COVID-19

CDC Public Health Science Agenda for COVID-19

Building the Evidence Base for Ongoing COVID-19 Response

Updated Jan. 5, 2022

Priority COVID–19 Public Health Science Questions

As the public health response to the COVID-19 pandemic continues to evolve, routine identification and dissemination of priority COVID-19 public health science questions can promote efforts by the Centers for Disease Control and Prevention (CDC) and public health partners to fill critical scientific gaps and inform evidence-based decision-making through public health surveillance and epidemiologic research. The priority questions outline the critical scientific gaps identified by the CDC COVID-19 Response, CDC programs, and other public health partners that, if addressed, could provide significant, timely, and measurable improvements in public health outcomes.

The CDC COVID-19 Response Strategic Science Unit (SSU) systematically collects input from multiple entities across the CDC Response and from external public health partners to identify and update these questions as part of the CDC Public Health Science Agenda for COVID-19. These questions have been updated approximately every 4 months since April 2021 to ensure their timeliness, relevance, actionability, and impact. To address these questions, CDC authors have published over 1,000 scientific articles, indexed by priority topic here: COVID-19 CDC Publications Database. This update presents input gathered during October–December 2021, and spans **7** topic areas:

Health equity

Vaccines

Variants

Prevention strategies

Testing

Natural history, transmission, breakthrough infections, and reinfections

Within these topic areas, **14** 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 (e.g., other government agencies, academics, the private sector). Other relevant questions are found in the complementary science agendas of other federal agencies, including National Institutes of Health (NIH) and Environmental Protection Agency (EPA)

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Post-COVID conditions and other health impacts

Importantly, these questions also serve to expand the evidence base to accelerate progress toward reducing COVID-19 disparities and achieving health equity (CDC COVID-19 Response Health Equity Strategy). A health equity priority question was added in December 2021 to address health equity research gaps that do not necessarily fall within the other priority questions; however, health equity science remains a fundamental consideration to all priority questions, and therefore there is some overlap in health equity science activities across questions.

Key activities: 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
- Understanding trends in disparities in COVID-19 illnesses, hospitalizations, deaths, post-COVID conditions, and orphanhood, including by age group, sex, race, ethnicity, social class, underlying medical conditions, and place of residence, to identify opportunities for additional intervention
- Measuring progress toward equitable vaccination availability and coverage, including by race, ethnicity, social class, and place of residence
- Evaluating differences in timeliness, effectiveness, and efficiency of COVID-19 vaccination programs in communities of varying demographic composition, socioeconomic status, geographic location, policy environment, and population size to identify opportunities for improvement
- Evaluating which initiatives and policies (e.g., to incentivize or mandate COVID-19 vaccination) have measurably improved vaccination equity and coverage
- Measuring and addressing differences in adherence to community and workplace COVID-19 prevention strategies, such as vaccination (including drivers of vaccine hesitancy and perceptions about vaccine adverse events), by age group, gender, race, ethnicity, social class, underlying medical conditions, and place of residence
- Characterizing and reducing barriers to vaccination among persons reporting intent to vaccinate but who have not yet been vaccinated
- Characterizing outpatient and inpatient treatment of severe COVID-19 in various populations, including by age group, sex, race, ethnicity, social class, place of residence, and insurance status
- Measuring and addressing disparities in COVID-19–associated second-order consequences in children, for example, orphanhood or caregiver death, poverty, food insecurity, violence, adverse childhood experiences, mental health threats, and educational disruptions

Vaccines

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

Key activities
- Measuring differences in vaccine effectiveness in various populations and settings, including by age group, underlying medical condition, and product type
- Measuring impacts of pediatric vaccination on SARS-CoV-2 transmission and disease burden

- Developing recommendations for timing, periodicity, and administration of primary series and booster vaccine doses for various populations: *children, elderly, immunocompromised persons, pregnant or breastfeeding persons, nursing home residents, healthcare personnel, frontline workers, and other persons disproportionately affected by COVID-19*
- Measuring vaccine effectiveness with mixed vaccine products or extended intervals between doses
- Evaluating vaccine effectiveness, sequence, and timing among persons who were previously infected with SARS-CoV-2
- Evaluating effectiveness of primary series and booster vaccines against post-COVID conditions
- Measuring impacts of vaccine coverage on SARS-CoV-2 infections, hospitalizations, deaths, and orphanhood among persons disproportionately affected by COVID-19
- Characterizing threshold levels for vaccine effectiveness against illness, hospitalization, and death to determine whether vaccination recommendations may need to be updated in the future for new variants
- Understanding how primary series and booster vaccine coverage, domestically and globally, might affect dispersion of SARS-CoV-2 through travel
- Conducting modeling studies: *how many hospitalizations and deaths have vaccines averted, how many deaths could have been averted had vaccination coverage been higher, cost-effectiveness of vaccination in the United States, impact of vaccination of parents and school personnel on protecting children too young to receive COVID-19 vaccine*
- Analyzing data on health communications for COVID-19 vaccines to improve communication strategies

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

Key activities
- Evaluating strategies to build trust in CDC recommendations for use of COVID-19 vaccines
- Understanding socioeconomic and other social determinants that could affect vaccination: *identifying and engaging diverse populations with high levels of vaccine hesitancy, prioritizing geographic locations with inequitable access, developing effective solutions to overcoming barriers to access, building capacity for state and local health departments and community- and faith-based organizations to address social and behavioral drivers of vaccine demand/uptake, vaccination in private settings versus mass vaccination events*
- Evaluating differences in timeliness, effectiveness, and efficiency of COVID-19 vaccination programs in communities of varying demographic composition, socioeconomic status, geographic location, and population size to identify opportunities for improvement
- Characterizing intended and unintended impacts of vaccine mandates and policies that ban vaccine mandates
- Addressing vaccine hesitancy among pregnant persons, parents/guardians of minor children, and adolescents
- Identifying industries and workplace types associated with low vaccination uptake
- Evaluating strategies to effectively counter vaccine misinformation and disinformation
- Tracking and responding to changes in vaccine-related questions, concerns, and reports about adverse events over time, particularly for pediatric vaccination
- Addressing barriers to ensure vaccine providers check Immunization Information Systems (IIS) prior to vaccination to reduce vaccine administration errors

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

Key activities
- Assessing potential risks and benefits in various populations, including pregnant persons, children, adolescents and young adults, the elderly, people with underlying medical conditions, immunocompromised persons, and

persons disproportionately affected by COVID-19

- 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 impact of COVID-19 vaccination on routine and seasonal vaccinations

Variants

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

Key activities
- Measuring prevalence and incidence of variants of concern in various populations and settings, including among the origins and destinations of travelers to the United States and among immunocompromised persons
- Tracking evolution of new variants, particularly in immunocompromised populations
- Increasing timeliness and accuracy of regional estimates of variant proportions in circulation in the United States and globally
- Determining the optimal level of timeliness and accuracy of genomic surveillance needed to effectively detect and track variants
- Improving data quality: *enhancing genomic surveillance, increasing social and demographic data completeness, integrating travel history, ensuring a representative sample of specimens*
- Effectively communicating health information about variants to the public
- Characterizing the effect of changing SARS-CoV-2 nomenclature on the grouping of variants, and how it impacts prevention strategies based on variant circulation
- Exploring wastewater surveillance, including for persons living in congregate settings and other populations at risk for COVID-19

6. How do SARS-CoV-2 variants affect diagnostics, vaccine effectiveness, clinical outcomes, transmissibility, and public health interventions? ⌃

Key activities
- Ensuring diagnostic methods remain robust for the changing genetic landscape of SARS-CoV-2, including rapid evaluation of diagnostics for sensitivity of detecting new variants
- Measuring changes in effectiveness of COVID-19 vaccines and other public health interventions against SARS-CoV-2 variants in various populations and settings
- Measuring differences in transmissibility of SARS-CoV-2 variants in various populations and settings, by vaccination status
- Understanding changes in adherence to recommended prevention strategies and vaccine uptake related to the public's understanding of variants
- Developing strategies to rapidly inform public health action as circulation of variants changes
- Characterizing clinical impact of variants in pediatric and adult populations
- Tracking changes in tissue tropism/receptor binding in relation to clinical presentations and outcomes

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, including schools and workplaces, particularly where vaccination coverage is low?

Key activities
- Developing and communicating evidence-based health recommendations and information on COVID-19 prevention
- Evaluating levels and types of personal protective equipment (PPE), including masks, and engineering controls (e.g., ventilation, air flow, and building design considerations) indicated in various occupational and other settings
- Reducing barriers to implementation of effective prevention strategies, including in communities, schools, and workplaces
- Evaluating effectiveness of prevention strategies, including contact tracing, 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 COVID-19 hospitalizations and deaths, including by age group, sex, race, ethnicity, social class, underlying medical conditions, and place of residence
- Measuring differences in implementation, acceptability, and uptake of non-pharmaceutical interventions and other prevention strategies by social, demographic, geographic, cultural, and environmental factors
- Understanding which prevention strategies and non-pharmaceutical interventions have been effective in other countries in various settings and populations

8. When should SARS-CoV-2 prevention strategies and non-pharmaceutical interventions in various populations and settings be adjusted, for example based on vaccination coverage, variant prevalence, community transmission, or transitioning into an endemic disease control phase?

Key activities
- Developing indicator thresholds to guide public health actions, such as implementing or relaxing prevention strategies including non-pharmaceutical interventions
- Evaluating whether geography-based data indices on social determinants of health, such as the Social Vulnerability Index and Area Deprivation Index, can inform decisions about implementing or relaxing prevention strategies to reduce health disparities
- Measuring community-level economic impacts of prevention strategies and non-pharmaceutical interventions
- Evaluating travel-related interventions for domestic and international travel

Testing

9. How effective are at-home/self-testing, rapid diagnostic testing, point-of-care testing, routine screening, and serial testing strategies on reducing outbreaks, reducing disease burden, detecting potential surges, evaluating criteria for reopening, and detecting re-introduction of SARS-CoV-2 into low transmission settings?

Key activities

- Addressing needs for expanded testing, and adopting approaches to increasing testing capacity domestically and globally
- Evaluating and communicating appropriate recommendations for quarantine and isolation for individuals and households
- Measuring whether barriers to testing access might delay diagnosis of COVID-19, including by age, sex, race, ethnicity, social class, or place of residence
- Evaluating effective strategies to increase equitable access to testing, including for populations disproportionately affected by COVID-19
- Evaluating cost-effectiveness of testing strategies
- Determining testing recommendations based on vaccination status or change in variants
- Evaluating how prior infection, vaccination, and booster doses affect test performance characteristics for authorized tests
- Evaluating household testing strategies to protect household members at varying levels of risk for severe COVID-19 (e.g., multigenerational households)
- Determining community conditions for routine screening
- Evaluating community acceptability of different testing strategies
- Evaluating self-testing: *accuracy and reliability for detecting symptomatic and asymptomatic infection among vaccinated and unvaccinated persons, receptivity in various social and demographic populations, adequacy of training, integration into public health reporting systems, use in specific settings (e.g., schools, homeless shelters, correctional facilities), effectiveness in reducing or preventing SARS-CoV-2 transmission, utilization in populations disproportionately affected by COVID-19, validation of results tied to a specific person, acceptability and feasibility for use as risk mitigation or harm reduction measures over diagnostic tests*
- Improving collection of demographic and epidemiologic data associated with testing data
- Evaluating testing guidance for international travelers, particularly for persons traveling from areas where emerging variants are prevalent

Natural history, transmission, breakthrough infections, and reinfections

10. 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: *the role of prior immunity (infection or vaccine-mediated), the proportion of different variants, among immunocompromised persons, in various settings (e.g., occupational, educational, congregate living), the occurrence of and risk factors for severe illness or death*
- Improving data completeness for demographic and social determinants of health variables, and methods for handling missing data
- Understanding whether the ability to classify newly reported infections as a reinfection differs across racial and ethnic groups or other demographic characteristics based on data quality and completeness or other factors
- Evaluating impact of testing guidance on reinfection reporting
- Characterizing risk factors for reinfection in various populations and settings, including by age group, sex, race, ethnicity, social class, and place of residence
- Characterizing risk factors for breakthrough infections among vaccinated children
- Characterizing risk factors for severe illness with breakthrough infections

- Evaluating to what extent breakthrough infections contribute to further SARS-CoV-2 transmission and whether this differs by variant
- Conducting genomic sequencing to identify infections with SARS-CoV-2 variants among immunocompromised persons
- Measuring adverse pregnancy and birth outcomes with SARS-CoV-2 infection

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

Key activities
- Characterizing seasonality and impact of other respiratory viruses on SARS-CoV-2 transmission, domestically and globally
- Evaluating policies and adherence levels to effective interventions (e.g., masking, ventilation, distancing, and other effective interventions)
- Evaluating impact of domestic and international travel policies on SARS-CoV-2 transmission
- 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 in endemicity for human populations

12. What are reliable immune correlates of protection from SARS-CoV-2 infection and accurate ways to measure this? ⌃

Key activities
- Expanding diagnostic capabilities to distinguish infection versus vaccine-mediated immunity
- Measuring differences in strength and duration of protection afforded by infection versus vaccine-mediated immunity, and by both (prior infection and subsequent vaccination)
- Characterizing factors impacting duration of immunity
- Assessing waning immunity and potential need for vaccine boosters
- Assessing immunity to variants or anticipating breakthrough infection by specific variants
- Measuring variation of serological correlates by demographic and clinical characteristics
- Determining whether post-infection immunity should be linked to CDC testing guidance
- Evaluating measures for population-level immunity, including changes over time due to waning immunity and other factors

Post-COVID conditions and other health impacts

13. 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 relation to health equity measures
- Characterizing risk factors: *SARS-CoV-2 infection or reinfection characteristics, underlying biological mechanisms, variants*
- Assessing prevention measures for post-COVID conditions, including COVID-19 vaccination
- Assessing potential health and economic impacts of post-COVID conditions (e.g., inability to work)

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14. 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
- Implementing workplace policies and practices to improve worker resilience and reduce adverse mental health effects of the COVID-19 pandemic
- Measuring changes to other health epidemics and diseases impacted by the COVID-19 pandemic, including increases in drug-related overdoses, obesity, diabetes, STIs, and decreases in vaccination coverage beyond COVID-19, and developing evidence-based health communications and interventions to address these changes
- Measuring prevalence and incidence of COVID-19–associated second-order consequences among children, including orphanhood and caregiver death, poverty, food insecurity, violence, adverse childhood experiences, mental health threats, and educational impacts
- Understanding how the effect of the pandemic on income, housing, employment, caregiving, childcare, and other factors have exacerbated health inequities in non-COVID conditions
- Evaluating health and economic impacts to workers and families from changes in employment status related to the COVID-19 pandemic

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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

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- **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 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