least able to give informed consent—a fact that is rarely mentioned in public calls for trial diversification. Yet, as the history of HIV clinical trials in the global south showed, poverty, a fear of being HIV positive, and the hope of gaining access to medical care drove trial participation.[5] In numerous trials, research subjects were caught between the competing interests of regulatory bodies, pharmaceutical companies,

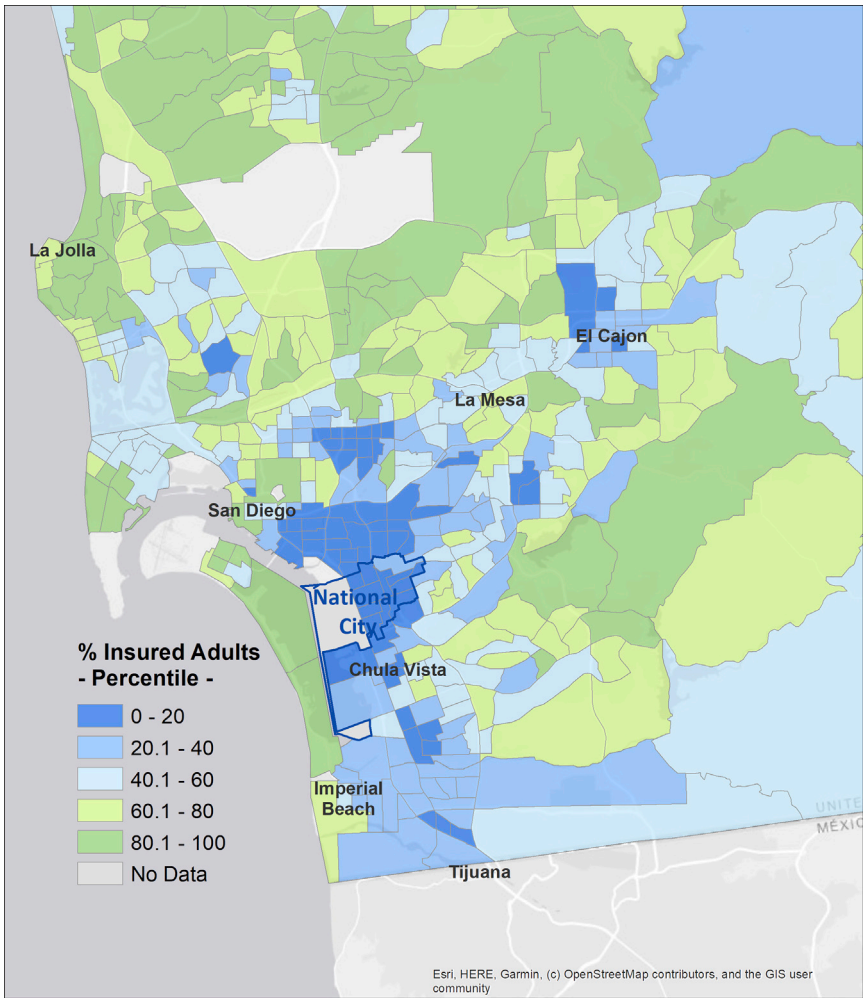

Figure 1. Spatial Distribution of Percent Insured Adults (2018) in San Diego County, Where National City Is Highlighted

Source: Percent of population without health insurance by census tract, https://www.cdph.ca.gov/Programs/OHE/Pages/CC-Health-Vulnerability-Indicators.aspx.

and health crises.[6] Scientific practices and ethical standards sometimes diverged, leading to gross violations.[7]

The history of medical research on BIPOC populations is littered with instances of manipulated or nonexistent consent that persist today (see for example Harriet Washington's archive of how incarcerated people in the US "consent" to potential life-threatening, risky, and painful experiments because it is the only way to have minimum contact with medical staff).[8] This history matters because it makes the work of diversifying trial populations more difficult. Many structurally disadvantaged communities justifiably withhold trust in scientific knowledge. This broken trust will not be restored simply by recruiting more diverse trial participants. Rather, it demands a rethinking of practices such as informed consent, which must be situated within broader frameworks of medical racism and structural violence.[9]

Patchwork Care

Finally, we question the quality of care provided in clinical trials as a justification for their location in underserved communities. Like other clinical trials, the AstraZeneca/UCSD trial promises only temporary care to trial participants. Instead of bolstering existing public health infrastructure, care will be dispensed through "mobile (and temporary) clinics." Doctors, nurses, and staff will be "bused" into National City for the duration of the trial. The parachuting in of medical experts to poor communities has been rightfully criticized for failing to produce necessary long-term and structural changes necessary to redress health inequities. After the trial and follow ups are completed, the infrastructure of clinics, doctors, and nurses will vanish. Meanwhile, a resource of untold commercial value—biological and genomic data—will have been extracted in the name of care.

This temporary care provided by clinical trials also fails to address the root causes of disparities in COVID-19 infection rates and resulting disproportionate impacts in BIPOC communities. Discussions of racial diversity often end up promoting notions of racial or ethnic determinism through reifying markers of genetic difference at the expense of attending to social and structural factors. For example, the largest genome-sequencing study of drug response in African American and Latino children with asthma—who have reduced albuterol response as compared to white children—found genetic variants that led to reduced lung capacity and lower immune response. These genetic variants were used to explain albuterol's weakened effect on Black and Brown children. While these findings are undoubtedly important, they codify a fallacious genetic basis of race as explaining ethnic health disparities and exclude the impacts of structural racism such as the effects of living in less-desired locations with poor air quality.[10]

In efforts to recruit Latinx people into the UCSD/AstraZeneca trial, we worry that a similar obfuscation is underway. Reports on the National City trial have foregrounded the vulnerability of

the population to COVID-19, without acknowledging socio-economic etiologies. Community activists and environmental justice researchers from National City have long argued that the intersecting interests of the military, shipyard industry, and traffic emissions have resulted in the intentional and disproportionate releasing and dumping of toxic environmental waste into the community's land, air, and water sources for decades (https://www.sandiegouniontribune.com/opinion/commentary/story/2020-07-15/uss-bonhomme-richard-environmental-racism-commentary). National City is home to four times as much toxic and hazardous waste than La Jolla, where UCSD is located (https://www.environmentalhealth.org/index.php/en/where-we-work/local/national-city).[11] Children in National City have significantly higher asthma hospitalization rates (122/100,000) compared to children in other cities in the county (87/100,000). These forms of structural violence are not acknowledged or addressed by the UCSD/AstraZeneca's trial's design.[12]

We ask researchers to critically interrogate whether or not their commitments to diversity and to serving historically marginalized communities can have their intended effect without addressing histories of environmental racism.

Beyond Extraction

If, as a best-case scenario, the National City trial is an attempt by pharmaceutical companies and university medical systems to "atone" for past neglects, it is an inadequate atonement.[13] Although clinical trials in "underserved" communities are being done in the name of diversity, equity, and inclusion, they lack strategies for redressing structural inequities, which can result in BIPOC people feeling like guinea pigs. Clinical trials claiming to serve "underserved" communities must always have clear and credible reasons for including distinctions of class and race in any study to root out the likelihood of social injustice in medical practice. Considerations of equity must pervade all phases of the vaccine development process—from trial to delivery to cost to distribution. Entry into BIPOC communities for trials and other interventions must not only acknowledge but redress historical and structural harms that have produced ill health in the first place. Otherwise, the notion that clinical trials offer "opportunities" to underserved communities' rings hollow.

We recognize this is a tall order for medical professionals, yet it is more crucial than ever. It requires new forms of relationship building and collaboration with BIPOC communities. It demands BIPOC communities have a stake in processes of scientific and medical development. They must be brought into decision-making processes fully, not just as experimental subjects, but through participatory design and engagement. Emergencies cannot be used to justify prolonging the necessary work of building infrastructure and redressing systemic racism. By failing to redress the structural conditions of ill health affecting communities of color and using them as opportunities for biological data extraction, clinical trials are in danger of producing new forms of vulnerability.

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DECLARATION OF INTERESTS

The authors have no conflicts of interest to declare.

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