

COVID-19: current status and lessons for the future

May 17, 2021

Martin J. Cannon, Ph.D.

Department of Microbiology and Immunology, UAMS

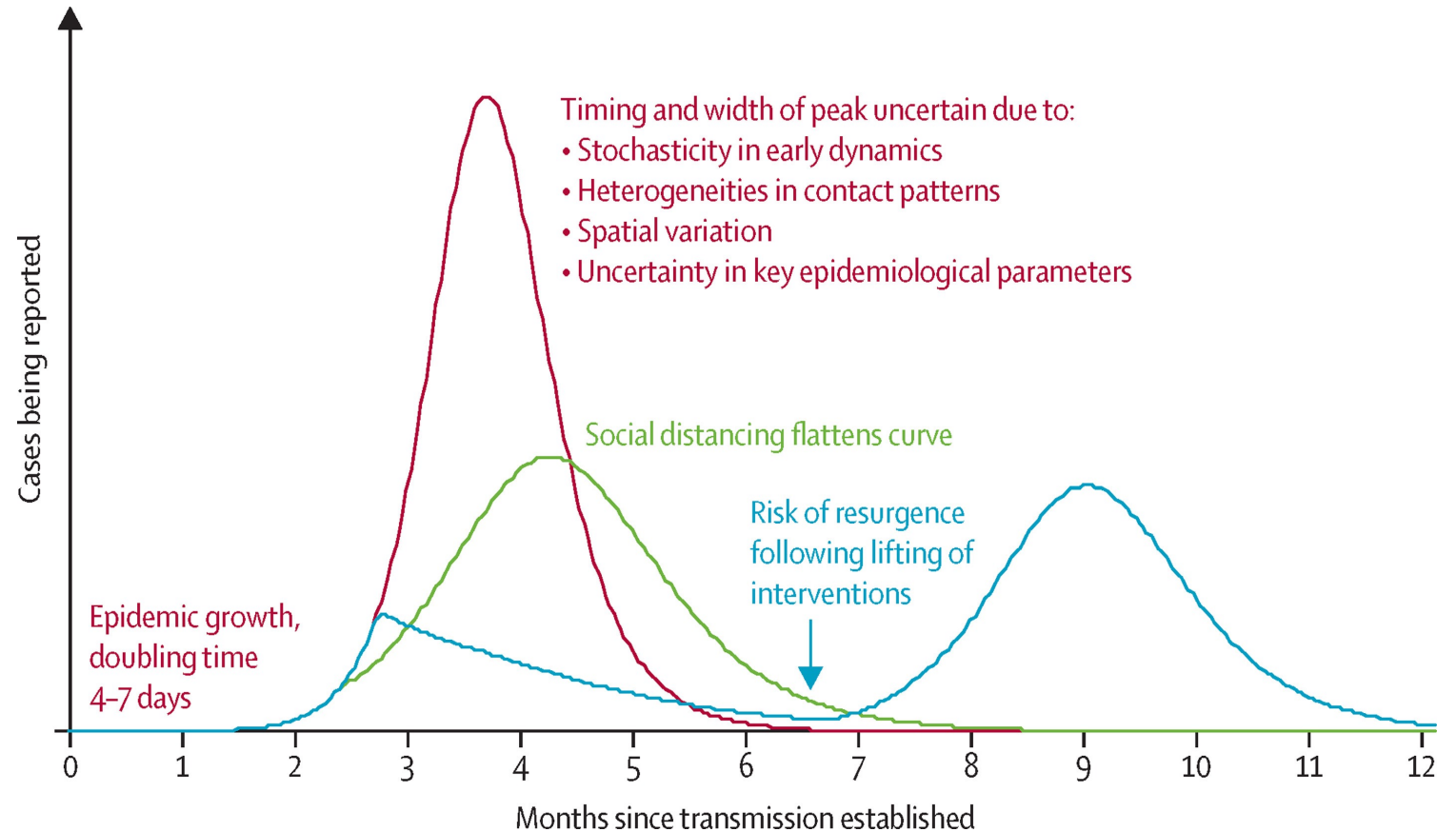
mjcannon@uams.edu

What happens if/when we ease off restrictions on socialization?

- There has been increasing social and economic pressure to relax containment policies
- This may seem like a bad idea from a public health perspective, but the socioeconomic impact of extended containment of transmission can also be devastating
- Consequences will be mitigated by extensive uptake of vaccination
- **Prediction from April 2020:** Restrictions will be eased at some point (my best guess would be June), and we will probably see a rebound in cases, and putting us back on the ascending part of the curve
- **What happened? Pretty much as predicted – a big increase in cases in the fall/winter of 2020**
- COVID-19 infection has followed the classic course of a pandemic, progressing through several cycles over an extended period
- Rate of infection declined rapidly in the spring of 2021, as the vaccination program advanced

COVID-19 transmission models

- Baseline simulation with case isolation only (red)
- Flattening the curve through social distancing (green)
- More aggressive social restrictions (blue), followed by risk of rebound when restrictions are eased
- [https://doi.org/10.1016/S0140-6736\(20\)30567-5](https://doi.org/10.1016/S0140-6736(20)30567-5)
- Always a risk of resurgence when containment measures are eased under any of these models, so red and green curves may be misleading....COVID-19 won't just go away



What is the frequency of mild or asymptomatic cases?

- This is largely unknown, but it matters because it has a considerable epidemiologic impact
- Study from Iceland, which tests very extensively, indicated that 50% of positive tests for COVID-19 were from individuals who had no symptoms
- Limited study in China found that 130 (78%) of 166 new infections identified over 24 hours (April 1) were asymptomatic
<https://doi.org/10.1136/bmj.m1375>
- Chinese study is difficult to interpret, since this takes a snapshot, and asymptomatic cases may yet develop symptoms
- Suggests that true frequency of COVID-19 infection may be far higher than numbers based only on testing symptomatic individuals

What is the impact of a high frequency of asymptomatic/mild COVID-19 cases?

- This would likely raise the estimated R_0 value and secondary attack rates, and also raise the threshold for herd immunity
- On the plus side, a much higher frequency of infection would suggest that populations can reach a threshold for herd immunity earlier than thought
- The downside is that asymptomatic COVID-19⁺ individuals may still transmit infection to others
- A high frequency of asymptomatic cases would raise an argument that lockdown policies are ineffective, while also causing an economic meltdown
- Antibody testing will provide more reliable data, and will aid in decisions on when to relieve stay-at-home orders and ease restrictions on social distancing

Racial disparities

- Limited data, since most states don't take race into account when reporting COVID-19 incidence
- However, a number of jurisdictions have reported disproportionately high COVID-19 incidence relative to population of blacks (e.g., Illinois, Michigan, Louisiana)
- President Trump was baffled....“Why is it that the African-American community is so much, numerous times more than everybody else?”
- Longstanding inequalities mean African-Americans are less likely to be insured and more likely to have existing health conditions
- African Americans are also more likely to work in jobs that involve close contact: they do not have the luxury of working from home
- Disparities in testing can lead to worse outcomes

Are there effective drugs for treatment of COVID-19?

The big news for 2021 has been the widespread introduction of SARS-COV-2 vaccines

- Some countries have done better than others....the UK, US and Israel have been notably successful
- Widespread evidence of inequities in global vaccine distribution

SARS-CoV-2 vaccine types

- **RNA vaccines**

Pfizer-BioNTech: modified mRNA encoding SARS-CoV-2 spike protein encapsulated in lipid nanoparticles

Moderna: essentially the same as above

- **Adenovirus vector vaccines**

Oxford-AstraZeneca: modified chimpanzee adenovirus ChAdOx1 encoding SARS-CoV-2 spike protein

Johnson and Johnson: Ad26 encoding SARS-CoV-2 spike protein

Sputnik V (Russia): two vector vaccine, Ad5 and Ad26, encoding SARS-CoV-2 spike protein. First dose is Ad26, second dose is Ad5

Convidecia (China): (Ad5-nCOV) encoding SARS-CoV-2 spike protein

SARS-CoV-2 vaccine types

- **Inactivated virus vaccines**

Coronavac (Sinovac, China): Phase III trial in Brazil showed 50% efficacy at preventing symptomatic infection, 83% effective in preventing mild cases from needing treatment. Phase III trial in Turkey showed 83% efficacy (March 2021)

Covaxin (India): efficacy reportedly 81% (April 2021)




























Covivac (Russia): no efficacy data

- **Subunit vaccines:**

EpiVacCorona (Russia): three peptide fragments of SARS-CoV-2 spike protein conjugated to a carrier protein (itself a fusion of a viral nucleocapsid protein and a bacterial maltose-binding protein)

RBD-Dimer (China): dimeric form of SARS-CoV-2 spike receptor-binding domain









How some of the Covid-19 vaccines compare

| Company | Doses | Storage |
|---|---|---|
| RNA | | |
|  Pfizer (BioNTech) |  |  -80 to -60°C (6 months) and 2 to 8°C (for up to 5 days) |
|  Moderna |  |  -25 to -15°C (6 months) and 2 to 8°C (for 30 days) |
| Viral vector | | |
|  Oxford-AstraZeneca |  |  2 to 8°C (6 months) |
|  Sputnik V (Gamaleya) |  |  -18.5°C (liquid form) 2 to 8°C (dry form) |
|  Johnson & Johnson (Janssen) |  |  2 to 8°C (3 months) |
| Inactivated virus | | |
|  CoronaVac (Sinovac) |  |  2 to 8°C |
|  Sinopharm |  |  2 to 8°C |
|  Covaxin (Bharat Biotech) |  |  2 to 8°C |
| Protein-based | | |
|  Novavax |  |  2 to 8°C |

Source: Wellcome Trust, BBC research



How some of the Covid-19 vaccines compare

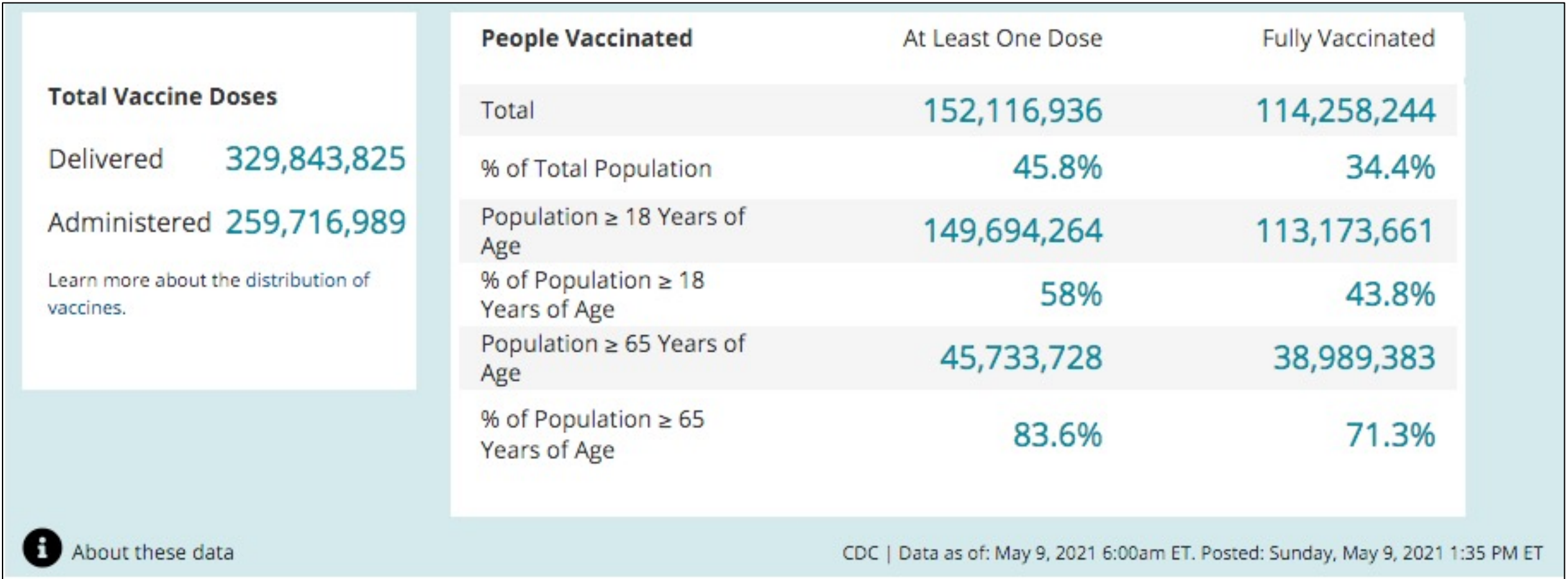
| Company | Type | Doses | How effective* | Storage | Cost per dose |
|--|---|--|----------------|--|---------------|
|  Oxford Uni-AstraZeneca | Viral vector (genetically modified virus) | x2  | 62-90% | Regular fridge temperature | £3 (\$4) |
|  Moderna | RNA (part of virus genetic code) | x2  | 95% | -20C up to 6 months | £25 (\$33) |
|  Pfizer-BioNTech | RNA | x2  | 95% | -70C | £15 (\$20) |
|  Gamaleya (Sputnik V) | Viral vector | x2  | 92% | Regular fridge temperature (in dry form) | £7.50 (\$10) |

*preliminary phase three results, not yet peer-reviewed

Source: Respective companies, WHO



COVID-19 vaccinations in the US, as of May 9, 2021



- Arkansas has administered 1.9 million doses, at 62,960 per 100K of population (currently ranked 48th of 50 states)
- 36.5% have received at least one dose, and 27.5% are fully vaccinated (VT, MA lead with 59% receiving at least one dose)
- 69.97% of distributed vaccines in Arkansas have been administered (ranked 47th – NM leads at 89.41%)

Pfizer vaccine-elicited neutralization against new SARS-CoV-2 variants

Several recent SARS-CoV-2 variants are cause for concern in the US, including **California B.1.429**, **New York B.1.526** and the **UK B.1.1.7** lineage with a new E484K substitution in the Spike protein

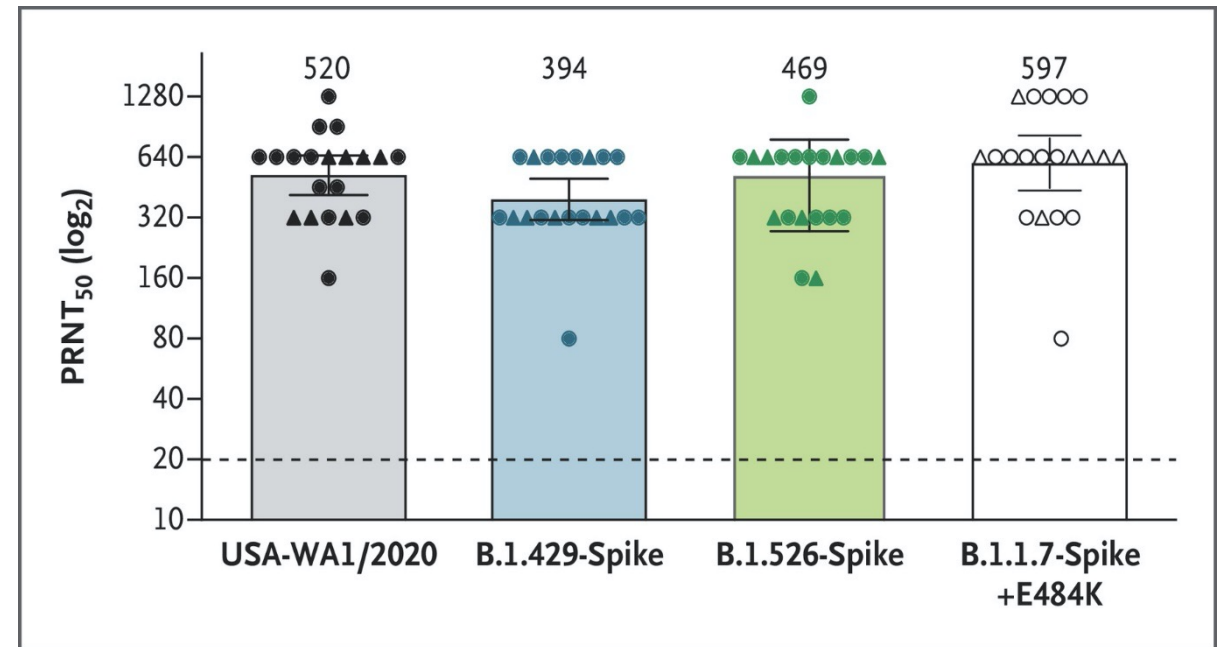
Tested serum neutralization of SARS-CoV-2 USA-WA1/2020 isolated in January 2020 and recent variants after administration of two doses of the Pfizer vaccine (BNT162b2)

50% plaque reduction neutralization testing (PRNT) showed that variants remain susceptible to neutralization, i.e., vaccination remains effective

Y Liu et al, NEJM May 12, 2021

Watch this space: serum from Pfizer vaccinees about 67% less potent against B.1.617 variant, which is predominant in India, and has been detected in the US

M Hoffmann et al, bioRxiv, May 5, 2021



SARS-CoV-2 vaccine side effects

- Injection site: pain redness. Swelling
- Systemic: tiredness, headache, muscle pain, chills, fever, nausea
- Very rare association of blood clots with AstraZeneca, J & J vaccines, possibly related to use of adenovirus vector
- Thrombosis-thrombocytopenia syndrome, associated with antibody response to platelet factor 4 (PF4)
<https://www.nejm.org/doi/full/10.1056/NEJMe2106315?query=TOC>
- J & J vaccine briefly paused after reports of six cases
- Total of 209 cases following AstraZeneca vaccine

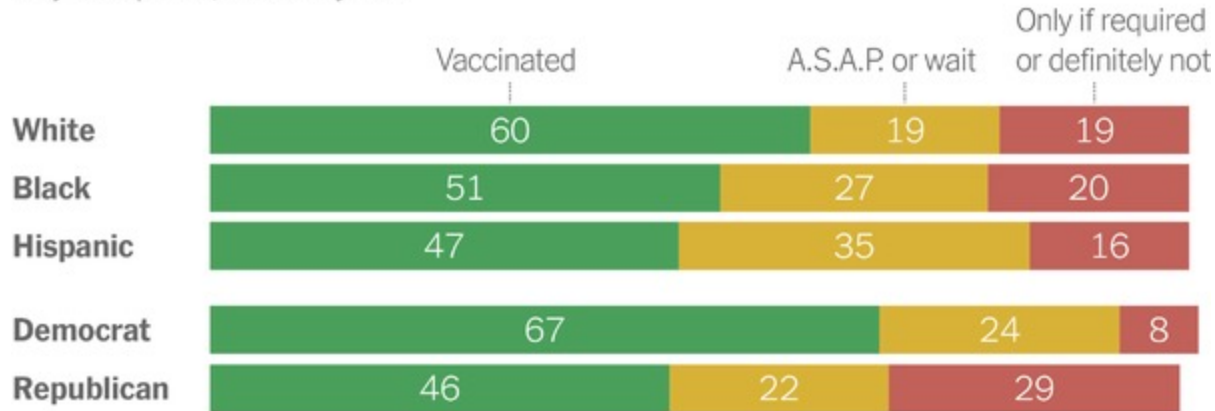
Impact of SARS-CoV-2 variants on vaccine efficacy

- The B.1.117 (UK) variant is currently the most prevalent in the US – available COVID-19 vaccines afford solid protection
- The B.1.167 variant is predominant in India, and has been picked up in 1-3% of COVID-19 infections in the US – this variant appears to be more transmissible, and prevalence is likely to increase
- The B.1.1.7 (Alpha), B.1.351 (Beta), P.1 (Gamma), B.1.427 (Epsilon), B.1.429 (Epsilon), and B.1.617.2 (Delta) variants circulating in the United States are classified as variants of concern
- Current evidence suggests that vaccination affords protection against B.1.167 (Alpha) and other variants
- Viruses change constantly – vaccine formulations may need to be adjusted in response to viral evolution

The vaccine class gap

Vaccine Attitudes

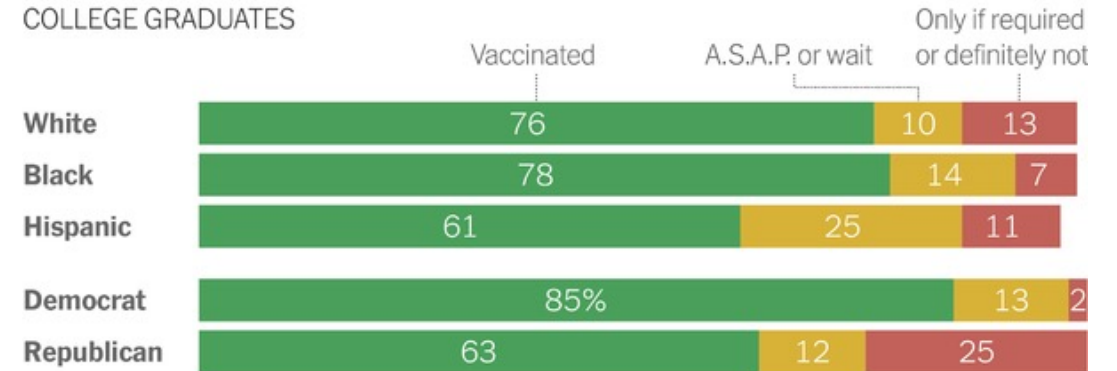
People chose one of five categories: vaccinated; want to be A.S.A.P.; wait and see; only if required; definitely not.



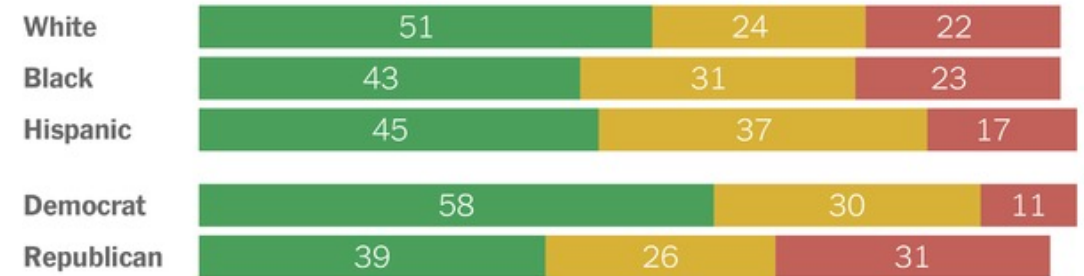
- Two distinct demographic groups show greater vaccine hesitancy – Republicans and racial minorities
- Also a huge class gap according to education level, i.e., working class versus professional
- Different racial groups of similar education levels can look remarkably similar
- Vaccine access may also contribute to class gap, notably for working class minorities

Vaccine Attitudes by Class

COLLEGE GRADUATES



NON-GRADUATES



Random survey of 2,097 adults conducted from April 15 to April 29, 2021.
Not all figures total to 100 percent; some people did not give an answer.

Vaccine hesitancy and the anti-vaxxers

- Lack of vaccine acceptance will ultimately be the biggest barrier to containment of COVID-19 infection
- Reasons are highly complex, usually based on misinformation
- Miami school bans vaccinated teachers!

<https://www.nytimes.com/2021/04/26/us/florida-centner-academy-vaccine.html>

Some creative incentives for vaccination

<https://www.theguardian.com/us-news/2021/may/12/ohio-coronavirus-vaccine-lottery-1-million>

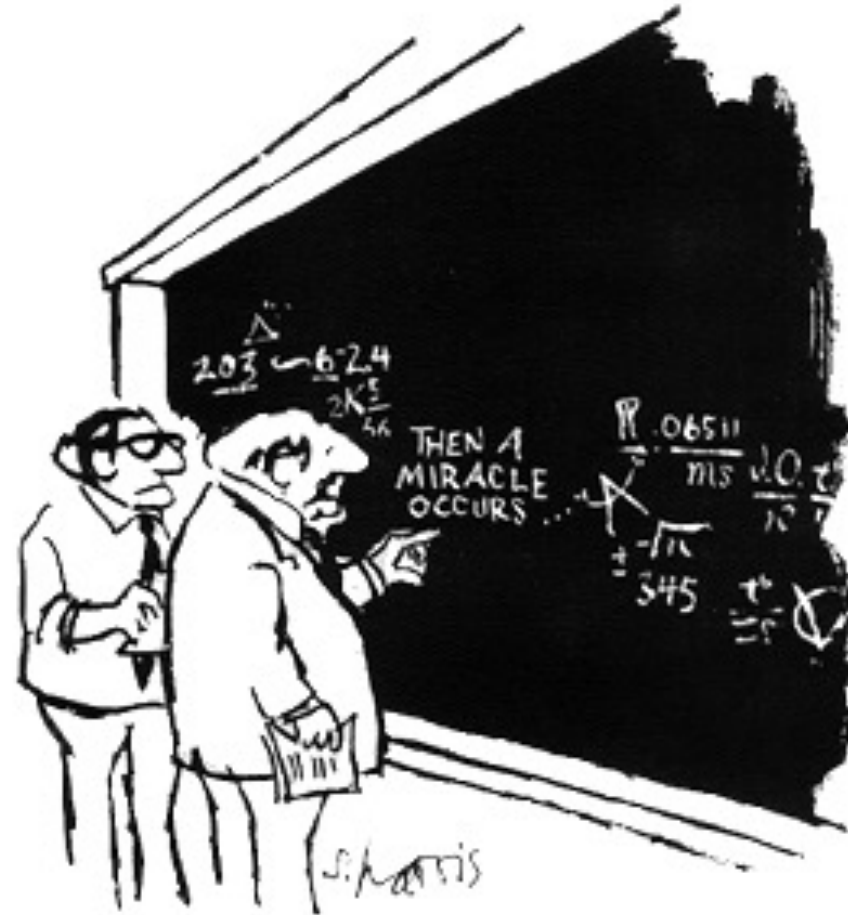


Incentives for vaccination

- <https://www.nejm.org/doi/full/10.1056/NEJMp2107719?query=TOC>
- Vax-a-Million, \$1 million prizes in Ohio, full scholarships for college
- Ohio's vaccination rates double after state vaccine lottery
- CVS offers a series of prizes, including a cruise, tickets to the Super Bowl, \$5,000 cash
- Many companies offer gift cards or paid time off for employees who get vaccinated
- Lots of creative ideas....
- <https://www.aarp.org/health/conditions-treatments/info-2021/vaccine-incentives.html>



Questions?



mjcannon@uams.edu