"Race, ethnicity, and health disparities in US children with COVID-19: a review of the evidence and recommendations for the future"

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Key points:

- American Indian/Alaska Native, Black, and Hispanic/Latino children in the United States have had disproportionately higher case rates, hospitalizations and deaths related to COVID-19. They also have had less access to medical care throughout the pandemic.
- American Indian/Alaska Native and Black children are significantly underrepresented in COVID-19 vaccine clinical trials.

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ABSTRACT

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Coronavirus disease 2019 (COVID-19) is an important cause of morbidity in children in the United States (U.S.). Moreover, the U.S. has witnessed significant disparities affecting American Indian/Alaska Native, Black, and Hispanic/Latino children, stemming from systemic racism and social-structural inequalities and not differences in innate biological susceptibility.

We review what is known on COVID-19 and health disparities in disease burden, access to care, pharmaceutical interventions, and clinical research in children, with a focus on the U.S. context. In addition, we propose strategies to communicate scientific data in ways that do not promote racism and biological susceptibility themes, and to address pediatric disparities in clinical infectious diseases research.

Introduction

In the United States (U.S.), the health impacts of the novel coronavirus disease 2019 (COVID-19) pandemic has been unevenly distributed by race and ethnicity.[1] These disparities may have deepened during recent COVID-19 surges attributable to the Delta and Omicron variants.[2, 3]

Race and ethnicity are socially constructed, historically determined, and culturally reproduced categories. Health disparities reflect the effects of systemic racism and should not be misconstrued as evidence of biological determinism (the concept that human characteristics are rigidly determined by hereditary factors largely unaffected by environmental factors).[4,5] The authors acknowledge that race and ethnicity as categories of analysis are deeply complicated, potentially reductive, and often problematic. Nonetheless, in many contexts, and especially in the U.S., they provide a useful lens for tracking and understanding health disparities, as they are frequently measured and closely intertwined with other social-structural determinants of health, including poverty and healthcare access. For this reason, we chose to utilize the racial/ethnic categories used in the U.S. Census for the purposes of this review. When comparing groups throughout this manuscript, White race is often use as the reference as we are following the data reporting per the primary studies cited, but we do not recommend utilizing White centering language when reporting original data.

The published literature on disparities by race and ethnicity in COVID-19 outcomes in the U.S. have focused largely on adults. There have been limited published manuscripts focused on pediatric health disparities observed during the COVID-19 pandemic.

In this article, we summarize what is known on COVID-19 and pediatric health disparities in disease burden, access to care, pharmaceutical interventions, and clinical research related to COVID-19, with a particular focus on the U.S. We chose the U.S. as a very large, diverse geographic context with which we are most familiar, and this is further justified by the fact that, as of this writing, the U.S. has reported more confirmed COVID-19 cases and deaths than any other country in the world.[6] Finally, we propose strategies to communicate scientific data in ways that do not promote racism and biological susceptibility themes, and to address pediatric disparities in clinical infectious diseases research.

Health disparities in the burden of COVID-19 in children

Acute COVID-19

Between February 2020 and January 2022, approximately 8.5 million children were infected with SARS-CoV-2 in the U.S.[7] Centers for Disease Control and Prevention (CDC) data show that the case rate per 100,000 population among American Indian/Alaska Native children has been consistently higher than other racial groups across all ages. During the peak of the Omicron surge in early 2022, children from all non-White racial groups had higher case rates when compared to White children.[8] (**Figure 1**) These disparities reflect the impacts of poverty, social vulnerability and systemic racism, which are manifested as differences in household crowding, healthcare access, and caregivers' occupation/employment.[9-11]

In the U.S., approximately 0.02% of children infected with SARS-CoV-2 have required hospitalization.[8] Hospitalization rates due to COVID-19 have been higher among Black and Hispanic/Latino children when compared to non-Hispanic White children. During the earliest phase of the pandemic, COVID-NET data indicated hospitalization rates of 16.4 per 100,000 among Hispanic/Latino children and 10.5 per 100,000 among Black children – corresponding to 5- to 8-fold higher rates than White children.[11] According to the National COVID Cohort Collaborative, increased odds of severe disease and hospitalization among Black children persisted with the advent of the Delta variant, and COVID-NET data indicated that Black children accounted for 47.1% of children hospitalized at the beginning of the Omicron surge in December 2021.[13, 14]

As of April of 2022, the U.S. registered 1,484 COVID-related pediatric deaths. Hispanic/Latino children comprise 32.4% of all pediatric deaths despite representing approximately 26% of U.S. children and non-Hispanic Black children comprised 19.4% of pediatric deaths despite representing 13.7% of the pediatric population. American Indian/Alaska Native and Native Hawaiian/Other Pacific Islander children, in particular, have experienced disproportionate risk for mortality, comprising 1.5% and 1.2% of pediatric COVID-related deaths, respectively, despite representing 0.8% and 0.2% of U.S. children.[8, 15]

Multisystem Inflammatory Syndrome in Children (MIS-C)

MIS-C is a rare but serious condition that typically occurs within 4 weeks after SARS-CoV-2 infection.[16] As of May 2, 2022, CDC reported cumulative totals of 8,210 MIS-C cases and 68 deaths.[8]

During the early phase of the COVID-19 pandemic in the U.S., MIS-C incidence per 1,000,000 person-months was 9-fold higher among Black and Hispanic/Latino children, and 3-fold higher among Asian or Pacific Islander children, versus White

children.[17] Hispanic/Latino and Non-Hispanic Black children have continued to be disproportionately affected by MIS-C, comprising 57% of reported cases with available race and ethnicity information as of May 2, 2022. [8]

Moreover, severity of MIS-C may differ by race or ethnicity. One national surveillance study reported increased odds of intensive care unit admission and decreased cardiac function among non-Hispanic Black children versus non-Hispanic White children with MIS-C.[18] Though the exact cause of these disparities is not known, potential contributing factors from the cited study include insufficient access to health care, increased prevalence of underlying medical conditions, and increased exposure to environmental pollutants. It remains unclear if the disparities in the burden of MIS-C are entirely attributable to disparities in SARS-CoV-2 infection. Some studies have reported that the observed burden of MIS-C in Black and Hispanic/Latino children exceeded expected burden based on corresponding SARS-CoV-2 infection rates.[17, 19] Undercounting of COVID-19 cases, however, probably differs by race and ethnicity due to disparities in testing access. Although measures of poverty, social vulnerability and systemic racism have not been routinely collected in MIS-C surveillance data, one small case-control study from the first year of the pandemic found that MIS-C patients hospitalized at three academic centers had lower neighborhood socioeconomic status, had increased social vulnerability, and were more likely to be Black or Hispanic/Latino.[20] Larger, high-quality studies are needed to understand the complex interactions between race, ethnicity, other social-structural determinants of health, and risk for MIS-C over time.

The pandemic's impact on other health and social outcomes

Disparities in health and social outcomes not directly attributable to SARS-CoV-2 infection itself have also been observed in children from racial and ethnic minority groups during the COVID-19 pandemic. These disparities reflect collateral damage of the pandemic and the societal response: school closures, social isolation, reduced access to in-person healthcare, impact on caregivers, and large-scale diversion of public health and social safety net infrastructure to the pandemic response. These outcomes include rates of prematurity,[21, 22] congenital syphilis,[23, 24] long-term breastfeeding,[25, 26] incomplete routine childhood vaccination coverage,[27, 28] diabetic ketoacidosis,[29, 30] food insecurity,[31, 32] inability to engage in virtual learning,[33] adherence to treatment for chronic conditions,[34] mental health emergencies[35] and suicide attempts,[36] among others.[9, 32] These are compounded over the loss of loved ones including parents and grandparents causing burdens of bereavement and grief that have disproportionately affected children from specific racial or ethnic minorities.[37] Paradoxically, child poverty in the US fell to historic lows during the first two years of the pandemic due to aggressive policy initiatives,[38] but rollbacks may disproportionately affect children from racial and ethnic minority groups.

Health disparities in pediatric COVID-19 access to care and pharmaceutical interventions

Access to SARS-CoV-2 testing

Disparities in testing rates have been reported across the United States, primarily impacting racial and ethnic minorities, and rural and low-income communities.[39-41] Using publicly available statelevel dashboards, Pond et al found that only 8 states reported testing data by race and ethnicity, and that Hispanic/Latino individuals received significantly fewer tests per case than non-Hispanic/Latino individuals.[42] The Health Resources and Services Administration's Health Center Program showed that among persons with known race/ethnicity who received testing, 36% were Hispanic/Latino, 38% were non-Hispanic White, and 20% were non-Hispanic Black; however, the percentage of positive test results were 56% Hispanic/Latino, 24% non-Hispanic White, and 15% non-Hispanic Black.[43] Other studies have shown larger differences in testing by preferred language and insurance status.[44] Identified challenges to achieve equitable testing are insufficient number of walk-in testing sites in the most affected communities, no access to private transportation to drive-up testing sites, and lack of accurate information on testing criteria, availability, and cost.[39] It has been shown that increasing access to testing in highly affected communities can increase outpatient evaluations and concomitantly decrease test-positivity and hospitalizations.[45]

Access to telehealth

The COVID-19 pandemic prompted the rapid expansion of telehealth services in the U.S., with slower uptake among pediatric populations.[46]

Access to technology, internet connection, digital literacy and English proficiency are essential to receive telehealth services.[47-49] Recent studies have identified disparities in the delivery of telehealth services to historically underserved communities.

National survey data on telehealth use among adults and children in 2021 showed that telehealth utilization was lowest among the uninsured (9.4%), and highest among those with Medicaid (29.3%) and Medicare (27.4%).[50] Yet, the lowest rates of video-enabled telehealth services were reported among respondents who self-identified as Asian American/Pacific Islander, Black or Hispanic/Latino; and those with lower education and income.[50] Medical providers practicing in areas with a high social vulnerability index were more likely to use telephone (audio only) as the primary telehealth modality than providers in low social vulnerability index areas (41.7% vs 23.8%; P <.001).[51]

Limited English proficiency is another important barrier to access telehealth services, and in particular video telemedicine.[52] Patients with limited English-proficiency have half the odds of using telehealth services compared with English-proficient patients, even after accounting for sociodemographic factors and health status.[52] Incentivizing and requiring integration of interpreter services into telehealth platforms may contribute to telehealth equity.

Access to COVID-19 therapeutics

Therapeutic options for children with COVID-19 remain limited. As of this writing, remdesivir and dexamethasone are mainstays for hospitalized children with severe disease.[52] In the outpatient setting, remdesivir, ritonavir-boosted nirmatrelvir and the anti-SARS-CoV-2 monoclonal antibody (mAb) bebtelovimab can be considered.[54] Other mAbs were available prior to the emergence of the Omicron variant. Administration of remdesivir and mAb therapy require most patients to travel to major pediatric centers as they are not available in all hospitals or pediatrician offices. In addition, the supply of ritonavir-boosted nirmatrelvir and mAbs has been distributed on allocation through federal and state public health agencies.[55] As a result, not only availability but also access for children is limited.

Even when indicated, access to therapies in the US may differ by race and ethnicity. A study that assessed COVID-19 treatment by race and ethnicity between November 2020 and August 2021 among 41 different U.S. health care systems found that Hispanic, Black, and Asian patients received mAb therapy 22-58% less often than did non-Hispanic White patients. Though less dramatic, differences were also noted in inpatient settings, where Asian, Black, and Hispanic/Latino patients received dexamethasone less often than did White patients. [56] In another study among kidney transplant recipients, Black and Hispanic/Latino patients were less likely to receive mAb therapy for COVID-19.[57]

Aside from logistical difficulties in accessing outpatient therapies, several social and cultural factors have been noted to influence a person's decision to accept these therapies even when recommended by their medical provider, including White race, non-Hispanic ethnicity, English as a primary language, and social support.[58-60] Data on disparities in access and parental acceptance of COVID-19 therapies among U.S. children are lacking.

Access to COVID-19 vaccines

Disparities in the receipt of COVID-19 vaccines exist based on race and ethnicity and rural versus urban populations. Since August of 2021, full vaccine coverage in people 12 years and older has remained lower among those identified as American Indian/Alaska Native (45.1%), Black (44.4%), Hispanic/Latino (41.8%), and Native Hawaiian/Other Pacific Islander (45.1%) versus Asian (68.5%) and White (59%).[61] Given the efforts from federal, state, local organizations and pharmacies, >90% of eligible children lived within 5 miles of an active COVID-19 vaccine provider within 4 weeks of the vaccine becoming available[62] which suggests that alternative reasons may explain persistent disparities in vaccine hesitancy and medical mistrust, which disproportionately affect Hispanic/Latino and non-Hispanic Black adults in the U.S.[63, 64]

It is also important to note that people living in urban areas have a higher rate of full vaccination coverage than those living in rural areas (67.2% versus 49%, respectively, as of April 17th, 2022).[65] Access to healthcare has been an important problem for rural communities during the COVID-19 pandemic in the U.S., but other factors are likely to play a role in this vaccine coverage gap.[66] One survey reported that 40% of parents living in rural areas did not receive the recommendation to get the COVID-19 vaccine from their child's primary care provider compared to only 8% of parents living in urban areas.[67]

Health disparities in pediatric COVID-19 research

Clinical trials have historically lacked diversity, enrolling predominantly White, male participants, and therefore, have not been representative of the general population.[68] Information on the safety and efficacy of therapies among a variety of racial and ethnic groups has been one hypothesized benefit of more diverse clinical trial enrollment,[69] but we are not aware of contemporary recommendations that modify indications or dosing of any anti-infective agents solely on the basis of race or ethnicity. Such hypotheses run the risk of medicalizing socially constructed categories and misapprehend the true benefit of diversity in clinical trial enrollment during a pandemic caused by a novel pathogen: improved and accelerated access to new and repurposed drugs among historically underserved populations that are also at highest risk for poor outcomes.

Some reasons clinical trials may lack diversity include mistrust of the team or process, stigma of participation, time and transportation constraints, and unclear understanding of the potential value of participating.[3, 69, 70] Some participants may need accommodations to participate, such as information provided in their preferred language, flexible time to participate, and transportation.[70] Importantly, the potential costs of clinical trial participation are an underappreciated barrier that may prevent low-income individuals from enrolling in clinical trials. Medicare recipients and private payers have been able to get these costs covered by insurance for several years. In December of 2020, Congress passed the \$900 billion COVID-19 relief package and \$1.4 trillion omnibus spending bill which includes legislation that now guarantees coverage of such costs for all Medicaid recipients for the first time in the program's history, which may help address the cost barrier for some individuals.[71]

In addition to lack of racial and ethnic diversity in clinical trials, children are not typically included in the initial phases of clinical trials which often leads to extrapolation of adult data for treatment of children. However, it is well known that children have complex pharmacokinetic characteristics that vary with age and are unique from adults.[72] Like adult trials, there is a lack of diversity in pediatric clinical trials.[73]

This lack of diversity in clinical trials seems absurd given the disproportionate burden of cases, hospitalization and death among American Indian/Alaska Native, Black, and Hispanic/Latino populations.[74, 75] The proportion of people from racial and ethnic minority groups included in many of the major COVID-19 vaccine and therapeutic trials has not been representative of the proportion of these groups in the general US population. Additionally, children were excluded in the early vaccine and therapeutic trials. This has led to a paucity of data for optimal therapeutic management of children with COVID-19 and has resulted in off-label use of treatments.[76]

The COVID-19 vaccine trials of the BNT162b2 vaccine in children and adolescents included a great majority of White participants. American Indian/Alaska Native and Black children were underrepresented in both trials[77,78]; notably there were no American Indian/Alaska Native children in the vaccine trial for 5–11-year-olds.[77] A summary of the initial vaccine trials (for children and adults) and racial/ethnic characteristics of participants is included in **Table 1**.

Most of the randomized controlled trials on COVID-19 therapies are limited to patients aged 18 years and above. The racial and ethnic make-up of each trial, when available, was highly variable and is summarized in **Table 2**. Of note, this table is not intended to be inclusive of all studies conducted but highlights pivotal trials and the participants who were included. For comparison, we provide the racial and ethnic breakdown of the general U.S. population in **Supplementary Table 1**.

Conducting clinical trials during a pandemic is difficult, and these studies have provided information that has saved countless lives. However, these studies did not always have participants reflective of the racial and ethnic make-up of the U.S. Though some studies were multi-national—and global equity in pharmaceutical access is certainly a laudable goal—ensuring diversity in trial enrollment should have been a major priority given the disproportionate impact of COVID-19 on racial and ethnic minority groups. Indeed, normalizing the collection and reporting on other social-structural determinants such as social vulnerability index[79] and Medicaid beneficiary status may represent simple and efficient steps towards ensuring equity in clinical trial enrollment and early access to novel therapies.

Recommended strategies to decrease disparities in clinical research

It is important that investigators address racial and ethnic equity throughout the different steps of clinical research to decrease disparities and inequality. This should be considered while formulating a research question, applying for funding, collecting and analyzing data, and reporting data to both the scientific community and the public. We summarize some practical strategies to decrease disparities in clinical research, and for investigators to communicate data without promoting racism in **Figure 2**.

Conclusion

Our review of the evidence indicates that morbidity attributable to acute COVID-19, MIS-C, and a variety of other adverse health and social outcomes have not been evenly distributed among all U.S. children. Unequal availability and access to vaccines and therapeutics further contribute to health disparities, and it is urgent that such disparities be described and addressed by the pediatric infectious diseases and public health communities. Disparities in clinical trial enrollment represent a missed opportunity to afford early access to new, potentially beneficial therapeutics in the face of novel and emerging pathogens. We hope this manuscript serves to summarize and highlight the ongoing health disparities in the impact of the COVID-19 pandemic among U.S. children but also as a call to action to work towards decreasing these disparities and mitigate its effects on children's health.

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TABLES/FIGURES

 Table 1. Racial and ethnic make-up of several key COVID-19 vaccine trials

Vaccine manufacturer	Trial design	Age of participants	Racial & Ethnic make-up of participants ^a						
	N ²		American Indian or Alaska Native n (%)	Asian n (%)	Black n (%)	Hispanic/Latino n (%)	White n (%)		
	Phase 2/3 randomized placebo- controlled trial assessing safety, immunogenicity, and efficacy of BNT162b2 vaccine[77]	5-11 years	Not reported	137 (6%)	147 (6.5%)	478 (21.1%)	1790 (79%)		
Pfizer-BioNTech	Phase 3 randomized, placebo- controlled, observer-blinded trial assessing safety, immunogenicity, and efficacy of BNT162b2 vaccine[78]	12-15 years	7 (0.31%)	143 (6.3%)	109 (4.8%)	262 (11.6%)	1933 (85.5%)		
P	Phase 2/3 multinational, placebo- controlled, observer-blinded pivotal efficacy trial assessing safety and efficacy of BNT162b2 vaccine[80]	≥16 years	201 (0.5%)	1608 (4.3%)	3492 (9.3%)	10543 (28%)	31266 (82.9%)		
Moderna	Phase 3 randomized, observer- blinded, placebo-controlled trial to assess efficacy and safety of mRNA- 1273 SARS-CoV-2 vaccine[81]	≥18 years	233 (0.8%)	1382 (4.6%)	3090 (10.2%)	6235 (20.5%)	24024 (79.2%)		
Johnson &	Phase 3 international, randomized,	≥18 years	187 (0.4%)	1430	8515	19837 (45.4%)	25696		

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Johnson's	double-blinded, placebo-controlled		(3.3%)	(19.4%)	(58.7%)
Janssen	trial assessing safety and efficacy of				
	single dose Ad26.COV2.S vaccine				
	against COVID-19[82]				

^aThe total within each row may exceed 100% if study participants reported multiple races/ethnicities.

Table 2. Racial and ethnic make-up of several key COVID-19 therapeutic trials

Medication type	Medication	Trial design	Age of participants	Ra	cial & Eth	nic make	-up of participant	s ^a
		Nai		American Indian or Alaska Native n (%)	Asian n (%)	Black n (%)	Hispanic/Latino n (%)	White n (%)
	xO	Double-blind, randomized, controlled trial of intravenous remdesivir vs placebo[83]	≥18 years	7 (0.7%)	135 (12.7%)	226 (21.3%)	250 (23.5%)	566 (53.3%)
	ral Remdesivir	Randomized, open-label, phase 3 trial comparing 5 days to 10 days of remdesivir[84]	≥12 years	Not reported	45 (11.5%)	44 (11.2%)	Not reported	276 (70.4%)
Anti-viral		Randomized controlled trial: patients randomized to one of four trial medications (including remdesivir) or local standard of care[85]	≥18 years	Reported	by geogra	phic regior	n, not by race and e	ethnicity
		Double-blind, randomized controlled trial comparing 3 days of outpatient remdesivir vs placebo[86]	≥12 years	14 (2.5%)	36 (6.4%)	42 (7.5%)	235 (41.8%)	452 (80.4%)

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		Phase 2/3 open-label study evaluating safety, tolerability and pharmacokinetics[87]	28 days – < 18 years		No	t currently	available	
	Paxlovid	Phase 2/3, double-blind, randomized, controlled trial of Paxlovid vs placebo[88-90]	≥18 years [90]	191 (8.5%) [90]	315 (14.0%) [90]	110 (4.9%) [90]	1011 (45.0%) [90]	1607 (71.5%) [90]
	Molnupiravir	Phase 3, double-blind, randomized, controlled trial of molnupiravir vs placebo[91]	≥18 years	29 (3.7%)	18 (2.3%)	47 (6.1%)	452 (58.3%)	403 (52.0%)
N CC	Bamlanivimab & etesevimab	Phase 2–3, randomized, double-blind, placebo- controlled trial of bamlanivimab & etesevimab vs placebo[92]	≥12 years	3 (0.3%)	38 (3.7%)	83 (8.1%)	304 (29.4%)	896 (87.4%)
Monoclonal antibodies	Casirivimab & imdevimab	Phase 1-3, randomized, double-blind, controlled trial of low-dose vs high- dose casirivimab & imdevimab vs placebo[93]	≥18 years	2 (1.0%)	3 (1.0%)	35 (13.0%)	153 (56.0%)	224 (81.0%)
	Sotrovimab	Phase 3, randomized, double-blind, control trial	≥18 years	1 (<1.0%)	34 (6.0%)	38 (7.0%)	368 (63.0%)	506 (87.0%)

		of sotrovimab vs placebo[94]	sci	<u>6</u>				
	Bebtelovimab	No clinical data from placebo-controlled trials published at this time. FDA authorized for use, as it retains activity against the omicron variant[54, 95]	*FDA authorized for ≥12 years[53]		No	t currently	available	
	, Q'E'	Randomized, open-label, controlled trial of standard of care alone vs standard of care plus dexamethasone[96]	≥18 years		Not	specified		4689 (73.0%)
Corticosteroids & Immunomodulators	Dexamethasone	Blinded, parallel group, stratified, randomized controlled trial comparing 12 mg/day to 6 mg/day of IV dexamethasone[97]	≥18 years	Reported by country, not by race and ethnicit			city	
	Tocilizumab	Randomized, open-label, controlled trial of standard of care alone vs standard of care plus tocilizumab[98]	≥18 years	rs Not specified			3127 (76.0%)	
	Baricitinib	Phase 3, double-blind,	≥ 18 years	316 (21.2%)	174 (11.7%)	75 (5.0%)	100 (31.3%) *Reported in	920 (61.6%)

randomized, controlled	the U.S. only
trial comparing baricitinib	
vs placebo[99]	

^aThe total within each row may exceed 100% if study participants reported multiple races/ethnicities.

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Figure 1. COVID-19 weekly cases per 100,000 population among children in the U.S. during the peak of the Omicron sublineage BA.1 surge (01/15/2022) by age group and race and ethnicity.[8]

Figure 2. Suggested strategies to decrease disparities in research and for investigators to communicate data without promoting racism.

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REFERENCES

- Gold, J.A.W., L.M. Rossen, F.B. Ahmad, et al., *Race, Ethnicity, and Age Trends in Persons Who Died from COVID-19 - United States, May-August 2020.* MMWR Morb Mortal Wkly Rep, 2020. 69(42): p. 1517-1521.
- Taylor, C.A., M. Whitaker, O. Anglin, et al., COVID-19-Associated Hospitalizations Among Adults During SARS-CoV-2 Delta and Omicron Variant Predominance, by Race/Ethnicity and Vaccination Status - COVID-NET, 14 States, July 2021-January 2022. MMWR Morb Mortal Wkly Rep, 2022. 71(12): p. 466-473.
- 3. Clark, L.T., L. Watkins, I.L. Pina, et al., *Increasing Diversity in Clinical Trials: Overcoming Critical Barriers*. Curr Probl Cardiol, 2019. **44**(5): p. 148-172.
- Fain, K.M., J.T. Nelson, T. Tse, and R.J. Williams, *Race and ethnicity reporting for clinical trials in ClinicalTrials.gov and publications*. Contemp Clin Trials, 2021. 101: p. 106237.
- 5. Chowkwanyun, M. and A.L. Reed, Jr., *Racial Health Disparities and Covid-19 Caution and Context*. N Engl J Med, 2020. **383**(3): p. 201-203.
- 6. Our World in Data. *Daily new confirmed COVID-19 deaths per million people*. Available at: https://ourworldindata.org/explorers/coronavirus-data-explorer. Accessed 17 May 2022.
- American Academy of Pediatrics. More Than a Half-million New COVID-19 Cases in Children Reported in One Week: Cumulative Pediatric Cases Since Pandemic's Onset Exceed 8.5 Million Available at: https://www.aap.org/en/news-room/newsreleases/aap/2021/more-than-a-half-million-new-covid-19-cases-in-children-reported-inone-week-cumulative-pediatric-cases-since-pandemics-onset-exceed-8.5-million/. Accessed 18 April 2022.
- 8. Centers for Disease Control and Prevention. *COVID Data Tracker*. Available at: https://covid.cdc.gov/covid-data-tracker/#datatracker-home. Accessed 15 April 2022.
- 9. Smitherman, L.C., W.C. Golden, and J.R. Walton, *Health Disparities and Their Effects* on Children and Their Caregivers During the Coronavirus Disease 2019 Pandemic. Pediatr Clin North Am, 2021. **68**(5): p. 1133-1145.
- Chen, J.T. and N. Krieger, *Revealing the Unequal Burden of COVID-19 by Income, Race/Ethnicity, and Household Crowding: US County Versus Zip Code Analyses.* J Public Health Manag Pract, 2021. 27 Suppl 1, COVID-19 and Public Health: Looking Back, Moving Forward: p. S43-S56.
- Hamidi, S. and I. Hamidi, Subway Ridership, Crowding, or Population Density: Determinants of COVID-19 Infection Rates in New York City. Am J Prev Med, 2021. 60(5): p. 614-620.
- 12. Kim, L., M. Whitaker, A. O'Halloran, et al., *Hospitalization Rates and Characteristics of Children Aged <18 Years Hospitalized with Laboratory-Confirmed COVID-19 COVID-*

NET, 14 States, March 1-July 25, 2020. MMWR Morb Mortal Wkly Rep, 2020. **69**(32): p. 1081-1088.

- Martin, B., P.E. DeWitt, S. Russell, et al., Characteristics, Outcomes, and Severity Risk Factors Associated With SARS-CoV-2 Infection Among Children in the US National COVID Cohort Collaborative. JAMA Netw Open, 2022. 5(2): p. e2143151.
- 14. Marks, K.J., M. Whitaker, O. Anglin, et al., *Hospitalizations of Children and Adolescents with Laboratory-Confirmed COVID-19 COVID-NET, 14 States, July 2021-January 2022.* MMWR Morb Mortal Wkly Rep, 2022. **71**(7): p. 271-278.
- 15. U.S. Census Bureau. *Decennial Census* 2020.Available at: https://data.census.gov/cedsci/table?q=United%20States. Accessed 16 April 2022.
- 16. Centers for Disease Control and Prevention. *Multisystem Inflammatory Syndrome in Children (MIS-C) Associated with Coronavirus Disease 2019 (COVID-19)*. Available at: https://emergency.cdc.gov/han/2020/han00432.asp. Accessed 12 May 2022.
- Payne, A.B., Z. Gilani, S. Godfred-Cato, et al., *Incidence of Multisystem Inflammatory* Syndrome in Children Among US Persons Infected With SARS-CoV-2. JAMA Netw Open, 2021. 4(6): p. e2116420.
- Abrams, J.Y., M.E. Oster, S.E. Godfred-Cato, et al., Factors linked to severe outcomes in multisystem inflammatory syndrome in children (MIS-C) in the USA: a retrospective surveillance study. Lancet Child Adolesc Health, 2021. 5(5): p. 323-331.
- Stierman, B., J.Y. Abrams, S.E. Godfred-Cato, et al., Racial and Ethnic Disparities in Multisystem Inflammatory Syndrome in Children in the United States, March 2020 to February 2021. Pediatr Infect Dis J, 2021. 40(11): p. e400-e406.
- 20. Javalkar, K., V.K. Robson, L. Gaffney, et al., *Socioeconomic and Racial and/or Ethnic Disparities in Multisystem Inflammatory Syndrome*. Pediatrics, 2021. **147**(5).
- Marin Gabriel, M.A., M. Reyne Vergeli, S. Caserio Carbonero, et al., *Maternal*, *Perinatal and Neonatal Outcomes With COVID-19: A Multicenter Study of 242 Pregnancies and Their* 248 Infant Newborns During Their First Month of Life. Pediatr Infect Dis J, 2020. 39(12): p. e393-e397.
- 22. Allotey, J., E. Stallings, M. Bonet, et al., *Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis.* BMJ, 2020. **370**: p. m3320.
- Bowen, V.B., R. McDonald, J.A. Grey, A. Kimball, and E.A. Torrone, *High Congenital Syphilis Case Counts among U.S. Infants Born in 2020.* N Engl J Med, 2021. 385(12): p. 1144-1145.
- 24. Centers for Disease Control and Prevention. *Sexually Transmitted Disease Surveillance* 2020. Available at: https://www.cdc.gov/std/statistics/2020/overview.htm#Syphilis. Accessed 12 May 2022.
- 25. Popofsky, S., A. Noor, J. Leavens-Maurer, et al., *Impact of Maternal Severe Acute Respiratory Syndrome Coronavirus 2 Detection on Breastfeeding Due to Infant Separation at Birth.* J Pediatr, 2020. **226**: p. 64-70.
- Beauregard, J.L., H.C. Hamner, J. Chen, et al., *Racial Disparities in Breastfeeding Initiation and Duration Among U.S. Infants Born in 2015*. MMWR Morb Mortal Wkly Rep, 2019. 68(34): p. 745-748.
- 27. Ackerson, B.K., L.S. Sy, S.C. Glenn, et al., *Pediatric Vaccination During the COVID-19 Pandemic.* Pediatrics, 2021. **148**(1).

- Sabnis, S.S. and J.H. Conway, Overcoming Challenges to Childhood Immunizations Status. Pediatr Clin North Am, 2015. 62(5): p. 1093-109.
- Chambers, M.A., C. Mecham, E.V. Arreola, and M. Sinha, *Increase in the Number of Pediatric New-Onset Diabetes and Diabetic Ketoacidosis Cases During the COVID-19 Pandemic*. Endocr Pract, 2022. 28(5): p. 479-485.
- 30. Lavik, A.R., O. Ebekozien, N. Noor, et al., *Trends in type 1 diabetic ketoacidosis during COVID-19 surges at seven US centers: highest burden on non-Hispanic Blacks.* J Clin Endocrinol Metab, 2022.
- 31. The Hamilton Project. About 14 Million Children in the US Are Not Getting Enough to Eat. Available at: https://www.hamiltonproject.org/blog/about_14_million_children_in_the_us_are_not_get ting enough to eat. Accessed 19 April 2022.
- 32. Suarez-Lopez, J.R., M.R. Cairns, K. Sripada, et al., *COVID-19 and children's health in the United States: Consideration of physical and social environments during the pandemic.* Environ Res, 2021. **197**: p. 111160.
- 33. Baykadar, S. and A. Guveli. Inequalities in home learning and schools' provision of distance teaching during school closure of COVID-19 lockdown in the UK. Available at: https://www.iser.essex.ac.uk/research/publications/working-papers/iser/2020-09.pdf. Accessed 19 April 2022.
- 34. Plevinsky, J.M., M.A. Young, J.K. Carmody, et al., *The Impact of COVID-19 on Pediatric Adherence and Self-Management*. J Pediatr Psychol, 2020. **45**(9): p. 977-982.
- Leeb, R.T., R.H. Bitsko, L. Radhakrishnan, et al., Mental Health-Related Emergency Department Visits Among Children Aged <18 Years During the COVID-19 Pandemic - United States, January 1-October 17, 2020. MMWR Morb Mortal Wkly Rep, 2020. 69(45): p. 1675-1680.
- 36. Jones, S.E., K.A. Ethier, M. Hertz, et al., Mental Health, Suicidality, and Connectedness Among High School Students During the COVID-19 Pandemic - Adolescent Behaviors and Experiences Survey, United States, January-June 2021. MMWR Suppl, 2022. 71(3): p. 16-21.
- Kidman, R., R. Margolis, E. Smith-Greenaway, and A.M. Verdery, *Estimates and Projections of COVID-19 and Parental Death in the US.* JAMA Pediatr, 2021. 175(7): p. 745-746.
- 38. Wise, P.H. and L.J. Chamberlain, Adversity and Opportunity-The Pandemic's Paradoxical Effect on Child Health and Well-being. JAMA Pediatr, 2022.
- 39. Tan, T.Q., R. Kullar, T.H. Swartz, et al., *Location Matters: Geographic Disparities and Impact of Coronavirus Disease 2019.* J Infect Dis, 2020. **222**(12): p. 1951-1954.
- 40. Hendricks, B., R. Paul, C. Smith, et al., *Coronavirus testing disparities associated with community level deprivation, racial inequalities, and food insecurity in West Virginia.* Ann Epidemiol, 2021. **59**: p. 44-49.
- 41. Lieberman-Cribbin, W., S. Tuminello, R.M. Flores, and E. Taioli, *Disparities in COVID-*19 Testing and Positivity in New York City. Am J Prev Med, 2020. **59**(3): p. 326-332.
- 42. Pond, E.N., L. Rutkow, B. Blauer, et al., *Disparities in SARS-CoV-2 Testing for Hispanic/Latino Populations: An Analysis of State-Published Demographic Data.* J Public Health Manag Pract, 2022.
- Romero, L., L.Z. Pao, H. Clark, et al., *Health Center Testing for SARS-CoV-2 During the COVID-19 Pandemic - United States, June 5-October 2, 2020.* MMWR Morb Mortal Wkly Rep, 2020. 69(50): p. 1895-1901.

- 44. Heintzman, J., J. O'Malley, M. Marino, et al., *SARS-CoV-2 Testing and Changes in Primary Care Services in a Multistate Network of Community Health Centers During the COVID-19 Pandemic.* JAMA, 2020. **324**(14): p. 1459-1462.
- 45. Perez, N.P., D.C. Xerras, L.S. Aldrich, et al., *The impact of broadening COVID-19 testing eligibility on communities of color - A lesson for overcoming structural barriers to health care.* Prev Med Rep, 2022. **26**: p. 101744.
- 46. Koonin, L.M., B. Hoots, C.A. Tsang, et al., *Trends in the Use of Telehealth During the Emergence of the COVID-19 Pandemic United States, January-March 2020.* MMWR Morb Mortal Wkly Rep, 2020. **69**(43): p. 1595-1599.
- Lieneck, C., E. Weaver, and T. Maryon, *Outpatient Telehealth Implementation in the* United States during the COVID-19 Global Pandemic: A Systematic Review. Medicina (Kaunas), 2021. 57(5).
- 48. Dixit, N., Y. Van Sebille, G.B. Crawford, et al., *Disparities in telehealth use: How should the supportive care community respond?* Support Care Cancer, 2022. **30**(2): p. 1007-1010.
- Gray, D.M., II, J.J. Joseph, and J.N. Olayiwola, *Strategies for Digital Care of Vulnerable Patients in a COVID-19 World—Keeping in Touch*. JAMA Health Forum, 2020. 1(6): p. e200734-e200734.
- 50. Assistant Secretary for Planning and Evaluation. *National Survey Trends in Telehealth Use in 2021: Disparities in Utilization and Audio vs. Video Services*. Available at: https://aspe.hhs.gov/sites/default/files/documents/4e1853c0b4885112b2994680a58af9ed/ telehealth-hps-ib.pdf. Accessed 18 April 2022.
- 51. Chang, J.E., A.Y. Lai, A. Gupta, et al., *Rapid Transition to Telehealth and the Digital Divide: Implications for Primary Care Access and Equity in a Post-COVID Era*. Milbank Q, 2021. 99(2): p. 340-368.
- Rodriguez, J.A., A. Saadi, L.H. Schwamm, D.W. Bates, and L. Samal, *Disparities In Telehealth Use Among California Patients With Limited English Proficiency*. Health Aff (Millwood), 2021. 40(3): p. 487-495.
- 53. National Institutes of Health. *COVID-19 Treatment Guidelines. Special Considerations in Children*. Available at: https://www.covid19treatmentguidelines.nih.gov/special-populations/children/. Accessed 18 April 2022.
- 54. U.S. Food and Drug Administration. *Fact Sheet for Healthcare Providers: Emergency Use Authorization for Bebtelovimab.* Available at: https://www.fda.gov/media/156152/download. Accessed 18 April 2022.
- 55. Department of Health and Human Services, Administration of Strategic Preparedness and Response. *COVID-19 Therapeutics Locator*. Available at: https://covid-19-therapeutics-locator-dhhs.hub.arcgis.com/. Accessed 18 April 2022.
- 56. Wiltz, J.L., A.K. Feehan, N.M. Molinari, et al., *Racial and Ethnic Disparities in Receipt of Medications for Treatment of COVID-19 United States, March 2020-August 2021.* MMWR Morb Mortal Wkly Rep, 2022. **71**(3): p. 96-102.
- 57. Klein, E.J., A. Hardesty, K. Vieira, and D. Farmakiotis, *Use of anti-spike monoclonal antibodies in kidney transplant recipients with COVID-19: Efficacy, ethnic and racial disparities.* Am J Transplant, 2022. **22**(2): p. 640-645.
- 58. Bierle, D.M., R. Ganesh, C.G. Wilker, et al., *Influence of Social and Cultural Factors on the Decision to Consent for Monoclonal Antibody Treatment among High-Risk Patients*

with Mild-Moderate COVID-19. J Prim Care Community Health, 2021. **12**: p. 21501327211019282.

- Al Shamsi, H., A.G. Almutairi, S. Al Mashrafi, and T. Al Kalbani, *Implications of Language Barriers for Healthcare: A Systematic Review*. Oman Med J, 2020. 35(2): p. e122.
- 60. Patel, J.A., F.B.H. Nielsen, A.A. Badiani, et al., *Poverty, inequality and COVID-19: the forgotten vulnerable*. Public Health, 2020. **183**: p. 110-111.
- 61. Centers for Disease Control and Prevention. *Trends in Demographic Characteristics of People Receiving COVID-19 Vaccinations in the United States*. Available at: https://covid.cdc.gov/covid-data-tracker/#vaccination-demographics-trends. Accessed 20 April 2022.
- 62. Kim, C., R. Yee, R. Bhatkoti, et al., *COVID-19 Vaccine Provider Access and Vaccination Coverage Among Children Aged 5-11 Years - United States, November* 2021-January 2022. MMWR Morb Mortal Wkly Rep, 2022. **71**(10): p. 378-383.
- 63. Khubchandani, J. and Y. Macias, *COVID-19 vaccination hesitancy in Hispanics and African-Americans: A review and recommendations for practice.* Brain Behav Immun Health, 2021. **15**: p. 100277.
- 64. Kricorian, K. and K. Turner, *COVID-19 Vaccine Acceptance and Beliefs among Black and Hispanic Americans.* PLoS One, 2021. **16**(8): p. e0256122.
- 65. Centers for Disease Control and Prevention. *COVID-19 Vaccination Equity*. Available at: https://covid.cdc.gov/covid-data-tracker/#vaccination-equity_vacceq-pop12. Accessed 20 April 2022.
- Murthy, B.P., N. Sterrett, D. Weller, et al., Disparities in COVID-19 Vaccination Coverage Between Urban and Rural Counties - United States, December 14, 2020-April 10, 2021. MMWR Morb Mortal Wkly Rep, 2021. 70(20): p. 759-764.
- 67. Sparks, G., L. Hamel, A. Kirzinger, M. Stokes, and M. Brodie. COVID-19 Vaccine Monitor: Differences in Vaccine Attitudes Between Rural, Suburban, and Urban Areas. Kaiser Family Foundation. Available at: https://www.kff.org/coronavirus-covid-19/pollfinding/kff-covid-19-vaccine-monitor-vaccine-attitudes-rural-suburban-urban/. Accessed 20 April 2022.
- 68. Giusti K, H.R., Krasnow M. Addressing Demographic Disparities in Clinical Trials. 2021 06/11/2021 [cited April 16th 2022].
- Gray, D.M., 2nd, T.S. Nolan, J. Gregory, and J.J. Joseph, *Diversity in clinical trials: an opportunity and imperative for community engagement*. Lancet Gastroenterol Hepatol, 2021. 6(8): p. 605-607.
- 70. U.S. Food and Drug Administration. Enhancing the Diversity of Clinical Trial Populations - Eligibility Criteria, Enrollment Practices, and Trial Designs Guidance for Industry. Available at: https://www.fda.gov/media/127712/download. Accessed 16 April 2022.
- Takvorian, S.U., C.E. Guerra, and W.L. Schpero, A Hidden Opportunity Medicaid's Role in Supporting Equitable Access to Clinical Trials. N Engl J Med, 2021. 384(21): p. 1975-1978.
- 72. Joseph, P.D., J.C. Craig, and P.H. Caldwell, *Clinical trials in children*. Br J Clin Pharmacol, 2015. **79**(3): p. 357-69.

- 73. Rees, C.A., A.M. Stewart, S. Mehta, et al., *Reporting of Participant Race and Ethnicity in Published US Pediatric Clinical Trials From 2011 to 2020.* JAMA Pediatr, 2022: p. e220142.
- 74. Tai, D.B.G., A. Shah, C.A. Doubeni, I.G. Sia, and M.L. Wieland, *The Disproportionate Impact of COVID-19 on Racial and Ethnic Minorities in the United States*. Clin Infect Dis, 2021. 72(4): p. 703-706.
- 75. Centers for Disease Control and Prevention. *Disparities in COVID-19 Illness*. Available at: https://www.cdc.gov/coronavirus/2019-ncov/community/health-equity/racial-ethnic-disparities/increased-risk-illness.html. Accessed 16 April 2022.
- 76. Hwang, T.J., A.G. Randolph, and F.T. Bourgeois, *Inclusion of Children in Clinical Trials of Treatments for Coronavirus Disease 2019 (COVID-19)*. JAMA Pediatr, 2020. **174**(9): p. 825-826.
- 77. Walter, E.B., K.R. Talaat, C. Sabharwal, et al., *Evaluation of the BNT162b2 Covid-19 Vaccine in Children 5 to 11 Years of Age.* N Engl J Med, 2022. **386**(1): p. 35-46.
- Frenck, R.W., Jr., N.P. Klein, N. Kitchin, et al., Safety, Immunogenicity, and Efficacy of the BNT162b2 Covid-19 Vaccine in Adolescents. N Engl J Med, 2021. 385(3): p. 239-250.
- 79. Islam, S.J., A. Nayak, Y. Hu, et al., *Temporal trends in the association of social vulnerability and race/ethnicity with county-level COVID-19 incidence and outcomes in the USA: an ecological analysis.* BMJ Open, 2021. **11**(7): p. e048086.
- 80. Polack, F.P., S.J. Thomas, N. Kitchin, et al., *Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine*. N Engl J Med, 2020. **383**(27): p. 2603-2615.
- 81. Baden, L.R., H.M. El Sahly, B. Essink, et al., *Efficacy and Safety of the mRNA-1273* SARS-CoV-2 Vaccine. N Engl J Med, 2021. **384**(5): p. 403-416.
- Sadoff, J., G. Gray, A. Vandebosch, et al., Safety and Efficacy of Single-Dose Ad26.COV2.S Vaccine against Covid-19. N Engl J Med, 2021. 384(23): p. 2187-2201.
- 83. Beigel, J.H., K.M. Tomashek, L.E. Dodd, et al., *Remdesivir for the Treatment of Covid-*19 - Final Report. N Engl J Med, 2020. **383**(19): p. 1813-1826.
- 84. Goldman, J.D., D.C.B. Lye, D.S. Hui, et al., *Remdesivir for 5 or 10 Days in Patients with Severe Covid-19*. N Engl J Med, 2020. **383**(19): p. 1827-1837.
- 85. Consortium, W.H.O.S.T., H. Pan, R. Peto, et al., *Repurposed Antiviral Drugs for Covid-*19 - Interim WHO Solidarity Trial Results. N Engl J Med, 2021. **384**(6): p. 497-511.
- 86. Gottlieb, R.L., C.E. Vaca, R. Paredes, et al., *Early Remdesivir to Prevent Progression to Severe Covid-19 in Outpatients*. N Engl J Med, 2022. **386**(4): p. 305-315.
- 87. Gilead. Phase 2/3 Interim Data Evaluating the Safety, Tolerability and Clinical Outcomes of Veklury (Remdesivir) in Pediatric Patients with COVID-19 Presented at CROI 2022. Available at: https://www.gilead.com/news-and-press/press-room/pressreleases/2022/2/phase-23-interim-data-evaluating-the-safety-tolerability-and-clinicaloutcomes-of-veklury-remdesivir-in-pediatric-patients-with-covid19-presente. Accessed 17 April 2022.
- 88. U.S. Food and Drug Administration. Coronavirus (COVID-19) Update: FDA Authorizes First Oral Antiviral for Treatment of COVID-19. Available from: https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-updatefda-authorizes-first-oral-antiviral-treatment-covid-19. Accessed 17 April 2022.
- 89. Hammond, J., H. Leister-Tebbe, A. Gardner, et al., *Oral Nirmatrelvir for High-Risk, Nonhospitalized Adults with Covid-19.* N Engl J Med, 2022. **386**(15): p. 1397-1408.

- 90. U.S. Food and Drug Administration. . Fact Sheet for Healthcare Providers: Emergency Use Authorization for Paxlovid. Available at: https://www.fda.gov/media/155050/download. Accessed 17 April 2022.
- Jayk Bernal, A., M.M. Gomes da Silva, D.B. Musungaie, et al., *Molnupiravir for Oral Treatment of Covid-19 in Nonhospitalized Patients*. N Engl J Med, 2022. 386(6): p. 509-520.
- 92. Dougan, M., A. Nirula, M. Azizad, et al., *Bamlanivimab plus Etesevimab in Mild or Moderate Covid-19*. N Engl J Med, 2021. **385**(15): p. 1382-1392.
- 93. Weinreich, D.M., S. Sivapalasingam, T. Norton, et al., *REGEN-COV Antibody Combination and Outcomes in Outpatients with Covid-19*. N Engl J Med, 2021. 385(23): p. e81.
- 94. Gupta, A., Y. Gonzalez-Rojas, E. Juarez, et al., *Early Treatment for Covid-19 with SARS-CoV-2 Neutralizing Antibody Sotrovimab.* N Engl J Med, 2021. **385**(21): p. 1941-1950.
- 95. National Institutes of Health. COVID-19 Treatment Guidelines. Therapeutic Management of Nonhospitalized Adults with COVID-19. Available at: https://www.covid19treatmentguidelines.nih.gov/management/clinicalmanagement/nonhospitalized-adults--therapeutic-management/. Accessed 17 April 2022.
- 96. Group, R.C., P. Horby, W.S. Lim, et al., *Dexamethasone in Hospitalized Patients with Covid-19*. N Engl J Med, 2021. **384**(8): p. 693-704.
- 97. Group, C.S.T., M.W. Munch, S.N. Myatra, et al., Effect of 12 mg vs 6 mg of Dexamethasone on the Number of Days Alive Without Life Support in Adults With COVID-19 and Severe Hypoxemia: The COVID STEROID 2 Randomized Trial. JAMA, 2021. 326(18): p. 1807-1817.
- 98. Group, R.C., Tocilizumab in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial. Lancet, 2021. 397(10285): p. 1637-1645.
- 99. Marconi, V.C., A.V. Ramanan, S. de Bono, et al., *Efficacy and safety of baricitinib for the treatment of hospitalised adults with COVID-19 (COV-BARRIER): a randomised, double-blind, parallel-group, placebo-controlled phase 3 trial.* Lancet Respir Med, 2021.
 9(12): p. 1407-1418.
- 100. Ginther, D.K., W.T. Schaffer, J. Schnell, et al., *Race, ethnicity, and NIH research awards*. Science, 2011. **333**(6045): p. 1015-9.
- 101. Sharma, A. and L. Palaniappan, *Improving diversity in medical research*. Nat Rev Dis Primers, 2021. **7**(1): p. 74.
- 102. National Academies of Sciences, Engineering, and Medicine 2022. *Improving Representation in Clinical Trials and Research: Building Research Equity for Women and Underrepresented Groups*. Washington, DC: The National Academies Press. Available at: https://doi.org/10.17226/26479. Accessed 26 July 2022.
- 103. University of Texas College of Education. *Considerations for Equity-Centered Research*. Available at: https://texcep.education.utexas.edu/equity-centered-research. Accessed 27 July 2022.
- 104. The Annie E. Casey Foundation. *Step-by-Step Guide on Using Equity Principles in Social Science Research*. Available at: https://www.aecf.org/blog/step-by-step-guide-on-using-equity-principles-in-social-science-research. Accessed 27 July 2022.
- 105. Andrews, K., J. Parekh, and S. Peckoo. *A guide to incorporating a racial and ethnic equity perspective throughout the research process*. Available from:

https://www.childtrends.org/publications/a-guide-to-incorporating-a-racial-and-ethnic-equity-perspective-throughout-the-research-process. Accessed 26 July 2022.

C

106. Flanagin, A., T. Frey, S.L. Christiansen, and A.M.A.M.o.S. Committee, *Updated Guidance on the Reporting of Race and Ethnicity in Medical and Science Journals.* JAMA, 2021. **326**(7): p. 621-627.

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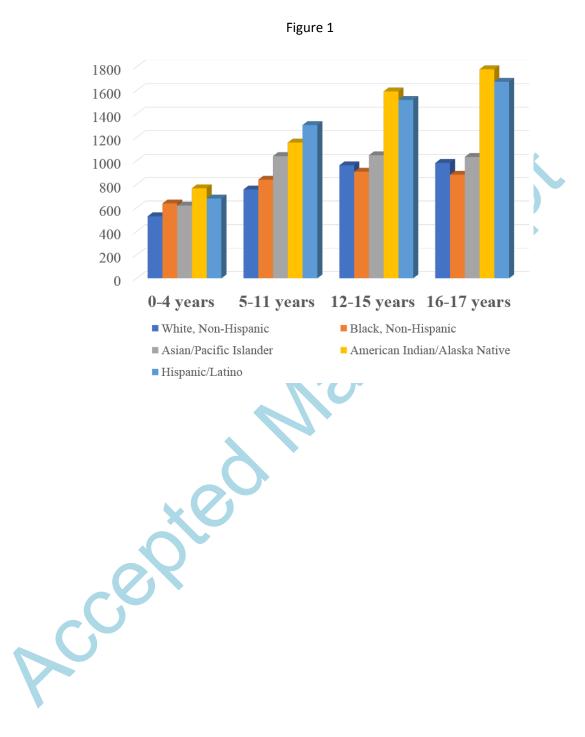


Figure 2

Increasing presence of underrepresented populations in clinical trials

- Investigators should be aware of the inequities in social determinant of health that affect racial and ethnic minorities.
 The research workforce should be representative of diverse racial, ethnic, and socioeconomic backgrounds.[100, 101]
- · Ensure diversity in Institutional Review Board (IRB) and engage community members in local IRBs.[102] · Academic institutions should value faculty investment in community-engaged research.[102]
- · In clinical trials, strive to provide flexible hours, transportation, and offer telehealth visits when appropriate.[70]
- Make research teams accessible via several platforms (e.g., website, email, landline).[102]

Best practices for funding research [102]

- Funding agencies should diversify their scientific committees to implement a more inclusive research agenda.
 Priority should be given to study proposals that include a representative population and engage community partners.
- · Funding agencies should acknowledge the increased efforts and financial resources needed to recruit/retain diverse
- study participants.

- Generating new research questions with an equity-focused perspective

 Research teams should have members from diverse backgrounds with a connection to the study population.[103]
- Research teams should foster relationships and community engagement early during clinical trials.[70, 101]
 Community representatives should have input into the research question(s) to ensure their needs are addressed,
- preferred methods of inquiry are determined, and that the proposed research will benefit the community.[103,104]
- Research questions should reflect the community's values and perspectives of the study participants.[105]
 Research should be aimed at promoting equity[104] and ensure that recruiting protocols do not potentiate

inequities.[103] • Ensure culturally relevant measures are used.[103]

Analyzing data from an equity standpoint

- · Prioritize analyses that can impact action, such as changes in practices and policies.[103]
- · Investigators should consider how some data may increase vulnerabilities. [103]
- Investigator should explore within-group variation.[103,104]
 If disparities are noted, the structural factors responsible should be named. [103]

Reporting data to the scientific community

- Investigators should promote the use of non-stigmatizing terms when referring to certain groups of people.[106] · Race and ethnicity differences should be considered and interpreted in the context of other sociodemographic factors,
- cultural practices, and social determinants of health and reported in a way that reflects all these factors Increasing diversity on editorial boards of medical journals can help minimize biases in publication.[102]
- <u>Reporting data to the public</u>[105] Collaboration with the community is important to identify audiences and best platforms for result dissemination
- Stereotyping and victim-blaming the study participants should be avoided.
 Language utilized to report data should be appropriate for the identified audiences, considering a communication team
- and/or outside expert consultation if needed.
- Report of findings should be accompanied by a plan to maintain interest and engagement in the future, so commitm
 with the community does not end with the conclusion of the research study.