COVID-19: Update More Than Ever A Moving Target

Vistage September 25, 2020

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Global COVID-19 (9/25/2020)



Johns Hopkins Univ. Coronavirus Resource Center

EPIDEMIOLOGY & TRANSMISSION



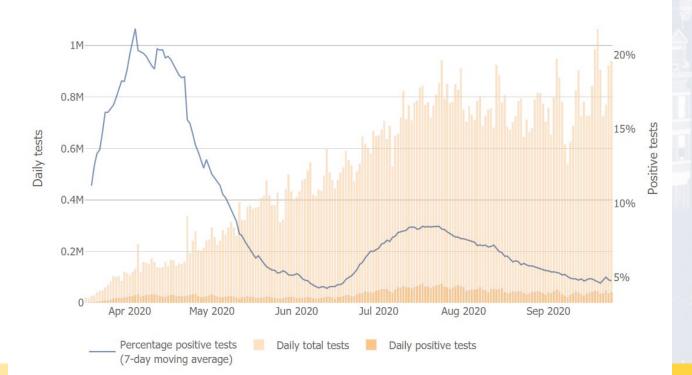
United States Testing Trends 7 –day moving average (9/25/20)

DAILY STATE-BY-STATE TESTING TRENDS

See daily changes in tests performed and positivity rates

SHARE: f y in





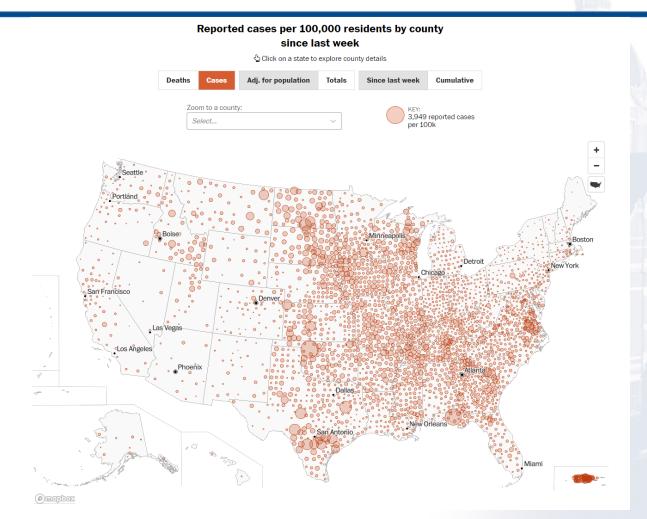


Percent of new tests that are positive

Display a different dataset Percent positive Map View **Overview** • 5.0% 10.0% 15.0% 20.0% 25.0% 30.0% ME AK VT NH WA ID MT ND MN IL WI MI NY RI MA OR NV WY SD IΑ IN ОН PA NJ CT UT KY CA CO NE MO WV VA MD DE ΑZ NM KS AR TN NC SC DC OK LA MS AL GΑ HI TX FL



COVID CASES/100,000 – 7d average



From: Turbulent Gas Clouds and Respiratory Pathogen Emissions: Potential Implications for Reducing Transmission of COVID-19

JAMA. 2020;323(18):1837-1838. doi:10.1001/jama.2020.4756

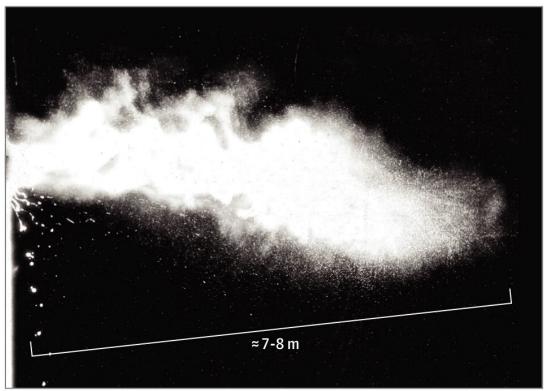


Figure Legend:

Multiphase Turbulent Gas Cloud From a Human Sneeze













Transmission Dynamics of COVID-19 Outbreaks Associated with Child Care Facilities — Salt Lake City, Utah, April-July 2020

Early Release / September 11, 2020 / 69

Adriana S. Lopez, MHS1; Mary Hill, MPH2; Jessica Antezano, MPA2; Dede Vilven, MPH2; Tyler Rutner2; Linda Bogdanow2; Carlene Claflin2; Ian T. Kracalik, PhD1; Victoria L. Fields, DVM1; Angela Dunn, MD3; Jacqueline E. Tate, PhD1; Hannah L. Kirking, MD1; Tair Kiphibane2; Ilene Risk, MPA2; Cuc H. Tran, PhD1 (View author affiliations)

Children who likely got COVID-19 at two Utah child care centers spread it to household members



12 kids likely got COVID-19 in 2 child care centers; 3 didn't have symptoms



12 people who had contact with the children outside the child care centers got infected* including some parents and siblings

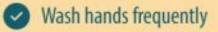


1 parent required hospitalization

SLOW THE SPREAD OF COVID-19 IN CHILD CARE CENTERS

"confirmed or probable







Encourage adults and children 2 years and older to wear masks Clean and disinfect frequently



CDC.GOV

bit.ly/MMWR91120

MMWR

September 25, 2020

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Travel risks

Transportation

Nearly 11,000 people have been exposed to the coronavirus on flights, the CDC says



Melaku Gebermariam with Grupo Eulen, uses an electrostatic spraying process before passengers board a Delta Air Lines flight at Reagan National Airpor on July 22, 2020. (Evelyn Hockstein/For The Washington Post)

By Ian Duncar

September 19, 2020 at 4:50 p.m. EDT

CDC incompletely contact traced 1600 people "says some of those travelers subsequently fell ill, in the face of incomplete contact tracing information and a virus that incubates over several days, it has not been able to confirm a case of transmission on a plane."

"One person with COVID-19 infected 15 others during a long-haul flight from London to Vietnam in early March"

"A 27-year-old woman in business class as the primary source of the outbreak."

"Noted that long flights in particular have become a matter of increasing concern as many countries have started lifting flight restrictions despite...the ongoing pandemic."



EMERGING INFECTIOUS DISEASES®

EID Journal > Volume 26 > Early Release > Main Article

Disclaimer: Early release articles are not considered as final versions. Any changes will be reflected in the online version in the month the article is officially released.

Volume 26, Number 11—November 2020

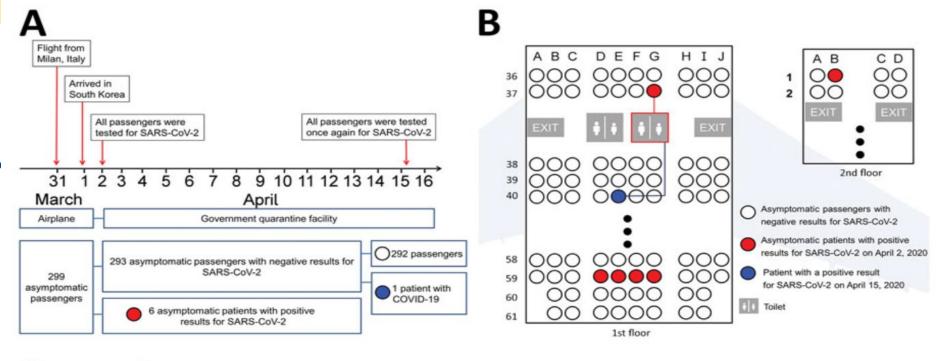
Dispatch

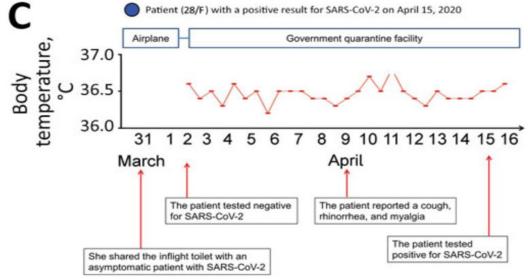
Asymptomatic Transmission of SARS-CoV-2 on Evacuation Flight

Flying risks? Little known, perception is low

299 Asx passengers, Milan → South Korean, March 31, 2020
--mean age 30.0, 44.1% male
11 hr flight, then quarantined x 14 days

All wearing N95 masks (except meals/toilet), > 6 ft for preboarding Flight is full, no seat separation





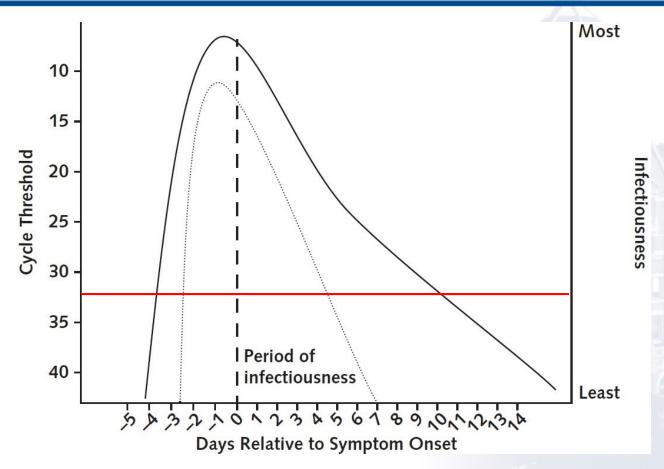


Asymptomatic Transmission The Diamond Princess

- 2666 passengers, 1045 crew
 - Total 3711
- 712 (~20%) infected
- 13 deaths
 - Case fatality rate1.8%

- 72-79% asymptomatic
- Estimate asx cases =
 11-84% transmissions

When are you most infectious?



symptomatic adults (dotted line) and respiratory tract viral load with time (solid line) red line (> 33 Cycle threshold generally not infectious)

Who transmits?— The Superspreaders

Setting (Reference)	Cases/Total at Risk (Attack Rate), n/N (%)	Index Case	Key Features	
Korean call center (136)	94/216 (43.5)	Not identified in report	Most cases found on the 11th floor of the call center: indoors with workers in very close proximity	
Church in Arkansas (55)	35/92 (38)	Pastor was presymptomatic and then symptomatic during series of events he led at church	Events included 5 indoor church- related events over several days, some of which included singing	
Wedding in Jordan (137)	76/350 (21.7)	Bride's father had fever, cough, and runny nose starting 2 d before event	2-h indoor wedding ceremony; additional 9 confirmed case patients who did not attend wedding were household contacts of those who did	
Choir in Washington state (138)	53/61 (86.7)	1 person had "cold- like" symptoms starting 3 d before event	2.5 h in multipurpose room with chairs close together; question of whether singing aerosolized the virus	
U.S.S. Theodore Roosevelt (140)	~1000/1400 (~60–70)	Not identified in report	Close quarters; social distancing, mask use, and avoiding common areas all associated with decreased risk	
Overnight camp in Georgia (139)	260/354 (78) of those who were tested had positive results (out of 597 who attended)	Not identified in report	Staffers but not campers were expected to wear cloth masks; windows and doors of cabins were not opened to increase ventilation; activities included "daily vigorous singing and cheering"; lodging consisted of 31 cabins with an average of 15 persons in each cabin	
International business conference in Boston (141)	At least 90 direct cases leading to sustained local transmission with progeny virus found in at least 35% of infections thereafter in Boston area during a major outbreak and exported to multiple other states	Presumed single introduction from Europe to Boston via this conference	Conference details not described in the manuscript, although presumed hours of close, indoor, unmasked contact	

- Superspreaders
- Estimates
 10-20% of infected
 → 80% of cases
- High viral load likely important



What about in a household?

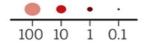
- Overall—meta-analysis of 40 studies
 - Secondary attack rate 18.8% (95% CI, 15.4% to 22.2%)
 - Higher for spouse/partner
 - Lower for other household members
 - Variable, depending on environmental factors
- Rates only lower if mask wear & social distancing in household
 - Strongly suggested for high risk people

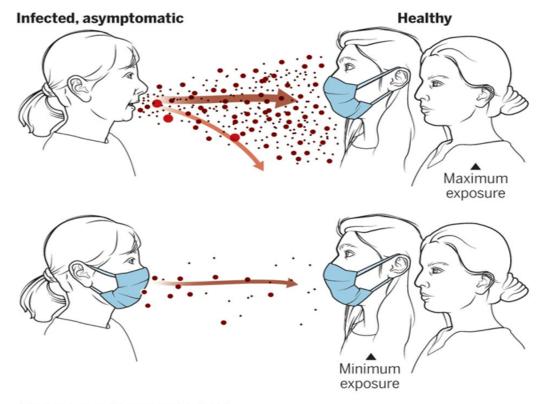
Masks—The Current Best Thing

Masks reduce airborne transmission

Infectious aerosol particles can be released during breathing and speaking by asymptomatic infected individuals. No masking maximizes exposure, whereas universal masking results in the least exposure.

Particle size (μm)





Folded handkerchief

Leaked from the top the mask

© 0.5 sec. After the start of the emulated cough.

Homemade double-layered stitched mask

Off-the-shelf cone style mask (non N95 mask)





0.97 sec.

0.47 sec.

(0.2 sec.

() 0.2 sec.

Average distance traveled by airborne droplets. (in inches)

Uncovered Bandana (Elastic T-shirt material) Folded handkerchief (Cotton) Off-the-shelf cone style mask (Unknown)

Stitched mask (Quilting cotton)*

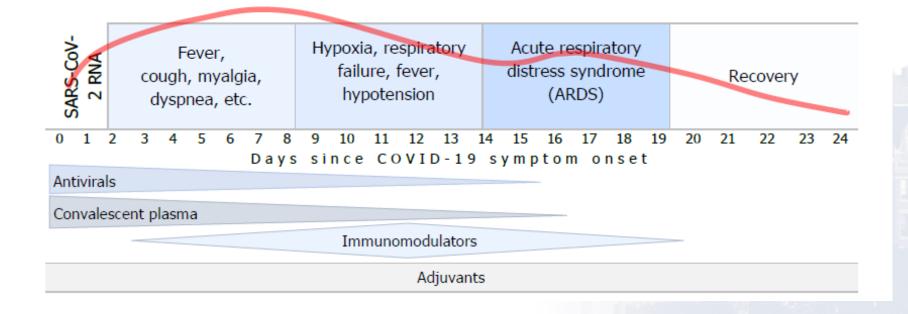
also escaped from the top edge.

*Researchers found that, of the masks they studied, a stitched, double-layered cotton mask was most effective in preventing droplets from being emitted forward. Most of the escape was from the gap between the nose and mask. Droplets traveled further out of the cone mask and

Source: Siddhartha Verma, Manhar Dhanak and Jaho Frankenfield of Florida Atlantic University Alberto Cervantes/THE WALL STREET JOURNAL

GRAPHIC: V. ALTOUNIAN/SCIENCE

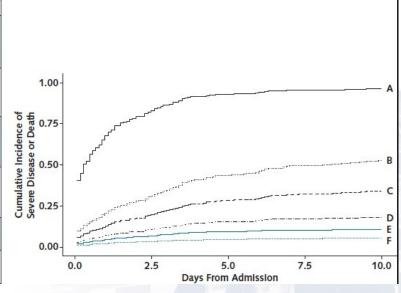
Range of COronaVIrus Disease-2019



80% without symptoms or mild illness

Johns Hopkins Medical Institutions COVID-19 Hospitalizations

Patlent	Description	Cumulative Incidence of Severe Disease or Death		
		2 Days	4 Days	7 Days
Α	81-year-old Black woman with diabetes and hypertension; BMI, 35 kg/m²; respiratory rate, 32 breaths/min; febrile; high CRP level; D-dimer level > 1 mg/L	80%	92%	96%
В	69-year-old Black man with diabetes, coronary disease, and hypertension; BMI, 38 kg/m²; respiratory rate, 23 breaths/min	28%	41%	50%
С	47-year-old Black man with diabetes and hypertension; BMI, 34 kg/m²; respiratory rate, 18 breaths/min; febrile; detectable troponin level	18%	27%	32%
D	79-year-old White man with a CCI of 0; BMI, 24 kg/m²; respiratory rate, 19 breaths/min; afebrile; detectable troponin level	10%	15%	18%
E	60-year-old White woman with a CCI of 0; BMI, 28 kg/m²; respiratory rate, 18 breaths/min; afebrile	6%	9%	11%
F	39-year-old Latinx man with a CCI of 0; BMI, 23 kg/m²; respiratory rate, 18 breaths/min; afebrile	3%	5%	5%



832 Consecutive, hospitalized patients

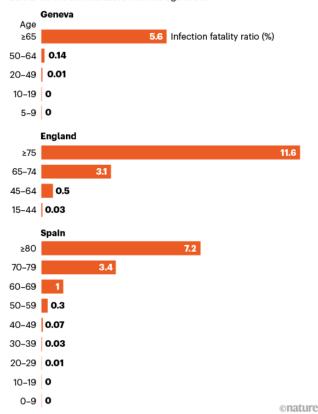
Overall mortality ~ 16%

Factors → mortality: age, nursing home residence, comorbid conditions, obesity respiratory symptoms, respiratory rate, fever, and certain lab values

Age & Gender Mortality Risks

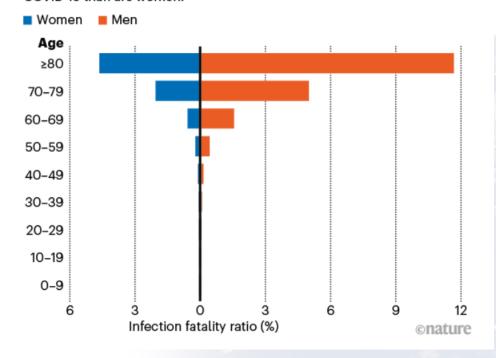
RISK WITH AGE

A person's age is the strongest predictor of their risk of dying of COVID-19. The risk increases from the age of 50.



VULNERABLE MEN

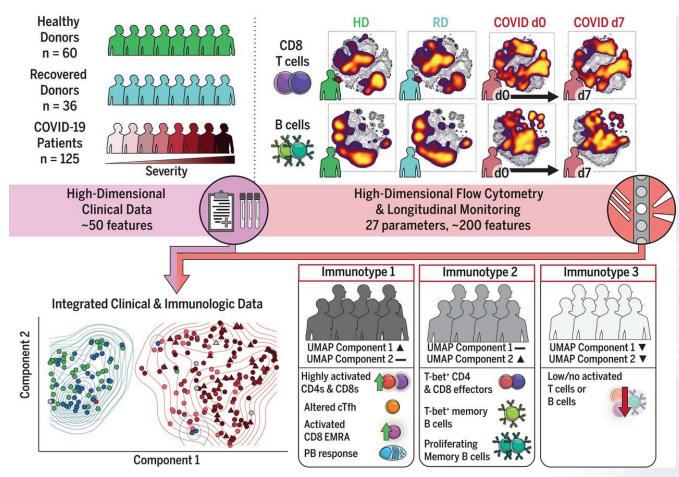
A study in Spain found that men are at higher risk of dying from COVID-19 than are women.



Source: Ref. 4; Ref. 1; Nature analysis based on Ref. 2

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COVID-19 Three Potential Patient Characteristics



Immunotype 1 =
Severe disease
Robust activated CD4s
Hyperactivated or
exhausted CD8s

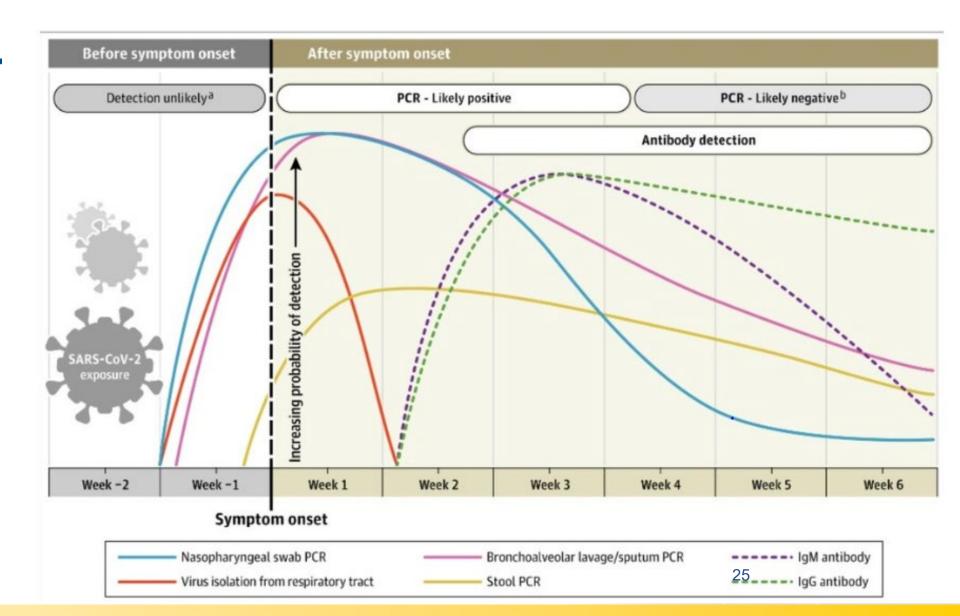
Immunotype 2 =
Less CD4 activation
> Memory B cells

Immunotype 3 =
Negative correlation with
disease severity
Lack activated T cells and
B cells

DIAGNOSTICS



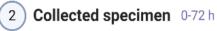
Test Sensitivity Varies With Time Since Symptom Onset



COVID-19 Diagnostic Test through RT-PCR

1) Nasopharyngeal swab <15 min

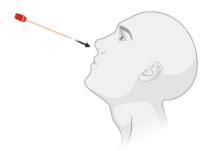
Cotton swab is inserted into nostril to absorb secretions.

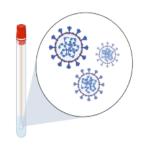


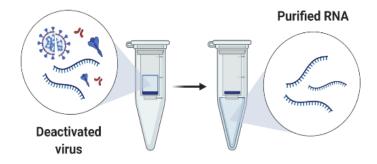
Specimen is stored at 2-8°C for up to 72 hours or proceed to RNA extraction.

3 RNA extraction ~45 min

Purified RNA is extracted from deactivated virus.



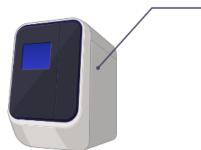


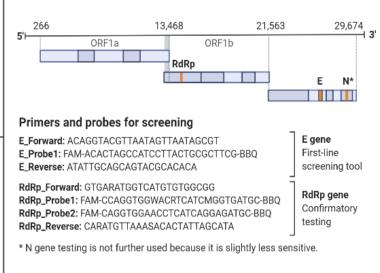


4 RT-qPCR ~1 h per primer set

Purified RNA is reverse transcribed to cDNA and amplified by qPCR.

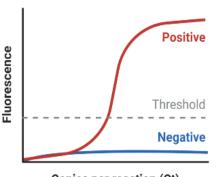
Retro transcription





5 Test results real-time

Positive SARS-CoV2 patients cross the threshold line within 40.00 cycles (< 40.00 Ct).



Copies per reaction (Ct)

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FACT SHEET FOR HEALTHCARE PROVIDERS

Sofia SARS Antigen FIA – Quidel Corporation

Updated: June 9, 2020

Coronavirus
Disease 2019
(COVID-19)



US Government, commandeered All machines for sale

→ nursing homes July 2020

What does it mean if the specimen tests negative for the virus that causes COVID-19?

A negative test result for this test means that antigens from SARS-CoV-2 were not present in the specimen above the limit of detection. However, a negative test result does not rule out COVID-19 and should not be used as the sole basis for treatment or patient management decisions, including infection control decisions. Antigen tests are known to be less sensitive than molecular tests that detect viral nucleic acids. Therefore, negative results should be treated as presumptive and confirmed with a molecular assay, if necessary for patient management.



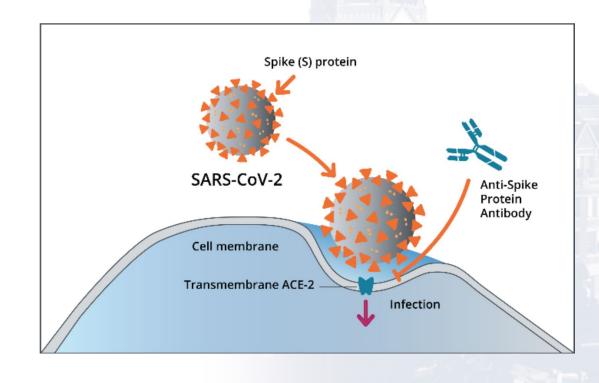
COVID-19 Molecular v. Antigen

Table 2. Summary of Some Differences between RT-PCR Tests and Antigen Tests

	RT-PCR Tests	Antigen Tests	
Intended Use	Detect current infection	Detect current infection	
Analyte Detected	Viral RNA	Viral Antigens	
Specimen Type(s)	Nasal Swab, Sputum, Saliva	Nasal Swab	
Sensitivity	High	Moderate	
Specificity	High	High	
Test Complexity	Varies	Relatively easy to use	
Authorized for Use at the Point-of- Care	Most devices are not, some devices are	Yes	
Turnaround Time	Ranges from 15 minutes to >2 days	Approximately 15 minutes	
Cost/Test	Moderate	Low	

SARS-CoV-Antibody Testing

- A positive test may reflect exposure to other coronaviruses
- A positive test should not be taken as evidence of immunity
- A positive test does not mean a COVID-19 diagnosis

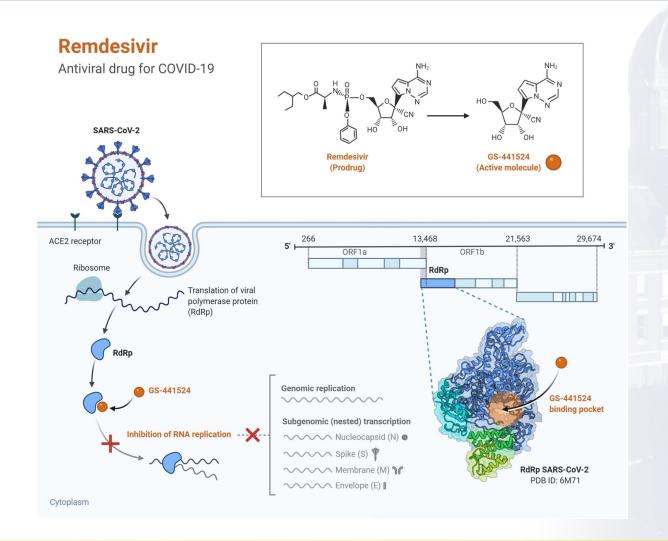




TREATMENT



Antiviral Therapy: Remdesivir





ORIGINAL ARTICLE

Remdesivir for the Treatment of Covid-19 — Preliminary Report

J.H. Beigel, K.M. Tomashek, L.E. Dodd, A.K. Mehta, B.S. Zingman, A.C. Kalil, E. Hohmann, H.Y. Chu, A. Luetkemeyer, S. Kline, D. Lopez de Castilla, R.W. Finberg, K. Dierberg, V. Tapson, L. Hsieh, T.F. Patterson, R. Paredes, D.A. Sweeney, W.R. Short, G. Touloumi, D.C. Lye, N. Ohmagari, M. Oh, G.M. Ruiz-Palacios, T. Benfield, G. Fätkenheuer, M.G. Kortepeter, R.L. Atmar, C.B. Creech, J. Lundgren, A.G. Babiker, S. Pett, J.D. Neaton, T.H. Burgess, T. Bonnett, M. Green, M. Makowski, A. Osinusi, S. Nayak, and H.C. Lane, for the ACTT-1 Study Group Members*

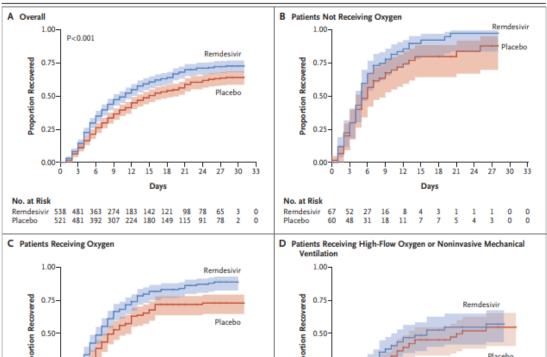
14 d day (28d in analysis) No virologic data

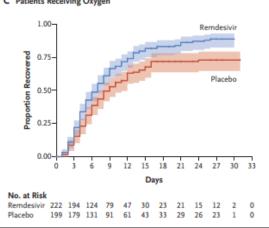
15d → 11d Length of stay

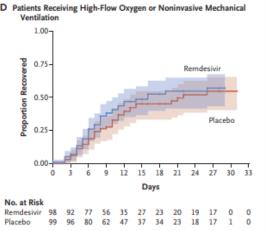
Appears safe

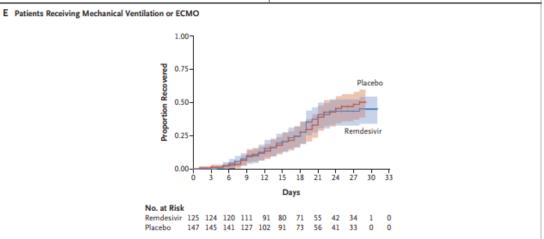
Mechanically ventilated or ECMO patients don't Appear to benefit

O2 requiring (largest group) Most benefit









Dexamethasone Trial Arm (RECOVERY Trial, Horby NEJM 2020)

- Target: hyperinflammatory state, trial halted
- UK trial
 - 2104 v. 4321 controls
- NNT avoid 1 death
 - Ventilated patients: 8
 - Mortality rate 40% → 28%
 - On oxygen: 25
 - Mortality rate 25% → 20%
 - No benefit if not on oxygen, trend toward worsening



- Home / News & Events / FDA Newsroom / Press Announcements / FDA Issues Emergency Use Authorization for Convalescent Plasma as Potential Promising COVID-19 Treatment, Another Achievement

FDA NEWS RELEASE

FDA Issues Emergency Use Authorization for Convalescent Plasma as Potential Promising COVID-19 Treatment, Another Achievement in Administration's Fight Against Pandemic



- No RCTs support use (early terminations or Phase II)
 - Li et al; Gharbharan et al; Agarwal et al (PLACID, n = 464)
- Political pressure accusations

Preliminary Data from Convalescent Plasma Expanded Access Program Adjust Mortality— Graded Dose Effect (High v. Low Titer)

- 76 patients, 7d mortality if hospital days
 - $\le 3 8.7\%$ [95% CI 8.3%-9.2%]
 - $\ge 4 11.9\% [11.4\% 12.2\%] p < 0.001)$
- 30 day mortality 21.6% vs. 26.7%, p<0.0001
- High titer v. low titer
 - 7 day mortality
 - 8.9% (6.8%, 11.7%) v. 13.7% (11.1%, 16.8%) (p=0.048)
 - 30 day morality
 - High titer, pooled 0.77 [0.63-0.94] for 30 days



LOCAL GUIDANCE/REGULATIONS + COMPANY POLICIES

RETURN TO WORK



CDC: Return to Work (9/11/20 update)

- Social distance in shared spaces
 - -≥6 feet
 - More if older adults and at risk for severe COVID-19
 - Indoor spaces > risk than outdoor spaces
- Avoid close contact with others on your commute to work

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CDC: Return to Work (9/11/20 update)

- Avoid sharing objects and equipment
- Clean and disinfect frequently touched surfaces and objects
 - To disinfect, use these <u>EPA-registered</u> disinfectantsexternal icon.



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VACCINES

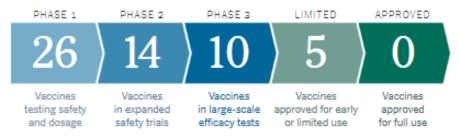


The COVID-19 Vaccine Race

> 300 candidate vaccines

Coronavirus Vaccine Tracker

By Jonathan Corum, Sui-Lee Wee and Carl Zimmer Updated September 23, 2020



All two injections except: JNJ & CanSinoBio (single inj)

Vaccines in Phase 3 trials

- Moderna (mRNA)
- BioNTech/Pfizer (mRNA)
- CanSinoBio* (Ad5)
- Gamaleya* (Ad5/Ad26)
- Oxford/AstraZeneca (ChAdOx1)
- Sinovac* (inactivated)
- Wuhan Inst/Sinopharm (inactivated)
- Sinopharm* (inactivated)
- Murdoch (BCG vaccine)
- JNJ (Ad26)

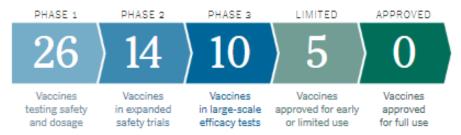


First Available Phase 3 results? Full results likely > 6 months later

> 300 candidate vaccines

Coronavirus Vaccine Tracker

By Jonathan Corum, Sui-Lee Wee and Carl Zimmer Updated September 23, 2020



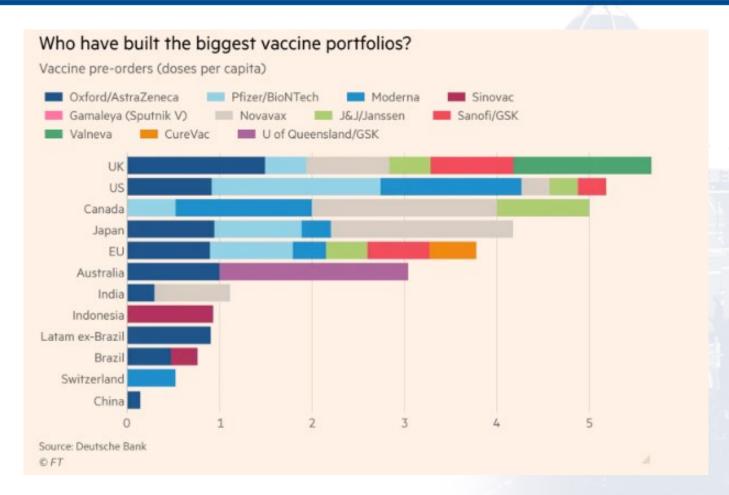
All two injections except: JNJ & CanSinoBio (single inj)

Vaccines in Phase 3 trials

- Moderna (mRNA) DEC or JAN?
- BioNTech/Pfizer (mRNA) NOV-DEC?
- CanSinoBio* (Ad5)
- Gamaleya* (Ad5/Ad26)
- Oxford/AstraZeneca (ChAdOx1)
- Sinovac* (inactivated)
- Wuhan Inst/Sinopharm (inactivated)
- Sinopharm* (inactivated)
- Murdoch (BCG vaccine)
- JNJ (Ad26)



Vaccine Portfolio





Pandemic still severe
Global effect
Worries for this winter
Likely only US hope = vaccines (Spring)
WEAR MASKS

QUESTIONS?

