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REopening Archives, Libraries, and Museums

Briefing: Vaccines, Variants, and Ventilation

A Briefing on Recent Scientific Literature Focused on SARS-CoV-2 Vaccines and Variants, Plus the Effects of Ventilation on Virus Spread

Dates of Search: 01 January 2021 through 14 June 2021

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This document synthesizes various studies and data; however, the scientific understanding regarding COVID-19 is continuously evolving. This material is being provided for informational purposes only, and readers are encouraged to review federal, state, tribal, territorial, and local guidance. The authors, sponsors, and researchers are not liable for any damages resulting from use, misuse, or reliance upon this information, or any errors or omissions herein.

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INTRODUCTION

Purpose of This Briefing

- Access to the latest scientific research is critical as libraries, archives, and museums (LAMs) work to sustain modified operations during the continuing severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic.
- As an emerging event, the SARS-CoV-2 pandemic continually presents new challenges and scientific questions. At present, **SARS-CoV-2 vaccines and variants in the US** are two critical areas of focus. The effects of **ventilation-based interventions on the spread of SARS-CoV-2** are also an interest area for LAMs. This briefing provides key information and results from the latest scientific literature to help inform LAMs making decisions related to these topics.

How to Use This Briefing: This briefing is intended to provide timely information about SARS-CoV-2 vaccines, variants, and ventilation to LAMs and their stakeholders. Due to the evolving nature of scientific research on these topics, the information provided here is not intended to be comprehensive or final. As such, this briefing should be used in conjunction with other timely resources to ensure decision-making reflects the latest scientific understanding. Continual re-evaluation of SARS-CoV-2 policies is highly recommended as new scientific discoveries are published.

About This Briefing

- Battelle conducted a systematic search of scientific literature about SARS-CoV-2 vaccines, variants, and ventilation. This briefing summarizes those findings.
- Research questions:
    1. What implications does SARS-CoV-2 vaccination in the US have for public health interventions and policies, especially related to indoor environments?
    2. How do SARS-CoV-2 variants currently circulating in the US differ from the original strain in terms of spread, transmissibility, surface attenuation, and effectiveness of public health interventions?
    3. What effects do ventilation and ventilation-based interventions (e.g., heating, ventilation, and air conditioning systems (HVAC)) have on the spread of SARS-CoV-2 in indoor environments?
- Dates of search: 01 January 2021 to 14 June 2021. Newest items labeled "[New]"
- Additional information about the methods used to conduct the literature search and create this briefing is included later in the document.

About REALM

REopening Archives, Libraries, and Museums (REALM) is a research project conducted by OCLC, the Institute of Museum and Library Services (IMLS), and Battelle to produce and distribute science-based COVID-19 information that can aid local decision-making regarding operations of archives, libraries, and museums.

View reports published by REALM.

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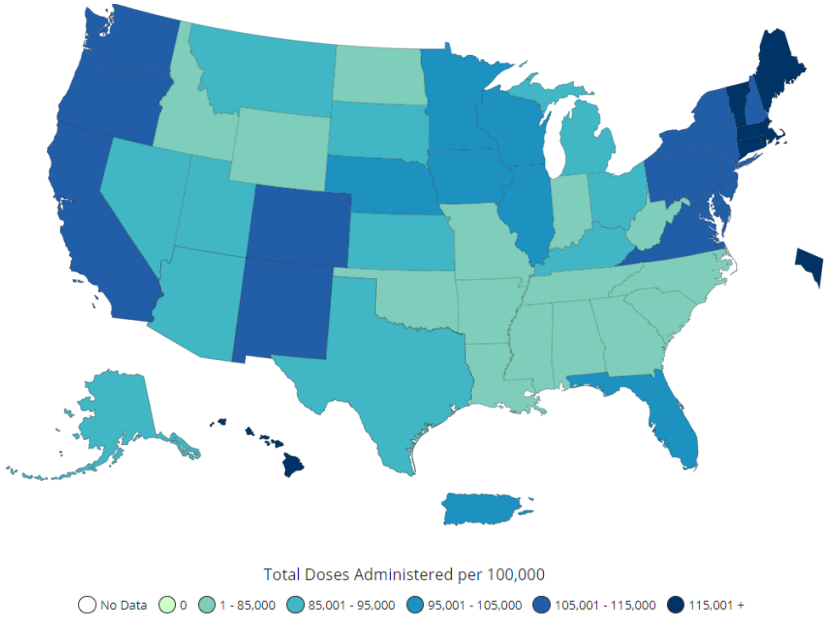
BACKGROUND INFORMATION: VACCINES AND VARIANTS

SARS-CoV-2 Vaccines

- Vaccination efforts in the US are underway.
- The CDC reports updated vaccination numbers daily on a COVID-19 data tracker.[1]
- Three safe and effective vaccines are distributed under the US FDA Emergency Use Authorization:[2]
  - Pfizer-BioNTech: 2-dose series, 21 days apart[3]
  - Moderna: 2-dose series, 28 days apart[4]
  - Janssen (Johnson & Johnson) (J&J): Single dose[5]
- CDC recommends individuals get the first vaccine that is available for their age group.[3]
- On April 23, 2021, CDC and FDA recommended use of the J&J vaccine after a brief pause in the US. Both agencies noted women 50 years of age and younger should be made aware of an increased risk of a rare adverse event that involves blood clots. [5]

Total Doses Administered Reported to the CDC by State/Territory per 100,000 of the Total Population (as of 29 June 2021)



**Vaccination rates by county are also available

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SARS-CoV-2 Vaccines

- CDC recommends that everyone age 12 or older get a COVID-19 vaccine.[6]
  - [New] CDC noted increased reports of heart-related inflammation in teens and young adults after COVID-19 vaccination, but COVID-19 vaccination is still recommended for everyone age 12 or older because benefits continue to outweigh risks.[3]
- Vaccines are widely available now, and the US government is working to make vaccines free and available to everyone.[6]
- CDC has indicated that people who are fully vaccinated can resume some activities they stopped due to the pandemic. CDC continues to review infection rates across the country and release guidance on precautions that both vaccinated and non-vaccinated people should take to stop the spread of COVID-19.[7]
  - Lists of what may and may not be safe to change after full vaccination are on the CDC website.

More information about finding local vaccination sites: [7]

- **Vaccines.gov**
- **Text a zip code to 438829**
- **Call 800-232-0233**

Variants of SARS-CoV-2

What is a Variant?

- **Viruses inherently replicate, which can result in genetic changes or mutations**. After enough mutations occur, the new version is called a variant. As expected, multiple SARS-CoV-2 variants have been found in the US and abroad during this pandemic.
- Sometimes new variants emerge and disappear, and other times new variants emerge and persist.[8]

Types of Variants[9]

- There are three types of variants. The types differ based on the possibility of the variant to affect people negatively, such as increased transmissibility. In order from least to most negative effects:
  - Variants of Interest (VOI)
  - Variants of Concern (VOC)
  - Variants of High Consequence (VOHC)
- As of this report, in the US there are seven VOI, six VOC, and zero VOHC.[9]

Why is it important to track variants?

Monitoring variants can help find out:

- How the virus changes over time into new variants
- How these changes affect aspects of the virus
- How the changes might impact health.[10]

Variants of SARS-CoV-2

CDC Variants of Concern (VOC)

"A variant for which there is evidence of an increase in transmissibility, more severe disease (increased hospitalizations or deaths), significant reduction in neutralization by antibodies generated during previous infection or vaccination, reduced effectiveness of treatments or vaccines, or diagnostic detection failures." [9]

Information about reported cases of variants by region and state is available from the CDC.

Current Variants of Concern in the US (as of 29 June 2021) [9]

Variant	WHO Label	First Detected	Other Names
B.1.1.7	Alpha	United Kingdom (UK)	20I/501Y.V1
B.1.351	Beta	South Africa	20H/501.V2
P.1	Gamma	Japan/Brazil	20J/501Y.V3
B.1.427	Epsilon	US – California	20C/S:452R
B.1.429	Epsilon	US – California	20C/S:452R
[New] B.1.617.2	Delta	India	20A/S:478K

What does neutralization mean?
Neutralization is when antibodies, part of the body's defense, bind to a virus and block infection. Vaccines cause the body to build up the antibodies that inhibit viruses.[10]

SUMMARY OF FINDINGS: SYSTEMATIC SEARCH OF SCIENTIFIC LITERATURE ABOUT SARS-COV-2 VACCINES, VARIANTS, AND VENTILATION

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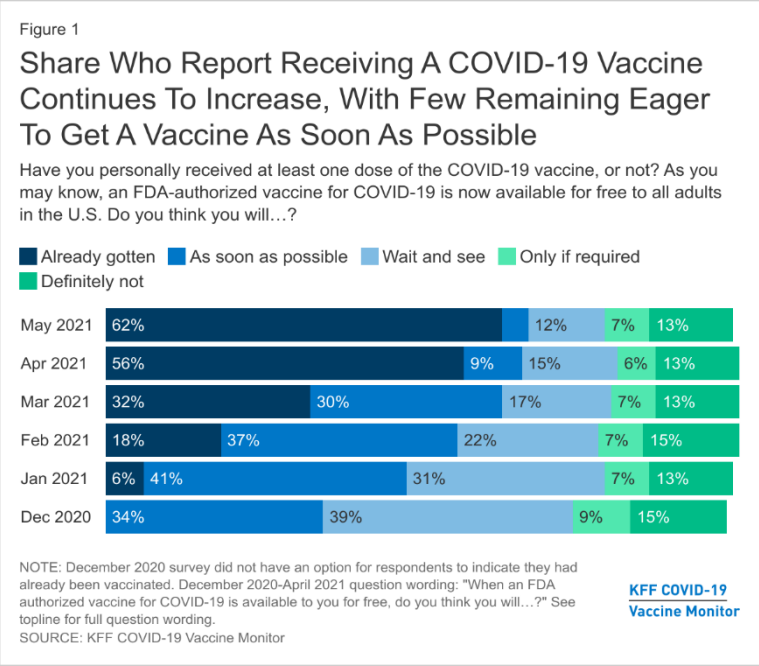
Studies About SARS-CoV-2 Vaccines

Studies About SARS-CoV-2 Vaccines

The Kaiser Family Foundation COVID-19 Vaccine Monitor is an ongoing research project that utilizes surveys and qualitative data to track the public's attitudes and experiences with COVID-19 vaccines.[11]



[New] **Key Findings from May 2021 Monitor**

- Steady progress in vaccine uptake: 62% of U.S. adults reported getting at least one dose of a vaccine (up from 56% in April).
- Over a third in the "wait and see" category plan to get a COVID-19 vaccine within three months, but one-third plan to wait over a year.
- Younger adults and Black adults remain disproportionately likely to say they will wait and see before getting a vaccine, while Republicans, rural residents, and White Evangelical Christians are disproportionately likely to say they will definitely not get vaccinated.
- 43% of surveyed adults say that CDC guidance on the activities that vaccinated and unvaccinated people can safely engage in is confusing and hard to follow.
- 41% of parents with adolescents say their adolescent (ages 12-17) has already received a COVID-19 vaccine or will right away. About 25% of parents with children <12 say they will get their children vaccinated as soon as possible, and 33% say they will "wait and see."

Studies About SARS-CoV-2 Vaccines

Impact of Vaccines

- Long-term impacts of the vaccines are still being studied.
- Studies continue to show that COVID-19 vaccines offer protection against the infectiousness, transmissibility, and disease burden of SARS-CoV-2.[12,13,14][New]
- [New] A recent preprint article on vaccine efficacy (VE) estimates for COVID-19 vaccines found:[15]
  - COVID-19 vaccines reduce transmission rates by approximately 54% (range of 38-66%).
  - Average VE against COVID-19 is 85% (95% CI: 71 - 93%) after a full course of vaccination.
  - VE against severe disease, hospitalization, or death averages close to 100%.
- [New] A prospective cohort study of healthcare workers, first responders, and other frontline workers found that mRNA VE was 90% after 14 days past full vaccination.[16]

Studies About SARS-CoV-2 Vaccines

Impact of Vaccines (Continued)

- [New] Data from six models found that high vaccine coverage and moderate use of nonpharmaceutical interventions (e.g., masks and physical distancing) can lead to low COVID-19 hospitalizations and death in the US. A sharp decline is projected by July 2021.[17]
- Positive tests for COVID-19 after receiving both doses of vaccine (Moderna or Pfizer) are rare according to data from two California healthcare systems that studied healthcare workers' infection rates after vaccination.[18]
  - Although absolute risk of testing positive for SARS-CoV-2 after vaccination was slightly higher than the risks reported in clinical trials, the healthcare workers' demographics were different than those in the clinical trials and healthcare workers were at higher risk of exposure.[18]
- Similarly, a recent study of healthcare professionals at Mayo Clinic sites found that the adjusted vaccine effectiveness was > 96% following two doses of Moderna or Pfizer.[19]

Studies About SARS-CoV-2 Vaccines

Impact of Vaccines (Cont.)

- Antibodies produced by the Moderna vaccine lasted for ***at least*** 119 days after the first vaccination.[20]
- A study on response to the Pfizer-BioNTech mRNA vaccine showed that after a single dose, persons who had a prior COVID-19 infection saw an antibody response that was similar to that of people without prior infection who received two doses.[21]
- Four months of national surveillance data in Israel showed that two doses of Pfizer-BioNTech were highly effective across all ages (16+) at preventing SARS-CoV-2 infections, COVID-19-related hospitalizations, severe disease, and death, including those caused by the B.1.1.7 SARS-CoV-2 variant.[22]
- [New] Data from Israel identified a strong negative association between vaccination rate at the community level and the risk of infection for unvaccinated members of the community, but further studies are needed to understand whether and how vaccination campaigns can impact herd immunity.[23]

Studies About SARS-CoV-2 Vaccines

Impact of Vaccines: Subpopulations

- Older Adults:
  - [New] In the US, there has been a decrease in COVID-19 cases, emergency department visits, hospital admissions, and deaths among older adults, which are the age group with the highest vaccination rates.[24]
  - [New] In a multistate network of US hospitals, vaccines (Pfizer-BioNTech or Moderna) were 94% effective against COVID-19 hospitalization among fully vaccinated older adults (ages 65 and up) and 64% effective among partially vaccinated older adults.[25]
  - A recent German study found reduced antibody responses in people ages 80 or older compared to people ages 60 or younger who received the Pfizer-BioNTech vaccine. The authors noted that the elderly population needs to be closely monitored after vaccination and may require earlier revaccination and/or an increased vaccine dose.[26]

Studies About SARS-CoV-2 Vaccines

Impact of Vaccine: Subpopulations (Cont.)

- Pregnant women: Preliminary findings of vaccine safety (mRNA vaccines) for pregnant persons did not show any obvious safety signals to pregnancy or neonatal outcomes, but continued monitoring was recommended.[27-28, 29-30][New]
- [New] Rural: Residents of rural communities are at increased risk for severe COVID-19 outcomes and have less vaccine coverage (38.9%) than urban populations (45.7%).[31]
- [New] Adolescents: A study found the Pfizer-BioNTech vaccine had a favorable safety profile and was highly effective against COVID-19 in 12- to 15-year-olds. On May 10, 2021, the FDA emergency use authorization was expanded to include persons 12 years of age or older based on the data from this study.[32]

Studies About SARS-CoV-2 Vaccines

Vaccine Hesitancy and Vaccine Safety

- Vaccine safety is assessed during the development process and is still continuously monitored.[33-38] While states have expanded vaccine eligibility, surveys continue to show "vaccine hesitancy" remains a concern for ensuring equitable vaccination coverage among all populations.[39-40]
- Factors potentially related to vaccine hesitancy include concerns over vaccine safety, trust in government recommendations, perceived political interference, education, income, race/ethnicity, and perceived threat of COVID-19.[41-49]
- The CDC and FDA recommended a pause in administration of the J&J vaccine to allow for a safety review by CDC's Advisory Committee on Immunization Practices (ACIP). The pause was lifted 10 days later, and vaccinations resumed.[50]

Studies About SARS-CoV-2 Vaccines

Health Communication and Misinformation

- Scientists have called for efforts to address miscommunication and misinformation on COVID-19 vaccines and restore trust in health authorities.[51-53] Vaccine acceptance will be impeded by misinformation and poor public health communication strategies.[53-56]
  - [New] Although it's important to address misinformation, some researchers think social media companies need to work with public health experts to engage vaccine-hesitant groups online rather than ban or censor them from the platforms.[57]
- Equitable access to COVID-19 vaccines among racial/ethnic minorities is a key concern. Researchers have identified that COVID-19 continues to disproportionally impact the Black community, further worsening health disparities already present due to racism and its effects on social and economic factors.[40,58-62][New]
- A rapid expert consultation recommended emphasizing support for vaccines, leveraging endorsements, focusing on hesitant individuals, and engaging communities to increase confidence in vaccines.[63]

What is Still Unknown About SARS-CoV-2 Vaccines?[2,7,64]

- How long immunity lasts for different vaccines
- How well the vaccines keep people from spreading SARS-CoV-2 to others, even without symptoms
- How and when vaccines will be available for children under 12 years old
- How well different vaccines will protect against future SARS-CoV-2 variants
- How dosing with two different vaccines for first and second doses can affect efficacy (e.g., Pfizer then Moderna)
- Efficacy in sub-populations (elderly, pregnant women, children/adolescents)

Key CDC Resources About SARS-CoV-2 Vaccines

- CDC website - Vaccines for COVID-19
- Community-Based Organizations COVID-19 Vaccination Toolkit
- Interim Public Health Recommendations for Fully Vaccinated People
- Key Things to Know About COVID-19 Vaccines
- Facts about COVID-19 Vaccines:
  - English version
  - Spanish version
- COVID-19 Vaccinations in the United States

Studies About SARS-CoV-2 Variants

Studies About SARS-CoV-2 Variants

Spread, Transmissibility, and Infectivity

- Several studies suggested that emerging SARS-CoV-2 variants, specifically the B.1.1.7 and B.1.351 variants, are more transmissible than the early lineage variant.[65-71]
  - One study found that in the US, the B.1.1.7 variant is ~50% more transmissible than other circulating variants, has a growth rate of ~7.5% per day, and has a doubling rate of 1.5 weeks.[72]
  - Another study found that the B.1.1.7 variant has an estimated 43-90% higher reproduction number than preexisting variants in England, 45–66% higher than those in Denmark, and 56-63% higher than those in the US.[73]
  - A study in France showed that from 25 January to 16 February 2021, SARS-CoV-2 infections from variants (B.1.1.7, B.1.351, and P.1) were associated with more rapid spread of SARS-CoV-2 infections than anticipated, such that by February 16, more than half of infections in the country were caused by variants.[74]

Legend: Names for Variants of Concern in the US*

Variant	WHO Label
B.1.1.7	Alpha
B.1.351	Beta
P.1	Gamma
B.1.617.2	Delta
B.1.427	Epsilon
B.1.429	Epsilon

***as of 29 June 2021**[10]

Studies About SARS-CoV-2 Variants

Spread, Transmissibility, and Infectivity (Cont.)

- Certain mutations in the B.1.1.7 and B.1.351 variants and SARS-CoV-2 substrains have been found to be linked with increased transmissibility and infectivity.[75-79]
- Findings have shown that the higher infectivity and rapid spread of the B.1.1.7 variant may be linked to the higher viral load found in samples from people with the variant.[80]
- A study of the spread of COVID-19 in the US by county found that regions with high proportions of two SARS-CoV-2 variants with a specific mutation (the G614 mutation) had higher spread rates than regions with lower proportions of those variants.[81]
- A study found the stability of the B.1.1.7 variant in aerosols in different environmental conditions (varying temperature, relative humidity, and simulated sunlight) was similar to other previously identified variants, suggesting that the increased transmissibility of B.1.1.7 is not due to an enhanced ability to survive in the environment.[82]

Studies About SARS-CoV-2 Variants

Spread, Transmissibility, and Infectivity (Cont.)

- [New] A study showed that secondary attack rate (spread of disease within a family or other group) in households with SARS-CoV-2 variant of concern (VOC) cases (B.1.1.7, B.1.351, and P.1) was 31% higher than households with non-VOC cases. These results highlight the increased transmissibility of VOCs.[83]
- [New] A study examining the outbreaks of the B.1.1.7 variant in childcare centers and related households found similar secondary attack rates among children and adults: 23% vs. 30% in childcare centers and 32% vs. 39% in households.[84]
  - The study findings suggest that susceptibility and infectiousness of children ages 1 to 6 years old is higher for B.1.1.7 compared to the early lineage variant and may be increasing toward adult rates of infection.[84]

Studies About SARS-CoV-2 Variants

Outcomes Severity for Variants (compared to original version of SARS-CoV-2)

- Studies have found that the B.1.1.7 variant is associated with increased mortality in England compared to pre-existing variants.[85-86]
- A study found that SARS-CoV-2 persisted longer in people infected with the B.1.1.7 variant (16 days) compared to those infected with other variants (14 days).[87]
- [New] Preliminary data from a study of hospitalized patients with severe SARS-CoV-2 infection showed that the B.1.351 variant was linked to higher risk for short-term (60-day) mortality compared to the B.1.1.7.[88]

Studies About SARS-CoV-2 Variants

Outcomes Severity for Variants (Compared to original version) (Cont.)

- Research suggests that specific mutations that have been identified in SARS-CoV-2 variants are associated with varying severity of COVID-19 illness:
  - One study identified five mutations of the virus that were associated with mild outcomes and 17 mutations that were associated with severe outcomes.[89]
  - One study indicated that a common mutation found in all currently identified VOCs (the D614G mutation) is not associated with more severe disease outcomes.[90]
  - Two mutations identified in SARS-CoV-2 variants were found to have opposing outcomes. One mutation (in gene N [P13L]) was associated with decreased deaths and decreased cases per million, whereas another mutation (in gene ORF3a [Q57H]) was linked to decreased deaths and increased cases per million.[91]
- Findings from a study examining global data showed a potential link between a variant with the S-D614G mutation and increased case severity.[92]

Studies About SARS-CoV-2 Variants

Risk of Reinfection

- Case reports highlight instances of reinfection with the B.1.1.7 and P.1 SARS-CoV-2 variants following previous infection with the early lineage virus.[93-95]
- One study reported that the B.1.351 variant has an “unusually large number of mutations,” some of which might be linked to immunoescape (i.e., the virus escapes being stopped by the immune system). Thus, it is unclear whether infection for one SARS-CoV-2 strain offers protection against reinfection by another strain.[96]
- A study found that the B.1.1.7 and B.1.351 variants are more resistant to neutralization (i.e., they are less likely to lose infectivity), which suggests there was evidence of the possibility of reinfection with these strains.[97]
- Despite there being a possibility of reinfection with VOCs, one study showed no evidence of increased reinfection rates in the presence of the B.1.1.7 variant.[70]

Studies About SARS-CoV-2 Variants

Impact of Therapies and Vaccines on the Variants

- A study showed that plitidepsin and ralimetinib, two host-directed drugs used in the treatment of SARS-CoV-2, as well has remdesivir have antiviral effects against both the early lineage and the B.1.1.7 variant of SARS-CoV-2.[98]
- As SARS-CoV-2 variants continue to emerge, it is possible that current COVID-19 vaccines will not be as effective against future variants. However, several studies have shown that current vaccines are effective against most of the current VOCs.[99]
  - [New] A recent preprint found that the average vaccine efficacy is 86% (95% CI: 65 - 84%) for the B.1.1.7 variant, 61% (95% CI: 43 - 73%) for B.1.1.28 (related to P.1 variant), and 56% (95% CI: 29 - 73%) for B.1.351.[15]
- The Pfizer-BioNTech vaccine appears to be highly effective against the B.1.1.7, B.1.351, P.1 lineage, variants of SARS-CoV-2,[100-103][New] and the D614G mutation.[75,104]
  - The Pfizer-BioNTech vaccine was found to neutralize the B.1.1.7-spike+E484K B.1.526-spike virus and B.1.429-spike virus (though slightly lower).[105]

Studies About SARS-CoV-2 Variants

Impact of Therapies and Vaccines on the Variants (cont.)

- The Moderna mRNA-1273 vaccine has been shown to maintain neutralizing activity against all circulating SARS-CoV-2 variants except the B.1.351 variant, which has shown some resistance to the vaccine.[106-108]
- [New] A study examined the presence of neutralizing antibodies (NAbs) in healthcare workers who had been vaccinated or infected with SARS-CoV-2 six months prior.[109]
  - Findings showed that 97% of participants who were fully vaccinated with the Pfizer-BioNTech vaccine had detectable NAbs against the B.1.1.7 and B.1.1351 variants.[109]
  - Only 60% of previously infected participants had detectable NAbs against B.1.1351.[109]
  - These findings highlight the need for people previously infected with SARS-CoV-2 to receive vaccinations.[109]

Studies About SARS-CoV-2 Variants

Impact of Therapies and Vaccines on the Variants (cont.)

- Findings indicated that a single dose of the Pfizer-BioNTech or Moderna vaccines may increase neutralizing activity against the B.1.1.7, B.1.351, and P.1 variants for individuals who were previously infected with SAR-CoV-2.[110,111]
  - A study showed that after two doses of the Pfizer-BioNTech vaccine, people who were previously infected with SARS-CoV-2 developed increased neutralizing antibodies by a factor of 5.2 against B.1.1.7, 6.5 against B.1.351, 4.3 against P.1, and 3.4 against original SARS-CoV-2 (compared to people who had not been previously infected).[112]

Studies About SARS-CoV-2 Variants

Continued Use of Established Mitigation Strategies

- Studies show that it is critical to continue existing public health strategies (e.g., physical distancing, hand hygiene, mask wearing, people quarantining after exposure) to reduce the transmission of SARS-CoV-2 variants while vaccine coverage expands.[113-115]
- A study using an epidemiological model showed that – accounting for variants, reinfection, and optimal control – relaxing mitigation measures early would lead to a sharp increase in new cases.[116]
- A model examining the impact of social distancing measures in France on the spread of SARS-CoV-2 showed that although these measures reduced the effective transmission rate of previously circulating SARS-CoV-2 strains, they did not lead to a decline in the spread of the B.1.1.7 variant due to the variant's more efficient transmission.[117]
  - These findings suggest that maintaining rigorous mitigation strategies alongside increased vaccination may be the most effective way to minimize the spread of the B.1.1.7 variant.[117]

Studies About SARS-CoV-2 Variants

Continued Use of Established Mitigation Strategies (Cont.)

- A study of the spread of the B.1.1.7 variant in Portugal over a six-week period showed a deceleration in the growth rate of the variant after physical distancing measures were put in place.[118]
- [New] A study examining how well various inactivation strategies work against the B.1.1.7 and B.1.351 variants found that both variants were inactivated by heat, soap, and ethanol, suggesting that existing disinfection strategies remain effective.[119]

What is Still Unknown About SARS-CoV-2 Variants?[2,9]

- How transmissible some variants of SARS-CoV-2 are for certain demographics (e.g., older adults)
- The likelihood of reinfection due to SARS-CoV-2 variants
- How the infectious dose (amount of virus needed for infection) differs between variants and the early lineage
- How these variants may affect existing therapies, such as vaccines.
- How widely variants have spread in the US and abroad
- How well variants are detected using current SARS-CoV-2 tests

Key CDC Resources About SARS-CoV-2 Variants

- Variants and Genomic Surveillance for SARS-CoV-2
- About Variants of the Virus that Causes COVID-19
- Variant Proportions (US COVID-19 Cases Caused by Variants)
- Science Brief: Emerging SARS-CoV-2 Variants

Studies About the Effects of Ventilation on SARS-CoV-2

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Studies About the Effects of Ventilation on SARS-CoV-2

General Findings

- Many of the studies used carbon dioxide as a proxy for SARS-CoV-2 to measure the degree of ventilation in a space.[120-124] In other words, testing of ventilation methods with active virus was not conducted.
  - Excess CO_2 concentration has been shown to trend with relative risk of infection. Carbon dioxide concentration can serve as a proxy for infection risk, and sensors are relatively inexpensive.[125]
- Theoretically, many factors influence whether ventilation is successful in the elimination or decrease of SARS-CoV-2 particles in the air, including
  - Activities taking place in the space,
  - Number of infectious people in a space and their viral load,
  - Air change rate, natural vs. mechanical ventilation, presence of air filtration.[126]
- Air purification or ventilation alone is not enough to decrease virus particles to below guideline levels, but ventilation, purification, and implementation of other mitigation measures (mask wearing, occupancy restrictions, surface cleaning) can reduce risk of infection drastically.[127-129]

Studies About the Effects of Ventilation on SARS-CoV-2

General Findings (Cont.)

- Researchers created an app to determine exposure times and occupancy levels based on ventilation, room specifications, and other parameters.[130]
- A 'state of the literature' review published in April 2021 determined that the quality of evidence was low, in terms of understanding the role of ventilation systems in mitigating or promoting spread of COVID-19.[131]
- Modeling research has shown that the probability of infection may be influenced more by how close a person is to someone carrying SARS-CoV-2 than by the amount of fresh air in a space.[132,133]
- [New] HVAC systems tend not to be built for airborne infection control and may only operate at a small fraction of the room air change rate needed to stop virus spread.[133]
  - [New] Air may need to be circulated more frequently in high traffic areas (e.g., communal space and bathrooms).[134]

Studies About the Effects of Ventilation on SARS-CoV-2

Air Purification

- A study using surrogate viruses to test the effectiveness of air purification devices found that a HEPA H14 filter eliminated 99% of bacteriophages under perfect conditions.[135]
- Similarly, another study found that aerosol concentration decreased 90% after 30 minutes of running four air purifiers in a classroom with windows and doors closed.[136]
- Additionally, the optimal positioning of air purifiers was in front of the source of aerosols (e.g., an infectious person), on the ground.[137]
- Another study showed higher viral load concentrations when the air purifier was placed farther away from the particle emitter (range: 1.2m – 8.4m).[138]
- The most appropriate air purifiers to use against SARS-CoV-2 are those that use HEPA filters, ionizers, or ultraviolet germicidal irradiation (UVGI).[139]

Studies About the Effects of Ventilation on SARS-CoV-2

Air Purification (Cont.)

- [New] Researchers designed and tested a low-cost air purification device using a box fan, MERV-13 filter, and a cardboard support.[140]
  - [New] Researchers tested this purification device at approximately two air changes per hour, which is typical of a classroom built before 1989. This homemade purifier was found to reduce the risk of airborne transmission in a classroom setting, lowering the percentage of suspended aerosols in the room to as low as 1% when placed next to the ventilation source.[140]
- [New] Purification devices that can demonstrate removal of 99.99% of pathogens are eligible for FDA approval for medical and home-health use.[141]
- [New] Filters should fit snugly in their housings to mitigate filter bypass and should be replaced according to the instructions on the filter.[142]
- [New] PPE should be worn when replacing air filters to reduce exposure to viral particles.[142]

Studies About the Effects of Ventilation on SARS-CoV-2

HVAC Systems

- There is a risk that HVAC systems could worsen spread of COVID-19 if not designed or modified to maximize circulation of virus-free air into a space.[137,143]
- Displacement ventilation systems, or those “designed to vertically stratify indoor air by temperature (warm air at the top of the room, colder air at the bottom) and remove warmer air” were found most likely to reduce risk of SARS-CoV-2 transmission via HVAC.[134,143-145]
- Conversely, another study found that unstable or neutrally stratified air (warm air at the bottom of the room, or no discriminate layers of warm or cold air) reduced the risk of infectious aerosols remaining at one height in the breathing environment.[113]
- Increasing the fraction of outdoor air and using a MERV-13 filter (rather than a MERV-8 filter) were found to be more likely to reduce spread of SARS-CoV-2 between adjoining rooms.[146]

Studies About the Effects of Ventilation on SARS-CoV-2

HVAC Systems (Cont.)

- Ventilation at only one point in a room is unlikely to efficiently remove virus particles in the absence of other precautions (e.g., masks, social distancing, etc.).[147]
- Inadequate or inappropriately positioned ventilation may lead to virus hotspots or increased surface deposition.[143-144,147]
- Incorporation of UV-C light into duct systems was shown to inactivate 99.98% of virus in the air that passed through the duct.[134]
  - [New] Upper room ultraviolet germicidal irradiation (UVGI) can also be used to disinfect warm air as it rises toward the ceiling. UVGI can be used with displacement ventilation or ceiling fans to continually mix and disinfect the air in the room.[133-134]
  - [New] In-duct UVGI used in conjunction with in-duct filters (e.g., HEPA) can significantly reduce viral load in indoor air.[148]

Studies About the Effects of Ventilation on SARS-CoV-2

HVAC Systems (Cont.)

- [New] Increasing air change rates can lead to higher energy costs. These costs can be offset by 'smart' systems, which only ventilate rooms when they are occupied, and also by natural ventilation.[149-151]
- [New] Air diffusers and return vents located in such a way that circulated air is contained in one physical space (also called localized flow regimes) may mitigate the spread of contaminated air.[134]
- [New] Outdoor air dampers can be opened beyond the minimum settings to reduce indoor air recirculation (weather and temperature permitting).[142]
- [New] It may be beneficial to run HVAC at maximum outdoor airflow for a period of time (e.g., 2 hours) before a space is occupied.[142]

Studies About the Effects of Ventilation on SARS-CoV-2

Historic Buildings & Natural Ventilation

- In a school system in Switzerland, natural ventilation was performed during breaks and decreased the amount of carbon dioxide from 1600ppm to 1097ppm.[121]
- In a study of New York City school buildings, transmission was found to be lower in older buildings compared to newer buildings, likely due to “greater outdoor airflow” (i.e., drafts).
  - Transmission rate was also found to be lower in schools with mechanical ventilation (when compared to natural ventilation).[152]
- A study of a historic building in Jeddah (Saudi Arabia) found that the number of windows opened (large windows with cross ventilation) was positively correlated with ventilation rates, while wind speed and direction were not.[153]
- Conversely, it was found that atypically low wind speed and wind direction in a naturally ventilated building may have contributed to a COVID-19 outbreak in Hong Kong.[120]

Studies About the Effects of Ventilation on SARS-CoV-2

Historic Buildings & Natural Ventilation (Cont.)

- [New] Another study found that natural ventilation from adjacent windows reduced infection risk better than natural ventilation from opposite windows.[154]
- [New] Fans can be placed in open windows to increase the effectiveness of natural ventilation. Air should exhaust to the outdoors.[142]

Studies About the Effects of Ventilation on SARS-CoV-2

Effects of Temperature & Humidity

- Because ventilation with outdoor air is more difficult in colder months, researchers have estimated that airborne infection risk is double that of summer months.[123,139,155]
  - During these months, monitoring indoor carbon dioxide as a proxy for ventilation is recommended and should not exceed 1000 ppm.[155]
  - In the absence of carbon dioxide monitoring, attention should be paid to areas where stagnant air is more likely.[155]
- Researchers in another study recommended further research on humidification of air, which could increase the speed at which SARS-CoV-2 particles drop to the ground or surfaces.[156]
- [New] The taller a building is, the more prone it is to stack effect, especially in colder climates. Stack effect occurs when pressure differences between floors cause air to stagnate on upper floors. This effect may also cause a reversal of airflow and contaminants may spread to other areas of the building.[157]

What is Still Unknown About the Impact of Ventilation on SARS-CoV-2?

- Consensus on how to best configure, upgrade, or design ventilation systems to mitigate the spread of SARS-CoV-2
- How proximity to air purifiers (close to emitter vs. far away) impact the amount of virus particles present in a space
- Whether variants that are more transmissible can be mitigated using the same ventilation methods that are effective for other strains
- How results may differ if ventilation-related studies used SARS-CoV-2 instead of surrogate substances (e.g., carbon dioxide)
- [New] How to best to utilize UVGI (upper room and/or in-duct) to reduce the number of virus particles in a space
- [New] Whether plexiglass barriers do more harm than good by impeding air flow[158]

Key CDC Resources About Ventilation to Mitigate SARS-CoV-2

- Ventilation in Buildings
- COVID-19 Employer Information for Office Buildings
- Improving Ventilation in Your Home
- Ventilation and Coronavirus (COVID-19) (Environmental Protection Agency resource)

HOW THIS BRIEFING WAS CREATED (METHODOLOGY)

How This Briefing Was Created

- In January 2021, REALM stakeholders developed Phase 3 research questions. An additional question related to ventilation was added in May 2021.
- Battelle developed search strings that included variations of the term “SARS-CoV-2” and novel terms for vaccine and variants using Boolean operators. The Boolean operator “AND” was used to separate SARS-CoV-2 and research question terms, while different variations of the virus name and keywords related to the research question were grouped by category using parentheses and the Boolean operator “OR” (e.g., ["SARS-CoV-2" OR "2019-nCoV" OR "COVID-19"] AND [vaccine OR variant]). Search strings are included in the appendix.
- Battelle developed research question keywords using ad hoc test searches and comparison against known relevant articles, and databases were selected (Scopus, SciTech, Web of Science, and MEDLINE) to provide comprehensive search capacity and inclusion of smaller databases.
- The initial search string included a time criterion to capture articles published in January 2021 and after. Subsequent searches were executed on two-week durations. Note: when the ventilation research question was added in May 2021, articles were searched from 01 January 2021 forward to cover the same time period as the other research questions.

How This Briefing Was Created (cont.)

- Battelle staff reviewed the titles and abstracts of search results to select those most relevant to the research questions for additional examination.
- The DHS Master Question List for COVID-19 and CDC Morbidity and Mortality Weekly Reports (MMWR) were reviewed to verify the completeness of the search results (i.e., to double-check that relevant articles were not missed by the search strings).
- Battelle staff analyzed the relevant articles to identify key subtopics and prioritize high-value articles. Summaries of the articles, organized by subtopic, were presented to OCLC, IMLS, and REALM working groups for feedback.
- Battelle summarized the results for this briefing, which is a cumulative report that builds on prior briefings by adding new relevant research findings published 18 May to 14 June 2021. Additional information was also added from the CDC to provide context on the key topics.
- Battelle will continue to review articles gathered by the search on a biweekly basis, and this briefing will continue to be updated iteratively with new information.

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APPENDIX: SEARCH STRINGS

Database	Strategy: Vaccines and Variants of SARS-CoV-2
Scopus	((TITLE-ABS (coronavir* OR covid OR "COVID-19" OR "SARS-CoV-2" OR "2019-nCoV") AND TITLE-ABS (spread* OR transmi* OR infect* OR reinfect* OR virulence OR neutraliz* OR sever* OR evad* OR airborne OR aerosol* OR occupation* OR infectiv* OR mortality OR morbidity OR death*) AND TITLE-ABS (variant OR vaccine OR mutat* OR mutant* OR lineage OR immun* OR strain)) AND NOT TITLE-ABS (receptor OR inflamm* OR peptide* OR nanomaterial OR ace2 OR polymerase OR "IgA" OR patient* OR assay* OR ligand* OR protease OR hiv))
SciTech	(ti,ab(coronavir* OR covid OR "COVID-19" OR "SARS-CoV-2" OR "2019-nCoV") AND ti,ab(spread* OR transmi* OR infect* OR reinfect* OR virulence OR neutraliz* OR sever* OR evad* OR airborne OR aerosol* OR occupation* OR infectiv* OR mortality OR morbidity OR death*) AND ti,ab(variant OR vaccine OR mutat* OR mutant* OR lineage OR immun* OR strain)) NOT ti,ab(receptor OR inflamm* OR peptide* OR nanomaterial OR ace2 OR polymerase OR "IgA" OR patient* OR assay* OR ligand* OR protease OR hiv)
Web of Science	TS=(coronavir* OR covid OR "COVID-19" OR "SARS-CoV-2" OR "2019-nCoV") AND TS=(spread* OR transmi* OR infect* OR reinfect* OR virulence OR neutraliz* OR sever* OR evad* OR airborne OR aerosol* OR occupation* OR infectiv* OR mortality OR morbidity OR death*) AND TS=(variant OR vaccine OR mutat* OR mutant* OR lineage OR immun* OR strain) NOT TS=(receptor OR inflamm* OR peptide* OR nanomaterial OR ace2 OR polymerase OR "IgA" OR patient* OR assay* OR ligand* OR protease OR hiv)
MEDLINE	(TI (coronavir* OR covid OR "COVID-19" OR "SARS-CoV-2" OR "2019-nCoV") AND TI (spread* OR transmi* OR infect* OR reinfect* OR virulence OR neutraliz* OR sever* OR evad* OR airborne OR aerosol* OR occupation* OR infectiv* OR mortality OR morbidity OR death*) AND TI (variant OR vaccine OR mutat* OR mutant* OR lineage OR immun* OR strain) NOT TI (receptor OR inflamm* OR peptide* OR nanomaterial OR ace2 OR polymerase OR "IgA" OR patient* OR assay* OR ligand* OR protease OR hiv)) OR (AB (coronavir* OR covid OR "COVID-19" OR "SARS-CoV-2" OR "2019-nCoV") AND AB (spread* OR transmi* OR infect* OR reinfect* OR virulence OR neutraliz* OR sever* OR evad* OR airborne OR aerosol* OR occupation* OR infectiv* OR mortality OR morbidity OR death*) AND AB (variant OR vaccine OR mutat* OR mutant* OR lineage OR immun* OR strain) NOT AB (receptor OR inflamm* OR peptide* OR nanomaterial OR ace2 OR polymerase OR "IgA" OR patient* OR assay* OR ligand* OR protease OR hiv))

Database	Strategy: Effects of Ventilation on Spread of SARS-CoV-2
Scopus	(TITLE-ABS (coronavir* OR covid OR "COVID-19" OR "SARS-CoV-2" OR "2019-nCoV") AND TITLE-ABS (spread* OR transmi* OR persist* OR mitigat* OR purif* OR reduc*) AND TITLE-ABS (indoor OR office OR "climate controlled" OR ambient OR air OR airborne OR aerosol* OR hvac OR merv OR filter* OR filtrat* OR ventilat* OR hepa)) AND NOT TITLE-ABS (pollution OR particulate* OR hospital* OR nosocomial OR animal OR wastewater OR sewage OR "intensive care" OR patient OR phenotype OR clinical OR polymerase) AND (LIMIT-TO (PUBYEAR , 2021))
SciTech	(TS=(coronavir* OR covid OR "COVID-19" OR "SARS-CoV-2" OR "2019-nCoV") AND TS=(spread* OR transmi* OR persist* OR mitigat* OR purif* OR reduc*) AND TS=(indoor OR office OR "climate controlled" OR ambient OR air OR airborne OR aerosol* OR hvac OR merv OR filter* OR filtrat* OR ventilat* OR hepa)) NOT TS=(pollution OR particulate* OR hospital* OR nosocomial OR animal OR wastewater OR sewage OR "intensive care" OR patient OR phenotype OR clinical OR polymerase) AND PUB YEAR= 2021
Web of Science	(TI (coronavir* OR covid OR "COVID-19" OR "SARS-CoV-2" OR "2019-nCoV") OR AB (coronavir* OR covid OR "COVID-19" OR "SARS-CoV-2" OR "2019-nCoV")) AND (TI (spread* OR transmi* OR persist* OR mitigat* OR purif* OR reduc*) OR AB (spread* OR transmi* OR persist* OR mitigat* OR purif* OR reduc*)) AND (TI (indoor OR office OR "climate controlled" OR ambient OR air OR airborne OR aerosol* OR hvac OR merv OR filter* OR filtrat* OR ventilat* OR hepa) OR AB (indoor OR office OR "climate controlled" OR ambient OR air OR airborne OR aerosol* OR hvac OR merv OR filter* OR filtrat* OR ventilat* OR hepa)) NOT (TI (pollution OR particulate* OR hospital* OR nosocomial OR animal OR wastewater OR sewage OR "intensive care" OR patient OR phenotype OR clinical OR polymerase) OR AB (pollution OR particulate* OR hospital* OR nosocomial OR animal OR wastewater OR sewage OR "intensive care" OR patient OR phenotype OR clinical OR polymerase)) Date of Publication: 20210101-20211231
MEDLINE	(ti,ab(coronavir* OR covid OR "COVID-19" OR "SARS-CoV-2" OR "2019-nCoV") AND ti,ab(spread* OR transmi* OR persist* OR mitigat* OR purif* OR reduc*) AND ti,ab(indoor OR office OR "climate controlled" OR ambient OR air OR airborne OR aerosol* OR hvac OR merv OR filter* OR filtrat* OR ventilat* OR hepa)) NOT ti,ab(pollution OR particulate* OR hospital* OR nosocomial OR animal OR wastewater OR sewage OR "intensive care" OR patient OR phenotype OR clinical OR polymerase) Date: After January 01 2021

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