Supplement to
American Journal of
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A PUBLICATION OF
AMERICAN PUBLIC HEALTH ASSOCIATION

Racial Disparities in Cancer Care | Access to Care for Transgender Veterans | Hepatitis C Among US Veterans | Battling Tobacco Use at Home | [illegible] | How Might the Provision of Culturally Competent Services Be Enhanced for American Indian and Alaska Native Veterans? | Improving Trends in Gender Disparities | Suicidality Among Hispanic and African American Veterans Following Surgery

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COVER: Phyll Opoku-Gyimah, co-founder and director of UK Black Pride, addresses LGBTI+ protesters in Parliament Square before the first-ever Reclaim Pride march on July 24, 2021, in London, United Kingdom. Reclaim Pride replaced the traditional Pride in London march, which many feel has become too commercial and strayed from its roots in protest, and was billed as a Peoples Pride march for LGBTI+ liberation. Campaigners called for the banning of LGBTI+ conversion therapy, the reform of the Gender Recognition Act, the provision of a safe haven for LGBTI+ refugees, and for LGBTI+ people to be decriminalized worldwide, and marched in solidarity with Black Lives Matter.

Cover concept and selection by Aleisha Kropf. Photo by Mark Kerrison/In Pictures via Getty Images. Printed with permission.

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AMERICAN PUBLIC HEALTH ASSOCIATION
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Promoting public health research, policy, practice, and education is the *AJPH* mission. As we widen our scope to embrace global issues, we also sharpen our focus to support the needs of public health practitioners. We invite contributions of original unpublished research, opinion and commentary, and letters to the editor.

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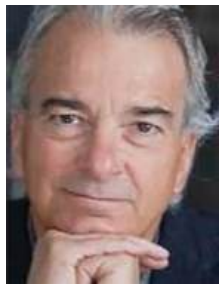
OPEN-THEMED RESEARCH

Why Is *AJPH* Publishing More Than Other Major Journals About Race and Racism?



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Every editor of color, and their colleagues on diverse editorial teams, understands that being a person of color is a liability in interactions with the health care system. A complex array of factors—including the organization and structure of the health care system and the training and job opportunities of its personnel—coalesce to produce a health care system that does not treat everyone equitably, particularly when the patient's race and ethnicity are involved.

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DOI: https://doi.org/10.2105/AJPH.2021.306461

4 Years Ago

Cardiovascular Disease in Sexual Minorities

Sexual minority women exhibited greater cardiovascular disease risk related to tobacco use, alcohol consumption, illicit drug use, poor mental health, and body mass index, whereas sexual minority men experienced excess risk related to tobacco use, illicit drug use, and poor mental health. . . . CVD risk differed across racial/ethnic groups, with Latina and Black sexual minority women experiencing greater CVD risk than did heterosexual women of the same race. . . . It appears that nonrural sexual minority individuals experience greater CVD risk than do their heterosexual peers. . . . [E]vidence . . . supports the need to target CVD risk in sexual minorities, particularly sexual minority women. These data indicate that clinicians and public health practitioners should develop primary and secondary prevention interventions that reduce CVD risk in sexual minorities.

From AJPH, *April 2017*

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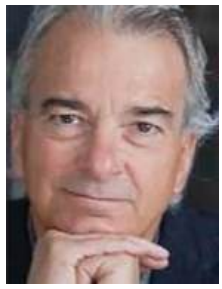

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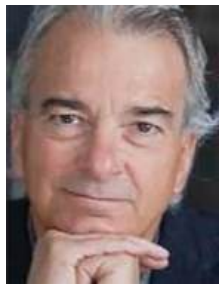

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The Two Waves of the COVID-19 Pandemic in Africa

Salyer et al. performed the first comprehensive review of COVID-19 data from all 55 African Union member states collected between February 14 and December 31, 2020. By December 31, African countries reported 2 763 421 COVID-19 cases and 65 602 deaths, accounting for 3.4% of cases and 3.6% of deaths globally. More than 80% of reported cases were from 9 of the 55 countries, and 18 countries reported case fatality rates greater than the global rate of 2.2%. At the peak of the first wave in July 2020, on average, 18 273 new cases were reported daily. During the second wave, this number increased to 23 790. However, the number of member states with stringent social measures decreased from 48 during the first wave to 36 as of December 31, 2020. Salyer et al. concluded that the African continent's second wave of the COVID-19 pandemic was more severe than its first wave .

Citation. Salyer SJ, Maeda J, Sembuche S, et al. The first and second waves of the COVID-19 pandemic in Africa: a cross-sectional study. *Lancet*. 2021;397(10281):1265–1275. https://doi.org/10.1016/S0140-6736(21)00632-2

The Mediation of Excess COVID-19 Risk Through Deprivation Among Underrepresented Populations

Although there is growing evidence that COVID-19 risk is disproportionately higher among underrepresented populations, there is a dearth of evidence regarding the influence of material deprivation on this association. The authors conducted a mediation analysis involving a 4-way counterfactual approach using UK Biobank data with linked COVID-19 outcomes to determine the role of deprivation in the excess risk of COVID-19 among ethnic minorities. Models that shifted 25% of the most deprived individuals from deprivation resulted in a 40% to 50% reduction of excess COVID-19 risk among South Asian and Black individuals, suggesting that policies targeting material deprivation could substantially reduce the excess risk of COVID-19 in underrepresented populations.

Citation. Razieh C, Zaccardi F, Islam N, et al. Ethnic minorities and COVID-19: examining whether excess risk is mediated through deprivation. *Eur J Public Health*. 2021; Epub ahead of print. https://doi.org/10.1093/eurpub/ckab041

Brazilians' Self-Rated Health During the COVID-19 Pandemic

The spread of COVID-19 in Brazil prompted its government to release recommendations and various initiatives, such as physical distancing and business closures, with the goal of preventing transmission. Szwarcwald et al. used results from the ConVid Behavior Survey—a cross-sectional Web-based study carried out from April through May 2020 in Brazil—to identify factors contributing to lower self-rated health during the COVID-19 pandemic. The authors found that 29.4% of the 45 161 participants included in the study reported worsening health, with women having significantly greater odds of reporting worsening health. People who reported seeking mental health care, seeking care for COVID-19, sleep problems, worsening back pain, depression, sedentary behaviors, and adhering to social distancing, among other factors, were associated with reporting worsening health status. The authors conclude that a multitude of social, health, and behavioral factors have affected self-rated health during the COVID-19 pandemic in Brazil.

Citation. Szwarcwald CL, Damacena GN, Barros MBA, et al. Factors affecting Brazilians' self-rated health during the COVID-19 pandemic. *Cad Saude Publica*. 2021;37(3):e00182720. https://doi.org/10.1590/0102-311X00182720

Ethical Implications for Potential LGBTQ+ Discrimination of Using COVID-19 Patient Data

Multiple countries in the Asia-Pacific region are using big data to identify and track COVID-19–positive individuals and to alert others of possible exposure to COVID-19. The use of big data in tracking COVID-19 cases is pivotal but poses significant ethical concerns for individual privacy.

The authors used the principle of double effect, which states that 4 conditions must be met to use data with both good and bad effects, to determine whether data usage was ethical in specific circumstances. For example, the second clause of the principle of double effect states that a good effect must not result from a bad effect. In South Korea, information disclosure on COVID-19 cases revealed secondary issues, including stigmatization of LGBTQ+ (lesbian, gay, bisexual, transgender, queer) neighborhoods and revealing LGBTQ+ status to families of those affected. This analysis highlights the need to deliberate about surveillance tools that use private data before releasing the data to the public to retain public trust and privacy.

Citation. Ngan OMY, Kelmenson AM. Using big data tools to analyze digital footprint in the COVID-19 pandemic: some public health ethics considerations. *Asia Pac J Public Health*. 2021;33(1):129–130. https://doi.org/10.1177/1010539520984360

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Modern Capitalism as a Threat to Health

Mary T. Bassett, MD, MPH

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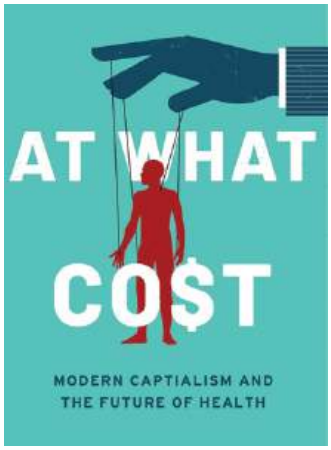

At What Cost: Modern Capitalism and the Future of Health
By Nicholas Freudenberg
New York, NY: Oxford University Press; 2021
Hardcover: 416 pp.; $29.95
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Nicholas Freudenberg, a professor of public health at the New York City's public university, has long been insightful about the many ways that society affects health, from HIV infection to incarceration. His previous book, *Lethal but Legal*,[1] described how corporate practices not only permitted but also promoted consumption that is harmful. In recent years, he has turned his attention to examining how the food system became an important contributor to the avalanche of obesity and a host of other diseases. He helped frame the notion of "corporate determinant" of health and the more commonly used phrase, "commercial determinant," which add corporate and commercial activity to the list of societal determinants of health. It was at a meeting in Bangkok, Thailand, in early 2019 that I first heard Freudenberg talk about modern capitalism as a root cause of the apocalyptic scenarios that we now face—floods, droughts, fires, frayed safety nets, and the worst pandemic in a century. At the time I thought that in a setting far from home, at a session hosted by the progressive People's Health Movement,[2] he felt encouraged to discuss capitalism, which is rarely referenced in the US public health. But Freudenberg has always been outspoken, wherever he is, and, in fact, he was sharing the thinking that we have now in book form.

MODERN US CAPITALISM AS A ROOT CAUSE OF ILL HEALTH

Anyone who cares about health, the environment, our food, dignity, and fairness should read *At What Cost: Modern Capitalism and the Future of Health*. It is truly a brave survey of a serious topic. In the United States, it takes courage to be critical of capitalism. More than other wealthy nations, the United States has kept alive the notion of the so-called "communist menace" and lurking socialism. Of wealthy countries, only the United States endured the McCarthy period. *At What Cost* makes a compelling case to extend examination beyond health-harming corporate actions—Big Tobacco, Big Food, Big Pharma, and now Big Tech—to explore the social and economic relations that entrench and enable such behavior. The most important message of this book is that capitalism, particularly the rapacious form of 21st century US capitalism, with its greatly accelerated income inequality, is not inevitable. Our very planet, let alone the people and other living things that inhabit it, depend on controlling a system whose logic is profit.

Modern capitalism is a sweeping topic. The book ably breaks it down into manageable parts, beginning with the distinguishing features of modern capitalism: globalization, financialization, market concentration, privatization, deregulation, tax cuts, and austerity. I was not familiar with the word "financialization." It refers to the growing dominance of finance over manufacturing. A variety of ways of packaging and moving around money are now a key way of generating profits. Then, to make these interrelated phenomena practically meaningful, Freudenberg shows how they work to affect what he calls the

"pillars of health": food, education, health care, work, transportation, and social connections. There is the rise of ultraprocessed foodstuffs made with ingredients that do not exist in a home kitchen. And there is the emergence of publicly funded, privately managed charter schools; Ubers to skip that subway ride; and gadget-galore medicine. Reading the book, you will see how all trace their logic to these characteristics of capitalism. For example, Uber would like to maintain the use of cars for transportation and take over a chunk of the public transport market. This makes continued car transport, including driverless cars, appealing. But pouring cars onto the streets, leaving it to humans to stay out of the way, seems unlikely to end road carnage and will not end air pollution or consumption of fossil fuels. But only the market is in charge, and no one is "in charge" of the big picture. Through case examples, with clear compelling prose, we see how these abstract concepts manifest in everyday life. Each section ends with how an alternative vision is possible. Drivers organize; teachers strike in defense of childhood.

A FRESH LOOK AT CURRENT CHALLENGES

I learned a lot. For example, New York City's pioneering 2006 restriction of artificial trans fat in restaurant food eventually led the US Food and Drug Administration to remove these unhealthy fats from our food supply.[3] But a consequence was a massive increase in demand for palm oil. Globally, palm oil production has a devastating environmental impact. Likewise, I reflected on the US focus on food components—sugar, salt, fat, calories—as bad actors, whereas Freudenberg highlights how Monteiro et al. from Brazil showed how the food preparation process—ultraprocessing—more than particular components makes for unhealthy food[4]; how tax cuts for wealthy individuals and corporations created the budget shortfalls used to justify budget cuts to social safety nets; and how global trade agreements forced patent restrictions for lifesaving pharmaceuticals on poor nations, protecting private profits, which is now playing out with global access to COVID-19 vaccinations.

I have spent many years thinking about racism in the United States and its impact on health. *At What Cost* invokes transport apartheid and food apartheid as consequences of the US racial hierarchy. Freudenberg acknowledges Ibram X. Kendi's image of racism and capitalism as "conjoined twins" with neoliberalism reinforcing US systemic racism. But racism joins the author's list of challenges—sexism, climate crisis, etc. In contrast, I find racism not only a driver of inequality but also foundational to US capitalism. For this reason, racism deserves a more prominent place than Freudenberg offers in the understanding of US capitalism. Africans were captured and kept in bondage for their labor. The purpose of racism is not to make Black people miserable; it is exploitation. The embrace of White supremacy is all I can find to explain why such a large slice of the White working class chooses class collaboration over class solidarity. Much of the failure to challenge modern capitalism has foundered on reluctance to acknowledge this actual history of the United States: a country that began as a settler colony and procured land through genocidal campaigns against the people whom the Europeans found here. Enslaved people then worked this land. This profitable, bloodstained enterprise catapulted the United States into the ranks of wealthy nations and helped establish the brand of capitalism we have today.

The usual argument is that poor and working-class White people have been misled by racism, which causes them to overlook their own exploitation and instead blame their problems on Black people. Furthermore, it is the failure to make compelling the "racism harms everyone" argument that permits this misunderstanding to persist. I have heard this rationale for many, many years. If White people understood that everyone can win, and no one has to lose, we would have a different politics. Heather McGhee's *The Sum of Us* eloquently makes this case.[5] The costs of our contemporary brand of capitalism are all around us. The United States departed from the upward life expectancy trajectory of other wealthy nations around 1980, and 2015 marked a decline that the COVID-19 pandemic has accelerated.[6,7] The recent Lancet Commission on Public Policy in the Trump Era showed that had the United States' trajectory of life expectancy increase remained in the middle of the pack of G7 nations (which also includes Canada, France, Germany, Italy, Japan, and the United Kingdom), more than 450 000 total deaths would not have occurred.[6] Not since 1964 has the majority of White voters voted for a Democrat for president. Is this narrative of "being misled" accurate? Or, as Isabel Wilkerson suggests in *Caste: The Origins of Our Discontent*, does the "long game" indeed favor White racial solidarity?[8] Kendi's "conjoined twins" tells the truth because, in the United States, racism and capitalism share the same heart.

A White choice for solidarity was on display in the global outpouring following the police murder of George Floyd. My daughter recounted a protest in New Orleans, Louisiana, where thousands in

a multiracial group marched through the city and adjoining areas. The group approached a parish once known as a "sundown" parish, meaning no Black people allowed after sundown, where police in military attire stood in the street. The march leaders, mostly young people of color, called out on bullhorns: "White people to the front." I will not forget the awe in my daughter's voice as she said, "And Mom, they went." There have been Whites who died for Black rights over many generations, but this felt different.

Freudenberg ends by making plain that although better technology is often credited, health advancements most importantly are attributable to social movements that improve overall living conditions. The book does not take responsibility for crafting a path to undoing modern capitalism, but invokes the role of social activism and calls for public health to align itself with a large array of diverse social movements. In 2015, it felt brave to talk about racism.[9] *At What Cost* tells us that now it is time to be brave and talk about capitalism. Freudenberg has good company. Thomas Piketty's *Capital* became a bestseller[10]; Case and Deaton titled their bestselling book *Deaths of Despair and the Future of Capitalism*.[11] I suspect that a conversation about capitalism also will take us to one about racism. AJPH

ACKNOWLEDGMENTS

M. T. Bassett conceptualized and wrote this book review based on her remarks made at an online book launch hosted by the CUNY Graduate School of Public Health and Health Policy and Scholars Strategy Network on March 16, 2021.

CONFLICTS OF INTEREST

The author reports no conflicts of interest.

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Twenty Years After 9/11: The Public Health Preparedness We Need Now

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September 11, 2021 (9/11) will mark 20 years since the terrorist attacks on the World Trade Center and the Pentagon, the foiled attempt to hijack Flight 93, and the subsequent anthrax attacks in October. Significant strides in advancing local, state, and national public health preparedness through investments that build core preparedness and emergency response capabilities have been made since. Twenty years after 9/11, COVID-19 demonstrated that our nation's public health readiness, despite the tireless efforts of committed and skilled public health professionals who have admirably responded, was compromised by disconnected local, state, and federal data systems and disease surveillance capacity; an inadequate medical supply chain to meet demand for personal protective equipment; insufficient surge capacity to meet the national demand for contact tracing and case investigation; and varied attention to building equity and community resilience activities into ongoing response and recovery efforts. So, do we have the preparedness we need? The answer is mixed.

SUSTAINABLE INVESTMENTS OR BOOM-AND-BUST

Before 9/11, the US Centers for Disease Control and Prevention (CDC) bioterrorism preparedness program consisted of a $40 million annual cooperative agreement with states that was focused on building state and territorial capacity for preparedness planning, epidemiology, and surveillance; building biological and chemical laboratory capacity; and implementing the Health Alert Network. Congress appropriated nearly $1 billion to the CDC in fiscal year 2002, and the agency reorganized its preparedness activities in support of states and territories, including the creation of a new national center now known as the Center for Preparedness and Response. With these federal resources, states and territories created preparedness programs that were far more robust than before 9/11, guided by a set of 15 emergency preparedness and response capabilities, first promulgated in 2011, which now serve as the national standards for public health preparedness planning.

The need for governmental public health to integrate new preparedness and response capacities with established response partners required public health professionals to learn and use the Incident Command System and National Incident Management System components in both day-to-day and emergency operations. Since 9/11, public health and medical entities have used the Incident Command System structure to carry out activities prescribed by the Federal Emergency Management Agency's National Response Framework, specifically Emergency Support Function 8, which addresses the provision of public health and medical services during times of major emergencies and disasters. Public health preparedness is now a core part of the nation's homeland security efforts, with the original focus areas of bioterrorism preparedness expanded to a comprehensive set of capabilities that include emergency operations coordination, fatality management, mass care, medical countermeasure dispensing and administration (including the Strategic National Stockpile), responder safety, and volunteer management.

Congress has had a significant role in establishing our modern public health preparedness system and in preparing the nation for the future. The Public Health Security and Bioterrorism Preparedness and Response Act of 2002 (Pub L No. 107–188) amended the 1994 Public Health Service Act (Pub L No. 78–410) to improve preparedness planning and coordination, established state and territory cooperative agreement funding programs for public health and hospital and health care preparedness, and created the National Pharmaceutical Stockpile Program. In 2006, the Pandemic and All-Hazards Preparedness

Act (PAHPA; Pub L No. 109-417) established a new Assistant Secretary for Preparedness and Response in the Department of Health and Human Services; provided new authorities for several federal programs, including the advanced development and acquisitions of medical countermeasures; and called for the establishment of a quadrennial National Health Security Strategy. In 2013, PAHPA was reauthorized in the Pandemic and All-Hazards Preparedness Reauthorization Act (Pub L No. 113–5), allowing continued funding for public health and medical preparedness programs and granting state health departments greatly needed flexibility in dedicating staff resources to meeting critical community needs in a disaster. In 2019, PAHPA was reauthorized as the Pandemic and All-Hazards Preparedness and Advancing Innovation Act (Pub L No. 116-22), which sustained vital public health and health care programs and authorized the use of the Public Health Emergency Fund when the secretary determines there is significant potential for or outright declares a public health emergency.

The first 20 years of public health preparedness and response is characterized by large initial investments in preparedness programs and the establishment and demonstration of the capabilities and capacities needed to integrate with emergency management partners. Significant accomplishments included planning efforts that ensure compliance with the Incident Command System and National Incident Management System in state and local health structures, exercising and demonstrating emergency plans to test staff and systems capabilities, and recruiting public health preparedness subject matter experts for health agency roles. However, efforts to quantify readiness over the past 20 years have validated mixed results in the states. These findings are well documented in Trust for America's Health Ready or Not? report series, the National Health Security Preparedness Index, the Johns Hopkins Center for Health Security's Global Health Security Index, and various reports of the Bipartisan Commission on Biodefense, among several other reports.

A consistent finding of these reports, echoed by many national public health advocacy groups, is the need for sustained investment in preparedness to address the "boom-and-bust" cycle of budget increases during emergencies and decreasing investments post hoc and the need for investments to support public health infrastructure and capabilities to address both everyday and emergency events. Since the recession of 2008, and with waning attention to public health emergencies, agencies' preparedness investments and resources needed to sustain progress have declined. Although some of the decline in funding has been made up with one-time emergency supplemental appropriations for large-scale disasters such as the H1N1 influenza, Ebola, Zika, and now COVID-19, these supplemental funds are restricted to specific uses to address a given emergency. Consequently, despite funding increases during emergencies, public health agencies were unable to sustain temporary workforce expansions or to implement enterprise-wide data systems, as emergency funding has been emergency-specific and ebbed as the emergency's intensity decreased.

COVID-19, PREPAREDNESS, AND THE FUTURE

COVID-19 could motivate us to change this boom-and-bust cycle and move national preparedness efforts forward by building sustained public health capacity. With more than $51 billion allocated to state and territorial health agencies to respond to and recover from COVID-19, health departments now have significant resources dedicated to epidemiology and laboratory capacity enhancements ($30.4 billion), workforce expansion ($7.4 billion), and data modernization ($1.1 billion). These funds are intended to be used for COVID-19–related activities, but some may also be used to support other infectious disease response and cross-cutting capacities, such as information technology and workforce improvements. These new investments will help support long-term capacity building, especially in the areas of disease investigation and surveillance, laboratory services, data systems improvements, and health equity—especially if they are sustained with longer term investments in our nation's public health infrastructure.

As we look at the public health preparedness needed now, a lesson learned from COVID-19 and many other disasters over the past 20 years becomes strikingly obvious: disasters and public health emergencies exacerbate and worsen disparities among persons of color, underresourced communities, and disabled Americans. If the first 20 years of public health preparedness were formative in developing public health's formal role as an emergency responder, the next 20 should advance an agenda that addresses health equity, community resilience, and the social and political factors that affect health. Disaster and emergency recovery programs should focus less on restoration, or "bouncing back," and more on helping communities bounce forward to conditions that are improved by the opportunities these emergencies present.

Readiness for catastrophic infectious disease events such as the COVID-19 pandemic, but also natural disasters including Hurricane Katrina and Superstorm Sandy, illustrates the benefits of deliberately focusing on efforts that build resiliency and rebuild with equity and sustainability in mind. The importance of community engagement's role in crafting policy to reduce social vulnerability cannot be overstated. The COVID-19 pandemic provides us the opportunity to return to a next normal in which community members are active in rebuilding and redesigning their public health and health care systems in a way that is governed and guided locally, developed with state guidance and input, and supported with federal resources. One such model of community resilience is under way in Rhode Island, where the state health department has supported Health Equity Zones development and local efforts to build healthier, more resilient communities.

So, do we have the preparedness we need now? The past 20 years suggest that a state of complete and total preparedness for all public health emergencies may not be a realistic goal. Nevertheless, efforts should be placed on cultivating and maturing a coordinated national response and building local community resiliency to respond to and bounce forward from events that overwhelm typical public health operations. Building core capabilities for emergency response alongside efforts to promote place-based, community-led approaches to building healthy and resilient communities are the work of the next 20 years. The more prepared we are for large-scale emergencies, the better we will be in rapidly detecting, responding to, and preventing more typical emergencies, such as foodborne illnesses, health care–associated infections, vaccine-preventable diseases (e.g., measles), and mass casualty events. AJPH

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Puncturing Hubris . . . and Insularity: The 1942 Yellow Fever Vaccine Disaster and COVID-19

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See also Löwy, p. 1654.

The past year has not been a good one for US public health hubris. As is now well-known, in 2019, the Global Health Security Index—produced by the Johns Hopkins Center for Health Security, the Nuclear Threat Initiative, and the Economist Intelligence Unit—ranked 195 countries in terms of their preparedness to "prevent, detect, and rapidly respond" to infectious disease threats.[1] The United States ranked first in overall scoring. The COVID-19 pandemic, of course, turned such notions of preparedness and exceptionalism on their respective heads, with "hubris" only one of the many charges leveled at the US response to the pandemic.[2,3] Yet this was not the first disastrous example of US public health hubris. And as a historian, I displayed at least my own ignorance and insularity, if not quite hubris, in missing a telling earlier example.

In the spring of 2020, amid the first surge of COVID-19, I cowrote a historical examination of "Biomedical Research in Times of Emergency."[4] My colleagues and I, relying solely on English-language sources, drew attention to the opportunities attendant to increased investment in (and concentration of) research, but also to the potential hazards of pressurized research. We noted that "urgency can induce shortcuts that compromise quality,"[4(p297)] and pointed to the United States' World War II yellow fever vaccine disaster as a telling example. In the spring of 1942, in the context of a mass vaccination campaign with yellow fever vaccine produced at the Rockefeller Institute in New York City for millions of US servicemen fighting overseas, over 40 000 men developed acute hepatitis presenting as jaundice. And although the vaccine's association with an unknown filterable virus would not be recognized for several years (with the virus itself only identified as the hepatitis B virus after several decades), the apparent relationship of the acute hepatitis to the human serum that was used in the production of the vaccine was determined within several weeks, with vaccination halted accordingly. As my colleagues and I summarized: "Relying on untested human serum, they unknowingly used a contaminated sample to formulate the vaccines and infected tens of thousands of GIs with hepatitis."[4(p297)] And yet, as Ilana Löwy relates elsewhere in this issue (p. 1654), my own North–South (or at least US–non-US) historiographic insularity was paralleled decades earlier by US North–South hubris at the very center of the yellow fever vaccine story.

In fact, the US yellow fever vaccine–associated hepatitis fiasco had been preceded by an earlier such association in Brazil only two years previously. And the Rockefeller team in New York City was aware of this association. As Löwy relates, Rockefeller Foundation experts had actually founded the virology laboratory of the Brazilian Yellow Fever service at the Oswaldo Cruz Institute in Rio de Janeiro, with certain Rockefeller experts working with their Brazilian colleagues in the 1930s to develop a form of the attenuated 17D yellow fever virus strain vaccine amenable for mass production. In their rollout of the vaccine within the country in the late 1930s, the Brazilian Yellow Fever service implemented a rigorous post-vaccination surveillance program—based, as Löwy puts it, on such humble tools as "a 'vaccination book,' a pen, and labor-intensive collection, transmission and tabulation of data" (p. 1658)—and by early 1940 had detected more than 1000 cases of jaundice, with 22 associated deaths. As Löwy further relates, the team in Rio de Janeiro, after a careful process of elimination, concluded that year that the cause of such jaundice was the normal human serum included to stabilize the vaccine. They in turn discarded the existing batches of the vaccine. Back in New York City, though, such concerns were minimized. Engaged in the limited production of the vaccine since 1938, the Rockefeller team there had found few cases of jaundice—but they had scarcely looked for any. When it came time for the scaling-up of vaccine

manufacture, concerns over the need to rapidly intensify production with known methods prevailed over those regarding associated jaundice raised in Brazil. As it turns out, the Rockefeller team did not just passively or "unknowingly" use a contaminated sample; rather, as Löwy describes, they had actively chosen to downplay concerns raised by their partners from the apparent periphery.

Eight decades later, as tropical medicine and international health have transformed into "global health," North–South collaborations and partnerships have further proliferated. Amid this proliferation, scholars have raised concerns over North–South funding and power imbalances that shape aspects of the research enterprise, ranging from the questions to be answered and the interventions that are proposed to the distribution of project funding and the order of authorship in articles stemming from such projects.[5–7] Even beyond these structural inequities, moreover, lay issues of mutual trust and confidence among collaborators,[8] as they apparently did eight decades prior. And yet there remain important benefits to such collaborations, if done well, in settings of mutual trust and empowerment, and with appropriate humility.

Such considerations of humility, as demonstrated by the Global Health Security Index and the COVID-19 pandemic, can spread outward to national assessments and notions of exceptionalism as well. And it can extend to historians writing from their own "centers." This can range from broad claims to "decenter" historical accounts[9] to a simple acknowledgment of the vast realms of work being conducted beyond our own self-constructed orbits—disciplinary, geographic, or otherwise. I'm not overly ashamed to have missed in-depth earlier accounts, in non–English-language publications, of yellow fever vaccination outside the United States.[10,11] But I did miss them. More than anything, I'm grateful for Ilana Löwy's updating of the account of this history of yellow fever vaccination in Brazil, and of demonstrating its relevance for present-day North–South public health hubris, especially in the midst of the COVID-19 pandemic. As my colleagues and I wrote a year ago: "We would do well to retain the due humility and ongoing self-examination that the virus seems to have demanded in so many respects to this point."[4(p298)] This remains true a year later, whether examining yellow fever vaccines from eight decades ago or the COVID-19 virus and its impacts, with which we all continue to engage. AJPH

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Reaching Intermittent Tobacco Users With Technology: New Evidence

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See also Mays et al., p. 1686.

Waterpipe (hookah) smokers, unlike cigarette smokers, are typically intermittent users who are rarely motivated to quit, making them difficult to reach with interventions. Mays et al. (p. 1686) conducted a randomized controlled trial of a six-week tailored text message intervention to reduce waterpipe smoking in young adults. Intent-to-treat results revealed that 43% of participants in the tailored text condition self-reported waterpipe cessation at six months versus 35% in an untailored text condition and 28% in an assessment-only control condition. Such a simple, inexpensive intervention that can easily be disseminated has high potential for impact on this type of tobacco use. Although many existing evidenced-based tobacco-cessation services are delivered in the health care system, interventions that operate outside the health care system are needed, particularly for young adults who may not regularly interact with health care providers and who may not even consider themselves smokers.

One challenge for implementing this type of intervention in the real world will be in determining how to engage waterpipe smokers who are not usually actively seeking to quit. Participants in the study by Mays et al. responded to advertisements for a study about "waterpipe tobacco beliefs and behavior" and received $100 for completing assessments. In the absence of financial incentives, people who are not ready to change may be reached by engaging them on a topic that resonates with their interests and values. For example, we reached mothers of adolescent daughters to reduce their permissiveness to allow their daughters to use tanning beds by creating a Facebook group–delivered campaign on mother–daughter communication about adolescent health, a topic of high interest to mothers.[1] The campaign involved twice daily posts for a year but a fraction (15%) of those posts (approximately two per week) were on the topic of tanning beds. Findings revealed that the campaign was successful in reducing mothers' permissiveness in allowing their daughters to use tanning beds.[2] Text-based interventions could use this "embedded messaging" approach so that the text campaign could be on a highly engaging topic for young adults and include a small proportion of messaging on waterpipe smoking.

The bulk of text messages in both text conditions in Mays et al. provided education about the health harms and addictiveness of waterpipe tobacco use. Such education helps correct commonly held misconceptions about the risks of this type of tobacco use. However, future studies could incorporate other strategies known to affect long-term change in tobacco use, such as setting a quit day, refusal skills, coping strategies for cravings, and access to tobacco-cessation medication when appropriate. A recent clinical trial for e-cigarette cessation in young adults demonstrated that a text intervention including these strategies was effective at promoting vaping cessation.[3]

Even though much intervention content was educational, the tailored text messages of Mays et al. were based on baseline characteristics as well as brief answers to questions, primarily regarding the participant's knowledge of waterpipe health risks and addictiveness. Interestingly, the tailored text condition did not outperform a nontailored text condition, which is in line with the extant literature indicating that tailoring has not consistently increased effects of text-messaging interventions.[4] Recently, interest has grown in using just-in-time adaptive intervention approaches to improve the effects of tailored interventions by tailoring content to coincide with moments of opportunity, receptivity, or

vulnerability.[5,6] If momentary tailoring variables for waterpipe use could be identified and monitored with mobile technology (e.g., presence at a party, urges to use), messages could be timed to engage momentary targets (e.g., peer pressure, cravings) on a just-in-time basis. Building on the notion of context sensitivity, future research should explore whether a generic, one-size-fits-all decision rule is optimal for text-messaging interventions to reduce waterpipe tobacco use. Different people may benefit from different messages at different times; that is, the optimal dosing of messages may be person specific, and person-specific decision rules may be required to optimize intervention effects.[7]

Although the text intervention decreased waterpipe smoking, the majority of the sample in Mays et al. also used at least one other tobacco product at baseline in addition to waterpipe tobacco. Specifically, 29% were current cigarette smokers and 68% had used a tobacco product other than waterpipe or cigarettes in the past 30 days. This is a strength of the study, as it likely accurately reflects the frequency of other tobacco product use among waterpipe smokers in the United States.[8] However, cessation outcomes reflect only waterpipe smoking, and the use of other tobacco products is neither incorporated into the definition of cessation nor reported at follow-ups. The possibility exists that those who reduced waterpipe use concurrently increased use of other tobacco products, making the effect of the text interventions on overall tobacco risk profile unclear. The possibility of compensatory tobacco use may have been increased by the fact that the content of several of the intervention text messages sought to raise the perceived harm of waterpipes *relative to* other tobacco products (e.g., one text to participants read, "The large amount of smoke from hookah delivers more cancer-causing chemicals than cigarettes"). Future studies should examine how the interventions affected the perceived risk of waterpipe *versus* that of other tobacco products and if such changes in relative risk drive compensatory tobacco use.

Because of how waterpipe cessation was defined, caution is warranted when comparing the cessation rates and effect sizes reported by Mays et al. to other tobacco-cessation interventions. An intent-to-treat cessation rate of 43% is reported at six-month follow-up for the tailored text intervention, representing an odds ratio of 1.9 relative to assessment-only control. By itself, this seems remarkable for a low-cost tobacco-cessation intervention. However, the majority of other recent clinical trials targeting combustible tobacco define cessation as abstinence from the target combustible tobacco product, as well as other (i.e., not specifically targeted) combustible tobacco products.[9] Recent guidelines regarding clinical trials of combustible cigarette cessation from the Society for Research on Nicotine and Tobacco recommend (1) reporting the use of all tobacco products at outcome assessments, and (2) defining cessation of combustible cigarettes as abstinence from combustible cigarettes and all other combustible tobacco products.[9] Although these guidelines are about trials of combustible cigarettes, much of the rationale for these recommendations applies to waterpipe use as well. Defining cessation as abstinence from all combustible tobacco products would also allow biological verification of short-term abstinence, which is the current gold standard in tobacco cessation.[10]

Overall, we are cautiously enthusiastic about these new findings. This intervention addresses an important unmet need for waterpipe cessation and could be a valuable component of a multicomponent tobacco-cessation program. Given the proliferation of ways to smoke tobacco and consume nicotine, further work is needed to determine whether interventions targeting one form of tobacco use have a net harm reduction effect considering all other forms as well. AJPH

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Tobacco Control Leaders Call for a Balanced Assessment of the Risks and Benefits of Nicotine Vaping

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See also Balfour et al., p. 1661.

The role of e-cigarettes, or nicotine vaping products, in tobacco control has been controversial from the outset. Early divisions among public health experts led to polarized coverage in the media, confused messages to the public, and inconsistent policymaking between jurisdictions. For many authorities in the United States, the potential health harms of e-cigarettes and youth-vaping concerns were overriding considerations. For others (most notably in the United Kingdom), those risks have been balanced more explicitly against the potential benefits for smokers of easy access to nicotine vaping products. As more and better evidence becomes available and continues to accrue, some consensus should be possible on the individual elements of this complex policy question. It remains, however, a significant challenge to integrate that evidence into a holistic view of the major risks and benefits associated with nicotine vaping products.[1]

In this issue of *AJPH*, 15 past presidents of the Society for Research on Nicotine & Tobacco—the world's leading scientific society for the study of smoking—review the evidence underpinning US policy on nicotine products, mainly e-cigarettes. They briefly cover the health risks of vaping, the potential for e-cigarettes to increase smoking cessation, and concerns about youth nicotine vaping. The context is staggering success in reducing smoking rates to historic lows, especially among US youths, and the announcement of the aim to reduce tobacco use prevalence to less than 5% by 2030.[2]

These eminent authors conclude that the "singular focus of US policies on decreasing youth vaping" (Balfour et al. [p. 1661]) has been a distraction from the larger goal of tobacco control, namely reducing smoking and its harms. They point out that despite widespread experimentation, frequent use remains much more common among youths who smoke, and if vaping were to lead to more youth smoking then we would see some evidence of it by now. Population surveillance data show the reverse: youth smoking continues to fall and at a faster rate than before. It seems at least plausible that vaping has contributed to this decline, with vaping replacing smoking among US youths.

The authors also point out that the number of nonsmoking young people who might be at risk from the potential harms of nicotine addiction is far smaller than the number of smokers in the United States (1 in 7 of the population) at real and evident risk of serious harm from their smoking who could benefit from increased smoking cessation. To be clear, they are not arguing that vaping should be promoted as overall beneficial, just that a more appropriate balance should be struck between the likely potential harms and benefits.

The problem with the current focus in the United States on youth vaping is that many measures to discourage vaping, such as flavoring bans, taxes, and e-cigarette sales restrictions, may reduce smoking cessation and effectively protect smoking.[3,4]

There is another risk in antivaping policies intended to protect youths. In seeking to tell a strong story, we are in danger of misleading the public. The authors contrast public perception with the conclusions of the US National Academy of Sciences and the Royal College of Physicians. Nearly half of Americans incorrectly believe e-cigarettes to be at least as harmful as smoked tobacco. The effect has been worsened by the EVALI (e-cigarette or vaping use-associated lung injury) outbreak caused by adulterated marijuana products and wrongly ascribed to nicotine vaping devices. The harm to health from this misattribution has had effects far beyond the United States and continues to this day.[5,6] The price is a high one, as smokers, doctors, and governments are put off supporting an approach to quitting that can be twice as effective as licensed medicines.[7] Overemphasis of the risks of vaping leads to cognitive bias that means we are inclined to reject the benefits highlighted, for example, in

the recent Cochrane review.[8] Public health risks stealing the industry's clothes, becoming the new merchants of doubt.

Balfour et al. offer a refreshingly clear policy prescription for the United States: the US Food and Drug Administration should implement its plan to reduce the nicotine in cigarettes while ensuring the availability of reduced risk products and should permit advertising only if it encourages smokers to switch; smoked tobacco should be taxed heavily and e-cigarettes only modestly; rather than banning flavored e-cigarettes, their sale should be confined to age-restricted vendors; government Web sites should address the concerns about youth vaping realistically and the benefits of smokers switching separately. In search of a model for a government's realistic presentation of risks and benefits, we would do well to look to the example of New Zealand's Quit Strong campaign[9] and vaping facts Web site.[10]

Alas, one of the unintended consequences of highly successful tobacco policies in the United States, the United Kingdom, and elsewhere has been to increase inequalities. As Balfour et al. point out:

> African Americans suffer disproportionately from smoking-related deaths. . . . Today's smokers come disproportionately from lower education and income groups, the LGBTQ community, and populations suffering from mental health conditions. (p. 1667)

The authors suggest that to affluent Americans "today's smokers may be nearly invisible" (p. 1667). If doctors, academics, and policymakers have few smokers among their friends and families, the task of making smoking obsolete may look almost done. And when they find their adolescent sons and daughters—youths for whom smoking cigarettes had become all but unthinkable—using new nicotine products, it is no surprise that they are alarmed, even though the use may be only short lived or occasional.

Balfour et al. are to be commended for their efforts to bring more light and less heat to tobacco policy. The arguments are framed in the US context but have obvious international relevance. We can only hope that their contribution is received well by open minds. Antivaping policies are underpinned by a commendable passion to protect youth welfare and a fear that the hard-won reductions in youth smoking could be lost. These legitimate concerns about harm must be balanced by recognition of the potential benefits for the multitude of people who still take their nicotine the old way and who are often also experiencing multiple disadvantages. AJPH

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E-Cigarettes and Harm Reduction: An Artificial Controversy Instead of Evidence and a Well-Framed Decision Context

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See also Balfour et al., p. 1661.

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In this issue of *AJPH*, a distinguished group of tobacco control researchers and practitioners call for a more balanced look at e-cigarettes for reducing the enormous and persistent burden of smoking-caused morbidity and premature mortality—a worthy goal. The article is built around the artifice of a controversy between "fervent opponents" of harm reduction who emphasize risk to young people and "enthusiastic supporters" who want to facilitate smoking cessation and reduce harm with e-cigarettes. This "controversy" exists because we lack evidence on the long-term consequences of policies that promote the use of e-cigarettes for harm reduction, both for the smoking adults who switch to them and for the youths who start using them. Of course, we cannot see or model far enough into the future to have credible projections of the impact of regulatory decisions made now, decisions that will undoubtedly have long-term, generational repercussions.

In our comments, we redirect focus to an alternative framing that should underlie decision making on the place of e-cigarettes in the tobacco marketplace. The key principle is captured in the public health impact standard for modified risk products of the Family Smoking Prevention and Tobacco Control Act. Such products must:

> (1) significantly reduce harm and the risk of tobacco-related disease to individual tobacco users; and (2) benefit the health of the population as a whole taking into account both users of tobacco products and persons who do not currently use tobacco products.[1(p123)]

However, lacking from this principle of the act and from the commentary by Balfour et al. (p. 1661) and others is a sufficiently deep explication of the risk trade-offs inherent in advancing e-cigarettes as a harm-reduction strategy for smokers. If switching to e-cigarettes has benefits, they accrue to the smokers who may perhaps quit or reduce their use of cigarettes because of the switch, thus lowering their risk of tobacco-related morbidity and mortality while remaining nicotine addicted. If there are harms, they largely fall on youths and young adults, who are at risk for becoming addicted to nicotine across their lifetimes and sustaining the inevitable consequential adverse health effects. This is an intergenerational trade-off: possible immediate health benefits for older persons versus longer term and quite uncertain health risks for younger individuals.

The authors' review leads them to conclude that e-cigarettes' risk trade-off benefits population health overall. We do not agree that the evidence presented is sufficient to support their conclusion. Their evidence comes from a selective and opaque review process that does not meet standards for systematic review or for evidence integration, as in the US Surgeon General reports on smoking and health.[2] In particular, the risks of nicotine (and e-cigarettes specifically) for youths are minimized in the face of much (uncited) longitudinal evidence of its dangers (e.g., increase in the frequency and intensity of cigarette smoking, risk of nicotine dependence).[3] Nicotine is a known addictive chemical; disposable and pod-based products that administer nicotine in very high concentrations with little adverse sensory effect are addicting youths now. E-cigarettes do harm the adolescent's still-developing lungs, and e-cigarette– and vaping-associated lung injury outbreak points to the dangers of inhaling unregulated aerosols from carefully engineered devices intended to maximize the aerosol dose reaching the lungs.

Balfour et al. conclude that the potential for harm reduction for smokers should motivate action, given the

evidence they cite and their judgment on e-cigarettes' potential for risk reduction. Although the authors find the balancing of e-cigarettes' risks and benefits to be acceptable, doesn't that weighing depend on who you are? For those who benefit directly and perhaps their families, e-cigarettes would likely seem a preferable alternative to combustible cigarettes. Change the perspective to that of a parent whose underage child becomes nicotine addicted; for that perspective, we propose that the child's addiction is an unacceptable outcome of a harm-reduction strategy for adults. Remember that the nicotine-addicted smoker has alternatives—quitting "cold turkey" or turning to Food and Drug Administration (FDA)-approved agents and other interventions.[4] Moreover, if e-cigarettes can be an effective cessation aid, why have companies not sought their approval as a cessation aid through the FDA's Center for Drug Evaluation and Research?

The question to be answered for decisions on e-cigarettes—and the risk trade-offs—needs to be better specified; in the current marketplace for tobacco products (or in a better regulated future marketplace), does the availability of e-cigarettes in commercial outlets lower the prevalence of tobacco product use among adult cigarette smokers and reduce the frequency of tobacco-caused disease without increasing nicotine addiction among young people? This question is not addressed by the highly artificial randomized clinical trials on e-cigarettes and cigarette-smoking cessation, which focus only on the method of nicotine delivery (i.e., via e-cigarettes). There is some evidence that e-cigarettes may be associated with increases in smoking cessation among those who use e-cigarettes daily (compared with those who use alternative cessation methods).[4] The findings of trials that provide free e-cigarettes (vs conventional cessation therapy) also indicate increased cessation with the e-cigarette intervention.[5] However, we do not know whether the effectiveness and reach of e-cigarettes as a cessation aid depend on ready availability in retail locations (e.g., in vape shops, pharmacies, and convenience stores), which has the consequence of making them more accessible to youths.

How will the evidence be generated to better inform decisions on the least risky approach for youths that makes e-cigarettes available to smokers for harm reduction? Much research is in progress with support from the Tobacco Regulatory Science Program of the National Institutes of Health. That research is directed at many of the critical gaps for decisions on e-cigarettes, but only "real-world" experience will provide an answer to this question. Modeling is critical for bringing together the evidence and forecasting what might happen, but projections are inevitably subject to uncertainty, particularly as they are extended further and further into the future, into a marketplace with completely unknown features.

Notably, Balfour et al. do not discuss the tobacco industry in their article. The authors' silence on the industry is remarkable; we do not trust the tobacco industry, despite Philip Morris International's protestation of a new direction, which is an echo of past false promises. The media are currently carrying a pronouncement from the chief executive officer—"A Letter to All Who Aspire to a Better Future"—with the tagline "Unsmoke the Future."[6] The verbiage does not say "Unnicotine the future." Many of the editorial's authors have been through the "tobacco wars." Are they willing to trust the industry not to sacrifice public health for profit? The authors conclude this article with a discussion of the social justice issues related to cigarette smoking and the disproportionately high burden of tobacco-related disease morbidity and mortality in certain populations, including those of low socioeconomic status, racial and ethnic minorities, sexual and gender minorities, and those with comorbid conditions. We point out that the tobacco industry generated many of these disparities using egregious marketing tactics to target the most vulnerable of individuals.

We agree that the FDA is at a critical decision-making juncture on e-cigarettes and public health, as the marketplace continues to diversify with noncombustible tobacco products, including not only e-cigarettes but other heated tobacco products. Since the FDA took jurisdiction over e-cigarettes with the Deeming Rule in 2016, its approach to e-cigarettes has not been aggressive, coherent, or consistent.[7] Action was finally proposed in 2020 to counter the surge in youths' e-cigarette use driven by flavored products, particularly those of JUUL.[8] The national strategy of reducing nicotine delivery by combustible cigarettes has been set aside, and the FDA's overall course in the Biden administration is undeclared.[9] The public health research and practice communities can be most helpful to setting this course by providing the needed evidence and facilitating its interpretation in a well-framed decision context. An unneeded schism and polarization are antithetical to what should be happening now. AJPH

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Changing the Narrative and Accelerating Action to Reduce Racial Inequities in Maternal Mortality

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See also MacDorman et al., p. 1673.

In this issue of *AJPH*, MacDorman et al. (p. 1673) add a new analysis of cause of death data, underscoring that inequities in maternal mortality persist. Findings highlight the importance of identifying causes and accelerating actions to address racial inequities in maternal mortality. This is essential for changing the narrative about why Black people are more likely to experience pregnancy-related deaths than are non-Hispanic White, Hispanic, and others. We must use methods of inquiry that continue to ask why at each level (https://bit.ly/2TwnO4l; Figure 1). Asking why leads us away from "mother blame" narratives or a singular focus on health behaviors of birthing people and toward naming structural racism as a root cause and assessing unequal treatment in the health care system.[1]

The authors report that the maternal mortality rate for Black people is 3.5 times that of White people. Their analysis on cause of death addresses why we see these unacceptable inequities. Their findings suggest that the excess maternal deaths are attributable to higher rates of eclampsia and preeclampsia, postpartum cardiomyopathy, and obstetric embolism. Thus, increased vigilance for cardiovascular problems during and after pregnancy may reduce disparities in maternal mortality.

To understand why Black people have higher death rates from eclampsia and preeclampsia, postpartum cardiomyopathy, and obstetric embolism—despite mortality from these conditions being 60% to 70% preventable—we must go beyond addressing individual risk factors. Numerous scholars have described the unique stress and discrimination Black women face across their lifetimes and the toll this takes on health (https://bit.ly/3iKonjy). Additionally, people of color are less likely to receive preventive health services irrespective of income, neighborhood, comorbid illness, or insurance type, and they often receive lower quality care. Therefore, Black and Indigenous people[2] frequently contend with delays in care or diagnosis for cardiovascular and other diseases that increase the risk of maternal mortality.

But why are Black people so much less likely than their White peers to receive risk appropriate care based on standards? Evidence indicates the need for access to care before, during, and after pregnancy. Access to care is necessary but insufficient to achieving equitable outcomes, and Black pregnant and birthing people are disproportionately served by poorer quality institutions. One study found that predominantly Black-serving hospitals were more likely than predominantly White-serving hospitals to perform worse on 12 of 15 quality indicators for labor and delivery.[3] Additionally, Black birthing people are far more likely than their White peers to report being treated unfairly or unjustly by providers.[4–6] Finally, even the best quality preventive care cannot eliminate disparities in maternal mortality if Black people do not have equitable access to key social determinants of health. Study after study finds that people of color in the United States are disproportionately unable to access resources critical to health and well-being.

The disparities in Black maternal mortality and severe maternal morbidity are rooted in structural racism and slavery's legacies.[7] These legacies and resulting policies and practices shape access to social determinants of health, access to high-quality health care, and the implicit and explicit biases that affect how Black people are treated in health care settings. Racism is expressed through bias and unequal treatment in health care, lack of access to high-quality and equitable care, and lack of continuous health coverage or access.[8]

How do we begin to address these problems? A focus on systems instead of individuals is key. And policy action must focus on drivers that have an outsize impact on health and well-being, including economic stability, neighborhood

FIGURE 1— **The 5 Whys: Understanding Root Causes of Maternal Mortality**

and physical environment, food security, and community safety. Health care coverage and access to systems of high-quality prenatal care are critical; however, we cannot expect health care to "fix" or make up for nonmedical contributors during nine months of prenatal care. Policies must be informed by a deep understanding of historical structural inequities and incorporate the perspectives and solutions of Black pregnant and birthing people and their communities.

We need policies that advance health coverage beyond pregnancy and make investments in equity-oriented primary health care.[9] Because more than half of pregnancy-related mortality is preventable, targeted improvements to health coverage and care—including services that address physical, reproductive, and behavioral health needs—can help reduce mortality disparities.

Across the life course, greater attention to preventive and primary health care

and health coverage is necessary. Medicaid expansion provides coverage for people who lack the resources to pay for health care out of pocket. Extending Medicaid postpartum coverage one full year is urgent. Under the American Rescue Plan Act, all states can extend Medicaid postpartum coverage for one year. Medicaid pays for nearly half of US births, and in some states upward of two thirds. Yet for many, pregnancy-related Medicaid coverage currently extends only to 60 days postpartum. Too many people who lose their Medicaid coverage shortly after a birth simply fall through the cracks.

Improving quality, safety, and equity of care must be a priority. Delays in recognition, diagnosis, or treatment are key aspects of these inequities. Multiple studies have pointed to the rates of "failure to rescue" (death in the setting of severe morbidity), which disproportionately affect people of color.[10] Other studies find differences in access to critical care interventions[11] and unmanaged underlying health conditions, including cardiovascular disease, infections, and metabolic disorders.[12] Addressing these delays requires understanding why systems allow Black people to experience these delays disproportionately. Better recognition of and accountability for inequities in these delays and missed diagnoses are essential. As the authors note, implementing safety bundles to standardize care and increasing awareness may help address this issue. Additionally, a closer examination is required of how medicine and nursing are taught, and of the guidelines and tools employed in clinical decision-making. Moreover, it also involves implementation of routine patient experience measures that can quantify experiences of racism and discrimination in obstetric settings to build accountability and support quality improvement through an equity lens.[13]

We know there are real, concrete steps we can take to put the United States on the path to an antiracist, equitable health care system where people of color have the necessary ingredients for a thriving existence that results in healthy pregnancies and births. Let's change the narrative, tackle the root causes head on, and accelerate the pace of change. AJPH

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From Restrictions to Outright Challenges: Abortion Laws and Population Health

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See also Vilde et al., p. 1696.

The landmark 1973 *Roe v. Wade* decision in the United States established a woman's legal right to abortion before fetal viability. Despite this constitutional right, abortion access has become increasingly difficult, as state legislatures have since enacted more than 1000 restrictive laws and regulations. The recent tilt of the US Supreme Court to a more hostile position on the right to choose has emboldened some states to propose legislation not only restricting access to abortion services but also prohibiting abortion outright. The Supreme Court later this year will hear a case concerning a Mississippi law that would ban most abortions after 15 weeks, a direct challenge to the 1973 *Roe* decision. The court's ruling on the Mississippi case could alter or even overturn the constitutional right established by *Roe v. Wade*.

A reversal of this right would have public health consequences and would widen existing social and health inequities. Stripped of the right to choose termination of pregnancy, individuals face difficult options and negative consequences. For example, they might resort to illegal and dangerous abortions, or stay in unhealthy relationships, sometimes sustaining long-lasting psychological and physical harm. Findings from the study by Vilda et al. (p. 1696), included in this issue, underscore the importance of a woman's right to make sexual and reproductive health decisions and the potentially lethal impact the removal of that right could have.

Emerging evidence reveals that abortion restrictions may have unintended public health consequences. As Vilda et al. observe, state-level abortion restrictions are associated with a higher state-level maternal mortality rate. In addition, in a recent study we conducted using data from the US Cohort Linked Birth/Infant Death Files,[1] we observed a significant relationship between the number of restrictive abortion laws and the odds for infant mortality (Figure 1). These results suggest that such restrictions have detrimental effects on women's and infants' health.

Abortion-restricting laws may have multiple direct and indirect causal pathways leading to poor maternal and infant health. If a woman is compelled to give birth when a pregnancy is not wanted, her mental and physical well-being can be compromised. Furthermore, when safe abortion services are not legally available and easily accessible, some women with unwanted pregnancies turn to risky alternatives to end their pregnancies. At the same time, restrictive laws may serve as indicators of other social and political dynamics at play in certain states, reflecting a climate that might further disadvantage the health and agency of women.

WIDENING SOCIAL AND HEALTH INEQUITIES

In the United States, access to abortion and family planning services varies significantly across states. Geographical variability in access will continue to grow, as several states have recently approved laws to protect abortion rights. State differences will exacerbate current social and health inequities. When abortion services are not widely and universally available, women from disadvantaged backgrounds are disproportionately affected. Those with financial means can travel out of state and pay for legal services, whereas their poorer counterparts cannot.

Infant and maternal mortality rates are highest among the non-Hispanic Black population.[2,3] In our study, non-Hispanic Black infants born in states with Medicaid restrictions experienced a greater odds of mortality compared with those born in states with no such restrictions.[1] These restrictions may limit options for non-Hispanic Black mothers if they cannot afford to pay for abortion services.

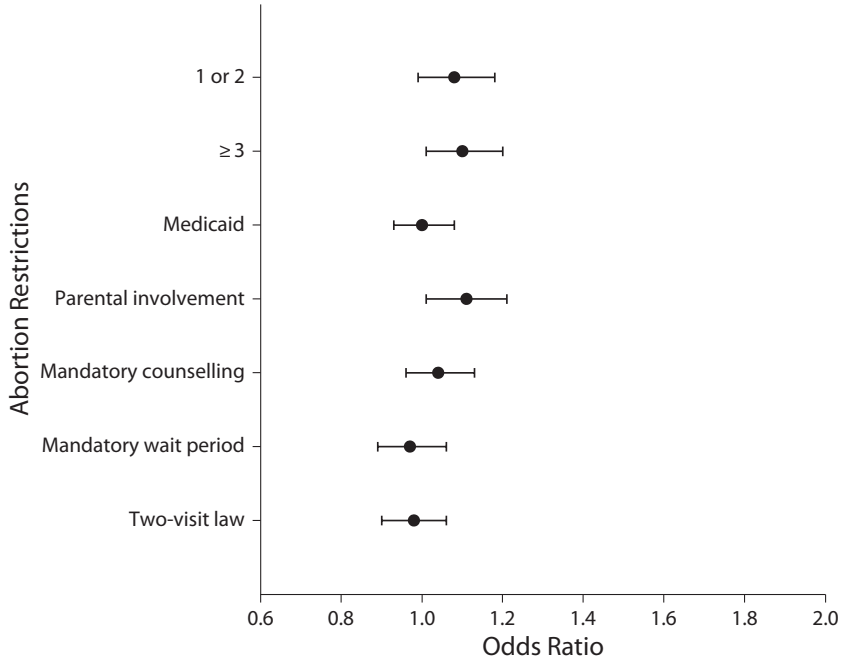

FIGURE 1— Relationship Between the Number of Abortion Restrictions and the Odds for Infant Mortality

Note. Whiskers indicate 95% confidence intervals.
Source. Pabayo et al.[1]

Although Vilda et al. did not observe a relationship between restrictions and maternal mortality rates among non-Hispanic Black mothers, as the authors note, it may be the result of limited statistical power. Nonetheless, further restrictions may increase existing health inequities between non-Hispanic White mothers and those who are more likely to experience structural barriers (e.g., non-Hispanic Blacks, adolescents, and women from rural settings).

FUTURE RESEARCH AGENDA

Although a significant relationship between abortion restrictions and maternal and infant mortality has been identified, causality cannot be inferred. Previous research has shown an association between legalized abortion and lower infant mortality rates and a link between funding for family planning and abortion services and lower infant mortality rates,[2] but causal methods were not used.[3] Future work must incorporate causal inference methods such as difference-in-differences and interrupted time series using observational data to determine whether the enactment of laws is causally associated with the timing of past and upcoming restrictions (all necessary methodological assumptions having been met).

To investigate a causal relationship between state-level sexual and reproductive health indicators and maternal mortality rates, researchers conducted a quasiexperimental, population-based difference-in-differences study.[4] Interestingly, to our knowledge, causal methods have not been used to study the possible effect of the *Roe v. Wade* decision on health outcomes such as infant and maternal mortality rates, although researchers have employed interrupted time series to assess the impact of the decision on the rates of homicide of young children.[5] Going forward, studies should include individual-level data to inform our understanding of the impact of abortion restrictions, an understanding that currently relies primarily on evidence gleaned from ecological studies using aggregated data.

REPRODUCTIVE RIGHTS ARE HUMAN RIGHTS

According to the sexual and reproductive health framework, reproductive rights are human rights.[6,7] Oppression occurs when structures prevent individuals from deciding for themselves the optimal timing and conditions for childbearing. Beyond examining abortion laws themselves, policymakers may need to apply the reproductive justice framework to achieve equity in reproductive issues in the United States. The justice framework acknowledges how our reproductive lives reflect our complex social context. Achieving optimal maternal, infant, and sexual and reproductive health will require addressing multiple structural and systemic issues. Beyond access to safe and legal abortion, additional upstream factors to target include more comprehensive sexual health education, greater access to contraception, and gender equity in pay.

More than 72 million women in the United States are of reproductive age (15–49 years). Laws that weaken legal and regulatory frameworks that support sexual and reproductive rights may be contributing to rising maternal mortality rates in the United States. Although restrictive, the policies examined in the study by Vilda et al. and in our study are still in the constitutionality established

by *Roe v. Wade*. Recent legislation directly challenging *Roe v. Wade* may have a far more harmful public health impact and may increase social and racial inequities.

The US public needs to take an active stance to protect sexual and reproductive rights. States such as California and New York have recently passed laws to protect the right to have an abortion. However, federal legislation, such as the Women's Health Protection Act—reintroduced by Congress in June—is needed to achieve full and effective reproductive health care for the entire nation. Ensuring dignity, autonomy, and the right to choose is a necessary part of any comprehensive strategy to promote maternal and infant health and to address persistent health inequities. AJPH

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Structural Racism, Poverty, and Sexism Shape the History of and Response to Childhood Maltreatment Among Incarcerated Individuals

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In their impressive analysis, Bodkin et al.[1] show how high rates of childhood maltreatment are among incarcerated individuals in Canada and how these rates compare with those in the general population. Their work thus highlights two facts we build on. First, that prisons and jails are filled with people who are simultaneously the perpetrators, victims, and witnesses to maltreatment. Yet the violence inflicted on them as children usually receives attention only when they commit truly gruesome acts; the traumas of someone convicted of dealing drugs, committing robbery, or even engaging in domestic violence simply do not register much—dare we say, most—of the time. Second, structural racism, poverty, and sexism shape both (1) inequities in incarceration and maltreatment, and (2) responses to them.

The execution of Lisa Montgomery on January 13, 2021, and the media coverage of her life and crimes provide a poignant example of our core arguments. Montgomery was the first woman to be executed by the federal government in more than 70 years and was executed for a truly horrific crime. She befriended and then ultimately murdered a pregnant woman, abducting the unborn child (who, fortunately, ultimately survived) and passing the child off as her own before her eventual arrest. Montgomery's crime was far from her first experience with violence though. She endured years of physical and sexual abuse as a child, often perpetrated by her caregivers, and entered adulthood with severe mental health and substance abuse problems.

The violence Montgomery endured at the hands of adults for virtually her entire childhood drew international attention but, importantly, did not save her from execution. The sad reality is that when we think about violence in the context of incarcerated individuals, we tend to focus—both as a society and as a legal system—on the violence that incarcerated individuals inflict on others and never, or at least rarely, on the violence that incarcerated individuals have been exposed to. As a result, we are rarely forced to reckon with the core contradictions of incarceration: contemporary prisons represent, at best, an ineffective site of intervention for traumatized people; tend to create more opportunities for experiencing violence; and, as with the child welfare system, reflect historical legacies of marginalization and neglect.

PREVALENCE OF CHILDHOOD MALTREATMENT

Although Montgomery's response to the abuse and neglect she experienced was unique—almost no incarcerated individuals have committed such heinous crimes, and many individuals who experience abuse and neglect never go on to engage in crime at all—the fact that she experienced abuse and neglect as a child was hardly unique among incarcerated individuals, as Bodkin et al. demonstrate in their meta-analysis. Some specifics on the study itself may be helpful at this point, as many of us know a bit about childhood maltreatment or a bit about the incarcerated population but little about both.

Maltreatment broadly refers to physical, sexual, or emotional abuse as well as neglect. In Canada, as elsewhere, witnessing or being victimized by violence is a salient predictor of later incarceration. Estimates of maltreatment experiences in the general population vary greatly across studies and definitions, but, as a rough frame of reference, 12% of children in the United States have experienced maltreatment that was substantiated by child protective services agencies at some point.[2] In studies

using caregiver reports, 38% of children have experienced maltreatment at some point.[3] By contrast, the average incarcerated person in Canada experienced some form of maltreatment (66%), with very high rates of physical abuse (48%), emotional abuse (52%), and neglect (52%) experiences during childhood. Among women, sexual abuse was especially common; half of all incarcerated women reported an instance of sexual abuse. Such findings conform well to those in the United States.[4] Moreover, the racial disparities in incarceration experiences in the United States largely mirror racial disparities in child welfare involvement that occurs much earlier; institutional engagement with child welfare systems in early life and prison systems in adulthood are thus common for marginalized populations.

DURATION AND SEVERITY OF MALTREATMENT

Prevalence rates of any form of maltreatment among incarcerated people are thus astonishingly high. Prevalence rates—for both the incarcerated population and the general population—capture the difference between any maltreatment and no maltreatment, however, and thus provide no information about the duration and severity of maltreatment—what we can think of as the "texture" of maltreatment. As scholars doing qualitative research on incarcerated individuals have long noted, incarcerated people can be thought of as living what sociologist Bruce Western has called "lifetimes of violence."[5] This means, simply put, that incarcerated people have experienced overlapping, sustained, severe episodes of maltreatment beginning as children and extending well into adulthood at rates that are almost certain to be higher, on average, than those of individuals who have experienced maltreatment in the general population.

Consequently, the incarcerated population has experienced both any maltreatment at a higher rate than the general population and serious, sustained childhood maltreatment at a higher rate than others who have experienced childhood maltreatment. They are doubly disadvantaged when it comes to childhood maltreatment, which is virtually certain, whether through the maltreatment itself or through child protective services contact, to do them grave harm.[6] To return to the example we opened with in the introduction, saying that incarcerated people have experienced maltreatment at higher rates than the general population is similar to saying that Montgomery committed homicide; it is factually true but likely misses so much of the texture that it is not the full story.

Tackling the overlap between maltreatment and incarceration experiences is further complicated by the fact that maltreated individuals later convicted of crimes often trigger risky victim stereotypes, activating disgust rather than sympathy responses and creating opportunities for further victimization while incarcerated. Correctional facilities tend to have high rates of physical and sexual victimization—and this is especially the case for women when it comes to sexual victimization, some of which may come at the hands of staff.[7] Making a precise estimate of how often this sort of victimization happens is exceedingly difficult, leading to highly divergent estimates of the prevalence of victimization. Nonetheless, it is important to remember that incarceration likely adds yet another layer to the victimization individuals have faced.

CRIMINAL LEGAL SYSTEM INCORPORATION

Although there are many policies that could stem from recognizing both the fact and the texture of maltreatment incarcerated individuals have been subjected to, we focus on just two. First, we strongly agree with Bodkin et al.,[1] who argue for trauma-informed care for incarcerated individuals to address their experiences both inside and outside correctional settings. Second, and more controversially, we suggest a need to rethink sentencing on the basis of childhood trauma and system failures, which may well not be limited to maltreatment. At the sentencing phase, crimes committed are displayed for all to see so they can be scrutinized. Yet crimes endured by the person being sentenced that may have shaped their actions are hidden completely or sanitized by legal and institutional language. A more just system might consider the harms inflicted on people as children as seriously as the harms they inflicted on others. AJPH

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Taking an Anti–Health Inequity Approach to Counter the Unfair Burden of Poor Health

Sandro Galea, MD, DrPH, and Roger Vaughan, DrPH, MS

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See also Akré et al., p. 1610, MacDorman et al., p. 1673, and Vilda et al., p. 1696.

In the 1990s Margaret Whitehead defined health inequities—often referred to in the United States as "health disparities"—as health differences that are avoidable, unnecessary, and unjust.[1] More recent work (e.g., by Braveman[2]) has done much to sharpen our understanding of why we need specific efforts to counter fundamental inequities if we are to achieve health equality. After the George Floyd national reckoning with racial inequities, the concept of antiracism—deliberate efforts to counter systemic and historical forces that discriminate against particular racial groups—has entered the public conversation, elevating the visibility of one particular dimension of efforts that can help push us toward equity.[3] This evolving thinking has made it ever more clear that addressing long-standing inequalities that stem from unjust conditions requires deliberate action to counter that injustice. This perspective, which we should perhaps call an "anti–health inequity" approach, makes clear that the work of public health is inextricable from the work of social justice, simply because equality of health outcomes is unachievable without deliberate action to tackle the forces that create the inequity in the first place. Informed by this thinking, recent work has suggested, for example, that Black–White health disparities, resting as they often do on long-standing wealth disparities, may be unattainable without reparations for the Black population to contribute to narrowing Black–White wealth gaps.[4]

These concepts are, at this point, becoming embedded in the mainstream of public health thinking[5,6] and are likely not particularly new to readers of this journal. They do remain, however, far from the broader cultural mainstream. Three articles in this issue of *AJPH* illustrate well the persistence of health inequities and point to the need for specific efforts that are anti-inequity to mitigate the unjust burden of poor health.

THE UNJUST GAPS

The first illustration of this point concerns the COVID-19 moment. Recent work has shown well that one of the consequences of the COVID-19 pandemic has been an increase in the burden of poor mental health nationwide. This work has also shown how this is unevenly borne, as groups with fewer assets shoulder much of the burden of depression and anxiety nationally.[7] Akré et al. (p. 1610) in this issue of *AJPH* add to this literature by showing that the rates of depression, anxiety, and alcohol use were higher among LGBTQ+ (lesbian, gay, bisexual, transgender, queer and other spectrums of sexuality and gender) people than among cisgender straight/heterosexual populations. This article documents an important health inequality, but it builds on a large body of work that has shown that this inequality stems from fundamental unnecessary and unjust marginalization of sexual minority groups.[8] An awareness of this work suggested long before COVID-19 swept the country that the burden of poor mental health would be borne disproportionately by marginalized groups.[9] An anti–health inequity approach would have called for us, nationally, to invest resources to mitigate this unjust burden of poor health in this population, and it certainly suggests that we do so after such events in the future.

The second illustration concerns the long-standing problem of racial inequities in maternal mortality. The work by MacDorman et al. (p. 1673) confirms the extraordinarily greater risk—more than threefold—of maternal mortality among Black compared with White women and notes the prominence of four causes—eclampsia and preeclampsia, postpartum cardiomyopathy, obstetric embolism, and obstetric hemorrhage—that together account for 59% of the documented Black–White inequities. The importance of this work

centers on its documenting the core causes of these persistent racial inequities, paving a pathway of opportunity toward narrowing them. Although the science is imperfect, these conditions are reasonably well understood, and careful monitoring during pregnancy can result in substantially reduced morbidity and mortality rates. An anti–health inequity approach would call for a doubling down on efforts to monitor these conditions among Black women specifically, aiming to reduce maternal mortality in this group, and thus narrowing health gaps.

In the third article, Vilda et al. (p. 1696) document the relationship between state-level policies that restrict abortion access and maternal mortality. They show that states with more restrictive abortion policies had a 7% increase in total maternal mortality. Although this analysis does not document the relation between these policies and racial differences in maternal mortality, the evidence on racial gaps in maternal mortality strongly suggests that these restrictive abortion policies are contributing to greater inequities. This, therefore, points to policy action as being critical to anti–health inequity work and clearly calls out the more than 1000 policies and regulations that have been put in place aiming to reduce access to abortion care since *Roe v Wade*.

AN ANTI–HEALTH INEQUITY APPROACH

Health inequities do not arise passively. They are a fundamental feature of unjust distribution of the conditions that create health. Much as countering the effects of racism requires an antiracist approach, countering the unjust conditions that give rise to health inequities requires an explicit anti–health inequity approach. That would be consonant with a public health agenda that sees its role as generating the conditions that create health, equitably, for all. AJPH

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Are We There Yet? The American Journey to Safer City Streets

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Last year, Helsinki, Finland, and Oslo, Norway, announced a stunning accomplishment: after decades of sustained effort, both densely populated capital cities recorded zero deaths among cyclists and pedestrians in 2019.[1] Their achievement is remarkable proof that efficient urban mobility need not come at the cost of human lives. It also stands in stark contrast to the lackluster traffic safety record of similarly sized municipalities in the United States. How can American cities close the gap to their European counterparts? The Vision Zero framework provides one roadmap by which urban America might navigate toward safer streets.

Originating in Sweden in 1995, Vision Zero rejects the conventional transportation planning paradigm that makes trade-offs between road user safety and considerations such as traffic flow, driver expectations, and cost. Instead, Vision Zero embraces a simple premise: the only acceptable number of serious traffic injuries is zero.[2] Under this framework, policymakers, road users, city traffic engineers, urban planners, law enforcement, and vehicle manufacturers work together to design a transportation system that tolerates human error, minimizes crash risk, and mitigates the risk of injury even if a crash occurs.[2] As demonstrated in Oslo and Helsinki, this often means using protected bicycle lanes and pedestrian bridges to separate vulnerable road users from vehicles, controlling vehicle speed with chicanes and speed humps, preventing head-on collisions with median barriers, and decreasing kinetic energy transfer at potential collision sites using modern roundabouts.[2] Between 2010 and 2017, these and other interventions reduced pedestrian fatalities by 23% in Finland and by 54% in Norway, yet pedestrian deaths increased by 38% in the United States over the same period.[3]

While American cities might have something to learn from their Scandinavian counterparts, the striking variability in vulnerable road user fatality rates across urban America suggests that many US cities can also learn from successes closer to home (Figure 1). Boston, Massachusetts, and Seattle, Washington, for example, have publicly committed to Vision Zero. To make progress toward a goal of zero traffic deaths and serious injuries by 2030, the City of Seattle performed a data-driven bicycle and pedestrian safety analysis to help prioritize intersection safety improvements, developed a safety-focused transportation master plan, standardized speed limits on most residential streets (nonarterial, 20 miles per hour [mph]; arterial, 25 mph), expanded the use of red-light cameras and other forms of traffic safety enforcement, accelerated the installation of leading pedestrian intervals (in which the "walk" signal is illuminated three to seven seconds before the vehicle green light, enhancing pedestrian visibility), created a crash review task force, and committed millions of dollars to enhance a cycling network that will include almost 200 miles of protected bike lanes and greenways.[7] The City of Boston struck an interdisciplinary Vision Zero Task Force, created a Vision Zero Action Plan, lowered the default speed limit on city streets from 30 mph to 25 mph, curtailed vehicle speeds in some residential neighborhoods using speed humps and curb extensions, opened sight lines and installed leading pedestrian intervals to improve pedestrian visibility at select intersections, made capital investments in bicycle lane safety, and committed to periodically publishing crash data that allow citizens to hold city decision-makers accountable.[8] It would be naïve to suggest simple causality, but these two cities have 65% fewer vulnerable road user fatalities per capita than Detroit, Michigan; Memphis, Tennessee; or El Paso, Texas—similarly sized US cities that have yet to commit to Vision Zero.

New York City's experience since adopting the Vision Zero framework in 2014 refutes the common misconception that traffic safety interventions are unacceptably costly. Vision Zero principles motivated ambitious and wide-ranging changes to traffic safety

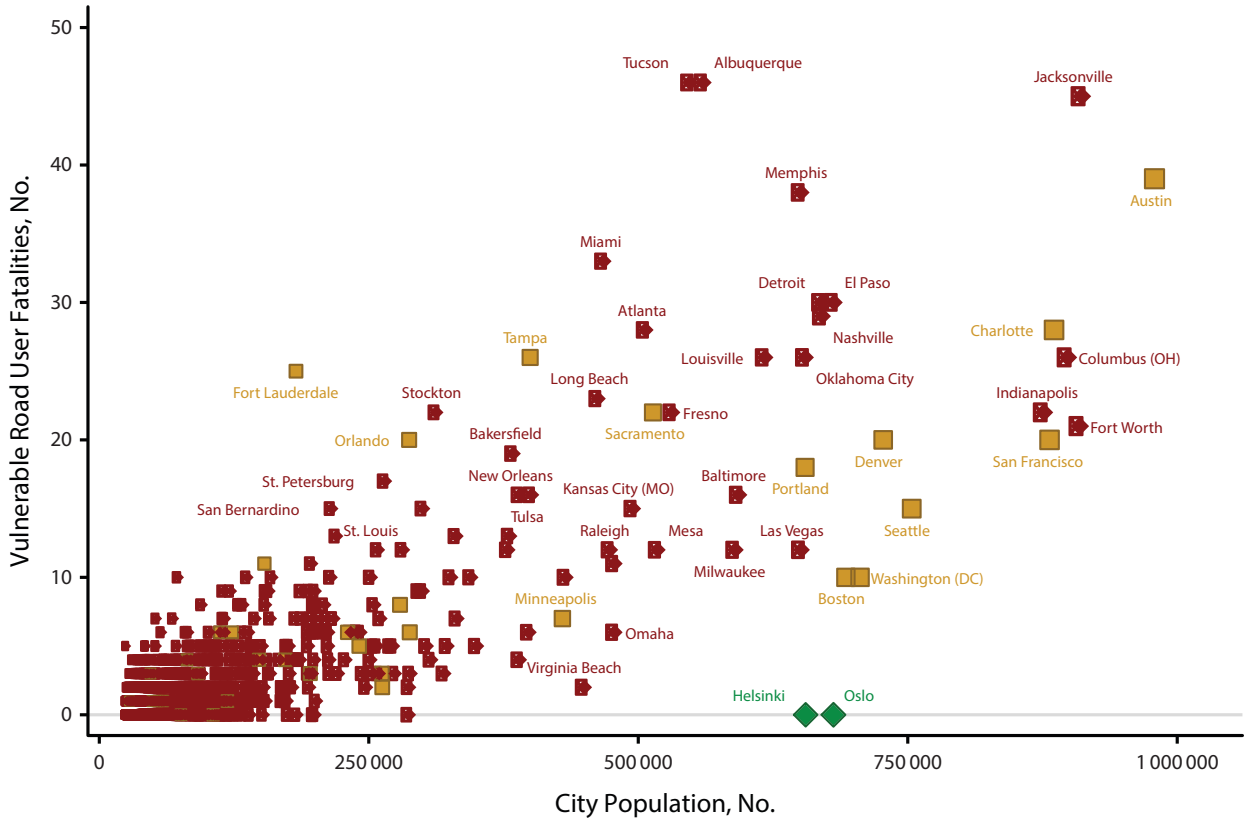

FIGURE 1— Vulnerable Road User Fatalities in US Cities in 2019

Note. Scatterplot depicting the number of pedestrian and cyclist fatalities for 1513 US cities with a population between 25 000 and 1 million residents. X-axis indicates the city population; y-axis indicates the number of traffic fatalities in 2019; dot size indicates the city population; circles indicate US cities outside of the Vision Zero Network; squares indicate US cities within the Vision Zero Network; diamonds indicate Nordic cities.[4–6] American cities with fewer than 1 million residents account for 82% of all US urban vulnerable road user fatalities. An analogous figure including all cities with more than 25 000 residents can be found in the Appendix (available as a supplement to the online version of this article at http://www.ajph.org).

legislation, education, engineering, and enforcement, culminating in an impressive 33% reduction in pedestrian fatalities over the first six years of the initiative.[9] One inexpensive and highly effective legislative intervention reduced the default speed limit from 30 to 25 mph for the vast majority of city streets, producing a 39% reduction in injuries and fatalities on affected roadways.[10] An analysis using data from the New York City Department of Transportation concluded that protected bike lanes are highly cost effective (incremental cost-effectiveness ratio of $1297 per quality-adjusted life year gained, far below the conventional $50 000 per quality-adjusted life year willingness-to-pay threshold for medical interventions).[11] Similar analyses using empirical data found that Neighborhood Slow Zones and speed limit enforcement cameras save money and save lives.[12,13] Instead of portraying traffic safety interventions as an onerous expense, US cities might find Vision Zero initiatives are more politically palatable when framed as both an ambitious American "moon shot" and a financially prudent investment.

While larger, densely populated American cities individually report the highest absolute number of traffic deaths, efforts to reduce urban road risks should also focus on less populous urban areas. Though this strategy seems counterintuitive, it illustrates a form of the prevention paradox: half of America's urban vulnerable road user fatalities occur in cities smaller than Mobile, Alabama (population 189 809).[14] Smaller cities and towns often lack the resources and experience to make progress against Vision Zero targets, suggesting that state governments may need to supply capital and expertise to enable rapid reductions in road morbidity and mortality. Progress in smaller cities could be accelerated by evidence-informed safety-focused changes to state speed, seatbelt, and impaired driving laws, and by removal of state-

level restrictions on photo-radar speed enforcement, automated red-light cameras, and random sobriety checkpoints.[15]

The elimination of pedestrian and cyclist fatalities in two European capitals is a giant leap toward the ambitious eradication of all types of serious traffic injury. Relentless application of Vision Zero principles has allowed Helsinki and Oslo to lead the way. Now it is time for American cities to catch up. AJPH

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Direct and Indirect Mental Health Consequences of the COVID-19 Pandemic Parallel Prior Pandemics

Mark É. Czeisler, AB, Mark E. Howard, PhD, MBBS, and Shantha M. W. Rajaratnam, PhD

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A century ago, Karl Menninger, MD, documented adverse mental health consequences of the 1918 influenza pandemic,[1–3] publishing a case series of patients with postinfluenza mental illness. He concluded, "There is also no doubt but that influenza was the direct cause of thousands and thousands of [psychiatric] cases"[3(p244)] and cited evidence of mental illness during pandemics as early as 1385.[3] In his classic textbook, William Osler, MD, wrote in 1899, "Among the most important of the nervous sequelae [of influenza] are depression of spirits, melancholia and . . . dementia."[4(p97)] As Julius Althaus, MD, wrote in 1892, "[there were] A good many people who, without being actually laid up with definite symptoms of grip [influenza], yet seemed to some extent to be under the influence of the poison, as shown by such symptoms as general languor and depression"; sometimes "such endurable despondency as to make the patient feel that death was preferable to the state in which he found himself, and suicide the only means of relief," and other times "other symptoms . . . causing the patients to make themselves drunk with alcohol or morphine, in order to find relief."[5(p24,25)]

Advances in psychiatry and data collection methodologies limit comparisons of mental health consequences of earlier pandemics and those observed during the COVID-19 pandemic, and pathogenic mechanisms of mental health conditions may vary. Nevertheless, these earlier descriptions have striking parallels with adverse mental health documented during recent epidemics.[6,7] For example, patients hospitalized for SARS (severe acute respiratory syndrome) or MERS (Middle East respiratory syndrome) commonly experienced acute confusion, depressed mood, anxiety, impaired memory, and insomnia.[6]

DIRECT MENTAL HEALTH EFFECTS

Emerging evidence highlights the importance of monitoring and addressing potential postacute neuropsychiatric sequelae of COVID-19. Analysis of 81 million electronic health records revealed that one third of COVID-19 survivors were diagnosed with neurologic or psychiatric conditions within six months.[7] Patients with COVID-19 had an increased risk of such diagnoses compared with patients with other conditions (e.g., vs influenza, a 78% and 44% increased risk of first-time and any such diagnoses, respectively). Among patients with COVID-19, those admitted to intensive care had a 187% and 58% increased risk of first-time and any incident neurologic or psychiatric diagnosis. Heterogenous conditions observed (e.g., anxiety, ischemic stroke, intracranial hemorrhages, dementia, parkinsonism)[7] may result from direct brain injury following viral infection, particularly given evidence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) invasion of the central nervous system[8] or from systemic factors, including inflammation, immune dysregulation, and adverse medical treatment responses.[8] Even persons with mild COVID-19 and otherwise asymptomatic SARS-CoV-2 infection may experience psychiatric symptoms.[7]

INDIRECT MENTAL HEALTH EFFECTS

In addition to potential direct neuropsychiatric impacts of these viral infections, socioeconomic disruptions caused by pandemics and their mitigation can have indirect mental health consequences. Menninger asserted that the 1893 European financial panic was "*indirectly* [emphasis added] due to the depressing effect of . . . influenza, and the mutual loss of confidence and enthusiasm which it is well known to produce."[3(p243,244)] Measuring indirect

mental health effects of infectious disease outbreaks is particularly difficult, especially given differing sociopolitical contexts (e.g., World War I during the 1918 pandemic). However, evidence from the COVID-19 pandemic reveals considerably elevated levels of adverse mental health symptoms compared with prepandemic years, even in the absence of widespread SARS-CoV-2 transmission. As early as April 2020, anxiety and depression symptoms in the United States were two to four times as prevalent as in 2019—and similarly high in Australia despite exceptionally low COVID-19 prevalence.[9]

During the COVID-19 pandemic, governments have implemented stringent mitigation policies, including stay-at-home orders, gathering bans, economic shutdowns, school closures, and travel bans to reduce SARS-CoV-2 transmission. As unemployment, loneliness, and social isolation increased and financial security and social interaction decreased, factions of resistance emerged, perhaps because of adjustment disorders with disturbance of conduct, including norm-violating or inappropriate conduct (e.g., mask refusal), aggressive behavior (e.g., violent protests, purposefully exposing others to SARS-CoV-2), and other maladaptive reactions (e.g., substance use). US Army major George Soper, who discovered asymptomatic transmission of typhoid in the United States, commented on these social dynamics during the 1918 pandemic: "It does not lie in human nature for a man who thinks he has only a slight cold to shut himself up in rigid isolation as a means of protecting others."[10(p502)] That attitude is apparent today, as moral appeals for mutual protection from COVID-19 have often fallen on deaf ears amid socioeconomic disruption of uncertain duration.

People who embrace public health guidance may experience social isolation, concerns of COVID-19 morbidity and mortality, and grief and guilt associated with the isolated deaths of loved ones. Some may feel resentment toward what Paul Farmer, MD, PhD, designates containment nihilism, referring to approaches that abandon public health measures to contain SARS-CoV-2 and instead endorse enormous mortality to achieve population-level immunity. By June 2020, 40.9% of 5412 surveyed US adults reported adverse mental health symptoms or substance use, and suicidal ideation was twice as prevalent as in 2018.[11] Young adults, unpaid caregivers, Black persons, Latinx persons, essential workers, people with disabilities, and individuals with psychiatric or substance use conditions have disproportionately experienced adverse mental health symptoms. Anxiety and depression symptom levels among US adults continued to climb through February 2021,[12] likely representing direct and indirect effects of the COVID-19 pandemic complemented by seasonality. Provisional data indicate that US deaths classified as suicides declined by 2677 in 2020 versus 2019.[13] However, unintentional injury deaths increased by 19 136 during the same interval, driven by a record increase in drug overdose deaths.[13] Taken together, deaths of despair increased substantially in 2020.

RESPONDING TO MENTAL HEALTH NEEDS

Longstanding inadequate funding of mental and behavioral health services has left countries underprepared to respond to mental health needs during the COVID-19 pandemic. Despite an estimated $1 trillion economic cost of anxiety and depression alone—and a four-to-one benefit–cost ratio for investment in relevant treatment—mental health expenditure accounted for less than 2% of 2017 government health budgets.[14] Addressing the chronic underinvestment in mental health infrastructure can reduce the impact of such unique challenges, with added benefits for population-level health and productivity. Fortunately, early indicators of mental health effects of the pandemic[9,11] led the US president to sign Executive Order 13954, allocating $425 million to address mental health, the opioid crisis, and suicide. Moreover, the US Congress has allocated $1.15 billion to study postacute sequelae of COVID-19, including neuropsychiatric sequelae.

A comprehensive pandemic response will require recognition of both direct and indirect mental health consequences of the COVID-19 pandemic. Failure to recognize that COVID-19 is among the infectious diseases that may directly cause psychiatric conditions has led some policymakers to incorrectly conclude that adverse mental health consequences of the pandemic are driven solely by mitigation, creating a false choice between COVID-19 containment and preserving mental health. Similarly, failure to appreciate that fear, bereavement, and pandemic-associated life disruption can have adverse mental health consequences could lead policymakers to allocate mental health resources only to those who have had SARS-CoV-2 infection. Moreover, social determinants of health and the impacts of systemic and institutional racism and economic downturns compound pandemic-related stressors. Parallel stressors are, however, not unique to the COVID-19 pandemic; the 1918 influenza pandemic occurred during World War I alongside sociopolitical turmoil.

In describing the commonality of depression following influenza observed by internists and general practitioners in the wake of the 1918 influenza pandemic, Menninger states, "'Since I had influenza' is the touchstone of many a clinical history of depression."[2(p257)] Public health, societal, and medical efforts can help to reduce this experience with COVID-19. Public health prevention efforts should include promotion of COVID-19 prevention measures and coordination of COVID-19 vaccine distribution. Societal efforts should include integrated and sustained community-wide education campaigns and interventions to reduce social and health inequalities, both backed by strong legislative platforms. Medical efforts should prioritize expansion of mental health care access, as the already considerable percentage of US adults with unmet mental health care needs increased by 27% during the pandemic[13] and many countries rely on out-of-pocket payment for mental health services.[15] Increased, equitable access to tele–mental health services, digital mental health programs, and safe in-person services may mitigate the long-term consequences of neglecting this overlooked aspect of the pandemic.

Moreover, given evidence of neuropsychiatric consequences of SARS-CoV-2 infection,[7,8] enhanced mental health monitoring of all individuals who contract SARS-CoV-2 may be warranted, with recognition that psychiatric symptoms experienced by patients with COVID-19 may reflect experiential aspects of COVID-19 (e.g., self-stigma) or indirect mental health effects of the pandemic, which are not mutually exclusive from potential direct brain effects of COVID-19. Given the potential for mental health challenges affecting patients more broadly, integration of mental and behavioral health services into medical practices could help to better support community mental health needs.

With the global prevalence of laboratory-confirmed SARS-CoV-2 infections approaching 200 million in July 2021 and the true number of infections considerably larger, greatly enhanced research and clinical initiatives are needed to characterize and address the direct and indirect mental health consequences of the COVID-19 pandemic and to mitigate the detrimental impacts of mental health stigmatization. As Menninger warned in 1919,[2] failure to do so could further overwhelm underprepared US and global mental health care systems, the shortcomings of which were exposed beginning early during the current pandemic.[15] AJPH

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A Four-Year Follow-Up to "Hosting Syrian Refugees": Challenges, Resilience, and Small Joys During COVID-19

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"In Syria, we say, *Kul ta-kheer feeh kheer*—every delay has some goodness in it!" Noor, a 35-year-old refugee from Syria told me jovially on the phone as we discussed a major delay in an unemployment check she needed to pay bills in January. Over the past year, I have watched the COVID-19 pandemic disrupt the lives of 11 refugee families in central Pennsylvania, including Noor's, and I have been struck by the resilience and hope they exhibit in the face of hardship.

I am part of a team of students from Penn State College of Medicine who have helped lead a refugee initiative since 2016.[1] When our leadership team published a reflection on its efforts in *AJPH* in 2017, the group had just begun to focus on food security, education, and social support, using grant funding for weekly trips to a Harrisburg, Pennsylvania, farmers market, offering tutoring services, and developing trusting relationships with families still adjusting to their adoptive country. Even after the group's original leaders graduated, new students like me have maintained the effort year after year. But in 2020, COVID-19 disrupted not only our normal activities but also the day-to-day lives of the families we serve.

I will never forget the first few weeks of the pandemic in March 2020. I had recently taken on my role codirecting the initiative, when suddenly I was receiving an overwhelming number of calls from Noor and families asking for help applying for unemployment. Those who I had come to know for their self-reliance and quick settlement into new lives were now losing their jobs, and one family had even fallen ill with COVID-19. Our team was worried—we had never dealt with such complex needs before and were unfamiliar with the unemployment system. As we sought to navigate the bureaucracy, we found that telephone lines for assistance were always busy. Moreover, the application system was difficult to comprehend even for a native English speaker, and there were no jobs available even for those most desperate to return to work. Along with classmates, I spent hours filling out forms, translating them into Arabic, communicating with landlords, and trying to keep our tutoring efforts afloat online via WhatsApp. I lost nights of sleep worrying about our families—COVID-19 had put their financial security, housing, and mental health in jeopardy.

One rainy day in October, after I had struggled with their unemployment applications, I was invited to the home of Hanna and Ahmed, a married couple from Syria. Still frazzled, I was surprised when I was ushered into a warm, inviting living room, neatly decorated with a large birdcage and potted plants on the windowsill. Hanna and Ahmed chatted with me as their three-year-old daughter waddled to and fro, pigtails bouncing in the air, and two parakeets chirped and flitted about their cage. As the rain drizzled against the window, I could not believe the happiness that permeated this home. I had been so distraught at the hardships they were facing, but here I found calm. Even as Hanna solemnly shared hardships—that she had lost siblings in the Syrian war, that other siblings still lived in tents, that her children were struggling to learn English in an inner-city public school—she and Ahmed also shared how grateful they were to be safe and sound in the United States. They gave me homemade baklava to take home and excitedly taught me to make Turkish coffee. Hanna and Ahmed did not invalidate their hardships with gratitude, but they made clear that struggle can coexist with happiness.

Practically speaking, policies and systems that provide affordable, language-accessible social services will aid people like Noor, Hanna, and Ahmed in future crises. However, this past year has not only highlighted the urgent need for such changes but also taught me that suffering is not all encompassing. For people who are resilient, even a time of crisis rife with delays can contain small joys. AJPH

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A Statewide Voluntary Movement Addressing the Shortage of Medical Supplies During the COVID-19 Pandemic

Martin Krause, MD, Andrew Henderson, BS, BA, Daniel Griner, BA, Olivia S. Rissland, PhD, Jeremy Beard, PE, MS, and Karsten Bartels, MD, PhD, MBA

During the COVID-19 pandemic, a shortage of personal protective equipment compromised efficient patient care and provider safety. Volunteers from many different backgrounds worked to meet these demands. Additive manufacturing, laser cutting, and alternative supply chains were used to produce, test, and deliver essential equipment for health care workers and first responders. Distributed equipment included ear guards, face shields, and masks. Contingent designs were created for powered air-purifying respirator hoods, filtered air pumps, intubation shields, and N95 masks. (*Am J Public Health*. 2021;111(9): 1595–1599. https://doi.org/10.2105/AJPH.2021.306364)

During the early stages of the COVID-19 pandemic, the rapid spread of severe acute respiratory syndrome coronavirus 2 via aerosolized particles as well as the high demand for and limited reusability of medical equipment led to a shortage of personal protective equipment (PPE) and compromised patient care and provider safety.[1,2]

INTERVENTION

An ad hoc group of stakeholders and volunteers came together to design, validate, manufacture, and distribute PPE for health care workers and first responders.

PLACE AND TIME

This Colorado-wide initiative began in March 2020 and was consolidated as Make4Covid. A digital community was created using Mighty Networks (Mighty Software, Palo Alto, CA) and Slack (Slack Technologies, San Francisco, CA) channels. Private donations from individuals, foundations, businesses, and state grants were accepted via the https://make4covid.co homepage. A total of $316 400 was used for raw materials and fabrication costs (61%); specialized design, testing, and prototyping services (30%); professional fees and services (8%); and gifts to volunteers (1%). Notably, the bulk of logistics and shipping were provided in-kind, warehouse spaces were donated, and additional materials were supplied in-kind by both individuals and organizations.

PERSON

After a core interdisciplinary group spearheaded the project, a broader coalition of more than 100 partner organizations bundled their efforts and connected through the make4covid.co Web site. As of this writing, this group has grown to more than 2200 volunteers (Figure 1).

PURPOSE

With the temporary closure of production facilities and the disruption of supply chains during the pandemic, these local efforts enabled the procurement of scarce supplies through creative problem solving, and philanthropic efforts served to offset costs for recipients.

IMPLEMENTATION

Sewing machines, 3-D printers, and laser cutters located across a network of more than 500 homes, small businesses, public schools, libraries, and university labs were used to produce face shields, cloth masks, and ear guards at scale. Designers and clinicians evaluated and

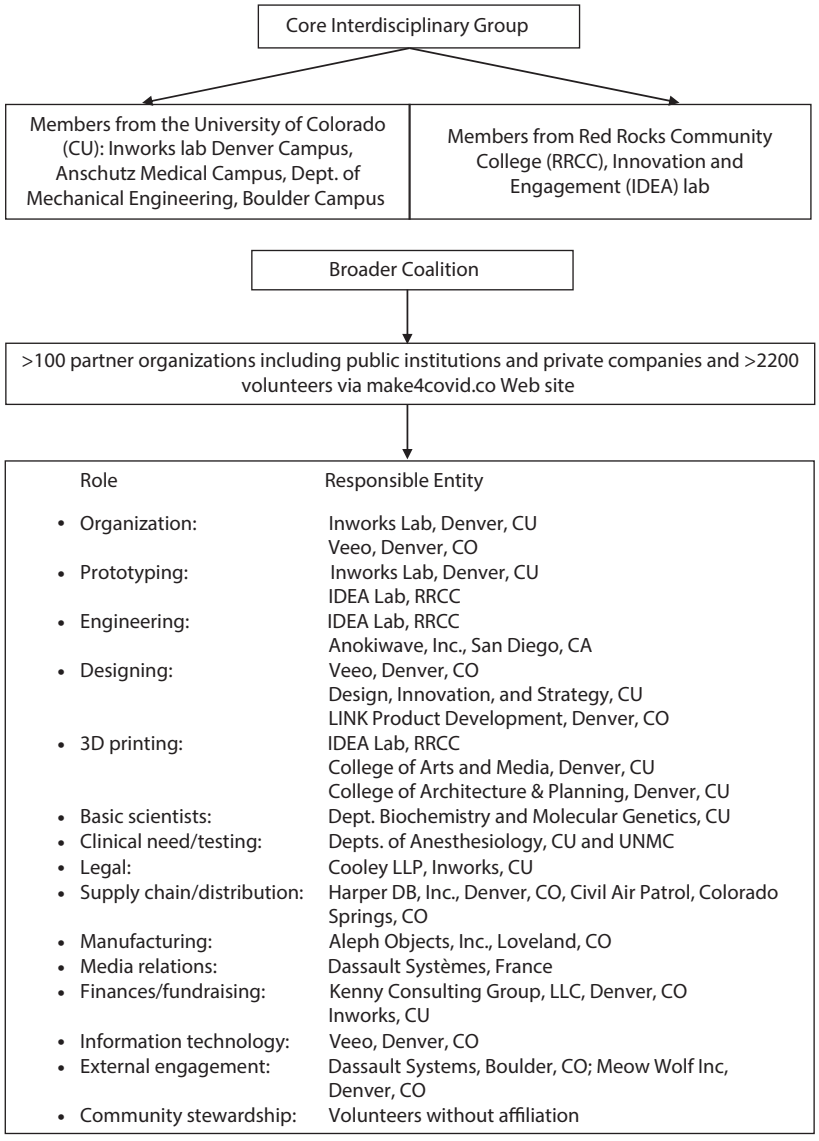

FIGURE 1— Key Stakeholders of Make4Covid.co, Which Designed, Validated, Manufactured, and Distributed Essential Equipment for Health Care Workers and First Responders in Hospitals, Nursing Homes, and Schools: United States, 2020

Note. LLC = limited liability company; LLP = limited liability partnership.

adapted open-source designs. Two experienced medical designers used an extended network of contacts available from the greater Make4Covid community to bring working prototypes on location and asked users targeted questions. Qualitative review with hospital staff included several prototypes across multiple products and involved fit tests across diverse staff to assess ergonomics, breathability, stability, and coverage. Novel or complex products, such as powered air-purifying respirators (PAPRs) and intubation shields, were brought on-site for mock procedures. Products were tested weekly or at critical points in the design and were revision controlled to ensure appropriate iterative changes. Qualified designs were published on a "Start Making" page for distributed production. Once approved, legal counsel for adherence to emergency use authorizations was sought. This process continued after publication, and meaningful revisions to designs were made over time following similar mechanics. In addition to qualitative analysis and codevelopment with clinicians, products were tested quantitatively whenever feasible.

Strict sanitation guidelines were followed in all participating locations.

Because many of the makers did not have a background in sanitation, guidelines included redundant sanitation methods through commonly available cleaning products (e.g., rubbing alcohol) at each step in the distribution chain. In addition, in-person contact was kept to a minimum, and, when unavoidable, Centers for Disease Control and Prevention guidelines were followed to prevent transmission between volunteers.

A network of volunteers and nonprofit transport organizations packaged and delivered PPE to recipients. Collection points were established at partner locations, and a hub-and-spoke model was used to consolidate products at a central location. The State Emergency Operations Center supported the effort, allowing the Civil Air Patrol to provide logistical support for collection, quality control, and distribution. A group of skilled makers provided technical support through recurring video meetings and were instrumental in translating quality control feedback to the entire network. The same group provided agile, short production runs of customized face shields to meet specialized needs in dental and emergency medicine.

Additionally, intubation shields, novel mechanical ventilators, ventilator connectors, reusable N95 respirators, PAPR hoods, and filtered air pumps were designed and prototyped using a combination of the distributed manufacturing network and traditional manufacturing techniques such as injection molding.

Legal counsel specializing in medical products assisted in meeting Food and Drug Administration (FDA) emergency use authorizations and crafting usage waivers. Local medical device manufacturers assisted in material selection and clean room assembly of PAPRs and N95 prototypes. The N95 respirators were iteratively tested to the National Institute for Occupational Safety and Health (NIOSH) equivalent standards at the State of Colorado's emergency testing facility.

In preparation for an anticipated ventilator shortage, a novel ventilator prototype using industrial high-speed valve technology was pilot tested in a swine model.

EVALUATION

Facilities in desperate need of vital equipment were provided with 127 866 pieces of PPE (Table 1). This ensured the safety of patients, health care workers, teachers, and schoolchildren. A dashboard was publicly available at the Make4Covid Web page specifying the number of delivered PPE, volunteers, partners, and weeks in operation.

TABLE 1— Delivered Personal Protective Equipment (PPE) and Recipients of PPE Served by Make4Covid.co: United States, 2020

	No. or No. (%)
PPE deliveries	
Face masks	12 426
Adult size	7 839
Child size	4 587
Face shields[a]	91 687
Complete face shields	78 314
Replacement of clear shields	13 373
Upgrades	
Visors	1 428
Padding	574
Sewn back straps	6 178
Ear savers	23 773
Total[b]	127 886
PPE recipients	
Clinics, medical offices	84 (22)
Home care, assisted living, nursing homes, hospices	61 (16)
Dental practices	55 (14)
Hospitals, medical centers	47 (12)
Education, schools	27 (7)
First responders: police, corrections, fire, EMS	18 (5)
Government, emergency response, health departments	19 (5)
Community organizations, underserved areas	26 (7)
Native American aid	3 (1)
Essential workers	43 (11)
Total	383

Note. EMS = emergency medical services.

[a]The total number of face shields delivered includes complete face shields and replacement of clear shields but excludes upgrades for face shields.
[b]Total number of PPE components delivered includes face masks, face shields, and ear savers but excludes upgrades for face shields.

ADVERSE EFFECTS

Before taking advantage of these resources, health care entities had to account for several issues. For example, demand for PPE needed to be anticipated. Second, products procured through nonstandard sources needed to be assessed for compliance with applicable regulatory policies.[3] A particular challenge was procuring filter media that met NIOSH standards consistently. This material requires specialized machinery and technical knowledge to create, putting it outside the network's fabrication capabilities. Despite multiple accepted purchase orders with reliable manufacturers of N95 media, governmental authority overrode each attempt. Attempts to validate filter media from two new domestic manufacturers identified unacceptable variations of filter performance. Although the products met many of the levels of protection required, the lack of reliable filter media prevented N95 respirators and PAPR pumps from meeting all requirements under the prevailing emergency use authorizations and NIOSH standards. Prototypes of novel mechanical ventilators have been tested on test lungs and animal models but would require clinical trials and FDA emergency use authorization if ventilators became scarce. Another logistic issue involved distributing equipment to more rural areas in need, which made the operation highly dependent on nonprofit aviation organizations such as Angel Flight West and Civil Air Patrol.

SUSTAINABILITY

Novel local production infrastructure developed during the COVID-19 pandemic could be used for health care emergencies in the future when complex supply chains collapse and national response programs are overwhelmed.[4] Laser cutting and 3-D printing, also known as additive manufacturing, proved to be innovative production solutions for medical equipment made from commonly available materials and could, therefore, be used in upcoming health care challenges. Out of necessity, institutional and private manufacturers created alternate approaches to conventional mechanical ventilation methods during this pandemic, such as supplies enabling ventilatory splitting or designing alternative ventilators.[3] Although mostly tested in experimental settings, these emerging techniques could become crucial for future pandemics caused by airborne pathogens.[5] Lastly, the production of reusable instead of disposable parts, which can then be sanitized chemically or sterilized by ultraviolet radiation,[1,3,6,7] is currently being tested by organizations such as Make4Covid and could become a more sustainable solution to depleted inventories of medical equipment and for environmental protection.

PUBLIC HEALTH SIGNIFICANCE

Volunteer-driven programs similar to Make4Covid.co have been essential for the health care community on state and national levels.[3,6] There is no question that without these efforts, many more health care providers and patients would have been infected and could have died. AJPH

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History of Methadone and Buprenorphine Opioid Agonist Therapy Among People Who Died of an Accidental Opioid-Involved Overdose: Rhode Island, January 1, 2018–June 30, 2020

Benjamin D. Hallowell, PhD, Heidi R. Weidele, MPH, Mackenzie Daly, MPA, Laura C. Chambers, PhD, MPH, Rachel P. Scagos, MPH, Lisa Gargano, PhD, MPH, and James McDonald, MD, MPH

To guide intervention efforts, we identified the proportion of individuals previously engaged in opioid agonist therapy among people who died of an accidental opioid-involved overdose. Most individuals (60.9%) had never received any prior buprenorphine or methadone treatment. Individuals who died of an overdose in 2020 had a similar demographic profile and treatment history compared with prior years. To prevent additional accidental opioid-involved overdose deaths, efforts should be directed toward linking individuals to care. (*Am J Public Health*. 2021;111(9):1600–1603. https://doi.org/10.2105/AJPH.2021.306395)

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In 2018, the rate of accidental drug overdose deaths in Rhode Island was 50% higher than the national average.[1] Despite its numbers gradually declining for the previous three years, Rhode Island in 2020 was on track to have its highest number of accidental overdose deaths ever recorded.[2] Prior engagement with opioid agonist therapy among this population is currently unknown. Additionally, it is unclear whether individuals previously in recovery were disproportionally affected by the opioid and COVID-19 syndemic in 2020.[3]

INTERVENTION

To guide intervention efforts and determine whether individuals in recovery were disproportionally affected by the syndemic, we identified the proportion of individuals previously engaged in opioid agonist therapy (methadone: January 2010–June 2020; buprenorphine: April 2016–June 2020) among people who died of an accidental opioid-involved overdose.

PLACE AND TIME

This analysis was performed by the Rhode Island Department of Health (RIDOH) in July 2020. To inform prevention activities, results were presented internally and to external partners in August 2020 and to the public in September 2020.

PERSON

All accidental opioid-involved overdose deaths (defined as those with opioids listed as a cause of death) occurring in Rhode Island between January 1, 2018, and June 30, 2020, were identified using data from the Office of the State Medical Examiner (OSME). To ensure that complete treatment history could be obtained, out-of-state residents were excluded from the analysis. Of the 815 accidental overdose deaths occurring during the study period, 697 involved opioids, of which 626 occurred among Rhode Island residents.

PURPOSE

The objective of the analysis was to identify the proportion of individuals previously engaged in methadone or buprenorphine treatment for opioid use disorder by year of death. The results from this analysis helped RIDOH identify whether prevention efforts should be

directed toward providing additional support to individuals in long-term recovery, currently engaged with treatment, or never engaged in treatment.

IMPLEMENTATION

To obtain treatment information for all accidental opioid-related overdose deaths, OSME data were linked with the Rhode Island Prescription Drug Monitoring Program (PDMP) and the Rhode Island Behavioral Health On-Line Database (RI-BHOLD) to obtain prior buprenorphine and methadone treatment history, respectively. To do this, a unique identifier was created using the last five letters of an individual's last name, the first three letters of their first name, and their date of birth. Using this identifier, OSME data were linked to Rhode Island Vital Records to ensure accuracy of matching characteristics and to obtain their social security number. Individuals who did not link were manually matched; four individuals could not be linked, so only their OSME identifier was used for the analysis. This identifier was also used to obtain decedents' prescription history for buprenorphine products approved by the Food and Drug Administration for opioid agonist therapy, as recorded in the PDMP from April 1, 2016, to June 30, 2020. For individuals who did not match to the PDMP, a second unique identifier using Vital Records information was created and the linkage was reperformed. Methadone treatment history between January 1, 2010, and June 30, 2020, was obtained from RI-BHOLD. Individuals were first matched by social security number (96% of matches) and then by full name and date of birth. For this analysis, buprenorphine treatment was assumed based on dispensed medication and the days' supply and includes buprenorphine dispensed by out-of-state pharmacies. With methadone, by contrast, treatment is primarily given through direct observed therapy, receipt of treatment is known, and data on methadone treatment received out of state are not available.

For the analysis, demographic characteristics from OSME, buprenorphine prescription history from the PDMP, and methadone treatment history from RI-BHOLD were compared by year of death. Any treatment history was defined as receipt of any prior buprenorphine prescription or methadone treatment. To determine whether an individual stopped treatment within 30 days of death or whether they were engaged in treatment at the time of death, we utilized the last day an individual received methadone treatment or the fill date of the buprenorphine prescription and the days' supply. Categorical measures were compared with χ^2 tests. Analyses were performed in SAS version 9.4 (SAS Institute, Cary, NC).

EVALUATION

Overall, most accidental opioid-related overdose deaths occurred in males (76.8%), non-Hispanic Whites (78.3%), and those aged 25 to 44 years (53.2%; Table 1). When demographic characteristics by year of death were compared, no significant differences were observed.

Overall, 245 individuals (39.1%) who died of an accidental opioid-involved overdose between January 2018 and June 2020 received any prior methadone or buprenorphine treatment for opioid use disorder based on the available data; of those, 170 (27.2%) received any prior methadone treatment and 151 (24.1%) received any prior buprenorphine (Figure 1; Table A, available as a supplement to the online version of this article at http://www.ajph.org). Although more data are available for people who died in later time periods, the proportion of individuals who received any prior treatment was similar from 2018 to 2020 ($P = .7$). Among individuals who received methadone or buprenorphine treatment, 60 (24.5%) were enrolled in treatment at the time of death and 47 (19.2%) died within 30 days of treatment cessation. The proportion of individuals who died in the 30 days following treatment cessation increased somewhat, from 16% in 2018 and 2019 to 29% in 2020.

When demographic characteristics by any treatment history were compared, individuals who were non-Hispanic White had a higher proportion engaged in treatment (44.9%) compared with non-Hispanic Black (16.0%) and Hispanic (21.8%) individuals. Additionally, 48.2% of individuals who matched to the PDMP for any controlled substance prescription were engaged in treatment, compared 13.4% for individuals who did not match (Table 1). When stratified by treatment type (methadone and buprenorphine), similar results were obtained.

Of note, data from the PDMP are limited to after April 1, 2016, and data from RI-BHOLD are limited to after January 1, 2010, so some individuals likely received treatment that predates the available data, particularly for buprenorphine. Unfortunately, we cannot determine from this analysis if the low proportion of individuals in treatment reflects individuals who

TABLE 1— Demographic Characteristics of Rhode Island Residents Who Died of an Accidental Opioid-Related Overdose, Stratified by Prior Treatment History: Rhode Island, January 1, 2018–June 30, 2020

	Overall, No. (%)	Any Prior Methadone or Buprenorphine Treatment[a]		*P*[b]
		Yes, No. (%)	No, No. (%)	
Age, y				.002
18–24	33 (5.3)	< 5 (. . .)	31 (8.1)	
25–34	159 (25.4)	61 (24.9)	98 (25.7)	
35–44	174 (27.8)	80 (32.7)	94 (24.7)	
45–54	124 (19.8)	51 (20.8)	73 (19.2)	
55–64	114 (18.2)	44 (18.0)	70 (18.4)	
≥ 65	22 (3.5)	7 (2.9)	15 (3.9)	
Gender				.029
Female	145 (23.2)	68 (27.8)	77 (20.2)	
Male	481 (76.8)	177 (72.2)	304 (79.8)	
Race/ethnicity				< .001
Non-Hispanic White	490 (78.3)	220 (89.8)	270 (70.9)	
Non-Hispanic Black	50 (8.0)	8 (3.3)	42 (11.0)	
Hispanic (any race)	78 (12.5)	17 (6.9)	61 (16.0)	
Other	8 (1.3)	0 (0.0)	8 (2.1)	
Matched to PDMP for any controlled substance prescription[c]				< .001
Yes	462 (73.8)	223 (91.0)	239 (62.7)	
No	164 (26.2)	22 (9.0)	142 (37.3)	

Note. PDMP = Rhode Island Prescription Drug Monitoring Program. The sample size was n = 626.

[a]Includes buprenorphine products Food and Drug Administration–approved for opioid agonist therapy dispensed between April 1, 2016 and June 30, 2020, and methadone treatment received between January 1, 2010 and June 30, 2020.
[b]χ^2 test.
[c]Matching indicates an individual was dispensed any schedule II-V medications or opioid antagonists between April 1, 2016 and June 30, 2020.

want treatment but have barriers to access or are not currently interested in treatment.

ADVERSE EFFECTS

We are not aware of any adverse events that occurred because of this analysis.

SUSTAINABILITY

We plan to reperform this analysis regularly until this information is no longer needed to direct prevention activities of RIDOH and its partners in response to the syndemic.

PUBLIC HEALTH SIGNIFICANCE

In Rhode Island, most individuals (60.9%) who died of an accidental opioid-involved overdose had not received any prior methadone or buprenorphine treatment for opioid use disorder. Despite a 33% increase in accidental opioid-involved overdose deaths in January through July 2020 compared with the same time period in 2019,[2] this study did not identify any differences in demographic characteristics or treatment history by year of death. The high proportion of individuals engaged in treatment who had received a prior controlled substance prescription suggests that, for this population, individuals who are more connected to the health care system may be more likely to initiate treatment. Additionally, the lower proportion of individuals engaged in treatment among younger age groups (< 25 years of age) and among non-Hispanic Black, Hispanic, and other minority racial/ethnic groups suggests that additional outreach efforts should be directed at linking these populations to care. To help address the opioid epidemic in Rhode Island, efforts to promote harm reduction practices, link

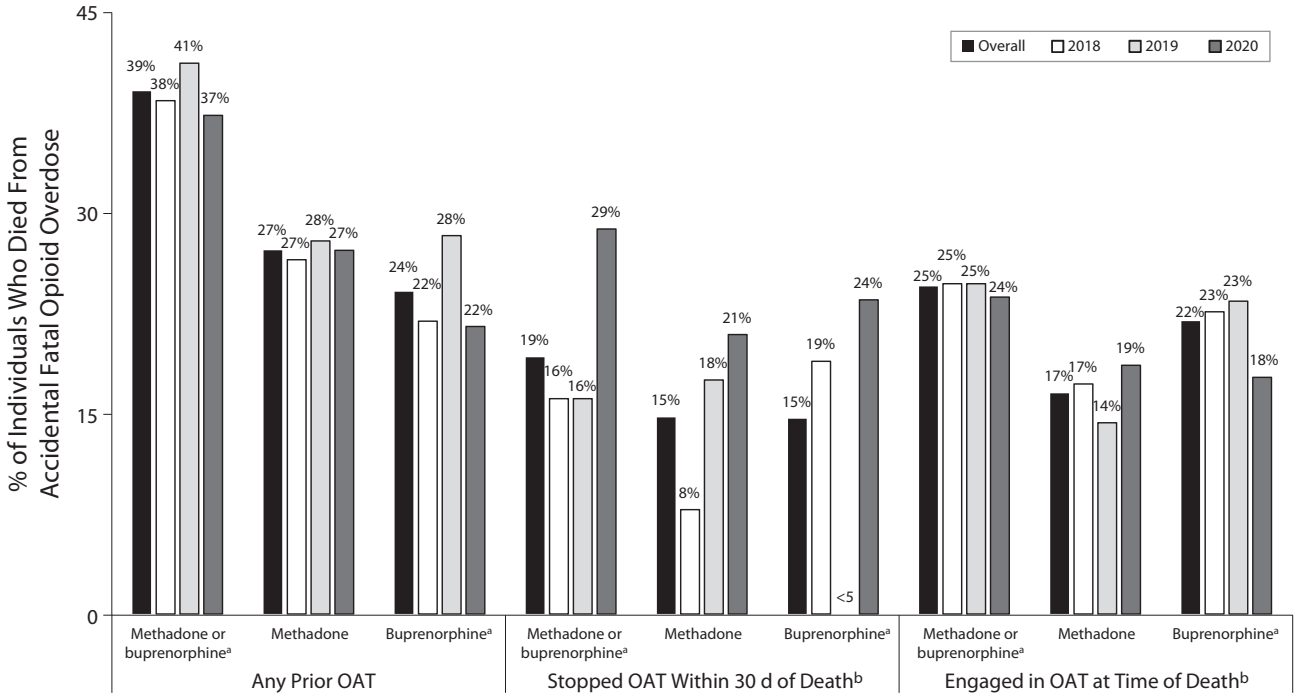

FIGURE 1— Methadone and Buprenorphine Treatment Characteristics Among Rhode Island Residents Who Died of an Accidental Opioid-Related Overdose: Rhode Island, January 1, 2018–June 30, 2020

Note. OAT = opioid agonist therapy. The sample size was n = 626.
[a]Includes buprenorphine products Food and Drug Administration–approved for opioid agonist therapy dispensed between April 1, 2016, and June 30, 2020, and methadone treatment received between January 1, 2010, and June 30, 2020.
[b]Limited to individuals who received buprenorphine or methadone treatment. Calculated from the last day an individual received methadone treatment or the fill date of the buprenorphine prescription and the days' supply.

individuals to treatment, identify facilitators that help link individuals to care, and remove barriers that limit utilization and retention should continue to be a priority. AJPH

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B. D. Hallowell, H. R. Weidele, and M. Daly collected the data. B. D. Hallowell, H. R. Weidele, M. Daly, L. C. Chambers, and J. McDonald analyzed and interpreted results. All authors contributed to study conceptualization and design and draft manuscript preparation, reviewed the results, and approved the final version of the manuscript.

CONFLICTS OF INTEREST

The authors have no conflicts of interest to disclose.

HUMAN PARTICIPANT PROTECTION

This study was deemed exempt by the Rhode Island Department of Health (RIDOH) institutional review board; data were stored on encrypted servers at RIDOH.

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The Need for COVID-19 LGBTQ-Specific Data

Lisa Bowleg, PhD, MPH, and Stewart Landers, JD, MCP

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See also Cahill, p. 1606, Akré et al., p. 1610, and Sell and Krims, p. 1620.

No data, no problem. Social epidemiologist Nancy Krieger's aphorism deftly captures the politics that surround the sizable gaps in data on COVID-19's impact among US lesbian, gay, bisexual, transgender, and queer [LGBTQ] communities.[1]

LGBTQ communities in the United States have made substantial social and legal gains. Yet many challenges remain, such as employment discrimination; political attacks on transgender youths; hate crimes, particularly against Black transwomen; religion-based discrimination[2]; and, in the case of COVID-19, public health data collection. Indeed, the largest global health crisis in more than a century has magnified numerous public health data gaps for LGBTQ communities.

LGBTQ activists, scholars, and national organizations, such as the National Academy of Medicine, the Williams Institute, and the Fenway Institute, have long advocated better sexual and gender minority (SGM) status data collection.[3,4] Accordingly, there has been an uptick in data collected systematically—and predominantly but not exclusively—by federal government surveys to better understand LGBTQ health concerns, needs, assets, and inequities. Despite concerns that LGBTQ stigma and discrimination would complicate data collection, evidence documents that LGBTQ data can be feasibly and efficaciously collected.[5]

LGBTQ people are not a mutually exclusive group, but rather intersect with other communities at increased and disproportionate risk for COVID-19 morbidity and mortality and adverse socioeconomic impact. Thus, government public health data collection efforts are essential to reflect the intersectional complexity of the real world. Indeed, the Gallup Organization's private representative polling data indicate that a growing number of US adults now identify as LGBTQ, including proportionately more Latino and non-Latino Black and Asian Americans.[6]

Sell and Krims (p. 1620) and Cahill (p. 1606) highlight that the void of SGM data on the prevalence and socioeconomic impact of COVID-19 is not inconsequential. Data from the Williams Institute documents that sexual minority people of color were twice as likely as their White counterparts to test positive for COVID-19. Sell shows that compared with their cisgender heterosexual counterparts (22%), 40% of sexual minority people work in service jobs subject to COVID-19 shutdowns. Evidence of the high correlation between smoking and respiratory illnesses such as COVID-19 and the fact that sexual minorities smoke at higher rates than sexual majorities are a further cause for concern.

Alas, the federal government bears much of the responsibility for the no data, no problem conundrum. As Cahill notes, as of May 2021 no federal agency had issued guidance recommending or requiring SGM status data collection for COVID-19 testing, care, and vaccination. In the absence of federal data on COVID-19 by SGM status, nongovernmental sources seek to fill the void. Using private data on the mental health impact of COVID-19, Akré et al. (p. 1610) document that LGBT people reported worse mental health and problem drinking during the COVID-19 pandemic than their cisgender heterosexual counterparts.

Collectively, the articles in this special section make a convincing argument for the need for SGM data in general, and during a global pandemic in particular. SGM data are urgently needed to assess the scope of the pandemic among diverse LGBTQ communities and inform the development of effective and LGBTQ-specific community-tailored interventions. These would include LGBTQ-segmented messaging in general public health messages as well as more targeted LGBTQ advertising (e.g., TV shows, magazines, Web sites).

Despite the considerable strides that activists, researchers, and public health officials have made in increasing public health SGM data collection, these articles highlight that LGBTQ people also remain intersectionally invisible in much of the response to COVID-19, despite evidence of clear problems and data gaps in COVID-19–related surveillance as well as mental and substance use. Consequently, there is a dire public health need to redouble advocacy efforts to boost SGM data, through either federal or state regulation, to effectively identify, address, and

intervene in the COVID-19 pandemic in diverse LGBTQ communities. AJPH

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Still in the Dark Regarding the Public Health Impact of COVID-19 on Sexual and Gender Minorities

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See also Bowleg and Landers, p. 1604.

More than a year into the COVID-19 pandemic, we know little about how COVID-19 is affecting lesbian, gay, bisexual, transgender, queer, and intersex (LGBTQI) people. This is because only five states and the District of Columbia have taken steps to collect sexual orientation and gender identity (SOGI) data, including intersex data, and none has yet reported any COVID-19 prevalence data by SOGI. As of July 2021, no federal agency had issued guidance recommending or requiring SOGI data collection in COVID-19 testing, care, and vaccination. This is a major public health surveillance opportunity that more states and the federal government should address forthwith.

As recently noted in *AJPH*,[1] sexual and gender minority (SGM) people may be at elevated risk of infection by the novel coronavirus because of a number of factors: greater likelihood of working in frontline occupations such as retail and food services, higher rates of poverty, and concentration in urban areas. This is especially true of people of color who are SGM. SGM populations also have higher rates of relevant risk factors (e.g., smoking and vaping) and comorbidities (e.g., asthma, cardiovascular disease, diabetes, cancer) that correlate with complications from COVID-19.[2]

As public health officials moved toward COVID-19 vaccine distribution in late 2020, SGM rights groups and civil rights groups encouraged state health directors to include SGM populations, people of color, immigrants, and other marginalized populations in their dissemination strategies. This is necessary because there are high rates of medical mistrust in SGM communities related to previous experiences of discrimination and abuse. This is especially true among Black[3] and Indigenous SGM populations, transgender people,[4] intersex people,[5] and older adults. Lesbian and bisexual women[6] and transgender people[7] are less likely to access routine, preventive health care. This could affect the likelihood that they will know how to access the COVID-19 vaccine and be willing to trust those offering it.

Public health authorities and health care providers should conduct affirmative outreach and enlist trusted community leaders to promote vaccination in Black and Indigenous communities, immigrant communities, SGM communities, and other communities in which medical mistrust is high. They should also collect SOGI data at vaccination, testing, and care to ensure that SGM populations are accessing these critical health care services equitably. More than 125 SGM health advocacy organizations sent a letter to the Association of State and Territorial Health Organizations in December 2020 asking them to do just this.[8]

DATA COLLECTION AND REPORTING

During 2020 SGM health advocates at the state and federal levels engaged in countless meetings and communications with public health officials and elected legislators, urging them to take steps to encourage or require SOGI data collection and reporting in the COVID-19 pandemic. This is an update on the results of those efforts as of May 2021. It is based on conversations with advocates, local journalists, and state and federal public health officials, including members of the Council of State and Territorial Epidemiologists.

The District of Columbia and five states—California, Oregon, Nevada, Pennsylvania, and Rhode Island—are collecting or trying to collect SOGI data in testing.

In spring 2020 Pennsylvania governor Tom Wolf announced that the state would collect SOGI data.[9] State health secretary Rachel Levine, MD, wrote health care providers, requesting "that you collect and report SO/GI data for all COVID-19 patients" and noting that "this is a top priority of the Wolf Administration, as the collection of this data will help inform public health policy decisions, drive health care delivery, and ultimately improve population health"

(https://bit.ly/3yKJ6tR). Pennsylvania's COVID-19 Dashboard reports race/ethnicity, gender, and age data for people with COVID-19 but does not yet report SOGI data (https://bit.ly/3jQX8pB).

California passed a law in 2015 requiring the routine collection of SOGI data in health care whenever race and ethnicity data are collected. In September 2020 Governor Gavin Newsom signed SB 932, a bill sponsored by Senator Scott Wiener requiring SOGI data collection and reporting in COVID-19 testing. Those who test positive are asked their SOGI.

According to a California LGBTQI activist, there have been two major problems in implementation. First, many people who are tested at drive-through and pop-up sites are not being asked their SOGI because "the California Department of [Public] Health is saying these are not health care sites and don't need SOGI data collection." Second, even if SOGI data are reported to the laboratories that process the test results, the labs are not forwarding SOGI data to the California Department of Public Health. "The data dies in the lab," the advocate said, "because the federal form doesn't require SOGI data" (oral personal communication, January 15, 2021).

This form, the Centers for Disease Control and Prevention's (CDC's) case report form, does not ask for SOGI information, and its sex options are "male, female, other, unknown." The labs told Senator Wiener and Mark Ghaly, California Secretary of Health and Human Services, that the problem was that Health Level Seven International (HL7), an international standards body, does not have SOGI standards. In response, Wiener and Ghaly wrote to the HL7 Public Health Working Group, asking that it immediately "modify its standards to include SOGI data in such a way that ensures interoperability between California's laboratories and the state's electronic disease reporting and surveillance system" and stating that "HL7's current lack of SOGI data standards is impeding California's efforts to measure, with the goal of ultimately ensuring, health equity for the state's LGBTQ and gender-nonconforming residents."[10] Although HL7 tends to move slowly, its chief executive officer Charles Jaffe quickly wrote back to the California leaders, offering "to provide guidance and identify key questions on the technical specifications needed to report this data from labs to state electronic disease reporting and surveillance systems." Jaffe said that HL7 "is committed to helping all states and their partners use relevant HL7 standards to improve COVID-19 reporting—for the LGBTQ community and other vulnerable populations."[11]

Meanwhile, California is the only state publicly reporting SOGI in COVID-19 data, although it is not prevalence data (https://covid19.ca.gov/equity). Instead, California reported that, as of May 7, 2021, it had sexual orientation data for 9.5% of the individuals who had died of COVID-19 and for 16.0% of the people who had tested positive for COVID-19. Gender identity data were more complete: the state had gender identity data for 99.0% of cases and 99.5% of deaths. (The gender identity response options are female, male, trans female/trans woman, trans male/trans man, genderqueer/gender nonbinary, not listed, and I prefer not to say.) California is trying to collect SOGI data only for individuals who test positive for COVID-19, not for each individual who gets tested.

California does not report whether SGM people are more likely to be diagnosed with COVID-19 than the majority or general population or whether SGM people are more likely to die from COVID-19.

San Francisco County and Los Angeles County in California are two of the only municipalities in the country to collect SOGI data. San Francisco collects and reports SOGI data in health and human services. A December 2020 report mentioned the COVID-19 pandemic as complicating data collection efforts but did not report COVID-19–related SOGI data.[12] Los Angeles County announced in June 2020 that it would collect SOGI data from people testing for COVID-19, but it has not yet released the data publicly.[13] In March 2021, seven frustrated California state legislators called for an audit of the state health department's collection of SOGI data related to the COVID-19 pandemic.[14]

In Oregon, SOGI data collection is starting to happen. A 2013 mandate that race/ethnicity, disability, language, and age data be collected in health care was expanded in October 2020 to include SOGI. In Nevada, contact tracers are asking patients about SOGI. Neither Oregon nor Nevada is publicly reporting SOGI data yet, nor is the District of Columbia.

In Rhode Island, case investigators call all individuals newly diagnosed with COVID-19 and ask several demographic questions, including SOGI. Individuals who test positive can also indicate their SOGI online on a case interview form. Rhode Island is analyzing data but has not reported any publicly yet.

IMPORTANCE OF INTERSECTIONAL DATA

There is preliminary polling data that SGM disparities in COVID-19 intersect with racial/ethnic disparities. A Williams Institute analysis of Axios–Ipsos survey

data from fall 2020 found that LGBTQI people of color were more likely than were straight, cisgender people of color to test positive for COVID-19 and were twice as likely to test positive for COVID-19 as LGBTQI White people.[15]

An analysis recently published in *Vaccines* of online survey data found that Black and Native American gay men and other men who have sex with men (MSM) in the United States were less willing than were White MSM to get vaccinated for COVID-19, whereas Asian American MSM were more likely to get vaccinated. There was no significant difference between Latino MSM and non-Hispanic White MSM.[16]

NEED FOR FEDERAL GOVERNMENT LEADERSHIP

Despite repeated outreach to US Department of Health and Human Services and CDC leaders throughout 2020, including CDC's Health Equity COVID-19 Strike Team and the COVID-19 Rapid Response Team, as of July 2021 the federal government had not issued guidance encouraging or requiring SOGI data collection in COVID-19 testing, care, or vaccination. SGM health advocates are hopeful that this will soon change, given the Biden-Harris administration's strong support for SOGI nondiscrimination and health equity and new CDC director Rochelle Walensky's career of providing HIV prevention and care to SGM patients. Health professional associations, such as the Council of State and Territorial Epidemiologists, should formally encourage the CDC to take this important step.

It is also imperative that the National COVID Cohort Collaborative (N3C), a project of the National Center for Advancing Translational Sciences, add SOGI to its COVID-19 Clinical Data Warehouse Data Dictionary. N3C states that collaborators can "contribute and use COVID-19 clinical data to answer critical research questions to address the pandemic" and that researchers can examine "associations between COVID-19 patient outcomes and social determinants of health" (https://ncats.nih.gov/n3c). Yet by not including SOGI, N3C does not allow for research on SGM populations' experiences with COVID-19.

COVID-NET, a network of 100 large hospitals meant to represent the US population, should also collect and report SOGI in COVID-19 care, testing, and vaccination.

At an April 2021 meeting of the Biden-Harris administration's COVID-19 Health Equity Task Force, Joneigh Khaldun, chair of the task force's Data, Analytics and Research Committee, spoke of the need for SOGI data collection and reporting in the COVID-19 pandemic. Hopefully, this will become a formal recommendation of the COVID-19 Health Equity Task Force soon.

Following more than a year of inaction by the federal government and most states, it is critical that other states and the federal government follow the lead of California, Oregon, Nevada, Pennsylvania, Rhode Island, and others and take steps to collect and report SOGI data in COVID-19 testing, care, and vaccination. This is a health equity imperative. AJPH

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CONFLICTS OF INTEREST

The author has no conflicts of interest to declare.

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Depression, Anxiety, and Alcohol Use Among LGBTQ+ People During the COVID-19 Pandemic

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See also Bowleg and Landers, p. 1604.

Objectives. To describe disparities in depression, anxiety, and problem drinking by sexual orientation, sexual behavior, and gender identity during the COVID-19 pandemic.

Methods. Data were collected May 21 to July 15, 2020, from 3245 adults living in 5 major US metropolitan areas (Atlanta, Georgia; Chicago, Illinois; New Orleans, Louisiana; New York, New York; and Los Angeles, California). Participants were characterized as cisgender straight or LGBTQ+ (i.e., lesbian, gay, bisexual, and transgender people, and men who have sex with men, and women who have sex with women not identifying as lesbian, gay, bisexual, or transgender).

Results. Cisgender straight participants had the lowest levels of depression, anxiety, and problem drinking compared with all other sexual orientation, sexual behavior, and gender identity groups, and, in general, LGBTQ+ participants were more likely to report that these health problems were "more than usual" during the COVID-19 pandemic.

Conclusions. LGBTQ+ communities experienced worse mental health and problem drinking than their cisgender straight counterparts during the COVID-19 pandemic. Future research should assess the impact of the pandemic on health inequities. Policymakers should consider resources to support LGBTQ+ mental health and substance use prevention in COVID-19 recovery efforts. (*Am J Public Health*. 2021;111(9): 1610–1619. https://doi.org/10.2105/AJPH.2021.306394)

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Public health strategies to combat COVID-19 transmission have focused on reducing exposure by encouraging mask wearing or through policies promoting physical distancing. Such efforts may have unique health ramifications for lesbian, gay, bisexual, transgender, queer, and other people of diverse sexual identities and sexual behaviors (herein referred to as LGBTQ+). For example, stay-at-home orders that aim to address COVID-19 transmission may not adequately consider whether they are feasible or possibly even unhealthy or unsafe for some segments of LGBTQ+ communities. LGBTQ+ people make up between 20% and 40% of the homeless population,[1] and many LGBTQ+ college students were forced to return to unsupportive family situations.[2,3] The COVID-19 mitigation strategies may also have more severe unintended consequences experienced by LGBTQ+ people, such as heightened loneliness and social isolation.[4]

LGBTQ+ populations experience disproportionately high poor mental health outcomes. Previous research has found that general life stressors (e.g., work, finances) as well as qualitatively unique LGBTQ+ specific stressors, such as discrimination, result in mental health tolls.[5-8] A recent study found that the impact of these stressors may accumulate, resulting in a greater risk of negative affect (i.e., propensity for negative emotions) and poor self-identity among LGBTQ+ people. Moreover, greater experiences of identity-related stressors exacerbated the impact of general stress on negative affect.[8] Alcohol use and misuse are also more prevalent among LGBTQ+ populations.[9] These substance use disparities may be driven by challenging psychosocial experiences, which have been shown to increase the risk of engaging in maladaptive

coping behaviors, particularly when such stressors are appraised as being severe and outside of one's control.[10] There is strong evidence that structural and social inequities contribute to mental health and substance use disparities experienced by LGBTQ+ people.[5,11,12] However, there are no empirical studies to our knowledge that have explicitly examined potentially widening disparities among sexual orientation, sexual behavior, and gender identity groups during the COVID-19 pandemic. The LGBTQ+ population is a diverse group of people whose races, nationalities, genders, sexualities, ages, abilities, and other social identities shape the social inequalities that they experience.[13] The unique lived experiences and vulnerabilities that LGBTQ+ people contend with may put them at higher risk for depression, anxiety, and high alcohol use during the COVID-19 pandemic.

The current literature on the COVID-19 pandemic has not yet characterized differences in health by sexual orientation, sexual behavior, and gender identity.[14] It is imperative to monitor the mental health and substance use of LGBTQ+ communities during the pandemic to establish points of intervention and prevent potential widening health inequities, including in depression, anxiety, and problem alcohol use experienced by LGBTQ+ persons versus their cisgender straight counterparts.[3] This study aimed to examine mental health and alcohol use patterns among LGBTQ+ and cisgender straight adults during the COVID-19 pandemic.

METHODS

We used data from the Uncovering COVID-19 Experiences and Realities (UnCOVER) Study, which consisted of a large sample of adults from 5 major metropolitan statistical areas in the United States: Atlanta, Georgia; Chicago, Illinois; New Orleans, Louisiana; New York, New York; and Los Angeles, California (n = 3245). Data were collected from May 21, 2020, to July 15, 2020. Participants were recruited through distribution lists from panel providers via Qualtrics Research Services. Panel providers identified and randomly selected participants who matched the specified target criteria. Inclusion criteria for this study included current residence in 1 of the designated market areas of the 5 metropolitan areas of interest, age 18 years or older, ability to read and understand English, and self-identification as Asian, Black, Hispanic/Latinx, or White. Participants who consented to participation completed the study questionnaire online through the Qualtrics survey platform. Quota sampling by race/ethnicity and geographic area was employed to ensure more equal representation across these demographics. Identical recruitment caps were set for each metropolitan area and racial/ethnic group within the metropolitan area. Because of recruitment difficulties, caps were increased to reach the target sample size (n = 3200).

Measures

The main variable of interest was self-reported sexual orientation identity, sexual behavior, and gender identity. To ascertain sexual identity, respondents were asked, "Which of the following best describes your sexual orientation?" The responses were heterosexual or straight, gay or lesbian, or bisexual. To obtain sexual behavior respondents were asked, "In your lifetime, who have you had sex with?" Responses were men only, women only, both men and women, and I have not had sex. Gender identity was derived from 2 questions. First, respondents were asked, "What is your gender?" Responses were man/male or woman/female. The respondents were asked, "What sex were you assigned at birth?" We combined each of these into a single explanatory variable to categorize respondents by both gender identity and sexual orientation. First, those who identified as women and were assigned male at birth and those who identified as men and were assigned female at birth were considered transgender. Otherwise, if gender and sex were congruent, participants were categorized as cisgender. We then defined sexual orientation with the gender identity as follows: (1) participants who identified as gay or lesbian we categorized as cisgender gay or lesbian, (2) participants who identified as bisexual as cisgender bisexual, (3) participants who ever engaged in any same-sex sexual behaviors but were not lesbian, gay, bisexual, or transgender were considered to be cisgender, non–LGBT-identified men who have sex with men and women who have sex with women (cisgender MSM/WSW) and (4) cisgender straight people identified as straight, were not transgender, and reported no same-sex sexual behavior. Because of the low sample size of transgender participants (n = 19), we were unable to create subgroups of sexual orientation for transgender participants.

Outcomes Variables

We used Patient-Reported Outcomes Measurement Information System (PROMIS) measures to assess depression, anxiety, and problem drinking during the COVID-19 pandemic. These instruments were developed and validated by the National Institutes of

Health. PROMIS scales are scored by summing responses across items to obtain a raw composite score. Raw scores are then converted to a US standardized T-score to assist with the interpretation of findings. The US mean is 50 with a standard deviation of 10.[15]

The short version of the PROMIS depression and anxiety measures each consisted of 4 items. The stem of each measure was modified to ask participants how often they had experienced each item specifically "during the COVID-19 or coronavirus pandemic." The PROMIS depression scale assessed the extent to which participants felt hopeless, worthless, helpless, and depressed. The PROMIS anxiety scale assessed how often participants felt fearful, found it hard to focus on anything other than their anxiety, felt their worries overwhelmed them, and felt uneasy. Participants scored each of the items using a 5-point Likert-type scale with response choices of never, rarely, sometimes, often, and always. Greater scores indicate elevated depression and anxiety symptoms with a maximum score of 20.

We used the PROMIS Alcohol Use Negative Consequences 7-item short-form scale to assess problem drinking.[16] A screening item assessed whether the participant drank any type of alcoholic beverage during the COVID-19 pandemic. Participants who reported that they did not drink were considered not to experience any problem drinking during the COVID-19 pandemic. Participants were asked to report the extent that they felt the following "during the COVID-19 or coronavirus pandemic": they spent too much time drinking, drank heavily at a single sitting, drank too much, drank more than planned, had trouble controlling drinking, had difficulty stopping drinking after 1 or 2 drinks, and had difficulty getting the thought of drinking off their mind. Items were scored on a 5-point Likert-type scale with responses of never, rarely, sometimes, often, and always. Higher scores indicate elevated alcohol use problems.

Changes in Mental Health and Alcohol Use

To examine whether levels of depression, anxiety, and problem drinking reported by participants were different from those before the COVID-19 pandemic, we included 3 single-item questions. To assess changes in depression or anxiety, participants were asked if "during the COVID-19 or coronavirus pandemic" they experienced "more, less, or about the same level" of (1) feeling anxious or worried and (2) feeling depressed. To create a binary outcome variable, we dichotomized the responses (i.e., [1] more or [2] less or about the same level). Participants who reported any alcohol consumption during the COVID-19 pandemic were asked if "compared to before the COVID-19 or coronavirus pandemic," their alcohol use "decreased," "stayed the same," or "increased." Participants were classified as greater drinking during the COVID-19 pandemic versus the same, less, or no drinking. We created a binary outcome variable for this measure by dichotomizing the responses (i.e., [1] increased or [2] decreased or stayed the same).

Covariates

Covariates included the following: age group (18–26, 27–49, 50–64, and ≥ 65 years), sex assigned at birth (male and female), race/ethnicity (African American/Black, Asian, Hispanic/Latinx, and White), educational attainment (less than high school, high-school degree, some college or an associate's or technical degree, and bachelor's degree or higher), household income in relation to the federal poverty level (FPL; according to the US Department of Health and Human Services: https://aspe.hhs.gov/prior-hhs-poverty-guidelines-and-federal-register-references) based on household size and number of children younger than 18 years (< 100% of the FPL, 100%–138% of the FPL, 139%–400% of the FPL, and > 400% of the FPL); relationship status (married or partnered; in a romantic relationship; widowed; and single, divorced, or separated); health insurance (uninsured, private, public, and other); and city of residence (Atlanta, Chicago, Los Angeles, New Orleans, and New York City).

Statistical Analysis

We describe differences in demographic and socioeconomic characteristics of the sample by sexual identity, sexual behavior, and gender identity. We specified multivariable linear regression models examining each outcome variable (anxiety, depression, and problem drinking). We conducted all analyses using Stata/MP version 16.1 (StataCorp LP, College Station, TX). We reported *P* values and 95% confidence intervals and considered findings statistically significant at a *P* value of .05 or less. We used an a priori Bonferroni correction to adjust for multiple comparisons significance level of 0.0125. To ensure that there were not issues of collinearity in the multivariate regression models, we used the variance inflation factor (vif) and tolerance (1/vf) to test for multicollinearity in each of the models. The average vif was 1.82 and all 1/vf were greater than 0.10. There were no issues with multicollinearity in any of the models.

RESULTS

The distribution of participant characteristics by sexual orientation, sexual behavior, and gender identity is presented in Table 1. LGBTQ+ respondents were more likely to report "more than usual" depression, anxiety, and drinking during the pandemic compared with cisgender straight respondents (Table 2). LGBTQ+ respondents had higher depression scores during the pandemic compared with cisgender straight respondents: 42.5% of lesbian or gay, 53.5% of bisexual, 46.7% of MSM/WSW, and 47.4% of transgender respondents reported feeling depression "more than usual," as compared with 36.3% of cisgender straight respondents ($\chi^2 = 32.3$; $P < .001$).

LGBTQ+ respondents had higher anxiety scores during the pandemic compared with cisgender straight respondents. We found that 63.3% of lesbian or gay, 69.7% of bisexual, 63.1% of MSM/WSW, and 57.9% of transgender respondents reported feeling depressed "more than usual" compared with 57.8% of cisgender straight respondents ($\chi^2 = 14.4$; $P < .01$). LGBTQ+ respondents had higher problem drinking scores during the pandemic compared with cisgender straight respondents. Compared with 13% of cisgender straight respondents, 8.3% of lesbian or gay, 17.1% of bisexual, 22.1% of MSM/WSW, and 10.5% of transgender respondents reported that their "alcohol use increased" ($\chi^2 = 12.9$; $P < .01$). Overall, multivariable linear regression analyses revealed that LGBTQ+ respondents had higher levels of depression, anxiety, and problem drinking during the pandemic (Tables 3 and 4). In models controlling for sociodemographic (e.g., age, sex, race, income, education, insurance, and relationship status) covariates, some statistically significant associations emerged: cisgender lesbian and gay participants had higher levels of depression (b = 2.10; 95% confidence interval [CI] = 0.36, 3.84) and anxiety (b = 1.52; 95% CI = −0.29, 3.32), and problem alcohol use (b = 2.20; 95% CI = 0.82, 3.58) compared with cisgender straight adults (Table 4). Cisgender bisexual participants reported higher rates of depression (b = 4.09; 95% CI = 2.76, 5.43), anxiety (b = 3.52; 95% CI = 2.13, 4.90), and problem alcohol use (b = 1.37; 95% CI = 0.32, 2.43) compared with cisgender straight participants. Cisgender MSM/WSW also had higher levels of depression (b = 3.31; 95% CI = 1.58, 5.04), anxiety (b = 3.05; 95% CI = 1.25, 4.84), and problem drinking (b = 3.80; 95% CI = 2.42, 5.17) compared with cisgender straight participants. Transgender respondents also had higher levels of depression, anxiety, and problem drinking than cisgender straight participants, but associations were not statistically significant.

DISCUSSION

Our findings suggest that certain LGBTQ+ subgroup populations had higher levels of anxiety, depression, and problem drinking during the COVID-19 pandemic compared with their cisgender straight counterparts. Inequities in these outcomes may have been exacerbated during the COVID-19 pandemic. In general, we found that cisgender bisexual participants reported the highest levels of depression and anxiety and were more likely to report that their depression and anxiety were greater during the pandemic compared with other sexual orientation, sexual behavior, and gender identity groups. Social support and relationships are important dimensions that can support the mental health of LGBTQ+ people. Stress and coping frameworks posit that social resources positively influence mental health and can serve as buffers under conditions of stress.[17] Social support can include emotional support (e.g., expressions of love), informational support (e.g., providing beneficial information), and instrumental support (i.e., providing a helping hand).[18] Previous research suggests that biphobia, including bisexual invisibility within the LGBTQ+ contexts, may lead to the social exclusion of bisexual people[19] and may result in psychological tolls, such as poorer self-concept (lower positive attributes associated with one's sexual identity), lack of integration between sexual identity and other social identities, and more incongruent self-identities.[20] The psychosocial resources and buffers may have been further diminished, particularly for bisexual people, during the COVID-19 pandemic, magnifying depression and anxiety during this period.

More broadly, LGBTQ+ people have historically faced barriers to accessing health care services and more limited provider understanding of their health needs. In tandem with experiences of exclusion within LGBTQ+ contexts, these experiences contribute to poor mental health and substance use outcomes in this population.[21] A recent report that documents the experiences of LGBTQ+ people during the COVID-19 pandemic demonstrates that they are experiencing higher rates of job loss, lost wages, food insecurity, and difficulty accessing health care.[22] These experiences of reduced resources and economic instability can be contributing to

TABLE 1— Demographic, Socioeconomic, and Mental Health Characteristics of Study Participants From the UnCOVER Study in 5 US Metropolitan Areas During the COVID-19 Pandemic by Sexual Orientation, Sexual Behavior, and Gender Identity: May 21, 2020–June 15, 2020

	Cisgender Straight (n = 2753), No. (%)	Cisgender Gay or Lesbian (n = 120), No. (%)	Cisgender Bisexual (n = 228), No. (%)	Cisgender MSM/WSW (n = 122), No. (%)	Transgender Person (n = 19), No. (%)	Total (n = 3242), No. (%)
Age, y						
18–26	571 (20.7)	33 (27.5)	135 (59.2)	22 (18.0)	5 (26.3)	766 (23.6)
27–49	854 (31.0)	38 (31.7)	65 (28.5)	55 (45.1)	9 (47.4)	1021 (31.5)
50–64	607 (22.0)	22 (18.3)	16 (7.0)	27 (22.1)	2 (10.5)	674 (20.8)
≥ 65	721 (26.2)	27 (22.5)	12 (5.3)	18 (14.8)	3 (15.8)	781 (24.1)
Sex at birth						
Male	954 (34.7)	63 (52.5)	37 (16.2)	41 (33.6)	5 (26.3)	1100 (33.9)
Female	1799 (65.3)	57 (47.5)	191 (83.8)	81 (66.4)	14 (73.7)	2142 (66.1)
Race/ethnicity						
Black	697 (25.3)	32 (26.7)	71 (31.1)	42 (34.4)	4 (21.1)	846 (26.1)
Asian	531 (19.3)	16 (13.3)	41 (18.0)	13 (10.7)	6 (31.6)	607 (18.7)
Hispanic/Latinx	391 (14.2)	23 (19.2)	57 (25.0)	17 (13.9)	3 (15.8)	491 (15.1)
White	1134 (41.2)	49 (40.8)	59 (25.9)	50 (41.0)	6 (31.6)	1298 (40.0)
Education						
< high school	555 (20.2)	21 (17.5)	70 (30.7)	18 (14.8)	5 (26.3)	669 (20.6)
High-school degree	853 (31.0)	39 (32.5)	90 (39.5)	49 (40.2)	7 (36.8)	1038 (32.0)
Some college or associate's or technical degree	839 (30.5)	33 (27.5)	43 (18.9)	26 (21.3)	5 (26.3)	946 (29.2)
≥ bachelor's degree	506 (18.4)	27 (22.5)	25 (11.0)	29 (23.8)	2 (10.5)	589 (18.2)
Household income, % FPL[a]						
0–99	343 (12.5)	25 (20.8)	80 (35.2)	16 (13.2)	5 (27.8)	469 (14.5)
100–138	183 (6.7)	9 (7.5)	27 (11.9)	12 (9.9)	1 (5.6)	232 (7.2)
139–400	1120 (40.8)	44 (36.7)	74 (32.6)	50 (41.3)	8 (44.4)	1296 (40.1)
> 400	1101 (40.1)	42 (35.0)	46 (20.3)	43 (35.5)	4 (22.2)	1236 (38.2)
Relationship status						
Married, marriage-like, or partnered	1195 (43.4)	37 (30.8)	36 (15.8)	54 (44.3)	8 (42.1)	1330 (41.0)
Romantic relationship	243 (8.8)	16 (13.3)	43 (18.9)	20 (16.4)	2 (10.5)	324 (10.0)
Widowed	914 (33.2)	60 (50.0)	126 (55.3)	36 (29.5)	5 (26.3)	1141 (35.2)
Single, divorced, or separated	401 (14.6)	7 (5.8)	23 (10.1)	12 (9.8)	4 (21.1)	447 (13.8)
Health insurance type						
Uninsured	296 (10.8)	14 (11.7)	35 (15.4)	13 (10.7)	3 (15.8)	361 (11.1)
Private	1207 (43.8)	52 (43.3)	71 (31.1)	45 (36.9)	9 (47.4)	1384 (42.7)
Public	1197 (43.5)	51 (42.5)	112 (49.1)	57 (46.7)	7 (36.8)	1424 (43.9)
Other	53 (1.9)	3 (2.5)	10 (4.4)	7 (5.7)	0 (0)	73 (2.3)

Continued

TABLE 1— Continued

	Cisgender Straight (n = 2753), No. (%)	Cisgender Gay or Lesbian (n = 120), No. (%)	Cisgender Bisexual (n = 228), No. (%)	Cisgender MSM/WSW (n = 122), No. (%)	Transgender Person (n = 19), No. (%)	Total (n = 3242), No. (%)
City						
Atlanta, GA	625 (22.7)	27 (22.5)	46 (20.2)	20 (16.4)	2 (10.5)	720 (22.2)
Chicago, IL	586 (21.3)	19 (15.8)	47 (20.6)	27 (22.1)	4 (21.1)	683 (21.1)
Los Angeles, CA	673 (24.4)	29 (24.2)	53 (23.2)	26 (21.3)	7 (36.8)	788 (24.3)
New Orleans, LA	224 (8.1)	7 (5.8)	20 (8.8)	12 (9.8)	2 (10.5)	265 (8.2)
New York, NY	645 (23.4)	38 (31.7)	62 (27.2)	37 (30.3)	4 (21.1)	786 (24.2)

Note. FPL = federal poverty level; MSM = men who have sex with men; UnCOVER = Uncovering COVID-19 Experiences and Realities; WSW = women who have sex with women.

Source. UnCOVER data 2020.
[a]FPL according to the US Department of Health and Human Services (https://aspe.hhs.gov/prior-hhs-poverty-guidelines-and-federal-register-references).

TABLE 2— Estimated Prevalence of Self-Reported Increases in Depression, Anxiety, and Alcohol Use and Mean PROMIS Score for Mental Health and Problem Drinking for Participants in the UnCOVER Study During the COVID-19 Pandemic Stratified by Sexual Identity, Sexual Behavior, and Gender Identity: 5 US Metropolitan Areas, May 21, 2020–July 15, 2020

	Cisgender Straight (n = 2753), % or Mean (SD)	Cisgender Gay or Lesbian (n = 120), % or Mean (SD)	Cisgender Bisexual (n = 228), % or Mean (SD)	Cisgender MSM/WSW (n = 122), % or Mean (SD)	Transgender Person (n = 19), % or Mean (SD)	Total (N = 3245), % or Mean (SD)
Depression***						
Less or same	63.7	57.5	46.5	53.3	52.6	61.8
More	36.3	42.5	53.5	46.7	47.4	38.2
Anxiety**						
Less or same	42.2	36.7	30.3	36.9	42.1	41.0
More	57.8	63.3	69.7	63.1	57.9	59.0
Alcohol**						
Less or same	87.0	81.7	82.9	77.9	89.5	86.2
More	13.0	18.3	17.1	22.1	10.5	13.8
Depression	53.5 (10.29)	56.36 (11.23)	61.67 (10.12)	57.91 (9.98)	55.93 (11.30)	54.36 (10.54)
Anxiety	56.74 (10.71)	58.74 (11.75)	64.37 (10.11)	60.95 (10.11)	59.96 (11.82)	54.36 (10.55)
Alcohol	42.87 (7.48)	45.52 (9.20)	44.31 (8.54)	47.64 (10.58)	42.97 (8.77)	43.25 (7.84)

Note. MSM = men who have sex with men; PROMIS = Patient-Reported Outcomes Measurement Information System; UnCOVER = Uncovering COVID-19 Experiences and Realities; WSW = women who have sex with women. The 5 metropolitan areas were Atlanta, GA; Chicago, IL; Los Angeles, CA; New Orleans, LA; and New York, NY.

Source. UnCOVER data set 2020.
$^{*}P < .05$; $^{**}P < .01$; $^{***}P < .001$.

disparities in mental health outcomes and increased alcohol use found in the study. To address health disparities between LGBTQ+ and cisgender and straight populations, as well as within LGBTQ+ communities, health care providers and pandemic response teams must ensure that there are not only sufficient resources but also tailored public health strategies. There is a dearth of identity-affirmative and culturally competent mental health care for LGBTQ+ people, with only 13% of mental health facilities offering LGBTQ+ services according to the 2016 National

TABLE 3— Unadjusted Linear Regressions Predicting PROMIS Scores for Depression, Anxiety, and Problem Alcohol Use in UnCOVER Study Participants: 5 US Metropolitan Areas, 2020

	Depression, b (95% CI)	Anxiety, b (95% CI)	Alcohol Use, b (95% CI)
Intercept	53.50 (53.10, 53.90)	56.74 (56.30, 57.10)	42.87 (42.60, 43.20)
Sexual orientation, sexual behavior, and gender identity			
Cisgender straight (Ref)	1	1	1
Cisgender gay or lesbian	2.86 (0.97, 4.74)	2.00 (0.042, 3.95)	2.64 (1.22, 4.07)
Cisgender bisexual	8.17 (6.78, 9.56)	7.63 (6.19, 9.08)	1.44 (0.39, 2.49)
Cisgender MSM/WSW	4.41 (2.54, 6.28)	4.21 (2.27, 6.15)	4.77 (3.36, 6.18)
Transgender person	2.43 (–2.23, 7.08)	3.23 (–1.60, 8.05)	0.10 (–3.41, 3.61)

Note CI = confidence interval; MSM = men who have sex with men; PROMIS = Patient-Reported Outcomes Measurement Information System; UnCOVER = Uncovering COVID-19 Experiences and Realities; WSW = women who have sex with women. Sample size was n = 3242. The 5 metropolitan areas were Atlanta, GA; Chicago, IL; Los Angeles, CA; New Orleans, LA; and New York, NY.

Source. UnCOVER data set 2020.

TABLE 4— Adjusted Linear Regressions Predicting PROMIS Scores for Depression, Anxiety, and Problem Alcohol Use in the Participants: UnCOVER Study, 5 US Metropolitan Areas, 2020

	b (95% CI)	b (95% CI)	b (95% CI)
Intercept	55.46 (53.6, 57.3)	56.84 (55.0, 58.70)	42.58 (41.1, 44.00)
Sexual orientation, sexual behavior, and gender identity			
Cisgender straight (Ref)	1	1	1
Cisgender gay or lesbian	2.10 (0.36, 3.84)	1.52 (–0.29, 3.32)	2.20 (0.82, 3.58)
Cisgender bisexual	4.09 (2.76, 5.43)	3.52 (2.13, 4.90)	1.37 (0.32, 2.43)
Cisgender MSM/WSW	3.31 (1.58, 5.04)	3.05 (1.25, 4.84)	3.80 (2.42, 5.17)
Transgender person	0.74 (–3.63, 5.12)	1.25 (–3.29, 5.79)	0.19 (–3.28, 3.67)
Age, y			
18–26 (Ref)	1	1	1
27–49	−2.59 (–3.58, –1.60)	−2.53 (–3.55, –1.50)	1.50 (0.71, 2.29)
50–64	−6.60 (–7.78, –5.41)	−6.29 (–7.52, –5.07)	−0.94 (–1.88, 0.001)
≥ 65	−10.05 (–11.40, –8.65)	−10.32 (–11.8, –8.88)	−4.04 (–5.15, –2.93)
Sex at birth			
Male (Ref)	1	1	1
Female	1.73 (1.02, 2.44)	3.06 (2.32, 3.80)	−1.55 (–2.11, –0.98)
Race/ethnicity			
Black (Ref)	1	1	1
Asian	0.89 (–0.15, 1.93)	1.13 (0.05, 2.20)	−2.19 (–3.01, –1.36)
Hispanic/Latinx	1.31 (0.21, 2.41)	1.56 (0.42, 2.70)	−0.10 (–0.97, 0.77)
White	2.89 (1.99, 3.79)	2.89 (1.96, 3.82)	0.70 (–0.01, 1.42)
Education			
< high school (Ref)	1	1	1
High-school degree	1.57 (0.63, 2.50)	1.54 (0.57, 2.51)	1.05 (0.31, 1.80)
Some college or associate's or technical degree	1.01 (–0.007, 2.03)	1.44 (0.38, 2.49)	1.07 (0.26, 1.88)
≥ Bachelor's degree	1.79 (0.63, 2.95)	1.86 (0.66, 3.07)	1.23 (0.31, 2.15)

Continued

TABLE 4— Continued

	b (95% CI)	b (95% CI)	b (95% CI)
Household income, % FPL[a]			
0–99 (Ref)	1	1	1
100–138	−0.05 (−1.54, 1.45)	0.00 (−1.54, 1.55)	0.94 (−0.24, 2.13)
139–400	−0.51 (−1.58, 0.57)	−0.14 (−1.25, 0.97)	1.64 (0.79, 2.49)
> 400	−1.63 (−2.83, −0.43)	−1.06 (−2.31, 0.18)	2.38 (1.43, 3.34)
Health insurance type			
Uninsured (Ref)	1	1	1
Private	−2.65 (−3.82, −1.49)	−2.14 (−3.35, −0.94)	−1.43 (−2.36, −0.51)
Public	−1.73 (−2.92, −0.54)	−1.06 (−2.29, 0.18)	−0.48 (−1.42, 0.47)
Other	−3.39 (−5.78, −0.99)	−3.66 (−6.14, −1.18)	−3.08 (−4.97, −1.18)
Relationship status			
Married, marriage-like, or partnered (Ref)	1	1	1
Romantic relationship	2.71 (1.45, 3.96)	2.89 (1.59, 4.19)	1.42 (0.42, 2.41)
Widowed	1.16 (0.27, 2.05)	0.65 (−0.27, 1.58)	−0.04 (−0.74, 0.67)
Single, divorced, or separated	0.69 (−0.38, 1.75)	0.05 (−1.05, 1.15)	0.07 (−0.77, 0.91)
City			
Atlanta, GA (Ref)	1	1	1
Chicago, IL	1.37 (0.36, 2.38)	1.58 (0.53, 2.63)	0.66 (−0.15, 1.46)
Los Angeles, CA	1.93 (0.92, 2.94)	1.70 (0.66, 2.75)	0.84 (0.040, 1.64)
New Orleans, LA	1.17 (−0.19, 2.53)	0.77 (−0.64, 2.18)	0.90 (−0.18, 1.97)
New York, NY	1.65 (0.64, 2.66)	2.31 (1.27, 3.36)	0.15 (−0.65, 0.95)

Note. CI = confidence interval; FPL = federal poverty level; MSM = men who have sex with men; PROMIS = Patient-Reported Outcomes Measurement Information System; UnCOVER = Uncovering COVID-19 Experiences and Realities; WSW = women who have sex with women. Sample size was n = 3242.

Source. UnCOVER data set 2020.

[a]FPL according to the US Department of Health and Human Services (https://aspe.hhs.gov/prior-hhs-poverty-guidelines-and-federal-register-references).

Mental Health Services Survey.[23] There is also a known lack of culturally competent mental health care providers for LGBTQ+ people.[24] It is essential that providers get the necessary training to provide affirming and supportive care for this population during the pandemic.

In addition, as many LGBTQ+ people have reported difficulty accessing health care during the pandemic,[22] implementing nontraditional modalities for providing services may be necessary. It is imperative that services, such as telehealth, be strengthened to better reach LGBTQ+ communities to address mental health and substance use during the pandemic. Online and application-based social interaction, support, and networking have been receiving particular attention and interest over the years, particularly during the COVID-19 pandemic.[25,26] Mobile health applications and other virtual services may also be leveraged to further support the mental health of LGBTQ+ people, especially during this period. Delivery of mental health assessments are feasible and acceptable through both short messaging system and mobile-based applications.[27,28]

Limitations

The primary limitation of this study was the nonprobabilistic sampling design. Our findings may be sensitive to selection bias resulting in systematic errors as survey respondents may differ from nonrespondents in ways that matter for measuring the impact of the pandemic on mental health among LGBTQ+ populations. Another limitation is that the study did not ascertain whether people had nonbinary gender identities, were genderqueer, or had agender identities. Furthermore, the survey did not inquire about other possible sexual orientation identities. The characteristics of those participating in survey panels and who are included in provider distribution lists are potentially different from those of the general US population. An additional limitation of the study was the small number of

transgender participants in the survey (n = 19). We recognize that the small number of respondents may result in spurious findings, wide confidence intervals, and results that are not generalizable. When weighing the option of whether to include transgender respondents in the analysis, we determined that we would prefer to include their findings with caution rather than exclude them from the analysis.

With that being said, a strength of the current study is the recruitment of a relatively large sample without the use of sexual orientation, sexual behavior, and gender identity criteria, thus reducing the potential for systematic response bias along this dimension compared with research utilizing more targeted sampling methods. Moreover, the large number of participants we recruited enabled us to disaggregate LGBTQ+ participants, allowing us to provide a more nuanced portrait of this population. Although the number of transgender participants in our study was small (n = 19; 0.59%), their representation in our study is similar to that of the US population estimate (0.60%).[29] While these specific analyses were underpowered and combined all transgender persons into 1 group eliding potential differences across gender and sexual orientation, we are aware of no other studies that have described mental health and substance use among transgender people during the COVID-19 pandemic. Moreover, the average scores of depression, anxiety, and alcohol use in our study sample are similar to national estimates and scores in other studies of the same scale in similar groups.[30–32] We recommend that future studies oversample transgender participants to permit more robust analysis.

Another limitation is the cross-sectional design of this study, which only allowed us to assess mental health during a single period during the pandemic. Moreover, the study was limited to an urban US sample and may not be generalizable to rural LGBTQ+ populations. In addition, as the survey asked questions about past experiences, responses may be subject to participant recall bias. In particular, the questions assessing depression, anxiety, and alcohol use before the pandemic did not have a specific time frame (e.g., past 12 months or lifetime). Still, we were able to infer whether the snapshots we obtained represent a change from levels before the pandemic through self-report. Regardless, deducing causality was not the aim of this observational study.

Conclusions

Our study contributes to the COVID-19 literature by characterizing disparities in mental health and alcohol use during the pandemic between cisgender LGBTQ+ and cisgender straight people. By using self-identification and behavioral dimensions of LGBTQ+ identity, our study characterizes mental health and alcohol use among LGBTQ+ people during the pandemic in a way that most epidemiological surveillance data have not yet done. Our findings highlight the need for future health research to disaggregate data on LGBTQ+ populations. Future research needs to expand surveillance efforts to include assessment of sexual identity, sexual behavior, and gender identity to better understand the concurrent and long-term impact of the COVID-19 pandemic on health inequities experienced by LGBTQ+ people.[33] Such research may also inform strategies to support LGBTQ+ mental health and substance use prevention. Sexual orientation and gender identity data should be routinely collected during the COVID-19 pandemic and beyond. National collection of sexual orientation and gender identity data will allow for future research to explicitly examine LGBTQ+ people's experiences during the COVID-19 pandemic contributing to the understanding of how and why inequities in mental health and substance use outcomes occur among sexual identity, sexual behavior, and gender identity groups. AJPH

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CONTRIBUTORS

E. R. Akré and A. Anderson conceptualized the presented idea. D. H. Chae supported the development of the theory, and E. R. Akré and A. Anderson performed the analysis. E. R. Akré and N. A. VanKim verified the analytical methods. K. W. Chung designed the tables. E. R. Akré, A. Anderson, K. Stojanovski, and D. H. Chae contributed to the interpretation of the results. E. R. Akré took the lead in writing the article. All authors provided critical feedback, helped shape the research, and

commented on the article. D. H. Chae supervised the findings of this work.

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CONFLICTS OF INTEREST

The authors have no conflict of interest to declare.

HUMAN PARTICIPANT PROTECTION

The Tulane Institutional Review Board and Human Protection Resource Office deemed this study to be exempt from human participant review because the research conducted only included interactions involving survey procedures, and (a) the information collected cannot be used to readily identify participants, and (b) any disclosure of responses outside would not reasonably place participants at risk.

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Structural Transphobia, Homophobia, and Biphobia in Public Health Practice: The Example of COVID-19 Surveillance

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See also Bowleg and Landers, p. 1604.

Public health surveillance can have profound impacts on the health of populations, with COVID-19 surveillance offering an illuminating example. Surveillance surrounding COVID-19 testing, confirmed cases, and deaths has provided essential information to public health professionals about how to minimize morbidity and mortality.

In the United States, surveillance has also pointed out how populations, on the basis of geography, age, and race and ethnicity, are being impacted disproportionately, allowing targeted intervention and evaluation. However, COVID-19 surveillance has also highlighted how the public health surveillance system fails some communities, including sexual and gender minorities. This failure has come about because of the haphazard and disorganized way disease reporting data are collected, analyzed, and reported in the United States, and the structural homophobia, transphobia, and biphobia acting within these systems.

We provide recommendations for addressing these concerns after examining experiences collecting race data in COVID-19 surveillance and attempts in Pennsylvania and California to incorporate sexual orientation and gender identity variables into their pandemic surveillance efforts. (*Am J Public Health*. 2021;111(9):1620–1626. https://doi.org/10.2105/AJPH.2021.306277)

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At the time of this writing, after having reviewed publications and public health and press Web sites, and after discussions with experts in the field, we can report that not a single public health surveillance reporting system at any level (e.g., local, state, or federal) in the United States has publicly reported the impact of COVID-19 on sexual or gender minorities (SGMs). This is more than a year since the first-reported COVID-19 case in the United States and despite literature documenting higher rates of COVID-19 risk factors among SGM communities providing a compelling argument that SGM people may be disproportionately burdened by COVID-19. SGM communities have consequently had to estimate the impact of COVID-19 by extrapolating from data in other studies on the prevalence of underlying risk factors for COVID-19 infection. This extrapolation process, which requires major assumptions, is how SGM communities have had to confront every public health emergency they have faced in the past 50 years.

Of the 10 medical conditions identified by the Centers for Disease Control and Prevention (CDC) as risk factors for severe illness from the virus that causes COVID-19, there is evidence that lesbian, gay, bisexual, and transgender (LGBT) people are at higher risk than the general population for nearly all of them.[1] These risk factors include smoking; lung, anal, and breast cancer; chronic obstructive pulmonary disease; heart conditions; obesity; type 2 diabetes mellitus; and immunocompromised state.[2–9] Despite documented higher rates of these risk factors among SGM communities, federal, state, and local agencies in charge of monitoring infectious diseases have almost universally failed to collect the data necessary to determine and lessen the impact of COVID-19 infection in these

communities. Excluding SGM communities from public health data collection has previously been identified as public health malpractice.[10] The spread of COVID-19 in these communities provides a tangible case study of the consequences of this continuing malpractice.

The influence data can have on policies, programs, and funding is evidenced in our response to COVID-19 for populations for which data are available. Race, ethnicity, age, and socioeconomic status have all been shown to be independently and together associated with COVID-19–related infections and deaths.[11] While these data are often incomplete, existing data have brought a spotlight on how some populations are differentially impacted and interrelated. However, for SGMs, these data are not just incomplete, they are nonexistent. The need to determine the toll of COVID-19 on SGM communities is pressing, as well as a determination of how these population characteristics interact and compound with each other. For example, Black transgender individuals are almost certainly likely to experience COVID-19 very differently from White cisgender gay, lesbian, and bisexual people because of systemic racism and transphobia.[1]

At the beginning of the pandemic, more than 100 lesbian, gay, bisexual, transgender, and queer (LGBTQ) and ally organizations, including the Gay and Lesbian Medical Association, Fenway Health, Whitman Walker Health, SAGE, the New York Transgender Advocacy Group, and the National Queer Asian Pacific Islander Alliance signed an open letter aimed at health professionals and the media highlighting the increased risks of COVID-19 infection in SGMs. The letter writers provided extensive suggestions for community-based organizations, health care centers, medical professionals, and the media that have not been met, including "Ensuring surveillance efforts capture sexual orientation and gender identity as part of routine demographics."[12] A second letter was issued in April 2020 with 170 allied organizations urging the collection of sexual orientation and gender identity (SOGI) data, yet SOGI data collection is still barely occurring.[13]

Because SOGI variables are rarely ever included in public health data collection efforts, public health experts investigating the health of these communities are almost always left to make conjectures about diseases such as COVID-19 on the basis of limited information about these communities in other areas of health. The concern expressed in the letter described previously is one such instance in which community members, knowing the risk factors for a new disease, surmised a need to respond.

For example, one risk factor that disproportionately affects SGM communities is smoking. COVID-19 is a respiratory infection, and smoking increases the likelihood of severe COVID-19. Lesbian, gay, and bisexual (LGB) people in the United States are 1.52 times more likely to report current cigarette use than non-LGB people.[14] This not only places LGB persons at elevated risk for severe COVID-19 infection, but also for lung cancer, liver cancer, colorectal cancer, prostate cancer, breast cancer, cardiovascular disease, chronic obstructive pulmonary disease, and type 2 diabetes, which are further risk factors for severe COVID-19 infection.[15] LGBT people also have higher rates of asthma, another respiratory condition that may increase risk of severe COVID-19 infection (21% in LGBT adults vs 14% in non-LGBT adults).[16,17]

Very few studies have been conducted on HIV-infected individuals with COVID-19. However, people with HIV infection are more likely to have serious chronic medical issues, including cardiovascular and lung disease, immune suppression, and other chronic conditions that arise with old age.[18,19] All of these medical conditions place one at higher risk for severe COVID-19 infection. Mirzaei et al. note that while HIV-positive people had similar risk factors to HIV-negative people for COVID-19 infection, severe morbidity and mortality co-occurring in HIV and COVID-19 infection were most affected by the presence of multiple diseases and age.[20] A second 2020 study found that severe clinical outcomes were common among patients with HIV diagnosed with COVID-19. Risk for severe COVID-19 infection among HIV-positive individuals was higher for those with comorbidities and low CD4 cell counts[18]

In addition to the previously mentioned concerns, sexual minorities are at greater risk for hypertension and cardiovascular disease. A review conducted by Caceres et al. on cardiovascular disease in SGMs found that sexual-minority men and women are at elevated risk for heart disease.[5] Heart conditions and hypertension are other medical conditions identified by the CDC that lead to increased risk of severe COVID-19 infection.

Furthermore, there are also social determinants and inequities that put SGM people at higher risk for infection and other harms during the COVID-19 pandemic. These social determinants and social inequities faced by SGM people are clear, obvious, and have been well documented for decades. For example, SGMs are health insured at

lower rates than cisgender heterosexual people and have higher poverty rates, and nearly 1 in 10 LGBT individuals are unemployed.[16,21–23] This results in decreased access to lifesaving care such as HIV medications and gender-confirming surgery for transgender individuals.[8]

Another cause for concern is that 40% of LGBT people work in service jobs as opposed to 22% of cisgender heterosexuals.[23] LGBT persons are more likely to lose their jobs as industries shut down, putting them at greater risk for job insecurity and poverty.[8] In addition, LGBT individuals that have remained in the workforce during the pandemic are more likely to be in physical contact with people during the pandemic, which places them at higher risk for COVID-19 infection. Furthermore, transphobia, homophobia, and biphobia in the workplace decreases access to social services and fosters an unsupportive environment, which can lead to poor health outcomes.[8,24]

Social isolation and parental and family rejection are also potential COVID-19 risk factors disproportionately affecting SGMs. These problems can lead to a cascade of negative mental health effects, especially in younger populations and the elderly.[22,25] Because many schools have closed, SGM youths are forced home to live with often unsupportive families and lose access to various school supports. It has been estimated that one third of LGBT youths experience parental rejection.[23] LGBT youths who are rejected by their families are 8 times more likely to attempt suicide and 6 times more likely to have depression.[23] Parental rejection often forces youths out of their homes, which we see reflected in rates of homelessness, which disproportionately affects SGMs.[8,25] In addition, LGB adults have 3 times greater risk for opioid use disorder than heterosexual adults.[26]

Older LGBT individuals are more likely to be single, living alone, and estranged from their biological families. It has been estimated that there are 2.7 million LGBT adults aged older than 50 years in the United States.[27] Isolation and lack of familial and social support are all significant burdens facing older LGBT people.[23] In addition, older lesbian, gay, bisexual, transgender, and queer plus (LGBTQ+) individuals are less likely to seek medical attention, are less likely to have a primary care provider, and may fear discrimination from health care providers—all of which present significant barriers to accessing health care.[28]

It is also important to note the lack of homogeneity among SMG populations to understand how LGBT individuals experience various health outcomes. Not only are cisgender lesbians likely to have different health experiences than transgender lesbians, but there will also be differences across other characteristics such as race and ethnicity. For example, gay and bisexual men are the population most heavily impacted by HIV and made up 69% of new HIV infections in 2018.[6] When broken down by race/ethnicity, Black/African American gay and bisexual men made up 37% of new diagnosis, followed by Hispanic/Latino gay and bisexual men at 30%, followed by White gay and bisexual men at 27%. Having all of the aforementioned variables would illuminate COVID-19–related health disparities by SGM status and race and ethnicity.

We could easily expand upon this brief review of risk factors for contracting COVID-19 and for worse outcomes resulting from COVID-19 infections in SGMs, but the indirect evidence presented here should engender tremendous concern among all public health professionals. It certainly has incited intense concern among public health professionals who focus on the health of SGMs, as well as within these communities.

Unfortunately, as is most often the case for investigating the health of SGMs, in this review, we have had to rely on indirect data and deductive reasoning to understand an emerging health concern. But deductive reasoning only gives us a blurry window into actual concerns and needs. We are left wondering, once again, how our response to an epic public health tragedy would have played out if better data were available. The absence of SOGI variables in public health surveillance systems is public health malpractice that was predicted and should have been averted.

COVID-19 SURVEILLANCE IN THE UNITED STATES

Summarizing the current COVID-19 data collection and surveillance system is no easy task. The public health surveillance system in the United States was constructed in a piecemeal manner over the past century as technology, culture, and public health needs shifted, resulting in multiple data collection channels and reporting pathways. While case and mortality data for COVID-19 are reported to the CDC through separate surveillance systems (National Notifiable Disease Surveillance System and the National Vital Statistics System, respectively), laboratories are required to report data to the Department of Health and Human Services (HHS).[29,30] Although data can be submitted directly to HHS, data can also be sent to state health departments or officials first, adding a second step. Data can also be

submitted through Teletracking, a patient flow automation system.[31] Clearly, the current system allows substantial room for error, being decentralized across 50 states and territories, and with no centralized data collection pathway. Other limitations include incomplete case reporting data, incomplete laboratory data streams with diagnostic data compiled from a variety of sources, and critical information missing in mortality data, including race and ethnicity data.[30]

THE EXAMPLE OF RACE AND ETHNICITY DATA

Previous research on health inequities for Black Americans and other race and ethnicity groups in the United States combined with data on race and ethnicity reported during the COVID-19 pandemic has led researchers and academics to conclude that Black Americans in particular are at higher risk for COVID-19 infection and death because of factors such as racism, housing inequities (i.e., crowding housing conditions where people cannot socially distance), lack of access to health care, and higher rates of employment in the service industry. Given past atrocities perpetrated by some within the medical community and the current negative effects of systemic racism on Black health, it is imperative that the medical community earn the trust of Black Americans seeking care and continue education and outreach. The COVID-19 vaccination campaign provides an opportune moment to do so. For example, concordant messaging from Black doctors increases information-seeking behavior among Black communities.[32] As a result of these findings, research has been conducted to increase our knowledge of COVID-19 infection in Black Americans in the United States, and there are health and policy recommendations to reduce COVID-19 infection in this population, as well as efforts to foster education and provide resources at the local and the national level among the Black population.[33,34] Ethnicity is another important social determinant of health, as Hispanic/Latinx individuals in the United States are hospitalized at more than 3 times the rate as White individuals for COVID-19 infection and experience an infection rate that is 1.3 times higher. This is of concern given the growing Hispanic/Latinx population in the United States.

The guidance, policies, and laws that dictate the collection of race and ethnicity data in existing systems are helpful models for understanding how SOGI data can also be collected and reported. Numerous guidelines pertain to the collection of race data in public health surveillance with the most recent, in relationship to COVID-19, being issued on June 4, 2020. This guidance requires the collection of demographic data including race "to ensure that all groups have equitable access to testing, and allow us to accurately determine the burden of infection on vulnerable groups."[35]

Despite guidance and years of efforts to include valid and reliable measures of race and ethnicity in surveillance data, the systems used to monitor disease in the United States are failing. As has been historically the case with the reporting of other diseases, race data are frequently missing, and, when collected, they are not collected in standard categories or using methods that have been evaluated to minimize error. Krieger et al. reported that data on race were missing for 50% of individuals included in the CDC COVID Data Tracker as of September 16, 2020.[36] Reporting of race data has only improved slightly in the 5 months since then, with 48% of cases missing race/ethnicity data at the beginning of March 2021. Furthermore, data reporting from The COVID Tracking Project indicates that some of the states with the most missing data might have higher concentrations of racial and ethnic minorities, indicating that the impact of COVID-19 in Black communities might be underestimated.[37]

It is imperative to examine effects of COVID-19 for those marginalized by race in addition to their SGM status, as there is evidence that individuals with double or triple minority status experience disproportionate morbidity. Data from The Williams Institute at the University of California, Los Angeles found that LGBT people of color are twice as likely as White LGBT individuals to test positive for COVID-19, highlighting the increased risk for those who live at the intersection of racial minority and SGM status.[38] In addition, the CDC's *Morbidity and Mortality Weekly Report* published an analysis on COVID-19 in February of 2021 on outcomes for SGM by race/ethnicity. The authors concluded that risk for COVID-19 may be magnified for non-White SGMs. Furthermore, they acknowledged that the data are not being collected, and emphasized the need for intersectional SGM data to improve health equity.[1]

INADEQUATE PROGRESS IN DATA COLLECTION

Because years of systemic discrimination and oppression in the United States are reflected in our health care and medical system, there are currently no data being collected on COVID-19

testing, infection rates, or deaths among SGMs, with the exception of Pennsylvania, California, District of Columbia, and Illinois, whose efforts have not yielded publicly reported findings at the time of this writing. More than 500 000 people have died from COVID-19 infection to date, yet we have no information regarding how many of them were SGM individuals.[11] The federal government's lack of initiative and action in regard to collecting SGM data in COVID-19–infected patients as well as through contact tracing demonstrates negligence given the concerns described previously.

Only Pennsylvania, California, Illinois, and the District of Columbia have made attempts to collect SOGI data in any part of their COVID-19 surveillance systems. The Illinois Behavioral Risk Factor Surveillance System survey had existing questions on SOGI, and, in 2020, a module on COVID-19 was added. While the District of Columbia is said to be collecting SOGI data, there is little evidence of this, and no data are available.[1] These limited attempts provide models that can be evaluated and potentially used elsewhere.

Pennsylvania initiated a systematic data collection process through governor Tom Wolf's orders. The state acted swiftly and announced the data collection program on March 13, 2020.[39] The Pennsylvania Department of Health, which uses Sara Alert for case surveillance, case investigation, and contract tracing, has been modified to include questions on SOGI.[40] In addition, the Pennsylvania Department of Health requested that the eHealth Authority Board of Pennsylvania require the state's 6 health information centers to gather data on SOGI by using electronic medical records. We could not find any publicly reported results from these data collection efforts. Nonetheless, Pennsylvania's commitment and eventual success in gathering SOGI data should be evaluated as a possible model for other states.

In California, we see a second strategy—the introduction of SOGI data collection through state-level legislation. California Governor Gavin Newsom signed Senate Bill 932 on September 26, 2020. The bill requires an option to collect data on sexual orientation and gender minority status when gathering data and reporting cases of communicable diseases, including COVID-19.[41] This is an important success as California is the first state to pass a law that requires SGM data collection for all communicable diseases. Still, there are major concerns with waiting for legislation to be passed to address SOGI data collection.

In addition, in July of 2020, Health and Human Services of California set forth emergency legislation that required local health departments and providers to collect SOGI data given voluntarily to understand the effects of COVID-19 on SGM populations.[1]

California State Senator Scott Weiner expressed his frustrations with needing legislation in California to start SOGI data collection saying:

> I wish I had not been forced to introduce this legislation . . . . I usually don't say that. This is frankly an issue that should've been taken care of already . . . . Frankly, even without the law, or a law, the State of California and our counties, and our healthcare providers should already be collecting this data.[42]

Senator Weiner brings up 2 key points: (1) the importance of collecting SGM data has been made clear by empirical evidence and human rights organizations, and it should be a given that these data would be collected during the COVID-19 pandemic, and (2) that there can and should be local efforts in a state to collect SOGI data even when we do not see movement at the state or federal level. Unfortunately, despite clear need for SOGI data, New York, California, Oregon, New Jersey, and the District of Columbia are the only places where SOGI data collection is mandated for any purpose other than hate crimes.[1,43] Weiner also commented that there is also no data collection around hospitalization and death rates for LGBT people. Furthermore, he concluded that SGMs are often an afterthought even though we have the means and resources to collect these important data.[42]

We note here that executive orders (as in Pennsylvania) and legislation (as in California) are only the first step toward data collection. The process of implementing questions on sexuality and gender, training health professionals, and monitoring data for accuracy and quality is not an insignificant undertaking as is evidenced in the collection of race and ethnicity data which has not fulfilled existing recommendations.

RECOMMENDATIONS

The public health surveillance system's noncollection of SOGI data is public health malpractice and also evidence of structural homophobia, biphobia, and transphobia. These concerns were identified long before the emergence of COVID-19, which emphasizes the harmful impact these problems can have on SGM communities when not addressed or even publicly recognized by the people and agencies that control public health surveillance systems.

There are not easy fixes to these problems because the system itself is broken, as evidenced by the haphazard and incomplete collection of race data. However, steps must be taken to begin recognizing the concerns of SGMs. While we recommend that the CDC and other public health surveillance experts begin to think about modern ways to overhaul the systems that are failing so many marginalized communities, steps can be taken within the confines of the existing system to right some historic wrongs.

First, we recommend that HHS and CDC issue guidance about the collection of SOGI data like their guidance on race and ethnicity data in relationship to COVID-19. We also recommend that research be funded to further the development of valid and reliable measures of sexual orientation identity and gender identity, as well as pilot studies testing the collection of these data in surveillance systems that can eventually be scaled up to the federal level. In the meantime, states, like Pennsylvania and California, can take the lead by implementing SOGI data collection efforts, and consequently serve as examples for other states and the federal government as they develop models to ensure the next public health emergency fully addresses the concerns of SGM populations otherwise overlooked. AJPH AJPH

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Health Data Disparities in Opioid-Involved Overdose Deaths From 1999 to 2018 in the United States

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Objectives. To examine temporal trends in the classification of opioid-involved overdose deaths (OODs) and racial variation in the classification of specific types of opioids used.

Methods. We analyzed OODs coded as other or unspecified narcotics from 1999 to 2018 in the United States using data from the National Vital Statistics System and the Centers for Disease Control and Prevention.

Results. The total proportion of OODs from unspecified narcotics decreased from 32.4% in 1999 to 1.9% in 2018. The proportion of OODs from unspecified narcotics among African American persons was approximately 2-fold greater than that of non-Hispanic White persons until 2012. Similarly, the proportion of OODs from unspecified narcotics among Hispanic persons was greater than that of White persons until 2015. After we controlled for death investigation system, African American persons had a higher incidence rate of OODs from unspecified narcotics compared with White persons.

Conclusions. There have been significant improvements in the specification OODs over the past 20 years, and there has been significant racial disparity in the classification of OODs until about 2015. The findings suggest a health data disparity; the excessive misclassification of OODs is likely attributable to the race/ethnicity of the decedent. (*Am J Public Health*. Published online ahead of print June 29, 2021:e1627–e1635. https://doi.org/10.2105/AJPH.2021.306322)

White persons have higher rates of opioid use and opioid-involved overdose deaths (OODs) compared with African American persons.[1,2] The higher rate of opioid use among White persons is in part attributed to racial differences in prescribing practices.[3,4] There is preliminary evidence that suggests that population-adjusted rates of opioid use among African American persons is approaching that of non-Hispanic White persons.[5,6] Nationally, there has been a rapid change in the illicit opioid supply, particularly illicitly manufactured fentanyl and fentanyl analogs (i.e., synthetic opioids).[7,8] Although initially mixed with heroin, illicitly manufactured fentanyl is increasingly being found in supplies of cocaine, methamphetamine, and counterfeit prescription pills, which increases the number of populations at risk for an opioid-involved overdose.[9,10] This is also reflected by the growth in OODs; the annual percent change in OODs among African American persons now outpaces White persons.[6,11] The convergence of OOD rates among African American persons with White persons may additionally be explained, in part, by the inequitable allocation of prevention and intervention resources.[11]

Typically, when an overdose death occurs, coroners or medical examiners determine the cause of death and complete a death certificate. The information listed on the death certificate is then coded according to the guidelines of the *International Classification of Diseases, Tenth Revision* (*ICD-10*) to allow standardized classification and analysis of the causes of death.[12] The actual coding of the medical information on the death certificates is done by the National Center for Health Statistics (NCHS) using software that automates and standardizes the process.[13] For deaths involving opioid analgesics, this process is less than perfect for surveillance purposes because coroners and medical examiners exercise varying approaches to recording the drug's contribution to the

death on the death certificate. Among deaths with drug overdose as the underlying cause, the type of opioid is indicated by the following *ICD-10* multiple cause-of-death codes: opium (T40.0), heroin (T40.1), natural and semisynthetic opioids (T40.2), methadone (T40.3), synthetic opioids other than methadone (T40.4), and other and unspecified narcotics (T40.6).[14] OODs that are missing the opioid involved in the death because of lack of sufficient toxicological testing or failure to record the results from the toxicological testing are assigned the T40.6 *ICD-10* multiple cause-of-death code (used interchangeably as "other or unspecified narcotic" and "unspecified opioid"), essentially a misclassification of the OOD.[15] When there is no information on the drug involved in the overdose death, the T50.9 *ICD-10* code (other and unspecified drugs, medicaments, and biological substance) is used.[15]

Evidence-informed preventive and treatment strategies are often absent or inconsistently implemented in African American communities; a lack of quality data may contribute to the dearth of preventive strategies. African American persons are less likely to be recommended psychiatric or addiction treatment services after clinical evidence of an intentional drug overdose, including those related to opioids.[16] Studies have shown that African American persons are less likely to access or receive targeted medications for opioid use disorder such as buprenorphine and methadone[7] as well as naloxone, which have been shown to reduce OODs.[4] In addition, there has been a steady decline in the availability of publicly funded substance use disorder treatment centers; this decline has been most apparent in counties with larger percentages of African American residents.[17]

Compounding the issue, compared with privately funded substance use treatment programs, publicly funded programs are less likely to have a physician on staff and have lower utilization rates of US Food and Drug Administration–approved medications for substance use disorders.[18] Nationally representative data demonstrate that buprenorphine treatment is concentrated among White persons and those with private insurance or who self-pay.[19]

Resources to decrease and treat opioid misuse and prevent OODs should be culturally competent, include special populations, and be allocated on the basis of need; these factors require valid and reliable data.[20] VanHouten et al. suggested that gender-responsive and -specific interventions may be needed given the changing trends of opioid misuse among women aged 30 to 64 years; there were larger increases in prescription opioid misuse among this population over time but no increases in synthetic opioid use.[21] Hadland et al. recently highlighted the national paucity of opioid use disorder treatment facilities with programming for pregnant and postpartum women, and programs for adolescents are limited.[22] Without a health equity–focused lens, these important differences by gender and age would be missed. We examined racial disparities in OODs from unspecified narcotics. The lack of data (or misclassification of data) may hinder the development of effective and targeted prevention and intervention efforts to reduce OODs.

METHODS

We obtained the count of OODs from the National Vital Statistics System (NVSS) Multiple Cause of Death (inclusive of Underlying Cause of Death) public use data files from 1999 to 2018.[13] We calculated age-adjusted death rates with population totals obtained from the Centers for Disease Control and Prevention (CDC) Wide-ranging Online Data for Epidemiologic Research (WONDER).[23] We calculated age-adjusted death rates based on the direct method by the NCHS. We calculated age-adjusted death rate by applying age-specific crude death rates (R_i) to the US standard population age distribution:

$$(1) \qquad \sum \left(\frac{P_{si}}{P_s}\right) R_i$$

where P_{si} is the standard population for age group i, and P_s is the total US standard population (all ages combined). NCHS adopted the year-2000 population of the United States as the standard population. The CDC WONDER considers death counts of 20 or fewer unreliable for statistical analysis, so death counts of 20 or fewer were suppressed.

Drug overdose deaths are based on the following *ICD-10* underlying causes of death: X40–X44 (unintentional), X60–X64 (suicide), X85 (homicide), or Y10–Y14 (undetermined intent). Among deaths with drug overdose as the underlying cause, OOD is indicated by the following *ICD-10* multiple cause-of-death codes: T40.0 (opium), T40.1 (heroin), T40.2 (natural/semisynthetic opioids), T40.3 (methadone), T40.4 (synthetic opioids), and T40.6 (other and unspecified narcotics).[6] OODs that are missing the opioid involved in the death due lack of sufficient toxicological testing or failure to record the results from the toxicological testing are assigned the T40.6 *ICD-10* multiple cause-of-death code.[15]

The current study focused on OODs with the *ICD-10* multiple cause-of-death code T40.6 "other or unspecified narcotics," herein referred to as

unspecified narcotics. The NVSS allows the selection or exclusion of multiple causes of death; for this study we only included OODs from unspecified narcotics (i.e., T40.6), excluding T40.0 to T40.4 *ICD-10* codes (i.e., OODs from specific opioids). Previous investigations have examined racial differences in OODs (i.e., T40.0–T40.6)[11]; this investigation sought to examine racial/ethnic differences in the misclassification of OODs (i.e., T40.6).

To explore possible differences in OOD classification by death investigation system, we obtained death investigation systems by state for 2015 from the CDC.[24] The death investigation systems include centralized medical examiners (n = 16 states), county- or district-based medical examiner systems (n = 6), county-based systems with a mixture of coroner and medical examiner offices (n = 14), and county-, district-, or parish-based coroner systems (n = 14; Table A, available as a supplement to the online version of this article at http://www.ajph.org).

We calculated the number of OODs from unspecified narcotics separately for the total population and stratified by race and ethnicity (i.e., non-Hispanic White, non-Hispanic African American, and Hispanic) from 1999 to 2018 using NVSS Mortality Multiple Cause Files. We used the χ^2 test to compare the annual proportion of deaths from unspecified narcotics among all OODs between non-Hispanic African American (now referred to as African American), non-Hispanic White (now referred to as White), and Hispanic persons over time (Table 1). We used Bonferroni correction to correct *P* values because of pairwise comparisons; adjusted *P* values are presented.

We used Joinpoint Regression Program (version 4.5.0.1; National Cancer Institute, Bethesda, MD) to examine the trends in age-adjusted death rates attributable to unspecified narcotics (i.e., annual percent change [APC]) by race and ethnicity from 1999 to 2018. APC assumes constant percentage change every year on a log scale until a shift in slope occurs. The APC within 2 adjacent joinpoints is calculated as

$$(2) \qquad APC = (e^{\beta} - 1) \times 100$$

Coefficient (b) is the estimated average change (slope) obtained from linear regression:

$$(3) \qquad \log(y) = \alpha + \beta w$$

where *y* is the age-adjusted death rates, and *w* is number of years within 2 adjacent joinpoints. Here, b captures the fixed effect of time on age-adjusted death rates. The Joinpoint model uses the Akaike information criterion and Bayesian information criterion to determine when and how often the APC changes (number of joinpoints).

We used generalized estimating equations with negative binomial link to examine the relationship between race/ethnicity and OODs from unspecified narcotics by state, controlling for the death investigation system. Given the limited number of OODs from unspecified narcotics by race/ethnicity and state, we aggregated the number of OODs from unspecified narcotics by 2 ten-year periods: 1999–2008 and 2009–2018. We used the logarithm of all OODs by race/ethnicity as an offset variable to estimate the incidence rate of OODs from unspecified narcotics among all OODs. Significant findings are reported for α levels below 0.05.

RESULTS

Table 1 shows the number of OODs in the United States from unspecified narcotics and the proportions of these deaths among total OODs by race/ethnicity for 1999 to 2018. The total proportion of OODs from unspecified narcotics in the United States decreased from 32.4% in 1999 to 1.9% in 2018. While the proportion of OODs classified as unspecified narcotics has decreased over time, the proportion of OODs from unspecified narcotics among African American persons was approximately 2-fold greater than that of White persons until 2012, and the difference was significantly higher until 2013 (χ^2 test, 2.1%–28.5% higher; $P < .01$). For example, in 1999, the proportion of OODs from unspecified narcotics among African American persons was 56.0% compared with 27.5% among White persons (χ^2 test $P < .01$). African American persons continued to have a statistically significantly higher proportion of OODs classified as unspecified narcotics until 2013 ($P \leq .01$ in each year). From 2014 to 2018, the differences in proportion of OODs from unspecified narcotics dropped below 10% for White and African American persons, and there was no statistically significant difference in unspecified narcotics classification ($P > .05$).

Hispanic persons also had a greater proportion of OODs from unspecified narcotics compared with White persons until 2015 (1.3% to 11.2% higher; $P < .05$), the difference was not statistically significant from 2016 to 2018. Hispanic persons had a lower proportion of OODs from unspecified narcotics compared with African American persons until 2012 (1.6% to 23.6% lower; $P < .01$); from 2013 to 2016 the proportion of OODs from unspecified narcotics was higher in Hispanic compared with African American persons (0.5% to 1.0% higher; $P < .05$).

Figure 1 shows racial/ethnic variation in the trends in age-adjusted OOD rates classified as unspecified narcotics from

TABLE 1— Number of Opioid-Involved Overdose Deaths From Unspecified Narcotics and Proportions Among Total Opioid-Involved Overdose Deaths by Race/Ethnicity: United States, 1999–2018

	OOD From Unspecified Narcotics, No.,[a] (%)[b]				*P*		
Year	United States	White Persons	African American Persons	Hispanic Persons	White vs African American Persons[c]	White vs Hispanic Persons[d]	African American vs Hispanic Persons[e]
1999	2609 (32.4)	1561 (27.5)	633 (56.0)	343 (32.4)	< .01	< .01	.06
2000	2559 (30.4)	1573 (25.3)	607 (53.2)	317 (36.5)	< .01	< .01	< .01
2001	2539 (26.7)	1635 (22.4)	551 (49.1)	292 (33.4)	< .01	< .01	< .01
2002	2752 (23.1)	1864 (19.9)	532 (43.3)	299 (27.6)	< .01	< .01	< .01
2003	2703 (20.9)	1797 (17.4)	536 (44.4)	322 (27.7)	< .01	< .01	< .01
2004	2307 (16.8)	1628 (14.4)	374 (33.5)	254 (24.2)	< .01	< .01	< .01
2005	2348 (15.7)	1655 (13.5)	352 (28.8)	286 (24.5)	< .01	< .01	< .01
2006	2207 (12.6)	1577 (11.0)	341 (22.2)	251 (19.1)	< .01	< .01	< .01
2007	2125 (11.5)	1535 (9.9)	318 (24.1)	231 (17.0)	< .01	< .01	< .01
2008	2275 (11.6)	1682 (10.3)	292 (22.6)	255 (17.2)	< .01	< .01	< .01
2009	2100 (10.3)	1583 (9.3)	254 (18.4)	215 (14.6)	< .01	< .01	< .01
2010	1934 (9.2)	1492 (8.3)	209 (15.6)	192 (14.0)	< .01	< .01	< .01
2011	2196 (9.6)	1667 (8.7)	251 (16.9)	226 (13.8)	< .01	< .01	< .01
2012	2130 (9.2)	1601 (8.3)	258 (15.9)	205 (11.9)	< .01	< .01	< .01
2013	1899 (7.6)	1488 (7.2)	179 (9.3)	198 (10.1)	.01	< .01	< .01
2014	1528 (5.3)	1223 (5.2)	131 (5.7)	141 (6.7)	.99	.048	.019
2015	1545 (4.7)	1218 (4.5)	135 (4.9)	145 (5.8)	.99	.049	.019
2016	1471 (3.5)	1128 (3.4)	166 (3.8)	147 (4.3)	.53	.050	.028
2017	1206 (2.5)	929 (2.5)	139 (2.5)	106 (2.7)	.99	.99	.99
2018	877 (1.9)	650 (1.8)	102 (1.7)	102 (2.3)	.99	.13	.09

Note. OOD = opioid-involved overdose death.

[a]Number of deaths from unspecified narcotics is counted as the number of deaths in which *International Classification of Diseases, Tenth Revision* (*ICD-10*) codes[12] for underlying causes are X40–X44, X60–X64, X85, or Y10–Y14 with multiple causes including T40.6 and excluding T40.0–T40.4.
[b]Number of OODs are the number of deaths in which *ICD-10* codes[12] for underlying causes are X40–X44, X60–X64, X85, and Y10–Y14 with multiple causes including T40.0–T40.4 and T40.6.
[c]*P* values were obtained by χ^2 test for 2 samples (non-Hispanic White vs non-Hispanic African American) proportions of OODs from unspecified narcotics among all OODs with Bonferroni correction.
[d]*P* values were obtained by χ^2 test for 2 samples (non-Hispanic White vs Hispanic) proportions of OODs from unspecified narcotics among all OODs with Bonferroni correction.
[e]*P* values were obtained by χ^2 test for 2 samples (non-Hispanic African American vs Hispanic) proportions of OODs from unspecified narcotics among all OODs with Bonferroni correction.

1999 to 2018. Among African American persons, the age-adjusted OOD rate attributable to unspecified narcotics was 1.83 per 100 000 in 1999 and decreased steadily over time to 0.22 per 100 000 in 2018. The APC was −9.71 ($P < .01$) with no change in the slope from 1999 to 2018. Among Hispanic persons, the age-adjusted OOD rate attributable to unspecified narcotics was 1.01 per 100 000 in 1999 and decreased steadily over time to 0.17 per 100 000 in 2018. The APC was −8.00 ($P < .01$) with no change in the slope from 1999 to 2018. Among White persons, the age-adjusted OOD rate attributable to unspecified narcotics was as 0.80 per 100 000 in 1999; the rate decreased to 0.65 per 100 000 in 2013 with an APC of −0.74 ($P = .16$). There was 1 joinpoint in 2013, with an accelerated decrease in APC to −13.38 ($P < .01$). Consistent with the χ^2 tests, the joinpoint analyses suggest a racial/ethnic disparity in OOD classification and an overall improvement in OOD classification over time.

Table 2 shows the proportion of OODs from unspecified narcotics among total OODs by state and race/ethnicity for 1999 to 2008 and 2009 to 2018. From

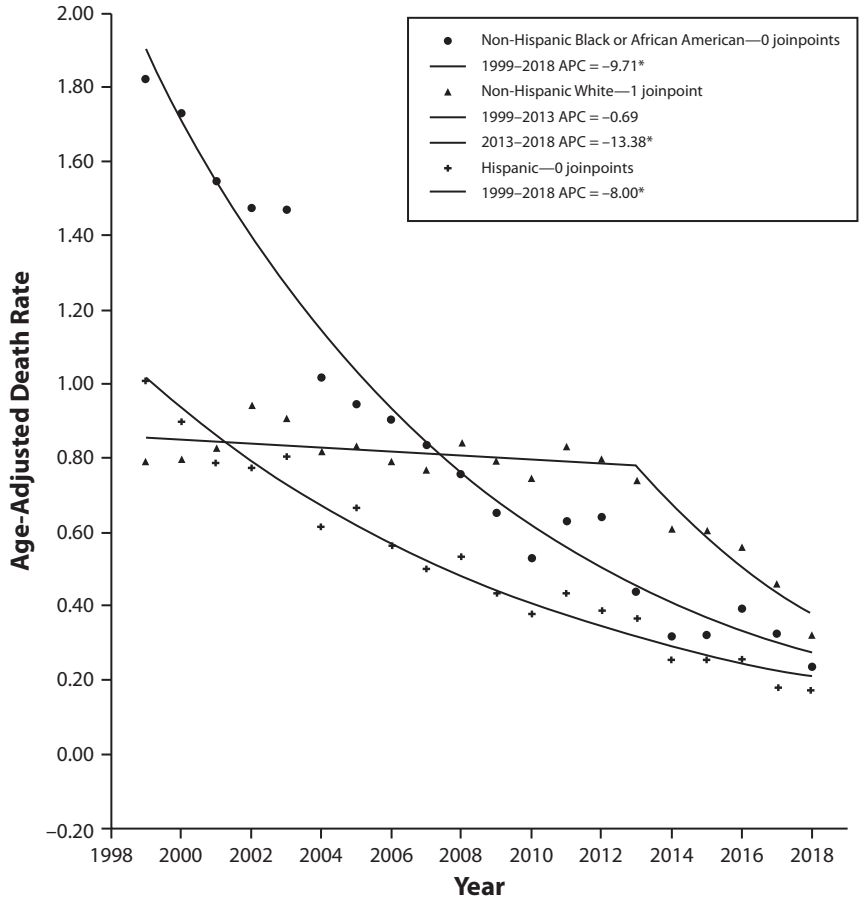

FIGURE 1— Annual Percent Change in Unspecified Narcotic Opioid-Involved Overdose Death Classification by Race/Ethnicity: United States, 1999–2018

Note. APC = annual percent change.

1999 to 2008, 28 states had OODs from unspecified narcotics of 10 or more in both African American and White persons for all years (32 states had death counts of 20 or fewer, which is unreliable for statistical analysis and therefore suppressed). Among these states, African American persons had a higher proportion of OODs from unspecified narcotics among all OODs compared with White persons in 25 states (89.3%). From 2009 to 2018, African American persons had a higher proportion of deaths from unspecified narcotics among OODs in 18 of 28 states (64.3%). From 1999 to 2008, Hispanic persons had a higher proportion of OODs from unspecified narcotics among all OODs compared with White persons in 15 of 16 states (93.8%). From 2009 to 2018, Hispanic persons had a higher proportion of deaths from unspecified narcotics among OODs compared with White persons in 9 of 18 states (50%).

We used generalized estimating equations with negative binomial link to examine the relationship between race/ethnicity (White persons as the reference group), death investigation system (centralized state medical examiner office as the reference group), and OOD classification by state. African American persons had a higher incidence rate of OODs from unspecified narcotics compared with White persons from 1999 to 2008 (incidence rate ratio [IRR] = 2.35; 95% confidence interval [CI] = 1.37, 4.03), but not in the period 2009 to 2018 (IRR = 1.21; 95% CI = 0.74, 1.99) after we controlled for death investigation system (Table 3). There was no significant difference in the incidence rate of OODs from unspecified narcotics when we compared Hispanic to White persons for 1999 to 2008 (IRR = 1.58; 95% CI = 0.89, 2.79) nor 2009 to 2018 (IRR = 1.33; 95% CI = 0.93, 1.90) while we controlled for the death investigation system. In a separate analysis (Table B, available as a supplement to the online version of this article at http://www.ajph.org), African Americans was used as the reference group. The incidence rate comparing Hispanic to African American persons was not statistically significant for 1999 to 2008 (IRR = 0.67; 95% CI = 0.36, 1.24) nor 2009 to 2018 (IRR = 1.10; 95% CI = 0.65, 1.86). Of note, the relationship between death investigation system and the incidence rate of OODs from unspecified narcotics was not statistically significant in either model, indicating that the death investigation system did not explain the incidence rate of OODs from unspecified narcotics.

DISCUSSION

This study revealed 2 important findings; namely, there have been significant improvements in the specification of OODs over the past 20 years, and there has also been a significant racial/ethnic disparity in the classification of OODs until around 2015. From 1999 to 2012, there was an average 2-fold difference in the proportion for African American compared with White persons. After we adjusted for the death investigation systems, African American persons had a higher incidence rate of OODs from

TABLE 2— Proportion of Opioid-Involved Overdose Deaths From Unspecified Narcotics Among Total Opioid-Involved Overdose Deaths by State and Race/Ethnicity: United States, 1999–2008 and 2009–2018

State	Proportion of Deaths From Unspecified Narcotics, %					
	White Persons, 1999–2008	White Persons, 2009–2018	African American Persons, 1999–2008	African American Persons, 2009–2018	Hispanic Persons, 1999–2008	Hispanic Persons, 2009–2018
Alabama	5.2	4.6	. . .	. . .	. . .	. . .
Alaska	12.7	4.1	. . .	. . .	. . .	. . .
Arizona	23.7	8.9	29.6	. . .	35.6	5.8
Arkansas	4.8	4.5	. . .	. . .	. . .	. . .
California	12.7	6.3	14.8	7.4	16.2	8.8
Colorado	22.7	5.5	42.1	13.6	36.5	7.2
Connecticut	14.4	4.6	16.7	. . .	13.8	4.2
Delaware	16.0	7.4	22.7	7.0	. . .	. . .
District of Columbia	40.4	. . .	58.0	5.2	. . .	. . .
Florida	5.1	2.1	6.4	1.8	5.4	2.2
Georgia	10.0	3.4	29.0	4.8	. . .	. . .
Hawaii	9.5	8.1	. . .	. . .	. . .	. . .
Idaho	7.9	5.3	. . .	. . .	. . .	. . .
Illinois	44.9	14.4	73.7	20.3	74.1	22.5
Indiana	15.3	8.4	32.1	8.1	. . .	9.0
Iowa	6.9	5.7	. . .	. . .	. . .	. . .
Kansas	5.1	3.9	. . .	. . .	. . .	. . .
Kentucky	6.5	5.4	. . .	7.4	. . .	. . .
Louisiana	12.0	8.6	20.8	12.5	. . .	. . .
Maine	12.1	1.7	. . .	. . .	. . .	. . .
Maryland	52.1	4.6	70.5	6.1	. . .	. . .
Massachusetts	59.0	13.8	71.3	15.6	72.0	10.5
Michigan	7.4	4.1	6.1	3.3	. . .	2.6
Minnesota	20.3	7.9	53.2	14.8	. . .	. . .
Mississippi	7.3	6.5	. . .	10.5	. . .	. . .
Missouri	5.5	5.0	5.0	3.4	. . .	. . .
Montana	3.5	3.5	. . .	. . .	. . .	. . .
Nebraska	4.3	3.3	. . .	. . .	. . .	. . .
Nevada	14.4	7.7	19.7	9.0	19.0	6.1
New Hampshire	24.0	2.1	. . .	. . .	. . .	. . .
New Jersey	16.5	3.6	19.2	3.7	19.3	3.7
New Mexico	4.0	3.8	. . .	. . .	4.1	2.9
New York	32.7	5.0	48.9	4.2	49.9	5.9
North Carolina	2.0	2.2	4.5	2.8	. . .	. . .
North Dakota	19.1	21.1	. . .	. . .	. . .	. . .
Ohio	6.9	3.2	9.9	2.7	. . .	2.3
Oklahoma	0.9	1.5	. . .	. . .	. . .	. . .
Oregon	8.3	3.7	. . .	. . .	. . .	. . .
Pennsylvania	13.0	4.3	12.3	3.1	31.4	5.1
Rhode Island	50.3	11.0	51.7	11.2	70.4	10.6

Continued

TABLE 2— Continued

State	Proportion of Deaths From Unspecified Narcotics, %					
	White Persons, 1999–2008	White Persons, 2009–2018	African American Persons, 1999–2008	African American Persons, 2009–2018	Hispanic Persons, 1999–2008	Hispanic Persons, 2009–2018
South Carolina	5.3	2.5	10.3	2.6	. . .	. . .
South Dakota	. . .	. . .	. . .	. . .	. . .	. . .
Tennessee	8.2	5.8	. . .	1.9	. . .	. . .
Texas	5.8	6.3	10.1	7.6	12.9	9.3
Utah	3.9	2.1	. . .	. . .	6.0	. . .
Vermont	5.0	. . .	. . .	. . .	. . .	. . .
Virginia	7.9	2.7	12.1	3.3	. . .	. . .
Washington	17.2	5.4	27.1	6.8	26.0	4.7
West Virginia	2.1	1.1	. . .	. . .	. . .	. . .
Wisconsin	3.4	2.9	6.0	2.4	. . .	. . .
Wyoming	16.0	12.5	. . .	. . .	. . .	. . .

Note. Ellipses indicate deaths from unspecified narcotics in the state were ≤ 20 by race by 10-year time period and suppressed.

unspecified narcotics compared with White persons for the period of 1999 to 2008. Similarly, there was a significant disparity between Hispanic and White persons in the classification of OODs until 2015—although the disparity was smaller compared with the African American–White disparity. After we controlled for death investigation system, there was no difference between Hispanic and White persons in the incidence of OODs from unspecified narcotics. By 2017, the unspecified OOD rate was less than 3% for all groups with no statistically significant differences.

The lack of quality data among minority populations, often described as health data disparities, is not uncommon. Rockett et al. found that race and ethnicity predicted potential misclassification of suicides; specifically, African American and Hispanic persons had excess suicide misclassification compared with White persons.[25] The authors suggested the misclassification, in part, may help explain the racial differences in reported suicide rates.[25] The presence of health data disparities was further elucidated by Huguet et al.; this study examined the prevalence of missing data from the National Violent Death Reporting System (NVDRS).[26] The NVDRS was developed in 2002 to improve data collection related to suicide after the Surgeon General's *Call for Action to Prevent Suicide*.[26] The study had 2 important conclusions: (1) African American persons had more missingness in the NVDRS compared with White persons, and (2) missingness by race was not related to the system used for death investigations (e.g., coroner, medical examiner). On the basis of the findings from the study, the authors suggested "that the death investigation may be conducted differently if the decedent is African American."[26(p193)] The excessive misclassification in OODs among African American persons found in our study for 1999 to 2008, even after we controlled for the death investigation system, mirrors the findings related to the misclassification of suicide.[25,26] Institutionalized racism, discriminatory practices, and implicit biases likely fuel the lack of quality data among deceased African American persons, data that are essential for allocating resources and implementing interventions. This gap in data predictably prevents identification of other racial disparities in health.

Limitations

With respect to limitations, there may be differences in the completeness and handling of overdose deaths by county and state, which may be related to use of the T40.6 *ICD-10* code.[27] Given the differential handling of death investigations across the country, the National Association of Medical Examiners published recommendations for OOD investigation in 2013, and these recommendations were updated in 2020.[28] There are 2 recommendations from that group relevant for this current study: (1) "Toxicological panel should be comprehensive, including potent depressant, stimulant, and antidepressant medications. Detecting novel

TABLE 3— Unspecified Narcotics by State Death Investigation System Type, Period, and Race/Ethnicity: United States, 1999–2008 and 2009–2018

	IRR (95% CI)
Intercept	0.06 (0.04, 0.10)
County-based mixture of medical examiner and coroner offices (Ref: centralized state medical examiner office)	0.95 (0.52, 1.72)
County- or district-based coroner offices (Ref: centralized state medical examiner office)	0.81 (0.45, 1.47)
County- or district-based medical examiner offices (Ref: centralized state medical examiner office)	0.58 (0.30, 1.14)
1999–2008 (Ref: 2009–2018)	2.93 (2.31, 3.71)
Black or African American persons, 1999–2008 (Ref: White persons)	2.35 (1.37, 4.03)
Black or African American persons, 2009–2018 (Ref: White persons)	1.21 (0.74, 1.99)
Hispanic persons, 1999–2008 (Ref: White persons)	1.58 (0.89, 2.79)
Hispanic persons, 2009–2018 (Ref: White persons)	1.33 (0.93, 1.90)

Note. CI = confidence interval; IRR = incidence rate ratio.

substances present in the community may require special testing," and (2) "When death is attributed to a drug or combination of drugs (as cause or contributing factor), the certifier should list the drugs by generic name in the autopsy report and death certificate."[28(p152)] The timing of the initial recommendations (2013), which aligned with increased funding to combat the opioid epidemic, also coincided with the rapid deceleration of OOD misclassification, and the last year there was a racial disparity in OOD misclassification between White and African American persons. The difference between White and Hispanic persons ended 2 years later. The use of death investigation systems data for a single year was also a limitation; however, only 1 state changed death investigation systems from 2004 to 2015.[24,29] Slight changes in death investigation systems by state over time are unlikely to influence the results. Lastly, there may be unmeasured, confounding factors that influence the detail and completion of death certificates for different racial/ethnic groups. Future studies should take an in-depth examination of death investigations by race, ethnicity, and socioeconomic status to identify inequities in death investigations.

Conclusions

Even in death, there are racial disparities that have the potential to have an impact on the health of minority populations. The overall improvements in OOD classification over time is likely attributable to increased funding to combat the opioid epidemic and subsequent improvements in testing and toxicology reporting.[12] The misclassification of OODs may not have been addressed if it only affected African American or Hispanic persons. The reduction in unspecified narcotic OODs in 2013 aligns with the CDC-defined OOD epidemic periods[1] marked by the widespread distribution of illicitly manufactured fentanyl and recommendations from the National Association of Medical Examiners surrounding OOD investigations. Interventions are inequitably distributed among African American and Hispanic persons in the presence of sufficient data; misclassified and missing data are likely to have a synergistic negative impact on the allocation of resources and preventive efforts and further health disparities. It is imperative that we continue to ensure equity in the classification of OODs and in the implementation of opioid-specific intervention strategies that account for race/ethnicity, gender, geographic, and contextual differences in OOD risk. AJPH

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CONTRIBUTORS

Adam J. Milam and Debra Furr-Holden conceptualized and designed the analysis. Ling Wang collected the data and performed the analysis. All authors wrote and approved the final article.

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CONFLICTS OF INTEREST

The authors have no conflicts of interest to report.

HUMAN PARTICIPANT PROTECTION

Institutional review board approval was not needed for this study because it used publicly available de-identified data.

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Mortality Before and After Border Wall Construction Along the US–Mexico Border, 1990–2017

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Objectives. To evaluate changes in mortality in US counties along the US–Mexico border in which there was substantial new border wall construction after the Secure Fence Act of 2006 relative to border counties in which there was no such border wall construction.

Methods. Using complete 1990 to 2017 mortality microdata and a quasi-experimental difference-in-differences design, we evaluated changes in overall (all-cause) mortality, mortality from drug overdose, and mortality from homicide in the 10 counties with substantial new border wall construction and 11 counties with no such construction. We fit a linear model, adjusting for population characteristics and county and year fixed effects, with Bonferroni adjustments for multiple comparisons. Sensitivity analyses included the addition of adjacent inland counties and modifications to the statistical model.

Results. Relative to counties without substantial new border wall construction, counties in which a substantial amount of new border wall was constructed exhibited a nonsignificant 0.02-percentage-point increase (95% confidence interval [CI] = −0.06, 0.10; $P > .99$) in overall mortality after construction. Border wall construction was not associated with changes in either deaths from overdose or deaths from homicide.

Conclusions. Wall construction along the US–Mexico border after the Secure Fence Act of 2006 was not associated with discernible changes in mortality. (*Am J Public Health*. 2021;111(9):1636–1644. https://doi.org/10.2105/AJPH.2021.306329)

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Most countries border other countries. In recent years, nations around the world have constructed physical barriers or walls between themselves and neighboring countries, raising the number of walls along national borders from about 15 a few decades ago to about 70 today, with roughly 1000 kilometers of new walls in Europe alone since 2015.[1–3] The implications of border walls for population health are potentially important. To date, however, little empirical evidence is available from population-wide individual-level data to assess the relationship between health outcomes and the building of border walls.

In the United States, the Secure Fence Act of 2006 led to the construction of 548 miles of new border wall along the 1954-mile US–Mexico border in a few short years.[4,5] Wall construction along the US–Mexico border after the Secure Fence Act resulted in changes in migration patterns, with a 0.4% reduction in the number of Mexican citizens (or approximately 50 000 people) living in the United States. Low-skilled workers in the United States saw their annual income per capita increase by $0.28 as a result of the reductions in low-skilled Mexican workers entering the country, and high-skilled workers saw a $2.73 decline in annual income per capita.[5] In addition, the Congressional Research Service found that, after fencing and other border resources were deployed in San Diego, California, fewer apprehensions of individuals attempting to cross the border from Mexico were recorded in that area.[6]

The US–Mexico border region has a unique population health profile embedded in a diverse and mobile population with varying economic and cultural features.[7] For the past 2 decades, certain populations of this region in the United States have been characterized by lower rates of health

insurance,[8,9] poorer physical health,[10] and a high prevalence of vector-borne infections,[11] food insecurity,[12] and chronic diseases.[7] The US–Mexico Border Health Commission, a binational entity created in 2000 between the US and Mexican governments, seeks to address public health challenges at the border through collaboration. Recently, the commission has identified poverty as one of the drivers of poor health in the region.[7] Many of the border counties have higher unemployment than the border states and the nation as a whole.[13] Environmental degradation on the border, resulting in water shortages and poor air quality, has also been linked to poor health in the region.[14]

Despite some studies on the economic effects of border wall construction and research on health at the US–Mexico border, little evidence exists on the potential effects of border walls on key population health outcomes such as mortality. Border walls between 2 countries might affect mortality in a variety of ways. For example, in the current US policy discussion over border wall funding, some have hypothesized that a border wall between the United States and Mexico could reduce mortality among US residents living near the border through preventing homicides and entry of illicit drugs.[15]

Although this rationale to protect lives has led to policy change, such as the US declaration of a national emergency at the US–Mexico border in February 2019 (which availed funds for border wall construction),[16] it has generally not been empirically tested. Only 2 studies to our knowledge have examined the health consequences of US–Mexico border wall construction. One focused on mortality in Mexico and revealed that an additional 1000 deaths could be attributed to border wall construction between 2007 and 2011 owing to an escalation of violence in Mexican localities after construction.[17] The other study showed that border infrastructure in response to the Secure Fence Act had no impact on property or violent crime rates in the counties in which the wall was built.[18]

We sought to contribute new evidence to this gap in knowledge by examining mortality before and after construction of the US–Mexico border wall. Using geospatial data demarcating where and when the border wall was built as part of the Secure Fence Act of 2006 and a quasi-experimental, difference-in-differences research design, we evaluated changes in mortality attributable to border wall construction.

Specifically, we examined changes in overall mortality, mortality from homicide, and mortality from drug overdose by comparing counties where there was substantial border wall construction with counties where there was no such border wall construction. Consistent with the public health rationale for wall construction posited by policymakers, we focused on counties near the border to test for a local treatment effect of the wall. In all of our analyses, we provide both treatment effects and 95% confidence intervals (CIs). Because we had a near complete registration of all US resident deaths on the border during the study period, any uncertainty (as reflected by the confidence intervals) reflects uncertainty in modeling the parameters rather than sampling uncertainty.

METHODS

We obtained mortality data from National Center for Health Statistics restricted use microdata files, which include records based on information from all death certificates filed in the 50 states and the District of Columbia.[19] We excluded deaths of nonresidents such as individuals not living in the United States, nationals living abroad, and residents of Puerto Rico, Guam, the Virgin Islands, and other US territories.

We assessed overall all-cause mortality as well as mortality from drug overdoses and homicides using underlying cause of death codes from the *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM*; National Center for Health Statistics, Hyattsville, MD) for deaths from 1990 to 1998 and the *International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM*; National Center for Health Statistics, Hyattsville, MD) for deaths from 1999 to 2017 (Table A, available as a supplement to the online version of this article at http://www.ajph.org). We computed crude mortality rates by dividing the total deaths for a county by the total number of residents in the county and multiplying by 100. Data on total number of residents in a county were obtained from the Bridged-Race Population Estimates Data Files within the Centers for Disease Control and Prevention's National Vital Statistics System.[20] Deaths were assigned to counties on the basis of the deceased's county of residence. In our primary analysis, we included only deaths in which individuals resided in the same state in which they died.

Data on border wall construction were obtained from US Customs and Border Protection, which published data on wall construction from 1962 to 2015 (this information was originally obtained via a Freedom of Information Act request by KPBS and Inewsource).[21] These files contained data on the year border wall construction was completed, the type of fencing used (the material of the barrier

as well as information on whether the barrier was aimed toward pedestrians or vehicles), and the coordinates of the section. We mapped border wall construction to the US border. Specifically, for each border county, we calculated the percentage of the county's border that had a border wall in a given year.

Using data on resident population available in the Bridged-Race Population Estimates Data Files, we extracted information on county race/ethnicity, sex, and age percentiles to be used as covariates in our primary analysis.

We extracted 2003 and 2013 Rural-Urban Continuum Codes data. These data provide a classification scheme that distinguishes metropolitan counties and nonmetropolitan counties by population size and degree of urbanization. Data range from 1 (most metropolitan) to 9 (least metropolitan).

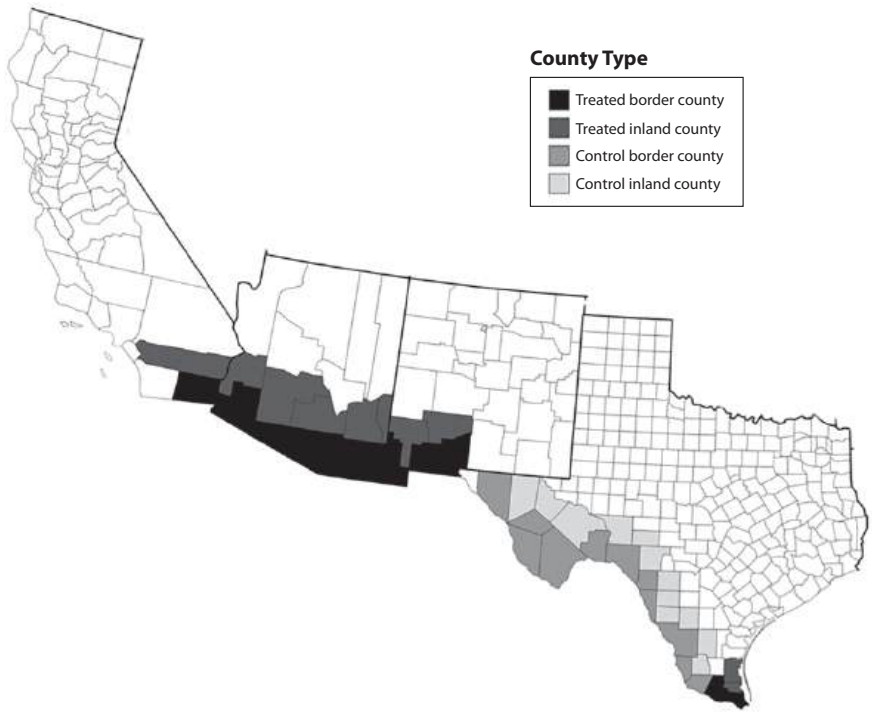

FIGURE 1— Treated and Control Border and Inland Counties: US States Bordering Mexico

Note. The primary sample included border counties in which there was wall construction (treated border counties) as a result of the Secure Fence Act of 2006 and border counties in which there was no construction (control border counties). Sensitivity analyses included their contiguous inland neighbors. Mapchart.net was used in creating the figure.

Defining Exposure

We defined exposure to the treatment—construction of the border wall—as the presence of a human-made barrier of any type at the US–Mexico border at the county level. The border wall comprised fencing for vehicles as well as fencing for pedestrians, depending on location. Vehicle fencing generally involved metal poles and aimed to block traffic from crossing. Pedestrian fencing varied in material and included corrugated steel landing mats, steel walls, steel walls with barbed wire, and barbed wire fencing.[21]

We defined our preintervention period as 2006 and all earlier years. Because much of the construction of border walls as part of the Secure Fence Act occurred during 2007 and 2008, we defined our postintervention period as 2009 and subsequent years. On the basis of the distribution of changes in the border wall after the Secure Fence Act, we defined treated counties as those with at least a 25-percentage-point increase in their border walls from 2006 to 2009. The 25-percentage-point cutoff was selected because it was empirically the point along the distribution of wall construction among border counties in which there was any notable change in the border wall after the Secure Fence Act. All treated border counties saw substantial wall construction from 2006 to 2009, with increases that ranged from 28 to 87 percentage points and an average change of 59 percentage points in the length of their borders with Mexico that had a wall (Figure A, available as a supplement to the online version of this article at http://www.ajph.org).

All other counties on the border were defined as control counties. We excluded San Diego, California and El Paso, Texas, from our analyses because both counties saw substantial wall construction before 2007. In total, there were 10 treated border counties and 11 control border counties.

To allow for the possibility of the health consequences of border wall construction extending beyond counties on the US–Mexico border, we also included inland counties immediately adjacent to border counties in our base sample. We defined inland treated and control counties according to whether they were contiguous with a treated or control border county. Thus, we defined an inland county that touches a treated border county but not a control border county as a treated inland county. There

were 10 treated inland counties. Similarly, we defined an inland county that touches a control border county but not a treated border county as a control inland county. There were 12 control inland counties. Two other counties contiguous with both a treated border county and a control border county were excluded. We grouped treated border counties with treated inland counties, which produced 20 total treated counties. In the same manner, we grouped control border counties with control inland counties, generating 23 total control counties. Treated and control counties are shown in Figure 1.

Statistical Analysis

For our main analysis, we used an ordinary least squares model and conducted a semiparametric difference-in-differences analysis to assess the association between the border wall and our 3 primary outcomes: overall (all-cause) mortality, mortality from drug overdose, and mortality from homicide. We defined pre-treatment as 1990 to 2006 and post-treatment as 2009 to 2017. Years 2007 and 2008 were washout years and were excluded from the analysis. We added county and year fixed effects to account for time-invariant factors within counties and years and clustered standard errors at the county level. We weighted counties by population size. We then estimated the following ordinary least squares difference-in-differences model:

$$(1)\ County\ Mortality\ Rate_{it} = \varphi + \tau(Treated)_i + \sum_1^{25} \beta(Treated * Year)_{it} + \sum_1^{20} \gamma(County)_i + \sum_1^{25} \vartheta(Year)_t + \gamma(X)_{it} + \varepsilon_{it}$$

In this model, the outcome is the mortality rate for a given cause of death in county i and year t. The difference-in-differences estimate is denoted by the coefficient of the product term β. This estimate is the average change in mortality rate for a given cause of death from 1990 to a given year for the treated counties in comparison with the control counties. To obtain our estimate of interest, we took the average of β for the 9 posttreatment years. The vector X refers to a set of county-level demographic covariates that include age (<20, 20–29, 30–39, 40–49, 50–64, ≥ 65 years), sex, and race/ethnicity. Race/ethnicity was categorized according to percentage Hispanic, non-Hispanic White, Black, and "other." As a result of small numbers of residents in several of the counties whose race/ethnicity was not Hispanic, non-Hispanic White, or Black, we created a single grouping for other race/ethnicity.

We assessed whether there were differential preintervention trends in the outcomes (over the period 1990–2006) by looking at the interaction between treatment and year as a continuous variable. Given the nature of the observational design, which is susceptible to confounding and selection effects, causal interpretation is limited. Nevertheless, approaching the results with any causal interpretation is generally aided by nondifferential preintervention trends in the outcomes between the treated and control groups.

Evaluating 3 outcomes in total, we used the Bonferroni correction to adjust for multiple comparison testing, and we report Bonferroni-corrected P values.

Sensitivity Analyses

We assessed the robustness of our model estimates to several sensitivity analyses. First, we repeated the main analysis absent county fixed effects, year fixed effects, and demographic characteristics to assess the stability of the model estimates given the importance of modeling choice in the setting of complete mortality data. Second, we estimated models without population weights, as differences across weighted and unweighted models might suggest model misspecification.[22] Third, we estimated models including 2006 as a washout year because some counties demonstrated modest increases in wall construction from 2005 to 2006.

Fourth, we modified the sample to include only deaths in which individuals both resided and died in the same county in the event that individuals died in a county separate from where they resided. Fifth, given the relatively small number of counties, we also derived P values for our main analysis (unweighted) from a nonparametric permutation test with 5000 replications. Permutation tests are free of distributional assumptions, and such a test was useful in this situation given the limited number of counties.[23] Finally, we repeated the main analysis but redefined treatment using a more intensive definition of border wall construction of at least a 60-percentage-point increase from 2006 to 2009 in a given county, because this was the approximate mean value of border change for treated counties.

RESULTS

Characteristics of counties in which there was border wall construction (treated) and those in which there was no construction (control) are shown in Table 1. Before wall construction, treatment and control counties had minor differences in their age distributions. Females made up 50.6% of

TABLE 1— Characteristics of the Study Population in Prewall (1990–2006) and Postwall (2009–2017) Counties: US States Bordering Mexico

	BEFORE BORDER WALL CONSTRUCTION		AFTER BORDER WALL CONSTRUCTION	
	Treatment Counties (n = 10)	Control Counties (n = 11)	Treatment Counties	Control Counties
Border counties[a]				
Age group, y, %				
< 20	33.85	34.08	30.28	29.30
20–29	13.42	12.60	13.85	12.56
30–39	13.81	13.04	11.68	11.65
40–49	12.46	12.14	11.59	11.74
50–64	13.66	14.70	17.18	17.85
≥ 65	12.81	13.44	15.41	16.90
Female, %	50.63	50.28	50.36	49.46
Race/ethnicity, %				
White	36.29	27.61	29.56	24.49
Hispanic	60.27	71.39	66.57	73.57
Black	1.66	0.46	1.79	0.87
Other	1.79	0.53	2.09	1.06
Population, no.				
Total	39 172 552	6 125 566	27 217 400	4 240 880
County mean	230 427	32 757	302 416	42 837
Border wall proportion of county, mean %[b]	8.31	0.10	67.43	1.25
RUCC mean[c]	3.6	6.5	3.7	5.7
Border and inland counties[a]				
Age group, y, %				
< 20	32.19	33.87	28.45	28.95
20–29	12.77	12.60	13.22	13.29
30–39	13.61	13.18	11.70	11.79
40–49	12.58	12.57	11.54	11.91
50–64	14.76	14.70	17.94	17.90
≥ 65	14.07	13.07	17.15	16.16
Female, %	49.86	49.83	49.50	48.63
Race/ethnicity, %				
White	43.47	27.43	38.09	23.04
Hispanic	51.50	71.41	55.81	74.92
Black	1.75	0.72	2.24	1.08
Other	3.28	0.44	3.86	0.96
Population, no.				
Total	119 027 664	8 072 383	88 742 512	5 279 253
County mean	350 081	20 645	493 014	25 504
Border wall proportion of county, mean %[b]	8.31	0.10	67.43	1.25
RUCC mean[c]	4.3	6.8	4.4	6.4

[a]We grouped treated border counties with treated inland counties, which produced 20 total treated counties. We grouped control border counties with control inland counties, generating 23 total control counties.

[b]We calculated border wall proportion of county as the total percentage of the county's border with a border wall in 2006.

[c]We used the 2003 and 2013 Rural-Urban Continuum Codes (RUCC), a classification scheme that distinguishes metropolitan counties and nonmetropolitan counties. RUCC 3 refers to counties in metropolitan areas with populations of less than 250 000. RUCC 4 refers to a population of 20 000 or more adjacent to a metropolitan area. RUCC 5 refers to a population of 20 000 or more not adjacent to a metropolitan area. RUCC 6 refers to a population of 2500–19 999 adjacent to a metropolitan area.[24]

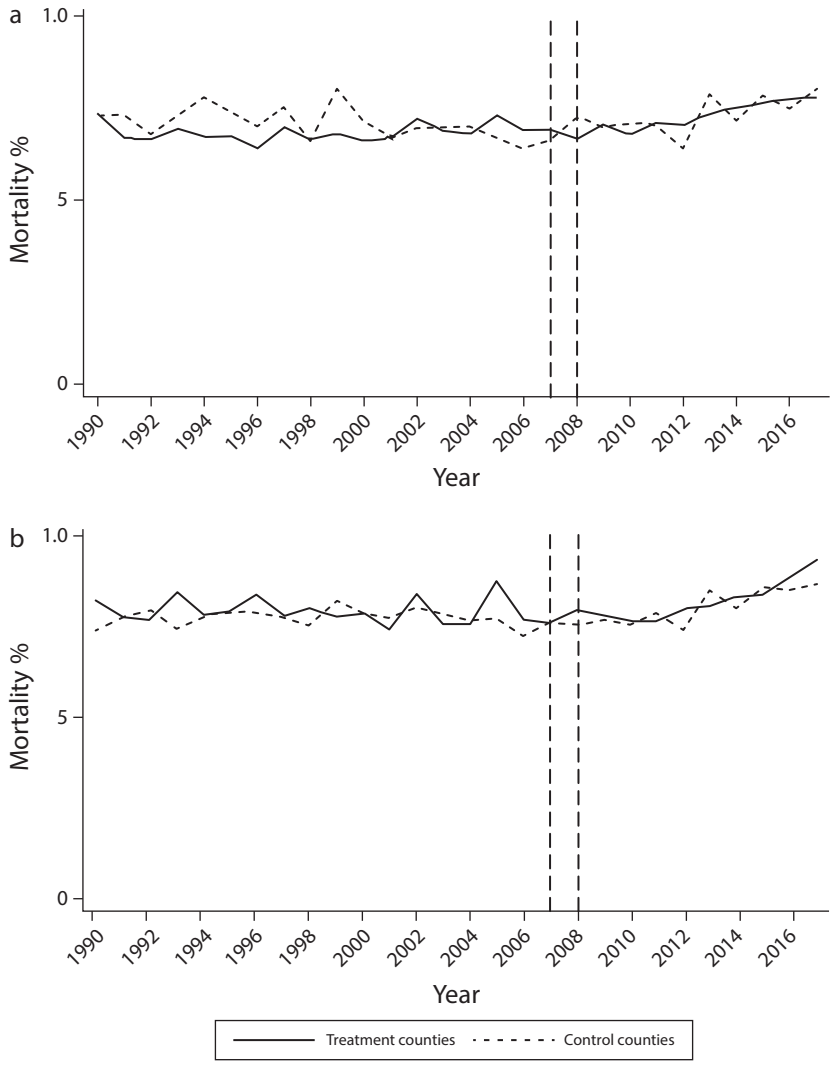

FIGURE 2— Mortality Rates per Year From 1990 to 2017 for (a) Treated and (b) Control Counties: US States Bordering Mexico

Note. Unadjusted annual overall mortality rates in treatment counties and control counties are shown, with vertical lines denoting the washout period around the construction.

treatment counties and 50.3% of control counties. Treatment counties were 36.3% White, 60.3% Hispanic, 1.7% Black, and 1.8% other. Meanwhile, control counties were 27.6% White, 71.4% Hispanic, 0.5% Black, and 0.5% other. Treatment counties had an average population of 230 427, whereas control counties had an average population of 32 757. We also provide demographic information for the sample, including inland counties, in Table 1.

Unadjusted trends in mortality rates for treated and control counties before border wall construction did not appear to diverge (Figure 2), including when inland counties were added to the sample (Figure 2). Among only border counties as well as the larger sample with inland counties, there were no statistically significant differences in preintervention trends for any category of mortality (Table B, available as a supplement to the online version of this article at http://www.ajph.org).

Adjusted results for our main sample comprising border counties are shown in Table 2. The adjusted difference-in-differences estimate of the change in overall mortality associated with border wall construction was a 0.02-percentage-point increase (or approximately 46 additional deaths per year based on the preintervention average county population of 230 427), but this result was not statistically significant (95% CI = −0.06, 0.10; $P > .99$). Similarly, border wall construction was not associated in adjusted analyses with either changes in deaths from drug overdose (−0.003-percentage-point change; 95% CI = −0.009, 0.002; $P = .68$) or changes in deaths from homicide (−0.001-percentage-point change; 95% CI = −0.006, 0.003; $P > .99$).

Adjusted results for our sample including inland counties are shown in Table 2. The change in overall mortality associated with border wall construction was smaller and similarly not statistically significant: 0.001 percentage points (95% CI = −0.09, 0.09; $P > .99$). Border wall construction was not associated with a change in deaths from overdose for this expanded sample of treatment counties relative to their controls. In this expanded sample, the change in deaths from homicide associated with border wall construction was a statistically significant 0.005-percentage-point increase (95% CI = 0.001, 0.010; $P = .045$).

We used sensitivity analyses to test the robustness of our main estimates. For overall mortality, the difference-in-differences estimate remained not statistically significant with alterations of covariates and model weights (Table C,

TABLE 2— Changes in Mortality Rates per Year in Prewall (1990–2006) and Postwall (2009–2017) Counties: US States Bordering Mexico

	TREATMENT COUNTIES			CONTROL COUNTIES			DIFFERENTIAL CHANGE			
	Prewall	Postwall	Change	Prewall	Postwall	Change	Unadjusted	Adjusted (CI)	*P*	Bonferroni corrected *P*[a]
Border counties only										
Overall mortality	0.685	0.734	0.050	0.711	0.733	0.022	0.028	0.020 (−0.063, 0.103)	.62	> .99
Drug overdose	0.006	0.014	0.008	0.002	0.006	0.004	0.005	−0.003 (−0.009, 0.002)	.23	.68
Homicide	0.005	0.004	−0.002	0.005	0.006	0.001	−0.003	−0.001 (−0.006, 0.003)	.6	> .99
Border and inland counties										
Overall mortality	0.791	0.820	0.029	0.771	0.805	0.034	−0.005	0.001 (−0.085, 0.087)	.98	> .99
Drug overdose	0.006	0.016	0.009	0.003	0.007	0.004	0.006	0.001 (−0.003, 0.006)	.6	> .99
Homicide	0.007	0.004	−0.003	0.006	0.005	−0.001	−0.001	0.005 (0.001, 0.010)	.02	.045

Note. Prewall and postwall outcomes are pooled average yearly mortality rates for each period. Years 2007 and 2008 were washout years and were excluded from the analysis. We computed crude mortality rates by dividing the total deaths for a county by the total number of residents in the county and multiplying by 100. We included county and year fixed effects and clustered standard errors at the county level. We weighted counties according to population size. We used ordinary least squares regression and estimated the model shown in Equation 1.

[a]We used the Bonferroni correction to correct for multiple comparison testing.

available as a supplement to the online version of this article at http://www.ajph.org). When we expanded the washout period to include 2006, the adjusted difference-in-differences estimate for overall mortality associated with border wall construction was 0.02 percentage points (95% CI = −0.06, 0.10; *P* > .99; Table D, available as a supplement to the online version of this article at http://www.ajph.org).

When we repeated the main analysis but changed the sample to include only deaths in which people both died and resided in the same county, the adjusted change in overall mortality analysis associated with wall construction was 0.02 percentage points (95% CI = −0.05, 0.09; *P* > .99; Table D). Similarly, when we used a permutation test, we also found a nonsignificant difference-in-differences estimates of the change in mortality (Table D). The difference-in-differences estimated remained small and nonsignificant when treatment was redefined (Table E, available as a supplement to the online version of this article at http://www.ajph.org).

DISCUSSION

Although many countries around the world are discussing the implications of border policies for the well-being of populations, little empirical evidence exists on the connection between border walls and health outcomes. In this study of counties near the US–Mexico border before and after the construction of border walls, we generally found no statistically significant association between border wall construction and mortality. This lack of association was robust to several sensitivity analyses, including variations in the statistical model and the sample. The exception was a modest relative increase in homicide deaths associated with wall construction in the sample that included inland counties.

Together, these results suggest that the border wall construction concentrated in 2007–2008 along the US southern border was not associated with observable large effects on overall mortality or mortality attributable to drug overdoses or homicide, which have been proposed as potential benefits of border wall construction.

Limitations

There are several limitations to this study. First, the data offered by US Customs and Border Protection provide information only on when a section of the wall was completed. The agency does not provide details on when the building of the section began. If wall construction started before 2006, this could attenuate estimates of its impact. However, the timing of the Secure Fence Act suggests that the majority of wall building began between 2007 and 2010, which informed our assignment of preintervention and postintervention periods.

Second, there were only a maximum of 43 counties in our analysis and 21 counties in the border-only analysis. This small sample size limited our statistical power, requiring larger effect sizes to be detected as statistically significant. However, because our data included the universe of all official recorded deaths among Americans in these counties

during the study period, the confidence intervals do not reflect sample uncertainty. Moreover, the lack of statistical significance was consistent when we conducted an inference analysis with a permutation test.

Third, it is possible that lagged effects occurred after 2017, the last year of mortality data we included in our study. However, this seems unlikely, and attribution of treatment effects during later years could be confounded by other societal or policy changes.

Another limitation is that our analyses do not capture the topography or environmental conditions that may have differentially affected the treatment and control counties. Nor does our study capture economic conditions that may have differentially affected these counties. Notably, all counties that could serve as controls were located in Texas. Thus, to the extent that counties in Texas may not serve as an ideal counterfactual for treatment counties from other states (e.g., as a result of policies that differentially affected Texas), our results may be biased. Also, because data from the Freedom of Information Act request did not include an explanation of why certain areas were selected over others for border wall construction, our results could be biased if the reason for selecting certain locations was associated with future mortality rates. Finally, the US mortality data did not capture migrants who may have died while attempting to cross the border.

Importantly, our study focused on mortality as the outcome. We could not observe nonmortality effects of the border wall. The possible effects of border wall construction on other meaningful outcomes, such as other health effects (e.g., mental health) and health behaviors, remain open for scientific inquiry.

CONCLUSIONS

In this study, we found that border wall construction in 2007–2008 along the US southern border was not associated with discernible changes in mortality. As countries around the world grapple with complex policy decisions surrounding their borders, this study offers one piece of evidence from the US context. AJPH

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CONFLICTS OF INTEREST

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HUMAN PARTICIPANT PROTECTION

No protocol approval was necessary for this study because no human participants were involved.

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Best Practices for Conducting Clinical Trials With Indigenous Children in the United States

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We provide guidance for conducting clinical trials with Indigenous children in the United States. We drew on extant literature and our experience to describe 3 best practices for the ethical and effective conduct of clinical trials with Indigenous children. Case examples of pediatric research conducted with American Indian, Alaska Native, and Native Hawaiian communities are provided to illustrate these practices.

Ethical and effective clinical trials with Indigenous children require early and sustained community engagement, building capacity for Indigenous research, and supporting community oversight and ownership of research. Effective engagement requires equity, trust, shared interests, and mutual benefit among partners over time. Capacity building should prioritize developing Indigenous researchers. Supporting community oversight and ownership of research means that investigators should plan for data-sharing agreements, return or destruction of data, and multiple regulatory approvals.

Indigenous children must be included in clinical trials to reduce health disparities and improve health outcomes in these pediatric populations. Establishment of the Environmental Influences on Child Health Outcomes Institutional Development Award States Pediatric Clinical Trials Network (ECHO ISPCTN) in 2016 creates a unique and timely opportunity to increase Indigenous children's participation in state-of-the-art clinical trials. (*Am J Public Health*. 2021;111(9)1645–1653. https://doi.org/10.2105/AJPH.2021.306372)

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The US population includes nearly 7 million Indigenous people, including 5 million American Indian and Alaska Native (AI/AN) people and 1.5 million Native Hawaiian and other Pacific Island people.[1] Overall, Indigenous people in the United States experience lower life expectancies, higher disease burden, and higher rates of all-cause mortality than other demographic groups, especially non-Hispanic White populations.[2] These health disparities include disproportionately high rates of infectious diseases, diabetes, behavioral health conditions, and many chronic conditions.[3] Indigenous children share this burden, with disproportionately high rates of asthma,[4] obesity,[5] and respiratory infections[6] compared with the general pediatric population.

Increasing evidence suggests that social and environmental determinants of health contribute significantly to these health disparities.[7] Among the more than 2 million Indigenous children in the United States in 2017, approximately 33% of AI/AN children and 21% of Native Hawaiian/Pacific Islander children lived in poverty, compared with 20% of the overall pediatric population.[1] AI/AN children are more likely than their peers in all other racial groups to live in rural areas, with limited access to health care.[8] Furthermore, Indigenous communities experience disproportionate rates of household crowding, lack of indoor plumbing and running water, indoor air pollutants, and environmental contamination.[9] These inequities are deeply rooted in historical policies of forced relocation, assimilation, and extermination of Indigenous societies that continue to threaten the health of Indigenous people today.[10,11] There is growing attention to Indigenous cultural

values and practices as key mechanisms for achieving positive health outcomes[12]; substantial work remains, however, to address health disparities in Indigenous communities, including children. One aspect of this work is ensuring that Indigenous children and their communities have access to state-of-the-art health care and clinical research.

NEED FOR PEDIATRIC TRIALS WITH INDIGENOUS CHILDREN

With limited exceptions such as cardiology and oncology, few clinical trials have been conducted with children, relative to adults.[13] Among 266 119 interventional studies registered on ClinicalTrials.gov (as of May 7, 2020), only 47 049 (18%) planned to enroll people aged 0 to 17 years. In the National Library of Medicine PubMed database, an unfiltered search combining terms for "clinical trial" and "pediatric," across all article types and all years, yielded about 56 000 citations. Adding "American Indian," "Native Hawaiian," or "Alaska Native" returned fewer than 100 articles total (Table 1). Thus, among articles in the database that contain the term "clinical trial," only 5% include the term "pediatric," and 0.007% mention Indigenous children in the United States.

The lack of pediatric clinical trials has resulted in fewer evidence-based therapies for children in all racial and ethnic groups, requiring clinicians to often rely on pharmacological treatments that have been researched in adults only.[13] This is problematic given age-based differences in pathophysiology and drug metabolism.[14] Congress passed the Pediatric Exclusivity Provision in 1997 to incentivize pediatric drug trials, followed by the Pediatric Research Equity Act of 2003, requiring pediatric tests of new drugs that are likely to be used in children.[15] However, no such requirements exist for pediatric trials to include Indigenous children, who may not benefit from interventions developed with general population samples.

Substantial challenges exist in enrolling Indigenous children in clinical trials, particularly those living in rural areas. Trials typically occur at large academic medical centers in urban areas; travel and financial burdens associated with participation limit access for children in rural areas, where many Indigenous children live.[16] Experiences with research misconduct in Indigenous communities have also resulted in distrust of researchers and clinical research, especially that involving children. Furthermore, Western scientific standards or practices may directly conflict with community priorities and values. For example, "gold standards" of clinical study design, such as randomization, may be fundamentally unacceptable in Indigenous communities that prioritize cultural values of equity and community benefit over equipoise. Understanding and overcoming these challenges is necessary for increasing Indigenous children's participation in clinical trials and improving child health outcomes.

TABLE 1— PubMed Advanced Search for Pediatric Clinical Trials With American Indian, Alaska Native, or Native Hawaiian Populations Unfiltered

Search Terms	Items Retrieved, No.
clinical trial	1 181 619
pediatric	912 165
(clinical trial) AND (pediatric)	56 288
((clinical trial) AND (pediatric)) AND (American Indian)	51
(((clinical trial) AND (pediatric))) AND (Native Hawaiian)	22
(((clinical trial) AND (pediatric)) AND (Alaska Native)	8

Note. As of May 7, 2020; 3:57 Alaska Time.

BEST PRACTICES FOR CLINICAL TRIALS WITH INDIGENOUS CHILDREN

The Environmental Influences on Child Health Outcomes Institutional Development Award States Pediatric Clinical Trials Network (ECHO ISPCTN) was established in 2016 to increase pediatric trials in rural and medically underserved areas.[17] The network's focus on environmental influences on child health aligns with the health needs and priorities of many Indigenous communities. However, little explicit guidance exists on how to develop and implement pediatric trials with Indigenous communities. Although a growing literature has emerged on the ethics of conducting clinical research with Indigenous communities, few of these articles mention children.[18] Through consideration of this literature and our experience conducting clinical research with Indigenous communities, we suggest 3 best practices for conducting pediatric clinical trials with Indigenous communities in the United States (Box 1). These practices are not novel, nor do we claim that they are original approaches for conducting

BOX 1— Best Practices for Conducting Pediatric Clinical Trials With US Indigenous Communities

Practice	Description
Early and sustained community engagement	Community leaders or delegates are involved in formulating research questions and approaches to ensure that research addresses only problems of interest to the community, involves participation of community members in research activities (not only as participants) in a manner that creates equitable and trusted partnership with shared interests and goals, and involves researcher commitment to the community and continuing relationship beyond any specific study.
Build Indigenous research capacity	Research and other activities that build research capacity in Indigenous communities, particularly among community members, in academic and nonacademic settings (e.g., tribal health organizations), through various roles (e.g., researcher, community advisor, institutional review board member) with the explicit intention of increasing knowledge, skills, resources, and leadership in self-determined research by Indigenous peoples for Indigenous peoples.
Support community ownership and oversight of research	Formal recognition (e.g., memorandum of understanding, contract, tribal resolution) that Indigenous community owns all data (e.g., recordings, transcripts, biospecimens) and has oversight authority over all research activities, including data storage and management procedures and dissemination activities, and that research is preapproved by community-led institutional review boards and other local regulatory entities as deemed appropriate and required by community leadership.

clinical research with Indigenous communities. Rather, we advocate here for their application to increase the clinical trial participation of Indigenous children, a population with substantial health disparities that is underrepresented in pediatric research. To illustrate each practice, we provide examples of clinical research with Indigenous children in Alaska, Hawaii, Montana, New Mexico, and Oklahoma. These studies preceded establishment of the ECHO ISPCTN and offer lessons for increasing pediatric clinical trials with Indigenous communities.

Early and Sustained Community Engagement

Early and sustained community engagement is essential to conducting clinical trials with Indigenous communities, particularly on sensitive topics such as child health. Community engagement is arguably the most important practice of doing research with Indigenous populations. Various models of community-engaged research exist, including community-based participatory research, participatory action research, and community engaged research. Woolf et al.[19] use "authentic engagement" to describe research in which Indigenous communities are "full partners in setting research priorities, forming research questions, and shaping the design, funding, conduct, and dissemination of studies."[19(p2)] The different models of community engagement all conceptualize research as an equitable, collaborative process between researchers and communities. Equitable research requires that all partners understand the importance of having a shared interest and emphasizes the development of meaningful, sustained relationships built on mutual trust and respect among all partners, by their own standards. Such partnerships center the unique and critical expertise of community partners, who are involved in some capacity in all aspects of the research. The processes by which researchers can identify appropriate community partners is an important consideration and will vary greatly by setting.

The Family Spirit intervention provides an example of effective university-based research using a community-based participatory research approach to engage Indigenous communities in clinical trial design and implementation.[20] Family Spirit is an evidence-based, culturally tailored home-visiting intervention program designed specifically for rural Native American families, and the first to provide evidence for the value of Indigenous home visitors for improving behavioral health disparities. The intervention is a 43-session curriculum administered by Indigenous paraprofessionals to adolescent mothers from 28 weeks' gestation until the child's third birthday. Expectant American Indian adolescents (n = 322; mean age = 18.1 years) from 4 southwestern reservation communities were randomly assigned in stratified blocks to Family Spirit plus optimized standard care or optimized standard care alone. Maternal and child outcomes were evaluated at 28 and 36 weeks' gestation, and 2, 6, 12, 18, 24, 30, and 36 months postpartum. The intervention improved parenting and maternal and child outcomes, and the trial had a retention rate of 83% at 36 months. Study partners attributed the trial's success to the community-based participatory research approach that involved Indigenous research staff who understood the culture, language, and local resources, and who were trusted by study participants. The study also

helped build a sustainable, scalable Indigenous workforce in participating communities.

Another example of effective community engagement in pediatric research is the Treatment Options for Type 2 Diabetes in Adolescents and Youth (TODAY) study, a multicenter clinical trial aimed at improving treatment of diverse youths with type 2 diabetes.[21,22] Researchers at the University of Oklahoma site of the study engaged Native American community leaders for several years before the study and built relationships within the community as clinical care providers. The researchers proposed a preliminary research design and then worked with the community to identify potential obstacles to participation, such as travel distances for families. This resulted in a modified design in which researchers provided the study intervention at a local tribal clinic, rather than a distant medical center. This trust-building process between university researchers and community partners on all aspects of the study included development of legal agreements and day-to-day operations that facilitated achieving study objectives. The TODAY study illustrates that community engagement is not a single event, but an ongoing, continual process of building and sustaining relationships that are experienced by all partners as mutually beneficial.

Thus, clinical research with Indigenous populations requires longitudinal community engagement from before study conceptualization to beyond completion. Community members participate actively in the research, not only as sources of data but also as consultants, decision-makers, recruiters, data collectors, analysts, authors, and regulatory authorities.

Build Indigenous Research Capacity

The term "capacity building" in health science research typically means the development of independent (principal) investigators, research networks, and scientific infrastructure. The National Institute of General Medical Sciences' Division for Research Capacity Building, for example, partners with other National Institutes of Health (NIH) agencies and the Indian Health Service to fund Native American Research Centers for Health (NARCH). NARCH grants are awarded to tribes and tribal organizations to build scientific expertise and infrastructure to conduct research and career enhancement activities that meet the health needs prioritized by the community. Building Indigenous research capacity requires developing necessary knowledge, skills, and resources to promote scientific studies selected by the AI/AN community and conducted by partnerships of health researchers from within and outside these communities. Walters and Simoni describe this as "decolonizing research capacity" and contend that research partners must work to "dismantle [colonial research paradigms] by embracing indigenous [sic] worldviews, engaging in collaborative research partnerships, building research capacity within universities and tribal communities, changing reward systems, and developing mentoring programs."[23(pS71)]

A slogan of the disability rights movement of the 1990s, the Latin idiom *nihil de nobis, sine nobis* (nothing about us without us), describes many Indigenous communities' resolve to not only benefit from clinical research but also to lead these efforts. To this end, some communities have established research infrastructures to develop and employ Indigenous health researchers and promote Indigenous-led research. For example, the Alaska Native Tribal Health Consortium and Southcentral Foundation, both Alaska Native–owned and –operated health organizations, established research departments within the organizations, with principal investigators, researchers, and grant administration personnel, many of whom are AI/AN. Both organizations have policies and procedures that govern how studies are selected, approved, implemented, and disseminated to community and scientific audiences.[24] Building capacity for state-of-the-art pediatric clinical trials in Indigenous communities requires the infrastructure, training, and opportunities for Indigenous people to lead these efforts.

One example of building Indigenous community capacity is the Wood Stove Interventions and Child Respiratory Infections in Rural Communities (KidsAIR) study, a randomized controlled trial aimed at reducing risk of lower respiratory tract infections through improvements in indoor air quality in young children residing in homes heated by wood stoves.[25] KidsAIR grew out of multiple community- and household-level intervention studies that highlighted the importance of community capacity building. Before KidsAIR, several rural communities implemented community-wide wood stove changeout programs to replace old heating units with improved technology stoves to reduce ambient exposures.[26] In 1 such program on the Nez Perce Indian Reservation in Idaho targeting indoor exposures, investigators recorded improvements in ambient exposures in 10 of 16 participating homes and noted the need for a

community-engaged approach to maximize both recruitment and the effectiveness of the intervention.[27] In addition, local research staff were critical to the conduct of the Asthma Randomized Trial of Indoor Air Quality and Smoke (ARTIS) study, a randomized trial designed to improve symptoms and related health measures in children with asthma residing in homes that used an older model wood stove as a primary heating source.[28]

KidsAIR includes children from rural and Indigenous communities in Montana and Alaska, as well as the Southwest. Extensive community engagement and community capacity building laid the foundation for the KidsAIR study. In addition to the ARTIS study, which demonstrated the importance of targeting indoor air quality in western Montana homes with wood stoves, results from more than 300 surveys administered in rural parts of Alaska identified specific air quality concerns as potential contributors to disparities in respiratory health in children.[29] Of note, community coordinators residing in each of the study areas were essential members of the research team and assisted with survey design and administration. The inclusion of Southwest communities in KidsAIR was based on findings, relationships, and needs identified during previous research with a pediatric cohort in the region, exemplifying the key role of sustained, long-term, and collaborative relationships in clinical research with Indigenous communities. Community staff outreach and feedback indicated community concerns about asthma and the need to do research, as well as provide solutions, setting the stage for expanding the study. Community coordinators lead data collection efforts at each KidsAIR study site, an approach that both builds research capacity in the community and facilitates the successful conduct of study-related activities.

The development of the 13-valent pneumococcal conjugate vaccine (PCV13) provides another illustration of building Indigenous research capacity. In the late 1990s, the rate of invasive pneumococcal disease among Indigenous children in Alaska's Yukon Kuskokwim (YK) Delta was 10 times that of their non-Native peers.[30] After introduction of the 7-valent pneumococcal conjugate vaccine, invasive pneumococcal disease rates among YK Delta children declined initially, only to increase dramatically again by 2007 because of the emergence of nonvaccine serotype disease.[31] During a tribal gathering, Indigenous Elders voiced support for the tribally owned YK Health Corporation's (YKHC's) participation in the late phase 3 clinical trial of the prelicensure PCV13 vaccine. The YKHC implemented the study in 24 rural villages, using a local research coordinator, and training tribal nurses and Indigenous community health aides to administer study vaccine. The PCV13 study enabled YKHC to develop and fund its own research program, which currently employs 3 permanent staff and 4 research nurses in 3 clinical studies. Furthermore, within 6 months of licensure, 91% of children in the region aged younger than 5 years received PCV13 vaccine, and invasive *Streptococcus pneumoniae* cases decreased 73%.[32]

Support Ownership and Oversight of Research

An increasing number of Indigenous communities have formed institutional review boards under 45 CFR 46, as well as Tribal Research Review Committees that do not fall under this statute.[33] These entities function to ensure that, in addition to meeting federal requirements, all research activities are ethical by community standards, that individuals and organizations in the community are appropriately engaged, and that the research aligns with community priorities. The levels and types of community approval vary. Oetzel et al.[34] investigated the relationship between the type of final approval for community-engaged projects and governance processes, productivity, and perceived outcomes among 294 federally funded studies in 2009. Tribal government or "government-type" agency approval was associated with communities having greater control of research, greater share of research resources, and more formal agreements about data ownership and research dissemination. These authors conclude that it is an "ethical imperative for communities (especially Native communities and other vulnerable populations) to adopt a model of governance focusing on [research] stewardship," similar to those established by many tribal health organizations in Alaska such as the Alaska Native Tribal Health Consortium and South-central Foundation.[24(p1161)] Researchers should be prepared to invest the necessary, often extensive, effort to identify and engage the individuals and entities with authority to approve research activities, as well as to establish a clear understanding of approval processes and expectations, which takes time and may involve navigating new or developing community structures, as well as modifying research plans or designs as deemed appropriate by community research oversight authorities.

For example, in response to several negative experiences with research, the Waianae Coast Comprehensive Community Health Center in Hawaii developed its own Health Center Research Committee, Community Advisory Group,

and institutional review board. A research group proposed a maternal health study that involved obtaining and analyzing salivary cortisol samples. However, some Native Hawaiian community members on the Health Center Research Committee voiced concerns that the saliva samples were biological specimens that contained cells and DNA and, therefore, needed special consideration. The community members stated that Native Hawaiians have traditionally believed, as with many other Indigenous cultures, that one's body, including hair and fluids, can be considered sacred or spiritual and should not be given away. Researchers relied heavily on the Health Center Research Committee and Community Advisory Group members for ways to better explain the research, including the purpose of the sampling, how procedures would be conducted in a way that respected the community, and the potential value of these test results to the community. Researchers' formative understanding of community concerns, demonstration of respectful testing, and working with the research laboratory on procedures to ensure the proper, culturally acceptable disposal of the human samples, showed respect for the Indigenous population and their worldview. This process took considerable time, but the study was eventually approved and successfully completed because, in part, of the researchers' willingness to adapt the study based on feedback from community authorities.

Pediatric trialists should be prepared to establish the appropriate type of agreement (e.g., memorandum of understanding, contract, tribal resolution) with legitimate approval bodies to formalize shared understanding and expectations about data ownership, management, storage, disposal, or return, as well as dissemination. These processes can take substantial time and should be factored into study timelines in funding applications. Researchers should expect that ownership of data (e.g., biospecimens, medical records, surveys, and interviews) will be retained by the community with additional consent required for secondary use and dissemination. Communities may assert their sovereign right to decline for data to be included in data repositories or used for future studies.

CONCLUSION

Indigenous children in the United States experience significant health disparities yet remain substantially underrepresented in clinical trials. Improving health outcomes in this pediatric population of more than 2 million children requires increasing their enrollment in clinical trials to ensure the development of effective, population-based interventions that can be successfully implemented. The dearth of clinical trials in Indigenous communities in the United States has resulted in little explicit guidance for researchers on the ethical conduct of pediatric trials with these populations. We have drawn on extant literature and our own experiences to identify 3 best practices for conducting pediatric trials with Indigenous communities: (1) early and sustained community engagement, (2) building Indigenous research capacity, and (3) supporting community ownership and oversight of research.

These practices are not specific to clinical trials or pediatric populations. Nor are they specific to research with Indigenous people in rural settings, although urban contexts may require other considerations—for example, how to identify appropriate community partners. Applying these practices does not guarantee a successful trial; it is the minimum requirement for one. Researchers should have no illusion that that these practices necessarily prevent conflicts, missteps, or even occasional crises in relationship between partners. For example, randomization, particularly to placebo or parallel group designs, may be unacceptable in some communities. While alternative trial designs (e.g., stepped wedge, delayed entry) may be acceptable, these conflicts may be irreconcilable and require a scientifically less rigorous approach in favor of a culturally more appropriate one. In our experience, however, these challenges can usually be overcome with relationships built on trust, equity, commitment, shared interests, and mutual benefit.

The case examples herein provide only an introduction, not a comprehensive guide, for conducting pediatric trials with Indigenous communities. As previously mentioned, decolonizing Indigenous research requires more than simply hiring local staff onto studies; it requires sustained commitment on the part of noncommunity researchers and funders (e.g., NARCH) to building Indigenous research capacity that goes beyond a single study and actively supports development of research structures that respect Indigenous peoples and sovereignty, including the right to data ownership and oversight. For example, the Alaska site of the ECHO ISPCTN reached a data-sharing agreement with the NIH that makes tribal approval a requirement for any researcher seeking to access or disseminate results from data collected from Alaska Native families participating in a network study. We have noted that identifying appropriate community partners and understanding research approval processes and expectations

TABLE 2— Total National Institutes of Health Extramural Funding to Institutional Development Award (IDeA) Program and Non-IDeA Program States, Combined and by Location: United States, Fiscal Year 2020

State	Funding, $
Non-IDeA states[a]	30.8 billion combined
California	4 873 379 566
Massachusetts	3 254 611 912
New York	3 112 927 263
Pennsylvania	2 012 759 114
North Carolina	1 968 510 312
Washington	1 588 938 213
Texas	1 495 164 387
Maryland	1 246 582 971
Illinois	1 100 476 076
Ohio	918 576 423
Michigan	890 081 214
Georgia	735 589 203
Florida	727 819 822
Connecticut	679 750 577
Tennessee	676 130 402
Missouri	670 766 929
Minnesota	669 561 614
Wisconsin	530 039 381
Colorado	475 284 058
Virginia	422 324 832
Oregon	420 261 738
Indiana	374 365 757
Alabama	369 367 577
New Jersey	330 270 251
Arizona	281 551 338
Utah	247 425 348
Foreign	242 351 436
District of Columbia	234 692 091
Iowa	217 827 324
Guam	2 058 324
American Samoa	497 841
Virgin Islands	403 329
IDeA states[b]	2.2 billion combined
Kentucky	239 834 370
Rhode Island	229 105 661
South Carolina	213 196 155
Louisiana	176 480 826
Nebraska	133 512 380
Oklahoma	125 197 845
Kansas	119 625 766
New Hampshire	119 623 590

Continued

requires navigating complex Indigenous community structures, necessitating researchers' time and effort to build relationships, trust, knowledge, and understanding. This is a critical process that will vary greatly by setting, and the importance of which cannot be overemphasized.

Pediatric trials have contributed to advances in the prevention, diagnosis, and treatment of many childhood illnesses. However, children remain underrepresented in clinical trials, and many treatments provided to children are based on research conducted with adults only. Indigenous children are not only underrepresented in pediatric clinical trials but also experience health disparities and environmental conditions that may differentially impact their health as well as the effectiveness of interventions compared with their peers. The need for increased inclusion of Indigenous children in clinical trials is particularly highlighted by the emergence of complex diseases, such as COVID-19, that manifest differently in children and disproportionately affect Indigenous communities.

The NIH Institutional Development Award (IDeA) program builds research capacity in states that historically have low levels of NIH funding (Figure A, available as a supplement to the online version of this article at http://www.ajph.org).[35] In fiscal year 2020, the 23 IDeA-designated states and Puerto Rico received only 7% of the $33 billion awarded for extramural research (Table 2). ECHO ISPCTN aims to increase pediatric clinical trials in these states, particularly in rural and medically underserved areas. Several of these states have the highest proportions of Indigenous children, presenting pediatric researchers with a unique and timely opportunity to partner with Indigenous

TABLE 2— Continued

State	Funding, $
New Mexico	112 437 059
Maine	103 673 732
Arkansas	75 960 965
Vermont	71 427 751
Delaware	54 867 373
Hawaii	52 881 131
Puerto Rico	49 611 681
West Virginia	45 482 645
Nevada	43 936 449
Mississippi	43 914 422
Montana	43 398 838
South Dakota	26 583 066
North Dakota	24 743 701
Idaho	18 296 519
Alaska	15 887 731
Wyoming	12 808 992

Source. US Department of Health and Human Services.[36]

[a]Includes 27 states, Guam, Virgin Islands, American Samoa, and foreign locations outside the United States or territories.
[b]Includes 23 states and Puerto Rico.

communities on state-of-the-art clinical trials. Doing so requires understanding the challenges and necessary considerations in doing this type of research. We suggest 3 best practices for conducting pediatric trials with Indigenous communities. We hope that future research elaborates on these practices as more pediatric researchers successfully engage with Indigenous communities to conduct clinical trials to reduce health disparities and improve child health outcomes.

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CONFLICTS OF INTEREST

The authors have no potential or actual conflicts of interest from funding or affiliation-related activities.

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This study describes published research and did not involve human participants.

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The 1942 Massive Contamination of Yellow Fever Vaccine: A Public Health Consequence of Scientific Arrogance

Ilana Löwy, PhD

See also Podolsky, p. 1565.

In the late 1930s, the 17D vaccine against yellow fever was produced in record time. 17D was and is an excellent vaccine. Its rapid diffusion led, however, to several problems, the most important among them being the 1942 massive contamination of the vaccine distributed to the US Army by the hepatitis B virus. The US part of this story is relatively well-known, but its Brazilian part much less so. In 1940, scientists who were producing the 17D vaccine in Rio de Janeiro found that it was contaminated by an "icterus virus" that originated in normal human serum. They solved this problem through the exclusion of human serum from vaccine production, but failed to persuade their US colleagues to do the same. The Rio experts, aware of the potential pitfalls of a new technology, carefully supervised the consequences of their vaccination campaigns. They were thus able to rapidly spot problems and eliminate them. By contrast, US scientists, persuaded of their technical superiority and distrustful of warnings that originated from a "less developed" country, neglected to implement basic public health rules. A major disaster followed. (*Am J Public Health*. 2021;111(9):1654–1660. https://doi.org/10.2105/AJPH.2021.306313)

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Discussion of the manufacture of COVID-19 vaccines is dominated by praise for their rapid development and diffusion. This is, we are told, an entirely unprecedented feat. Such self-congratulatory statements are not entirely accurate. Earlier emergencies stimulated the accelerated development of some vaccines. The most recent example was the Ebola vaccine—rapidly developed, licensed, and tested in the aftermath of the 2013–2016 outbreak.[1]

This essay describes an earlier event: the emergency production of the 17D yellow fever vaccine at the Rockefeller Institute virology laboratory in New York City during World War II. In 1941 and 1942, hundreds of thousands of doses of that vaccine were produced in record time and administered to US soldiers being sent to fight on the Pacific Front. Such rapid scaling-up of production of a viral vaccine was presented as an impressive endeavor. Alas, some batches of the vaccine were contaminated with a virus that induced jaundice (later identified as hepatitis B virus) that originated in one of the components of the vaccine, normal human serum. As a consequence, epidemiologists estimate that in spring 1942, between 40 000 and 50 000 US soldiers developed vaccine-related hepatitis.[2] The investigation that followed this outbreak acknowledged the existence of a severe public health problem, but presented it as unavoidable.[3] In 1942, when the vaccine was mass produced at the Rockefeller Foundation, scientists were not aware of the existence of an "icterus virus," transmissible by blood and other body fluids and resistant to heating to 56°C (then the usual method of inactivating pathogens in the serum), or of the presence of long-time carriers of such a virus. The investigation also praised the rapidity of the reaction of the Rockefeller Foundation virologists to this public health disaster. Merely a few weeks after the first report of jaundice in the US Army, they uncovered the culprit—human serum—and eliminated it from the vaccine's chain of production.[4]

The story omits to tell, however, that the same problem had arisen a year and half earlier in Brazil.[5] Brazilian and North American scientists who produced the 17D vaccine in Rio de Janeiro found that the most probable cause of jaundice linked with the yellow fever vaccine was contamination by an unknown virus present in the human serum, and that the manufacture of a serum-free 17D vaccine put an end to the incidence of postvaccination jaundice. The production of yellow fever vaccine in Rio de

Janeiro was made in close collaboration with the virology department of the Rockefeller Foundation. Researchers working in Brazil repeatedly warned their US colleagues about the serious dangers of use of human serum. They were not believed: scientists in a cutting-edge biomedical research center were not inclined to take lessons from researchers from a "peripheral" institution. As long as the New York laboratory produced only a small volume of the 17D vaccine, the maintenance of serum in the vaccine's composition probably had only limited consequences, but the situation changed dramatically with the mass production of this vaccine.

THE 17D VACCINE IN BRAZIL

The story of the yellow fever vaccine starts in the late 1920s, when successful infection of rhesus monkeys with yellow fever opened the way to production and testing of vaccines on the basis of killed or attenuated virus. The first vaccines made with a killed virus had limited efficacy only. In 1930, the virologist Max Theiler, who joined the Rockefeller Institute virology laboratory that year, successfully adapted the yellow fever virus to growth in a mouse brain, greatly facilitating its maintenance in the laboratory. Two years later, the director of the yellow fever laboratory at the Rockefeller Foundation, Wilbur Sawyer, together with his colleagues S. F. Kitchen and Wray Lloyd, developed the first live vaccine with an attenuated neurotropic yellow fever virus, 17E, grown in fertilized eggs. However, this virus was not sufficiently stable, and could be employed safely only when mixed with serum that contained antibodies against yellow fever.[6]

The virology laboratory of the Brazilian Yellow Fever Service at Oswaldo Cruz Institute, Rio de Janeiro (this laboratory was founded by experts from the Rockefeller Foundation), started a culture of the 17E strain in 1936. In 1937, a large epidemic of jungle yellow fever (yellow fever transmitted from jungle animals to people who live in proximity to a tropical forest) in the state of Parana led to a large-scale field trial of the 17E vaccine. Scientists who conducted this trial found that some of the vaccine's recipients developed complications such as serum sickness, rash, and jaundice; these complications were attributed to reaction to anti–yellow fever serum.[7] George Marshall Findlay and his colleagues from the Wellcome Foundation's virology laboratory in London, who also noted jaundice among people vaccinated in Africa, similarly doubted the role of the yellow fever virus itself.[8] Researchers therefore wished to develop a vaccine that could be administered without immune serum.

In 1937, Max Theiler, with his colleague Hugh Smith, developed another attenuated strain of yellow fever, 17D. Animal experiments and preliminary tests in humans indicated that 17D could be administrated without immune human serum.[9] That same year, Smith traveled from New York to Rio de Janeiro, where he and a Brazilian colleague, Henrique de Azevedo Penna, perfected the culture of 17D in fertilized eggs, making possible rapid production of a new vaccine. The 17D vaccine was first used in Brazil during an outburst of sylvatic yellow fever in Minas Gerais in December 1937. In 1938, 1 058 328 Brazilians were vaccinated with 17D.[10] Because of the unknown risks linked with distribution of a live vaccine for a dangerous disease, the Brazilian Yellow Fever Service staff elaborated a strict protocol of postvaccination surveillance. Each vaccination site had two tables: one for the preparation of the vaccine (diluted from a lyophilized stock) and another for records and paperwork. Data on each vaccinated person (name, age, sex, occupation, address) were recorded in a vaccination book. One copy of this book was kept locally and another in Rio. After a vaccination campaign in a given locality, physicians designated by the Yellow Fever Service visited this locality twice—once after a few weeks and then after a few months—to investigate the efficacy and potential secondary effects of the vaccine. The existence of detailed records of vaccination facilitated their task.[11]

The protocol elaborated in Brazil for the early 17D vaccination campaigns was maintained during the impressive scaling-up of the vaccination. In 1939 alone, more than a million Brazilians received the 17D vaccine.[12] In 1939 to 1941, there were several incidents of iatrogenic effects of the vaccine. The existence of these incidents led a researcher of the Oswaldo Cruz Institute, Angelo Moreira de Costa Lima, to accuse the Rockefeller Foundation experts of using Brazilians as guinea pigs.[13] This, however, was a minority opinion. The yellow fever vaccination campaigns were usually well accepted, probably because of fear of the disease, but also because the campaigns' organizers successfully mobilized the support of local authorities and local elites. Moreover, although vaccination incidents were far from negligible, the existence of an efficient follow-up mechanism made possible rapid detection of a problem and its elimination. As the Rockefeller Foundation's experts in Brazil explained, "the best protection against future accidents is the careful surveillance of vaccinated individuals."[14]

The main pitfalls of using a live, neurotropic vaccine maintained through multiple passages in fertilized eggs, were that the virus might be too weak (excessive attenuation) or too strong (insufficient attenuation), and contamination of the vaccine by an external infectious agent. During the mass production of the 17D yellow fever vaccine in Rio de Janeiro, all three types of accidents did occur. In 1939, a vaccination campaign in the state of Espirito Santo was followed by an epidemic of yellow fever. The cause, researchers in the Rio laboratory found, was that the virus used for vaccination was weakened through too many passages in fertilized eggs. Accordingly, they limited the number of such passages.[15] In June 1941, doctors observed a rise in incidence of encephalitis after a vaccination campaign in the state of Minas Gerais. An investigation concluded that the outbreak was induced by a batch of vaccine that contained an insufficiently attenuated virus. This incident led to a tightening of controls of attenuation of the virus through more frequents checks on its effects in laboratory animals.[16]

The most serious accident with the 17D vaccine in Brazil was, however, its contamination by a "jaundice agent." During a vaccination campaign in the state of Espirito Santo in late 1939 and early 1940, a postvaccine follow-up identified more than 1000 cases of jaundice, with 22 deaths. The Rockefeller Foundation experts and their Brazilian colleagues decided to halt immunization with 17D until they could find the source of this jaundice. First, they excluded the possibility that the jaundice was produced by a mutation of the yellow fever virus itself. There was no correlation whatsoever between jaundice and the level of antibodies against yellow fever. They then carefully examined all the components of the production chain, and through an elimination process arrived at the conclusion that the culprit was normal human serum, employed as a suspension fluid that protected the fragile yellow fever virus.[17] Virologists who had produced the yellow fever vaccine in Rio de Janeiro decided to discard all the old batches of vaccine. They imported a new strain of 17D from New York, and in the mid-1940s they started production of a vaccine in which the human serum was replaced by liquid from fertilized eggs. There were no more cases of vaccine-related jaundice in Brazil.[18]

The conclusion that serum can contain a jaundice-inducing "agent" was not very surprising. There had been numerous earlier reports of this phenomenon. Probably the most important among them was the description—made in 1919 by the South African professor of veterinary medicine Arnold Theiler—of jaundice in horses vaccinated against African horse sickness with a combination of live virus and horse immune serum. Theiler concluded that the jaundice—later named Theiler's disease—was induced by a previously unknown virus in the horse immune serum.[19] In 1939, Findlay and his colleagues proposed that jaundice observed in people vaccinated with 17D virus might have originated in normal human serum used to prepare this vaccine.[20] It is reasonable to assume that these studies were known to virologists confronted with the outbreak of postvaccine jaundice in Brazil. It is equally reasonable to assume that they were known to scientists who produced the 17D vaccine in New York, the more so because Max Theiler was Arnold Theiler's son, and Findlay and his colleagues at the Wellcome Foundation had frequent exchanges with Rockefeller Foundation experts. Virologists from the New York laboratory were also aware of the decision, made in Rio de Janeiro in 1940, to produce a serum-free yellow fever vaccine. Nevertheless, a year later, when the New York laboratory began a massive production of yellow fever vaccine for the US Army, its vaccine contained normal human serum.

THE 17D VACCINE IN NEW YORK

From 1938 on, the Rockefeller Institute virology laboratory in New York was engaged in small-scale production of the 17D vaccine (Sawyer became the head of the International Division of the Rockefeller Foundation in 1935, but continued to work part-time in the laboratory). Production of the vaccine increased in 1939, but remained limited. Demand for the vaccine increased steeply in 1940, however, with the growing probability of the United States entering the war and opening a Pacific Front. Sawyer and his collaborators Johannes Bauer and George Strode were initially reluctant to scale up vaccine production in their laboratory. Faced with the alternative of either increasing their production of the vaccine or entering into partnership with private industry, they nevertheless chose the first alternative.[21] In 1940, the virology laboratory's researchers considered the possibility of switching to production of a serum-free vaccine, but finally decided that a period of rapid scaling-up of manufacture was not the right time to modify a product that, they were persuaded, was already satisfactory.[22] Fred Soper, the head of the Rockefeller Foundation International Division in Latin America, strongly disagreed. The New York researchers believed that there were no complaints about their vaccine, he argued, because

they did not make any effort to find out whether such complaints existed. In one documented case, a Pan American Airways pilot, M. Koepke, reported in 1941 severe icterus following vaccination against yellow fever, but the follow-up of this case was rapidly dropped.[23] In December 1941, Sawyer nevertheless reiterated that the absence of complaints about the New York vaccine proved that they were taking adequate precautions to avoid contaminations.[24]

In 1941, the yellow fever laboratory of the Rockefeller Foundation was transformed into a production plant.[25] Between January 1, 1941, and April 9, 1942, it supplied the US Army with 141 batches of vaccine, that is, 7.7 million doses.[26] Whereas in 1941 the vaccine was mainly intended for the Navy and Air Forces, from December 1941, when the United States entered the war, the bulk of the vaccine went to the Land Army. The first cases of jaundice in the Army were reported in California in March 1942. Sawyer was at first reluctant to consider the possibility that the disease was induced by yellow fever vaccine. He and Bauer immediately traveled to California to investigate the jaundice outbreak, and on March 25 Sawyer wrote to Strode that he and Bauer were increasingly persuaded that it was a local event, unrelated to vaccination.[27] Things were, however, moving fast. In early April, jaundice cases among vaccinated soldiers appeared simultaneously in numerous sites. The majority of these cases were mild, but 17% were classified as moderately severe and 2% as very severe.[28] An emergency meeting of the New York virology laboratory decided on April 9 to halt the production of vaccine with human serum, and start the production of a serum-free vaccine.[29] On April 16, the surgeon general recommended stopping yellow fever vaccination until the arrival of new, serum-free batches.[30]

On July 24, 1942, US Secretary of War Henry L. Stimson reported that from January to July, vaccination against yellow fever had induced 28 525 cases of "yellow jaundice" and 62 deaths. The *Chicago Tribune* of July 28, 1942, reacted to this statement, and to the announcement of the death from hepatitis of Lieutenant Colonel Edward Platt Reed, chief of the Inspection Division of the Chicago District. The *Tribune* editorial protested the Army's decision to use a dangerous vaccine, adding that the majority of the vaccinated soldiers had a very remote chance of becoming infected with yellow fever. It concluded that the yellow fever vaccination was a sanitary disaster. Someone was guilty of a grievous error of judgment, and an inquiry was plainly needed to find who was responsible for this error.[31] In his editorial of August 1, 1942, the editor of the *Journal of the American Medical Association*, Morris Fishbein, vigorously rejected the *Chicago Tribune*'s accusations.

> There is every reason to believe that the occurrence of 62 deaths and some 28,000 cases of jaundice associated with the vaccination of millions of men is far less serious than would be an epidemic of virulent yellow fever among soldiers sent to tropical areas.

The *Tribune* editorial's call for an inquiry, Fishbein wrote, "presupposes a stupidity on the part of medical science which is wholly unjustified." By printing such accusations, the *Tribune* might create fear among soldiers, injure morale, and hamper the war effort.[32] An article in the *New York Times* of October 18, 1942, stated that the "tremendous hullabaloo" raised by one Chicago, Illinois, newspaper about postvaccine jaundice was totally unwarranted. An investigation "has been unable to discover anything that savors of negligence or that gives any cause for alarm."[33]

There was no external inquiry into the postvaccine icterus incident. The report of an internal investigation by the Rockefeller Foundation, published in 1944, estimated that more than 26 000 soldiers developed postvaccine hepatitis.[34] Later, epidemiologists estimated that at least 40 000 soldiers were hospitalized with this diagnosis, of a total of 300 000 soldiers immunized with contaminated batches of the vaccine, the largest known iatrogenic incident of vaccination in US history.[35] The internal investigation conducted in the virology laboratory linked jaundice-inducing batches of 17D vaccine with serum from individuals who had had jaundice in the past.[36] In the second half of 1942, three surgeons from the US Public Health Service injected 278 volunteers from an "institution with a population of at least 1700" (probably a prison) with suspected batches of yellow fever vaccine or sera of people who developed jaundice following vaccination, and displayed a transmission of jaundice through serum.[37] The commission that, in 1944, investigated the massive contamination of yellow fever vaccine by hepatitis virus exonerated the Rockefeller Institute virology laboratory from responsibility for this incident.[38] Sawyer's biographers acknowledge nevertheless that his involvement in the massive contamination of US soldiers harmed his reputation.[39] This also may have been the reason why he did not share the Nobel Prize awarded to Max Theiler in 1951 for his yellow fever studies.

The contamination of US soldiers by hepatitis B virus might have become a

long-term health disaster as well. Because hundreds of thousands of US soldiers were vaccinated with contaminated vaccine in early 1941, there was a serious risk of increased incidence of chronic liver disease in this population. This probably did not happen. Investigations made 40 years later did not find a significant increase in severe liver disease among recipients of contaminated batches of vaccine; it was concluded that although a "natural" infection with hepatitis B through contaminated syringes, blood and blood product, and sexual relationships led to chronicity in 5% to 10% of cases, the proportion of chronic cases was much lower among contaminated soldiers, probably because they were young, healthy, and above all had a single exposure to the virus.[40] These studies nevertheless uncovered a small excess of deaths from liver cancer among the infected soldiers.[41] One might add to those a possible excess of deaths from liver cirrhosis. In 2011, the *Tampa Bay Times* published an article entitled "St. Petersburg Woman Solves Mystery of Dad's 1958 Death," which reported that a woman whose father died from cirrhosis in 1958 heard about the contamination of soldiers with yellow fever vaccine, obtained evidence of vaccination of her father with a contaminated batch, presented this evidence to the Veterans Health Administration, and retroactively obtained veteran benefits for her mother.[42]

CONCLUSION: TECHNOLOGY AND TRUST

Sawyer's refusal to accept the Brazilian researchers' view of the important risks linked to inclusion of human serum in the 17D vaccine was attributed mainly to his conviction that the Brazilian epidemiological data were not solid enough to justify a modification that might have decreased the potency of the yellow fever vaccine.[43] In a 1944 article, Sawyer and his colleagues explained that they knew that researchers in Brazil connected an earlier episode of postvaccine jaundice to the presence of virus-containing human serum in the vaccine's production, but the "peculiar" traits of the Brazilian incident led them believe that in all probability "the yellow fever virus used in the preparation of the vaccine has become contaminated with an icterogenic agent during the cultivation in tissue cultures."[44] Sawyer and his colleagues disregarded the Rio de Janeiro group's claim that they carefully excluded the possibility of contamination of viral cultures themselves, probably because they did not trust virology studies conducted in Rio.[45] Accordingly, they became persuaded that the true cause of the end of the outbreak of postvaccine icterus in Brazil was not the exclusion of human serum from the vaccine, but the fact that the Rio group discarded their old viral cultures and started anew with a fresh strain of the virus imported from New York.[46]

Sawyer and his colleagues attributed the problems with the vaccine produced in the Rio de Janeiro laboratory to failure to adequately supervise the virus cultures in an "inferior" setting. They were confident that such problems would not arise in the cutting-edge virology laboratory in New York. Confident of the high quality of their product, they did not believe that it was important to provide a careful follow-up of the people vaccinated. Their claim that they had never encountered a problem with the vaccine produced in New York was grounded in the absence of complaints, not in field studies. Scientists who worked in Brazil, the great majority of whom were locally trained Brazilian doctors and technicians, had a very different attitude. They employed low-tech approaches to quality control: careful registering of information on each vaccinated individual, systematic and thorough postvaccination follow-up, and meticulous epidemiological investigation of suspicious cases. Their main research tools were a "vaccination book," a pen, and labor-intensive collection, transmission, and tabulation of data.

The yellow fever vaccine produced at Fiocruz (previously Oswaldo Cruz Institute) is still the 17D attenuated strain, and the vaccine department proudly preserves the first vials of the vaccine from 1937. In 2021, this vaccine is manufactured at the ultra-modern glass-and-steel building of Bio-Manguinhos, but this is a relatively new development. Until the early 21st century, yellow fever vaccine was produced in a modest building on the Fiocruz campus, lost among many other similar buildings, some dedicated to healing, some to teaching, and some to fundamental or applied research. The physical integration of the manufacture of vaccine with numerous other health-related activities was even more present in the late 1930s and early 1940s. Researchers from the Yellow Fever Service all took part in monitoring yellow fever outbreaks, producing and distributing vaccine, treating patients, and surveilling vaccinated people. The virology laboratory in New York, situated in the impressive building of the Rockefeller Institute—satirized in Sinclair Lewis's novel *Arrowsmith* under the name McGurk Institute—was in the early 1940s at the cutting edge of biomedical science. It is perhaps not surprising that many (though to be fair, not all) of the leading scientists at that institution had little confidence in knowledge produced by virologists who were working in a modest laboratory in a

peripheral country, relying mainly on elementary public health methods. Sawyer and other researchers at the Rockefeller Institute virology laboratory did not entirely disbelieve the results obtained in Rio de Janeiro; they just did not trust them sufficiently to act upon them and change their own behavior. In his *Journal of the American Medical Association* editorial of August 1942, Morris Fishbein criticized an assumption of "stupidity on the part of medical science."[47] Stupidity is probably not the right term. Excessive faith in (presumably) superior technology, distrust of (presumably) less knowledgeable "others," and neglect of basic public health approaches may be more accurate explanations.

Alas, doubts about the quality of studies made in the Global South—including those made in leading institutions by highly competent scientists—do not belong to the bygone past. In November 2015, two groups of Brazilian virologists—one from the Fiocruz Institute in Rio de Janeiro and led by Ana Maria Bispo, the other from Instituto Evandro Chagas in Ananindeua (Para state) and led by Pedro Vasconcelos—displayed links between the Zika virus and microcephaly. In Brazil, nobody doubted their findings; US experts were, however, skeptical. Peter Hotez, dean of the National School of Tropical Medicine at Baylor College of Medicine, explained in January 2017 that the initial reluctance of the Centers for Disease Control and Prevention (CDC) to accept the Brazilian scientists' work slowed the international response:

> even when the Brazilians found Zika virus in two women's amniotic fluid and in the brain of a microcephalic fetus, the CDC would not accept it until they had done it themselves. I saw that as hubris.[48]

The 2015–2017 Zika epidemic was mainly a regional phenomenon, with an especially high incidence in Brazil. The initial slowness of the international reaction to this epidemic therefore had a limited effect only on global public health. The slowness of European and North American reactions to Chinese publications from late January and early February 2020, which pointed to the danger of rapid propagation of a new coronavirus, had very different consequences.[49] AJPH

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CONFLICTS OF INTEREST

The author has no conflicts of interest to disclose.

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Balancing Consideration of the Risks and Benefits of E-Cigarettes

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See also Samet and Barrington-Trimis, p. 1572.

The topic of e-cigarettes is controversial. Opponents focus on e-cigarettes' risks for young people, while supporters emphasize the potential for e-cigarettes to assist smokers in quitting smoking. Most US health organizations, media coverage, and policymakers have focused primarily on risks to youths. Because of their messaging, much of the public—including most smokers—now consider e-cigarette use as dangerous as or more dangerous than smoking. By contrast, the National Academies of Science, Engineering, and Medicine concluded that e-cigarette use is likely far less hazardous than smoking. Policies intended to reduce adolescent vaping may also reduce adult smokers' use of e-cigarettes in quit attempts.

Because evidence indicates that e-cigarette use can increase the odds of quitting smoking, many scientists, including this essay's authors, encourage the health community, media, and policymakers to more carefully weigh vaping's potential to reduce adult smoking-attributable mortality.

We review the health risks of e-cigarette use, the likelihood that vaping increases smoking cessation, concerns about youth vaping, and the need to balance valid concerns about risks to youths with the potential benefits of increasing adult smoking cessation. (*Am J Public Health*. 2021;111(9):1661–1672. https://doi.org/10.2105/AJPH.2021.306416)

The use of nicotine-containing electronic- or e-cigarettes has divided the tobacco control community along a spectrum from fervent opponents to enthusiastic supporters. Opponents emphasize that vaping can cause nicotine addiction among young people and could lead some to become dependent cigarette smokers, possibly "renormalizing" smoking. They cite research indicating that nicotine may harm adolescents' developing brains. Some consider vaping's health risks substantial, and some question whether vaping decreases smoking cessation.[1] By contrast, proponents present evidence that vaping assists smokers in quitting smoking and believe that vaping poses far less risk to users' health than does smoking. Smoking among youths, they observe, has declined rapidly during vaping's ascendancy.[2]

Many US governmental health agencies[3–6] and nongovernmental medical[7,8] and health organizations[9–12] focus primarily on vaping's risks for young people. These organizations' pronouncements and their influence on policymakers and the media have had a profound impact on the public's understanding of vaping. A study of US news articles on e-cigarettes found that, from 2015 to 2018, 70% of articles mentioned vaping's risks for youths, while only 37.3% noted potential benefits for adult smokers.[13] Of respondents to a 2019 national survey, nearly half considered vaping nicotine just as harmful as or more harmful than cigarette smoking. Only 1 in 8 considered vaping less harmful. (The rest responded "I don't know."[14]) By contrast, the US National Academies of Sciences, Engineering, and Medicine[15] and the British Royal College of Physicians[16] have concluded that vaping is likely far less hazardous than smoking cigarettes.

The public's inaccurate perception worsened following a 2019 vaping-associated acute pulmonary disease outbreak (named "e-cigarette or vaping use-associated lung injury" [EVALI]) that caused 68 fatalities.[17] Media coverage was extensive. Several states and cities promptly banned retail and online sale of flavored e-cigarettes.[18] In early 2020, however, research attributed the illness to vitamin E acetate, an adulterant in illicit tetrahydrocannabinol (THC) vaping devices shown to produce pulmonary injury in animals.[19–21] A small percentage

of patients with EVALI reported vaping only nicotine, but they were primarily in states where THC was illegal, and most had no toxicology testing.[22] Once the potential harm of vitamin E acetate was publicized and adulterated THC removed from the market, the incidence of new cases fell precipitously.[19] Yet, after the outbreak, two thirds of respondents to a poll related the lung disease deaths to use of "e-cigarettes such as JUUL." Only 28% related the deaths to use of "marijuana or THC e-cigarettes."[23]

Scientists differ in their views of the relative risks and benefits of vaping nicotine, and of their implications.[1,2,24,25] Many, including this article's authors, believe that vaping can benefit public health, given substantial evidence supporting the potential of vaping to reduce smoking's toll. Our objective is to encourage more balanced consideration of vaping within public health and in the media and policy circles.

In the following pages we address:

- the health risks of vaping,
- the likelihood that vaping increases smoking cessation,
- the principal concerns about youth vaping, and
- balancing concerns about risks to youths with potential benefits for adult smokers.

THE HEALTH RISKS OF VAPING

According to the National Academies of Sciences, Engineering, and Medicine, "Laboratory tests of e-cigarette ingredients, in vitro toxicological tests, and short-term human studies suggest that e-cigarettes are likely to be far less harmful than combustible tobacco cigarettes."[15(p1)] The British Royal College of Physicians similarly concluded that "vaping isn't completely risk-free but is far less harmful than smoking tobacco."[16]

High-quality clinical and epidemiological data on vaping's health effects are relatively sparse. There are no data on long-term health effects, reflecting the relative novelty of vaping and the rapid evolution of vaping products. Determining even short-term health effects in adults is difficult because most adult vapers are former or current smokers.

Some studies find that vaping may worsen asthma, bronchitis, and cough, including among nonsmoking young people.[26,27] By contrast, a few studies found that smokers with asthma or chronic obstructive lung disease see symptoms improve after switching to e-cigarettes.[28,29] Randomized switching trials (cigarettes to e-cigarettes) document improvements in respiratory symptoms.[30,31]

Laboratory studies have reported potentially adverse effects of e-cigarette aerosol in cells and animals.[26,32] It is difficult, however, to extrapolate from exposure conditions in cells and animals to humans.[26] Human experimental studies have focused on acute effects,[33] which may not predict future disease. For example, e-cigarettes acutely impair tests of endothelial function, a common feature of cardiovascular disease, but when smokers switch from cigarettes to e-cigarettes, endothelial function normalizes.[34,35] A recent study detected no difference in biomarkers of inflammatory and oxidative stress in exclusive e-cigarette users and nonusers of either cigarettes or e-cigarettes.[36]

There is little evidence that e-cigarettes pose significant cancer risk.[15] However, some studies raise concerns that warrant long-term follow-up of vapers.[37,38]

Many scientists have concluded that vaping is likely substantially less dangerous than smoking because of the following[15,16]:

- The number of chemicals in cigarette smoke, greater than 7000,[39] exceeds that of e-cigarette aerosol by 2 orders of magnitude.[40,41]
- Among potentially toxic substances common to both products, cigarette smoke generally contains substantially larger quantities than e-cigarette aerosol.[42–44] However, e-cigarette aerosol contains some substances not found in cigarette smoke.[45]
- Biomarkers reflecting exposure to toxic substances are present at much higher levels in exclusive cigarette smokers than in exclusive vapers, and studies of smokers who switch to e-cigarettes find decreases in toxicant exposures.[31,46–50]
- Tests of lung and vascular function indicate improvement in cigarette smokers who switch to e-cigarettes.[28,29,34] Exclusive users of e-cigarettes (most being former smokers) report fewer respiratory symptoms than do cigarette smokers and dual users.[51]

However, questions remain.[52] Ongoing research will lend further insight into the products' absolute and relative dangers.

THE LIKELIHOOD THAT VAPING INCREASES SMOKING CESSATION

A growing body of evidence indicates that vaping can foster smoking cessation, although the evidence is not definitive.[53,54]

Randomized Trials

In an English smoking cessation randomized controlled trial,[55] smokers assigned to e-cigarettes achieved nearly twice the rate of biochemically confirmed smoking cessation at 1 year (18%) than smokers assigned to nicotine replacement therapy (9.9%); all received identical behavioral counseling. While 80% of those who quit with e-cigarettes were still vaping, they were no longer exposed to smoking's substantially higher risk.

A New Zealand trial found that at 6 months, nicotine patch with nicotine e-cigarettes outperformed patch with nicotine-free e-cigarettes and patch alone. Thus, in addition to aiding quitting when used alone, nicotine e-cigarettes may increase the effectiveness of existing cessation aids.[56]

Examining 26 randomized controlled trials, a recent Cochrane Review concluded that "There is moderate-certainty evidence that ECs [electronic cigarettes] with nicotine increase quit rates compared to ECs without nicotine and compared to nicotine replacement therapy."[53] Another meta-analysis drew similar conclusions, albeit with less certainty.[57] However, the US Preventive Services Task Force's smoking cessation practice guideline did not find the evidence convincing.[58] As such, and for reasons the Cochrane Review describes, more well-designed clinical trials are needed.

Noteworthy is the lack of trials by e-cigarette manufacturers in pursuit of regulatory agency approval to use e-cigarettes for smoking cessation, likely reflecting the profitability of selling e-cigarettes as consumer products, rather than medicinal devices.

Population Studies

Collectively, population studies' findings are consistent with a near doubling of quit attempt success, found in the randomized controlled trials, and the fact that e-cigarettes are smokers' most used aid in quit attempts.[59] Four studies[60–63] found significant increases in smoking cessation (10%–15%) that the authors associated with vaping. A Centers for Disease Control and Prevention study reported that, in 2018, 15.1% of smokers had quit smoking for 6 months or longer using e-cigarettes, compared with 3.3% using other noncigarette tobacco products and 6.6% using no tobacco products.[64] Another study identified a near doubling of self-reported cessation among users of e-cigarettes or varenicline compared with smokers not using these products.[65] Consistent with these population studies, simulation analyses have generally found that vaping increases smoking cessation, avoiding large numbers of premature deaths.[66–69]

Other researchers have found regular and frequent e-cigarette use to be associated with increased smoking cessation, while infrequent use was not.[70–75] This could reflect self-selection, with frequent vapers possibly liking vaping more and being more motivated to quit smoking. Infrequent vapers might use vaping as a temporary nicotine source where smoking is prohibited.[73,76]

Other researchers have reported reduced cessation rates among smokers who vape.[77,78] However, many failed to distinguish frequency of vaping, introducing the risk of the selection biases just noted. Other studies included only current vapers who also smoke, systematically excluding vapers who had successfully quit smoking.[53,78]

An often-cited meta-analysis found vapers' odds of quitting smoking 28% lower than for nonvaping smokers.[77] This analysis combined clinical trials, cohort studies, and cross-sectional analyses, an inappropriate practice for meta-analyses.[79] Furthermore, the individual studies' sources of bias could be compounded in a meta-analysis, possibly producing an incorrect result.[76]

Cigarette Sales

For years, US cigarette sales declined 2% to 3% annually. More recently, as vaping product sales increased, cigarette sales decreased much more rapidly. Conversely, following the EVALI outbreak and e-cigarette sales restrictions, sales of e-cigarettes fell and sales of cigarettes resumed their prevaping pattern.[80] Studies finding a positive cross-price elasticity of demand between cigarettes and e-cigarettes support the conclusion that the products are substitutes.[81,82]

Support for the plausibility of an inverse causal relationship between vaping and smoking comes from countries in which startling decreases in cigarette sales have accompanied rising sales of another novel nicotine product, heated tobacco products (HTPs). Like e-cigarettes, HTPs expose users to lower levels of toxicants than do cigarettes.[83] In Japan, HTP adoption from 2015 to 2019 was accompanied by cigarette sales declining by a third.[84] In both cases—HTPs in Japan and e-cigarettes in the United States—as sales of reduced-risk products rose, cigarette sales fell.

Unintended Consequences of Policies Restricting Vaping

Studies have found that policies intended to restrict e-cigarette use may

have unintentionally increased cigarette smoking. One study associated a Minnesota e-cigarette tax with increased adult smoking and reduced cessation, estimating that taxing e-cigarettes at the same rate as cigarettes nationwide could deter 2.75 million smokers from quitting smoking over a decade.[85] Two other studies found state restrictions on minors' access to e-cigarettes associated with higher adolescent cigarette smoking.[86,87]

Implications

Although not the final word, the totality of the evidence indicates that frequent vaping increases adult smoking cessation. Smokers unable to quit smoking with evidence-based cessation methods[88] should be well informed about the relative risks of vaping and smoking and vaping's potential to help them quit smoking. They should understand that, while the long-term health consequences are unknown, completely substituting vaping for smoking likely reduces health risks, possibly substantially.[15] Dual use of cigarettes and e-cigarettes will not have a comparable beneficial effect.[88] However, a period of dual use may be necessary for some smokers to transition from smoking. Because vaping itself poses some risk, the best advice is to eventually stop vaping as well.

THE PRINCIPAL CONCERNS ABOUT YOUTH VAPING

The principal objections to vaping regard 3 potential effects on youths:

- Vaping can cause nicotine addiction among young people who never would have tried smoking.
- Vaping by never-smoking youths may cause some to try smoking, risking "renormalizing" smoking among young people.
- Nicotine can harm developing brains, and vaping nicotine may have other adverse health effects.

Vaping as a Cause of Nicotine Addiction

Vaping likely addicts some young people to nicotine. However, the evidence does not suggest it is addicting very large numbers.[89] Jarvis et al. concluded that "Data . . . do not provide support for claims of a new epidemic of nicotine addiction stemming from use of e-cigarettes."[90] Jackson et al. recently reported that the e-cigarette–driven increase in nicotine product use among high-school students is not associated with an increase in population-level dependence.[89] Among tobacco-naïve youths, in addition to low vaping prevalence (9.1% in the past 30 days in 2020) and frequency (2.3% vaping ≥ 20 days in the past 30 days),[91] small percentages exhibited signs of nicotine dependence.[90]

Frequent use is much more common among current or former smoking youths than among never-smokers.[90] Many former smokers were already addicted to nicotine before initiating vaping. With high-school students' smoking declining at an increasing rate since youths began using e-cigarettes,[92,93] some may vape to reduce or quit smoking.

Nonetheless, to the extent that vaping creates nicotine addiction among otherwise tobacco-naïve youths, concerted efforts are needed to reduce youth vaping. The new minimum age of 21 years for purchasing tobacco products should help.[94] Governmental agencies[3,95] and voluntary organizations[12,96] disseminate vaping's risks to youths through Web sites, social media, and television campaigns. Voluntary organizations lobby Congress and state governments to adopt policies restricting youth access to e-cigarettes.

Recent policy attention has focused on restricting the availability of e-cigarettes with flavors,[97] a principal attraction for youths.[98-101] While flavor bans could reduce youth interest in e-cigarettes, they could also reduce adult smokers' vaping to quit smoking.[102–104] Like youths, adults prefer nontobacco flavors,[105] both groups favoring fruit and sweet flavors.[106,107]

Policies regarding flavors reflect the more general issue considered in this article: the need to create a balance between the sometimes-conflicting goals of preventing youth vaping and supporting adults' smoking cessation attempts, particularly for smokers unable or unwilling to quit otherwise.[108]

Vaping Causing Smoking Initiation

Prospective studies have found that young people who had vaped but never smoked cigarettes were more likely to have tried cigarettes several months to 2 years later than contemporaries who had neither smoked nor vaped.[15,109-113] Some commentators thus consider vaping a "gateway" into smoking.[114,115]

Other observers believe the relationship reflects a "common liability"[116]: young people who vape are generally more prone to risky behavior[117]; hence, they might be more likely to try smoking even without vaping.[118-121] Three recent studies have concluded that vaping likely diverts more young people from smoking than encourages them to

smoke.[122–124] Conversely, some prospective studies have found the vaping–smoking relationship strongest in youths at low risk of smoking.[125–127]

Obvious plausible correlates are often not considered, however.[128] Importantly, few studies include youths' use of other psychoactive substances, including marijuana and alcohol. In 1 study, inclusion of marijuana and 3 other variables eliminated the otherwise statistically significant link between vaping and subsequent smoking.[126,127] Most studies do not even consider previous use of tobacco products other than cigarettes. Adjustment for confounders substantially reduces the relationship between vaping and subsequently trying cigarettes.[129]

Numbers of cigarettes smoked at follow-up are frequently very low, only 1 or 2 in the past 12 months in one study.[130] Furthermore, the prospective studies generally have not examined progression to regular dependent smoking, with 1 recent exception.[131] Only a small proportion of youths who experiment with smoking become regular smokers. Kim and Selya found that while e-cigarette use was associated with ever trying smoking, it was not associated with current continued smoking.[119] Pierce et al. recently concluded the opposite.[131] Shahab et al. reported that less than 1% of US students who initiated nicotine or tobacco use with e-cigarettes were established cigarette smokers.[132]

If vaping causes some young people to try cigarettes, the aggregate impact must be small. A recent study[68] estimated that if vaping increases nonsmoking youths' odds of trying cigarettes by 3.5 (as reported by Soneji et al.[109]), smoking initiation among young adults would increase less than 1 percentage point. Furthermore, US survey data demonstrate that smoking among young people has declined at its fastest rate ever during vaping's ascendancy.[92,93,133] If vaping increases smoking initiation, other unknown factors more than compensate.

Nicotine Harming Developing Brains

Animal model studies have found that nicotine can affect maturation of brain parts associated with executive function and decision-making, potentially leading to more impulsive behavior, cognitive deficits, and greater likelihood to self-administer other drugs.[134,135] In addition, there is evidence in humans of neurological changes attributed to nicotine in the brains of adolescent smokers, interpreted by some as reflecting similar harmful effects to those in the animal models.[136,137]

These studies lead some researchers to suspect that adolescent nicotine use in any form may lead to long-term structural and functional brain changes with associated negative implications for cognition or impulse control.[138] However, given species differences and questions about the relevance of experimental animal nicotine dosing paradigms to human use patterns, the validity of extrapolation to humans is speculative. Whether impaired brain development with behavioral consequences occurs in young nicotine consumers is difficult to determine because of potential confounding of genetic and socioeconomic factors, the influence of other substance abuse, and the role of preexisting neuropsychiatric problems associated with youth smoking. Research has yet to isolate nicotine use in the adolescent years and then examine later sequelae. Still, concerns about brain function effects of nicotine exposure through vaping deserve serious examination.[98]

Concerns About Youth Vaping in Context

Several considerations raise the question of whether, for youth as a whole, vaping creates dangerous levels of nicotine exposure that would not have occurred in the absence of vaping.

- The large majority of nontobacco product–using young people do not vape and, thus, have no nicotine exposure.[90]
- Among those who vape, most do so infrequently; many are short-term experimenters.[90]
- Frequent vaping is most common among current or former smokers, individuals already exposed to nicotine.[91]
- The most dangerous form of youth exposure to nicotine, cigarette smoking, has declined at an unprecedented rate during the era of youth vaping.[92,93,133] Use of other tobacco products has declined as well.[139]

Still, concerns emanating from substantial increases in youth vaping in 2018 and 2019 are readily understandable and important to address. A sizable decline in 2020 is encouraging.[139] We must continue monitoring youth vaping, learning more about potential harms and identifying effective prevention strategies. However, as public health groups, the media, policymakers, and the general public focus on youth vaping, vaping's potential to help adults quit smoking too often gets lost. That may come at a significant public health cost. Fourteen percent of US adults smoke; smoking annually causes nearly half a

million deaths. Anything that can reduce that toll deserves serious attention.

With the focus on youths creating an environment in which smokers believe that vaping is as dangerous as or more dangerous than smoking,[14] many smokers struggling to quit may be unwilling to try vaping as an alternative. This likely translates into less smoking cessation than if smokers correctly understood the relative risks of vaping and smoking.

BALANCING CONCERNS ABOUT RISKS AND POTENTIAL BENEFITS

Research comparing vaping's risks for youths with potential benefits for adult smokers has found the latter to dominate,[66] potentially avoiding the smoking-produced loss of tens of millions of life-years.[67,68] Vaping cannot end cigarette smoking. But vaping can complement tried-and-true methods of reducing smoking, including taxes on combustible tobacco products, smoke-free workplace laws, marketing restrictions, plain packaging with graphic warning labels, antismoking media campaigns, tobacco-21 laws,[94] and evidence-based smoking cessation treatment.[88]

We believe the potential lifesaving benefits of e-cigarettes for adult smokers deserve attention equal to the risks to youths.[140] Millions of middle-aged and older smokers are at high risk of near-future disease and death. Quitting reduces risk.[88] Young people will not experience smoking-related (and conceivably vaping-related) chronic diseases for 3 decades, and likely not at all if they quit within a decade or 2. Social pressures to quit smoking will probably remain strong, and quitting aids may improve. Furthermore, as noted previously, the rate of smoking among young people has declined while vaping has increased.[92,93,133] Vaping may addict some youths to nicotine, but many fewer than popularly believed.[89,90]

Seeking a Sensible Mix of Policies

To date, the singular focus of US policies on decreasing youth vaping may well have reduced vaping's potential contribution to reducing adult smoking. Those policies include taxing e-cigarettes at rates comparable to cigarette taxes,[141] decreasing adult access to flavored e-cigarettes that may facilitate smoking cessation,[103] and convincing the public—including smokers—that vaping is as dangerous as smoking.[14]

The public health objective should be to develop policies and interventions that both reduce youth vaping and increase adult smoking cessation.[97,120,140,142] While an in-depth discussion of an optimal policy mix exceeds the scope of this article, we here present illustrative policies that would serve this objective. These are all in addition to conventional evidence-based prevention and cessation measures.

- Tax cigarettes and other combustible tobacco products heavily; impose a more modest tax on e-cigarettes. Taxes should be proportionate to risk. A much higher tax on combustibles will encourage adult smokers to quit smoking or to switch to less expensive e-cigarettes. By raising the price of e-cigarettes, a modest tax will discourage their use by price-sensitive youths.[141]
- Because both youth and adult smokers find e-cigarette flavors attractive,[98–107] banning all (or most) flavors risks reducing smokers' use of e-cigarettes to quit smoking[102–104] at the same time that it reduces youth vaping.[99,101] An alternative would be to limit the retail sale of flavored e-cigarettes to adult-only outlets such as vape shops. An imperfect policy for either goal, this approach could benefit both.
- Government agencies and health organizations should develop nuanced, targeted communications that emphasize the realistic concerns about youth vaping and, separately, the potential benefits of e-cigarettes as less-risky (but not risk-free) alternatives for adult smokers otherwise unable or unwilling to quit smoking.
- The US Food and Drug Administration (FDA) should strictly regulate e-cigarette advertising and marketing, prohibiting all marketing directed at, or attractive to, youths and young adults, including all "lifestyle" advertising. They should limit advertising to a "switch" theme directed clearly, and exclusively, to adult smokers otherwise unable to quit smoking.
- FDA should implement its thoughtful comprehensive 2017 plan,[143] mandating reduction of nicotine in cigarettes to levels incapable of sustaining addiction, while ensuring the availability of consumer-acceptable reduced-risk nicotine products. To achieve the latter, the agency should develop product standards for products like e-cigarettes, ensuring minimization of risk associated with the product class while maintaining consumer acceptability.

The Role of Nicotine in Tobacco-Produced Disease

FDA predicated its comprehensive plan on recognition of the continuum of risk in nicotine products.[143] Nicotine is the chemical in tobacco that fosters addiction. However, toxic constituents other than nicotine, predominantly in smoked tobacco, produce the disease resulting from chronic tobacco use.[143,144] Nicotine-yielding products vary in risk from FDA-approved nicotine replacement therapy products at the lowest end of the risk continuum to combustible cigarettes at the highest.

Unfortunately, the public has a distorted view of the dangers associated with nicotine per se. In a recent survey, 57% of respondents incorrectly agreed that "nicotine in cigarettes is the substance that causes most of the cancer caused by smoking." Only 18.9% disagreed. (The rest answered "Don't know.")[14] In a recent survey of physicians, 80% strongly, but incorrectly, agreed that nicotine causes cancer, cardiovascular disease, and chronic obstructive pulmonary disease.[145]

CONCLUSIONS

We share the very legitimate concerns about youth vaping with the entire field of public health. Our goal is to put those concerns in perspective. We agree with former Surgeon General C. Everett Koop who, in 1998, urged that "[A]s we take every action to save our children from the ravages of tobacco, we should demonstrate that our commitment to those who are already addicted . . . will never expire."[146] The latter appears at risk today.

While evidence suggests that vaping is currently increasing smoking cessation, the impact could be much larger if the public health community paid serious attention to vaping's potential to help adult smokers, smokers received accurate information about the relative risks of vaping and smoking, and policies were designed with the potential effects on smokers in mind. That is not happening.

The need to pay attention to adult smokers is particularly important from a social justice perspective. African Americans suffer disproportionately from smoking-related deaths, a disparity that, a new clinical trial shows, vaping could reduce.[31] Today's smokers come disproportionately from lower education and income groups, the LGBTQ (lesbian, gay, bisexual, transgender, and queer or questioning) community,[147] and populations suffering from mental health conditions[148] and from other drug addictions.[149] Smoking accounts for a significant proportion of the large life expectancy difference between affluent and poorer Americans.[150,151] For smokers with serious psychological distress, two thirds of their 15-year loss of life expectancy compared with nonsmokers without serious psychological distress may be attributable to their smoking.[152] Vaping might assist more of these smokers to quit.[148,153]

To the more privileged members of society, today's smokers may be nearly invisible. Indeed, many affluent, educated US persons may believe the problem of smoking has been largely "solved." They do not smoke. Their friends and colleagues do not smoke. There is no smoking in their workplaces, nor in the restaurants and bars they frequent. Yet 1 of every 7 US adults remains a smoker today.

Smoking will claim the lives of 480 000 of our fellow citizens this year alone. AJPH

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K. E. Warner wrote much of the original draft of the article and supervised revisions. N. L. Benowitz, S. M. Colby, D. K. Hatsukami, R. Niaura, N. A. Rigotti, and R. West drafted specific sections of the article or played lead roles in reviewing and revising article drafts. All authors reviewed all drafts critically, contributed significantly to revisions, and approved the final version of the article.

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The authors are former presidents of the Society for Research on Nicotine and Tobacco (SRNT), the world's leading professional organization dedicated to the subject. They are listed in alphabetical order. All 26 of the then–past presidents were invited to participate as co-authors of this article. (A 27th past president was the active president at the time of preparation of the article.) We were unable to reach one of them. Three were not included because of institutional commitments that they felt might be interpreted as conflicts of interest. The remaining 7 declined to co-author.

Note. The opinions expressed in this article are solely those of the authors. They do not represent those of SRNT, which has taken no organizational position on the issues discussed in this article and had no involvement in the preparation of this article.

CONFLICTS OF INTEREST

N. L. Benowitz is a consultant to Pfizer and Achieve Life Sciences, companies that market or are developing smoking cessation medications, and has been an expert witness in litigation against tobacco companies. S. J. Leischow is conducting a clinical trial supported by Achieve Life Sciences, which is developing a nonnicotine medication for smoking cessation, and has consulted with them. He also consulted more than 1 year ago for GSK, which is working to bring a new nicotine-replacement product to market, and he receives medication for a National Institutes of Health–funded smoking-cessation study from Pfizer. N. A. Rigotti receives royalties from UpToDate Inc for writing about smoking cessation and e-cigarettes and is a consultant for Achieve Life Sciences for an investigational smoking-cessation medication. R. West has undertaken research and consultancy for Pfizer and GSK, companies that manufacture smoking-cessation medications.

HUMAN PARTICIPANT PROTECTION

There were no human participants involved.

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Racial and Ethnic Disparities in Maternal Mortality in the United States Using Enhanced Vital Records, 2016–2017

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See also Galea and Vaughan, p. 1584.

Objectives. To better understand racial and ethnic disparities in US maternal mortality.

Methods. We analyzed 2016–2017 vital statistics mortality data with cause-of-death literals (actual words written on the death certificate) added. We created a subset of confirmed maternal deaths that had pregnancy mentions in the cause-of-death literals. Primary cause of death was identified and recoded using cause-of-death literals. We examined racial and ethnic disparities both overall and by primary cause.

Results. The maternal mortality rate for non-Hispanic Black women was 3.55 times that for non-Hispanic White women. Leading causes of maternal death for non-Hispanic Black women were eclampsia and preeclampsia and postpartum cardiomyopathy with rates 5 times those for non-Hispanic White women. Non-Hispanic Black maternal mortality rates from obstetric embolism and obstetric hemorrhage were 2.3 to 2.6 times those for non-Hispanic White women. Together, these 4 causes accounted for 59% of the non-Hispanic Black–non-Hispanic White maternal mortality disparity.

Conclusions. The prominence of cardiovascular-related conditions among the leading causes of confirmed maternal death, particularly for non-Hispanic Black women, necessitates increased vigilance for cardiovascular problems during the pregnant and postpartum period. Many of these deaths are preventable. (*Am J Public Health*. 2021;111(9):1673–1681. https://doi.org/10.2105/AJPH.2021.306375)

Significant disparities in maternal mortality between White and Black mothers have been recorded as long as national data have been available. In 1933, all states reported maternal deaths for the first time, and the mortality rate for Black mothers (1000 per 100 000 births) was 1.8 times the rate for White mothers (564 per 100 000).[1] These disparities have persisted, averaging 4 times higher for Black compared with White mothers as recently as 1990 to 1996,[2] with the most recent publication of 2018 maternal mortality rates showing a disparity of 2.5 times.[3] The breadth and persistence of these racial disparities have led to clinical,[4] policy,[5] and programmatic[6] initiatives. Compounding the challenges has been a lack of clarity in the measurement of maternal mortality.[7]

Vital statistics provide the official US maternal mortality estimates and also identify cases for more detailed review for other maternal mortality data systems such as the Pregnancy Mortality Surveillance System and maternal mortality review committees.[7] However, concerns about the accuracy of US vital statistics data used to measure maternal mortality have persisted for decades. Before 2003, the concern about accuracy of vital statistics data focused mainly on underreporting of maternal deaths.[8,9] With the 2003 standard revision of birth and death certificates, a pregnancy checkbox was added to address this underreporting,[10] and, as a result, more maternal deaths were captured on the death certificate.[11,12] However, recent validity studies found that the pregnancy checkbox also led to overreporting of maternal deaths (i.e., reproductive-aged women were counted as a maternal death with no

indication of pregnancy upon further validation), ranging from 21% in a 4-state study[13] to 50% in a Texas study.[14]

Another problem identified in vital statistics maternal mortality data is the large and increasing number of deaths coded to ill-defined causes. Studies found that 40% to 50% of maternal deaths were coded to ill-defined causes that do not provide any information as to the actual cause of death.[15,16] With so many deaths coded to ill-defined causes, it is impossible to accurately identify the leading causes of maternal death or the percent contribution of individual causes of death to maternal mortality disparities. To address these challenges, we developed a different cause-of-death coding method to increase the specificity of causes identified while greatly reducing the number of maternal deaths coded to ill-defined causes.[17] To correct for overreporting errors, we analyzed the cause of death literals (actual words written on the death certificate) to identify cases in which the decedent's pregnancy or postpartum status was not only identified by the pregnancy checkbox or a maternal mortality code on the death certificate but was also confirmed by specific terms written in the cause-of-death section of the death certificate—hereafter known as confirmed maternal deaths. The purpose of this study was to use this set of confirmed maternal deaths to re-examine racial and ethnic disparities in US maternal mortality, to identify the leading causes of maternal death by race and ethnicity, and to identify the specific causes of death that contributed the most to racial and ethnic disparities. Accurate information is critical to the development of preventive measures to address the profound racial/ethnic disparities in maternal mortality in the United States.

METHODS

US maternal mortality data used for national and international comparisons are based on information reported on death certificates filed in state vital statistics offices and compiled into national data through the National Vital Statistics System.[3] Physicians, medical examiners, or coroners are responsible for completing the medical portion of the death certificate, including the cause of death. The United States uses the World Health Organization (WHO) definition of maternal death: "The death of a woman while pregnant or within 42 days of termination of pregnancy, irrespective of the duration and the site of the pregnancy, from any cause related to or aggravated by the pregnancy or its management, but not from accidental or incidental causes."[18(p1238)] Late maternal deaths are those that occur from 43 days to 1 year after pregnancy.[18] Since 1999, cause-of-death data in the United States have been coded according to the *International Statistical Classification of Diseases and Related Health Problems, 10th Revision* (*ICD-10*).[18] Maternal deaths are those coded to *ICD-10* codes A34, O00–O95, and O98–O99, while late maternal deaths are coded to O96.[3,18]

We used the 2016 and 2017 US multiple cause-of-death data files from the National Center for Health Statistics (NCHS), with cause-of-death literals added. The cause-of-death literals are the actual words written in the cause-of-death section of the death certificate, which serve as the basis for assignment of *ICD-10* codes and provide much richer detail as to the actual circumstances of death. We created a subset of all possible maternal or late maternal deaths for coding. This included all females aged 10 to 54 years with a maternal code (A34, O00–O96, or O98–O99) in the multiple cause-of-death data or with pregnant or postpartum status indicated by the pregnancy checkbox.[17] For confirmed maternal deaths, the timing of death (maternal or late maternal) was identified by the pregnancy checkbox, together with information in the cause-of-death literals.

By 2016, all states except West Virginia had a pregnancy checkbox on their death certificate. West Virginia added the checkbox in 2017, and we included their data to be able to provide US estimates and because their inclusion or exclusion did not appreciably affect our findings. California had a nonstandard pregnancy question that ascertained whether the woman was pregnant at the time of death or up to 1 year before death. Given that more detailed information was not available, we included the California data and used the NCHS designation of whether these deaths were maternal or late maternal.[19]

Recoding Records to the Primary Cause of Death

NCHS coding practices specify that if the pregnancy checkbox indicates that the death occurred during or within 1 year of pregnancy, then the cause of death is automatically coded as a maternal or late maternal death, regardless of whether the condition was related to or exacerbated by the pregnancy. The only exception is for injury deaths (i.e., accidents, homicides, and suicides), which are coded to nonmaternal causes.[20] However, because of major problems with the pregnancy checkbox data,[13,14] we chose to examine each case independent of the checkbox. Thus, we recoded records with a pregnancy or postpartum mention in the cause-of-death literals as maternal deaths and

records with no such mention as nonmaternal causes.[17] This does not mean that the latter deaths were nonmaternal but merely indicates that we were unable to confirm pregnant or postpartum status from the cause-of-death literals. The recoding was done to increase the specificity of conditions coded and to provide an alternative code for cases in which it was unclear whether they were maternal deaths.

We developed an alternative coding strategy to identify the primary cause of death directly from the cause-of-death literals using methods described in more detail elsewhere.[17] We defined the "primary cause of death" as the cause of death that was the most likely, or primary, cause that led to the decedent's death, regardless of order of terms listed on the death certificate.[17] Standard underlying cause-of-death coding rules rely heavily on the order of causes listed and whether there is a plausible sequence of one cause leading to another.[18,20] However, maternal death certificates are often not filled out with proper cause-of-death sequencing. In these cases, an application of the standard cause-of-death coding rules often does not result in the most informative cause being selected as the underlying cause, a point explored in depth in a previous paper.[17] While assigning primary cause of death involves human judgment, we minimized bias by having all records jointly coded by 2 PhD epidemiologists trained at NCHS (M. F. M. and M. T.). Any discrepancies between the coders were resolved via individual case review and discussion, consultation with WHO and NCHS *ICD-10* coding manuals,[18,20] medical textbooks,[21] and with medical and coding experts. This coding reduced the percentage of maternal deaths coded to ill-defined causes (O26.8, O95, O99.8) from 43.5% in the NCHS-coded data to 2.5% among confirmed maternal deaths.

Late maternal deaths are coded to *ICD-10* code O96, which does not provide any information about the actual cause of death.[18] Thus, late maternal deaths with pregnancy mentions in the cause-of-death literals were coded to more specific maternal causes, while records with no such mention were coded to nonmaternal causes.

Analysis

We chose all "confirmed" maternal and late maternal death records for more detailed analysis. These were records in which specific terms indicating pregnancy or postpartum status (e.g., pregnant, postpartum, ectopic, amniotic) were written in the cause-of-death section of the death certificate.[17] This, together with the pregnancy checkbox being checked (in almost all cases), provides a high degree of confidence that these were in fact maternal or late maternal deaths.

We analyzed data separately for non-Hispanic White, non-Hispanic Black, and Hispanic women. Other race and ethnic groups were included in the total population but were not shown separately because of insufficient numbers of deaths to support a detailed cause-of-death analysis. An additional reason to restrict the analysis to non-Hispanic White, non-Hispanic Black, and Hispanic women is that race/ethnicity reporting is quite accurate on death certificates for these groups, but is less accurate for other racial/ethnic groups such Asians, Pacific Islanders, and Native Americans.[22] As not all states reported multiracial data in 2016 to 2017, we used NCHS bridged race data for our analysis.[23] NCHS provided bridged race data to reassign the 0.5% of US records reporting more than 1 race back to single-race categories using methods described elsewhere.[23] The purpose of this reassignment was to provide consistent racial categorization for data years when some states reported multiracial data and some did not.

We computed maternal mortality rates per 100 000 live births. We ascertained live births by race/ethnicity for the 2016 and 2017 data years from Centers for Disease Control and Prevention WONDER births online database.[19] Our population of maternal deaths includes those deaths that could be confirmed as maternal from specific terms listed in the cause-of-death literals. Thus, our maternal mortality rates likely underestimate the true levels of maternal death in the United States. In our analysis, we emphasized other estimates, specifically the ranking of leading causes of death, and maternal mortality rate ratios (MRRs). The advantages of this approach were to (1) identify a set of deaths that we can clearly confirm as maternal deaths, (2) improve the specificity of cause-of-death coding for these confirmed maternal deaths, and (3) greatly reduce the number of deaths coded to ill-defined causes. Thus, relative comparisons of maternal deaths and causes of death can be made with greater accuracy.

We ranked leading causes of maternal death from a longer tabulation list of causes of maternal death using NCHS ranking procedures.[17,24] We used our recoded primary cause data to identify the leading causes of maternal death for the total population and for non-Hispanic White, non-Hispanic Black, and Hispanic women. We compared maternal MRRs by race and ethnicity from our recoded data to corresponding rate ratios from NCHS data. The maternal MRR is the maternal mortality rate for

group A (e.g., non-Hispanic Black women) divided by the maternal mortality rate for group B (e.g., non-Hispanic White women).

We identified the causes of death that contributed the most to the non-Hispanic Black–non-Hispanic White maternal mortality disparity. This was done by computing the total difference in maternal mortality rates between non-Hispanic Black and non-Hispanic White women and the difference for each of the leading causes. The difference for each cause was then divided by the total difference to yield a percent contribution of each cause to the total difference.

Rates and ratios based on 10 to 19 deaths are shown but are flagged as being statistically unreliable, while rates based on fewer than 10 deaths are suppressed.[19] All statements in the text were tested for statistical significance and a statement that a rate is higher or lower than another rate indicates that the rates were significantly different at a *P* level of less than .05.

RESULTS

Among our study's confirmed maternal deaths, the 2016–2017 maternal mortality rate for non-Hispanic Black women was 3.55 times that for non-Hispanic White women (MRR = 3.55; Table 1). This ratio was higher than in the NCHS-coded data (MRR = 2.46). Numbers and rates are shown in Table A (available as a supplement to the online version of this article at http://www.ajph.org). The confirmed late maternal mortality rate (6 weeks to 1 year after delivery) for non-Hispanic Black women was 3.52 times that for non-Hispanic White women (MRR = 3.52). This ratio was also higher than in the NCHS-coded data (MRR = 2.14). The confirmed maternal MRR was not significantly higher for Hispanic than for non-Hispanic White women with ratios of 1.08 for maternal and 1.29 for late maternal deaths. This finding was in direct contrast with the NCHS-coded data, which found significantly lower maternal mortality rates among Hispanic compared with non-Hispanic White women (MRR = 0.76).

For the total population, obstetric embolism and eclampsia and preeclampsia were tied for the leading cause of maternal death (Table 2). The obstetric embolism category includes amniotic fluid embolism, pulmonary embolism, and any other type of embolism occurring during the pregnant or postpartum period. The third leading cause of maternal death was postpartum cardiomyopathy, followed by obstetric hemorrhage, and other complications of obstetric surgery and procedures (many from problems during cesarean section). Together, the 5 leading causes of maternal death accounted for nearly two thirds (65.7%) of confirmed maternal deaths. Rankings were similar for non-Hispanic White and Hispanic women (Table 2).

For non-Hispanic Black women, eclampsia and preeclampsia was the leading cause of death, followed by postpartum cardiomyopathy, obstetric embolism, and obstetric hemorrhage (Table 2). Ectopic pregnancy was the fifth leading cause of maternal death for non-Hispanic Black women but did not fall among the 5 leading causes for non-Hispanic White and Hispanic women. For non-Hispanic Black women, the risk of dying from eclampsia and preeclampsia (MRR = 5.06), and postpartum cardiomyopathy (MRR = 4.86) was about 5 times that for non-Hispanic White women.

The causes of death that contributed the most to the non-Hispanic Black–non-Hispanic White maternal mortality disparity were eclampsia and preeclampsia (22.1%), postpartum cardiomyopathy (19.1%), and obstetric embolism (11.0%; Table 2). If the non-Hispanic Black maternal mortality rate for these 3 causes could be reduced to non-Hispanic White levels, the overall maternal mortality disparity would be reduced by more than one half (52.2%). This is in contrast with the NCHS-coded data in which, by far, the largest contributor to the non-Hispanic Black–non-Hispanic White maternal mortality disparity was ill-defined causes (38.4%).[19]

For late maternal deaths, the leading cause of death was postpartum cardiomyopathy, accounting for 36.9% of all late maternal deaths for the total population, 32.4% of deaths for non-Hispanic White women, and 56.8% of deaths for non-Hispanic Black women (Table 3). Other causes of death that were important in the late maternal period were obstetric embolism, eclampsia and preeclampsia, and diseases of the circulatory system, although small numbers of deaths from these causes make a more detailed analysis infeasible.

For non-Hispanic Black women, the risk of late maternal death from postpartum cardiomyopathy was 6 times that for non-Hispanic White women (MRR = 6.16). About two thirds (66.4%) of the non-Hispanic Black–non-Hispanic White late maternal mortality disparity was attributable to postpartum cardiomyopathy.

DISCUSSION

Despite advances in public health, large racial and ethnic disparities in US maternal mortality remain a critical problem that calls into question our ability as a nation to treat all persons equally. Among confirmed maternal and

TABLE 1— Maternal Mortality Rate Ratios (MRRs) by Race/Ethnicity: United States, 2016–2017

	Maternal,[a] MRR (95% CI)[b]		Late Maternal,[c] MRR (95% CI)[b]		Combined Maternal and Late Maternal, MRR (95% CI)[b]	
	NCHS Coded	Confirmed	NCHS Coded	Confirmed	NCHS Coded	Confirmed
Non-Hispanic Black/ Non-Hispanic White	2.46 (2.20, 2.75)	3.55 (2.94, 4.28)	2.14 (1.79, 2.57)	3.52 (2.17, 5.71)	2.37 (2.16, 2.60)	3.55 (2.98, 4.22)
Hispanic/Non-Hispanic White	0.76 (0.66, 0.88)	1.08 (0.85, 1.36)	0.87 (0.70, 1.07)	1.29 (0.72, 2.26)	0.79 (0.70, 0.89)	1.11 (0.89, 1.36)
Non-Hispanic Black/ Hispanic	3.23 (2.78, 3.75)	3.30 (2.62, 4.19)	2.47 (1.96, 3.12)	2.73 (1.56, 4.92)	2.99 (2.64, 3.39)	3.21 (2.59, 3.99)

Note. CI = confidence interval; NCHS = National Center for Health Statistics.

[a]Deaths during pregnancy, birth, or up to 42 d postpartum.
[b]Rate ratio = maternal mortality rate for group A divided by maternal mortality rate for group B.
[c]Deaths between 43 and 365 d postpartum.

late maternal deaths, the non-Hispanic Black maternal mortality rate was 3.5 times the non-Hispanic White rate. The excess maternal mortality risk was focused among a few causes of death, and much of this excess mortality is preventable. Specific causes of death had even higher rate ratios. For example, maternal mortality risk was 5 times higher for non-Hispanic Black than for non-Hispanic White women for eclampsia and preeclampsia. These results are consistent with other studies documenting that Black women have higher rates of preeclampsia and eclampsia than do White women and are more likely to die from this complication.[25] Data suggest that 60% of maternal deaths related to preeclampsia are preventable, making this a critical area for intervention.[26] One recommended strategy is the implementation of a hypertension safety bundle in an effort to standardize care. This safety bundle includes provider and staff education on hypertension, protocols, treatment algorithms, and other key strategies to improve care for pregnant women with hypertension during delivery.[27]

Postpartum cardiomyopathy is another important contributor to the non-Hispanic Black–non-Hispanic White maternal mortality disparity, particularly among late (43 days to 1 year) maternal deaths.[28] For non-Hispanic Black women, the maternal mortality rate from postpartum cardiomyopathy was 5 times, and the late maternal mortality rate was 6 times that of non-Hispanic White women. Previous data suggest that Black women with postpartum cardiomyopathy are more likely to present with more severe symptoms and more advanced disease than White women.[29] Increasing awareness of cardiovascular disease in the postpartum setting by health care providers beyond obstetricians and gynecologists (e.g., emergency department physicians, primary care providers) may help to improve early diagnosis and treatment of this complication. Earlier detection is critical as a significant proportion of deaths from cardiomyopathy are thought to be preventable.[30]

For non-Hispanic Black women, obstetric embolism was the third and obstetric hemorrhage was the fourth leading cause of maternal death, with rates 2.6 and 2.3 times those for non-Hispanic White women, respectively. For both of these conditions, safety bundles have been recommended to standardize delivery care.[31] Similar to deaths from preeclampsia and cardiomyopathy, a significant portion of these deaths (up to 70% in the case of hemorrhage) are thought to be preventable.[32]

Strengths and Limitations

Strengths of this study included the use of cause-of-death literals, which provide richer detail on the specific circumstances of death: detail that is often lost during standard coding processes. For many women, an examination of the cause-of-death literals provided confirmation that the woman was pregnant or postpartum at the time of death, thus ensuring the accuracy of the maternal death attribution. Examination of the literals together with improved coding procedures also allowed us to reduce the percentage of deaths coded to ill-defined causes from 43.5% in the NCHS-coded data to 2.5% among confirmed maternal deaths, illustrating that most records initially coded to ill-defined causes actually contained more specific

TABLE 2— Five Leading Causes of Confirmed Maternal Death by Race and Hispanic Origin: United States, 2016–2017

	Total[a]		Non-Hispanic White[b]		Non-Hispanic Black[c]		Hispanic		Non-Hispanic Black/Non-Hispanic White, MRR (95% CI)	% Contribution to Non-Hispanic Black–Non-Hispanic White Disparity
	Rank	No. (Rate)[d]	Rank	No. (Rate)[d]	Rank	No. (Rate)[d]	Rank	No. (Rate)[d]		
All causes		615 (7.88)		230 (5.58)		232 (19.81)		109 (6.00)	3.55 (2.94, 4.28)	
Obstetric embolism (O88)	1	98 (1.26)	1	41 (0.99)	3	30 (2.56)	1	22 (1.21)	2.58 (1.55, 4.23)	11.0
Eclampsia and preeclampsia (O11, O13–O16)	1	98 (1.26)	2	32 (0.78)	1	46 (3.93)	3	13 (0.72)[e]	5.06 (3.16, 8.21)	22.1
Postpartum cardiomyopathy (O90.3)	3	86 (1.10)	4	29 (0.70)	2	40 (3.42)	5	11 (0.61)[e]	4.86 (2.93, 8.12)	19.1
Obstetric hemorrhage (O20, O43.2, O44–O46, O67, O71.0, O71.1, O71.3, O71.4, O71.7, O72)	4	82 (1.05)	3	31 (0.75)	4	20 (1.71)	2	19 (1.05)[e]	2.27 (1.22, 4.11)	6.7
Other complications of obstetric surgery and procedures (O75.4)	5	40 (0.51)	7	10 (0.24)[e]	6	14 (1.20)[e]	4	12 (0.66)[e]	4.93 (2.04, 12.4)	6.7

Note. CI = confidence interval; MRR = mortality rate ratio. Maternal deaths include those during pregnancy and up to 42 d postpartum.

[a]Includes other races not shown separately because of small numbers of deaths.
[b]For non-Hispanic White women, diseases of the circulatory system was the fifth leading cause of death with 16 deaths and a rate of 0.39.
[c]For non-Hispanic Black women, ectopic pregnancy was the fifth leading cause of maternal death with 18 deaths and a rate of 1.54.
[d]Per 100 000 live births.
[e]Rate considered statistically unreliable; based on 10 to 19 deaths in the numerator.

cause-of-death information. Our approach also provided greater cause-of-death detail for late maternal deaths, which is obscured with standard coding practices.

A major limitation of this study is that some actual maternal deaths were likely not included in our subset of confirmed maternal deaths when the certifier did not note the woman's pregnant or postpartum status in the cause-of-death section of the death certificate; thus, results may not be generalizable to all maternal deaths in the United States. Because of this, we emphasized rate ratios and percent contribution among confirmed maternal deaths rather than focusing on maternal mortality rates.

It is also possible that we made errors in coding the primary cause of death. We minimized this possibility through careful review and discussion of each identified case and consultation with additional resources when needed. Another limitation is that vital statistics coding procedures do not classify deaths from injuries (i.e., accidents, homicides, or suicides) in pregnant or postpartum women as maternal deaths, while these types of deaths (particularly suicides and drug overdose deaths) are sometimes included as maternal deaths in other studies.[33]

Public Health Implications

Our data suggest that racial and ethnic disparities in maternal mortality in the United States may be even more pronounced than previously reported and further highlight the urgent need to address this public health crisis. Both maternal and late maternal mortality rates for non-Hispanic Black women were 3.5 times those for non-Hispanic White women. For eclampsia and preeclampsia and postpartum cardiomyopathy, rates for non-Hispanic Black women were 5

TABLE 3— Four Leading Causes of Confirmed Late Maternal Death by Race/Ethnicity: United States, 2016–2017

	Total[a]		Non-Hispanic White		Non-Hispanic Black		Non-Hispanic Black/Non-Hispanic White, MRR (95% CI)	% Contribution to Non-Hispanic Black–Non-Hispanic White Disparity
	Rank	No. (Rate)[b]	Rank	No. (Rate)[b]	Rank	No. (Rate)[b]		
All causes		103 (1.32)		37 (0.90)		37 (3.16)	3.52 (2.17, 5.71)	
Postpartum cardiomyopathy (O90.3)	1	38 (0.49)	1	12 (0.29)[c]	1	21 (1.79)	6.16 (2.90, 13.74)	66.4
Obstetric embolism (O88)	2	14 (0.18)[c]		5 (. . .)		5 (. . .)	. . .	. . .
Eclampsia and preeclampsia (O11, O13–O16)	3	12 (0.15)[c]		3 (. . .)		6 (. . .)	. . .	. . .
Diseases of the circulatory system (O99.4)	4	11 (0.14)[c]		4 (. . .)		2 (. . .)	. . .	. . .

Note. CI = confidence interval; MRR = mortality rate ratio. Ellipses indicate that rates were not computed because there were < 10 deaths. Late maternal deaths are those occurring from 42 d to 1 y postpartum.

[a]Includes other races/ethnicities not shown separately because of small numbers of deaths. For example, there were only 21 late maternal deaths for Hispanic women, which was insufficient to support detailed cause-of-death analysis.
[b]Per 100 000 live births.
[c]Rates based on 10 to 19 deaths are considered statistically unreliable.

times those for non-Hispanic White women. These findings are especially concerning because the majority of deaths from these causes are preventable.[32]

The prominence of cardiovascular conditions (i.e., eclampsia and preeclampsia, embolisms, cardiomyopathy) among the leading causes of maternal death in general, and particularly for non-Hispanic Black women, highlight the urgent need to optimize women's health across the life course, manage chronic illness, and standardize care. The elevated risk of death for Black women across multiple causes of maternal mortality reveals the impact of structural racism on health and health care in the United States.[34,35] Differences in patient–doctor communication, bias, language issues, shared decision-making, and use of evidence-based practices may help to explain these disparities and warrant further investigation. Groups such as the Council on Patient Safety in Women's Health Care have identified specific steps that health care systems can take to promote equity in women's health.[36] Further research into the experiences of women of color can inform efforts to improve health care systems and, thus, improve the birthing experience for all women.[37]

Racial and ethnic disparities in maternal mortality are unacceptable. Efforts to improve quality of care and equity across the life course are critical to preventing maternal mortality and reducing disparities. Accurate data are vital to our efforts to end maternal mortality disparities. AJPH

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CONFLICTS OF INTEREST

The authors have no conflicts of interest.

HUMAN PARTICIPANT PROTECTION

The study was ruled as exempt from institutional review board review from the University of Maryland institutional review board because the study was based on death certificates and there were no living human participants.

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Prenatal Use of Medication for Opioid Use Disorder and Other Prescription Opioids in Cases of Neonatal Opioid Withdrawal Syndrome: North Carolina Medicaid, 2016–2018

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Objectives. To estimate use of medication for opioid use disorder (MOUD) and prescription opioids in pregnancy among mothers of infants with neonatal opioid withdrawal syndrome (NOWS).

Methods. We used linked 2016–2018 North Carolina birth certificate and newborn and maternal Medicaid claims data to identify infants with an NOWS diagnosis and maternal claims for MOUD and prescription opioids in pregnancy (n = 3395).

Results. Among mothers of infants with NOWS, 38.6% had a claim for MOUD only, 14.3% had a claim for prescription opioids only, 8.1% had a claim for both MOUD and prescription opioids, and 39.1% did not have a claim for MOUD or prescription opioids in pregnancy. Non-Hispanic Black women were less likely to have a claim for MOUD than non-Hispanic White women. The percentage of infants born full term and normal birth weight was highest among women with MOUD or both MOUD and prescription opioid claims.

Conclusions. In the 2016–2018 NC Medicaid population, 60% of mothers of infants with NOWS had MOUD or prescription opioid claims in pregnancy, underscoring the extent to which cases of NOWS may be a result of medically appropriate opioid use in pregnancy. (*Am J Public Health.* 2021;111(9):1682–1685. https://doi.org/10.2105/AJPH.2021.306374)

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Over the past 2 decades in the United States, the prevalence of opioid use and opioid use disorder (OUD) in pregnancy has substantially increased.[1] Medication for opioid use disorder (MOUD) is the recommended, evidence-based treatment of OUD in pregnancy.[2] Prior research shows that MOUD, compared with detoxification or continued opioid use, is associated with improved outcomes, including reduced risk of return to drug use, improved engagement in treatment and prenatal care, and higher birth weights.[3]

Neonatal opioid withdrawal syndrome (NOWS) is an expected and treatable condition following prenatal exposure to opioids, including MOUD.[4] NOWS is a drug withdrawal syndrome with symptoms including minor behavioral problems such as feeding difficulties and high-pitched crying and, less frequently, major problems such as failure to thrive and seizures.[4] Nationally, the incidence of NOWS has increased alongside increases in opioid use and OUD in pregnancy.[5]

Understanding the extent to which NOWS cases are related to prenatal use of MOUD or prescription opioids as directed by a health care provider can inform appropriate pre- and postnatal intervention and reduce stigma associated with NOWS diagnoses. In 2 Florida counties from 2010 to 2012, among mothers of infants with NOWS, 41% used MOUD and 22% used prescription opioids in pregnancy.[6] Across neonatal

intensive care units in 33 states from 2012 to 2013, among infants with NOWS, 41% of mothers used MOUD and 24% used prescription opioids in pregnancy.[7] In Tennessee from 2013 to 2016, 59% of mothers of infants with NOWS used MOUD in pregnancy.[8]

Although results from existing studies are informative, changes in opioid and other substance use patterns in pregnancy and enhanced efforts to engage pregnant populations in treatment signal a need for more recent estimates to inform current practice. Moreover, given that 80% of NOWS-related deliveries are funded by Medicaid,[5] a focus on this population, which has not been explicitly examined in prior studies, is warranted. We used 2016–2018 North Carolina Medicaid and birth certificate data to conduct a descriptive study, estimating MOUD and prescription opioid use in pregnancy among mothers of infants diagnosed with NOWS.

METHODS

We used the 2016–2018 North Carolina Composite Linked Birth (Babylove) files, which include linked birth certificate and newborn and maternal Medicaid claims data. Data management and linkage are conducted by the North Carolina State Center for Health Statistics.

We used newborn Medicaid claims and birth certificate data to identify singleton infants born in 2016 to 2018. We defined NOWS as a diagnosis code of neonatal withdrawal symptoms (*International Classification of Diseases, 10th Revision, Clinical Modification* [*ICD-10-CM*] code P96.1)[9] within 30 days of delivery.[10]

We estimated each woman's pregnancy period using gestational age at delivery on the birth certificate and date of delivery in Medicaid claims. We defined MOUD use as at least 1 claim in pregnancy with a National Drug Code for buprenorphine or naltrexone or a Healthcare Common Procedure Coding System code for buprenorphine, methadone, or naltrexone. We defined prescription opioid use as at least 1 claim in pregnancy with an opioid National Drug Code, excluding MOUD.

We restricted the sample to mothers of infants diagnosed with NOWS who had continuous enrollment (≤ 30 total gap days) in Medicaid during pregnancy (n = 3395). We calculated the number and proportion who had a claim for MOUD, prescription opioids, both MOUD and prescription opioids, and neither in pregnancy. We compared available maternal and infant characteristics from the birth certificate across groups.

RESULTS

From 2016 to 2018, among mothers of infants diagnosed with NOWS, 38.6% had a claim for MOUD only, 14.3% had a claim for prescription opioids only, 8.1% had a claim for both MOUD and prescription opioids, and 39.1% did not have a claim for MOUD or prescription opioids in pregnancy (Table 1).

Relative to other groups, there was a higher percentage of younger women among those with neither MOUD nor prescription opioid claims (37.1% < 25 years). Nearly all women with MOUD (91.1%) and both MOUD and prescription opioid claims (87.7%) were non-Hispanic White. There was a higher percentage of non-Hispanic Black women among those with prescription opioid claims only (20.5%) and with neither MOUD nor prescription opioid claims (29.5%). The percentage of women who used tobacco in pregnancy was highest among those with MOUD claims only (71.5%) and with both MOUD and prescription opioid claims (68.5%). The percentage of infants born full term and normal birth weight was highest among women with MOUD claims (85.9% and 85.9%) or with both MOUD and prescription opioid claims (82.4% and 80.1%).

DISCUSSION

In the 2016–2018 North Carolina Medicaid population, 60% of mothers of infants with NOWS had MOUD or prescription opioid claims in pregnancy. Specifically, nearly half had a claim for MOUD and more than 1 in 5 had a claim for prescription opioids. This is consistent with previous research[6,7] and documents the extent to which cases of NOWS may be due to medically appropriate opioid use in pregnancy.

Younger women and non-Hispanic Black women were underrepresented among mothers with MOUD or with both MOUD and prescription opioids in pregnancy. Previous studies have documented racial inequities in the treatment of OUD among pregnant populations.[11] In addition, more than two thirds of women with MOUD or with both MOUD and prescription opioids used tobacco in pregnancy. This is notable, as tobacco use is associated with a greater severity of NOWS.[12] Last, infants of mothers who had MOUD or both MOUD and prescription opioids in pregnancy were more likely to be full term and normal birth weight. This aligns with prior research[3] and reinforces the potential benefits of MOUD in pregnancy for infant outcomes.

Interventions including prescription drug monitoring programs and prescribing guidelines have been implemented to reduce opioid use in pregnancy and resulting NOWS among infants. However, we found that 60% of

TABLE 1— Maternal and Infant Characteristics Among Mothers of Infants With Diagnosed Neonatal Opioid Withdrawal Syndrome: North Carolina, 2016–2018

	All, No. (%) (n = 3395)	Only Medication for OUD Claims in Pregnancy, No. (%) (n = 1309)	Only Prescription Opioid Claims in Pregnancy, No. (%) (n = 484)	Medication for OUD and Prescription Opioid Claims in Pregnancy, No. (%) (n = 276)	Neither Type of Claim in Pregnancy, No. (%) (n = 1326)
Maternal age, y					
< 25	972 (28.6)	288 (22.0)	127 (26.2)	65 (23.6)	492 (37.1)
25–29	1287 (37.9)	555 (42.4)	181 (37.4)	100 (36.2)	451 (34.0)
30–34	822 (24.2)	359 (27.4)	110 (22.7)	84 (30.4)	269 (20.3)
≥ 35	314 (9.2)	107 (8.2)	66 (13.6)	27 (9.8)	114 (8.6)
Maternal race/ethnicity					
Non-Hispanic White	2577 (75.9)	1193 (91.1)	328 (67.8)	242 (87.7)	814 (61.4)
Non-Hispanic Black	542 (16.0)	41 (3.1)	99 (20.5)	11 (4.0)	391 (29.5)
Other non-Hispanic	185 (5.4)	49 (3.7)	45 (9.3)	16 (5.8)	75 (5.7)
Hispanic	91 (2.7)	26 (2.0)	12 (2.5)	7 (2.5)	46 (3.5)
Maternal education					
< high school	1008 (29.8)	370 (28.4)	158 (32.6)	73 (26.4)	407 (30.8)
High school or GED	1161 (34.3)	442 (33.9)	153 (31.6)	95 (34.4)	471 (35.6)
Some college	1155 (34.1)	471 (36.1)	161 (33.3)	105 (38.0)	418 (31.6)
College, graduate, or professional school	62 (1.8)	21 (1.6)	12 (2.5)	3 (1.1)	26 (2.0)
Maternal marital status					
Not married	2587 (76.2)	980 (74.9)	352 (72.7)	201 (73.1)	1054 (79.5)
Married	806 (23.8)	328 (25.1)	132 (27.3)	74 (26.9)	272 (20.5)
Tobacco use in pregnancy					
No	1271 (37.5)	373 (28.5)	201 (41.8)	87 (31.5)	610 (46.1)
Yes	2117 (62.5)	936 (71.5)	280 (58.2)	189 (68.5)	712 (53.9)
Infant gestational age					
< 37 completed weeks (preterm)	593 (17.5)	184 (14.1)	103 (21.3)	39 (14.1)	267 (20.2)
≥ 37 completed weeks (full term)	2801 (82.5)	1125 (85.9)	381 (78.7)	237 (85.9)	1058 (79.8)
Infant birth weight					
Low (< 2500 g)	680 (20.0)	231 (17.6)	107 (22.2)	55 (19.9)	287 (21.6)
Normal (≥ 2500 g)	2714 (80.0)	1078 (82.4)	376 (77.8)	221 (80.1)	1039 (78.4)

Note. OUD = opioid use disorder.

mothers of infants with NOWS were either receiving the standard of care for treatment of OUD or a prescription opioid from a health care provider in pregnancy, suggesting alternative directions for intervention. First, efforts to ensure equitable access to MOUD should be prioritized. An understanding of the lived experiences and treatment barriers among non-White pregnant populations with OUD can inform efforts to address racial inequities in MOUD receipt. Second, because NOWS is an expected outcome of medically appropriate opioid use in pregnancy, efforts to promote the uptake of interventions that are effective in reducing the severity of NOWS (including tobacco cessation programs for pregnant persons receiving MOUD or prescription opioids[12]) or in treating NOWS (such as the "Eat, Sleep, Console" method[13]) should be prioritized.

These results should be interpreted in the context of some limitations. Prior research suggests that NOWS is underidentified in administrative data.[10] Thus,

some infants with NOWS may have been misclassified as not having NOWS, and our results may underestimate NOWS. In addition, some opioid treatment programs dispensing methadone do not accept Medicaid and only accept cash or check payment. If women paid for MOUD with cash or a check, this would not have been captured in the Medicaid claims data. Thus, our results may underestimate MOUD. Last, our results are specific to the North Carolina Medicaid population and may not generalize to other populations.

CONCLUSIONS

In the 2016–2018 North Carolina Medicaid population, 60% of mothers of infants diagnosed with NOWS had a claim for MOUD or a prescription opioid in pregnancy. By highlighting the use of treatment and opioids as prescribed by a health care provider among mothers of infants with NOWS, these results provide insights for intervention and can be used to reduce stigma associated with NOWS. AJPH

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CONTRIBUTORS

A. E. Austin conceptualized and designed the study, interpreted the data, and drafted the article. V. Di Bona conceptualized and designed the study, analyzed and interpreted the data, and revised the article for important intellectual content. M. E. Cox, S. Proescholdbell, M. D. Fliss, and R. B. Naumann conceptualized the study, interpreted the data, and revised the article for important intellectual content. All authors approve of the final article as submitted.

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CONFLICTS OF INTEREST

The authors have no conflicts of interest to disclose.

HUMAN PARTICIPANT PROTECTION

This study was reviewed and approved by the institutional review board at the University of North Carolina at Chapel Hill.

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Tailored Mobile Messaging Intervention for Waterpipe Tobacco Cessation in Young Adults: A Randomized Trial

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See also Busch et al., p. 1567.

Objectives. To test a tailored mobile health (i.e., mHealth) intervention for waterpipe tobacco cessation in young adults.

Methods. From 2018 to 2020 at 2 US sites, we conducted a randomized trial with 349 waterpipe tobacco smokers aged 18 to 30 years randomized to control (no intervention), untailored, or tailored intervention arms. Intervention arms received a 6-week mHealth intervention conveying risks of waterpipe tobacco through text and images and strategies to enhance motivation and support quitting. The tailored intervention was personalized to baseline measures and intervention text message responses. Risk appraisals, motivation to quit, waterpipe smoking frequency, and cessation were assessed at 6 weeks, 3 months, and 6 months.

Results. At 6 months, cessation was higher in the tailored (49%) than the control arm (29%; odds ratio = 2.4; 95% confidence interval = 1.3, 4.2) and smoking frequency was lower in the tailored (mean = 3.5 days) than the control arm (mean = 4.3 days; $P = .006$). At interim follow-ups, significant differences in other outcomes favored the tailored intervention.

Conclusions. Tailored mobile messaging can help young adult waterpipe tobacco smokers quit. This scalable intervention is poised for population implementation. (*Am J Public Health*. 2021;111(9):1686–1695. https://doi.org/10.2105/AJPH.2021.306389)

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Waterpipe (i.e., hookah) smoking is a method of tobacco use in which tobacco (usually sweetened or flavored) is heated with charcoal, smoke passes through water, and the smoke is inhaled by the user. Waterpipe tobacco smoking poses risks of health harm (e.g., cancer, cardiovascular disease, respiratory disease) and addictiveness, and is understudied relative to other forms of tobacco use.[1–8] Among US adults, the prevalence of waterpipe tobacco smoking is low overall, but it is more common in certain subgroups (e.g., some racial/ethnic and sexual minorities) and most common among young adults aged 18 to 30 years.[9–12] In the Population Assessment of Tobacco and Health (PATH) Study (wave 1, total n = 45 971), 11% of young adults were past-30-day waterpipe tobacco smokers, and young adults comprised 78% and 88% of adults who smoked waterpipe tobacco daily or weekly and monthly, respectively.[10] Prospective PATH data show that although most young adults who smoke waterpipe tobacco do so intermittently (i.e., nondaily), many sustain use over time.[13] Young adults' waterpipe tobacco smoking is influenced by multiple factors, including appealing flavors, marketing, and use in social settings.[14,15] Importantly, young adults' misperceptions that waterpipe tobacco is not harmful or addictive are major factors contributing to waterpipe tobacco smoking.[14–19] Young adults also have low motivation to quit waterpipe tobacco smoking and believe quitting is easy, yet many develop dependence symptoms and have difficulty quitting.[6,20]

There is very limited research on waterpipe tobacco smoking cessation interventions in young adults. A 2015 Cochrane review found only 3 intervention studies, 1 of which focused on young adults.[21] Subsequent reviews included additional intervention studies,[22,23] but all found limited evidence for cessation interventions targeting young people. Furthermore, many interventions studied to date have low appeal and are less likely to benefit young adults because they focus on exclusive, daily waterpipe tobacco smokers.[21–23] The growth in young adult waterpipe use, associations with cigarette smoking,[24] and research gaps have produced calls to develop interventions addressing use patterns (i.e., nondaily smoking) and underlying misperceptions about risks in young adults.[21,23]

A recent study piloted a personally tailored, mobile health (i.e., mHealth) messaging cessation intervention for young adult waterpipe smokers.[25] Results demonstrated acceptability and feasibility of the intervention and preliminary effects on behavioral outcomes.[25] mHealth is a promising strategy for waterpipe tobacco cessation interventions among young adults for several reasons. First, most US young adults own a mobile phone and use their phone for text messaging,[26,27] and they are receptive to mHealth interventions.[26,28] This positions mHealth interventions for high reach in the target population. Second, mobile messaging systems can deliver messages with text and visual imagery (i.e., multimedia message service; MMS); this approach can enhance the effects of tobacco messaging.[29] Third, mHealth interventions are scalable with the potential to be freely available to the US population. Finally, mobile messaging systems can also deliver interventions interactively and tailor content to individual characteristics. Tailored messaging increased the effects of online and mHealth interventions for cigarette smoking cessation in previous studies.[30–32]

Pilot research[25] supports the use of personally tailored mHealth interventions for waterpipe tobacco cessation, but they have not been tested rigorously. The goal of this study was to test the efficacy of an interactive mHealth cessation intervention in young adult waterpipe tobacco smokers and examine if a personally tailored intervention had added effects compared with an untailored intervention. The primary outcomes were risk appraisals (i.e., perceived risk, worry), cessation, waterpipe tobacco smoking frequency, and motivation to quit at 6 months. We also report results of secondary outcomes at interim time points (6 weeks, 3 months) based on recommendations for tobacco cessation trials.[33]

METHODS

This study was a 2-site, 3-arm, parallel group randomized trial. All participants provided informed consent, and the participating institutions' institutional review boards approved all procedures.

Participants

From 2018 to 2020, we recruited participants from the community at 2 academic medical centers in the US Mid-Atlantic region. Recruitment advertisements sought young adults for a study about waterpipe tobacco beliefs and behavior and directed interested individuals to a Web site with study details and a link to an eligibility screener. Eligible participants were young adults aged 18 to 30 years who reported smoking waterpipe tobacco in the past month and on at least a monthly basis. We chose these behavioral eligibility criteria based on young adults' waterpipe tobacco smoking patterns and previous pilot work to ensure participants smoked waterpipe tobacco with sufficient frequency for a cessation intervention.[10,25] Eligible participants also had to be able to complete study procedures in English and agree to use a personal mobile phone to send and receive study text messages. There were no other explicit exclusion criteria (e.g., for other medical conditions or alcohol or substance use).

Procedures

Eligible individuals provided informed consent online, completed an online baseline assessment, and received basic information on the risks of waterpipe tobacco smoking.[34,35] Participants were randomized to 1 of the 3 trial arms: control, untailored intervention, or tailored intervention. Participants completed follow-ups online 6 weeks, 3 months, and 6 months after baseline. Participants received incentives for completing study milestones ($20 at baseline, $25 at 6 weeks, $25 at 3 months, and $30 at 6 months).

Randomization

We randomized participants in a 1:1:1 ratio to the 3 trial arms; the randomization sequence was prepared in blocks by a statistician not involved in the trial. We stratified randomization by whether participants reported infrequent (i.e., monthly) or frequent (i.e., daily or weekly) waterpipe tobacco smoking at baseline to ensure balance by the trial arms.

Control Arm

Participants in the control arm received no intervention; they completed assessments only.

Intervention Arms

The intervention was a 6-week mobile messaging intervention. Descriptions of the message content development, pretesting, and the intervention pilot were published previously.[34,36] Messages were delivered on 2 days each week for 6 weeks, a frequency and duration based on patterns of young adult waterpipe tobacco smoking[10] and recommendations for mHealth interventions.[37–39] The content was scheduled for all participants so the first message day occurred early in the week (Tuesday) and the second occurred before the weekend (Friday).

We developed the intervention based on recommendations for mobile interventions,[40] recommendations for waterpipe tobacco interventions,[41] and research on young adults' waterpipe tobacco beliefs and behavior.[35,42–45] The message content communicated the short- and long-term health harms, toxicant exposure, and addictiveness of waterpipe tobacco use.[40] The content was sequenced to avoid repetition and introduce new information over time.

We developed the 12 message themes to align with misperceptions about risks of waterpipe tobacco use in young adults from previous research.[44] Messages conveyed risks of waterpipe tobacco through text and visual imagery (i.e., MMS) with images selected to convey the core risk communicated in text.[34,36] The intervention was designed to enhance motivation to quit by building behavioral skills, increasing confidence, and providing strategies for behavior change.[46–48] Over 6 weeks, this progressed from thinking about risks to planning to avoid waterpipe tobacco smoking, incorporating behavioral substitutes, and making a plan to quit.

The first day was an introductory message preparing participants to start. Each message day thereafter, participants first responded to a text message prompt that engaged participants by posing questions about waterpipe tobacco use or beliefs about risks. After responding to the prompts, participants received the MMS risk message content.

In the untailored intervention arm, all participants received the same prompts and message content. In the tailored intervention arm, we personalized the MMS message content to participants' baseline waterpipe tobacco smoking frequency, baseline risk beliefs, and responses to the prompts during the intervention. For waterpipe tobacco smoking frequency, we categorized participants as infrequent (i.e., monthly) or frequent (i.e., daily or weekly) smokers at baseline. For risk beliefs, we used a 12-item measure of beliefs about the health harms and addictiveness of waterpipe tobacco at baseline to tailor the messages.[44] Each risk belief aligned with 1 of the messages, and we categorized participants' responses to each baseline risk belief item as "low" indicating they do not believe waterpipe tobacco smoking to be risky or "high" risk beliefs that waterpipe smoking has greater risks for tailoring.[36] We also tailored the content to participants' responses to the text message prompts, such as whether they reported smoking waterpipe tobacco. Example intervention messages are provided in Table A (available as a supplement to the online version of this article at http://www.ajph.org).

Measures

At baseline, we assessed age, gender, race, Hispanic ethnicity, educational attainment, employment status, and household income.[49] We measured cigarette smoking at baseline, defining cigarette smokers as those who have smoked at least 100 cigarettes in their lifetime and now smoke cigarettes every day or some days.[49] We assessed past-30-day use of other tobacco (large cigars, little cigars, cigarillos, smokeless tobacco, electronic cigarettes)[49] and summarized responses as any other tobacco use in the past 30 days (yes or no).[35] We also captured number of days in the past 30 days drinking alcohol.[49]

We assessed waterpipe tobacco risk appraisals at all time points using 4 items—2 for harms and 2 for addiction.[34,35,43] Perceived risk of harms (i.e., chance of disease) from smoking waterpipe tobacco was based on a 1 (no chance) to 7 (certain to happen) scale. Worry about harms was also measured on a 1 (not at all) to 7 (very much) scale. We used 2 similar items to measure perceived risk of addiction (1–7 scale) and worry about addiction (1–7 scale). Based on previous studies,[34,35,43] we created a summary risk appraisals outcome by averaging responses to the 4 items at each time point (Cronbach's $\alpha = .72$ at baseline, .76 at 6 weeks, .75 at 3 months, and .80 at 6 months). We also analyzed each item separately, the results of which are shown in Table B (available as a supplement to the online version of this article at http://www.ajph.org).

At baseline, we assessed waterpipe tobacco use frequency and dependence. We asked whether participants usually smoked waterpipe tobacco monthly, weekly, or daily and

categorized participants as infrequent (i.e., monthly) or frequent (i.e., daily or weekly) smokers.[25,34,35] We assessed use frequency as the number of days in the past 30 days that participants smoked waterpipe tobacco.[9] We administered the 6-item Waterpipe Tobacco Dependence Scale[8] and summed the items to create a score (range = 0–25) with higher values indicating greater dependence (Cronbach's $\alpha = .77$).[8]

At the follow-ups, we used a series of items to assess waterpipe tobacco smoking frequency and cessation.[9] The first item assessed whether participants smoked waterpipe tobacco "even 1 or 2 puffs" since the last assessment. Among those responding no, the next item asked whether they completely stopped smoking waterpipe tobacco (yes or no). This captured cessation at each follow-up as point-prevalence abstinence.[33] Among those who had not quit, we assessed waterpipe tobacco smoking frequency at the follow-ups as described previously. For those who quit, we coded waterpipe tobacco smoking as zero at follow-ups. We analyzed as outcomes whether participants reported that they quit smoking waterpipe tobacco completely (yes or no) and the number of days in 30 days participants smoked waterpipe tobacco at each time point.

We measured motivation to quit smoking waterpipe tobacco at baseline and at the follow-ups among those who did not report quitting using a single item with a 1 (not at all) to 7 (very) scale.[35,44]

Statistical Analysis

We used descriptive statistics to characterize the sample overall and by arm. For risk appraisals and motivation to quit, we tested mean differences by trial arm at each time point using general linear models. Levene's test confirmed homogeneity of variance assumptions for each model (i.e., all $P > .05$). We interpreted the F statistic for trial arm and pairwise differences in least squares means using Tukey's adjustment for multiple comparisons.

For frequency of use, we used the Wilcoxon rank sum test for differences by trial arm. We interpreted the Kruskal–Wallis χ^2 statistic for trial arm and the Wilcoxon z test for pairwise comparisons between arms.

We used logistic regression to test if cessation differed by arm at each time point. We interpreted the χ^2 statistic for trial arm and the odds ratios (ORs) and 95% confidence intervals (CIs) for differences in cessation between arms. We ran 2 models for this outcome. The first model used data from those completing follow-ups only. The second model assumed that all those lost to follow-up had not quit smoking waterpipe tobacco.

For all outcomes, our primary comparison was the 6-month time point; earlier time points were prespecified as secondary. Sensitivity analyses controlling for baseline covariates that were not balanced by randomization (gender, race, cigarette smoking) did not differ for any outcomes, so we report unadjusted results.

Sample Size

We conducted a priori power calculations to determine the sample size needed to test for differences in the primary outcomes at 6 months between the trial arms assuming 2-tailed α of .05, 80% power, and 80% retention at 6 months. To detect mean differences as small as Cohen's d of 0.37 between trial arms in risk appraisals, motivation to quit, and use frequency and differences in cessation as small as 19% between trial arms, we needed to enroll 330 participants at baseline.

RESULTS

We screened 576 individuals for eligibility (Figure 1); 167 were ineligible (29%), 6 declined to participate (1%), 17 (3%) were withdrawn because they were later determined to be ineligible (e.g., provided inconsistent age), and we were unable to contact 37 (6%) after screening. In total, 349 participants enrolled and were randomized (Figure 1).

Table 1 displays baseline characteristics overall and by arm. Participants averaged 24.0 (SD = 3.4) years of age, 54% were female, 58% were non-White race, and 11.5% were Hispanic ethnicity. Nearly two thirds (65%) were frequent waterpipe smokers, and participants smoked waterpipe on average 11.5 (SD = 9.1) of the past 30 days. Overall, 29% were current cigarette smokers, and 68% reported other tobacco use. There were more cigarette smokers in the control arm, participants in the control arm were more likely to be female, and participants in the untailored arm were more likely to be White race.

Retention was 93% at 6 weeks (n = 324), 93% at 3 months (n = 325), and 91% at 6 months (n = 319). Attrition at the 3-month and 6-month follow-ups was higher in the tailored intervention arm (11% and 13%) than the control (3% and 5%) and untailored intervention (7% and 8%) arms.

There were no significant differences in risk appraisals between trial arms at 3 months or 6 months (Table 2). At 6 weeks, the effect of trial arm was significant ($F_{2324} = 3.1$; $P = .045$). Risk appraisals were significantly greater in the tailored arm (mean = 4.2; 95%

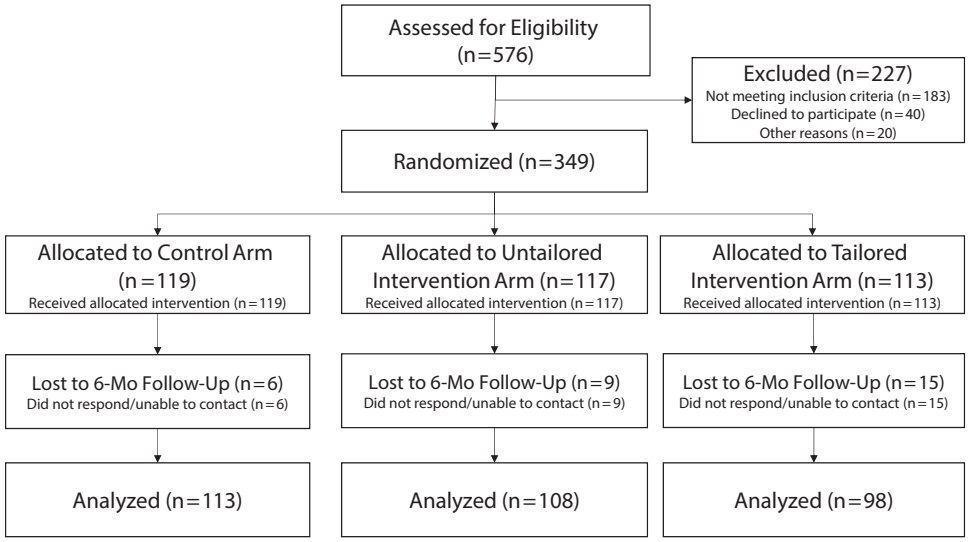

FIGURE 1— Flow Diagram for Randomized Trial of a Mobile Messaging Intervention for Waterpipe Tobacco Cessation in Young Adults: United States, 2018–2020

CI = 3.9, 4.4) than the control arm (mean = 3.8; 95% CI = 3.5, 4.0; $P = .039$). Results from analyses of individual items are shown in Table B.

At 6 months, waterpipe tobacco smoking frequency (Table 2) was significantly lower in the tailored arm (mean = 3.5 days; 95% CI = 2.0, 5.0) than the control arm (mean = 4.3 days; 95% CI = 3.0, 5.6; Kruskal–Wallis χ^2 for trial arm [2 *df*] = 9.2; $P = .010$; Wilcoxon $z = -3.1$; $P = .006$). At 6 weeks, smoking frequency was also significantly lower in the tailored arm than the control arm, and at 3 months it was significantly lower in the untailored and tailored arms than the control arm (Table 2).

Among those who did not quit smoking waterpipe tobacco, there were no significant differences in motivation to quit at 3 ($F_{2240} = 0.08$; $P = .923$) or 6 months by trial arm ($F_{2195} = 0.93$; $P = .398$; Table 2). Motivation to quit was significantly greater at 6 weeks in the tailored arm than the control arm (Table 2).

Table 3 shows outcomes for cessation. Using available data, at 6 months, cessation was significantly higher in the tailored arm (49%; OR = 2.4; 95% CI = 1.3, 4.2) than the control arm (29%; χ^2 for trial arm [2 *df*] = 8.8; $P = .012$). At 6 weeks and 3 months, cessation was significantly higher in the untailored and tailored arms than the control arm (Table 3). Assuming those lost to follow-up continued smoking waterpipe tobacco (Table 3), at 6 months, cessation was significantly higher in the tailored arm (43%; OR = 1.9; 95% CI = 1.1, 3.3) than the control arm (28%) but the overall effect of arm was no longer significant (χ^2 for trial arm [2 *df*] = 5.5; $P = .064$). At 6 weeks and 3 months, cessation was significantly higher in the untailored and tailored arms than the control arm (Table 3).

DISCUSSION

Our results demonstrate that a tailored mHealth messaging intervention increased cessation and decreased waterpipe tobacco smoking frequency among young adults. Although both the tailored and the untailored interventions affected outcomes at interim time points, for behavioral outcomes only, the tailored intervention effects were sustained to 6 months. These results build on previous research on waterpipe tobacco risk messages[34,35,45] by testing mHealth message delivery, demonstrating tailored messaging effects, and capturing behavioral outcomes.

There is limited research on waterpipe tobacco smoking cessation interventions for young adults[21–23] even though this is the age group in the United States when waterpipe tobacco smoking is most common.[9–12] This study is the first, to our knowledge, to demonstrate the efficacy of a tailored mHealth cessation intervention in young adult waterpipe tobacco smokers over a 6-month follow-up, filling a critical research gap. The mHealth intervention is highly scalable, aligning with major public health agencies' efforts to make mobile cessation interventions freely available. For example, the National Cancer Institute offers mHealth cessation programs for cigarette smoking and smokeless tobacco cessation, but not waterpipe tobacco

TABLE 1— Baseline Characteristics for Randomized Trial of a Mobile Messaging Intervention for Waterpipe Tobacco Cessation in Young Adults: United States, 2018–2020

	Overall (n = 349), Mean ±SD or % (No.)	Control (n = 119), Mean ±SD or % (No.)	Untailored Intervention (n = 117), Mean ±SD or % (No.)	Tailored Intervention (n = 113), Mean ±SD or % (No.)
Age	24.0 ±3.4	23.9 ±3.4	23.7 ±3.5	24.6 ±3.5
Gender				
Female	53.6 (187)	59.7 (71)	48.7 (57)	52.2 (59)
Male	46.4 (162)	40.3 (48)	51.3 (60)	47.8 (54)
Race				
White	42.1 (147)	42.9 (51)	36.8 (43)	46.9 (53)
Non-White	57.9 (202)	57.1 (68)	63.2 (74)	53.1 (60)
Hispanic ethnicity				
Yes	11.5 (40)	12.6 (15)	12.0 (14)	9.8 (11)
No	88.3 (308)	87.4 (104)	88.0 (103)	90.2 (101)
Education				
< college	16.0 (56)	13.4 (16)	20.5 (24)	14.2 (16)
Some college or higher	84.0 (293)	86.6 (103)	79.5 (93)	85.8 (97)
Employment				
Not full-time employed	58.1 (203)	56.3 (67)	63.2 (74)	46.0 (52)
Full-time employed	44.7 (156)	43.7 (52)	36.8 (43)	53.9 (61)
Annual household income, $				
≤ 50 000	65.3 (228)	62.2 (74)	63.2 (74)	70.8 (80)
> 50 000	34.4 (120)	37.8 (45)	35.9 (42)	29.2 (33)
Waterpipe smoking frequency				
Infrequent (i.e., monthly)	34.7 (121)	33.6 (40)	35.0 (41)	35.4 (40)
Frequent (i.e., weekly or daily)	65.3 (228)	66.4 (79)	65.0 (76)	64.6 (73)
Past-30-d waterpipe smoking, days	11.3 ±9.1	11.1 ±9.2	10.6 ±8.7	12.2 ±9.3
Waterpipe tobacco dependence	6.7 ±5.3	7.0 ±5.6	6.4 ±4.9	6.7 ±5.4
Motivation to quit waterpipe tobacco	2.7 ±1.6	2.9 ±1.6	2.5 ±1.6	2.6 ±1.6
Current cigarette smoker	29.2 (102)	37.8 (45)	24.8 (29)	24.8 (28)
Any other tobacco use, past 30 d	67.9 (237)	67.2 (80)	69.2 (81)	67.2 (80)
Days drinking alcohol, past 30 d	7.5 ±7.0	8.4 ±7.6	6.7 ±6.1	7.4 ±7.2

Note. For some variables (e.g., Hispanic ethnicity), numbers for categories do not sum to the total sample size because of sporadic missing data (1 or 2 cases in each instance).

cessation.[50] Our study provides the first evidence for a mHealth waterpipe tobacco smoking cessation intervention that can be implemented in this manner. Notably, waterpipe tobacco smoking is less prevalent than other forms of tobacco use (e.g., cigarette smoking) in the US population, but it is most common among young adults and it is associated with subsequent cigarette smoking initiation.[24] From a public health perspective, this intervention could be impactful if it is made available with other interventions designed to prevent and reduce tobacco use in young people overall.

A recent prospective analysis of US young adults' waterpipe tobacco smoking provides context for our findings.[13] Sharma et al. examined past-12-month waterpipe tobacco smoking over 3 years of PATH Study data, finding that 42% of young adults who smoked waterpipe tobacco at wave 1 continued smoking over the 3-year period, 47% discontinued by wave 3, and 11% discontinued at wave 2 and resumed smoking at wave 3.[13] This analysis examined past-12-month use, and it is unclear if "discontinuing" reflects cessation or

TABLE 2— Risk Appraisals, Past-30-Day Waterpipe Tobacco Smoking Frequency, and Motivation to Quit by Trial Arm: United States, 2018–2020

	Baseline (n = 349), Mean (95% CI)	6 Weeks (n = 324), Mean (95% CI)	3 Months (n = 325), Mean (95% CI)	6 Months (n = 319), Mean (95% CI)
Risk appraisals				
Control (A)	3.7 (3.5, 3.8)	3.8[C] (3.5, 4.0)	4.0 (3.7, 4.2)	4.0 (3.8, 4.3)
Untailored (B)	3.4 (3.2, 3.6)	3.9 (3.6, 4.1)	3.9 (3.7, 4.2)	4.0 (3.8, 4.3)
Tailored (C)	3.5 (3.3, 3.7)	4.2[A] (3.9, 4.4)	4.0 (3.8, 4.3)	4.3 (4.0, 4.5)
Waterpipe tobacco smoking frequency				
Control (A)	11.1 (9.4, 12.8)	7.8[C] (6.2, 9.5)	6.1[B,C] (4.6, 7.5)	4.3[C] (3.0, 5.6)
Untailored (B)	10.6 (9.0, 12.2)	5.4 (4.0, 6.8)	4.6[A] (3.2, 5.9)	4.0 (2.6, 5.2)
Tailored (C)	12.2 (10.4, 13.9)	5.4[A] (4.0, 6.8)	4.3[A] (3.0, 5.7)	3.5[A] (2.0, 5.0)
Motivation to quit				
Control (A)	2.9 (2.6, 3.2)	3.3[C] (3.0, 3.6)	3.8 (3.4, 4.2)	4.0 (3.5, 4.4)
Untailored (B)	2.5 (2.2, 2.8)	3.8 (3.4, 4.2)	3.9 (3.4, 4.3)	4.0 (3.5, 4.4)
Tailored (C)	2.6 (2.3, 2.9)	4.1[A] (3.7, 4.5)	3.9 (3.4, 4.4)	3.5 (3.0, 4.1)

Note. CI = confidence interval. For each time point, means for each outcome with different superscript letters differed significantly from the trial arm indicated (A = control; B = untailored; C = tailored) at $P < .05$. For risk appraisals and motivation to quit, comparisons of means are from general linear models with Tukey's adjustment for pairwise comparisons. For waterpipe tobacco smoking frequency, comparison of means is from Wilcoxon rank sum test and *z* test *P* values for pairwise comparisons. Waterpipe tobacco smoking frequency included all participants with those who quit at a given time point coded as 0. Motivation to quit only included those who had not quit smoking waterpipe tobacco at a given time point.

TABLE 3— Waterpipe Tobacco Cessation by Trial Arm at Follow-Up Time Points: United States, 2018–2020

	6 Weeks (n = 324)		3 Months (n = 325)		6 Months (n = 319)	
	%	OR (95% CI)	%	OR (95% CI)	%	OR (95% CI)
Available data						
Control	10	1 (Ref)	12	1 (Ref)	29	1 (Ref)
Untailored	24	2.8 (1.3, 5.8)	28	2.9 (1.4, 5.7)	38	1.5 (0.9, 2.6)
Tailored	22	2.5 (1.2, 5.2)	36	4.1 (2.1, 8.3)	49	2.4 (1.3, 4.2)
Assume lost to follow up continued smoking						
Control	10	1 (Ref)	12	1 (Ref)	28	1 (Ref)
Untailored	22	2.5 (1.2, 5.3)	27	2.7 (1.4, 5.4)	35	1.4 (0.8, 2.4)
Tailored	20	2.3 (1.1, 4.8)	33	3.7 (1.8, 7.2)	43	1.9 (1.1, 3.3)

Note. CI = confidence interval; OR = odds ratio. Table displays percentage reporting cessation and ORs (95% CIs) for cessation in the untailored and tailored intervention arms relative to the control arm at each time point. The first model with available data at each time point excludes those lost to follow-up. The second model at each time point assumes those lost to follow-up did not quit (i.e., continued smoking waterpipe tobacco).

intermittent use. However, the findings highlight the need to examine intervention outcomes over an extended follow-up. Some intervention effects we observed diminished over time, and assessing longer-term outcomes in the future will be important to determine if the effects are sustained and to assess maintenance of cessation and relapse.[51,52] This can guide future steps to optimize our intervention, such as testing adaptive models that provide additional support for those who do not quit or who relapse.[53]

Notably, many young adult waterpipe tobacco smokers are dual or poly tobacco users of other tobacco products.[13,54] In our sample, nearly one third

were cigarette smokers, and roughly two thirds used other tobacco. Although we observed intervention effects on waterpipe tobacco smoking, it is unclear if the intervention reduced tobacco use overall. Smoking cessation research has focused predominantly on exclusive tobacco product users (e.g., cigarette smokers) and existing interventions do not address dual or poly use.[55] Given the high prevalence of dual and poly use in young adults in general[55] and in young adult waterpipe smokers,[13,54] in future research it will be important to examine how interventions targeting waterpipe tobacco smoking affect other tobacco use outcomes in dual and poly users.

Limitations

This study has several important strengths, including a carefully developed mHealth intervention, rigorous trial design, and high retention. However, the findings should be interpreted in light of study limitations. We used remote (e.g., online, mobile) procedures for recruitment, data collection, and intervention delivery. These methods are increasingly used to improve efficiency of smoking cessation trials[56]; however, they are subject to limitations (e.g., potential reporting biases) that should be considered when interpreting the findings. We measured cessation by self-report. Although biochemically verified cessation is a gold standard in clinical trials,[57] established biomarkers (e.g., exhaled carbon monoxide, cotinine) cannot verify waterpipe tobacco smoking cessation in a population in which use of other combustible (e.g., cigarettes) and noncombustible (e.g., electronic cigarettes) products is common. Finally, assessing outcomes over a longer follow-up will provide more robust evidence on long-term intervention effects. We examined outcomes to 6 months as recommended for cessation trials,[33] but this will be important to understand if the effects are sustained.

Public Health Implications

This trial is the first, to our knowledge, to demonstrate the efficacy of a tailored mHealth messaging intervention for waterpipe tobacco smoking cessation in young adults. This is a scalable intervention model that aligns with ongoing efforts to make mHealth cessation interventions freely available to populations that need them. This study advances the science on waterpipe tobacco smoking cessation interventions, and the results suggest several important areas for further study. This includes examining long-term outcomes to assess if the effects are sustained and identify intervention optimization strategies for those who do not quit or who relapse, and examining intervention effects on other tobacco use in young adult dual and poly users. AJPH

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D. Mays and I. M. Lipkus conceptualized the study and acquired funding. D. Mays, A. C. Johnson, L. Phan, C. Sanders, and I. M. Lipkus collected the data. D. Mays, A. C. Johnson, and A. Shoben analyzed the data. D. Mays wrote the first draft of the article. All authors revised the article and read and approved the final article.

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CONFLICTS OF INTEREST

The authors have no conflicts of interest to disclose.

HUMAN PARTICIPANT PROTECTION

The study protocol was approved by the institutional review boards at Georgetown University and Duke University. The protocol for data analysis was also approved by the institutional review board at The Ohio State University.

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State Abortion Policies and Maternal Death in the United States, 2015–2018

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See also Liu et al., p. 1578, and Galea and Vaughan, p. 1584.

Objectives. To examine associations between state-level variation in abortion-restricting policies in 2015 and total maternal mortality (TMM), maternal mortality (MM), and late maternal mortality (LMM) from 2015 to 2018 in the United States.

Methods. We derived an abortion policy composite index for each state based on 8 state-level abortion-restricting policies. We fit ecological state-level generalized linear Poisson regression models with robust standard errors to estimate 4-year TMM, MM, and LMM rate ratios and 95% confidence intervals (CIs) associated with a 1-unit increase in the abortion index, adjusting for state-level covariates.

Results. States with the higher score of abortion policy composite index had a 7% increase in TMM (adjusted rate ratio [ARR] = 1.07; 95% CI = 1.02, 1.12) compared with states with lower abortion policy composite index, after we adjusted for state-level covariates. Among individual abortion policies, states with a licensed physician requirement had a 51% higher TMM (ARR = 1.51; 95% CI = 1.15, 1.99) and a 35% higher MM (ARR = 1.35; 95% CI = 1.09, 1.67), and states with restrictions on Medicaid coverage of abortion care had a 29% higher TMM (ARR = 1.29; 95% CI = 1.03, 1.61).

Conclusions. Restricting access to abortion care at the state level may increase the risk for TMM. (*Am J Public Health*. 2021;111(9):1696–1704. https://doi.org/10.2105/AJPH.2021.306396)

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Maternal mortality in the United States has remained unacceptably high over the past few decades compared with other high-income countries.[1,2] In 2020, the National Center for Health Statistics (NCHS) reported a national maternal mortality ratio (MMR, defined as deaths of women while pregnant or within 42 days of being pregnant, from any cause related to or aggravated by the pregnancy or its management, but not from accidental or incidental causes) at 17.4 per 100 000 live births for 2018.[3] In addition, wide racial disparities in maternal death persist, with non-Hispanic Black women being more than 2 to 3 times more likely to die from a pregnancy-related complication than non-Hispanic White women.[3,4] Furthermore, research shows that more than 60% of maternal deaths are preventable.[4]

Emerging evidence suggests that broader societal and policy factors may contribute to adverse maternal health outcomes and inequities.[5–7] Along with elevated maternal mortality rates, the past decade has witnessed an increasing passage of laws restricting access to abortion care.[8] Although the United Nations and the World Health Organization recognize abortion as a key component of reproductive health services and an important aspect of maternal and child health,[9,10] and despite *Roe v. Wade* (1973) guaranteeing the right to abortion in the United States, many states continue to undermine access to safe abortion care by imposing numerous policies and regulations. In 2015, nearly 400 abortion-restricting provisions were considered in 46 states, with 17 states enacting a total of 57 new abortion restrictions.[11] Such restrictions range from gestational age limits, ultrasound requirements, mandatory counseling, and waiting periods to insurance coverage limitations and targeted regulations on abortion providers.[8] As a result, access to abortion care varies greatly across the United States, with 6 states having only 1 abortion clinic in operation.[12]

While the link between restricted access to abortion care and maternal

mortality is well established in low- and medium-income countries,[13,14] the evidence base on the impact of abortion restrictions on maternal death in the United States is limited. Using 2007–2015 National Vital Statistics System data files from 38 states and the District of Columbia, a recent study found that the enactment of gestational age limits for abortion was associated with a 38% increase in maternal mortality, and a 20% reduction in Planned Parenthood clinics was associated with an 8% increase in maternal mortality.[5] In addition, growing evidence has linked abortion restrictions to other maternal and child health outcomes, including infant mortality,[15,16] child homicide deaths,[17] negative mental health outcomes among women who were denied abortion,[18,19] and adverse birth outcomes.[20,21]

The reproductive justice framework, developed by Black women and other women of color to address the histories and ongoing experiences of reproductive injustice in their communities, clarifies how policies that limit bodily autonomy may be associated with adverse reproductive health outcomes.[22] While abortion restrictions do not eliminate the occurrence of abortion, in a restrictive environment, abortion-seeking people with limited institutional power and access to resources will be the least able to obtain a safe and healthy procedure, and most likely to suffer an adverse reproductive consequence.[23,24]

Abortion-restricting laws may contribute to risk of maternal death via direct and indirect pathways. First, while legal induced abortion–related mortality is rare,[25] abortion restrictions can lead to an enhanced number of unsafe, illegal, or self-inflicted abortions, which have been shown to contribute to maternal mortality.[13] In addition, maternal death results from health-related complications developed or exacerbated during pregnancy, and, thus, women with chronic health conditions who are not able to access abortion care are forced to carry unwanted pregnancy to term even if their health and lives are in danger.[19] Findings of the longitudinal Turnaway Study, which evaluated the health and socioeconomic consequences of receiving or being denied an abortion in the United States, found that, while women whose health was imminently at risk were excluded from the study, 1 in 8 of the study's participants reported a health concern as a reason for seeking abortion.[19] Furthermore, while there is no evidence supporting negative lasting impacts from obtaining an abortion,[18] women forced to remain pregnant are more likely to remain in unhealthy relationships, suffer mental and physical health consequences, live in poverty, and have lower life satisfaction.[19]

The objective of this study was to examine the association between state-level variations in abortion policies and maternal death using the most recently available national maternal mortality data (2015–2018). We aimed to estimate the risk of maternal death associated with living in states with a higher number of abortion restrictions as compared with states with fewer restrictions. We hypothesized that, because of direct and indirect causes, a more restrictive abortion policy context within the state will be associated with greater risk of death during pregnancy and postpartum. In addition, given the vast racial disparities in maternal death, we examined heterogeneity in the hypothesized association by race/ethnicity.

METHODS

This study was a retrospective ecological analysis of the 2015–2018 maternal mortality file available through the NCHS. These data apply the new coding method for identifying maternal deaths while mitigating misclassification that resulted from the adoption of a standardized pregnancy-status checkbox on revised death certificates.

Outcome

Our primary analysis included women aged 10 to 44 years, given the substantial risk of misclassification of maternal deaths at more advanced maternal ages.[3,26] The primary outcome of interest was total maternal mortality (TMM), defined as a death while pregnant or within 1 year following the end of a pregnancy, from any cause related to or aggravated by the pregnancy or its management. We further divided these deaths by timing to identify maternal mortality (MM; those occurring during pregnancy or within 42 days of being pregnant) and late maternal mortality (LMM; those occurring between 43 days and 1 year following the end of a pregnancy) as additional outcomes of interest. Maternal deaths were identified based on underlying cause of death from the *International Statistical Classification of Diseases and Related Health Problems, 10th Revision* (*ICD-10;* 2nd ed. Geneva, Switzerland: World Health Organization; 2004). TMM included deaths with *ICD-10* codes O00–O99 and A34, excluding O97 codes, which apply to deaths occurring more than 1 year from the end of pregnancy. MM included deaths with *ICD-10* codes A34, O00–O95, and O98–O99. LMM included deaths with *ICD-10* code O96.[3,5] We computed the 4-year (2015–2018)

TMM, MM, and LMM ratios (deaths per 100 000 live births to women aged 10–44 years) for the total population in each state and the District of Columbia. Because of a nonstandard pregnancy checkbox question,[3] we excluded California from estimations of MM and LMM ratios. Data on live births by maternal age, residential state, and year were from the NCHS restricted-use natality file, available after application to and approval by NCHS. We merged counts of maternal death by state with counts of live births by state Federal Information Processing System codes to estimate TMM, MM, and LMM ratios.

Measures

We used an abortion policy composite index to quantify the extent of abortion-restricting policies in each state on January 1, 2015, the first year of data on mortality in this study. The index included 8 state-level policies limiting access to abortion care:

1. state-mandated counseling before abortion (i.e., abortion provider is required to read their patients information leaflets that are written in a way to dissuade patients from completing the abortion);
2. mandatory waiting periods (usually 24 hours) between counseling and abortion services;
3. mandatory ultrasound before abortion procedure (i.e., abortion provider is required to display or describe preabortion ultrasound images);
4. mandatory parental involvement laws for minors seeking abortion (i.e., a requirement that a parent be notified or give consent for an unmarried adolescent minor to obtain an abortion);
5. gestational age restrictions (i.e., limits on abortion after a specified point—e.g., 20 or more weeks of gestation—in pregnancy);
6. licensed physician requirement in providing abortion care (i.e., nonphysician health care providers, such as physician assistants, advanced practice registered nurses, or nurse midwives, are prohibited from providing abortion care);
7. denial of coverage for abortion in private insurance plans; and
8. restrictions on public funding for abortion (i.e., prohibitions against use of state Medicaid funds to pay for abortions).

We retrieved data on the 8 abortion regulations from January 2015 policy status reports compiled by the Guttmacher Institute.[27]

We computed the composite index based on a similar reproductive rights composite index developed by the Institute for Women's Policy Research[28] and previously used in reproductive health studies.[20,21] First, we coded each indicator as either 0 (policy not in effect) or 1 (policy in effect). Given that parental involvement requirement affects a small proportion of the abortion-seeking population, we assigned this policy a weight of 0.5, and the remaining indicators were given a weight of 1. To measure the cumulative impact of multiple abortion restrictions within a state over a single policy, we summed weighted indicators to compute a total composite index for each state. The internal consistency of the 8 policies was high (Cronbach $\alpha = 0.85$). In addition, to compare states with lower versus higher number of abortion-restricting policies, we categorized the composite index (low, moderate, high) with the highest tertile representing states with the highest number of abortion restrictions.

Covariates

Adjusted models included estimates of state-level poverty, unemployment, percentage of the population with college degree, percentage of the population that is non-Hispanic White, percentage of the population living in urban counties, percentage of the population that is foreign-born, and Medicaid expenditure per capita. We retrieved these measures from the US Census Bureau's American Community Survey and the Regional Economic Information System of the US Bureau of Economic Analysis. In addition, we included Medicaid expansion status in 2015 (retrieved from the Kaiser Family Foundation)[29] and 4-year (2015–2018) averages of the percentage of births covered by Medicaid and the percentage of births to women aged 35 years and older, aggregated from the NCHS natality files.

Statistical Analysis

We conducted descriptive analysis to characterize the variation of state-level TMM, MM, and LMM and contextual indicators across all states, and then separately by tertiles of abortion policy composite index. We then fit models examining the association between the abortion policy index (coded as a continuous variable) and TMM, MM, and LMM separately. We used a modified Poisson regression with cluster-robust standard errors to account for serial correlation of error terms within states to estimate the adjusted rate ratios (ARRs) and 95% confidence intervals (CIs) for all outcomes. To explore whether 1 abortion-restricting policy in particular may have been driving

associations between the composite index and the outcomes, we examined the associations between each outcome and each component of the abortion policy index separately. We weighted all models by the total number of live births by state (2015–2018). To test for heterogeneity by race/ethnicity, we fit the fully adjusted model with data aggregated by race/ethnicity and state and included an interaction term between the composite index and dummy variables for non-Hispanic Black and Hispanic populations.

Finally, we ran sensitivity analysis to confirm the robustness of our findings with an even more conservative age-restricted sample (i.e., decedents aged 10–39 years) to further reduce the possibility of misclassification.[3] We performed all statistical analyses with SAS version 9.4 (SAS Institute, Cary, NC).

RESULTS

From 2015 to 2018, there were 3785 total maternal deaths among women aged 10 to 44 years, including 2524 maternal deaths and 962 late maternal deaths. The 4-year TMM ratio across 50 states and the District of Columbia was 24.62 deaths per 100 000 live births, whereas MM and LMM ratios across 49 states (California excluded) and the District of Columbia were 17.78 and 7.02 deaths per 100 000 live births, respectively (Table 1). Crude TMM, MM, and LMM rates were significantly higher ($P < .05$) in states with the largest number of abortion restrictions (i.e., the highest tertile of the composite index).

In 2015, the abortion policy composite index ranged from 0 in California, Connecticut, Oregon, Vermont, and Washington to a high of 7.5 in Indiana, Kansas, Nebraska, and Oklahoma (mean = 3.75; SD = 2.5; Table A, available as a supplement to the online version of this article at http://www.ajph.org). Fifteen states had 2 or fewer abortion restrictions and were grouped in the lowest tertile of the composite index, while 17 and 19 states were clustered in the moderate (from 2.5 to 4.5 restrictions) and the highest (5.5 to 7.5 restrictions) tertiles, respectively. State groupings by tertile level of the abortion policy composite index are listed in Table 2 and shown visually in

TABLE 1— Total Maternal Mortality (TMM), Maternal Mortality (MM), and Late Maternal Mortality (LMM; 2015–2018) and State-Level Covariates (2015) by Tertile of State Abortion Policy Composite Index: United States

	All States (n = 51), Mean ±SD or No. (%)	Low (n = 15), Mean ±SD or No. (%)	Moderate (n = 17), Mean ±SD or No. (%)	High (n = 19), Mean ±SD or No. (%)
TMM per 100 000 live births	24.62 ±8.89	20.79 ±5.25	22.04 ±7.60	29.98 ±9.90
MM per 100 000 live births	17.78 ±7.13	14.83 ±3.89	15.81 ±6.10	21.73 ±8.21
LMM per 100 000 live births	7.02 ±2.86	6.32 ±2.34	6.23 ±2.73	8.25 ±3.03
Abortion policy composite index, 2015	3.75 ±2.46	0.73 ±0.65	3.41 ±0.91	6.42 ±0.71
Poverty (% of state population with income below federal poverty level[a])	14.85 ±3.17	13.81 ±3.38	14.29 ±2.78	16.16 ±3.02
Unemployment (% of state civilian population aged ≥ 16 y)	7.63 ±1.72	7.91 ±1.49	7.67 ±1.54	7.36 ±2.042
College graduates (% of state population aged ≥ 25 y)	28.66 ±5.87	33.36 ±6.19	27.47 ±5.33	26.01 ±3.7
Non-Hispanic White (% of state population)	75.99 ±13.63	71.13 ±19.99	80.45 ±8.30	75.84 ±10.26
Residence in urban county (% of state population)	74.11 ±14.89	77.97 ±19.92	76.22 ±13.58	69.17 ±10.02
Foreign-born population (% of state population)	9.25 ±6.12	13.10 ±7.35	8.95 ±5.71	6.47 ±3.52
Medicaid expenditure per capita (2011 US $)	3226 ±1170	3961 ±1412	3371 ±933	2518 ±691
Births to women aged ≥ 35 y, %	15.96 ±4.17	19.69 ±3.91	15.65 ±3.53	13.18 ±2.26
Births covered by Medicaid, %	40.64 ±9.06	38.75 ±8.44	41.09 ±7.50	41.51 ±11.07
Medicaid expansion status				
Yes	30 (58.81)	14 (93.33)	11 (64.71)	5 (26.29)
No	21 (41.19)	1 (6.67)	6 (35.29)	14 (73.71)

Note. All estimates for MM and LMM exclude data from California.

[a]Federal poverty level is according to the US Census Bureau's American Community Survey.

TABLE 2— States and Maternal Death by Tertile of State Abortion Policy Composite Index: United States, 2015–2018

Abortion Policy Index	No. of States	States	TMM (n = 3785), No. (%)	MM (n = 2524), No. (%)	LMM (n = 962), No. (%)
Low	15	CA, CT, DC, HI, IL, MD, ME, MT, NH, NJ, NM, NY, OR, VT, WA	1004 (26.53)	499 (19.77)	206 (21.41)
Moderate	17	AK, AZ, CO, DE, FL, IA, KY, MA, MN, NV, OH, PA, RI, TN, WI, WV, WY	999 (26.39)	714 (28.29)	285 (29.63)
High	19	AL, AR, GA, ID, IN, KS, LA, MI, MO, MS, NC, ND, NE, OK, SC, SD, TX, UT, VA	1782 (47.08)	1311 (51.94)	471 (48.96)

Note. LMM = late maternal mortality; MM = maternal mortality; TMM = total maternal mortality. All counts of MM and LMM exclude data from California.

Figure A (available as a supplement to the online version of this article at http://www.ajph.org).

In adjusted models, a 1-unit increase in abortion policy composite index was associated with a 7% increase in TMM (ARR = 1.07; 95% CI = 1.02, 1.12; Table 3). States with a licensed physician requirement had a 51% higher TMM (ARR = 1.51; 95% CI = 1.15, 1.99) and a 35% higher MM (ARR = 1.35; 95% CI = 1.09, 1.67), and states with restrictions on public funding for abortion had a 29% higher TMM (ARR = 1.29; 95% CI = 1.03, 1.61) compared with the states without these policies.

Associations between the remaining abortion policies and TMM and MM were not statistically significant. Associations between LMM and abortion restrictions were also not statistically significant.

Results from the fully adjusted models with the interaction terms for race revealed an association between the abortion policy composite index and TMM for non-Hispanic White (ARR = 1.06; 95% CI = 1.02, 1.11) but not non-Hispanic Black or Hispanic populations (Table 4).

Results from sensitivity analysis with an age-restricted sample were consistent with the primary analysis (see Tables B–D, available as supplements to the online version of this article at http://www.ajph.org). Adjusted associations between the abortion policy composite index and TMM remained significant, although attenuated in magnitude (ARR = 1.06; 95% CI = 1.02, 1.11). Attenuation of the associations between mandated licensed physicians as sole providers of abortion services and increased TMM and MM was evident in the age-restricted analysis as well (ARR = 1.48; 95% CI = 1.14, 1.92 for TMM and ARR = 1.28; 95% CI = 1.02, 1.60 for MM). Association between restriction on public funds for abortion

TABLE 3— Associations Between Total Maternal Mortality (TMM), Maternal Mortality (MM), and Late Maternal Mortality (LMM) and Abortion Policies: United States, 2015–2018

	TMM, ARR (95% CI)	MM, ARR (95% CI)	LMM, ARR (95% CI)
Abortion policy composite index	1.07 (1.02, 1.12)	1.02 (0.94, 1.10)	1.01 (0.95, 1.08)
State abortion policies (yes vs no)			
Mandated counseling	1.13 (0.90, 1.43)	0.98 (0.78, 1.23)	1.00 (0.77, 1.31)
Waiting period	1.16 (0.97, 1.38)	1.05 (0.77, 1.43)	0.99 (0.72, 1.36)
Ultrasound requirement	1.20 (0.96, 1.49)	1.07 (0.75, 1.52)	0.94 (0.70, 1.26)
Parent involvement for minors	1.09 (0.81, 1.46)	0.94 (0.70, 1.25)	1.25 (0.95, 1.63)
Gestational age restrictions	1.10 (0.94, 1.29)	0.91 (0.72, 1.14)	0.89 (0.70, 1.13)
Licensed physician requirement	1.51 (1.15, 1.99)	1.35 (1.09, 1.67)	1.12 (0.87, 1.45)
Private insurance coverage limited	1.26 (0.99, 1.59)	1.21 (0.93, 1.58)	1.20 (0.85, 1.70)
Public funds restricted	1.29 (1.03, 1.61)	1.09 (0.80, 1.49)	1.19 (0.87, 1.63)

Note. ARR = adjusted rate ratio; CI = confidence interval. All estimates for MM and LMM exclude data from California. All models adjusted for state-level poverty, unemployment, % population with bachelor's degree or higher, % non-Hispanic White population, % urban population, % foreign-born population, Medicaid expansion status, Medicaid expenditure per capita, average % of births covered by Medicaid, and average % of births to women aged 35 years or older.

TABLE 4— Associations Between Race-Specific Total Maternal Mortality (TMM), Maternal Mortality (MM), and Late Maternal Mortality (LMM), and Abortion Policy Composite Index, 2015–2018

	Non-Hispanic White			Non-Hispanic Black			Hispanic		
	TMM	MM	LMM	TMM	MM	LMM	TMM	MM	LMM
Abortion policy composite index, ARR (95% CI)	1.06 (1.02, 1.11)	1.05 (0.95, 1.15)	0.99 (0.92, 1.07)	0.98 (0.89, 1.08)	0.95 (0.80, 1.13)	0.99 (0.85, 1.15)	1.01 (0.94, 1.06)	0.98 (0.86, 1.13)	0.91 (0.79, 1.15)
No. of maternal deaths	1 728	1 165	489	1 210	848	312	615	366	115
No. of live births	8 082 036	7 564 573		2 233 216	2 139 606		3 626 302	2 733 569	

Note. ARR = adjusted rate ratio; CI = confidence interval. All estimates for MM and LMM and counts of deaths and live births in these columns exclude data from California. All models adjusted for state-level poverty, unemployment, % population with bachelor's degree or higher, % non-Hispanic White population, % urban population, % foreign-born population, Medicaid expansion status, Medicaid expenditure per capita, average % of births covered by Medicaid, and average % of births to women aged 35 years or older.

care and TMM was also marginally diminished in magnitude (ARR = 1.28; 95% CI = 1.04, 1.58). Finally, as we found in the primary analysis, there was a significant association between the abortion policy composite index and TMM among the non-Hispanic White population (ARR = 1.05; 95% CI = 1.01, 1.09).

DISCUSSION

Access to abortion care has been endorsed as a human right and a critical component of reproductive health services.[30] Restrictive abortion policies have been internationally recognized as a risk factor for maternal mortality,[10] yet more than 1000 laws or regulations restricting access to abortion care have been enacted in the United States since the 1973 Supreme Court decision in *Roe v. Wade*, with 483 of these restrictions enacted in the past decade.[31] Using the most recent and revised NCHS maternal mortality data, we examined the associations between the state abortion policy context and maternal death. We found that states with a higher number of abortion-restricting policies had a 7% increase in TMM. In addition, states with a licensed physician requirement had a 51% higher TMM and a 35% higher MM, and restrictions on state Medicaid funding for abortion was associated with a 29% higher TMM. These findings contribute to the growing evidence documenting the detrimental impact of a restrictive reproductive rights climate on maternal and infant health.[5,15,16,20,21]

Our findings suggest the cumulative impact of abortion restrictions on maternal death, adding to a limited body of empirical studies linking rising maternal mortality and reduced access to reproductive health services in the United States.[5] Our study is among the first to provide empirical evidence of an association between maternal death and state abortion policy climate. Of concern, we evaluated the status of state abortion restrictions in 2015, and subsequent years have seen numerous additional restrictions imposed in many, mostly Southern and Midwestern, states.[31,32] In 2019 alone, an unprecedented number of abortion restrictions were proposed across the United States, with 59 enacted in 19 states.[32]

On a macro level, states with higher numbers of abortion regulations and worse maternal mortality also have adverse confounding factors that have been shown to negatively affect maternal health.[6,7,33] In this study, states with highest numbers of abortion-restricting laws had the worst socioeconomic conditions. Such harmful social context, characterized by high poverty, a lack of health care safety net and paid family leave, systemic racism, and historical disinvestments in comprehensive community-oriented primary care, particularly in communities of color, are root causes of persistent racial inequities in maternal death.[33] Moreover, abortion-restricting policies often co-occur with other policies that seek to regulate women's sexuality and bodily autonomy—including limited access to publicly supported contraceptive services and supplies, lack of publicly funded family planning services, and inadequate sex education—despite their negative associations with sexual and reproductive health.[20,28]

We found that 2 abortion restrictions—requirement for licensed physician and prohibitions against use of Medicaid funds to pay for abortion care—are particularly prominent potential contributors to maternal death risk. A requirement that an abortion should be performed by a licensed physician—enforced by 39 states in 2015—is part of targeted and medically unnecessary requirements on abortion providers aiming to severely reduce the number of abortion providers and

thereby limit access to abortion care. Research shows that properly trained advanced practice nurses and physician assistants can competently perform abortion procedures,[34] and this restriction is one of many aimed at these professions that prevents them from addressing gaps in reproductive health care. Restrictions on Medicaid funds to pay for abortion care—imposed by 34 states in 2015—increase out-of-pocket costs, thus making abortion inaccessible to many low-income people. At the federal level, the Hyde Amendment prohibits the use of federal funds to pay for abortion procedures through Medicaid (except in cases of rape, incest, or life endangerment); however, the remaining 16 states use their own Medicaid funds to extend abortion care to low-income Medicaid enrollees. Research shows that abortion-seeking people living in states with Medicaid coverage bans experience higher financial barriers and prolonged abortion seeking, which increase the likelihood of being forced to carry a pregnancy to term.[24]

Our results indicate that risk of death during pregnancy and up to 1 year postpartum (TMM) is elevated in states with restrictive abortion climates. In this analysis, we were not able to identify how this relationship is sensitive to the timing of death relative to pregnancy as associations in the time-stratified outcomes of MM (during pregnancy and up to 42 days postpartum) and LMM (43 days to 1 year postpartum) were not significant. Maternal deaths are relatively rare events, and stratification by timing of death—in combination with the additional exclusion of California, the most populous state in the nation—may have had a negative impact on statistical power.

In addition, when stratified by race/ethnicity, the association between the abortion policy composite index and TMM was significant among non-Hispanic White population but not Black or Hispanic. Previous evidence has shown that women of all races and ethnicities experience negative impacts of abortion clinic closures and gestational age limits,[5] and, thus, our findings should be interpreted with caution. Counts of maternal deaths were considerably smaller among non-Hispanic Black and Hispanic populations compared with non-Hispanic Whites, potentially limiting power in stratified outcomes. The implications of a restrictive abortion climate on maternal health among non-Hispanic Black and Hispanic populations warrant further examination of contextual, policy, and provider factors (e.g., missed or delayed diagnosis, inadequate access to, or lack of continuity, of care) that may be more prevalent in these groups.

Study Limitations

This analysis had several limitations. First, we used an ecological, cross-sectional study design to increase the precision of our estimates and to minimize heterogeneity bias. As such, we avoided conclusions of causality. Second, we have relied on vital statistics to identify cases of maternal death, which are susceptible to misclassification when incorrect *ICD-10* code was assigned for underlying cause of death.[35] Moreover, evidence shows that misclassification most often results in overreporting of maternal deaths, especially among older women.[3,35] While we demonstrated consistency in findings across 2 age-restricted samples, the possibility of misclassification remains. Third, we acknowledge the possibility of residual confounding by state-level factors we were not able to measure. In addition, we cannot explore mortality among subgroups of women based on pregnancy intention in these data (i.e., separately among those whose pregnancy was intended and those who continued an unintended pregnancy). Finally, while we conducted the analysis at the state level, a geographic unit that does not capture local-area variations in abortion access, our findings have relevant implications for abortion-related policy decisions that occur at the state level.

Public Health Implications

In the context of persistently elevated maternal mortality and expanding state-level restrictions on reproductive health care access, we found associations between state abortion policy context and TMM. It is critical that state-level policies related to women's access to comprehensive reproductive health care services, including abortion, are evidence-based and guided by the primary goal of improving women's health and reducing maternal mortality. Our study provides evidence that decreasing the number of abortion restrictions across the states may reduce incidence of death during pregnancy and postpartum among all women in the United States. AJPH

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CONTRIBUTORS

D. Vilda designed the study, completed the analyses, and led the writing. M. E. Wallace supervised the study and assisted with the analyses and article writing. C. Daniel, M. Goldin Evans, C. Stoecker, and K. P. Theall contributed to the interpretation of the results and the writing of the article.

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CONFLICTS OF INTEREST

The authors have no conflicts of interest to report.

HUMAN PARTICIPANT PROTECTION

This study relied on secondary data containing no personal identifiers; therefore, no institutional review board approval was necessary.

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