San Francisco Village

COVID – 19
Research and Advisory Team:
Report and Recommendations #30
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This report contains a summary of the key updates on the status of Covid-19 that are more evident since our last report (June 14), along with our current recommendations for actions for SFV to consider taking. Sources include: CDC, WHO, SFDPH, CA DPH, Science Journal, Nature Journal, New England Journal of Medicine, Journal of the American Medical Association, Scripps Research Institute, Johns Hopkins Coronavirus Resource Center, UCSF Medical Grand Rounds, STAT, Institute for Health Metrics & Evaluation, the Covid Tracking Project, other clinical journals, reports from public health professionals, and news media.

RECENT FINDINGS

1) Largest study of COVID-19 transmission highlights essential role of super-spreaders

Extensive contact tracing in two southern Indian states offers the strongest evidence yet that a few super-spreading individuals are responsible for a disproportionate share of new coronavirus infections, according to a study published Wednesday in the journal Science. It also suggests that children are more efficient transmitters of the virus than widely believed.

A team of Indian and U.S. researchers examined data from 575,071 individuals who were tested after coming into contact with 84,965 people with confirmed cases of COVID-19. That's an average of seven contacts per case, and a cohort more than 10 times larger than in a previous study from South Korea that mapped how the virus was transmitted. Researchers found that just 8% of people with COVID-19 accounted for 60% of the new infections observed among the contacts. The finding underscores the essential role of super-spreaders in the COVID-19 pandemic: One individual or event, such as in a poorly ventilated indoor space, can trigger a high number of new infections, while others might not transmit the virus at all.

In the new study, researchers tracked down 78 people who had shared a bus or train with one of eight known infected people and sat within three rows of that person for more than six hours. Health workers visited these contacts at their homes to conduct follow-up screenings and determined that nearly 80% of them had contracted the coronavirus. By contrast, people who were known to be exposed to infected individuals in lower-risk environments — such as being in the same room but more than three feet away — became infected only 1.6% of the time. Super-spreading events are the rule rather than the exception. The results could help guide safety measures in places such as gyms, churches and choir practice spaces that have been locations for previous super-spreading events.

The study also found that although children younger than 17 were the least likely to die of COVID-19, they transmitted the virus at rates

similar to the rest of the population, underscoring the idea that the disease doesn't spare young people. One data point in particular holds implications for reopening schools: Children ages 5 to 17 passed the virus to 18% of close contacts their own age.

2) This Overlooked Variable Is the Key to the Pandemic
A lengthy and highly informative article in the Atlantic, which is worth reading https://www.theatlantic.com/health/archive/2020/09/k-overlooked-variable-driving-pandemic/616548/

Even after months of extensive research by the global scientific community, many questions remain open. Why, for instance, was there such an enormous death toll in northern Italy, but not the rest of the country? What happened in Guayaquil, Ecuador, in April, when so many died so quickly that bodies were abandoned in the sidewalks and streets? Why, in the spring of 2020, did so few cities account for a substantial portion of global deaths, while many others with similar density, weather, age distribution, and travel patterns were spared?

There *is* a potential, overlooked way of understanding this pandemic that would help answer these questions, reshuffle many of the current heated arguments, and, crucially, help us get the spread of COVID-19 under control. By now many people have heard about R0—the basic reproductive number of a pathogen, a measure of its contagiousness on average. But unless you've been reading scientific journals, you're less likely to have encountered *k*, the measure of its dispersion. The definition of *k* is simply a way of asking whether a virus spreads in a steady manner or in big bursts, whereby one person infects many, all at once. After nine months of collecting epidemiological data, we know that this is an *overdispersed* pathogen, meaning that it tends to spread in clusters, but this knowledge has not yet fully entered our way of thinking about the pandemic—or our preventive practices.

Overdispersion and super-spreading of this virus are found in research across the globe. A growing number of studies estimate that a majority of infected people may not infect a single other person. A recent paper found that in Hong Kong, which had extensive testing and contact tracing, about 19 percent of cases were responsible for 80 percent of transmission, while 69 percent of cases did not infect

another person. This finding is not rare: Multiple studies from the beginning have suggested that as few as 10 to 20 percent of infected people may be responsible for as much as 80 to 90 percent of transmission, and that many people barely transmit it. This kind of behavior, alternating between being super infectious and fairly noninfectious, is exactly what *k* captures. We can think of disease patterns as leaning deterministic or stochastic: In the former, an outbreak's distribution is more linear and predictable; in the latter, randomness plays a much larger role and predictions are hard, if not impossible, to make.

To fight a super-spreading disease effectively, policy makers need to figure out why super-spreading happens, and they need to understand how it affects everything, including our contact-tracing methods and our testing regimes. In study after study, we see that super-spreading clusters of COVID-19 almost overwhelmingly occur in poorly ventilated, indoor environments where many people congregate over time—weddings, churches, choirs, gyms, funerals, restaurants, and such—especially when there is loud talking or singing without masks. For super-spreading events to occur, multiple things have to be happening at the same time, and the risk is not equal in every setting and activity, Researchers identify "prolonged contact, poor ventilation, [a] highly infectious person, [and] crowding" as the key elements for a super-spreader event. Super-spreading can also occur indoors beyond the six-feet guideline, because SARS-CoV-2, the pathogen causing COVID-19, can travel through the air and accumulate, especially if ventilation is poor.

{The article goes onto describe in detail methods of contact tracing and testing that are suited to the overdispersion and super-spreading of this virus. The following paragraphs are a condensation of these methods}

Given that some people infect others before they show symptoms, or when they have very mild or even no symptoms, it's not always possible to know if we are highly infectious ourselves. We don't even know if there are more factors yet to be discovered that influence super-spreading. But we don't need to know all the *sufficient* factors that go into a super-spreading event to avoid what seems to be

a *necessary* condition most of the time: many people, especially in a poorly ventilated indoor setting, and especially not wearing masks.

In terms of contact racing, we should try to work *backwards* to see who first infected the subject. Because of overdispersion, most people will have been infected by someone who also infected other people, because only a small percentage of people infect many at a time, whereas most infect zero or maybe one person. As Adam Kucharski, an epidemiologist and the author of the book *The Rules of Contagion*, explained, if we can use retrospective contact tracing to find the person who infected our patient, and *then* trace the forward contacts of the infecting person, we are generally going to find a lot more cases compared with forward-tracing contacts of the infected patient, which will merely identify *potential* exposures, many of which will not happen anyway, because most transmission chains die out on their own. Similarly, the infectious person who is transmitting the disease is like the pandemic social butterfly: The average number of people they infect will be much higher than most of the population, who will transmit the disease much less frequently.

Another significant consequence of overdispersion is that it highlights the importance of certain kinds of rapid, cheap tests. Consider the current dominant model of test and trace. In many places, health authorities try to trace and find forward contacts of an infected person: everyone they were in touch with since getting infected. They then try to test all of them with expensive, slow, but highly accurate PCR (polymerase chain reaction) tests. But that's not necessarily the best way when clusters are so important in spreading the disease.

3) Safety and Immunogenicity of SARS-CoV-2 mRNA-1273 Vaccine in Older Adults

Testing of vaccine candidates to prevent infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in an older population is important, since increased incidences of illness and death from coronavirus disease 2019 (Covid-19) have been associated with an older age. We conducted a phase 1, dose-escalation, open-label trial of a messenger RNA vaccine, mRNA-1273. The trial was expanded to include 40 older adults, who were stratified according to age (56 to 70 years or ≥71 years).

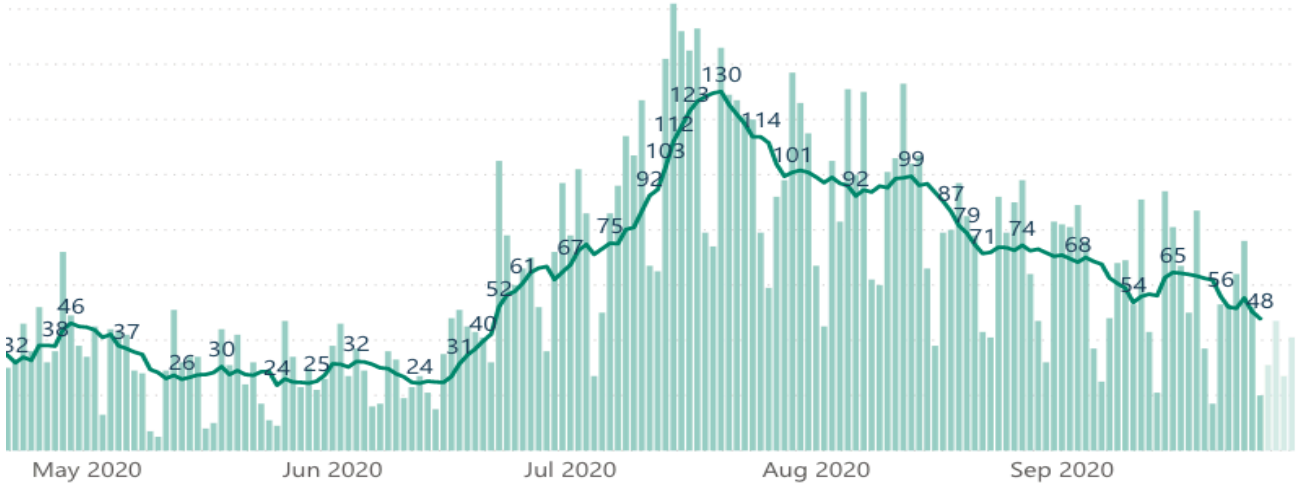
Solicited adverse events were predominantly mild or moderate in severity and most frequently included fatigue, chills, headache, myalgia, and pain at the injection site. Such adverse events were dose-dependent and were more common after the second immunization.

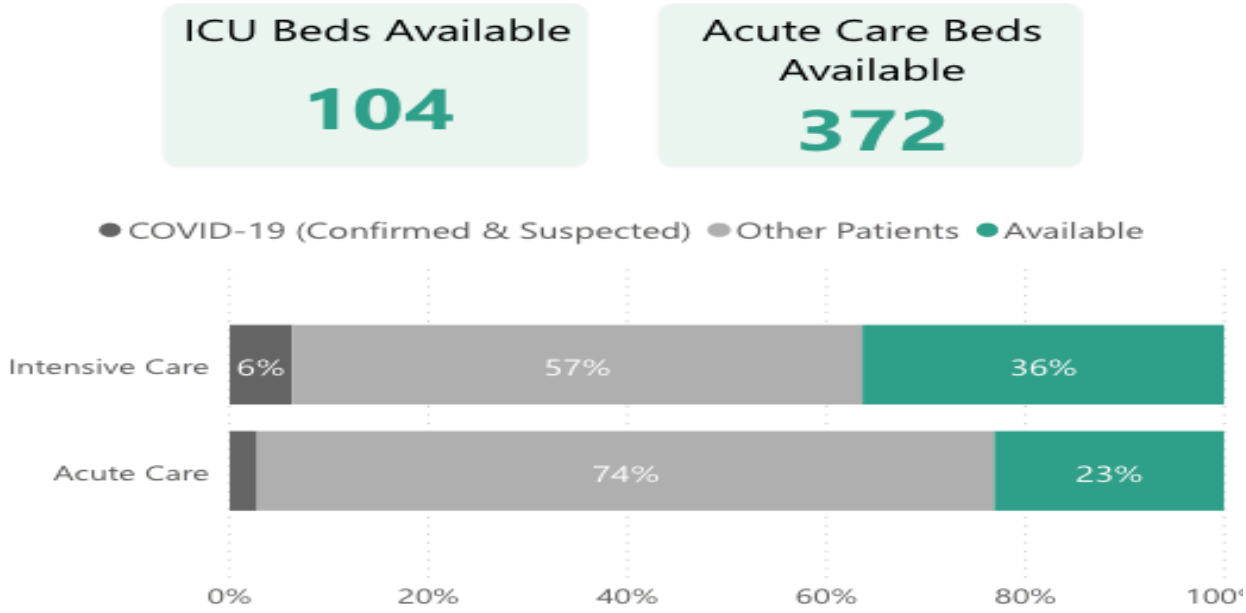
The mRNA-1273 vaccine induced high levels of both binding and neutralizing antibodies in older adults, and the time- and dose-dependent trends were similar to responses in younger adults; the responses after the second vaccination were similar to those observed in patients who had recovered from Covid-19 and had donated convalescent serum, including some who were severely ill. We must acknowledge that these assessments are qualitative; the small number of participants in each age and dose subgroup limits the power of efforts at quantitative assessment. These data also suggest that a second dose of vaccine is needed to achieve neutralizing antibodies in participants after the age of 56 years

SAN FRANCISCO

Total Positive Cases: 11,414
7-Day Average of New Cases: 48
Deaths: 107
R-Effective Rate: 0.93 (spread of Covid-19 is likely stable)

Number of New Cases and 7-Day Rolling Average





1) SF enters orange tier, which allows indoor dining and worship services.

As has been anticipated for two weeks now, San Francisco Mayor London Breed announced Tuesday that the city will resume allowing indoor dining effective Wednesday, September 30, at 25-percent capacity. And with the city's move into the state's "orange" tier for reopening, more things will be reopening as well including places of worship, movie theaters, and playgrounds. Restaurants and places of worship will have maximum capacity caps of 100 people or 25 percent, whichever is fewer.

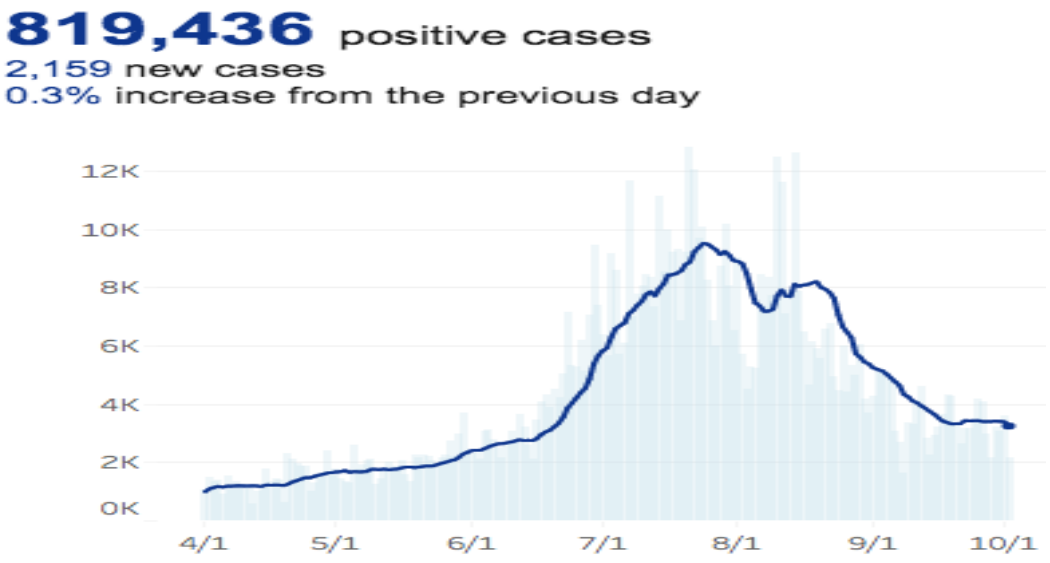
The "orange" tier, which indicates only moderate spreading of the coronavirus, actually allows for more lifting of restrictions than SF will be allowing — much as it did not immediately open restaurants and gyms as would have been allowed under "red" tier status, as limited capacity. Gyms and fitness studios were permitted to open at 10% capacity 2 weeks ago, after considerable lobbying from the industry.

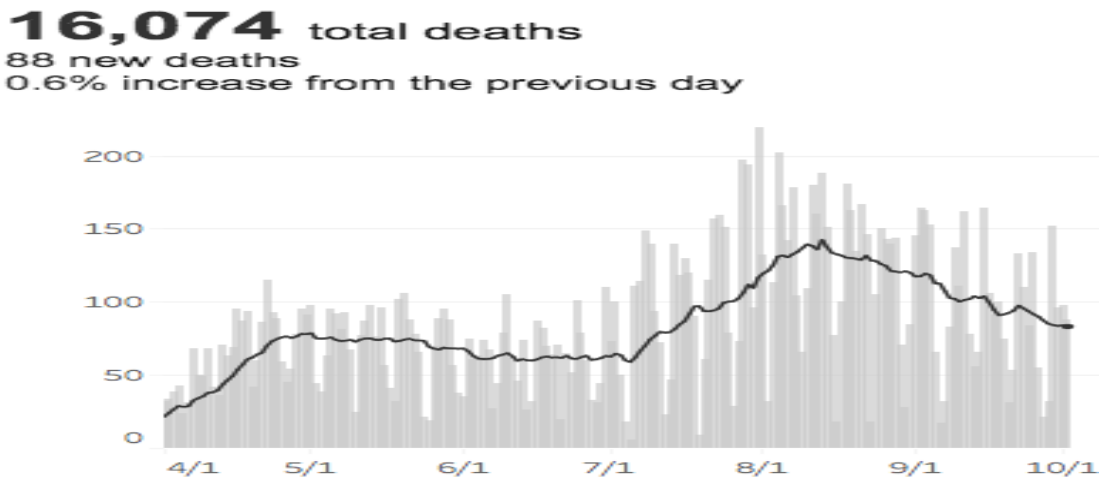
Apart from rural California counties where case counts have remained low throughout the pandemic, San Francisco is one of the first counties in the state to move from "red" to "orange" status.

2) UCSF researchers are testing a promising COVID-19 drug that could lessen symptoms and keep people out of the hospital.
The drug, which could eventually work on coronavirus much the way Tamiflu reduces flu symptoms, is being rolled out in a clinical trial at Zuckerberg San Francisco General Hospital, one of many U.S. sites that are enrolling volunteers for the study.

The medicine, made by the drug company Eli Lilly, is a type of drug called a monoclonal antibody that in preliminary studies appears to help people in early or mild stages of the disease. If proved effective, this class of drugs could help people with less severe symptoms — the majority of people who fall ill with the coronavirus — recover. It could also help people who are sick stay out of the hospital, thus preserving precious hospital capacity, and make people with the virus less infectious. Like Tamiflu, it would be an antiviral that helps shorten the duration of symptoms. It is unclear when such a drug, if effective in large studies, might be available to the public.

CALIFORNIA





- California has 819,436 confirmed cases to date.
- There were 3,590 newly recorded confirmed cases Thursday.
- The 7-day positivity rate is 2.8% and the 14-day positivity rate is 2.8%.
- There have been 14,868,431 tests conducted in California. This represents an increase of 96,580 over the prior 24-hour reporting period.
- As case numbers continue to rise in California, the total number of individuals who will have serious outcomes will also increase. There have been 16,074 COVID-19 deaths since the start of the pandemic.

1) California remains steady despite deadly day in SoCal.

Four counties in Southern California account for 70% of state's 151 deaths reported Tuesday. There were more coronavirus deaths reported Tuesday in California than on any other day in more than two weeks, according to data compiled by this news organization, but the daily average remained near its lowest point since the first week of July. Counties around the state reported a total of 151 new fatalities from COVID-19 on Tuesday — including more than 100 of those between four counties in Southern California — slightly increasing the average over the past week to about 84 per day. California's seven-day average of cases remained about flat, at about 3,275 per day, after there were another 3,260 new cases reported Tuesday. That figure dipped Sunday and Monday for the first time in weeks, to its lowest point since June 16.

UNITED STATES

Total Positive Cases: 7,367,537
Deaths: 209,162

1) A guide to how — and when — a Covid-19 vaccine could be authorized

The process of deciding when a vaccine appears to be safe and effective isn't as straightforward as the general public might believe. But it's important to understand it if we are to have confidence in these critical tools for helping to curb the pandemic.

a) When will vaccine makers have enough data?

A clinical trial is typically sponsored by a company making a vaccine candidate or an academic institution, or a partnership of both. But it is actually monitored by what is known as a data and safety monitoring board, or DSMB, a group of independent experts hired to make sure volunteers in the study are safe. In many studies, the DSMB has the ability to recommend stopping a study not only if a treatment is unsafe, but also if it is so clearly effective that continuing just wouldn't be ethical.

The DSMBs will conduct what's called an interim analysis after a certain number of people have been infected with Covid-19 and shown symptoms. Each of these cases is considered an "event," and each vaccine maker has set a different number of events as a threshold to conduct an interim analysis as part of their trial protocols.

Should a vaccine be approved, potentially for millions of people, after its efficacy has been shown based on a limited number of cases of Covid-19? Some experts say no. Eric Topol, the director of the Scripps Research Translational Institute, has been fervently saying that all the trials should continue beyond even their designed ends; while others say that while making a decision based on an interim analysis is fine.

b) The rules of approval

If and when a company believes its vaccine is safe and effective, it will then submit its data to the Food and Drug Administration. No Covid-19 vaccine is likely to be fully approved by the FDA in the near term,

because of requirements for manufacturing and follow-up that could take years. The FDA is expected instead to use a different authority by granting what is known as an emergency use authorization, or EUA. The bar for an EUA is low, and past EUAs have seemed unwise in hindsight. The challenge for the FDA will be to make sure that it brings its usual standards for a vaccine to the much more flexible emergency use authorization process. Reviewing data on a drug candidate normally takes a year, six months if it is fast, and three months at the fastest. Even a truncated review should take weeks.

c) Will the trials march on?
In the interim analyses that most people who follow medicine are used to, as soon as there is a clear result, the trial stops. But the plan for Covid-19 vaccines is different: Data from an interim analysis may be released if a vaccine is deemed inarguably effective — but volunteers may not be immediately told whether they are receiving vaccine or placebo. In other words, the study will remain "blinded." Participants receiving a placebo will not be switched immediately to the vaccine. The protocol is designed in a way that even if we would be able to file after an interim analysis, the protocol is designed to move on, at least for a certain amount of time

2) New research shows older adults are still often excluded from clinical trials
For years, researchers have called out a glaring gap in many clinical trials: Despite having far higher rates of many diseases, older adults are largely excluded from studies testing new therapies that might help them. Given how extensively experts have studied the issue of age disparities, though, it remains a significant problem — and one that has grown all the more pressing during the Covid-19 pandemic, given that the virus has hit older adults particularly hard. An analysis published this week found that older adults are likely to be excluded from more than half of Phase 3 Covid-19 trials on Clinicaltrials.gov — which could make it more difficult for researchers to evaluate doses, efficacy, and safety across all age groups.

Another paper, published this month in JAMA Internal Medicine, looked at the inclusion of older adults in cardiovascular clinical trials before and after the National Institutes of Health rolled out what's known as

the Inclusion Across the Lifespan Policy in January 2019. The policy requires anyone applying for NIH funding for studies involving human participants to include a plan for including people of all ages — or explain the scientific or ethical reason why they're not doing so.

Researchers looked at 97 cardiovascular trials listed on Clinicaltrials.gov and found that before the policy went into effect, one-third of trials had age limits. In the year after the policy went into effect, one-third of trials still had age limits. Age limits weren't the only factor that could limit enrollment of older adults. Two-thirds of the trials also used exclusion criteria that weren't specific to age, but which would disproportionately winnow out older adults, such as having preexisting conditions.

In another study, published in October 2019 in JAMA Oncology, researchers analyzed the average age of participants in 302 trials for breast, prostate, colorectal, or lung cancer, and compared it with the average age of patients worldwide with those diseases. On average, study participants were far younger than the real-world population affected by a disease. The biggest age disparities were seen in industry-funded studies and trials testing a targeted therapy. Another troubling finding: Those age gaps seemed to be widening over time.

Fixing the problems won't be as simple as changing the inclusion criteria for trials. There are a number of other barriers that affect whether older adults, including enrollment outreach and transportation concerns. Going forward, experts agree clinical trial sponsors will need to think creatively — and carefully — about the best ways to recruit and enroll older adults in a trial.

3) Expert panel recommends who should be first in line for COVID-19 vaccine.

The National Academies of Sciences, Engineering, and Medicine was tasked with looking at the ethical questions associated with distributing a lifesaving vaccine in the midst of a pandemic. The report was requested by the National Institutes of Health and the Centers for Disease Control and Prevention. The United States already is making millions of doses of COVID-19 vaccine before it's even known which candidate will end up working. Even so, rationing at the beginning will

be needed because it will take time to get shipping and delivery systems up and running smoothly. Distribution will happen by phase for different population groups.

- People in Phase 1a are critical to keeping the health care system functioning and are at high risk of exposure to sick patients. They're also at higher risk of then transmitting the virus to others, including family members.
- The second phase of vaccine distribution — Phase 1b — covers about 10% of the population. It includes people of all ages with underlying conditions like cancer, serious heart conditions, and sickle cell disease that put them at significantly higher risk of severe COVID-19 disease or death. This group includes people with two or more chronic conditions that put them at higher risk, including kidney disease, chronic obstructive pulmonary disease, obesity or diabetes. This phase also includes people 65 and older living in nursing homes, long-term care facilities, homeless shelters, group homes, prisons or jails.
- Phase 2 covers between 30% to 35% of people in United States. It includes teachers, school staff and childcare workers and critical workers in high-risk settings who can't avoid high-risk exposure to COVID-19, such as those working in the food supply system and public transit. Also included are all people over 65, because they account for about 80% of all reported COVID-19 deaths. Additionally, those who have one underlying condition that puts them at moderately higher risk, as well as people in homeless shelters or group homes and staff who work in those settings will have access to vaccine in this stage. People under 65 who are in prisons, jails, and detention centers and staffers also are included.
- Phase 3 covers between 40% and 45% of the population. It includes young adults and people who work in industries such as higher education, hotels, banks, exercise facilities and factories. Whether children are included in this group will depend if COVID-19 vaccines have been tested for safety and efficacy in younger age groups.
- Finally, Phase 4 will include everyone else residing in the U.S. who did not have access to the vaccine in prior phases, between 5% and 15% of the population.

The committee explicitly acknowledged the virus has disproportionally hit Black, Hispanic and Native American communities due to long-standing disparities in access to health care and poverty. In addition, people in these communities often have front-line jobs they cannot do from home, putting them at higher risk for contracting COVID-19. Because these communities face higher rates of hospitalization and death, the committee recommended special effort be made to deliver vaccine to people in high-vulnerability areas.

RECOMMENDATIONS

We have no new recommendations at this time.