Disclosures

• We have no relevant financial interests to disclose.
And Elsewhere...

Where new cases are **higher and staying high**
States where new cases are higher had a daily average of at least 15 new cases per 100,000 people over the past week. Charts show daily cases per capita and are on the same scale. Tap a state to see detailed map page.

New reported cases by day in the United States

States Currently Covered by the Order
Travelers from the following states and territories should quarantine upon arrival in Chicago: Alabama, Arkansas, Georgia, Iowa, Kansas, Kentucky, Louisiana, Mississippi, Missouri, Nebraska, North Dakota, Oklahoma, South Carolina, South Dakota, Tennessee, and Utah. The list will be updated every Tuesday and go into effect the following Friday at 12:01 a.m.

Where new cases are **higher but going down**

New reported deaths by day in the United States

And Abroad...

- Countries with rising rates of COVID-19
- implementing new restrictions:
  - UK
  - Israel
  - India
  - Argentina
  - Indonesia
  - Ukraine
  - Iraq
  - Spain
  - France

Source: ECDC, data to 15 Sep
mRNA vaccines

• 2 candidates in late stage trials: Moderna/NIAID mRNA-1273 and BioNTech/Fosun/Pfizer BNT162

• Advantages:
  • Development speed
  • Safety – no integration of into DNA, no viral particles

• Challenges:
  • Unintended immune reactions
  • Stability – need lipid nanoparticle to improve stability and get into cells
45 enrolled participants received their first vaccination between March 16 and April 14, 2020.

No serious adverse events were noted, and no prespecified trial halting rules were met.

Binding antibody IgG geometric mean titers (GMTs) to S-2P increased rapidly after the first vaccination, with seroconversion in all participants by day 15. Dose-dependent responses to the first and second vaccinations were evident.

After the first vaccination, neutralizing responses were detected in less than half the participants, and a dose effect was seen. However, after the second vaccination, responses were identified in serum samples from all participants.

Elicited CD4 T-cell responses that on stimulation by S-specific peptide pools were strongly biased toward expression of Th1 cytokines.
BioNTech/Fosun/Pfizer BNT162 b1/b2

- 195 healthy adults 18–55 and 65–85 years of age were randomized in an ongoing, placebo-controlled, observer-blinded dose-escalation study to receive 2 doses at 21-day intervals of placebo or either of 2 lipid nanoparticle–formulated, nucleoside-modified RNA vaccine candidates:
  - BNT162b1, which encodes a secreted trimerized SARS-CoV-2 receptor-binding domain
  - BNT162b2, which encodes a prefusion stabilized membrane-anchored SARS-CoV-2 full-length spike
- 2 vaccine candidates elicited similar dose-dependent SARS-CoV-2–neutralizing geometric mean titers (GMTs), comparable to or higher than the GMT of a panel of SARS-CoV-2 convalescent sera.
- BNT162b2 was associated with less systemic reactogenicity, particularly in older adults and was selected to advance to phase III study

RNA-Based COVID-19 Vaccine BNT162b2 Selected for a Pivotal Efficacy Study
doi: https://doi.org/10.1101/2020.08.17.20176651
Updates as of 9/13...

• Moderna enrollment is slowing – trying to increase diversity on enrollment

• The fraction of white participants being enrolled in the study has decreased over the last four weeks, from 73% to 68% to 67%, and finally down to 59% for the most recent week. Meanwhile, enrollment of Hispanic or Latino participants jumped from 17% to 22%, and Black or African Americans increased from 5% of enrollment three weeks ago to 11% of enrollment in the most recent week.

• Moderna is trailing Pfizer and BioNTech which had enrolled 25,189 patients in the phase 2/3 clinical trial testing its coronavirus vaccine, BNT162b2, as of an update on Sep. 7. In terms of diversity though, Moderna is ahead with 27% of participants coming from diverse communities, compared to Pfizer and BioNTech's 24%

• U of Chicago to start enrollment this week; UIC is already enrolling
Adenoviral Vectored Vaccines

- All genetic vaccines mimic a natural viral infection by forcing our bodies to produce viral proteins inside our cells. That spurs the T cells of our immune system to attack these vaccinated cells, and in the process, they learn to seek and destroy cells infected with the real virus in the future.

- Genetic material is added to the adenoviral construct, which is used to make proteins from the SARS-CoV-2 coronavirus called Spike glycoprotein (S). This protein is usually found on the surface of SARS-CoV-2 and plays an essential role in the infection pathway of the SARS-CoV-2 virus.
AZD1222 SARS-CoV-2 Vaccine (AstraZeneca/Oxford)

- Formerly known as ChAdOx1 nCoV-19, is made from a virus (ChAdOx1), which is a weakened version of a common cold virus (adenovirus) that causes infections in chimpanzees, that has been genetically changed so that it is impossible for it to grow in humans.

- The vaccine was safe and tolerated, with reduced reactogenicity when paracetamol was used prophylactically for the first 24 h after vaccination.

- Reactogenicity was reduced after a second dose.

- Humoral responses to SARS-CoV-2 spike protein peaked by day 28 post prime and cellular responses were induced in all participants by day 14.

- Neutralising antibodies were induced in all participants after a second vaccine dose. After two doses, potent cellular and humoral immunogenicity was present in all participants studied.

Lancet 2020; 396: 467–78
July 20, 2020 https://doi.org/10.1016/S0140-6736(20)31604-4
Updates as of 9/13...

• September 8 – trial suspended due to SAE in one volunteer
• Volunteer in UK developed transverse myelitis
• Enrollment restarted 4 days later in the UK, but not in the US – FDA investigation result is still pending
• Three Chicago hospitals, Northwestern, Rush and Stroger, are among the facilities around the world set to take part in the trial
Johnson & Johnson/Janssen Ad26.COV2.S

• Only published study to date: Preclinical study on primates shows a production of neutralizing antibody to the Spike protein

• Phase I/IIa trials underway – preliminary results are supposedly good, though not published

• Monovalent vaccine composed of a recombinant, replication-incompetent adenovirus type 26 (Ad26) vector, wh encodes SARS-CoV-2 spike (S) protein.

• Adenoviral vectors:
  1. Well characterized and easily manipulated
  2. Exhibit broad tropism infecting many dividing and non-dividing cells
  3. Platform allows for high yield
     • a. Adenovirus E1 region deleted (Ad26)
     • b. Clin/non-clin experience shows strong humoral and Th1 CMI w acceptable safety

• Previous Adenovial vectored vaccines: HIV, Ebola, RSV, Zika, malaria vaccines show good safety profile
  • Significant AEs: (>30%) malaise, fatigue, HA, myalgia.

• Planning underway for phase III study to begin later this month – University of Chicago will be a site
Sub-Unit Vaccines: Novavax NVX-CoV2373

• The company has received a $1.6 billion grant from the government’s Operation Warp Speed to have 100 million doses ready by early 2021.

• Novavax’s technology turns moth cells into factories for the Spike protein, which studs the surface of coronaviruses. Its vaccine combines several of the spike proteins in a nanoparticle.

• Working with Takeda on production of vaccine.

• Phase II studies ongoing; hope to produce results in 4th quarter.
Fairly Prioritizing Groups for Access to COVID-19 Vaccines

• First, prioritizing in-person health care workers and staff
  • Indirectly prioritizes disadvantaged groups because reducing disease spread facilitates the provision of treatments such as hemodialysis and chemotherapy, which disadvantaged individuals need more often.

• Second, prioritizing people engaged in essential high risk activities, such as in-person education, childcare, and food supply work
  • In-person workers are more likely to be socioeconomically disadvantaged than those able to work remotely. Prioritization among these workers should consider indirect benefit: if vaccination of those involved in education can contribute to reopening schools, this should precede vaccination of those involved in reopening other less beneficial venues, such as bars.

• Prioritizing people older than 65 years without high risk is ethically and legally more complex. Because early death correlates with disadvantage, prioritizing all patients 65 years and older is likely to exacerbate disadvantage. For instance, 30% of all non-White COVID-19 decedents are younger than 65 vs only 13% of White decedents. Although the risk of death from COVID-19 increases 7-fold between age 50 and 80, these estimates do not control for health conditions or exposure in residential settings.

• Prioritization should recognize that a healthy older person who can shelter in place is at different risk from a medically vulnerable older person in crowded housing. A preferable approach would reduce disparities by considering vulnerabilities.
Lilly announces proof of concept data for neutralizing antibody LY-CoV555 in the COVID-19 outpatient setting

September 16, 2020
- Primary endpoint of viral load change from baseline at day 11 was met for one of three doses; consistent effects of viral reduction seen at earlier time points

- Rate of hospitalizations and ER visits was 1.7 percent (5/302) for LY-CoV555 versus 6 percent (9/150) for placebo--a 72 percent risk reduction in this limited population

- LY-CoV555 was well-tolerated across all doses with no drug-related serious adverse events reported
# Remdesivir Studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>Intervention</th>
<th>Outcome</th>
</tr>
</thead>
</table>
| Wang Y et al.  
The Lancet, April 2020  
Double blind, placebo-controlled, multi-center, RCT | N=237 hospitalized patients with SARS-CoV2 virus, with CXR changes and O2<94% RA | Remdesivir 10 days vs. placebo, 2:1 | No associated difference in time to clinical improvement |
| Beigel JH et al.  
ACTT-1, NEJM May2020  
Double blind, placebo-controlled, multi-center, RCT | N=1063 hospitalized patients with SARS-CoV2 virus and CXR changes and O2<94% RA | Remdesivir x 10 days vs. placebo | Recovery time of patients receiving 10d of Rem vs. placebo was shorter (11 vs 15 days)  
No mortality difference bw drug (7.1%) and placebo (11.9%) |
| Goldman JD et al.  
NEJM, May 2020  
Randomized, open-label, phase 3 trial | N=397 hospitalized patients with SARS-CoV2, CXR changes and O2<94% RA | Remdesivir 5 vs. 10 days, 1:1 | Clinical status assessed day 14, assessed by a 7-point ordinal scale found no significant difference 5 v 10d  
Mortality lower 5d (8 v 11%) |
| Spinner, CD et al.  
JAMA, August 2020  
Randomized, open-label, multi-center phase 3 trial | N=584 hospitalized adults with moderate COVID-19 (pulmonary infiltrates and RA O2%>94) | 10 days remdesivir vs. 5 days remdesivir vs. standard of care, 1:1:1 | 5-day Rem group had statistically significantly higher odds of better clinical status (p=.02) vs. SOC on D11.  
No difference between 10-d and SOC groups (p=.18)  
*Mean length of treatment 5d v 6 d (10-d arm)  
*difference of unclear clinical importance |
Efficacy of Remdesivir in COVID-19

Erin K. McCreary, PharmD; Derek C. Angus, MD, MPH

- Optimal patient population is not clear
- Optimal duration of therapy is not clear
- Outcomes vs. placebo or a standard of therapy are not clear
- The effect of remdesivir if given with dexamethasome or other steroids are not clear

(Reuters) - U.S. hospitals have turned down about a third of their allocated supplies of the COVID-19 drug remdesivir since July as need for the costly antiviral wanes, the Department of Health and Human Services (HHS) confirmed on Friday.
Patients divided into two groups
- Metabolic syndrome (MetS) and non-Mets per WHO criteria

Criteria for MetS (3 of 5)
- Prediabetes or documented h/o diabetes
- Obesity BMI>30 kg/m²
- History of hypertension or antihypertensive medication
- TG>150 mg/dL
- HDL<50mg/dL for women and <40 mg/dL for men OR use of cholesterol-lowering medication with history for hypercholesterolemia

66% had metabolic syndrome, predominantly non-Hispanic black patients

MetS associated with increased odds of hospital mortality, ICU requirement, IMV and ARDS

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- TG>150 mg/dL
- HDL<50mg/dL for women and <40 mg/dL for men OR use of cholesterol-lowering medication with history for hypercholesterolemia
Table. Baseline Characteristics of Young Adults Age 18 to 34 Years With COVID-19

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No. (%)</th>
<th>Full case series (N = 3222)</th>
<th>No death or ventilation (n = 2879)</th>
<th>Death or ventilation (n = 343)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), y</td>
<td></td>
<td>28.3 (4.4)</td>
<td>28.3 (4.4)</td>
<td>28.3 (4.5)</td>
<td>.90</td>
</tr>
<tr>
<td>Men</td>
<td></td>
<td>1849 (57.6)</td>
<td>1626 (56.7)</td>
<td>223 (65.0)</td>
<td>.003</td>
</tr>
<tr>
<td>Race/ethnicity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White non-Hispanic</td>
<td>536 (16.6)</td>
<td>479 (16.6)</td>
<td>57 (16.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White Hispanic</td>
<td>350 (10.9)</td>
<td>324 (11.3)</td>
<td>26 (7.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black non-Hispanic</td>
<td>748 (23.2)</td>
<td>675 (23.4)</td>
<td>73 (21.3)</td>
<td></td>
<td>.14</td>
</tr>
<tr>
<td>Black Hispanic</td>
<td>14 (0.4)</td>
<td>13 (0.5)</td>
<td>1 (0.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other/unknown</td>
<td>1574 (48.9)</td>
<td>1388 (48.2)</td>
<td>186 (54.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black and/or Hispanic</td>
<td>1838 (57.0)</td>
<td>1669 (58.0)</td>
<td>169 (49.3)</td>
<td></td>
<td>.002</td>
</tr>
<tr>
<td>Discharge month</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>April 2020</td>
<td>1680 (52.1)</td>
<td>1495 (51.9)</td>
<td>185 (53.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>May 2020</td>
<td>1063 (33.0)</td>
<td>936 (32.5)</td>
<td>127 (37.0)</td>
<td></td>
<td>.004</td>
</tr>
<tr>
<td>June 2020</td>
<td>479 (14.9)</td>
<td>448 (15.6)</td>
<td>31 (9.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Region</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Northeast</td>
<td>1298 (40.3)</td>
<td>1161 (40.4)</td>
<td>137 (39.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>South</td>
<td>1130 (35.1)</td>
<td>1032 (35.9)</td>
<td>98 (28.6)</td>
<td></td>
<td>.002</td>
</tr>
<tr>
<td>Midwest</td>
<td>558 (17.3)</td>
<td>488 (17.0)</td>
<td>70 (20.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>West</td>
<td>233 (7.2)</td>
<td>195 (6.8)</td>
<td>38 (11.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any obesity, BMI ≥ 30</td>
<td>1187 (36.8)</td>
<td>1007 (35.0)</td>
<td>180 (52.5)</td>
<td></td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Morbid obesity, BMI ≥ 40</td>
<td>789 (24.5)</td>
<td>649 (22.5)</td>
<td>140 (40.8)</td>
<td></td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Asthma</td>
<td>545 (16.9)</td>
<td>495 (17.2)</td>
<td>50 (14.6)</td>
<td></td>
<td>.22</td>
</tr>
<tr>
<td>Hypertension</td>
<td>519 (16.1)</td>
<td>412 (14.3)</td>
<td>107 (31.2)</td>
<td></td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Smoking</td>
<td>513 (15.9)</td>
<td>472 (16.4)</td>
<td>41 (12.0)</td>
<td></td>
<td>.03</td>
</tr>
<tr>
<td>Diabetes</td>
<td>588 (18.2)</td>
<td>494 (17.2)</td>
<td>94 (27.4)</td>
<td></td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

• Outpatient adults getting testing in July 2020
• Random sample of SARS-CoV2 positive case participants, each matched with 2 negative controls
• Compared with case-patients, control patients were more likely to be non-Hispanic white (<0.01), have a college degree or higher (p<0.01) and report at least one underlying chronic medical condition
• COVID-19 positive contacts reported by 42% of cases and 14% of controls
  • Half of contacts were family members
• Restaurants, gyms, coffee shops, bars and religious gatherings of highest risk if NO KNOWN contact

10-80% of people with the SARS-CoV2 virus experience symptoms >3 weeks after acute infections.