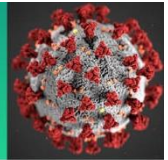


COVID-19 Science Update



From the Office of the Chief Medical Officer, CDC COVID-19 Response, and the CDC Library, Atlanta, GA.
Intended for use by public health professionals responding to the COVID-19 pandemic.

*** Available on-line at <https://www.cdc.gov/library/covid19> ***

Section headings in the COVID-19 Science Update align with the [CDC Science Agenda for COVID-19](#).

Prevention, Mitigation and Intervention Strategies

PEER-REVIEWED

[Safety and efficacy of the BNT162b2 mRNA COVID-19 vaccine](#). Polack *et al.* NEJM (December 10, 2020).

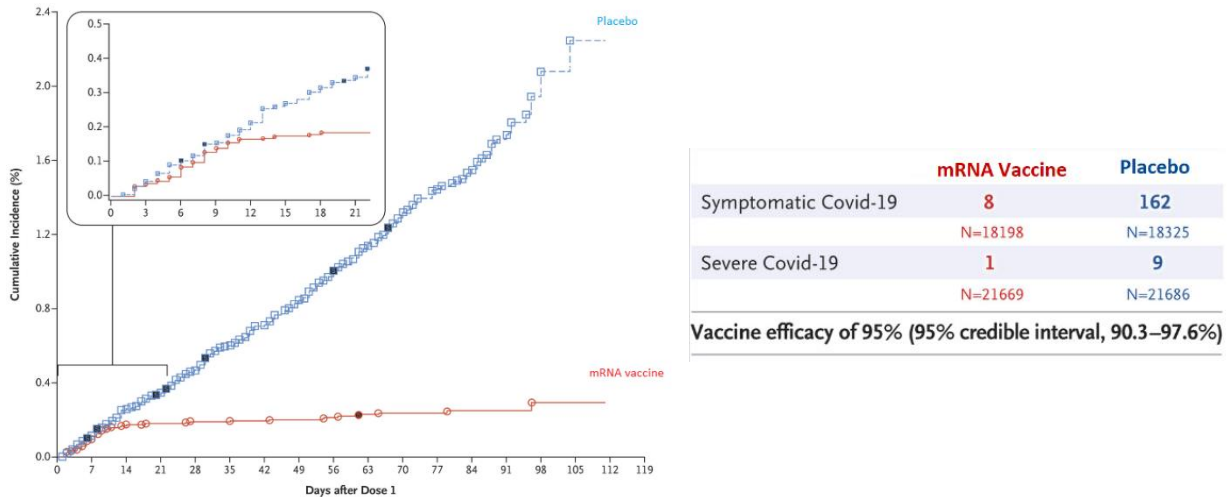
Key findings:

- The Pfizer/BioNTech SARS-CoV-2 spike protein mRNA vaccine candidate BNT162b2 was 95% efficacious in preventing symptomatic COVID-19 after two doses (Figure).
 - Similar vaccine efficacy was observed by age, sex, race, ethnicity, baseline body-mass index, and the presence of coexisting conditions.
- Participants receiving vaccine had higher rates of local reactions (pain, redness, swelling) and systemic reactions (fever, headache, muscle pain) compared with those receiving placebo.

Methods: Phase 2/3 safety and efficacy study of a SARS-CoV-2 spike protein mRNA vaccine candidate previously reported by [Walsh *et al.*](#) was assessed for a median of two months. Healthy persons ≥ 16 years old were randomly assigned 1:1 to receive two intramuscular doses of 30 μg placebo ($n = 21,728$) or BNT162b2 ($n = 21,720$) 21 days apart and followed for development of symptoms in which case they underwent viral testing for SARS-CoV-2. 8183 persons were included in the reactogenicity subset. **Limitations:** Safety and efficacy was studied for only 2 months and only in healthy persons; did not assess efficacy in asymptomatic persons or transmission potential of vaccinated persons.

Implications: In a remarkable historical public health achievement, the [FDA approved](#) the first mRNA COVID-19 vaccine that was developed in record time and that achieved 95% efficacy in a large randomized trial with minimal adverse events. Implementation should follow [ACIP's interim guidance](#), however there remains open questions, pointed out in [Callaway *et al.*](#), such as how much protection the vaccine offers, to whom, and for how long.

Figure:



Note: Adapted from Polack *et al.* Efficacy of COVID-19 mRNA vaccine compared to placebo by cumulative incidence of COVID-19 from the time of the first dose. Second dose given at day 21. Each symbol represents a COVID-19 case; filled symbols represent severe COVID-19 cases. The inset shows the first 21-day data on an enlarged y-axis. From NEJM, Polack *et al.*, Safety and efficacy of the BNT162b2 mRNA COVID-19 vaccine. Copyright © 2020 Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.

Analysis of measles-mumps-rubella (MMR) titers of recovered COVID-19 patients. Gold *et al.* MBio (November 20, 2020).

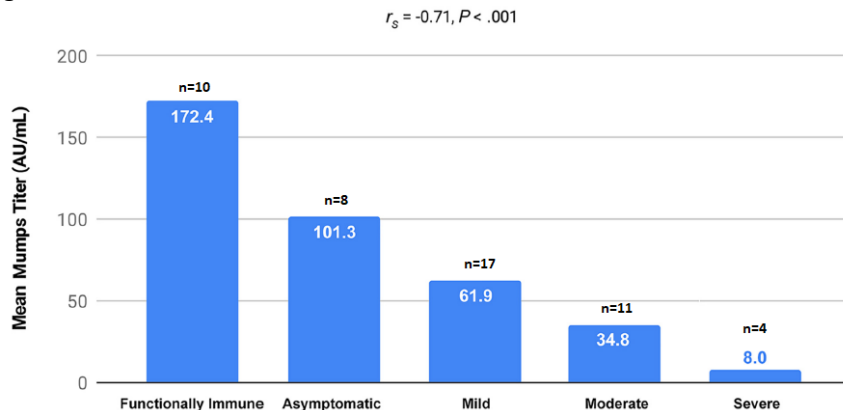
Key findings:

- There was a significant inverse correlation ($r_s = -0.71, p < 0.001$) between mumps virus IgG titers (but not measles or rubella) and COVID-19 severity among those vaccinated with the measles-mumps-rubella (MMR II) vaccine (Figure).

Methods: Retrospective descriptive analysis comparing MMR II IgG titers and COVID-19 severity in 80 participants with prior SARS-CoV-2 infection or exposure in the US, with or without prior MMR II vaccination. **Limitations:** Small sample size; no randomization of participants; limited generalizability.

Implications: A protective effect of mumps-specific antibodies could lead to new vaccination strategies for SARS-CoV-2. A large scale trial is underway that could help shed light on whether MMR vaccines can boost the immune response and be effective in preventing SARS-CoV-2 infection.

Figure:



Note: Adapted from Gold *et al.* Mean mumps titer values (in arbitrary units per milliliter) among the vaccinated group were compared in each of five COVID-19 severity categories based on symptom scores. Comparison of severity data were done with a Spearman's rank correlation coefficient, with the resulting r_s and p-values. Licensed under CC 4.0.

Detection, Burden, and Impact: Modeling Excess Mortality

Excess mortality reflects the full impact of the pandemic that that may go unmeasured due to undetected COVID-19 and other pandemic-related deaths.

PEER-REVIEWED

A. [All-cause excess mortality and COVID-19–related mortality among US adults aged 25-44 years, March-July 2020](#). Faust *et al.* JAMA (December 16, 2020).

Key findings:

- 76,088 persons aged 25 to 44 years died from all causes during March through July 2020; this was 11,899 more deaths (incident rate ratio 1.19, 95% CI 1.14-1.23) than expected.
 - 4,535 COVID-19 deaths accounted for 38% (95% CI 32%-48%) of the excess mortality.
 - Data are not yet available to account for the remaining excess deaths.

Methods: 2020 all-cause and COVID-19 deaths, from [provisional CDC data](#), were compared with expected all cause deaths for 2020 (calculated from 2015-2019 US population and mortality [counts](#)). **Limitations:** Incomplete data due to reporting lags.

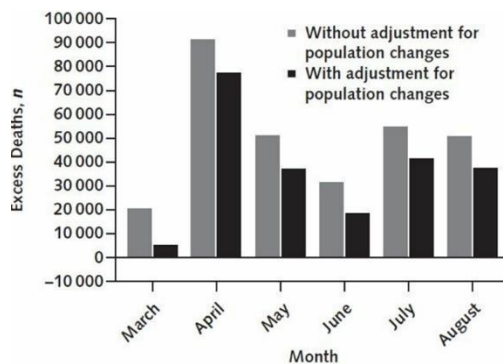
B. [Impact of population growth and aging on estimates of excess U.S. deaths during the COVID-19 pandemic, March to August 2020](#). Shiels *et al.* Annals of Internal Medicine (December 15, 2020).

Key findings:

- There were 1,671,400 US deaths from March to August 2020, compared with an average 1,370,000 deaths reported during the same months from 2015-2019.
 - Of these crude excess 301,400 deaths, 173,300 (57%) were related to COVID-19.
- After adjusting for changes in population structure, there were an estimated 217,900 excess deaths from March through August 2020, with 173,300 (80%) related to COVID-19 (Figure).
 - Diabetes, Alzheimer’s disease, and heart disease caused the most non-COVID-19 excess deaths.

Methods: Age-specific excess deaths in the US from March through August 2020 compared with 2015 to 2019 were estimated, accounting for changes in population size and age, using [provisional CDC data](#), [Underlying Cause of Death data](#), and [U.S. Census Bureau population estimates](#). Expected deaths were the number of deaths that would have occurred in 2020 if age-specific death rates were the same as in 2015 to 2019. **Limitations:** Provisional data are incomplete due to reporting lags, and excess deaths are likely underestimates.

Figure:



Note: Adapted from Shiels *et al.* Excess US total deaths, March to August 2020. Gray bars represent excess death estimates without adjustment for population changes, and **black** bars represent excess death estimates with adjustment for population changes. From Annals of Internal Medicine, Shiels *et al.*, Impact of population growth and aging on estimates of excess U.S. deaths during the COVID-19 pandemic, March to August 2020. Copyright © 2020 American College of Physicians. All Rights Reserved. Reprinted with the permission of American College of Physicians, Inc..

Implications for both studies (Faust *et al.* & Shiels *et al.*): After age adjustment, the majority of overall excess deaths in the U.S. in 2020 are related to COVID-19, which has impacted younger age groups as well.

Transmission

PEER-REVIEWED

[Evidence of long-distance droplet transmission of SARS-CoV-2 by direct air flow in a restaurant in Korea.](#) Kwon *et al.* Journal of Korean Medical Science (November 30, 2020).

SARS-CoV-2 is believed to be transmitted primarily through exposures to [respiratory droplets carrying the virus](#), following [close contact](#), typically defined as distances ≤ 6 feet and duration ≥ 15 minutes.

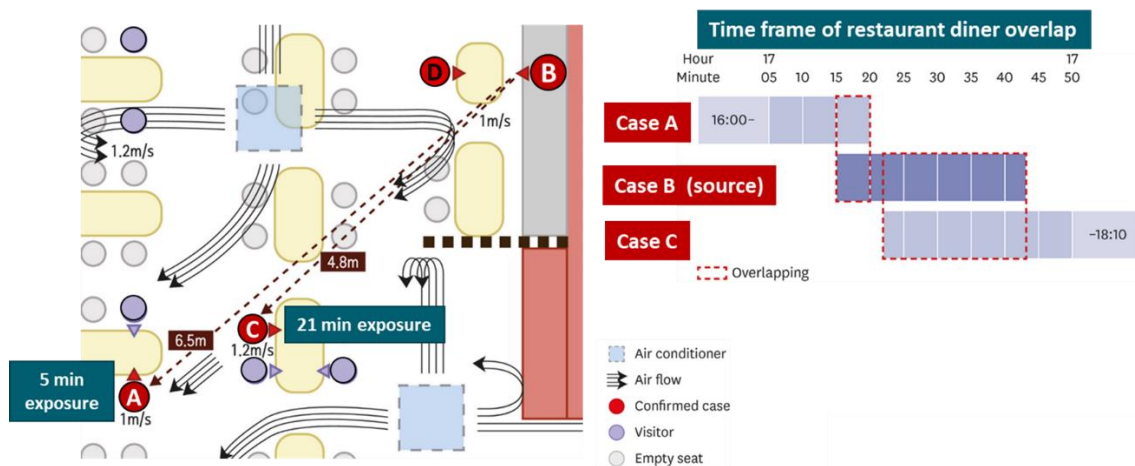
Key findings:

- An investigation revealed transmission of SARS-CoV-2 quickly at a distance >6 feet in a restaurant (Figure).
 - Case A overlapped with Case B, the source, for 5 minutes at a distance of 6.5 m (21 feet) (Figure).
 - Case C overlapped with Case B for 21 minutes at a distance of 4.8 m (16 feet) (Figure).
 - Only these 2 among 13 total unmasked staff and visitors were infected (attack rate 15.4%).
- Unlike other guests, Cases A and C were in the direct line of air flow from ceiling air conditioners (maximum 1.2 m/s) from source case B (Figure).

Methods: Epidemiologic and engineering investigations were used to identify cases and understand environmental exposures in an outbreak in Korea in June 2020. Researchers assessed closed-circuit television, table locations, timeline, and movement of cases and other people in the restaurant. Air speed and direction were measured by an anemometer. **Limitations:** Air flow measurements were simulations.

Implications: Droplet transmission can occur at ≥ 6.5 feet in a short time frame with direct air flow carrying the virus. Indoor spaces should have [proper ventilation](#) as well as physical distance and mask use to prevent transmission.

Figure:



Note: Adapted from Kwon *et al.* Schematic diagram of the outbreak restaurant equipped with ceiling-type air conditioners. The solid arrow streamlines represent the air flow directions. Curved air streamlines represent air from the ceiling air conditioners that is reflected from the wall or barrier toward the floor. The right panel shows the time of overlap of Case B with the two other cases (red dashed line). Case D was not infectious at the time of the event and was not considered in the investigation. Licensed under CC-BY.

[SARS-CoV-2 infection and transmission in educational settings: A prospective, cross-sectional analysis of infection clusters and outbreaks in England.](#) Ismail *et al.* Lancet Infectious Diseases (December 8, 2020).

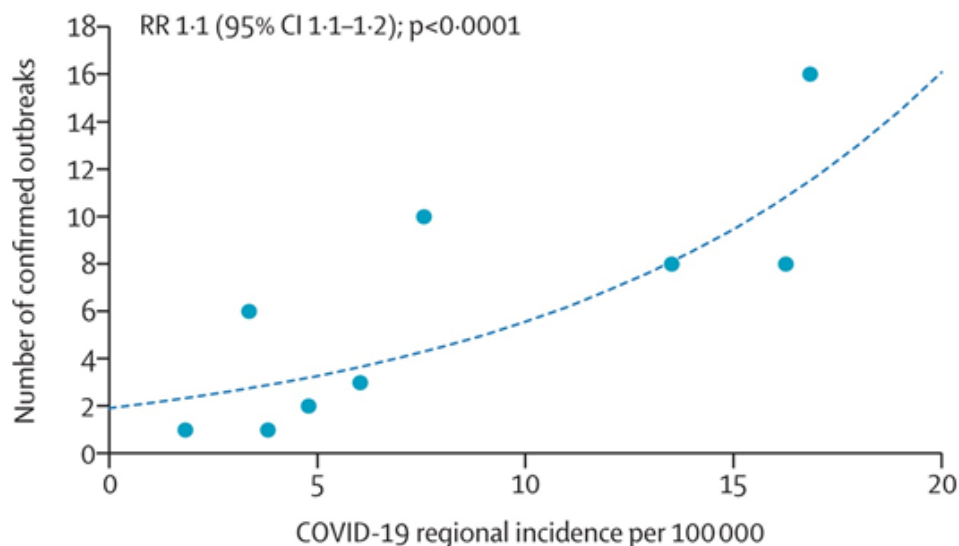
Key findings:

- The risk of SARS-CoV-2 infection in schools was low upon re-opening, and school-based outbreaks increased as the community incidence increased ($p < 0.0001$) (Figure).
- Staff had a higher incidence of SARS-CoV-2 than students and most cases linked to outbreaks were in staff members.
 - Of the 55 outbreaks, staff-to-staff transmission was most common (47%), followed by student-to-staff (29%), staff-to-student (15%), and student-to-student (9%).

Methods: Single case and outbreak data from a national database of schools and childcare settings in England from June 1 to July 17, 2020 were used to assess the correlation of school infection rates with population data and community incidence. Case rates were calculated using SARS-CoV-2 RT-PCR-confirmed cases and negative binomial regression. **Limitations:** Generalizability; cross-sectional design shows correlation not causation.

Implications: The overall risk of SARS-CoV-2 infection among staff and students is thought to be low; however, as [Flasche and Edmunds](#) noted, children are often asymptomatic and their cases could be missed. The strong correlation between COVID-19 outbreaks in schools and regional incidence emphasizes the importance of controlling community transmission to protect schools and allow for safe re-openings.

Figure:



Note: Adapted from Ismail *et al.* The number of confirmed school outbreaks increased as the regional COVID-19 incidence increased. Reprinted from The Lancet Infectious Diseases, Ismail *et al.*, SARS-CoV-2 infection and transmission in educational settings: A prospective, cross-sectional analysis of infection clusters and outbreaks in England. Copyright 2020, with permission from Elsevier.

Protection in Healthcare and Non-healthcare Work Settings

PEER-REVIEWED

[Assessing the effectiveness of using various face coverings to mitigate the transport of airborne particles produced by coughing indoors.](#) Li *et al.* *Aerosol Science and Technology* (December 4, 2020).

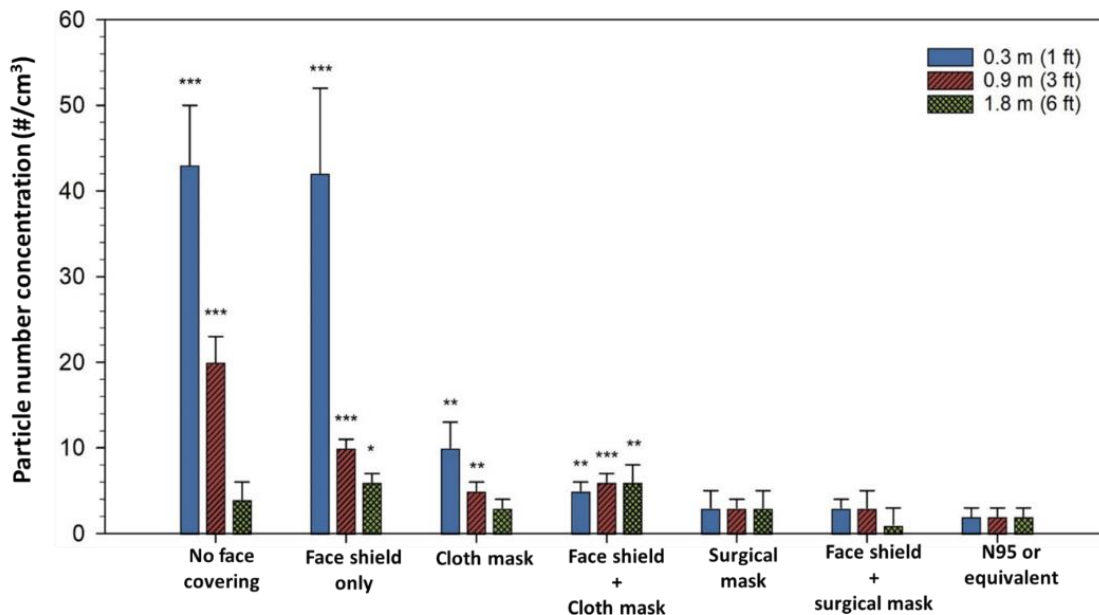
Key findings:

- The difference in concentrations of particles (PNC) detected when a volunteer coughed compared with background concentrations with no cough were impacted differently by various face coverings (Figure):
 - PNC increased approximately 40-fold after cough when using no covering or only a face shield.
 - PNC increased approximately 10-fold after cough using a cloth mask with or without a face shield.
 - PNC did not increase after cough when surgical masks or N95 respirators were used.
- 6 feet of distance reduced detected PNC as well as masks (Figure).

Methods: A volunteer coughed with and without a variety of face coverings, and cough-generated PNCs ranging from 0.01 to >1.0 μm , at 1, 3, and 6 feet away, were detected by an instrument indoors and compared to background with no coughing. **Limitations:** A single volunteer and setting; relationship between PNC and infectious SARS-CoV-2 dose unknown.

Implications: Cloth masks alone, but not face shields, were effective at reducing respiratory droplet spread, Surgical masks or N95 respirators were much more efficient. Data support recommendations to wear masks and maintain physical distance from others to prevent SARS-CoV-2 spread.

Figure:



Note: Adapted from Li *et al.* Background-subtracted particle number concentration (PNC) at 1, 3, and 6 feet away from a coughing volunteer under different face covering conditions. Error bars show the standard error of the mean. * $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$ compared with background PNC. Figure 2, Assessing the effectiveness of using various face coverings to mitigate the transport of airborne particles produced by coughing indoors. Li *et al.* *Aerosol Science and Technology*, reprinted by permission of The American Association for Aerosol Research, www.aaar.org.

Treatment

PEER-REVIEWED

The following paper evaluates if baricitinib, an inhibitor of immune and inflammatory responses given orally to treat moderate-to-severe rheumatoid arthritis, provides added benefit for COVID-19 treatment.

[Baricitinib plus remdesivir for hospitalized adults with COVID-19](#). Kalil *et al.* NEJM (December 11, 2020).

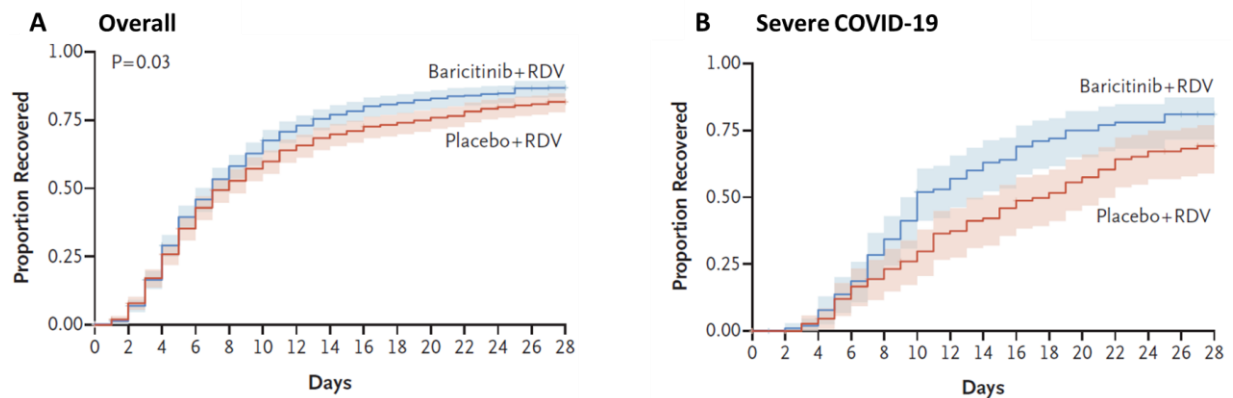
Key findings:

- COVID-19 patients receiving remdesivir (RDV) plus baricitinib compared with RDV plus placebo (control group) had:
 - Reduced recovery time (7 vs 8 days; RR 1.16, 95% CI 1.01-1.32, $p = 0.03$) (Figure).
 - Accelerated clinical improvements (OR 1.3, 95% CI 1.0-1.6).
 - Lower mortality at day 28 (5.1% vs.7.8%, HR 0.65, 95% CI 0.39-1.09).
 - Lower incidence of serious or nonserious adverse events ($p = 0.003$).
- The greatest improvement was seen in the most severe patients: 10-day recovery for RDV plus baricitinib compared with 18-day recovery for control group (Figure).

Methods: Double-blind, randomized, placebo-controlled trial (1:1 ratio) among 1033 patients across 8 countries. Patients were evaluated daily during hospitalization for 28 days. The primary outcome was time to recovery and the secondary outcome was status at day 15. **Limitations:** Unclear if benefits of baricitinib will be seen in patients receiving glucocorticoids

Implications: This study shows the data used by the FDA to grant an [EUA](#) for this treatment regimen on November 19, 2020.

Figure:



Note: Adapted from Kalil *et al.* Kaplan–Meier estimates of cumulative recovery across 28 days of the overall study population (A) and patients with severe COVID-19 receiving high-flow oxygen or noninvasive ventilation (B). RDV- remdesivir; shaded areas- 95% CI. From Kalil. Baricitinib plus remdesivir for hospitalized adults with COVID-19. NEJM. Copyright © 2020 Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.

Social, Behavioral, and Communication Science

PEER-REVIEWED

[Emergency preparedness and risk communication among African American churches: Leveraging a community-based participatory research partnership COVID-19 initiative.](#) Brewer *et al.* Preventing Chronic Disease (December 10, 2020).

The Fostering African American Improvement in Total Health (FAITH!) program is a partnership between the Mayo Clinic and 120 African American churches in the Minneapolis-St. Paul area. This article describes their community outreach efforts during the COVID-19 pandemic.

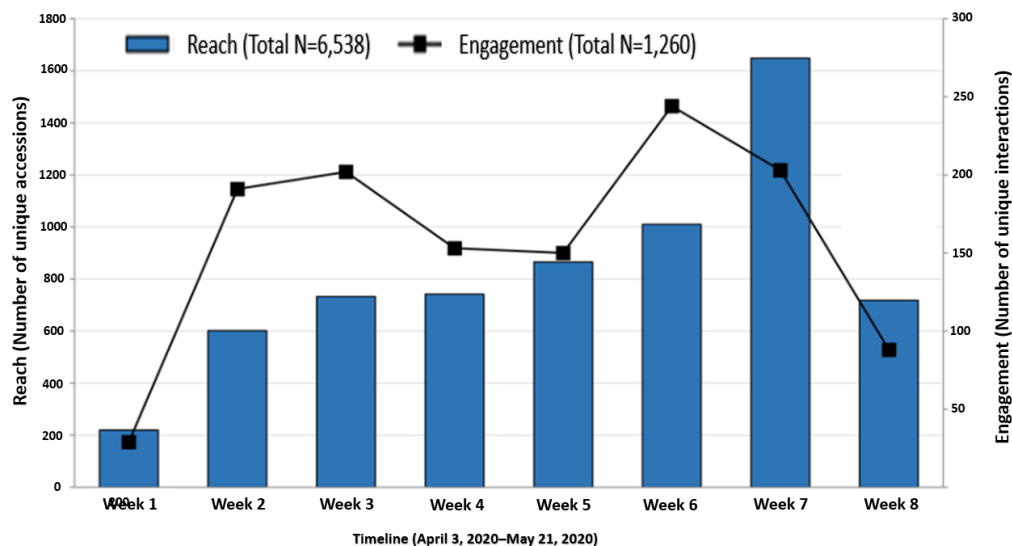
Key findings:

- Of 120 church leaders contacted, 32 (27%) responded to an emergency preparedness needs assessment and received an emergency preparedness kit.
- Social media engagement increased 8-fold in the first 7 weeks after implementation of COVID-19 community mitigation measures (Figure).
- Church leaders identified joint publications from the FAITH!/Mayo Clinic (n = 8), briefings by the Minnesota Governor (n = 8), and briefings by CDC (n = 7) as the most useful and reliable sources of information related to COVID-19.

Methods: In March 2020 a FAITH! COVID-19 Task Force was formed to develop emergency community preparedness plans. Task Force members disseminated emergency preparedness manuals, sent 230 email messages, and posted informative content on social media from April 3 to May 31, 2020. Evaluation looked at reach and engagement measured by unique persons viewing posts (“accessions”) or engaging in posts (with clicks, likes, *etc.*). **Limitations:** Generalizability to communities with less internet access.

Implications: Engaging trusted community leaders to create and deliver understandable messages could increase message visibility and adoption of recommendations in the event of an emergency such as the COVID-19 pandemic.

Figure:



Note: Adapted from Brewer *et al.* Facebook participation metrics of FAITH! COVID-19 Task Force’s weekly postings of emergency risk management messages during this 8-week project. Reach described **the number of unique accessions of the posting** while engagement refers to **the number of unique interactions**. Open access journal; all content freely available.

SARS-CoV-2 Vaccine Acceptance

High vaccine acceptance across society is crucial to attain coverage that would arrest transmission of SARS-CoV-2. Promoting acceptance requires identifying and reaching communities reluctant to vaccinate.

PREPRINTS (NOT PEER-REVIEWED)

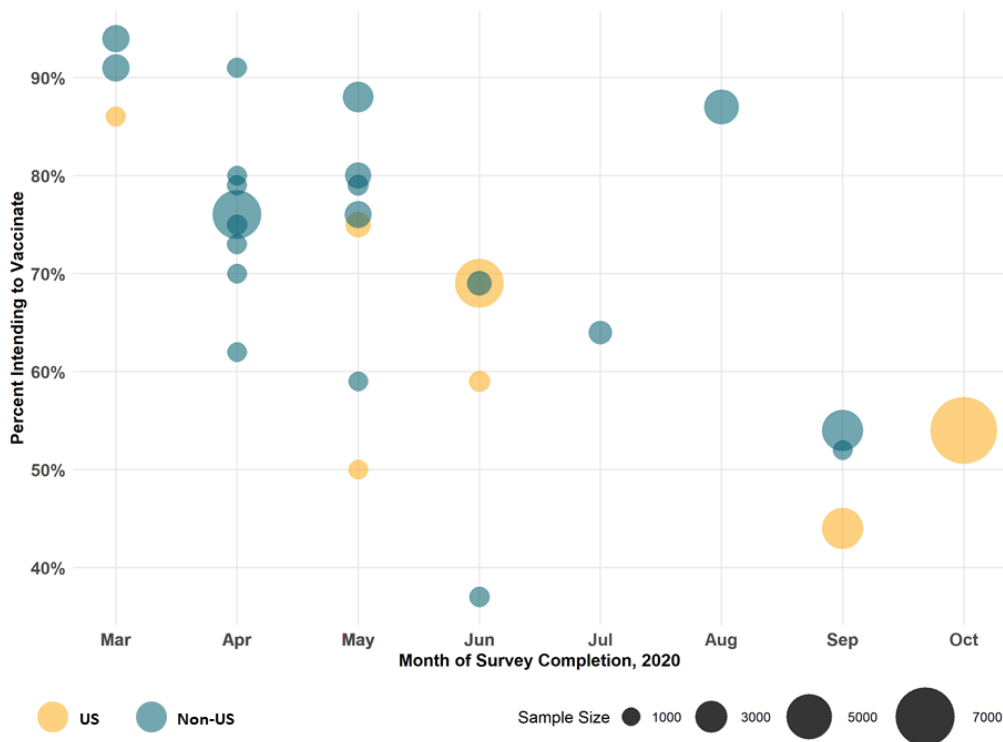
A. [International estimates of intended uptake and refusal of COVID-19 vaccines: A rapid systematic review and meta-analysis of large nationally representative samples.](#) Robinson *et al.* medRxiv (December 3, 2020).

Key findings:

- The general populations of 13 countries became less likely to vaccinate against SARS-CoV-2 from March to October 2020 (Figure).
 - From March to May 2020, 79% of respondents intended to vaccinate and 12% intended to refuse.
 - From June to October 2020, 60% of respondents intended to vaccinate and 20% intended to refuse.
- In the US, females, younger groups, people with lower income or education levels, and members of minority communities were less likely to vaccinate against SARS-CoV-2.

Methods: Nationally representative surveys including a question about intention or willingness to vaccinate were selected from databases for a systematic meta-analysis. 28 eligible articles from January to November 2020 captured 58,656 respondents from 13 countries. **Limitations:** Results largely relevant for North American and European populations.

Figure:



Note: Adapted from Robinson *et al.* Proportion of populations intending to vaccinate by country and time in **US** or **non-US** settings. Licensed under CC-BY.

B. [Intention of health care workers to accept COVID-19 vaccination and related factors: A systematic review and meta-analysis](#). Galanis *et al.* medRxiv (December 11, 2020).

Key findings:

- Of 8,847 healthcare workers (HCWs) surveyed across 11 studies, 5,354 (55.9%) indicated they intended to accept vaccination against SARS-CoV-2.
- Physicians reported greater vaccine acceptance (OR range: 1.59–7.76) in 5 studies compared to other healthcare professionals, such as nurses, paramedical staff, and pharmacists.

Methods: A meta-analysis of 11 studies that examined HCW intentions for vaccination. Eligible studies occurred between February and October 2020 in China, Democratic Republic of Congo, France, Greece, Hong Kong, Malta, Zambia, and the US. **Limitations:** HCWs may overstate acceptance because of social expectations; all studies were convenience samples; time trends not explored.

Combined implications for two summaries (Robinson *et al.* & Galanis *et al.*): Targeted messages, including towards healthcare workers, will be needed to improve acceptance of vaccines.

In Brief

Detection, Burden, and Impact

- Fitzpatrick *et al.* [Buyer beware: Inflated claims of sensitivity for rapid COVID-19 tests](#). Lancet. Highlights the importance of understanding the comparator used for sensitivity or percent positive agreement when evaluating new rapid diagnostic tests for SARS-CoV-2 infection.
- Rannan-Eliya *et al.* [Increased intensity of PCR testing reduced COVID-19 transmission within countries during the first pandemic wave](#). Health Affairs. RT-PCR testing intensity, defined as test-to-case ratio, was the most influential and significant ($p < 10^{-16}$) intervention to decrease the average reproduction number of SARS-CoV-2.
- Wurtzer *et al.* [Evaluation of lockdown effect on SARS-CoV-2 dynamics through viral genome quantification in waste water, Greater Paris, France, 5 March to 23 April 2020](#). Eurosurveillance. Early in the epidemic, wastewater surveillance of SARS-CoV-2 was sensitive enough to detect virus even with <10 hospitalizations of COVID-19 reported to surveillance systems.

Transmission

- Bulfone *et al.* [Outdoor transmission of SARS-CoV-2 and other respiratory viruses, a systematic review](#). Journal of Infectious Diseases. Analysis of 12 studies of respiratory infections suggest a lower but not zero risk of infection in outdoor settings, and relaxed mitigation efforts when outdoors may nullify this generally lower risk of infection.

Natural History of SARS-CoV-2: Spectrum and Clinical Course

- Owusu *et al.* [Characteristics of adults aged 18-49 years without underlying conditions hospitalized with laboratory-confirmed COVID-19 in the United States, COVID-NET - March-August 2020](#). Clinical Infectious Diseases. 22% of 513 younger adults without underlying medical conditions who were hospitalized with COVID-19 were admitted to ICU, 10% required mechanical ventilation, and 0.6% of patients died; study area covers approximately 10% of the US population.

- Lechner *et al.* [Course of symptoms for loss of sense of smell and taste over time in one thousand forty-one healthcare workers during the COVID-19 pandemic: Our experience](#). Clinical Otolaryngology. Nearly two-thirds of surveyed health care workers experienced sudden loss of smell or taste, and there was a strong correlation between loss of smell or taste and being diagnosed with COVID-19.
- Peckham *et al.* [Male sex identified by global COVID-19 meta-analysis as a risk factor for death and ICU admission](#). Nature Communications. A meta-analysis over 3 million reported global cases of COVID-19 showing that male patients have higher odds of admission to intensive care and death compared with female patients, despite having similar rates of COVID-19.

Natural History of SARS-CoV-2: Re-infection and Sequelae

- Arnold *et al.* [Patient outcomes after hospitalisation with COVID-19 and implications for follow-up: Results from a prospective UK cohort](#). Thorax. At 8-12 weeks post-admission, 74% of COVID-19 survivors had persistent symptoms and limitations in reported physical ability, and 35% had abnormalities in chest radiograph, exercise tests, blood tests and spirometry.
- Selhorst *et al.* [Symptomatic SARS-CoV-2 reinfection of a health care worker in a Belgian nosocomial outbreak despite primary neutralizing antibody response](#). Clinical Infectious Diseases. Reinfection of a 39-year-old immunocompetent health care worker with SARS-CoV-2 after an interval of 185 days was confirmed by genetic analysis showing that the two infections belonged to different SARS-CoV-2 clades; reinfection occurred despite a robust humoral response during the first infection.

Protection: Effectiveness of PPE

- Clapp *et al.* [Evaluation of cloth masks and modified procedure masks as personal protective equipment for the public during the COVID-19 pandemic](#). JAMA Internal Medicine. The filtration efficiencies of consumer grade masks averaged about 50% and varied widely by fabric (nylon>cotton) and tightness of fit; surprisingly, washing a 2-layer nylon mask increased the filtering efficiency from 56.3% to 79%.

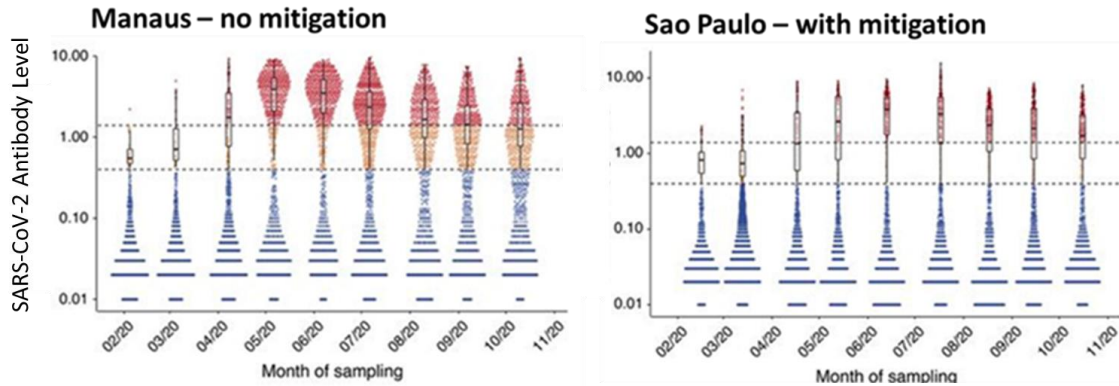
Protection: Strategies to Reduce Transmission

- Bluysen *et al.* [The effect of a mobile HEPA filter system on 'infectious' aerosols, sound and air velocity in the SenseLab](#). Building and Environment. A mobile HEPA filter system substantially decreased the number of particles when placed in front of a subject and may be a useful option if no ventilation is available, but the noisiness of the machine may be unacceptable to users.

Prevention, Mitigation, and Intervention Strategies

- Voysey *et al.* [Safety and efficacy of the ChAdOx1 nCoV-19 vaccine \(AZD1222\) against SARS-CoV-2: An interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK](#). Lancet. The adenoviral vector vaccine ChAdOx1 nCoV-19 had overall efficacy of 70.4% in preventing symptomatic COVID-19 and was associated with a low risk of adverse events. An [accompanying editorial by Knoll and Wonodi](#) describes how this vaccine has advantages for global distribution.
- Swan *et al.* [Vaccines that prevent SARS-CoV-2 transmission may prevent or dampen a spring wave of COVID-19 cases and deaths in 2021](#). medRxiv. Models the impact of vaccine on transmission based on how much the vaccine reduces infection and transmission of SARS-CoV-2 versus reducing symptomatic disease alone.

- Buss *et al.* [Three-quarters attack rate of SARS-CoV-2 in the Brazilian Amazon during a largely unmitigated epidemic](#). *Science*. The absence of mitigating measures in Manaus, the capital of Amazonas state of Brazil with a population of >2 million, led to widespread infection with an estimated 76% attack rate based on antibody levels in the community, compared to a 29% attack rate in neighboring Sao Paulo, with measures.



Note: Adapted from Buss *et al.* Population-level antibody levels (negative, intermediate, and high) in Manaus (Brazilian Amazon) and the neighboring city of Sao Paulo over the course of the COVID-19 pandemic. Licensed under CC-BY 4.0.

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