Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™

COVID-19

CDC Science Agenda for COVID-19

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Introduction

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 on a wide range of issues. From the beginning of the pandemic, CDC has been working with a wide array of partners to advance understanding of COVID-19. These efforts have focused on surveillance; epidemiologic investigations; mathematical modeling; development of laboratory diagnostics; protection of patients and workers; community mitigation strategies; and communications.

The CDC Science Agenda for COVID-19 builds on CDC's ongoing pandemic-related work. It articulates key areas of scientific inquiry and opportunities which chart a course for CDC, working with its partners, over a three-year period. 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 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 Science Agenda*

The goal of *The CDC 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 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 Science Agenda for COVID-19.*

The Science Agenda is a concise, high-level framework for the planning and prioritization of COVID-19 work conducted or supported by CDC. It complements areas of COVID-19 research addressed by scientists in other government agencies, academia, and the private sector.

As the COVID-19 pandemic and the public health response to it evolve, some knowledge gaps will close, and new ones will be identified. The broad-based nature of *The Science Agenda* will allow it to remain extant as knowledge of COVID-19 expands at an unprecedented pace.

Organization of *The Science Agenda*

The Science Agenda for COVID-19 is 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** are 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

CDC has established multiple systems of surveillance to monitor trends in COVID-19 disease in the United States and measure the impact of interventions. Surveillance studies are helping to estimate the proportion of cases that are asymptomatic or mild versus those that are severe or fatal. A key priority is the development, implementation, and evaluation of innovative, targeted strategies to rapidly detect early signals of COVID-19 in communities or settings of special interest such as schools, workplaces, or congregate living facilities.

CDC is utilizing serology testing to better understand how many infections with SARS-CoV-2 have occurred at different points in times in different locations. Seroprevalence surveys include large-scale geographic surveys, community level surveys, and smaller-scale surveys focusing on specific populations such as healthcare workers.

Surveillance strategies in international settings may include adaptation of established disease testing systems for other diseases (e.g., human immunodeficiency virus [HIV]) and leveraging existing partnerships (e.g., polio eradication programs).

Objective 2. Develop and optimize testing for SARS-CoV-2

Identifying new detection methods and strategies that improve the speed, accuracy, and sensitivity of diagnostics and are not reliant on reagents that can limit testing are a high priority.

CDC is pursuing multiple lines of research including evaluation of different types of specimens, assays, and serial testing strategies to optimize detection of acute and past SARS-CoV-2 infection; development of rapid, point-of-care diagnostic tests and multiplex testing systems to concurrently detect SARS-CoV-2 and influenza A and B; and identification of the most useful assays to advance understanding of community levels of

protection needed to interrupt transmission (i.e., herd immunity). Determining the optimal testing approach to differentiate natural infection from vaccination and developing other laboratory tools are essential to support the development and monitoring of COVID-19 vaccines.

CDC is continuing its work with the U.S. Food and Drug Administration and the National Institutes of Health to validate tests produced by commercial labs and other entities.

Objective 3. Utilize viral genomics to advance understanding of COVID-19 and mitigate its impact

CDC is using genomic sequencing to investigate the evolution, emergence, and spread of COVID-19 infections in communities and defined populations. Incorporation of viral genomic data with patient genomic, clinical, and epidemiologic data can lead to a better understanding of patient risk factors, clinical outcomes, and transmission dynamics. CDC, through its establishment of a new national viral genomics consortium,[3] is accelerating the release of SARS-CoV-2 sequence data into the public domain.

Large-scale sequencing studies to monitor the genetic diversity and stability of SARS-CoV-2 have the potential to offer clues on the impact of new virus variants on diagnostics, therapeutic agents, and vaccines.

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

Mathematical modeling is an important tool to help inform public health decision making. CDC, working with academic groups, uses probabilistic models to forecast the timing and trajectory of COVID-19 infections; the demand for hospital-based services; and deaths at the national, state, and sub-state levels. Models to forecast the impact of therapeutics, testing, vaccine, and mitigation strategies are also a priority.

Novel technological tools such as cell phone mobility data, for example, when used in combination with social, behavioral, and ethnographic information, offer the potential to assess the impact of community mitigation efforts, but require a thorough assessment of their practical utility.

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

The COVID-19 pandemic is affecting people's healthcare seeking behaviors for routine preventive and medical care. CDC is working with domestic and international clinical and public health partners to assess pandemic-related impacts on healthcare, special-needs care, routine public health activities, and priority disease elimination/control programs such as HIV, tuberculosis (TB), and neglected tropical diseases. Findings from these studies can be used to identify the best strategies and policies to maintain access to care, treatment, and preventive services with a focus on populations at increased risk for health disparities and inequities.

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

SARS-CoV-2 spreads easily and sustainably between people who are in close contact with one another. CDC is working with health departments and other domestic and international partners to support and conduct carefully planned and executed laboratory and epidemiologic studies to discern:

- the relative role of respiratory droplets versus aerosols
- the infectious dose of SARS-coV-2 by inhalation
- the role of non-respiratory routes of transmission, such as fecal-oral or blood
- the potential for spread through contact with contaminated surfaces and fomites
- the occurrence and risk factors for perinatal transmission

Objective 2. Identify host and virus factors associated with person-to-person transmission

CDC conducts and supports work to characterize the transmissibility of SARS-CoV-2 through all stages of disease; establish the relationship between viral burden and infectiousness; and identify host factors that contribute to higher viral load and prolonged virus shedding. Although transmission of SARS-CoV-2 from people who are asymptomatic has been well documented, clarifying the relative incidence of asymptomatic compared to symptomatic transmission of SARS-CoV-2 can help inform public health interventions to limit spread in workplaces and the community.

Objective 3. Assess and characterize transmission of SARS-CoV-2 across a spectrum of healthcare settings

CDC is working with public health and other partners to build on early epidemiologic and laboratory investigations, such as those in long term care facilities (LTCF), and advance a more nuanced understanding of risk and protective factors for transmission of SARS-CoV-2 among healthcare personnel (HCP) and patients in a wide array of healthcare environments, such as ambulatory care and first response settings. Comprehensive assessments of healthcare-associated transmission risks are essential to inform development and updating of tailored infection control guidance.

Objective 4. Evaluate transmission of SARS-CoV-2 in non-healthcare workplace and community settings/populations

Learning in real time where and how people are becoming infected with SARS-CoV-2 is essential to limiting spread of the virus through more targeted application of containment and mitigation measures. CDC conducts epidemiologic and laboratory investigations in collaboration with many partners to identify risk factors, refine estimates of epidemiologic parameters of transmission, and better understand the dynamics of SARS-CoV-2 transmission in settings and populations such as:

- workplaces, including critical infrastructure operations, with varying levels of worker density and interactions
- schools and universities
- households and other congregate living settings such as dormitories, correctional institutions, and shelters
- event and community gatherings
- conveyances
- children and adolescents
- other select populations, including persons at increased risk for health disparities and inequities
- superspreading events

These studies can help identify networks of transmission and provide insight into the interplay between workplace and community settings and the role of international, interstate, and intrastate travel in introducing and propagating community transmission.

Objective 5. Evaluate transmission of SARS-CoV-2 between people and animals

CDC works with the United States Department of Agriculture and state public health and animal health officials to evaluate SARS-CoV-2 infection in animals and assess if and how transmission occurs between people and animals in close contact with people, such as companion and farmed animals and wildlife. Investigations to evaluate transmission of SARS-CoV-2 between people and animals, including the potential establishment of new animal hosts and reservoirs through One Health response and collaborations with partners are essential to understanding how and why such spillover events occur and how they can be prevented.

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

CDC is working with clinical investigators, laboratorians, and pathologists to characterize complications associated with acute CoV-19 infection and assess any long-term sequelae. Investigation of multi-system inflammatory syndrome in children [MIS-C], for example, is one high priority focus. Identifying host, environmental, and viral factors that affect susceptibility to SARS-CoV-2 infection, illness severity, and outcome can lead to measures that reduce infection risk and temper the clinical course of infection. Ongoing research is seeking to clarify if, and to what extent, viral re-infection, viral reactivation, or persistent infection occurs and the role, if any, that repeated exposures to SARS-CoV-2 influence attack rates, disease course, and the potential for re-infection.

Objective 2. Characterize the immune response in infected persons

CDC, along with federal and academic partners, assesses humoral and cellular correlates of immune protection against SARS-CoV-2. Ongoing epidemiologic and laboratory studies will help determine the strength and time course of immunity and evaluate if host factors such as age, severity of disease, and immunocompromising conditions may be associated with differences in the immune response to natural infection and vaccines.

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

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

CDC is focused on the urgent need to develop and devise effective new methods to test:

- innovative personal protective equipment (PPE) that is reusable, long lasting, and more comfortable to wear, especially for extended periods of time and under a variety of conditions
- methods for decontamination/disinfection of PPE across a range of workplace settings which are effective but do not affect PPE performance
- the effectiveness of respiratory protection and other PPE to reduce transmission of SARS-CoV-2 in healthcare and non-healthcare work environments

CDC is examining the possible risks to patients, HCP and non-healthcare workers posed by shortages of PPE and the need to implement PPE optimization strategies, as well as the impacts of postponing elective surgery to conserve PPE supplies.

“Source control,” i.e., having patients, family members, and visitors wear a cloth face covering or facemask to contain their respiratory secretions, is theorized to reduce the risk of transmission of SARS-CoV-2 from symptomatic and asymptomatic people. CDC is supporting studies to evaluate the effectiveness of this practice and refine current recommendations as needed.

Objective 2. Assess strategies to reduce transmission of SARS-CoV-2 in healthcare and non-healthcare work settings

In addition to improvements in PPE, CDC is conducting and supporting study and evaluation of an array of control measures to maximize patient and worker safety and mitigate transmission of SARS-CoV-2 in the workplace such as:

- active engineering controls to reduce workers’ exposure to SARS-CoV-2
- translation of passive engineering controls (e.g., high ventilation rates, air filtration, directional airflow) used in healthcare environments into non-healthcare work settings
- effective disinfection/decontamination methods for reusable hospital/workplace

equipment

- administrative control strategies such as cohorting of patients and workers and modified work schedules to reduce worker density
- the utility of symptom monitoring and SARS-CoV-2 testing to facilitate rapid detection of infection and transmission among patients (e.g., LTCFs) and among healthcare and non-healthcare workers
- new tools (e.g., apps, sensors, or other novel biologic devices) to monitor exposures, symptoms, and COVID-19 infections in HCP and other workers

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

CDC supports innovative evaluation of the effectiveness of different strategies to limit transmission of SARS-CoV-2 with a particular focus on areas such as:

- masks and cloth face coverings, both as source control and protection, alone or in combination with other measures
- personal protective measures[4]
- community-wide mitigation measures and the impact of lifting them
- screening strategies to detect infected people including the use of new technologies for remote temperature measurement alone or in combination with other approaches such as visual assessments and questionnaires

Objective 2. Evaluate strategies to limit infection with SARS-CoV-2 in specialized settings or select populations

CDC is working with public health and other partners to build, broaden, and strengthen the evidence base for the use and effectiveness of mask/face coverings, personal protective measures, and the innovative application of engineering and administrative controls in specialized settings, such as congregate living settings; schools and

universities; conveyances; and event and community gatherings. Developing evidence-based approaches for preventing COVID-19 among populations at increased risk for health disparities and inequities and for people without ready access to respiratory and hand hygiene materials is a particular focus.

Objective 3. Develop methods to detect SARS-CoV-2 in the environment

CDC is engaged in activities to learn what role contaminated surfaces and equipment may play in transmission of SARS-CoV-2. Examples of areas of investigation include:

- optimizing environmental sampling and detection methodologies for viable SARS-CoV-2
- measuring the aerosol and environmental surface stability and viability of SARS-CoV-2 under varying environmental conditions
- assessing the potential contribution of building heating, ventilation, and air conditioning (HVAC) systems and equipment in the dissemination of viable SARS-CoV-2

Objective 4. Identify the most effective methods for contact tracing, testing, and monitoring

Tracing, testing, and monitoring contacts of persons with COVID-19 is a key strategy to limit the spread of SARS-CoV-2. The pandemic has called into focus a number of areas that require careful evaluation to optimize operational efficiency and outcome metrics for these activities such as:

- the utility (e.g., yield/effectiveness, staffing, and fiscal resources) of contact tracing at varying incidence rates of COVID-19 in a community/population
- the utility of different methods to identify, inform, and test contacts, including hard-to-reach populations and those at increased risk for health disparities and inequities
- the acceptability and utility of novel approaches such as digital tracing tools and technology to identify and monitor contacts' compliance with quarantine
- understanding attitudes about and barriers to contact tracing

Objective 5. Evaluate travel-related interventions

CDC, with the support of state and local health departments, examines the utility and limitations of travel-related interventions, such as entry restrictions, enhanced entry screening, and risk-based public health follow-up, to limit the spread of SARS-CoV-2 in the United States. Findings from these analyses can help drive development of innovative, efficient, and high-yield travel screening protocols to mitigate the importation and spread of infectious diseases related to domestic and international travel.

Objective 6. Optimize the acceptability, coverage, safety, and effectiveness of COVID-19 vaccines

An effective vaccine against SARS-CoV-2 is an essential tool to reduce the burden of COVID-19-associated illness, hospitalization, and death. CDC is actively engaged with a wide array of partners to:

- assess the acceptability of COVID-19 vaccines, especially among racial and ethnic minority populations and other high priority groups
- identify the best approaches for ensuring optimal coverage of COVID-19 vaccines across a range of populations and age groups, including hard-to-reach populations and those at increased risk for health disparities and inequities
- devise and implement enhanced safety monitoring capabilities, with particular focus on anticipated early recipients
- identify and evaluate technologic tools and innovative methods to more efficiently monitor vaccine receipt and safety
- estimate the safety, coverage, and effectiveness of COVID-19 vaccines across a range of available vaccines, populations, and outcomes

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

Targeted research to address gaps in knowledge about what sources of information different audiences, including people at increased risk for health disparities and inequities, consider trustworthy and how they prefer to receive information (e.g., social media, community-level communications) is an essential pre-requisite to effective messaging about COVID-19.

Objective 2. Optimize uptake of recommended behaviors and actions

CDC and others investigate the health beliefs shaped by messaging as well as the relationship between misinformation and adoption of risk or protective behaviors/recommended actions across a range of audiences. Findings can improve understanding of the role of misinformation in the communication environment and when and how CDC should respond to it. Social, economic, and behavioral factors also play a key role in adoption of recommended personal protective behaviors and community mitigation measures and require study.

Objective 3. Enhance CDC communication products and information tools

It is important for CDC to understand the reach, comprehension, acceptability and impact of its on-line materials and guidance. Only then can innovative and robust approaches be constructed to rapidly and effectively engage with different audiences, including people without access to internet services or disproportionately impacted by health disparities and inequities.

Communications research to test priority messages and products with intended audiences can assess if messages are clear, understandable, and help facilitate adoption of protective behaviors and actions.

Objective 4. Assess the social and mental health impacts of the pandemic

The social, behavioral, and mental health impacts of the COVID-19 pandemic need to be examined across a range of populations, age groups, and settings. Equally important is assessing community function and resilience throughout the pandemic period including the transition and recovery phases. Findings from such studies can assist in formulating more targeted advice and interventions to build resilience and improve mental health and well-being among vulnerable groups.

Priority Science Questions

As the evidence base and public health response to the COVID-19 pandemic continues to evolve, the routine identification and dissemination of priority science questions as part of *The CDC Science Agenda* can promote CDC's and public health partners' efforts to fill critical, time-sensitive scientific gaps to inform evidence-based decision making. During February–March 2021, the CDC COVID-19 Response's Strategic Science Unit (SSU)

systematically collected input from multiple entities across the Response. As a result of this process, 19 priority science questions emerged across six topic areas. The SSU aims to update these questions approximately every 3–4 months.

These science questions relate to the broad scope of CDC's scientific work, including surveillance, research, implementation science, and evaluation. Importantly, these questions also serve to expand the evidence base to accelerate progress toward reducing COVID-19 disparities and achieving health equity. In designing studies and analyses to address these questions, a population and place-based framework should be applied alongside the following principles: using data-driven approaches to identify contributing factors to reduce health disparities; fostering meaningful engagement with community institutions, organizations, and diverse leaders; leading culturally and linguistically responsive outreach; and reducing COVID-19-associated stigma associated with race and ethnicity and implicit bias.

Topics and Questions

(updated as of March 2021, listed in no particular order)

Variants

1. How do we effectively conduct surveillance of SARS-CoV-2 variants?
    - What are the standard case definitions and criteria for surveillance of SARS-CoV-2 variants, including variants of concern?
    - What are the key demographic variables needed as part of surveillance of SARS-CoV-2 variants, and how do we effectively integrate demographic data into molecular surveillance efforts?
    - What is the current prevalence and incidence of a given SARS-CoV-2 variant of concern overall and in various populations and settings?
    - What proportion or number of cases need to be sequenced to be reasonably certain that we are detecting, and can react to, changing SARS-CoV-2 variant prevalence across time and geography?
    - How do we enhance state and local capacity to address SARS-CoV-2 variants of concern, particularly among populations disproportionately affected by COVID-19?

2. How do SARS-CoV-2 variants affect diagnostics, therapeutics, vaccine effectiveness, clinical and public health outcomes, and transmissibility of the virus in various populations and settings?
    - How are prevention strategies, non-pharmaceutical interventions, healthcare and public health resource capacity, case investigations/contact tracing, and public health recommendations affected by SARS-CoV-2 variants?
    - How does the public's understanding of SARS-CoV-2 variants affect adherence to recommended prevention strategies and vaccine uptake?

Prevention strategies and non-pharmaceutical interventions

3. How do we effectively increase implementation and compliance with prevention strategies in various populations and settings, including congregate and critical infrastructure settings (e.g., K-12 schools, institutions of higher education, healthcare facilities, high-density worksites, long-term care facilities, group homes, prisons, homeless shelters, food industry, transportation)?
    - What policies and practices increase implementation of, and compliance with, school strategies?
    - How do we best measure compliance with prevention strategies such as mask wearing?
    - What are effective strategies to reduce barriers to the implementation of, and compliance with, prevention strategies, particularly among populations disproportionately affected by COVID-19?
    - How do vaccine availability and recommended non-pharmaceutical interventions affect people's willingness to take any of these prevention steps?
    - What are the best ways to communicate and frame messages around prevention strategies for various populations and settings?

4. How should prevention strategies and non-pharmaceutical interventions in various populations and settings be adjusted based on setting, rates of vaccination, community transmission, and variant prevalence?

5. What is the effectiveness and impact of implementing engineering controls for COVID-19 (e.g., high ventilation rates, air filtration, directional airflow, ultraviolet germicidal irradiation), and the new ASTM International Barrier Face Covering Standard on SARS-CoV-2 transmission in non-healthcare settings?

Vaccines

6. What is the impact of vaccine coverage rates on SARS-CoV-2 transmission, hospitalization, and death in various populations and settings?
    - How will vaccine uptake and the corresponding impact, including presumed decreases in hospitalization and death, affect future vaccine acceptance and prevention measures?

7. What is vaccine effectiveness and duration of protection afforded by vaccines against symptomatic disease and SARS-CoV-2 infection in various populations and settings?

8. What interventions, program decisions, and communication approaches are most effective at increasing equitable vaccination coverage, with a focus on vaccine access and vaccine confidence, among various populations and settings?
    - What strategies can increase equitable vaccine distribution and administration, particularly among populations disproportionately affected by COVID-19?
    - How can we identify settings or geographic locations where strategies should be

implemented to increase equitable vaccine access?

- How do socio-economic and other social factors and determinants (e.g., internet access, physical accessibility) affect vaccine access?
- How are program and operational decisions affecting vaccine access and vaccine confidence?
- How effective are current vaccine communication frames in various populations and settings, including populations disproportionately affected by COVID-19?

9. What is the risk for adverse events associated with COVID-19 vaccines, particularly among key sub-populations, including pregnant people, the elderly, and people with underlying medical conditions?

Testing

10. How do we effectively increase equitable access to testing for SARS-CoV-2 and testing rates among various populations and settings, including congregate and critical infrastructure settings (e.g., K-12 schools, institutions of higher education, healthcare facilities, high-density worksites, long-term care facilities, group homes, prisons, homeless shelters, food industry, transportation)?
    - What strategies can increase equitable distribution of testing services or platforms for SARS-CoV-2, particularly among populations disproportionately affected by COVID-19?
    - How can we identify settings or geographic locations where strategies should be implemented to increase equitable access to testing for SARS-CoV-2?
    - How do communication strategies for vaccine rollout affect attitudes and desire for testing among various populations?

11. How effective are serial testing strategies at the community level and in specific settings on reducing outbreaks, disease burden, and detecting potential surges in cases?
    - What is the cost-effectiveness and cost-benefit of serial testing strategies? And at what level of disease burden and vaccination coverage are serial testing strategies most useful?
    - Can serial testing strategies with antigen tests overcome limitations associated with decreased sensitivity compared with nucleic-acid amplification tests?

12. How do at-home testing and other new testing platforms for SARS-CoV-2 perform relative to currently approved or recommended tests in the detection of symptomatic and asymptomatic individuals, and in the presence of variants?
    - What is the receptivity to using at-home tests, and what are the barriers to use in various populations and settings?

Natural history, reinfection, health impact

13. How do we effectively conduct surveillance of SARS-CoV-2 reinfection?
    - What is the standard surveillance case definition and nomenclature for SARS-CoV-2 reinfection?
    - What is the prevalence and incidence of SARS-CoV-2 reinfection overall and in various populations and settings?
    - How does SARS-CoV-2 testing guidance affect reported rates of reinfection and estimates of true incidence?
    - What are the risk factors for SARS-CoV-2 reinfection in various populations and settings?
    - Is severe illness and/or death more or less common with SARS-CoV-2 reinfection? What are the risk factors associated with severe illness and/or death from reinfection?
    - How do underlying chronic medical conditions influence SARS-CoV-2 reinfection potential, particularly among populations disproportionately affected by COVID-19?
    - Is there geographical or temporal variation in SARS-CoV-2 reinfection?

14. How do we effectively conduct surveillance for post COVID-19 conditions?
    - What are the standard case definitions for the various post-acute versus long-term phases of COVID-19?
    - What are the prevalence and incidence of the various post-COVID-19 conditions overall and in various populations and settings?
    - With what frequency does SARS-CoV-2 infection or reinfection lead to late sequelae, particularly among populations disproportionately affected by COVID-19?
    - How do we assess disease burden among various populations, factoring in variations in access to healthcare and healthcare seeking behaviors?
    - What is the effect of ongoing media coverage of post COVID-19 health conditions on attitudes and prevention behaviors?

15. How do environmental factors (e.g., chemical and heavy metal exposures, air pollution, water quality, and the built environment) and physiological responses to those factors contribute to COVID-19 outcomes, particularly among populations disproportionately affected by COVID-19?

16. What are the correlates of protection from SARS-CoV-2 infection and how do we measure this (e.g., neutralizing antibodies, binding antibodies, memory B-cells, T-cell immunity)?
    - What are the diagnostic capabilities to discriminate between natural, vaccine-mediated, and variant immunity?
    - What factors impact SARS-CoV-2 immunity duration?

Transmission risk, dynamics

17. What role do fully vaccinated and previously infected individuals play in the transmission of SARS-CoV-2 and its variants?

18. How do we effectively detect asymptomatic transmission of SARS-CoV-2 in the community?
    - What is the impact and cost-effectiveness of various strategies to detect asymptomatic SARS-CoV-2 infection on community transmission?

19. What disease indicators and other factors best inform SARS-CoV-2 transmission dynamics and predict surges of community-level infection?

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.
3. See https://www.cdc.gov/coronavirus/2019-ncov/covid-data/spheres.html.
4. Personal protective measures include hand and respiratory hygiene, social distancing, surface disinfection.

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Content source: National Center for Immunization and Respiratory Diseases (NCIRD), Division of Viral Diseases