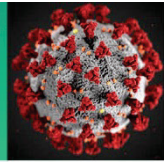


COVID-19 Science Update



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> ***

Modeling & Transmission: Bending the Curve

In the absence of a vaccine and therapeutics, population-based policies remain critical to reduce COVID-19 transmission. Social distancing has previously been used to slow the spread of communicable diseases, and science on the importance of this population-based policy in the context of SARS-CoV-2 continues to grow. The following two studies shed light on this topic.

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[Cluster of coronavirus disease associated with fitness dance classes, South Korea](#). Jang *et al.* Emerging Infectious Diseases (May 15, 2020).

Key findings:

- Of 217 adult students who participated in high-intensity aerobic dance classes across 12 facilities, 57 (26%) were infected with SARS-CoV-2 from contact with instructors.
- Classes where transmission occurred typically included 5–22 people in a 645 square-foot room (about the size of a 3-car garage) for 50 minutes.
 - No cases observed in classes with <5 participants.
- No students who took low-intensity classes (Pilates and yoga) from an infected instructor tested positive for SARS-CoV-2.

Methods: Contact tracing study in Cheonan, South Korea from February 15 to March 9, 2020. **Limitations:** Unclear whether any transmission occurred from instructors while presymptomatic.

[Strong social distancing measures in the United States reduced the COVID-19 growth rate.](#)

Courtemanche *et al.* Health Affairs (May 14, 2020).

Key findings:

- A combination of 4 social distancing measures in the US reduced the COVID-19 daily growth rate by 5% after 1–5 days, 7% after 6–10 days, 8% after 11–15 days, and 9% after 16–20 days.
- Without implementation of these measures, modelers estimated that COVID-19 cases would have been about 35 times higher than the observed number on April 27, 2020 (35,257,098 vs 978,047).
- Shelter in place orders and the closure of restaurants, bars, gyms, or other entertainment centers were the most effective measures to reduce the case growth rate compared with bans on large social gatherings (500+ people) and public school closures (Figures 1 & 2).

Methods: Analysis of the daily confirmed COVID-19 case growth rate in all US counties after the implementation of four government-imposed social distancing measures between March 1 and April 27, 2020. The model used event-study regression with multiple treatments and fixed effects for population density and resident's education,

political orientation, and age. *Limitations:* Underestimation of asymptomatic and mild cases and those not able to be tested; differences in case reporting practices by county were not accounted for in the model.

Figure 1

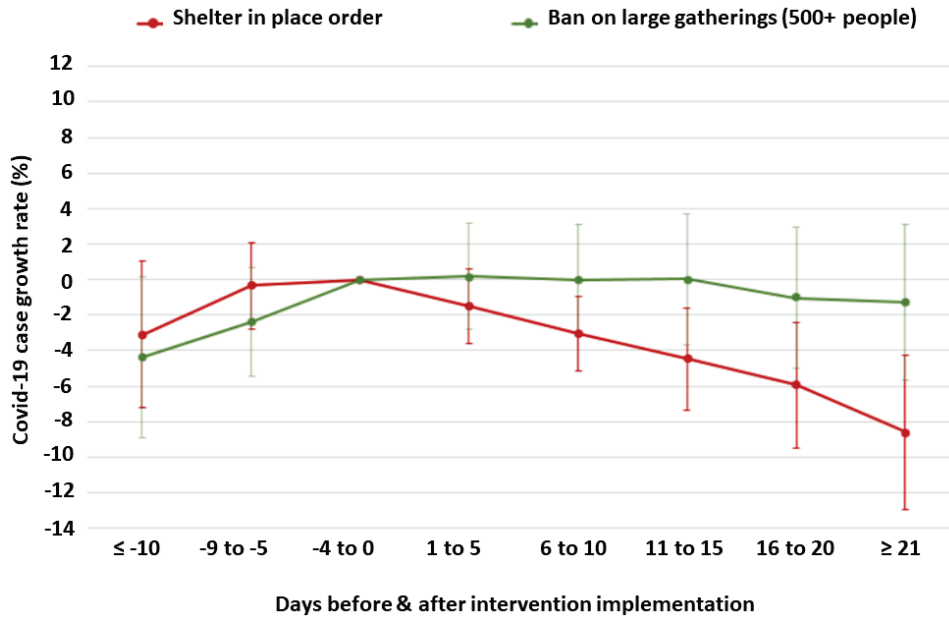
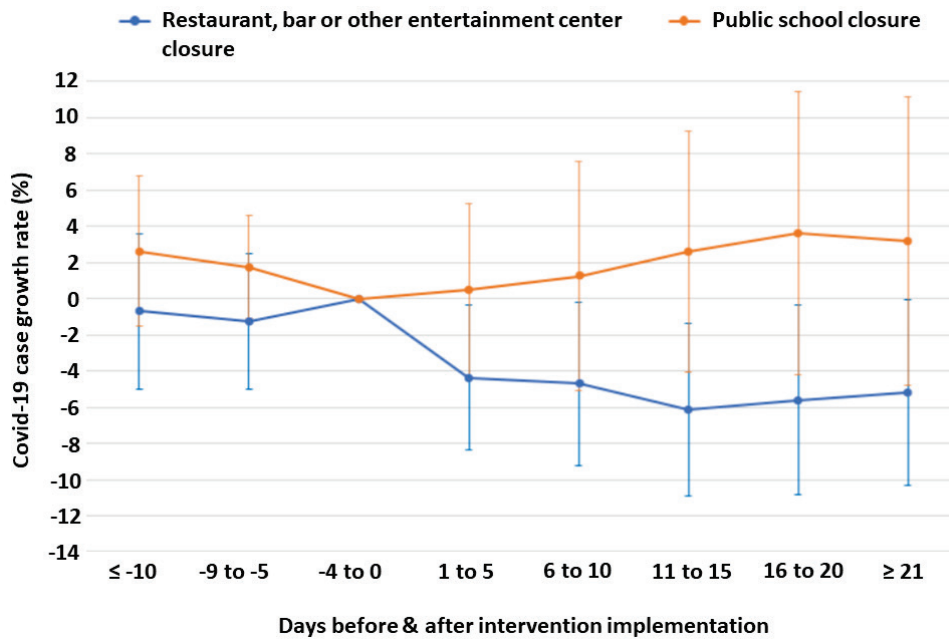


Figure 2



Note: Adapted from Courtemanche *et al.* Estimates of COVID-19 case growth rate change before and after the implementation of four government imposed social distancing measures. **Figure 1: shelter in place order** compared with **bans on large gatherings**. **Figure 2: restaurant, bar or other entertainment center closure** compared with **public school closure**. Used by permission from publisher.

Implications of 2 studies (Jang *et al.* & Courtemanche *et al.*): Social distancing measures can slow SARS-CoV-2 transmission. As restrictions are relaxed, it will be important to monitor possible transmission during various activities, including high-intensity aerobic exercise in enclosed spaces, even in small groups.

Clinical Treatment & Management

PEER-REVIEWED

[Use of prone positioning in nonintubated patients with COVID-19 and hypoxemic acute respiratory failure.](#) Elharrar *et al.* JAMA (May 15, 2020).

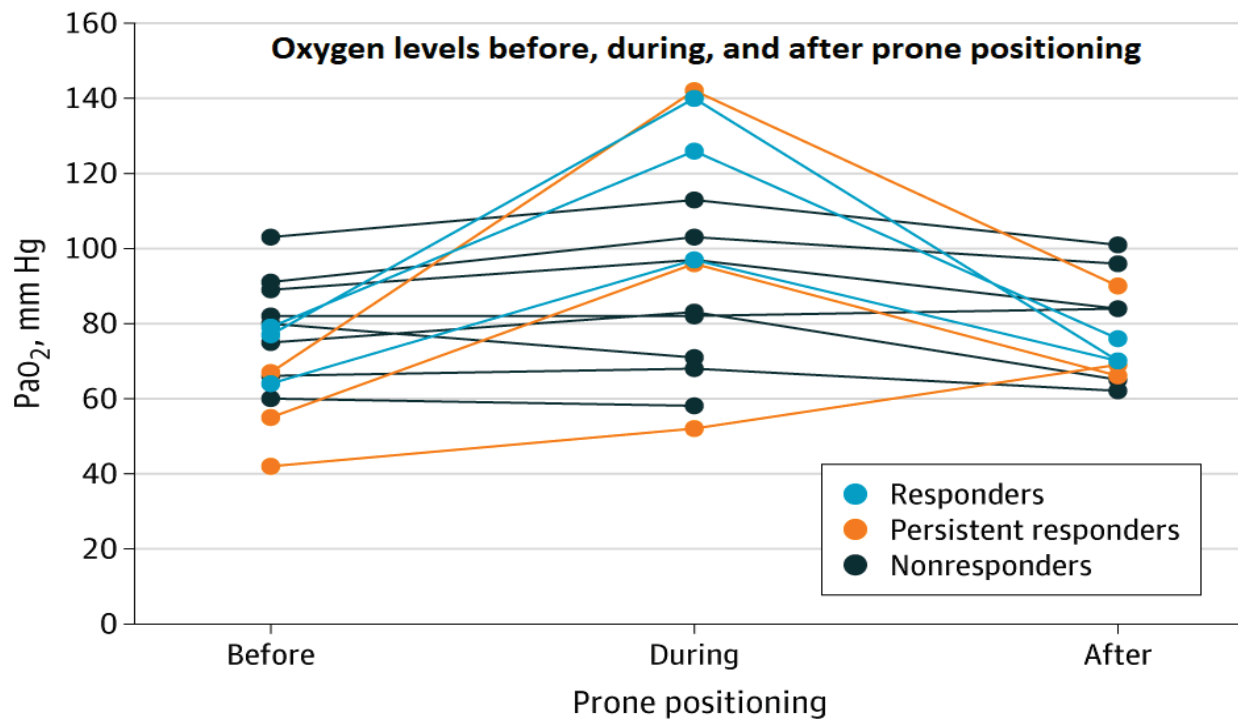
Key findings:

- Among 24 hospitalized, nonintubated COVID-19 patients requiring oxygen, 15 (63%) tolerated face-down (prone) positioning for >3 hours.
- 6 (25%) patients had $\geq 20\%$ increase in oxygen level during prone positioning (Responders) (Figure).
 - 3 (13%) had a persistent increase in oxygen level after being returned to the face-up position for 6–12 hours (Persistent Responders).

Methods: Prospective, single-hospital study of 24 patients with COVID-19 who required oxygen, but not intensive care. Oxygen level measured before, during, and after prone positioning. Response to prone positioning defined as $\geq 20\%$ increase in partial pressure of arterial oxygen (PaO₂). **Limitations:** Single center; small sample.

Implications: Prone positioning is commonly used for intubated, sedated patients and may benefit a subset of non-intubated COVID-19 patients. Further research on this issue is needed, and a clinical trial is underway.

Figure:



Note: Adapted from Elharrar *et al.* Individual partial pressure of arterial oxygen (PaO₂) variation among patients who sustained prone positioning for >3 hours. **Responders** had a PaO₂ increase $\geq 20\%$ during prone positioning. **Persistent responders** maintained a PaO₂ increase $\geq 20\%$ at least 6-12 hours after completing prone positioning. **Nonresponders** had a PaO₂ increase $< 20\%$ during prone positioning. Reproduced with permission from JAMA. doi:10.1001/jama.2020.8255. Copyright©2020 American Medical Association. All rights reserved.

Immunity Against Reinfection

B cells and T cells protect the body from repeated attacks by pathogens, including viruses. B cells make antibodies that coat viruses and neutralize their ability to infect cells. T cells recognize infected cells and either kill the cell (killer T cells) or help other immune cells fight infection (helper T cells). However, little is known about the human immune response to SARS-CoV-2. The following four studies shed light on this topic.

PREPRINT (NOT PEER-REVIEWED)

A. [Convergent antibody responses to SARS-CoV-2 infection in convalescent individuals.](#) Robbiani *et al.* bioRxiv (May 22, 2020). [Published](#) in Nature (June 18, 2020).

Key findings:

- Blood samples from 149 COVID-19 patients contained varying levels of antibodies able to neutralize virus and protect cells from infection with SARS-CoV-2.
- Neutralizing activity was strongest in patients who recovered from severe COVID-19.

Methods: Blood was collected from 149 people who had recovered from COVID-19, an average of 39 days after onset of symptoms and ≥ 14 days after symptom resolution. Antibodies reactive against SARS-CoV-2 were quantified with ELISA. Neutralizing activity was measured with pseudotyped virus assays. **Limitations:** Laboratory study; in vivo immunity against reinfection in patients recovered from COVID-19 not assessed.

PEER-REVIEWED

B. [Targets of T cell responses to SARS-CoV-2 coronavirus in humans with COVID-19 disease and unexposed individuals](#) Grifoni *et al.* Cell (May 14, 2020).

Key findings:

- Among 10 people who recovered from COVID-19, 7 (70%) had killer T cells and 10 (100%) had helper T cells specific to SARS-CoV-2, including the viral spike protein.
- 6 of 11 (55%) unexposed healthy controls also had SARS-CoV-2-specific helper T cells, consistent with cross-reactive T cell recognition possibly from prior infection with “common cold” coronaviruses.

Methods: Blood was collected from 20 adults who had recovered from COVID-19, 20–35 days after symptom onset and ≥ 14 days after symptom resolution. T helper and killer cells in samples from recovered COVID-19 patients and 11 healthy donors (collected before the COVID-19 pandemic) were tested for reactivity to SARS-CoV-2. **Limitations:** Small sample size; laboratory study; in vivo immunity to reinfection with SARS-CoV-2 not assessed.

PREPRINT (NOT PEER-REVIEWED)

C. [Presence of SARS-CoV-2-reactive T cells in COVID-19 patients and healthy donors.](#) Braun *et al.* medRxiv (April 22, 2020). [Published](#) in Nature (July 29, 2020).

Key findings:

- 15 of 18 (83%) COVID-19 patients with varying disease severity and 23 of 68 (34%) SARS-CoV-2 seronegative healthy donors had helper T cells specific to SARS-CoV-2; the latter finding may be consistent with cross-reactive T cell recognition from prior infection with “common cold” coronaviruses.

Methods: Helper T cells in blood samples collected from 18 patients with mild to critical COVID-19 and 68 healthy controls were tested for reactivity to SARS-CoV-2 spike protein. **Limitations:** Presence of killer T cells not

determined; time from symptom onset to sampling (time available to mount an immune response) was shorter for COVID-19 patients with critical compared with mild or moderate disease (range 2–11 vs 5–39 days).

PEER-REVIEWED

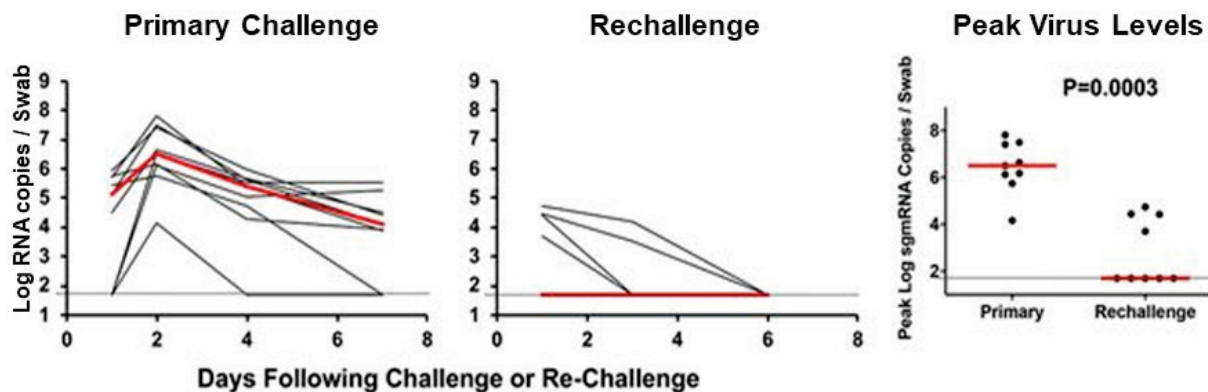
D. SARS-CoV-2 infection protects against rechallenge in rhesus macaques. Chandrashekar *et al.* *Science* (May 20, 2020).

Key findings:

- 9 rhesus macaques inoculated with SARS-CoV-2 developed pneumonia, high viral loads, neutralizing antibody, and cellular immunity.
 - All 9 rhesus macaques recovered.
- Upon rechallenge, the animals exhibited a robust increase in SARS-CoV-2-specific antibodies with rapid clearance of virus (Figure).

Methods: 9 rhesus macaques (monkeys) infected with SARS-CoV-2; humoral and cellular immune responses were examined; on day 35, all were rechallenged. **Limitations:** There are differences between SARS-CoV-2 infection in rhesus macaques and humans (e.g., rhesus macaques do not develop respiratory failure or die from SARS-CoV-2 infection); studies are needed to determine if SARS-CoV-2 infection leads to subsequent immunity in humans.

Figure:



Note: Adapted from Chandrashekar *et al.* Comparison of viral RNA from lung fluid following initial infection and rechallenge. Red bar is median viral load. Licensed under CC-BY 4.0.

Implications of 4 studies (Robbiani *et al.*, Grifoni *et al.*, Braun *et al.* & Chandrashekar *et al.*): Most people with COVID-19 develop neutralizing antibodies and helper T cells specific for SARS-CoV-2 that may help prevent reinfection. Similar defenses prevented reinfection of rhesus macaques with SARS-CoV-2. Studies are underway to ascertain whether a similar protective effect of natural infection with SARS-CoV-2 occurs in humans, which can help inform vaccine development.

COVID-19 and the GI System

The gastrointestinal (GI) system is often affected during COVID-19. The following two articles provide insight about the predictive value of combinations of symptoms and the prevalence of GI complications.

PEER-REVIEWED

[Are gastrointestinal symptoms specific for COVID-19 infection? A prospective case-control study from the United States.](#) Chen *et al.* *Gastroenterology* (May 12, 2020).

Key findings:

- GI symptoms were more common among people who tested positive (74%) than negative (53%) for SARS-CoV-2.
- Combinations of symptoms were more predictive of COVID-19 than individual symptoms, with specificities (ability to correctly identify those without the disease) of 94%-99%.
 - 88% of those with a combination of 5 symptoms (fever, diarrhea, loss of smell, taste, & appetite) tested positive for SARS-CoV-2; however, this suite of symptoms was seen in only one-quarter of people with confirmed COVID-19 (n = 24) (Figure).

Methods: Telephone survey of 340 adults tested for SARS-CoV-2 by NP swab RT-PCR (positive, 101; negative, 239) in one hospital; determined likelihood of combinations of COVID-19-related symptoms to predict presence (positive predictive value) or absence (negative predictive value) of infection with SARS CoV-2. **Limitations:** Timing of symptoms in relation to testing and diagnosis was unclear; mostly outpatients with mild to moderate symptoms.

Figure:

	n = 24	n = 29	n = 31	n = 42	n = 50	n = 52
Fever	✓	✓	✓	✓	✓	✓
Loss of smell	✓	✓	✓	✓	✓	
Loss of taste	✓	✓	✓	✓		✓
Diarrhea	✓	✓				
Loss of appetite	✓		✓			
Sensitivity	21%	25%	24%	33%	37%	38%
Specificity	99%	98%	97%	96%	95%	94%
PPV	88%	86%	77%	79%	74%	73%
NPV	75%	76%	75%	77%	78%	78%

Note: Adapted from Chen *et al.* Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of combinations of GI and non-GI symptoms for COVID-19. Each colored row denotes a different symptom. This article was published in *Gastroenterology*, Vol 159, Chen *et al.*, Are gastrointestinal symptoms specific for COVID-19 infection? A prospective case-control study from the United States, Page 1161-1163.e2, Copyright the AGA Institute 2020. This article is currently available at the Elsevier COVID-19 resource center: <https://www.elsevier.com/connect/coronavirus-information-center>.

[Gastrointestinal complications in critically ill patients with COVID-19.](#) Kaafarani *et al.* *Annals of Surgery* (May 1, 2020).

Key findings:

- 45% of 141 COVID-19 ICU patients had GI symptoms (e.g., abdominal pain, diarrhea, vomiting) on admission and 104 (74%) developed at least one GI complication while hospitalized, of whom:
 - 67% had abnormal liver function tests.
 - 56% had intestinal paralysis, 5% needed surgery, 3% had patches of dead bowel with SARS-CoV-2-induced small vessel thrombosis or bowel nerve injury proposed as possible causes of the injury (Figure).

Methods: 141 ICU patients with SARS-CoV-2 infection between March 13 and April 12, 2020 at one hospital in Massachusetts. **Limitations:** Case series; drug effects and metabolic and electrolyte disturbances in critically ill patients may have contributed to the findings.

Figure:



Note: from Kaafarani *et al.* ([Supplementary Appendix](#)) Diffuse yellowish areas of dead small bowel and colon. Available via Wolters Kluwer Public Health Emergency Collection through PubMed Central.

Implications of both studies (Chen *et al.* & Kaafarani *et al.*): Clinicians can recognize COVID-19 earlier, and respond appropriately to adverse events, by being alert to common GI symptoms and complications that have occurred among COVID-19 patients.

In Brief

- Lapolla *et al.* [Deaths from COVID-19 in healthcare workers in Italy - What can we learn?](#) *Infection Control & Hospital Epidemiology*. Examines COVID-19 health care worker deaths by category and medical specialty in Italy.
- Senghore *et al.* [Leveraging Africa's preparedness towards the next phase of the COVID-19 pandemic.](#) *Lancet Global Health*. Proposed mitigation strategies for resource-poor settings.
- Brown-Johnson *et al.* [PPE portraits-a way to humanize personal protective equipment.](#) *Journal of General Internal Medicine*. A way to humanize PPE by placing provider's photo on PPE.

- Ippolito *et al.* [Facepiece filtering respirators with exhalation valve should not be used in the community to limit SARS-CoV-2 diffusion](#). Infection Control & Hospital Epidemiology. Reminder that respirators with an exhalation valve will not be an effective means of source control.
- Cantwell M. [Watch the coronavirus' rampage through the body](#). Science. 4-minute video that demonstrates the pathogenesis of SARS CoV-2 infection throughout the entire body.
- West *et al.* [Applying principles of behaviour change to reduce SARS-CoV-2 transmission](#). Nature Human Behavior. How to enact behavior change in a time COVID-19? This is a discussion of the importance of developing and evaluating interventions to promote effective behavior change.
- Brewster *et al.* [Steam inhalation and paediatric burns during the COVID-19 pandemic](#). Lancet. Report of 30-fold increase in scald injuries in children based on the misconception that steam inhalation is beneficial in preventing and treating respiratory tract symptoms.
- Shaffer L. [15 drugs being tested to treat COVID-19 and how they would work](#). Nature Medicine. Listing of 15 drugs being examined as potential treatments for COVID-19.
- Berlin *et al.* [Severe COVID-19](#). NEJM. Discussion of the clinical management of severe COVID-19.
- Krammer *et al.* [Serology assays to manage COVID-19](#). Science. Discussion of serologic assays to measure antibodies to SARS CoV-2.
- Shumway *et al.* [Monitoring returning travelers during the early weeks of the COVID-19 pandemic: one US county's experience](#). American Journal of Public Health. Experience of San Bernardino County, CA in screening returning travelers for SARS-CoV-2.
- Faust *et al.* [Assessment of deaths from COVID-19 and from seasonal influenza](#). JAMA Internal Medicine. Comment on comparisons of SARS-CoV-2 mortality and seasonal influenza mortality.

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