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COVID-19: An Update for the Research Community

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Professor, Divisions of Infectious Diseases and Organ Transplantation Director, Transplant and Immunocompromised Host Infectious Diseases Service Director, NUCATS Center for Clinical Research Northwestern University Feinberg School of Medicine

21 October 2020



- Research Support[°]
 - AiCuris, Janssen, Shire
- Paid Consultation
 - Adagio, AlloVir, Celltrion, Cidara, Genentech/Roche, Janssen, Shionogi, Viracor Eurofins
- Unpaid Consultation
 - Romark

Northwestern

- Data & Safety Monitoring Board Participation
 - NIH, Janssen, Merck, SAB Biotherapeutics, Sequiris, Takeda, Vitaeris

As of 10/19/20; [°] Paid to Northwestern University.

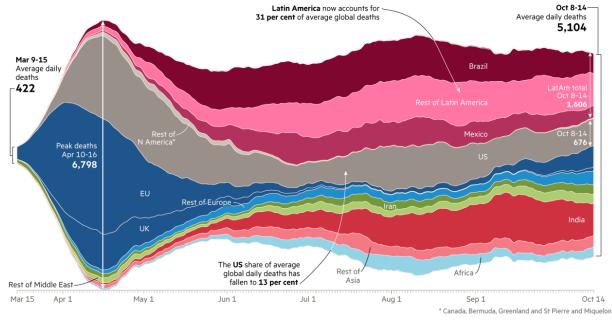
COVID-19 Update

- •Epidemiology
- •Prevention
 - •Masking and social distancing
 - Vaccines
- Treatment Options

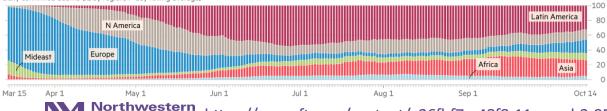
•What to Expect from the Flu Season

COVID-19: Current Global Situation

Daily deaths of patients diagnosed with coronavirus (7-day rolling average)



Daily confirmed deaths (%, by region, 7-day rolling average)

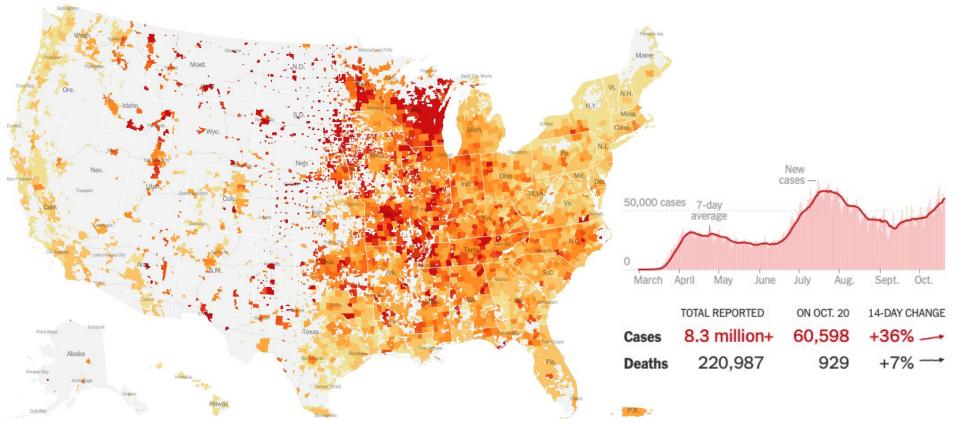




Medicine[®] https://www.ft.com/content/a26fbf7e-48f8-11ea-aeb3-955839e06441 - Accessed 21 October 2020

COVID-19: *Current Situation in the United States*

How the number of new cases has changed in the last two weeks

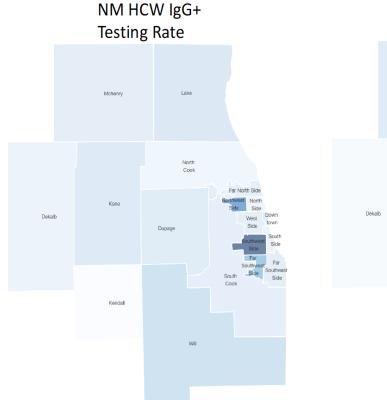


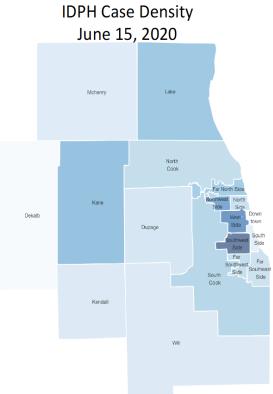
Northwestern Medicine* https://www.nytimes.com/interactive/2020/us/coronavirus-us-cases.html - Accessed 21 October 2020

Seropositivity of NM Employees: Seroprevalence Rate 4.8%

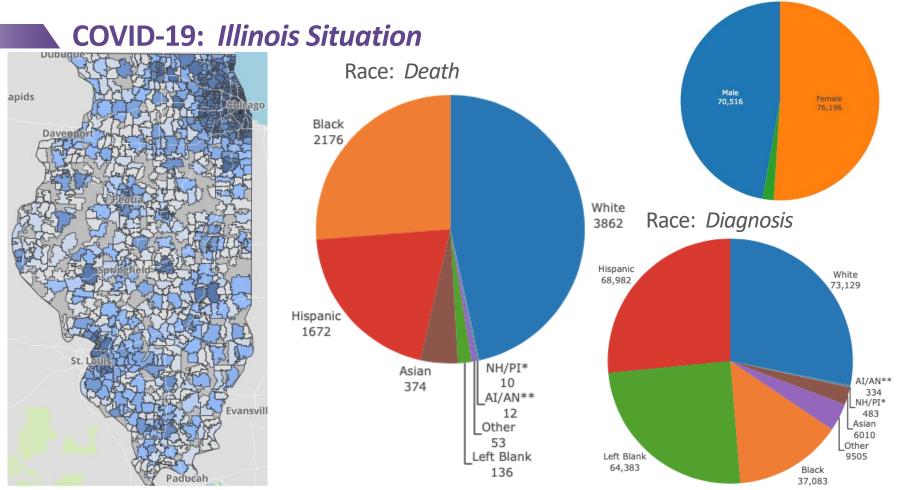
| Characteristics | IgG Positive % (95% CI) | Total (N) |
|-------------------------------------|---------------------------------|-----------|
| Age Category | | |
| - N | 316 | 6510 |
| - 18-29 | 97 (7.4% , 6.1 - 9%) | 1304 |
| - 30-39 | 97 (4.4%, 3.6 - 5.3%) | 2208 |
| - 40-49 | 60 (4.4%, 3.4 - 5.6%) | 1368 |
| - 50-59 | 47 (4.5%, 3.3 - 6%) | 1042 |
| - 60+ | 15 (2.6% , 1.4 - 4.2%) | 588 |
| Gender | | |
| - N | 316 | 6510 |
| - Female ^a | 256 (4.9%, 4.4 - 5.6%) | 5180 |
| - Male | 60 (4.5%, 3.5 - 5.8%) | 1330 |
| Race/Ethnicity | | |
| - N | 316 | 6510 |
| - Asian | 29 (4.6%, 3.1 - 6.5%) | 634 |
| - Hispanic/Latino | 46 (9.6% , 7.1 - 12.7%) | 477 |
| - Non-hispanic Black | 17 (8.5% , 5 - 13.2%) | 201 |
| - Non-hispanic White | 212 (4.3%, 3.8 - 5%) | 4877 |
| - Other/Multiracial/NA ^b | 12 (3.7%, 1.9 - 6.4%) | 321 |

Seropositivity by Neighborhood: NM HCW vs. IDPH Data





Northwestern Wilkins et al. medRxiv. 2020: doi.org/10.1101/2020.09.11.20192385.

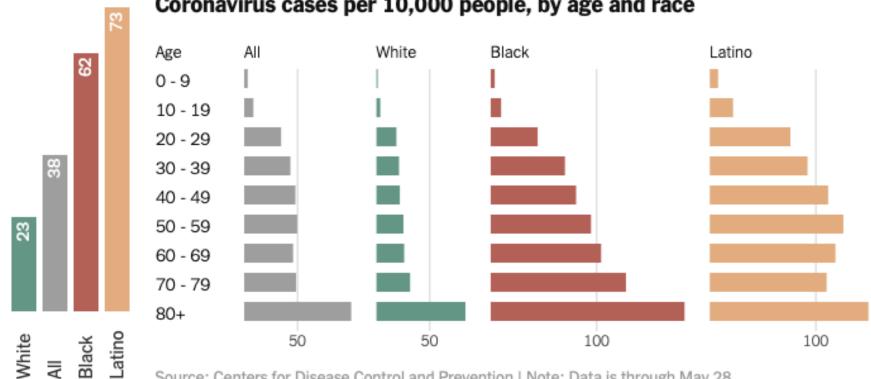


Northwestern Medicine[®]

https://www.dph.illinois.gov/covid19/covid19-statistics. Accessed 12 September 2020.

COVID-19: Special Populations - Minorities

Coronavirus cases per 10,000 people



Coronavirus cases per 10,000 people, by age and race

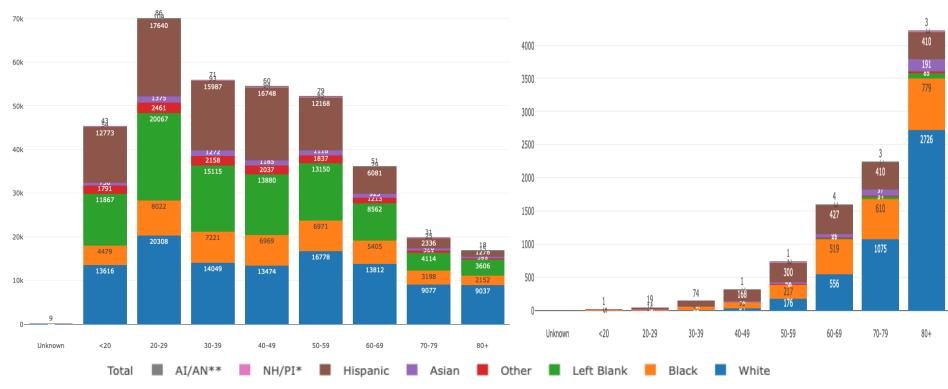
Source: Centers for Disease Control and Prevention | Note: Data is through May 28.

Northwestern https://www.nytimes.com/interactive/2020/07/05/us/coronavirus-latinos-african-americans-cdc-data.html

COVID-19: *Illinois Situation*

Diagnosis by Age

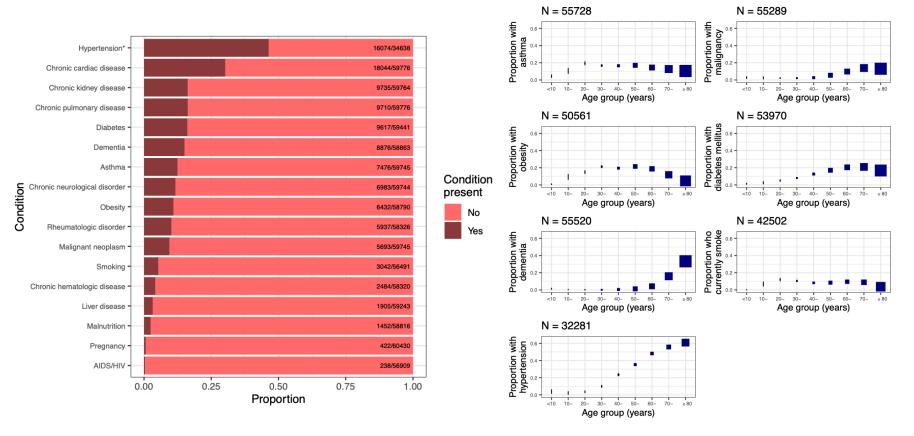
Death by Age



Morthwestern ht

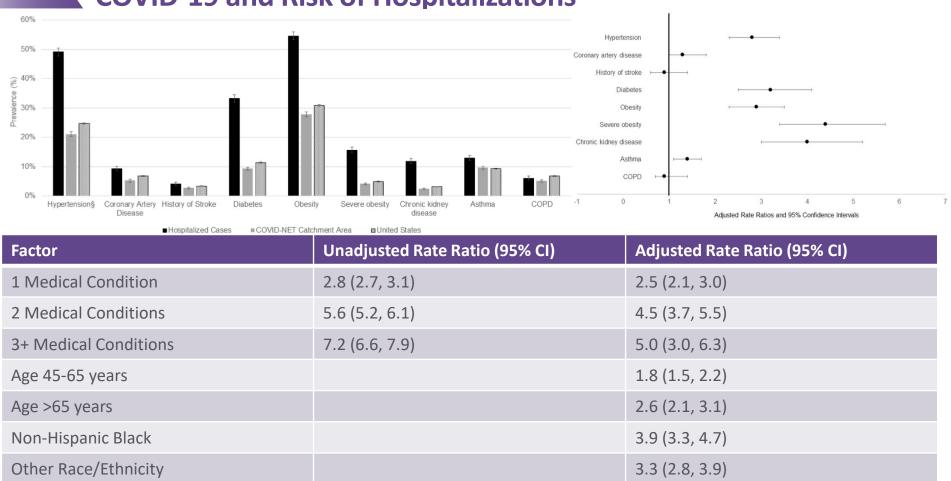
https://www.dph.illinois.gov/covid19/covid19-statistics. Accessed 21 October 2020.

COVID-19: *Epidemiology – Co-Morbidity*



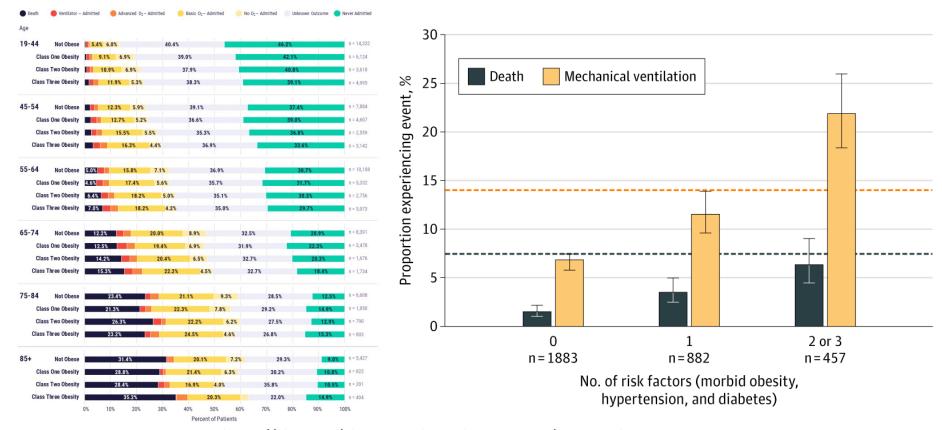
Morthwestern https://isaric.tghn.org. Accessed July 27, 2020.

Ko et al. Clin Infect Dis. 2020: doi.org/10.1093/cid/ciaa1419.



COVID-19 and Risk of Hospitalizations

COVID-19: Special Populations - Obesity





https://ehrn.org/obesity-and-covid-19-severity/ Accessed 12 Sept 2020

Cunningham et al. JAMA Internal Med. 2020: doi:10.1001/jamainternmed.2020.5313.

COVID-19: Symptoms



Muscle or body aches Vomiting or diarrhea New loss of taste or smell

Symptoms can range from mild to severe illness, and appear 2-14 days after you are exposed to the virus that causes COVID-19.

> Seek medical care immediately if someone has emergency warning signs of COVID-19. Trouble breathing Inability to wake or •

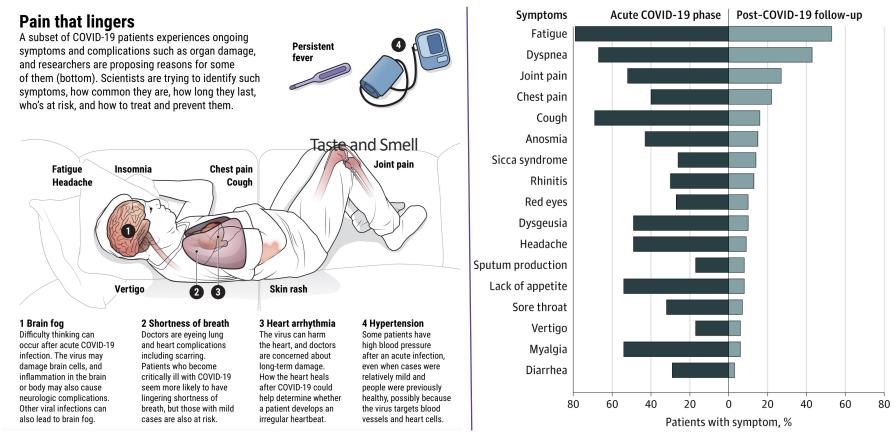
- Persistent pain or pressure in the chest
- New confusion

•

- stay awake
- Bluish lips or face

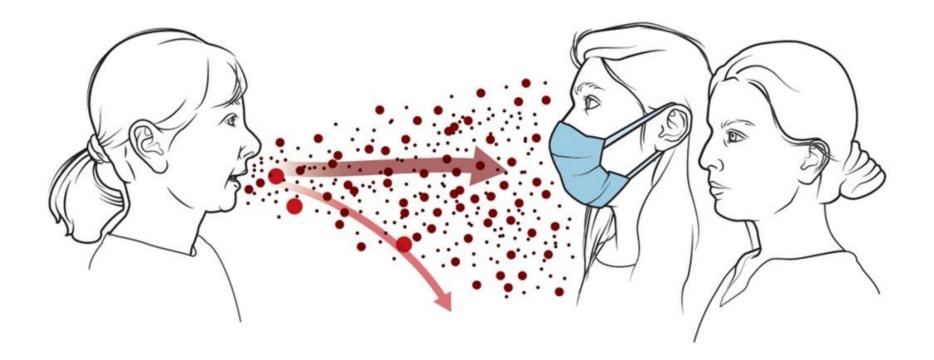


Long-Term Complications of COVID-19



Morthwestern Carfi *et ai.* JAMA. 2020;324(6):603-605. doi:10.1001/jama.2020.12603





Northwestern https://blogs.sciencemag.org/vis/2020/08/14/covid-a-visual-library/ Accessed 12 Sept 2020

COVID-19: *Transmission and Masks*

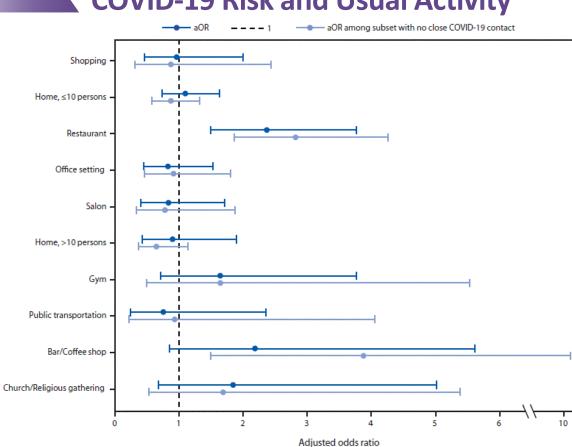
| Chance of Transmission | Asymptomatic COVID-19 Carrier | Uninfected Person |
|------------------------|----------------------------------|----------------------|
| HIGHEST | 2 | 8 |
| HIGH | 2 | |
| MEDIUM | | |
| LOW | | |
| LOWEST | 6 | ft → |
| PRACTICALLY NONE | | |

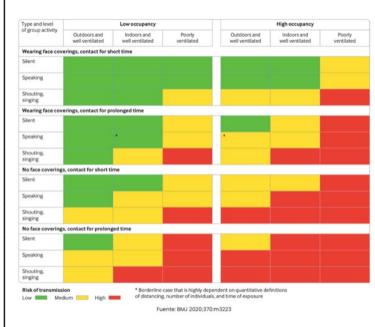


COVID-19: *Transmission and Masks*









COVID-19 Risk and Usual Activity

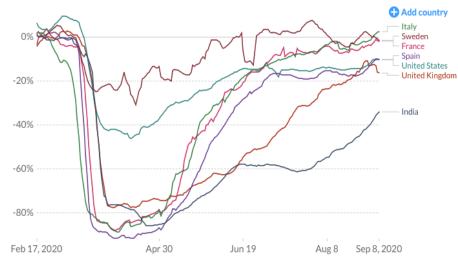
Northwestern Medicine[®]

Fisher et al. MMWR. 2020; 69:1258–1264.

Social Distancing: How the US Did Compared to Other Countries

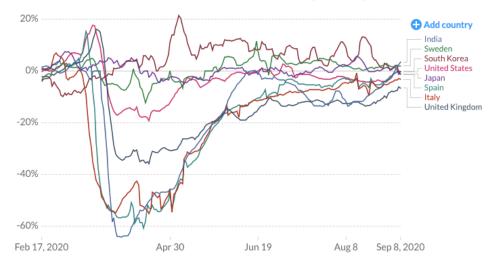
Change in Retail and Recreation Visits

Change in visitor numbers is measured relative to a baseline day; a baseline day is the median value from the 5-week period between Jan 3rd and Feb 6th 2020. This index is smoothed to the rolling 7-day average.



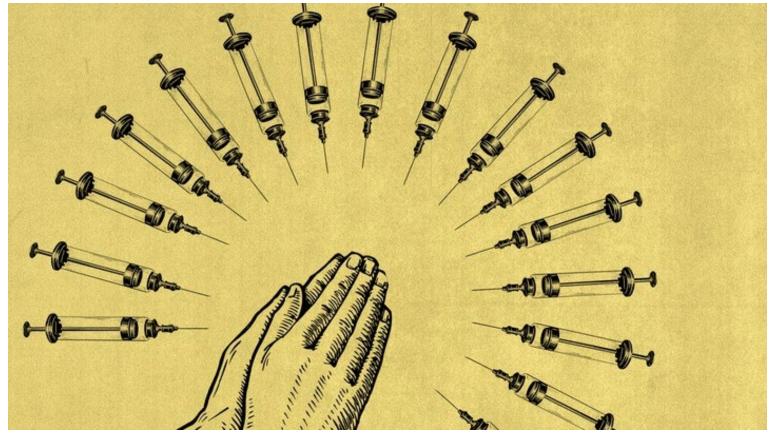
Change in Grocery and Pharmacy Visits

Change in visitor numbers is measured relative to a baseline day; a baseline day is the median value from the 5-week period between Jan 3rd and Feb 6th 2020. This index is smoothed to the rolling 7-day average.



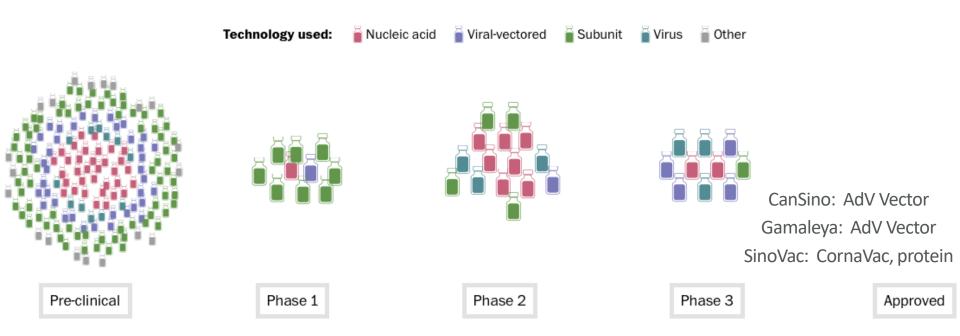
Northwestern https://ourworldindata.org/covid-mobility-trends Accessed 12 September 2020

SARS-CoV-2 Vaccines: Current Status



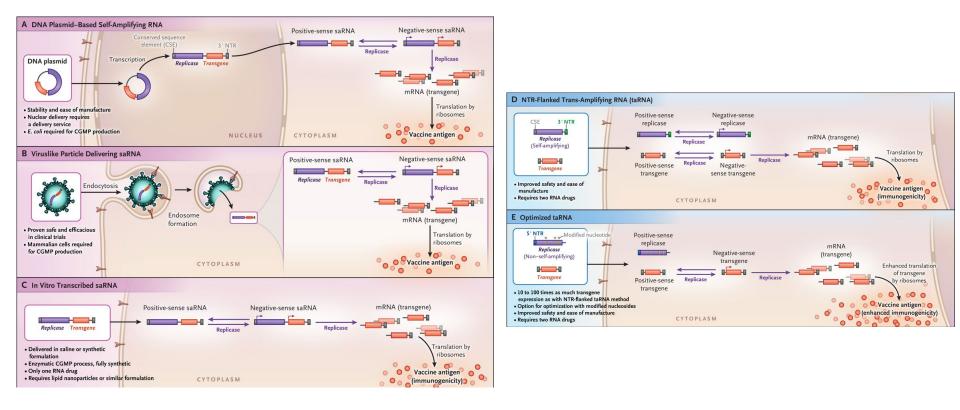


COVID-19: *Prevention - Vaccines*



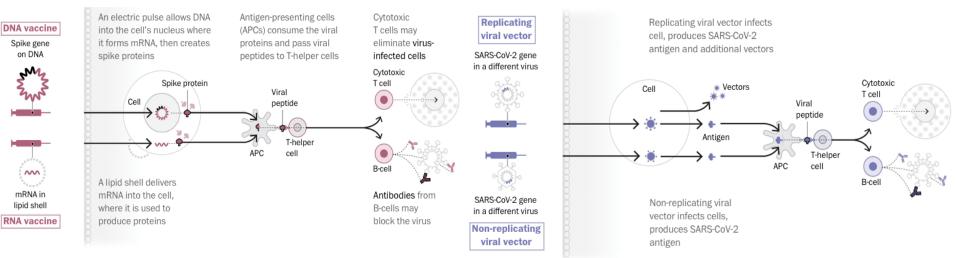
Morthwestern "These are the Top Coronavirus Vaccines to Watch." Washington Post. 13 October 2020.

COVID-19: RNA/DNA Vaccines



Medicine[®] Fuller DH, Berglund P. *N Engl J Med.* 2020;382:2469-2471.

COVID-19: RNA/DNA and Viral Vaccines



Nucleic acid vaccines, developed by ...

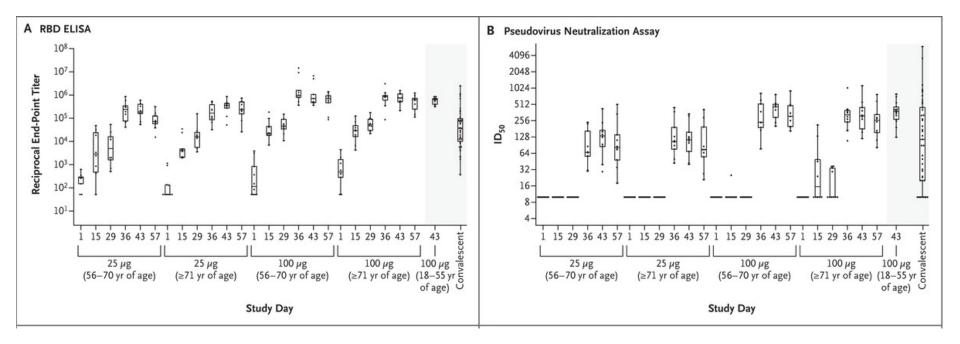
| Moderna; National Institutes of Health | PC | P1 | P2 | P3 | A |
|--|----|----|----|----|---|
| Pfizer; BioNTech; Fosun Pharma | PC | P1 | P2 | P3 | A |
| AnGes; Osaka University; Takara Bio | PC | P1 | P2 | P3 | A |
| Arcturus Therapeutics; Duke-NUS | PC | P1 | P2 | P3 | A |
| CureVac | PC | P1 | P2 | P3 | A |
| Genexine | PC | P1 | P2 | P3 | A |

Viral-vectored vaccines, developed by...

| AstraZeneca; University of Oxford | | | | i0 | |
|---|----|----|----|----|----|
| | | P1 | P2 | P3 | A |
| CanSino Biologics; Beijing Institute of Biotechnology* | PC | P1 | P2 | P3 | Δ. |
| | FU | FI | ΓZ | гэ | A |
| Gamaleya Research Institute* | PC | P1 | P2 | P3 | A |
| Johnson & Johnson, Beth Israel Deaconess Medical Center | PC | P1 | P2 | P3 | A |
| Institut Pasteur; Themis; University of Pittsburgh CVR; Merck | | | | | |
| Sharp & Dohme | PC | P1 | P2 | P3 | A |

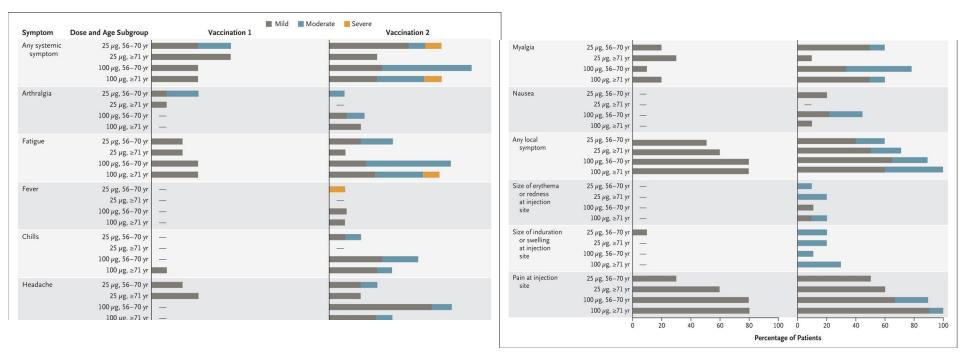
Northwestern "These are the Top Coronavirus Vaccines to Watch." Washington Post. 13 October 2020.

• Moderna/NIH (mRNA-1273): Lipid nanoparticle—formulated, mRNA encoding full-length spike glycoprotein trimer, S-2P, with two proline substitutions in the central helix in the S2 subunit



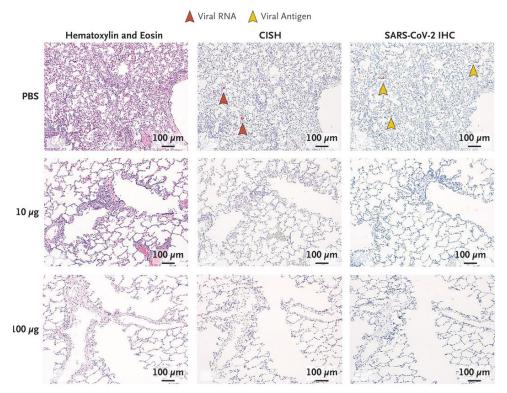
Northwestern Medicine^{*} Anderson *et al. N Engl J Med.* 2020: DOI: 10.1056/NEJMoa2028436.

• Moderna/NIH (mRNA-1273): Lipid nanoparticle—formulated, mRNA encoding full-length spike glycoprotein trimer, S-2P, with two proline substitutions in the central helix in the S2 subunit



Northwestern Medicine^{*} Anderson *et al.* **N Engl J Med**. 2020: DOI: 10.1056/NEJMoa2028436.

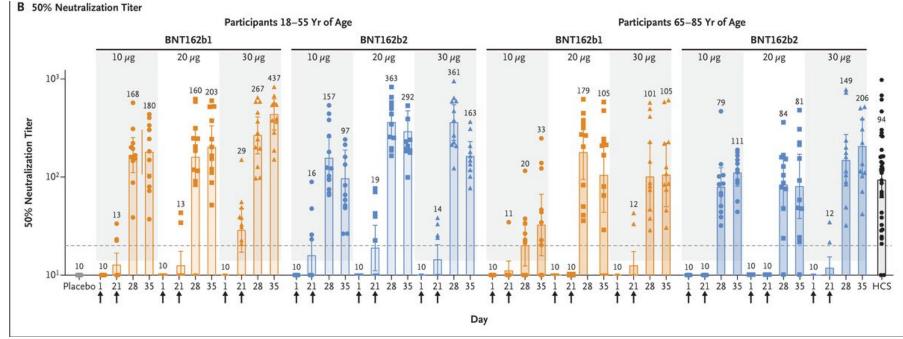
• Moderna/NIH (mRNA-1273): Animal Studies





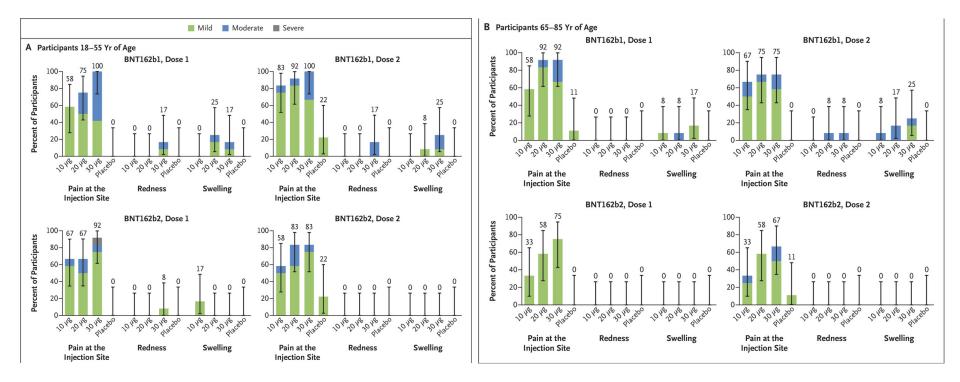
- BioNTech/Pfizer: Lipid nanoparticle-formulated, nucleoside-modified RNA vaccine candidates
 - BNT162b1: Secreted trimerized SARS-CoV-2 receptor-binding domain

o BNT162b2: Membrane-anchored SARS-CoV-2 full-length spike, stabilized in the prefusion conformation



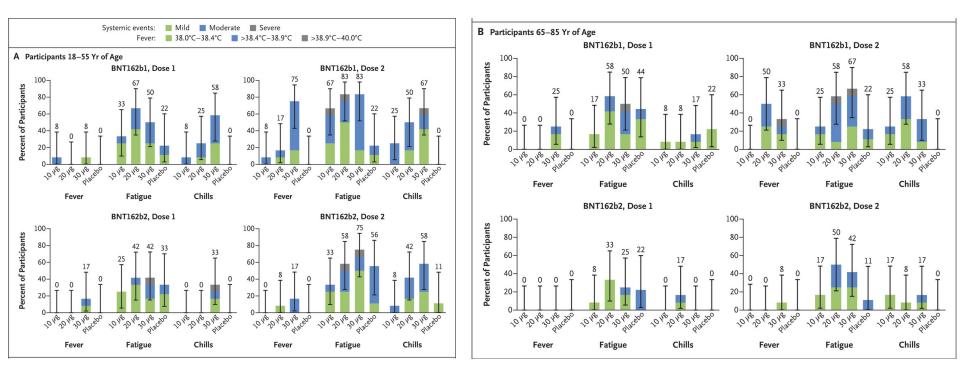
Northwestern Medicine^{*} Walsh *et al.* **N Engl J Med**. 2020: DOI: 10.1056/NEJMoa2027906.

• BioNTech/Pfizer: Lipid nanoparticle-formulated, nucleoside-modified RNA vaccine candidates



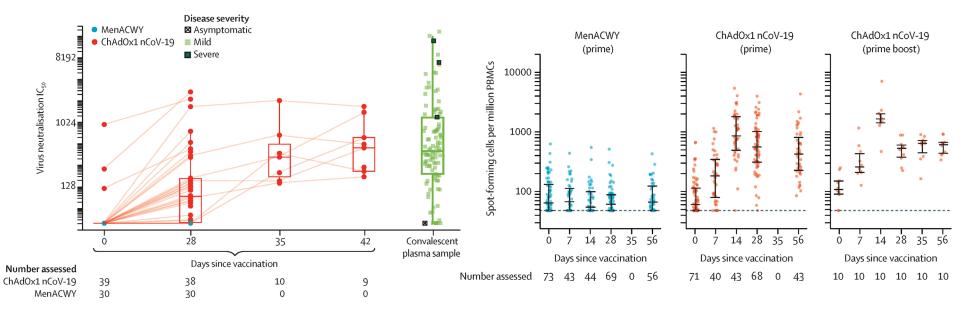
Northwestern Medicine^{*} Walsh *et al.* **N Engl J Med**. 2020: DOI: 10.1056/NEJMoa2027906.

• BioNTech/Pfizer: Lipid nanoparticle-formulated, nucleoside-modified RNA vaccine candidates



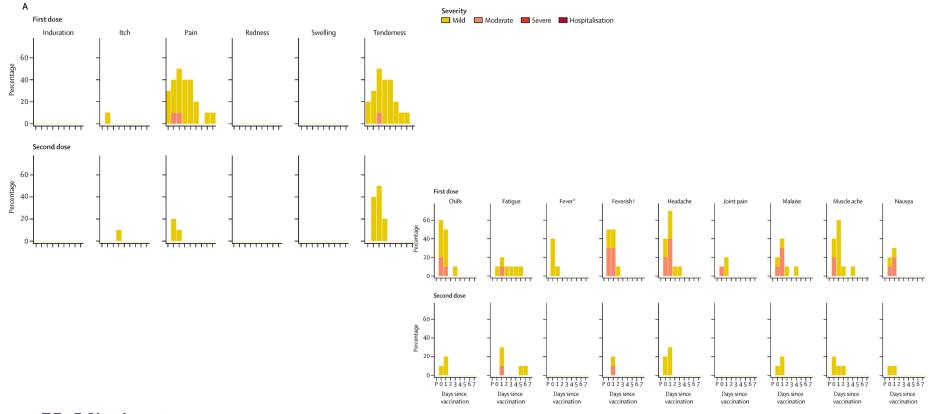
Northwestern Medicine^{*} Walsh *et al.* **N Engl J Med**. 2020: DOI: 10.1056/NEJMoa2027906.

• AstraZeneca/Oxford ChAdOx1 nCov-19: Chimpanzee adenovirus-vectored vaccine expressing the SARS-CoV-2 spike protein

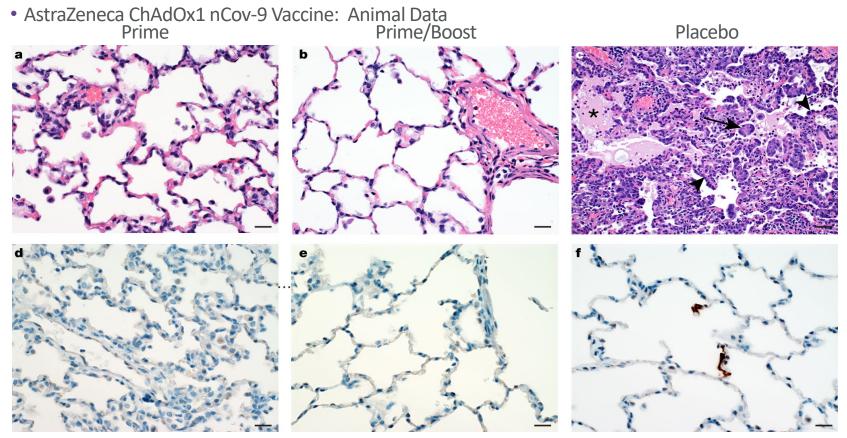


Northwestern Medicine^{*} Folegatti *et al. Lancet*. 2020: doi.org/10.1016/S0140-6736(20)31604-4.

AstraZeneca/Oxford ChAdOx1 nCov-19



Northwestern Medicine^{*} Folegatti *et al. Lancet.* 2020: doi.org/10.1016/S0140-6736(20)31604-4.



Northwestern Van Doremalen *et al.* Nature. 2020: doi.org/10.1038/s41586-020-2608-y.

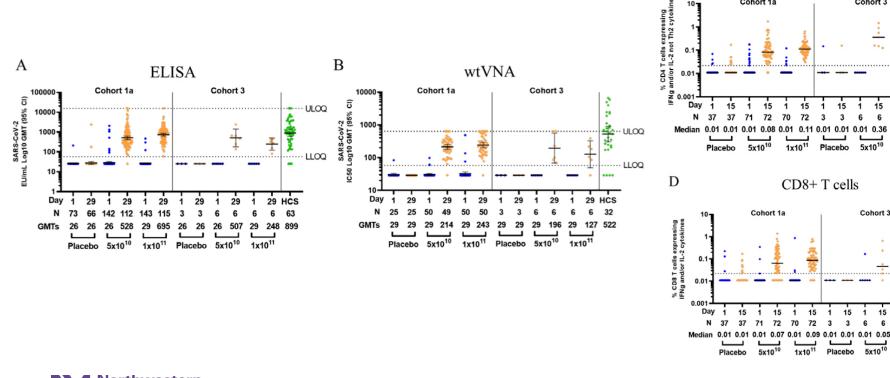
• JNJ-78436725/Ad26.COV2.S Vaccine: Non-replicating adenovirus 26 based vector expressing the stabilized pre-fusion spike (S) protein of SARS-CoV-2. Ad26.COV2.S С CD4+ Th1 cells

Cohort 1a

Cohort 3

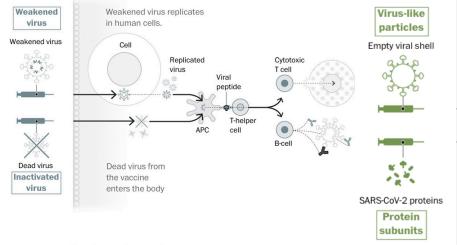
1x10¹¹

1x10¹¹

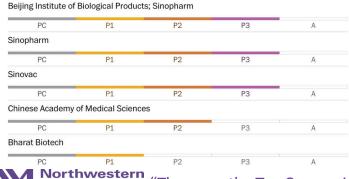


Northwestern Sadoff et al. medRxiv. 2020: doi.org/10.1101/2020.09.23.20199604. Medicine

COVID-19: *Protein Vaccines*



Weakened and inactivated virus vaccines, developed by...



Subunit vaccines, developed by...

2. 28

enter the body

Specific protein subunits,

such as the spike protein,

Empty viral shells look like the virus

but are not harmful because they have no genetic material

| Novavax | PC | P1 | P2 | P3 | A |
|---|----|----|----|----|---|
| Anhui Zhifei Longcom; Chinese Academy of Sciences | PC | P1 | P2 | P3 | A |
| Federal Budgetary Research Institution (FBRI) State Research Center of Virology and Biotechnology "VECTOR" | PC | P1 | P2 | P3 | A |
| Instituto Finlay de Vacunas | PC | P1 | P2 | P3 | A |
| SpyBiotech; Serum Institute of India | PC | P1 | P2 | P3 | A |

Cytotoxic

T cell

B-cell

Viral

APC

peptide

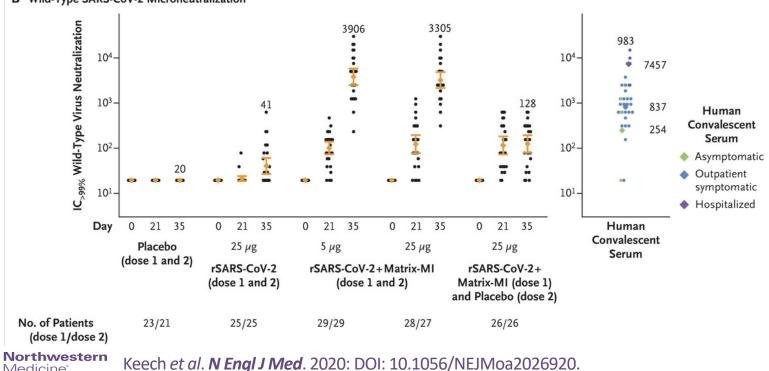
0

cell

T-helper

Northwestern Medicine^{*} "These are the Top Coronavirus Vaccines to Watch." Washington Post. 13 October 2020.

- Novovax: SARS-CoV-2 spike glycoprotein with Matrix-M1, a saponin-based adjuvant
 - Baculovirus Spodoptera frugiperda (Sf9) insect cell-expression system 0

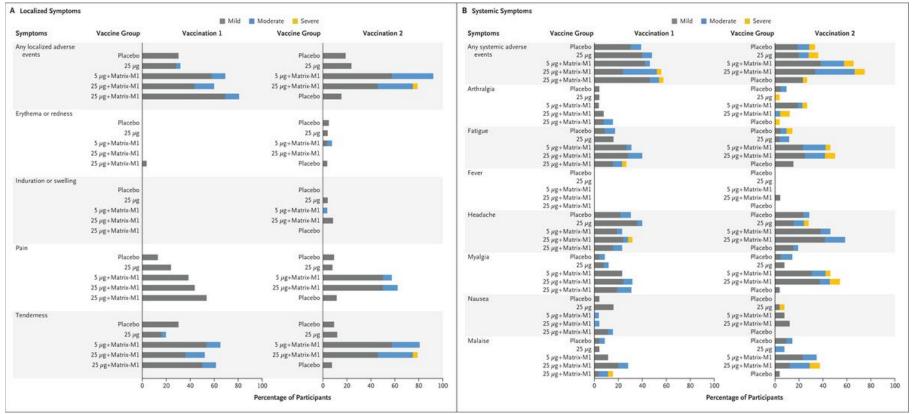


B Wild-Type SARS-CoV-2 Microneutralization

Medicine

COVID-19 Vaccines: RNA Vaccines

• Novovax:



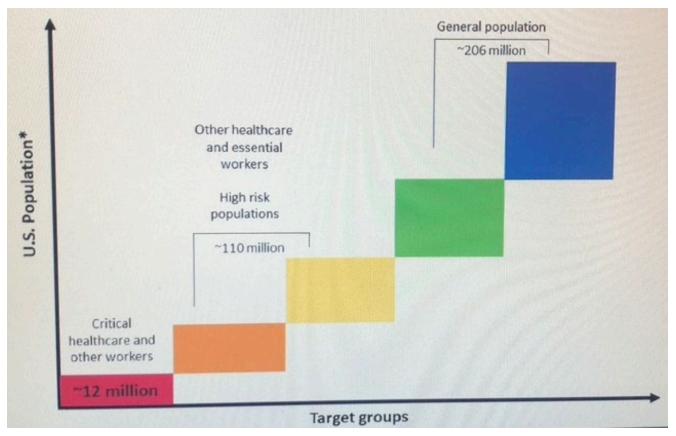
Northwestern Medicine^{*} Keech *et al.* **N Engl J Med.** 2020: DOI: 10.1056/NEJMoa2026920.

COVID-19: *Time to Vaccination*

| Phase 1 | Phase 2 | Phase 3 | Phase 4 |
|---|--|--|---|
| Phase 1a "Jumpstart Phase" High-risk health workers First responders Phase 1b People of all ages with comorbid and underlying conditions that put them at <i>significantly</i> higher risk Older adults living in congregate or overcrowded settings | K-12 teachers and school staff and child care workers Critical workers in high-risk settings—workers who are in industries essential to the functioning of society and at substantially higher risk of exposure People of all ages with comorbid and underlying conditions that put them at <i>moderately</i> higher risk People in homeless shelters or group homes for individuals with disabilities, including serious mental illness, developmental and intellectual disabilities or in recovery, and staff who work in such settings People in prisons, jails, detention centers, and similar facilities, and staff who work in such settings All older adults not included in Phase 1 | Young adults Children Workers in industries and occupations important to the functioning of society and at increased risk of exposure not included in Phase 1 or 2 | • Everyone residing in the United States who did not have access to the vaccine in previous phases |
| Equit crosscu consider | Itting for geographic areas ide | p, vaccine access should l ntified through CDC's So pecific index. | |
| rthwestern dicine [®] Natio | onal Academies of Sciences, | Engineering, and M | edicine. |

National Academies of Sciences, Engineering, and Medicine.

COVID-19: *Time to Vaccination*



Northwestern Medicine* Advisory Committee on Immunization Practices

Want to Help? Join a Study of SARS-CoV-2/COVID-19 Vaccine!

- Current COVID-19 Vaccine Trials
 - Multiple Centers in Chicago Participating
 - Priority given to high risk populations
 - Older adults
 - Minorities
 - Essential employees
 - \circ Sign Up Online
 - https://www.coronaviruspreventionnetwork.org

Help find a vaccine for COVID-19!

We're looking for:

- Adults aged 18 and older
- People who are more likely to be exposed to COVID-19, including:
 - People with underlying medical conditions
 - People with greater chances of exposure at their job
 - People who live or work in elder-care facilities
 - People over age 65
 - People who work in jails or prisons
 - People from racial and ethnic groups that have been impacted in greater numbers by the epidemic, such as African Americans, Latinx, and Native Americans
- If you are interested in being contacted about COVID-19 vaccine and other prevention studies, please register in the online Northwestern

COVID Prevention Trials Registry

https://is.gd/NUVaccineStudy You can also reach us via email at NUVaccineStudy@northwestern.edu or by calling 312-695-5012.



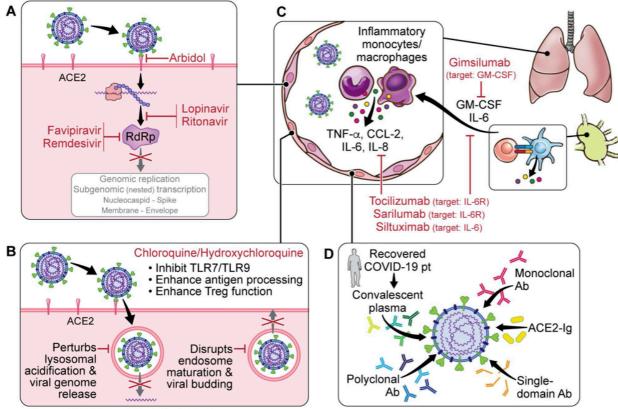








COVID-19: Management Options

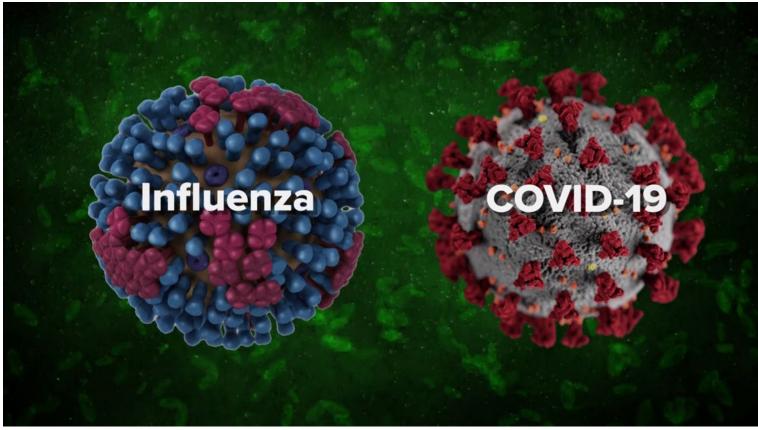


J Gregory ©2020 Mount Sinai Health System

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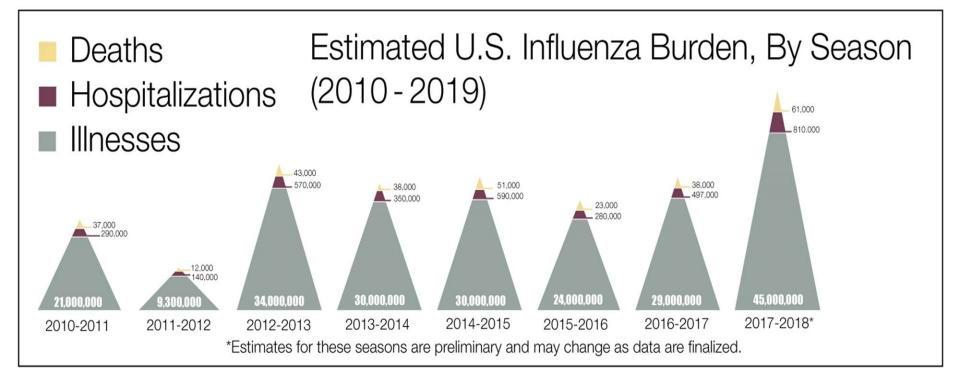
Vabret et al. Immunity. 2020: doi.org/10.1016/j.immune.2020.05.002.

COVID-19: *What Does the Future Hold?*



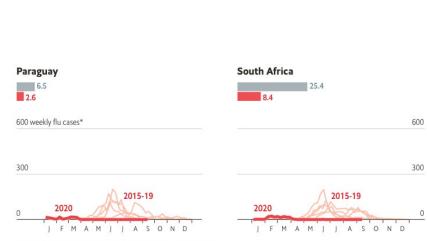


Influenza: What We Normally See



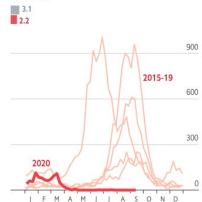


What We Know from the Southern Hemisphere



Argentina Deaths per 100,000 people 23.0 Covid-19 2020 Flu average 2015-19 16.2 900 weekly flu cases* Flu season 600 2015-19 300 2020 JFMAMJJASOND

2015-19

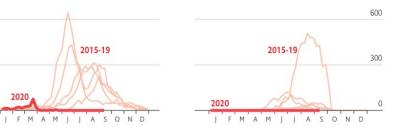


New Zealand 0.5 3.3

61.1

Australia





*As reported to WHO's Global Influenza Surveillance and Response System

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https://www.economist.com/graphic-detail/2020/09/12/the-southern-hemisphere-skipped-flu-season-in-2020

2020

Chile

600

300

12.7

900 weekly flu cases*

Influenza Vaccines: Knowing Which Vaccine to Get

- •Types of Influenza Vaccine
 - Standard Quadravalent Influenza Vaccine
 - High Dose Quadravalent Influenza Vaccine
 - Adjuvanted Quadravalent Influenza Vaccine
 - •Cell Culture Vaccines

oRecombinant Vaccine

Live Attenuated Vaccine



Influenza Vaccine: Composition and Recommendations

- 2020-2021 Influenza Vaccine Composition
 - A/Hawaii/70/2019 (H1N1)pdm09-like virus (updated)
 - A/Hong Kong/45/2019 (H3N2)-like virus (updated)
 - B/Washington/02/2019 (B/Victoria lineage)-like virus (updated)
 - B/Phuket/3073/2013-like (Yamagata lineage) virus
- Current Recommendations for Vaccine
 - $_{\odot}$ All individuals \geq 6 months of age should be vaccinated
 - $_{\odot}\,$ September and October are good times to get vaccinated
 - ° Contraindications: Egg allergy, Guillain-Barre Syndrome due to vaccine



Key Take Home Points

- •Get your flu shot (now is the time)
- •Where a mask whenever not at home
- •Expect a large second wave of disease this winter
- •COVID-19 is real
 - $_{\odot}$ Over 8,232,367 cases in the US
 - Over 438,967 (~5%) hospitalizations (39,230 currently hospitalized)
 - o Over 22,662 in ICU (5% of hospitalized; 8,178 currently in ICU)
 - Over 212,678 deaths (2.5% mortality, >20% if in ICU)

Obesity, hypertension and diabetes are key risk factors
 Medicine

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We're looking for:

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- People who are more likely to be exposed
- to COVID-19, including:
- People with underlying medical conditions
- People with greater chances of exposure at their job
- People who live or work in elder-care facilities
- People over age 65
- People who work in jails or prisons
- People from racial and ethnic groups that have been impacted in greater numbers by the epidemic, such as African Americans, Latinx, and Native Americans
- If you are interested in being contacted about COVID-19 vaccine and other prevention studies, please register in the online Northwestern

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Michael G. Ison, MD MS +1-312-695-4186 mgison@northwestern.edu



Sign Up to Participate in COVID-19 Vaccines

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We're looking for:

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- People who are more likely to be exposed to COVID-19, including:
 - People with underlying medical conditions
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 - People who live or work in elder-care facilities
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 - People who work in jails or prisons
 - People from racial and ethnic groups that have been impacted in greater numbers by the epidemic, such as African Americans, Latinx, and Native Americans

If you are interested in being contacted about COVID-19 vaccine and other prevention studies, please register in the online Northwestern

COVID Prevention Trials Registry

https://is.gd/NUVaccineStudy You can also reach us via email at NUVaccineStudy@northwestern.edu or by calling 312-695-5012.















