Vaccines, Variants, and Vigilance: Strengthening the COVID-19 Public Health Response through Partnerships and Collaborations

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Abstract: The United States Centers for Disease Control and Prevention (CDC), state, tribal, local, and territorial health departments, other U.S. government departments and agencies, the private sector, and international partners have engaged in real-time public health response to the coronavirus disease 2019 (COVID-19) pandemic, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Vaccination, variants, and vigilance were themes that arose in the second year of pandemic response in the United States. The findings included in this supplement emerged from these themes and represent some of the many collaborative partnership efforts to improve public health knowledge and action to reduce transmission, infection, and disease severity.

Keywords. COVID-19; SARS-CoV-2; CDC; public health; transmission; surveillance; vaccines; variants; vigilance.

Background

The coronavirus disease 2019 (COVID-19) pandemic has resulted in an enormous global health challenge; economic, medical, and public health systems have struggled to maintain essential functions. In response to the pandemic, the United States Congress appropriated emergency funding through the Coronavirus Aid, Relief, and Economic Security (CARES) Act (2020), the Coronavirus Response and Consolidated Appropriations Act (2021), and the American Rescue Plan Act of 2021 [1-3]. Along with this support, many sectors engaged in new partnerships and collaborations to address the challenges posed by the pandemic. The sectors included community, scientific, private, and public sectors; domestic and international partners; local, state, tribal, territorial, and federal governments; and public health and medical partners. These combined efforts led to the development of novel vaccines; vigilance which includes enhanced surveillance, monitoring, assessments, and evaluations; new SARS-CoV-2 diagnostics; increased understanding of the effectiveness of non-pharmaceutical mitigation measures, including masking, ventilation, and distancing; and novel treatments. These efforts also brought together many disciplines such as epidemiology, including data, laboratory, medical, and behavioral sciences. These multidisciplinary approaches maximized existing relationships and created new partnerships to combat a shared public health emergency.

The July 2021 Clinical Infectious Diseases (CID) COVID-19 supplement 'A Snapshot of Work by the COVID-19 Public Health Response' included research articles on the effects of the pandemic on a variety of U.S. sectors, including healthcare, construction, education, long-term care, and clinical laboratory work in 2020 [4]. This second supplement includes 25 articles from 337 different authors across 74 institutions. It represents significant efforts in domestic and international collaborations that have strengthened the U.S. Centers for Disease Prevention and Control (CDC) COVID-19 response over the past two years. This supplement is only one example of the many contributions of dedicated people. It highlights how partnerships can address evolving pandemic challenges in three key overlapping themes: vaccines, variants, and vigilance.

VACCINES

Effectiveness of COVID-19 vaccines on SARS-CoV-2 variants

The extraordinary speed with which several countries developed COVID-19 vaccines was a significant scientific achievement and a success story of innovation, dedication, creativity, collaboration, and cooperation. The U.S. Food and Drug Administration (FDA) issued emergency use authorizations (EUA)

for the first two mRNA COVID-19 vaccines: Pfizer BioNTech (BNT162b2) on December 11, 2020, and Moderna (mRNA-1273) on December 18, 2020 [5]. On February 27, 2021, FDA issued an EUA for the Janssen (Ad26.COV2.S) COVID-19 vaccine [5]. Interdisciplinary partnerships and cross-collaborations, a few of which are represented in this supplement, have demonstrated the real-world effectiveness of these and other COVID-19 vaccines in preventing severe illness, hospitalization, and death and have informed vaccine policy in populations not included in the vaccine trials [6].

Nursing home residents, who were not included in vaccine trials, have been disproportionately affected by the pandemic; as of the week ending May 29, 2022, 1,057,344 confirmed cases and 153,054 deaths were reported among U. S. nursing home residents [7]. In collaboration with partners including nursing home providers, state and local health departments, academic institutions, and international partners, CDC COVID-19-response staff examined vaccine effectiveness (VE) of COVID-19 vaccines in multiple settings using case-control, cohort, and outbreak methods [8-11]. Hatfield et al. determined mRNA VE in a partnership with a commercial nursing home provider of 105 nursing homes in 10 states. During the Delta variant predominance, VE against infection measured >150 days after the second dose was 33% (95%CI: -2%, 56%) for Pfizer-BioNTech and 77% (95%CI: 48%, 91%) for Moderna [8]. Collaboration among federal, state, and local public health departments demonstrated that the mRNA COVID-19 VE against infection was 64% in a Beta variant-driven outbreak in a skilled nursing facility [9]. Another group not included in vaccine trials is immunosuppressed patients; a cross-academic collaboration estimated the VE of a single dose of the Janssen vaccine against hospitalization; it was 70% overall; 55% among immunocompromised patients, and 72% among immunocompetent patients [10].

Procuring, storing, distributing, and understanding the real-world vaccine effectiveness of multiple new COVID-19 vaccines were some of the challenges that countries faced [12]. CDC staff assisted international partners in evaluating some of these COVID-19 vaccines. One such partnership evaluated a single dose of the CanSino Biologics (Adv5-nCoV) COVID-19 vaccine in a childcare worker cohort in Mexico; the adjusted VE was 20% against illness, 76% against hospitalization, and 94% against death [11]. Adjusted vaccine effectiveness against illness before Delta variant predominance (March 30–June 28, 2021) was 53%; this declined to 18% during Delta predominance. Before and amid the arrival of the Delta variant in Vietnam, a critical question was the role of the AstraZeneca (ChAdOx1 nCoV-19) COVID-19 vaccine for Vietnamese healthcare workers [13]. The collaboration between CDC and the Vietnamese government demonstrated that the vaccine effectively induced antibody response within the first three

months of receiving the 2-dose series, regardless of the interval between administering the first and second doses. Such collaborations and studies are essential as reassessments of vaccine effectiveness are frequently required to maintain an understanding of the effect of cumulative vaccinations, boosters, and infections, as well as the effect of new variants, on population susceptibility to infection and severe disease.

COVID-19 vaccine acceptability

Vaccine acceptance remains a critical public health issue and is dependent on multiple factors [14]; vaccination acceptability has affected vaccination rates which may have contributed to disparities by race, ethnicity, age, urbanicity, and region [15-17]. Understanding the drivers of vaccine hesitancy, acceptability, and inequalities are critical for CDC and partners to develop appropriate communications tools for providers and the public. The National Immunization Survey added the Adult COVID Module (NIS-ACM) in April 2021 in response to the COVID-19 pandemic to provide population-based, state, and local area estimates of COVID-19 vaccination coverage, attitudes, and intentions[18, 19]. Using these and similar data, jurisdictional and local vaccination programs can collaborate locally to develop culturally and linguistically appropriate, focused communication tools to improve vaccination rates and address disparities.

VARIANTS AND VIGILANCE

Monitoring the pandemic across settings

Vaccination status, viral variant, duration of exposure, prior infection, adherence to prevention measures, including isolation and quarantine guidance, and diagnostic tests all interact with social determinants of health. This includes where people live, work, learn, and play, influencing susceptibility, transmission, incidence, and outcomes of SARS-CoV-2 infection. Because interventions addressing social determinants of health involve influencing numerous settings, there is a need to engage multiple disciplines; expertise in these varied settings lie in numerous U. S. government agencies and public and private institutions; therefore, collaborations are essential to understand and address population needs.

Residential setting, where people live, is a social determinant of health; this supplement includes research on SARS-CoV-2 transmission in households where susceptible people may be exposed. Before widespread transmission of the Delta variant, compared to unvaccinated index cases, fully vaccinated index cases had a lower frequency of household transmission [20-22]. A multidisciplinary collaboration

demonstrated similar transmission rates during Delta and early Omicron predominance from vaccinated and unvaccinated index cases within households [23]. A similar multi-center partnership examined the transmission of other respiratory viruses and SARS-CoV-2 in 497 households with school-aged children, finding low transmission during low community incidence [24].

Occupational setting, where people work, another social determinant of health, presents a continued risk for SARS-CoV-2 transmission. Workers in both healthcare and non-healthcare settings have been disproportionately affected during the pandemic [25-27]. To investigate occupational exposures among workers in non-healthcare settings with SARS-CoV-2 infection, the CDC's National Institute of Occupational Safety and Health (NIOSH) surveyed more than 1,000 respondents in collaboration with six state health departments to collect and analyze more detailed work-related data than what is routinely available through national case surveillance [28]. In nursing homes, where people both work and live, the mingling of staff and residents makes prevention critical to reducing the risk of residents becoming infected. Zipfel et al. modeled how different screening or testing options and vaccination impact transmission in these settings [29].

Educational setting, where people learn, is another social determinant of health, has been important in understanding and mitigating the pandemic. Collaborations with educational institutions have been critical to understanding susceptibility in populations, risk of transmission, and how prevention activities can allow staff and students to teach and learn together safely in person. There are approximately 80 million students and staff across U. S. educational settings [30]. CDC collaborated with many institutes of higher education, state education agencies, and student associations [31-34]. One of these efforts described in the supplement involved collaboration across public health and educational agencies in Washington, D.C.; the investigators evaluated testing before school re-entry during the Omicron surge [32]. Another collaboration among 21 universities before the emergence of Omicron describes infections in student-athletes with partial or full vaccination coverage [33]. A partnership of federal, state, and institutions of higher education addressed a Delta outbreak in a university. Despite high vaccination rates, ongoing screening to detect and quarantine or isolate remained important in a high community transmission setting [34].

Leisure setting, where people play, is another social determinant of health and is highlighted in an article describing an outbreak at a concert in Seattle, Washington [35]. While the mask mandate and

congregate size limits for vaccinated persons had been lifted, a collaboration of private and public partners ascertained that one outbreak may have been facilitated by unvaccinated staff, limited masking, poor ventilation, and overcrowding.

Monitoring the general population

Understanding population-level past exposure to infection and vaccination can assist in pandemic planning. While vaccine effectiveness studies highlight that susceptibility to severe illness and hospitalization outcomes remains low after vaccination and boosting despite changes in variants, susceptibility to infection may increase with time since the last vaccine dose [36, 37]. Despite no clear serologic correlate of protection, SARS-CoV-2 antibody tests, which can distinguish between antibodies due to COVID-19 vaccines and infection, can provide prevalence estimates of post-vaccination and/or prior infection status. A collaboration among federal, state, local, territorial, academic, and commercial laboratories and blood centers spanning 50 states, the District of Columbia, and Puerto Rico reports, in this supplement, that among US blood donors, from January 2021 to December 2021, the combined seroprevalence from the previous infection, vaccination, or both, increased from 19.8% to 94.5% [38]. The same collaboration assessed the association between seropositivity and state-issued, county-specific nonpharmaceutical interventions (NPI) during different pandemic waves and found that multiple NPIs may be more effective than single NPIs in reducing infections [39]. Other supplement manuscripts describing serologic advances are an innovative 41-plex antibody immunity assay that used specimens provided by partners to differentiate influenza and four common human coronaviruses, as well as differentiate antibodies produced by SARS-CoV-2 infection and COVID-19 vaccine [40]. Finally, an early seroprevalence study in 2020 in Mozambique showed that younger people in certain occupations (healthcare workers, market vendors, and transport workers) and locations were more likely to have antibodies to SARS-CoV-2 [41].

In response to the pandemic, monitoring systems were either enhanced or developed with new and existing partners to improve understanding of infection and disease outcome trends. With close to real-time data [42, 43], risk groups [44] and real-world vaccine effectiveness among patients using electronic healthcare data systems and other sources have been described [45, 46]. A retrospective study using one system compared hospital-onset infections from pre-pandemic (2019) to those occurring during the first year of the pandemic and identified significantly higher odds of hospital-onset infections among COVID-19 inpatients [47]. Mortality has defined the severity of the pandemic; the United States alone

has now lost more than one million lives to COVID-19 [48]. A collaboration in Alaska found that infection during the Delta predominance was associated with a 2.4-fold increase in the odds of death and that vaccination was protective against mortality [49].

Monitoring special populations

In May 2020, the U.S. health departments began to report possible multisystem inflammatory syndrome in children (MIS-C) to CDC [50]. In this supplement, Miller et al. report that during Delta and early Omicron predominance, half of the MIS-C patients were aged 5–11 years old, 52% received intensive care unit (ICU)-level care, and 1.1% died. Only 3.0% of eligible patients were fully vaccinated before MIS-C onset [51].

Pregnant and post-partum women have a higher risk of severe illness from COVID-19 [52]. In one collaborative study, using a population-based retrospective cohort of all pregnancies with live birth or fetal death in Florida, after accounting for the trimester of infection, women infected during any trimester showed an increased risk of preterm, very preterm, and extremely preterm birth compared to women without COVID-19 during pregnancy and were more likely to be admitted to an ICU [53]. Using a population-based mother-baby linked longitudinal surveillance collaboration between CDC and state, local, and territorial HDs, Strid et al. found that compared to non-pregnant women of reproductive age, pregnant women had a higher risk of COVID-19 severity, ICU admissions, and invasive ventilation or extracorporeal membrane oxygenation during Delta variant predominance [54].

Case investigation and contact tracing

Although resource-intensive for the state, local, and territorial health departments, both in terms of human hours and financial expense, case investigation and contact tracing (CICT) has played a role in identifying people for testing and exposure notification. Stargel et al. describe how health departments developed, deployed, evaluated, and modified their CICT approach over time, depending on the jurisdiction's needs and the emerging variants [55]. At the state level, the surges sometimes overwhelmed the health department's capacity to identify people at risk for COVID-19 [56].

PARTNERSHIPS AND COLLABORATIONS: LOOKING FORWARD

This supplement includes examples of many collaborations that have been critical in providing data to guide the United States and the global public health response to reduce hospitalizations and deaths

from COVID-19. It is essential to consider diverse settings, long-term needs, cost-effectiveness, and additional creative solutions to sustain these relationships and momentum. The COVID-19 pandemic highlighted inequality and equity concerns; specific populations were disproportionately affected, including groups of certain ages, races and ethnicities, occupations, and those in congregate settings, with comorbid conditions and disabilities [57-59]. The immunocompromised and those unable to develop adequate immunity, including the elderly, continue to face the risk of severe outcomes of COVID-19. Additional partnerships that seek to improve population-level immunity by increasing vaccine coverage and the number of available therapies and supporting public health systems will enhance the response to the pandemic.

Limitations of public health partnerships and collaborations to mitigate the effect of the pandemic include social and historical factors and communication challenges. These relate to diminished trust in science and public health messages, which has led to resistance to contact investigation and tracing, reduced uptake of vaccines, and lowered acceptance and institution of public health guidance [14, 60]. Still, partnerships and collaborations have been instrumental in working toward fully restoring societal functions while protecting the public's health. Continuing to strengthen and learn from these partnerships and collaborations can pave the way toward a more equitable ongoing response to the impacts of this pandemic and those that follow.

Notes

Acknowledgments: The COVID-19 pandemic continues to affect populations adversely; extensive and strategic partnerships and collaborations remain critical to maintaining momentum to protect populations. This supplement is dedicated to the heroes and the people who lost their lives because of this pandemic.

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