

## COVID-19 DIGEST

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### *From the Cross-Campus Infectious Diseases COVID-19 Task Force*

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## EPIDEMIOLOGY

### LOCAL

As of today, **6,423 positive cases** and **58 deaths** have been reported in [San Francisco](#) with an average of 98 new cases diagnosed per day over the last 7-days. As of July 27, a record high of 112 patients were hospitalized across the city, including 5 transfers from outside of San Francisco. [California](#) now reports **485,372 confirmed COVID-19 cases** and **8,913 deaths**, the [positive test rate statewide](#) is stable at 7.5% over the last week, and as of July 27 6,896 persons were [hospitalized statewide](#), down slightly from a peak of 7,170 hospitalized patients with COVID-19 on July 21. Cases are surging in the 8 counties that make up the [Central Valley](#) (Fresno, Kern, Kings, Madera, Merced, San Joaquin, Stanislaus, Tulare), with over 16,500 infections reported in the last week alone and positive test rates ranging from 11% - 18%. On Monday Governor Newsom [announced additional resources](#) for testing and enabling effective quarantine would be directed towards these counties. Locally and statewide, glaring disparities continue to characterize the COVID-19 burden with the Latinx community being disproportionately affected.

### NATIONAL

The United States continues as the global epicenter of the COVID-19 pandemic with over **4.3 million reported cases** of COVID-19 and more than **150,000 deaths** across the United States. However, there are some signs that the case growth may be starting to plateau as the average cases added per day is currently 61,660 cases [over the last 5 days](#), a decrease for the first time since June. The majority of new cases continue to be reported from California, Florida, and Texas, and while there are some signs that new infections are starting to plateau in these hotspots, new reported cases [increased the most](#) in Oklahoma and Missouri and Ohio. Indiana, Kentucky, and Tennessee all reported concerning increases in test positivity over the last week. Nationally, deaths from COVID-19 have continued to increase over the last 3 weeks and on Tuesday [more than 1,300 deaths](#) were reported and 6 states (Florida, California, Texas, Arkansas, Montana, Oregon) [reported single-day highs](#). Amid the raging pandemic, professional sports leagues are attempting to resume play. Last Thursday Anthony Fauci threw the [first pitch](#) for the Washington Nationals on Major League Baseball's opening day. His pitch may have socially distanced from home plate, but a limited edition Topps baseball card commemorating the event [quickly became a best-seller](#) with more than 51,500 copies sold within 24 hours. On Monday, after playing the Phillies on Sunday evening, the Miami Marlins [announced](#) 12 players and staff were infected with COVID-19 (up to [18 as of Wednesday](#)). The Phillies' scheduled game against the Yankees on Tuesday has been postponed and the Marlins continue to quarantine in Philadelphia. The NBA is scheduled to restart their season on July 30 in a "bubble" created in Orlando, Florida. On Wednesday the NBA announced that [no players](#) had tested positive over the last 9 days of daily testing. The NHL, which is also attempting to complete the 2019 season in a "bubble", also announced [no new cases](#) over the last week of testing. The NFL is scheduled to start the 2020 season in September however many players are already [choosing to opt-out](#).

### GLOBAL

[Worldwide](#) there are currently over **16.8 million** reported cases of COVID-19 and **over 662,000 deaths**. The United States (4.3 million cases), Brazil (2.5 million cases), and India (1.5 million cases) lead the world. The [trajectories](#) of new cases continue to rise steeply in Brazil and India where over 60% and 12% of tests return positive respectively.

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## UP TO THE MINUTE DISPATCHES

### **Developing a safe, effective, inexpensive, easy to produce, and widely available vaccine is the holy grail to contain/end the SARS-CoV-2 pandemic**

An ideal vaccine would require no more than 2 vaccinations, protect vulnerable populations (older adults, those with comorbidities), confer protection for > 60 months, and reduce transmission. Over 120 vaccines are in development and recently promising Phase 1 results of 2 vaccine candidates were reported. [The first report](#) was a dose-escalation, open trial including 45 healthy adults aged 18-55 years who received 2 vaccinations, 28 days apart with 3 concentrations of an mRNA encoding a stabilized pre-fusion SARS-CoV-2 spike protein. A dose-dependent antibody response was observed, and after the 2<sup>nd</sup> vaccination, serum-neutralizing activity was detected in all participants, on par with the activity seen in convalescent serum isolated from SARS-CoV-2 patients. Adverse effects were reported in >50% participants, but no trial-limiting safety concerns occurred. In a [study](#) of non-human primates, this vaccine was effective at reducing viral replication and preventing clinical disease. The [second report](#), from the Oxford COVID Vaccine Trial Group, was a phase 1-2 single-blind randomized trial of a chimpanzee adenoviral vector vaccine expressing the SARS-CoV-2 spike protein. This vaccine had previously been proven immunogenic and protective against COVID-19 pneumonia in monkey, and in this trial was compared against a meningococcal conjugate vaccine as a control. No serious adverse events were reported in the COVID-19 arm. The humoral response to SARS-CoV-2 spike protein peaked at day 28, cellular responses were present in all participants by day 14, and neutralizing antibodies were induced in all participants after a 2<sup>nd</sup> vaccine dose. A similar safety and immunogenicity response was reported by the related CanSino biologics adenovirus vaccine trialed in China. **Conclusion:** Two vaccines against COVID-19 have elicited anti-SARS-CoV-2 immune responses in all participants without major safety concerns. Phase 3 trials are beginning.

### **RECOVERY trial: Dexamethasone as a mortality-decreasing therapeutic for COVID-19**

The RECOVERY trial, a large open-label, pragmatic, randomized, controlled trial in the UK comparing a range of possible treatments in those hospitalized with COVID-19, recently published a preliminary [report](#) analyzing dexamethasone outcomes. 2,104 patients received dexamethasone—6mg daily for up to 10 days—while 4321 patients received usual care. Overall, 22.9% of patients in the dexamethasone group versus 25.7% in the usual care group died within 28 days after randomization, the primary outcome. The incidence of death was significantly lower in the dexamethasone group for those who were intubated (29.3% vs. 41.4%) and for those receiving any form of oxygen therapy (23.3% vs. 26.2%). No benefit was found in patients receiving no respiratory support (17.8% vs. 14.0%). Limitations of this study include lack of information about the 1948 patients excluded and that all patients requiring supplemental oxygen who were not-mechanically ventilated were grouped in the analysis. Patients in this study did not receive remdesivir. **Conclusion:** Dexamethasone should be administered to hospitalized patients with COVID-19 requiring invasive mechanical ventilation, non-invasive ventilation, or high-flow nasal cannula. Given the increased mortality benefit in mechanically ventilated patients, dexamethasone should be considered in those outside the ICU with more severe respiratory compromise and higher oxygen need, such as patients on nasal cannula with persistently low oxygen saturation and requiring substantial supplemental oxygen (e.g.  $\geq 3\text{-}4\text{L O}_2$ ) or whose trajectory suggests increasing disease severity. More granular data on dexamethasone impact by oxygen requirement are needed. Patients who do not require supplemental oxygen should not receive dexamethasone for COVID-19. Factors to consider in determination of whether to withhold (or stop) steroids include uncontrolled invasive fungal infections, uncontrolled hyperglycemia, existing delirium, and other immunosuppressive medications. Use in pregnant patients should be discussed with OB/MFM as dexamethasone crosses the placenta. Remdesivir continues to be recommended for patients with hypoxia and COVID-19, and there is no contraindication with the use of dexamethasone. Further studies are needed to understand the potential added benefit of remdesivir and dexamethasone.

### **Is “cytokine storm” an appropriate term to describe the inflammatory response in patients with COVID-19?**

A recent [article](#) reported the results of plasma levels multiple cytokines (IL-1b, IL-1RA, IL-6, IL-8, IL-18 and TNFa) among four patient groups: 1) moderate COVID-19 (not admitted to the ICU, n=6); 2) severe COVID-19 (admitted to the ICU, n=9. 6 requiring mechanical ventilation); 3) non-COVID-19 ARDS (n=12); 4) sepsis (n=16). They found no significant

differences in the levels of these plasma cytokines among any of the groups. There was a trend for higher levels of IL-1RA and IL-6 in patients with severe versus moderate COVID-19. This finding is also supported by another [recent publication](#). However, a [study](#) that used flow cytometry and extensive characterization of circulating neutrophils, lymphocytes, and monocytes found extensive induction and immune lineages. A higher neutrophil to lymphocyte ratio correlated with the severity of a standard clinical measure of severity of critical illness (APACHE III score) as well as the severity of COVID-19 illness. **Conclusion:** Plasma biomarkers in severe COVID-19 patients are not markedly elevated when compared to critically ill patients with sepsis or ARDS and therefore may not be a sufficient approach to comprehensively understand the immunopathology of COVID-19 patients. Therefore, further studies that more broadly explore the immune response to COVID-19 to better understand the pathophysiology of clinical disease are needed.

### **What was the impact of statewide shelter-in-place orders on U.S. hospitalizations and mortality?**

In response to the COVID-19 pandemic, 42 states and the District of Columbia implemented statewide shelter-in-place orders (SIPOs) during March and April 2020. Using publicly available data from March 21 through May 15, 2020, researchers undertook an [event study](#) to determine the impact of SIPOs on hospitalizations and mortality in the U.S. They found that in 19 states with hospitalization data available, SIPOs significantly reduced the daily hospitalization growth rate two weeks after being implemented (3.2 percentage points)—the daily hospitalization growth rate decreased further to 8.4 percentage points after 6 weeks. In 42 states and the District of Columbia, the daily mortality growth rate significantly declined 3 weeks after implementing statewide SIPOs (2.9 percentage points) – after 6 weeks the daily mortality growth rate declined by 6.1 percentage points. It was estimated that between 250,000–370,000 deaths may have been averted by SIPOs; however, the authors noted multiple important limitations to the approach they used to derive these estimates. **Conclusion:** Shelter-in-place orders were effective early in the epidemic, and saved lives. Whether strict SIPOs should be reinstated (or instituted) in areas where the epidemic is out of control or if it can be controlled with universal masking and physical distancing is unknown.

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## **FAQ**

### **1. What are the key changes in the new CDC guidelines for discontinuing isolation?**

On July 17, the CDC updated guidelines for discontinuing transmission-based precautions in healthcare settings. There are 3 main changes: 1) the test-based strategy, i.e. requiring negative tests, is not recommended and replaced by a “time” based strategy ; 2) for patients with severe or critical illness or severe immunocompromise, the duration of time-based precautions was extended; 3) the time for isolation since last fever was shortened. With mild to moderate illness, precautions can be discontinued when all of the following criteria are met: a) 10 days have passed since symptom onset (or 10 days since initial positive test if asymptomatic); b) fever free for 24 hours without fever-reducing medication; c) symptoms have improved. With severe or critical illness or severe immunocompromise, 20 days must have passed since symptom onset, in addition to (b) and (c). **Conclusion:** Updated CDC guidelines on discontinuing isolation are consistent with emerging data regarding the duration of infectivity and, once healthcare systems adjust, should be easier to apply and less burdensome for patients.

### **2. How common are thrombotic events in hospitalized patients with COVID-19 infection?**

It has previously been observed that COVID-19 is associated with increased risk of thrombotic events. However, the incidence of thrombotic events has not been established. A recently published [observational study](#) of patients admitted to a large New York hospital system found that 16% of patients admitted with COVID-19 experienced thrombotic events including deep vein thrombosis, pulmonary embolism, myocardial infarction and ischemic stroke. Of patients admitted to the ICU, 29.4% had a thrombotic event. This rate was observed to be higher than that seen in patients admitted with H1N1 influenza during the [2019 pandemic](#). **Conclusion:** Thrombotic events in patients hospitalized with COVID-19 appear to be frequent. Clinicians should be aware of this association and remain vigilant for findings suggestive of venous or arterial thrombosis.

### 3. Why all the attention to COVID-19 (or lack of COVID-19) in Vietnam?

Vietnam has had an [astounding course with COVID-19](#), reporting only 446 cases since the beginning of the pandemic and zero deaths although a recent increase in cases have led to a prompt response. The father of the modern Vietnamese nation, Ho Chi Minh, [once noted](#) that, “The storm is a good opportunity for the pine and the cypress to show their strength and their stability” and Vietnam seemed to tackle its COVID-19 pandemic in that spirit. Perhaps engendered by their experience with SARS-CoV, Vietnam (a country of 100 million) acted swiftly, creating a National Response Plan by January 21, 2020 involving airport health screenings, physical distancing, travel bans on foreign visitors, a 14-day quarantine period for international arrivals, school closures, public event cancellations, and closure of non-essential services. The country was therefore [ready with extreme measures](#) by the time the first case of community transmission was reported on January 23, 2020 in Vietnam. Importantly, a strategy enforcing [population-level facial masking](#) when in public from January onwards was strictly enforced, one of the [pillars of pandemic control](#). Moreover, given economic restraints, Vietnam focused its testing [on high-risk and suspected cases](#) early on. Vietnam declared victory against COVID-19 and [moved to open its economy](#) on May 28, 2020. However, on Saturday July 25, 2020, the first case of community transmission in Vietnam since April [was reported in the central beach city of Danang](#) after life had essentially returned to normal. The government has been highly responsive, imposing [immediate lockdown of Danang](#) and travel restrictions, making the possibility of Vietnam controlling this new outbreak highly probable. Early and aggressive containment measures and a culture of masking since SARS in 2003 – with a highly adherent population- may be the key to Vietnam’s success.

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**UCSF Hospital Epidemiology and Infection Prevention COVID-19 webpage:**

<https://infectioncontrol.ucsfmedicalcenter.org/ucsf-health-covid-19-resources>

**San Francisco DPH link:** <https://www.sfdcp.org/infectious-diseases-a-to-z/coronavirus-2019-novel-coronavirus/>

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