COVID-19

CDC Public Health Science Agenda for COVID-19

Building the Evidence Base for Ongoing COVID-19 Response

Updated May 17, 2022

Priority COVID-19 Public Health Science Questions

As the public health response to the COVID-19 pandemic continues to evolve, considerable progress has been made. We now have more tools than ever to prevent COVID-19 from placing strain on communities and healthcare systems. With current high levels of vaccination and high levels of population immunity from both vaccination and previous infections, the risk of medically significant disease, hospitalization, and death from COVID-19 is greatly reduced for most people (see more on COVID-19 Community Levels). It remains important to collect data-driven information on key priority areas that can help CDC and public health partners continue to fill critical scientific gaps, build on knowledge gained and advances made, and inform evidence-based decision-making for continued intervention through public health surveillance and epidemiologic research.

CDC has developed priority questions around 8 thematic topic areas for *The CDC Public Health Science Agenda for COVID-19:*

- Health equity
- Vaccines
- Variants
- Prevention strategies
- Testing
- Treatment
- Natural history, transmission, breakthrough infections, and reinfections
- Post-COVID conditions and other health impacts

Within these topic areas, 15 priority public health science questions relate to the broad scope of CDC's scientific work, both in the United States and globally, including public health surveillance, epidemiologic research, implementation science, and evaluation. These questions also relate to ongoing work in the broader scientific community (such as other government agencies, academics, the private sector). Other relevant questions are found in the complementary science agendas of other federal agencies, including the National Institutes of Health (NIH), the Food and Drug Administration (FDA), the

Environmental Protection Agency (EPA), and the White House. This Science Agenda is intended to inform efforts by the broader public health research community. It is used to help direct and monitor CDC's scientific activities but is not a commitment by CDC to address every question.

Importantly, these questions also serve to expand the evidence base to accelerate progress toward reducing COVID-19 health disparities and achieving health equity in prevention, testing, treatment, and management of post-COVID conditions. Health disparities are differences in health among groups of people that are linked to social, economic, geographic, and/or environmental disadvantage (social determinants of health), and health equity is achieved when everyone has a fair and just opportunity to attain their highest level of health. Our health equity priority question considers populations experiencing COVID-19-related health disparities including, but not limited to: age, sex, race, ethnicity, sexual orientation, socioeconomic status, disability, underlying medical conditions (especially compromised immune status), education, occupation, place and type of residence (single versus congregate housing and urban versus rural settings), and other social determinants of health that may not necessarily fall within other priority questions. However, health equity science remains a fundamental consideration for all priority questions, and there is some overlap in health equity science activities across questions.

Two priority questions were added in March 2022 to address research gaps in evaluating equitable access to treatments for COVID-19 and the effectiveness of COVID-19 treatments in improving outcomes from COVID-19, post-COVID conditions, and other conditions unrelated to COVID-19.

Key activities of public health importance that fall within the question domain are noted under each question.

Health Equity

1. How can the public health community effectively identify and address health inequities to protect populations disproportionately affected by COVID-19?

Key activities:

- Identifying and monitoring trends in, and effects of, disparities in severe COVID-19 illnesses, hospitalizations, deaths, post-COVID conditions, as well as trends in access to vaccines and other prevention and treatment measures.
- Identifying and monitoring trends in, and effects of, disparities in COVID-19 associated second-order consequences in children (such as orphanhood or caregiver death, poverty, food insecurity, violence, adverse childhood experiences, adverse mental health conditions, and disruptions to education and childcare access)
- Understanding the social determinants of health that may contribute to these disparities in various populations to identify opportunities for interventions
- Evaluating the effectiveness of initiatives and policies, including broad communication and dissemination strategies, in facilitating equitable access to testing, vaccines, and treatments and identifying opportunities for improvement
- Evaluating which initiatives and policies (such as COVID-19 vaccination incentives or mandates) have improved vaccination equity and coverage in communities of varying demographic composition, socioeconomic status, geographic location, policy environment, and population size, both domestically and globally
- Characterizing outpatient and inpatient treatment of severe COVID-19 in populations affected by disparities related to social determinants of health, to identify opportunities for improvement
- Identifying and implementing targeted efforts to protect people with moderate or severe immunocompromising conditions, who might receive less protection by vaccines than others

Vaccines

2. What is the effectiveness and duration of immune protection afforded by COVID-19 primary series and booster vaccines?

Key activities:

- Measuring differences in vaccine effectiveness against symptomatic or severe COVID-19 illness in various populations and settings, including by country or region, single versus congregate settings, age groups, underlying medical conditions (including previous infection with SARS-CoV-2, the virus that causes COVID-19), product type (including mixed doses with more than one vaccine formulation), the number of doses, and the interval between doses
- Measuring effects of vaccination on SARS-CoV-2 transmission and disease burden
- Evaluating effectiveness of primary series and booster vaccines in reducing the likelihood of post-COVID conditions, including MIS-C
- Determining if post-vaccination testing in populations at risk for severe disease can inform the need for additional vaccine boosters, preexposure prophylaxis (such as monoclonal antibodies), treatment, or other clinical interventions

3. What communication approaches are most effective at increasing COVID-19 vaccination access and coverage?

Key activities:

- Evaluating strategies to build trust in CDC recommendations for use of COVID-19 vaccines and to increase vaccine uptake among people who have not yet been vaccinated
- Addressing vaccine hesitancy in communities of varying demographic composition and among special populations, including, but not limited to, adults aged 65 and older, residents of long-term care facilities, pregnant and lactating people, parents or guardians of minor children, adolescents, incarcerated or homeless populations, and healthcare providers, using culturally appropriate messaging
- Evaluating strategies to effectively counter vaccine misinformation and disinformation and encourage effective provider recommendations of COVID-19 vaccination as a part of routine care, especially for pediatric populations
- Tracking and responding to changes in vaccine-related questions, concerns, and reports about adverse events over time, particularly for pediatric vaccination
- Addressing barriers to vaccine providers checking Immunization Information Systems (IIS) prior to vaccination to reduce missed opportunities for vaccination

4. What are the risks associated with COVID-19 primary series and booster vaccines?

Key activities:

- Conducting vaccine safety analyses using various vaccine safety data sources, and developing accurate, timely, and transparent communication on potential adverse events and differences in potential adverse events by vaccine product
- Assessing effects of back-to-back vaccination against COVID-19 and other vaccine-preventable diseases, including seasonal influenza
- Characterizing the effect of COVID-19 vaccination on routine and seasonal vaccinations, domestically and globally
- Assessing potential risks in populations for which vaccination has only recently been approved or is not yet approved but poised to be (such as pediatric populations).

Variants

5. How can the public health community effectively and efficiently enhance surveillance for known and emerging SARS-CoV-2 variants?

Key activities:

- Tracking and measuring the proportion and incidence of emerging variant lineages in various populations and settings
- Using specialized surveillance strategies to identify importation of emerging variants, including testing travelers to the United States
- Improving the timeliness and accuracy of genomic surveillance and regional estimates of variant proportions in circulation in the United States and globally to effectively detect and track variants, including from wastewater surveillance
- Improving data quality of measures for detecting and tracking variants by enhancing genomic surveillance; increasing social and demographic data completeness; integrating epidemiologic and genomic data where available, including travel history; and ensuring a representative sample of specimens
- Effectively communicating health information about variants to the public

6. How do SARS-CoV-2 variants affect the performance of diagnostics, vaccine effectiveness, clinical outcomes, transmissibility, and treatments, and the outcome of public health interventions?

Key activities:

- Measuring changes in effectiveness of COVID-19 vaccines, treatments, and other public health interventions against SARS-CoV-2 variants in various populations and settings
- Measuring differences in the transmissibility of SARS-CoV-2 variants in various populations and settings, and by population vaccination status
- Understanding changes in adherence to recommended prevention strategies and vaccine uptake related to the public's understanding of variants
- Characterizing clinical impact and severity of variants in pediatric and adult populations

Prevention strategies

7. What effective prevention strategies and non-pharmaceutical interventions should be prioritized to reduce transmission of SARS-CoV-2 in various populations and settings?

Key activities:

- Reducing barriers to implementation of effective prevention strategies (such as masking, ventilation, distancing, and other effective interventions) in schools, workplaces, and other congregate settings when they are needed
- Evaluating effectiveness of prevention strategies, including testing, in settings at varying levels of vaccination coverage and varying levels of community transmission
- Evaluating which prevention strategies (jointly with vaccination) can measurably reduce disparities in severe COVID-19 illness, hospitalizations, and deaths

- Developing and communicating evidence-based health recommendations and information on COVID-19 prevention

Testing

8. How effective are at-home/self-testing, rapid diagnostic testing, point-of-care testing, routine screening, and serial testing strategies compared with laboratory-based nucleic acid amplification testing strategies on reducing outbreaks, reducing disease burden, detecting potential surges, and detecting re-introduction of SARS-CoV-2 into low transmission settings?

Key activities:

- Evaluating and identifying the most effective approaches to rapidly expand testing capacity when needed, as indicated by appropriate metrics
- Improving collection of demographic and epidemiologic data associated with testing, including the effect of testing on transmission
- Evaluating cost-effectiveness of testing strategies and developing testing recommendations that are effective for both vaccinated and unvaccinated people and consider the impact of emerging variants
- Evaluating ways to link at-home/self-testing with access to treatment

Treatment

9. What interventions, programs, and communication approaches are most effective at increasing equitable COVID-19 treatment access and coverage?

Key activities:

- Evaluating strategies to assess and build trust in use of SARS-CoV-2 oral antiviral treatment, including strategies to effectively counter oral antiviral misinformation and disinformation
- Tracking and responding to concerns about adverse events related to oral antivirals and other treatments, particularly for pregnant and lactating people and pediatric populations
- Assessing approaches for oral antiviral prescribing and dispensing, including telehealth
- Evaluating the relationship between testing demand and oral antiviral treatment availability
- Evaluating the benefits and risks of dispensing oral antiviral treatment at the time of COVID-19 testing, prior to disclosure of testing outcomes

10. How effective are treatment strategies at reducing disease burden and transmission?

Key activities:

- Addressing needs for expanded and equitable treatment access, and adopting approaches to increasing treatment availability domestically and globally
- Improving collection and analysis of epidemiologic data associated with treatment strategies in various populations and settings
- Conducting laboratory monitoring to rapidly identify oral antiviral resistant SARS-CoV-2 isolates

- Evaluating how SARS-CoV-2 treatments may influence the severity of COVID-19, post-COVID conditions, and other health conditions unrelated to COVID-19

Natural history, transmission, breakthrough infections, and reinfections

11. How does the public health community effectively and efficiently enhance surveillance for SARS-CoV-2 reinfections, breakthrough infections, vaccination, and various health outcomes?

Key activities:

- Measuring incidence of reinfection and associated risks
- Improving data completeness for demographic and social determinants of health variables, and methods for handling missing data
- Evaluating impact of reporting of infections and characterizing risk factors for reinfection in various populations and settings, including those experiencing health disparities related to social determinants of health
- Evaluating the effectiveness of new surveillance strategies to inform policy and personal action
- Characterizing risk factors for breakthrough infections leading to severe illness among vaccinated people
- Evaluating to what extent breakthrough infections contribute to SARS-CoV-2 transmission and whether these transmission rates differ by variant

12. What factors best inform SARS-CoV-2 transmission dynamics and predict surges of community-level infection?

Key activities

- Characterizing how the seasonality of other respiratory viruses (such as influenza) affects SARS-CoV-2 transmission, domestically and globally
- Evaluating whether geography-based data indices on social determinants of health, such as the Social Vulnerability Index and Area Deprivation Index, improve the accuracy of predicted surges in localized COVID-19 incidence
- Understanding the potential role of animal reservoirs of SARS-CoV-2 transmission to humans and sustaining environmental reservoirs
- Characterizing viral load and duration of shedding following infection by different host and virologic factors including age group, immune status, test type, virus variant, or infection and/or vaccine-mediated immunity
- Measuring rates of SARS-CoV-2 transmission and assessing risk of transmission by viral shedding dynamics, variant, and additional host and contact factors

13. What are reliable immune factors contributing to protection from SARS-CoV-2 infection and/or vaccination, and what are accurate ways to measure them?

Key activities:

- Expanding diagnostic capabilities to distinguish infection versus vaccine-mediated immunity
- Measuring differences in strength and duration of protection afforded by infection and/or vaccine-mediated immunity, variant type, disease severity and symptomatology
- Evaluating measures for population-level immunity from initial and booster vaccinations, and changes over time due to waning immunity and other factors

- Measuring variation of serological correlates by demographic and clinical characteristics

Post-COVID conditions and other health impacts

14. How does the public health community effectively conduct epidemiologic research on post-COVID conditions, overall and in various populations and settings?

Key activities:

- Developing standard case definitions for post-acute versus long-term phases of COVID-19
- Measuring and understanding the prevalence and incidence of various post-COVID conditions over time
- Measuring the burden of post-COVID conditions in health systems, to promote equitable access to care and quality of care
- Characterizing risk factors at the individual and population levels, including SARS-CoV-2 infection or reinfection characteristics, underlying biological mechanisms, and variant characteristics
- Assessing prevention measures for post-COVID conditions, including COVID-19 vaccination
- Assessing potential health and economic impacts of post-COVID conditions (such as inability to work or effects on daily activities)

15. What short- and long-term impacts from the COVID-19 pandemic are of the greatest public health importance, and what are the best ways to address them?

Key activities

- Measuring and improving mental health outcomes in the public health workforce and other frontline workforce populations to reduce adverse mental health effects of the COVID-19 pandemic
- Measuring changes to non-COVID-19 health epidemics and illnesses affected by the COVID-19 pandemic
- Understanding how the effect of the pandemic on income, housing, employment, caregiving, childcare, orphanhood, and other factors have exacerbated health and social inequities
- Evaluating evidence-based best practices for pre-pandemic planning and public health agency collaboration with specified sectors (such as healthcare, schools, and high-risk industries) to strengthen the overall public health infrastructure in an effective pandemic response
- Modeling long-term effects and differential burdens by population groups, communities, and countries

Background for the CDC Public Health Science Agenda for COVID–19

The COVID-19 pandemic is a formidable global public health challenge. Since the initial emergence of a novel coronavirus in late 2019, the spread of SARS-CoV-2 has been unrelenting, impacting nearly every aspect of society worldwide. The pandemic has required a substantial response by public health authorities at all levels.

The Centers for Disease Control and Prevention (CDC) is at the forefront of the public health response to the COVID-19 pandemic and is a respected source of data and information used by public health, medical, and policy decision makers. From the beginning of the pandemic, CDC has been working with a wide array of partners to advance understanding of COVID-19.

The CDC Public Health Science Agenda for COVID-19 builds on CDC's ongoing pandemic-related work. Importantly, the COVID-19 pandemic has underscored long-standing health disparities and inequities in the United States. Data-driven strategies are essential to address these disparities and improve the health outcomes of people disproportionately affected by COVID-19.[1] The work set out in *The CDC Public Health Science Agenda for COVID-19* is predicated on the use of culturally and linguistically appropriate approaches and methods and inclusion of populations at increased risk for health disparities and inequities to help reduce the impact of COVID-19 in these communities.

Goal of *The CDC Public Health Science Agenda*

The goal of *The CDC Public Health Science Agenda for COVID-19* is to guide the development of the evidence base needed to strengthen the public health actions, guidance, and policy essential to limit the spread and impact of SARS-CoV-2 and ultimately end the COVID-19 pandemic.

CDC's role and the scope of *The CDC Public Health Science Agenda*

CDC is providing leadership and technical expertise in the prevention and control of the COVID-19 pandemic by:

- employing public health fundamentals, including disease surveillance, laboratory detection, and epidemiologic investigation;
- identifying and implementing public health interventions to reduce disease transmission and the mitigation of its impact on health and well-being;
- developing evidence-based guidance and policies for disease prevention, detection, and control; and
- engaging in effective communication strategies to optimize uptake of protective behaviors and recommended actions.[2]

These key functions underpin *The CDC Public Health Science Agenda for COVID-19.*

Organization of *The CDC Public Health Science Agenda*

The CDC Public Health Science Agenda for COVID-19 was initially organized around a framework of six **Priority Areas**:

- Priority Area I. COVID-19 disease detection, burden, and impact
- Priority Area II. Transmission of SARS-CoV-2
- Priority Area III. Natural history of SARS-CoV-2 infection
- Priority Area IV. Protection in healthcare and non-healthcare work settings
- Priority Area V. Prevention, mitigation, and intervention strategies
- Priority Area VI. Social, behavioral, and communication science

For each of the six Priority Areas, a series of **Objectives** were described.

Priority Area I. COVID-19 Disease Detection, Burden, And Impact

Disease surveillance and laboratory detection are at the heart of CDC's mission and fundamental to the COVID-19 public health response. They underpin CDC's work with federal, state, tribal, local, and territorial (STLT), academic, and commercial partners to better understand the burden of COVID-19 disease and efforts to mitigate its diverse impacts, including the disproportionate impacts of COVID-19 on people at increased risk for health disparities and inequities. CDC supplements surveillance and laboratory methods with the modern tools of viral genomics and mathematical modeling.

- **Objective 1**. Develop new, or modify existing, methods of epidemiologic surveillance for COVID-19
- **Objective 2**. Develop and optimize testing for SARS-CoV-2
- **Objective 3**. Utilize viral genomics to advance understanding of COVID-19 and mitigate its impact
- **Objective 4**. Use mathematical modeling and other technological tools to forecast COVID-19 trends and measure the impact of interventions across a range of populations

- **Objective 5**. Assess and limit the impact of the COVID-19 response on healthcare services and public health programs in domestic and international settings

Priority Area II. Transmission of SARS-Cov-2

Understanding how SARS-CoV-2 is transmitted and the important factors that can facilitate its spread among people in healthcare, workplace, and community settings has been a high priority for CDC since the earliest days of the pandemic. This essential information is used to develop and update guidance about effective strategies to prevent, contain, and mitigate COVID-19.

- **Objective 1**. Refine understanding of SARS-CoV-2 transmission modes
- **Objective 2**. Identify host and virus factors associated with person-to-person transmission
- **Objective 3**. Assess and characterize transmission of SARS-CoV-2 across a spectrum of healthcare settings
- **Objective 4**. Evaluate transmission of SARS-CoV-2 in non-healthcare workplace and community settings/populations
- **Objective 5**. Evaluate transmission of SARS-CoV-2 between people and animals

Priority Area III. Natural History of SARS-Cov-2 Infection

The full spectrum of COVID-19 disease continues to unfold and confound in its clinical manifestations and requires careful study. CDC and its collaborators have been undertaking comprehensive clinical and laboratory investigations of confirmed cases across a range of age groups and populations to learn about the natural history of COVID-19 disease, associated medical complications, and the development of immunity.

- **Objective 1**. Define the spectrum and clinical course of SARS-CoV-2 infection
- **Objective 2**. Characterize the immune response in infected persons

Priority Area IV. Protection in Healthcare and Non-Healthcare Work Settings

Understanding and mitigating risks to patients, HCP, and non-healthcare workers across a range of settings is a high priority focus. CDC works to identify culturally and linguistically appropriate innovative strategies, tools, and practices which can supplement traditional infection control and worker safety measures to protect patients and reduce nosocomial and occupationally acquired SARS-CoV-2.

- **Objective 1**. Improve and assess the effectiveness of personal protective equipment
- **Objective 2**. Assess strategies to reduce transmission of SARS-CoV-2 in healthcare and non-healthcare work settings

Priority Area V. Prevention, Mitigation, and Intervention Strategies

CDC has disseminated a portfolio of prevention, mitigation, and intervention strategies tailored to specific settings and sectors to slow the spread of COVID-19 and protect individuals and communities. Evaluating the effectiveness of these strategies is critical to help refine public health guidance and recommendations. A key responsibility for CDC, in collaboration with STLT public health partners and academic and other researchers is monitoring the coverage, safety, and effectiveness of COVID-19 vaccines.

- **Objective 1**. Evaluate individual- and community-level strategies to limit infection with SARS-CoV-2
- **Objective 2**. Evaluate strategies to limit infection with SARS-CoV-2 in specialized settings or select populations
- **Objective 3**. Develop methods to detect SARS-CoV-2 in the environment

- **Objective 3**. Develop methods to detect SARS-CoV-2 in the environment
- **Objective 4**. Identify the most effective methods for contact tracing, testing, and monitoring
- **Objective 5**. Evaluate travel-related interventions
- **Objective 6**. Optimize the acceptability, coverage, safety, and effectiveness of COVID-19 vaccines

Priority Area VI. Social, Behavioral, And Communication Science

Effective communication requires community engagement; empowerment of individuals to take appropriate measures to reduce their risk; evaluation of risk communication methods and information gaps; and culturally and linguistically responsive materials and messengers. The effectiveness of risk reduction strategies, such as community mitigation or maximizing vaccine uptake, is dependent in part on understanding the barriers to implementation/acceptance, including economic and social determinants of health. Understanding the social, behavioral, and mental health impacts of the COVID-19 pandemic are as important as understanding the impacts to physical health.

- **Objective 1**. Understand where people receive information about the pandemic
- **Objective 2**. Optimize uptake of recommended behaviors and actions
- **Objective 3**. Enhance CDC communication products and information tools
- **Objective 4**. Assess the social and mental health impacts of the pandemic

Footnotes

1. Populations of special focus include racial and ethnic minority populations; people living in rural or frontier areas; people experiencing homelessness; essential and frontline workers; people with disabilities; people with substance use disorders; people who are justice-involved (incarcerated persons); and non-U.S.-born persons.
2. A CDC framework for preventing infectious diseases. See https://www.cdc.gov/ddid/docs/ID-Framework.pdf

Resources

1. CDC Coronavirus Disease 2019 (COVID-19)
2. ACIP COVID-19 Vaccine Recommendations
3. CDC Science Briefs
4. CDC COVID-19 Publications Database
5. MMWR COVID-19 Reports
6. CDC Office of Science
7. CDC Strategy for Global Response to COVID-19

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