

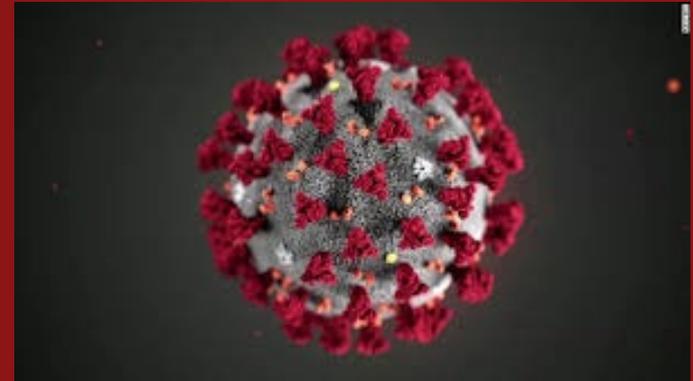


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Update on COVID-19: What have we learned so far?

Bonnie Maldonado, MD

July 21, 2020



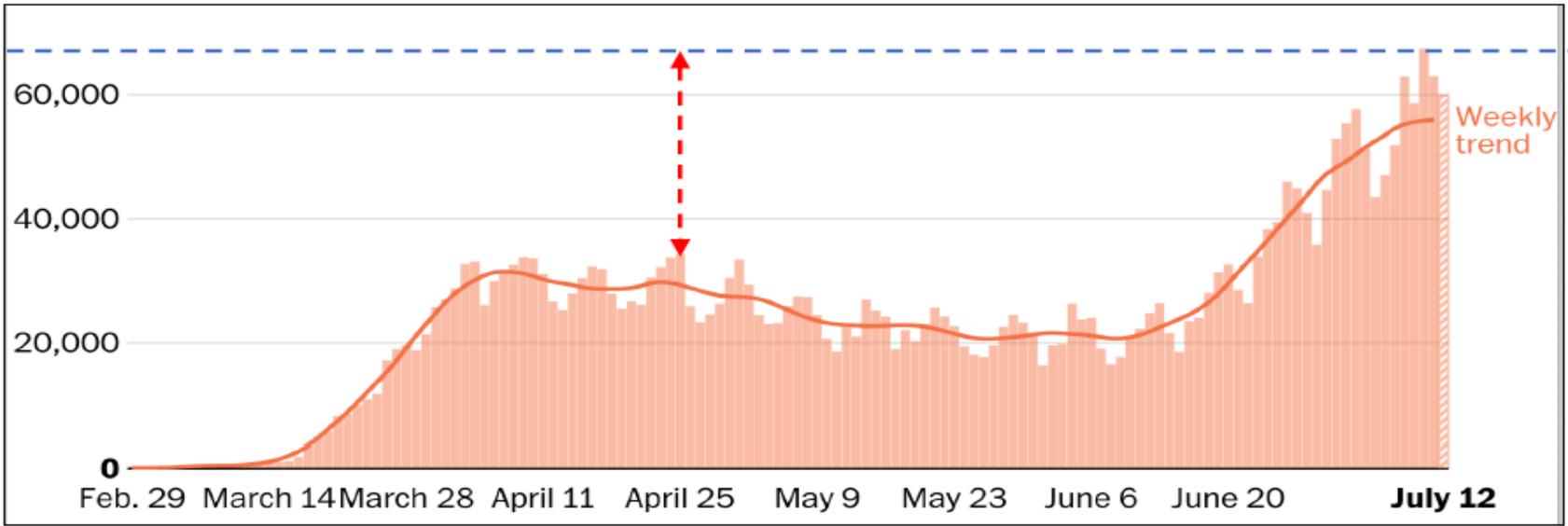
Objectives

- Epidemiology and Transmission
- Clinical Manifestation in Pediatrics and Pregnant Women
- Diagnostics and Treatment
- Returning to School?

COVID-19, United States, July 20, 2020

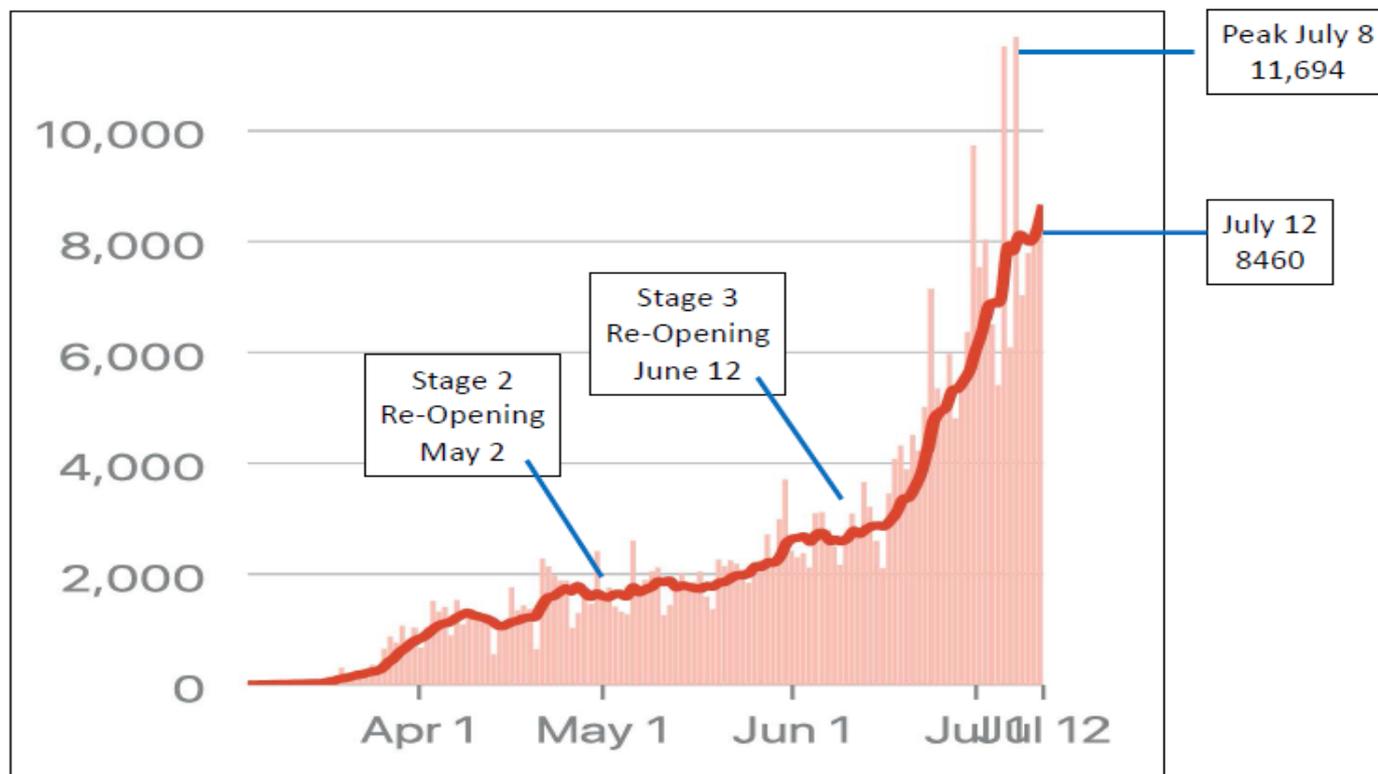
United States COVID-19 Cases/Day

<p>Previous High April 25 34,203 Cases</p>	<p>New High Above Previous High 33,008</p>	<p>New High nearly double earlier high July 10 67,211 Cases</p>
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https://www.washingtonpost.com/graphics/2020/national/coronavirus-us-cases-deaths/?itid=hp_hp-top-table-main_web-gfx-death-tracker%3Ahomepage%2Fstory-ans

Epidemiology of COVID-19 in California

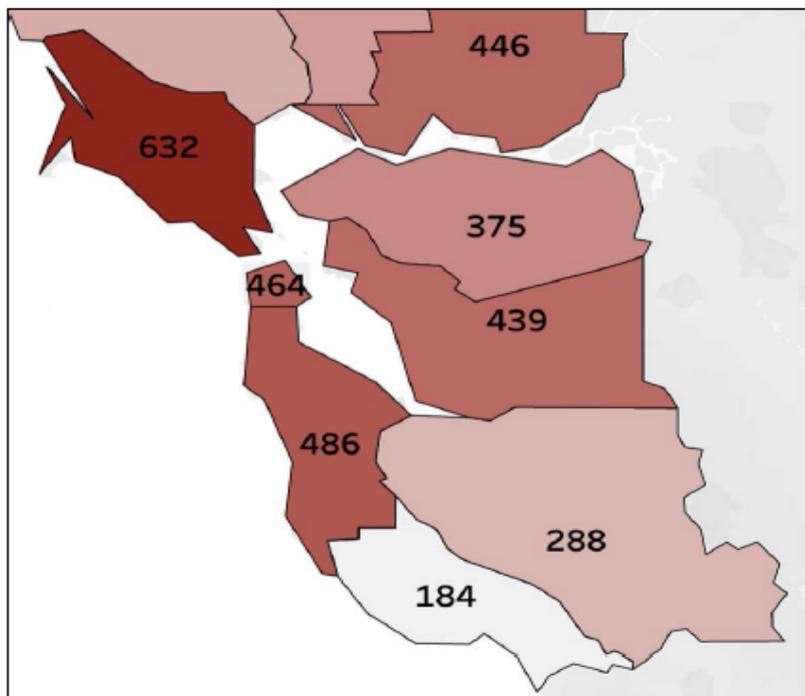


<https://covidtracking.com/data/state/california>

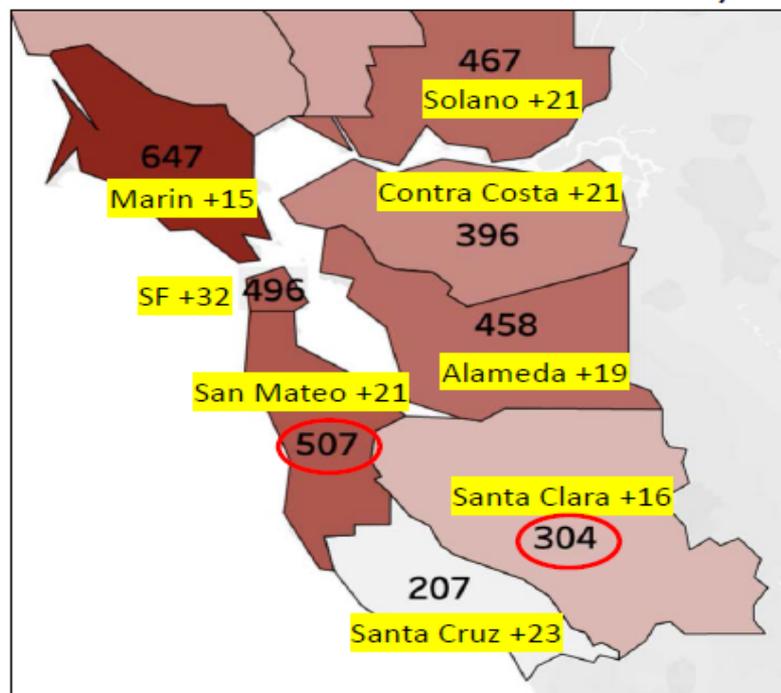
Epidemiology of COVID-19 in the SF Bay Area

Bay Area coronavirus cases per 100,000 residents

July 9



July 11



<https://www.mercurynews.com/2020/03/04/map-coronavirus-cases-in-the-bay-area/>

How important is aerosol transmission of SARS-CoV-2?

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It is Time to Address Airborne Transmission of COVID-19 FREE

Lidia Morawska ✉, Donald K Milton

Clinical Infectious Diseases, ciaa939, <https://doi.org/10.1093/cid/ciaa939>

“We appeal to the medical community and to the relevant national and international bodies to recognize the potential for airborne spread of COVID-19. There is significant potential for inhalation exposure to viruses in microscopic respiratory droplets (microdroplets) at short to medium distances (up to several meters, or room scale), and we are advocating for the use of preventive measures to mitigate this route of airborne transmission.”

- Size matters
 - Smaller (<5 μ) droplets can travel beyond 1-2 m
 - Viral RNA associated with droplets <5 μ can be recovered from air
- Analogy with SARS, MERS and other respiratory viruses
- One outbreak in a Chinese restaurant suggested aerosol transmission

- “Demonstrating that speaking and coughing can generate aerosols or that it is possible to recover viral RNA from air does not prove aerosol-based transmission; infection depends as well on the route of exposure, the size of inoculum, the duration of exposure, and host defenses.”
- $R_0 = 2.5$ – this is a small number given that people are infectious for about a week
- Secondary attack rates low (5%) but higher among close contacts (10-40%)
 - Risk to unmasked HCW 3%
- Few outbreaks suggest aerosol transmission
- Simple face masks highly effective
- **“...the balance of currently available evidence suggests that long-range aerosol-based transmission is not the dominant mode of SARS-CoV-2 transmission.”**

Klompas M, Baker MA, Rhee C. JAMA 2020 Jul 13 [Epub ahead of print].

The outbreak that didn't happen: Masks credited with preventing coronavirus spread inside Missouri hair salon

+ Add to list

Springfield, Mo., health officials braced for an outbreak. Now they say face coverings prevented one.

- 2 PCR-positive hairdressers in Springfield, Mo.
 - Worked 8 and 5 days, respectively
 - Both symptomatic
 - 139 customers exposed
- Posted sign “a mask is required to enter salon”
- Both hairdressers and all customers wore masks
- **No** secondary cases detected



Public health officials braced for a coronavirus outbreak after two stylists at this Great Clips hair salon in Springfield, Mo., tested positive for the virus last month. (USA Today Network/Reuters)

See also Hendrix MJ, Walde C, Findley K, Trotman R. Absence of apparent transmission of SARS-CoV-2 from two stylists after exposure at a hair salon with a universal face covering policy – Springfield, Missouri, May 2020. MMWR 2020 Jul 14; 69 [early release].



COVID-19 in US Children



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of Pediatrics



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Children and COVID-19: State-Level Data Report

[Critical Updates on COVID-19](#) / [Children and COVID-19: State-Level Data Report](#)

<https://services.aap.org/en/pages/2019-novel-coronavirus-covid-19-infections/children-and-covid-19-state-level-data-report/>



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State-based COVID-19 Reporting

- On July 9, the age distribution of reported COVID-19 cases was provided on the health department websites of 49 states, New York City, the District of Columbia, Puerto Rico, and Guam.
- Children represented 7.6% of all cases in states; over 200,000 children have tested positive for COVID-19 since the onset of the pandemic.
- A smaller subset of states reported on hospitalizations and mortality by age, but the available data indicated that COVID-19-associated hospitalization and death is uncommon in children.
- It appears that severe illness due to COVID-19 is rare among children.
- States should continue to provide detailed reports on COVID-19 cases, testing, hospitalizations, and mortality by age so that the effects of COVID-19 on children's health can continue to be documented and monitored.

COVID-19 in Children by State

A. Cumulative Child COVID-19 Cases, 7/9/20

Eleven states with 6,000+ cumulative child COVID-19 cases



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COVID-19 in US Children: Summary of State-Based Reporting



- **Cumulative Number of Confirmed Cases***
- 200,184 total child COVID-19 cases reported, representing 7.6% (200,184/2,651,066) of all cases
- Overall rate: 279 cases per 100,000 children in the population
- **Change in Child Cases, 6/25 – 7/9**
- 61,971 new child cases reported from 6/25-7/9 (138,213 to 200,184), a 45% increase in child cases
- **Testing***
- In 7 states reporting, children made up between 5.7%-10.9% of total state tests
- **Hospitalizations***
- In 20 states and NYC, children were 0.8%-2.9% of total reported hospitalizations
- Across states, between 0.7% and 9.1% of all child COVID-19 cases resulted in hospitalization
- **Mortality***
- In 42 states and NYC, children were 0%-0.5% of all COVID-19 deaths
- 22 states reported zero child deaths
- In states reporting, 0%-0.2% of all child COVID-19 cases resulted in death

COVID-19 IN PREGNANCY

Covid-19 Task Force for Obstetrics:

Iroque Igbinosa, Kelley Brennan Lee, Deirdre Lyell, Gill Abir, Kay Daniels, Alexis Davis, Ronald Gibbs, Yasser El-Sayed, Natali Aziz

June 30, 2020



Covid-19 and Pregnancy

- Presentation in Pregnancy
- Pregnancy Risk Factors and Outcomes
- Perinatal Outcomes
- LPCH Implementation of Protocols
- LPCH Experience
- Review of new CDC data (*MMWR 6/25/2020*)

Covid-19 Presentation in Pregnancy

-Given universal screening, significant asymptomatic
14/43 (33%) positive pts in NY per universal screening¹

-Symptomatic

--Fever (68%), cough (34%), malaise (7%), dyspnea (5%)

--Anosmia and/or ageusia not so commonly reported in pregnant women as in general population²

-Disease severity

--86% mild disease, 9.3% severe disease, and 4.7% critical disease¹

1. Breslin N, Gyamfi-Bannerman C, et al. Coronavirus disease 2019 among asymptomatic and symptomatic pregnant women...NY City hospitals. AJOG. MFM 2020.
2. Zaigham, et al. Maternal and Perinatal Outcomes with COVID-19: a systematic review of 108 pregnancies. Acta Obstetrics Gynecology Scand. 2020; 00:1-7

Covid-19 Pregnancy Risks

-Limited data pertaining to COVID-19 and effects on pregnant women

-Majority of data **have not demonstrated** increased risk of transmission or more severe complications/death in pregnant women compared to non-pregnant adult population

--New CDC study MMWR 6/25/2020 – pregnant patients may be at increased risk of complications

<https://www.cdc.gov/coronavirus/2019-ncov/hcp/pregnant-women-faq.html>

Covid-19 and Maternal Hospitalizations

- UKOSS Study: Characteristics of pregnant women with confirmed SARS-CoV-2 infection for whom data were available, UK, March 1 – April 14, 2020

Characteristics	Case women (N=427)	Control Women (N=694)	OR (95% CI)	aOR
	Number (%)	Number (%)		
Age: < 20	4 (1)	18 (3)	0.43 (0.14-1.28)	0.66 (0.14-.3.09)
20-34	248 (58)	477 (69)	1	1
>35	175 (41)	199 (29)	1.69 (1.31-.2.18)	1.35 (1.01-1.81)
BMI:	126(31)	337 (50)	1	1
18-25				
25-29	141 (35)	181 (27)	2.08 (1.54-2.81)	1.91 (1.37-2.68)
>29	140 (34)	155 (23)	2.42 (1.78-3.28)	2.20 (1.56-3.10)
Black or other minority group (all)	233 (56)	131 (19)	5.39 (4.11-7.07)	4.49 (3.37-6.00)
Pre-existing medical problems	145 (34)	166 (24)	1.64 (1.25-2.13)	1.52 (1.12-2.06)

Covid-19 and Perinatal Outcomes

-Initial reports^{1,2,3} showed **no vertical transmission** in 27 infants born to COVID-19 infected mothers

Negative testing 27/27 infants

Negative testing 9/9 infants for SARS-CoV-2 in amniotic fluid, cord blood, neonatal throat swab, breastmilk⁴

-Recent case reports/series

--Possible placental infection (live births and miscarriage)

--Possible vertical transmission from Italy and Canada^{5,6}

1. A A, et al. Evidence for and against vertical transmission. SARS-CoV136 2 (COVID-19). 2. Hui Zeng, MD1 ; Chen Xu, BS1 ; Junli Fan, MD1 138 ; et al. Antibodies in Infants Born to Mothers 139 JAMA. March 26, 2020. 140 do
3. Wang S, Guo L, Chen L, et al. A case report of neonatal COVID-19 infection in China 142 [published online ahead of print, 2020 Mar 12]. Clin Infect Dis. 2020;ciaa225. 4. Chen, et al Clinical characteristics of intrauterine vertical transmission. The Lancet. February 2020. 5. Kirtsman, CMAJ 2020. early-released May 14, 2020 6.Patanè L, et al, Vertical transmission of COVID-19: SARS-CoV-2 RNA on the fetal side of the placenta in pregnancies with COVID-19 positive mothers and neonates at birth, American Journal of Obstetrics & Gynecology MFM (2020).

LPCH and Covid-19 Protocols

- CDC/WHO/ACOG/AAP guidance
- One asymptomatic support person/caregiver for entire labor and delivery course
 - Two asymptomatic support persons during hospitalization
- Universal COVID-19 testing for all admitted patients
- Isolation of infants with suspected COVID-19 from other healthy infants
- Co-location of known/suspected COVID-19 mother and infant and breastfeeding decisions are determined using shared decision-making model

California: COVID-19 OB Experience

-Data from CMQCC and CPQCC

Covid-19 positive (and PUI) obstetric patients are presentations

--1-3 cases per week and many units have seen fewer

-Only a handful of pregnant/postpartum COVID-19 ICU admissions

--Several 2nd/3rd trimester cases were intubated but recovered and discharged pregnant

-Universal rapid COVID-19 testing in many L&D's

-Rate of positive tests among asymptomatic pregnant women across California

--~1.5% but many <1% (unlike NYC where many OB units have asymptomatic screen positive rates of 20-30%)

LPCH OB Experience

-Period: March 7-June 21 (Pre-op 4/13/20, Universal 4/25/2020)

Total PUI/Universal PATIENTS tested:	805
Total positive:	20 (2.5%)

Asymptomatic PATIENTS tested:	676
Asymptomatic positive:	6 (0.9%)

Symptomatic PATIENTS tested:	129
Symptomatic positive:	14(10.9%)

Stanford HCW- total=1.07%, asymptomatic =0.3%, symptomatic=3.5%

LPCH OB Experience

LPCH/Stanford Admissions:	20
Stanford (COVID-19 indications):	8 (2 in ICU, 1 PP-outside delivery)
LPCH (Obstetric indications) :	12
Delivered:	8 (5 VD, 3 CD- 2 repeat and 1 breech)
Neonatal Infections:	0

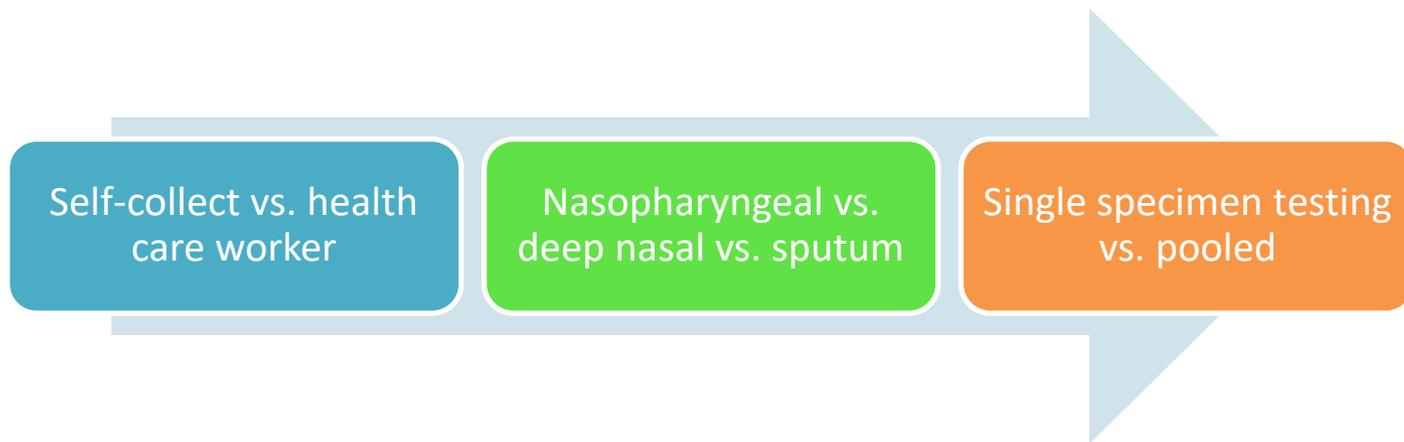
Stanford SARS-CoV-2 Testing Options

SARS-CoV-2 RT-PCR

SARS-CoV-2 Serology IgG & IgM

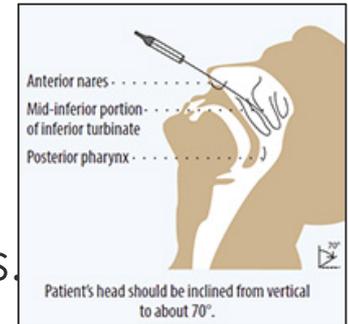
Variables Impacting Testing Capacity

- **Highest sensitivity assay:** COVID-19 RT-PCR assay performed on healthcare worker collected nasopharyngeal (NP) swab



- May choose options that increase testing capacity but impacts test sensitivity
- Increasing testing frequency can compensate for decreased sensitivity

Specimen Types & Collection Methods



Healthcare worker collected nasopharyngeal swab vs. self-collected tongue, nasal, and mid-turbinate – *symptomatic* individuals (1503 samples; ~500/group) [N Engl J Med. 2020. doi:10.1056/NEJMc2016321]

	Mid-Turbinate	Nasal (bilateral)	Tongue
Sensitivity % (95% CI)	96.2% (87.7-100)	94.0% (84.6-100)	89.8% (80.2-100)
Pearson correlation coefficient	0.86	0.78	0.48

Infectious Diseases Society of America Guidelines on Diagnosis of COVID-19: **Nasopharyngeal, mid-turbinate or nasal swabs** rather than oropharyngeal swabs or saliva alone for SARS-CoV-2 RNA testing in symptomatic individuals (Recommendation 2) [<https://www.idsociety.org/practice-guideline/covid-19-guideline-diagnostics/>]

FDA Approves Pooled PCR Testing



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FDA NEWS RELEASE

Coronavirus (COVID-19) Update: FDA Issues First Emergency Authorization for Sample Pooling in Diagnostic Testing

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Press Announcements

For Immediate Release: July 18, 2020

Today, the U.S. Food and Drug Administration reissued an emergency use authorization (EUA) to Quest Diagnostics to authorize its [Quest SARS-CoV-2 rRT-PCR test](#) for use with pooled samples containing up to four individual swab specimens collected under observation. The Quest test is the first COVID-19 diagnostic test to be authorized for use with pooled samples.

sample pooling in diagnostic testing to help health care providers follow current best practices

Content current as of:
07/18/2020

Regulated Product(s)
Medical Devices

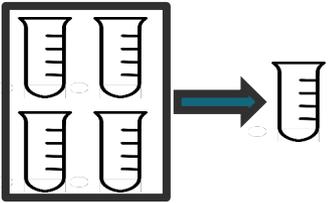
Health Topic(s)
Infectious Disease
Coronavirus

<https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-issues-first-emergency-authorization-sample-pooling-diagnostic>

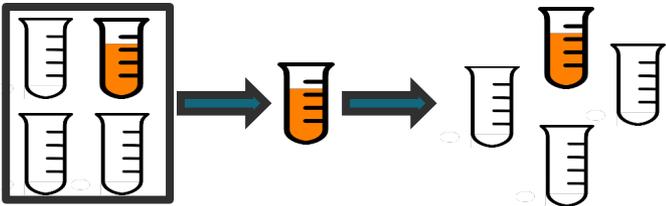


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Pooled (group) Testing



If a **pooled sample is negative** then all the individual specimens in the pool can be **reported as negative**



If a **pooled sample is positive**, then each specimen in the pool has to be **individually tested to identify the positive sample**.

Sensitivity

Repeat NP Swab Testing within 7 days (surrogate gold standard)

- Overall discrepancy: 3.5%
 - Stanford: 2.8%
 - Univ of WA: 4.3%
- Sensitivity: 96.5%
 - **Stanford: 97.2%**
 - Univ of WA: 95.7%

ACCEPTED MANUSCRIPT

Occurrence and Timing of Subsequent SARS-CoV-2 RT-PCR Positivity Among Initially Negative Patients ^{FREE}

Dustin R Long, MD, Saurabh Gombar, MD, PhD, Catherine A Hogan, MD, MSc, Alexander L Greninger, MD, PhD, Vikas O'Reilly Shah, MD, PhD, Chloe Bryson-Cahn, MD, Bryan Stevens, MD, Arjun Rustagi, MD, PhD, Keith R Jerome, MD, PhD, Christina S Kong, MD ... Show more

Author Notes

Clinical Infectious Diseases, ciaa722, <https://doi.org/10.1093/cid/ciaa722>

Published: 07 June 2020 Article history ▾

Specificity

12,739 Asymptomatic Health Care Workers tested

- COVID-19 positive rate: 0.3%
 - ~0.1% developed symptoms or had prior symptoms consistent with COVID
 - ~0.1% had repeat positive PCR or positive serology
 - **Estimated specificity: 99.93%**
 - 99.82%, if discount serology results

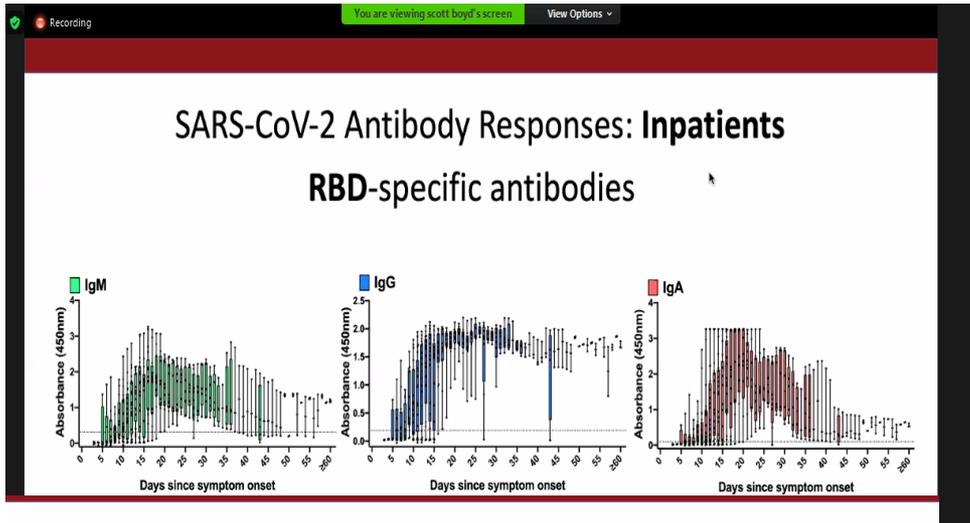
	1% Prevalence		10% Prevalence	
Specificity	PPV	NPV	PPV	NPV
99.93%	93.3%	100%	99.4%	99.7%
99.82%	84.5%	100%	98.4%	99.7%

CDC Interim Guidelines for Collecting, Handling, and Testing Clinical Specimens for COVID-19

Proper collection of specimens is the most important step in the laboratory diagnosis of infectious diseases. A specimen that is not collected correctly may lead to false negative test results.

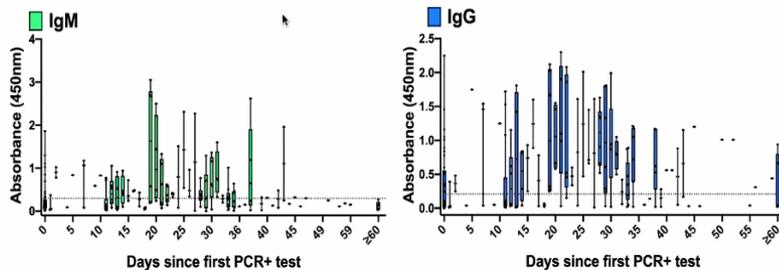
<https://www.cdc.gov/coronavirus/2019-nCoV/lab/guidelines-clinical-specimens.html>

SARS-CoV2 Serologic Responses



- Data from 40 inpatients
- PCR positive
- 396 time points
- Two months after symptom onset, IgM and IgA are near baseline but IgG still elevated

How do Outpatients and Asymptomatic Individuals Respond?



- 149 outpatients
- Lower antibody levels
- Rapid decrease, even for IgG





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Tracking and Treating New COVID-19 Infections and
Understanding Immunity in the San Francisco Bay Area



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COVID-19 Impact on Population Health and Healthcare Systems



- Healthcare systems are strained by the COVID-19 pandemic.
- Critical to investigate multiple therapeutic and alternative treatment strategies to avert the need for hospitalization.
- The Stanford University COVID-19 Translational Research Unit (COVID TRU) will help us meet this urgent demand.
- Stanford's strengths to design flexible and rigorous clinical trials, provide simultaneous innovative mechanistic studies, and build a pipeline of next-generation therapeutics.



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Epidemiology Impact on Designing Clinical Treatments for COVID-19



- Epidemiologic data indicates that ~80% of patients have no symptoms or mild COVID-19 infection.
- Although these individuals may not need hospitalization, they still experience respiratory symptoms, need to quarantine, and consequently lose productivity.
- More importantly, patients with mild disease still contribute to community disease transmission.
- **Limiting viral shedding from this group is crucial to controlling disease in the individual and spread of COVID-19, especially in households and close personal contacts.**

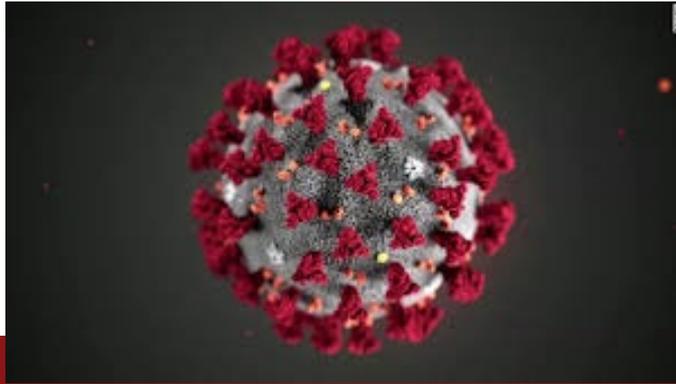
Stanford Medicine COVID-19 Efforts



- Household transmission studies
- Stanford COVID Clinical Trials Research Unit (COVID TRU)
 - Remdesivir
 - Lambda Interferon
 - Favipiravir
 - Pending: Camostat, monoclonal antibodies, inhaled remdesivir, vaccine trials
- Understanding immunity to SARS-CoV2
- When can we go back to “normal”?



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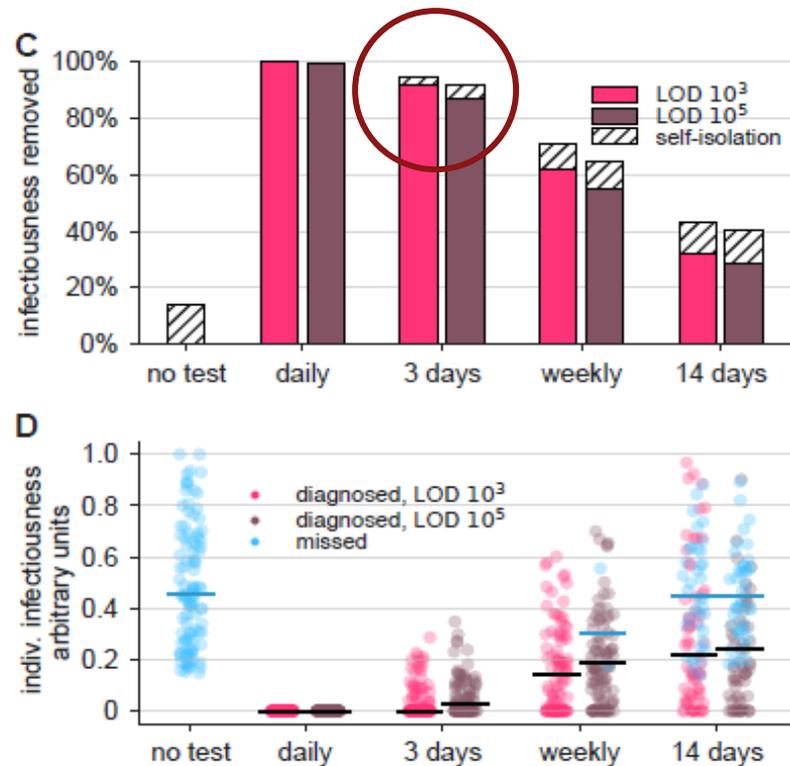
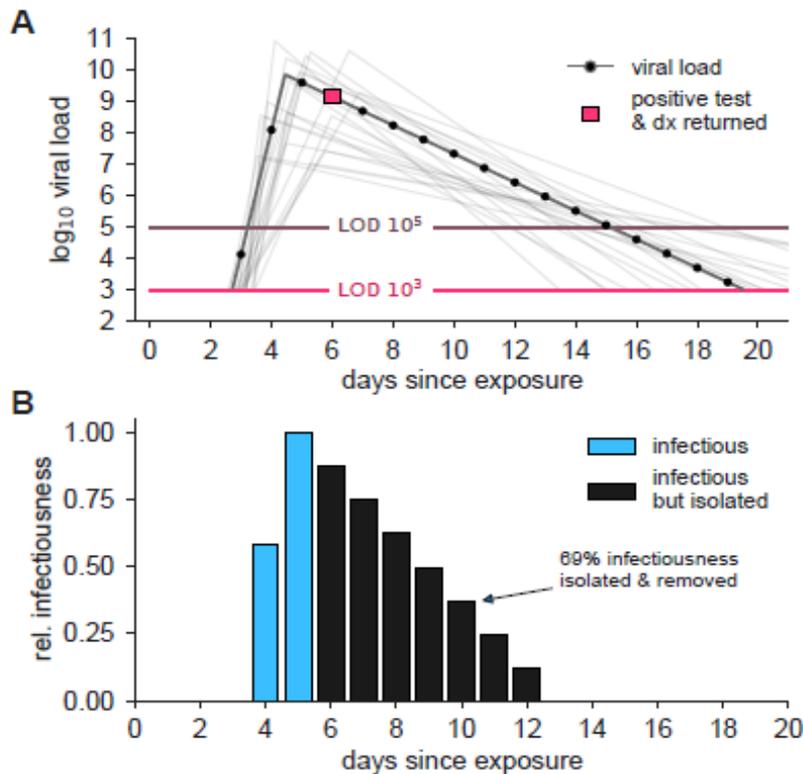
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SARS-CoV2 Surveillance and Testing – How Often and Which Test?

When Will We Get Back to “Normal”?

- Proposed interventions are based on a number of population-based assumptions:
- The disease will likely be circulating at an unknown rate for some unknown time even after staged reductions in community containment
 - A vaccine will not be available for several months or longer
 - Rapid viral testing and antibody testing will be available for real-time, population-based high throughput monitoring for new infections and possibly re-infections
 - Behavioral mitigation strategies (handwashing, social distancing) may be incompletely successful
 - Non-behavioral mitigation strategies are able to limit spread of disease.
 - Hospitalizations for affected individuals will likely be low but rapidly available

Test sensitivity is secondary to frequency and turnaround time for COVID-19 surveillance



Frequency versus Sensitivity

- Individuals would not isolate unless they were detected by surveillance testing.
- This analysis demonstrates little difference in averting infectiousness between the two classes of test.
- Dramatic reductions in total infectiousness of the individuals were observed by testing daily or every third day, 60% reduction when testing weekly, and < 40% under biweekly testing.
- Because viral loads and infectiousness vary across individuals, also analyzed the impact of different surveillance regimes on the distribution of individuals' infectiousness.
- Considering tests with LOD of 10³ and 10⁵, analogous to RT-qPCR and RT-LAMP / rapid antigen tests, respectively.



Back to School? What the AAP Says

- **AAP strongly advocates that the goal should be to have students physically present in school. This should happen with careful measures to keep students and staff safe, and with flexibility to adapt as needed to the community's prevalence of COVID-19.**
- Kids who are in school learn more than math, reading and science. They also learn social and emotional skills, get healthy meals and exercise, mental health support and other things that cannot be provided with online learning.
- Beyond supporting the educational development of children and adolescents, schools play a critical role in addressing racial and social inequity. This pandemic is especially hard on families who rely on school lunches, have limited access to the Internet or health care.
- **School leaders and local public health officials will need to work together to ensure safety for children, teachers and staff. They will need to be nimble and flexible, and ready to switch gears based on their community's prevalence of COVID-19 cases.**
- The evidence we have so far indicates that children and adolescents are less likely to have symptoms or severe disease resulting from SARS-CoV-2 infection. Studies so far have also shown that children are less likely to become infected, **and they are less likely to spread infection.** COVID-19 appears to behave differently in children and adolescents when compared with other common respiratory viruses, such as influenza.

<https://services.aap.org/en/news-room/working-with-the-media/speaking-points/talking-points-on-schools-reopening-guidance/?nfstatus=200&nftoken=388b602a-73e3-411f-85c1-62a90288990c&nfstatusdescription=SUCCESS%3a+Local+token+is+valid>

Back to School? What the AAP Says

- It is important to make the school environment safe for all those in the building. Physical distancing is especially important for adults, including teachers and staff. Cloth face coverings, frequent hand-washing and cleaning should be implemented.
- Decisions to alter the school schedule, such as partial days or alternate attendance days, or to temporarily close schools, must be made by local and state officials according to the prevalence of COVID-19 in the community. The goal should be to have students physically present in school as long as safety measures for students and staff can be met.
- **Reopening schools in a way that maximizes safety, learning, and the well-being of children will clearly require new investments in our schools. We call on our leaders to provide the resources necessary to ensure that funding does not stand in the way of safely educating and caring for our children.**
- **Children absolutely must be up to date on all vaccines, and AAP recommends all children are vaccinated for the flu and have had their physicals. New measles outbreaks or flu can cause severe illness or be life-threatening, and should not be taken lightly especially in the midst of the COVID-19 pandemic.**
- To help keep the virus from spreading, AAP has recommended physical distancing, cleaning and other practices for different age populations.



When Will We Get Back to “Normal”?

- Agreement to continue some community interventions
 - a. Continued restrictions on mass gatherings
 - b. Sheltering in place for older adults
 - c. Not reopening schools until the fall
 - d. Masks worn outdoors

- Staggered return to work



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Resources:

CDC:

<https://www.cdc.gov/coronavirus/2019-ncov/index.html>

<https://www.cdc.gov/coronavirus/index.html>

WHO:

<https://www.who.int/health-topics/coronavirus>

Santa Clara County Public Health:

www.sccgov.org/sites/phd-p/Diseases/novel-coronavirus

