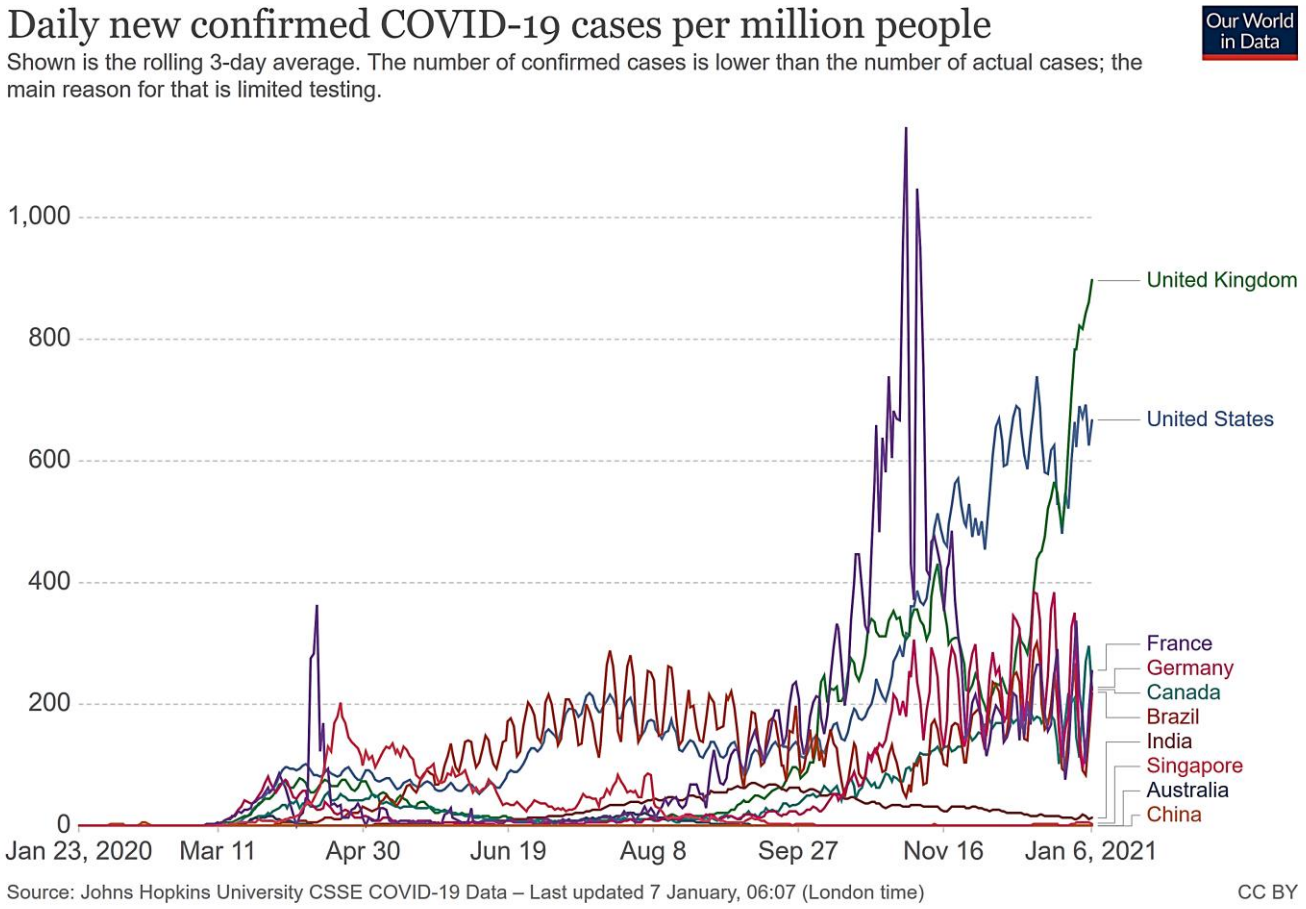
HERO TOGETHER

KEEPING COMMUNITIES
HEALTHY WITH VACCINATION

Learning Together about Vaccines for SARS CoV-2

Robert Califf, MD, MACC
Emily O'Brien, PhD

January 6, 2021 (last HERO Collaboratory GR presentation)



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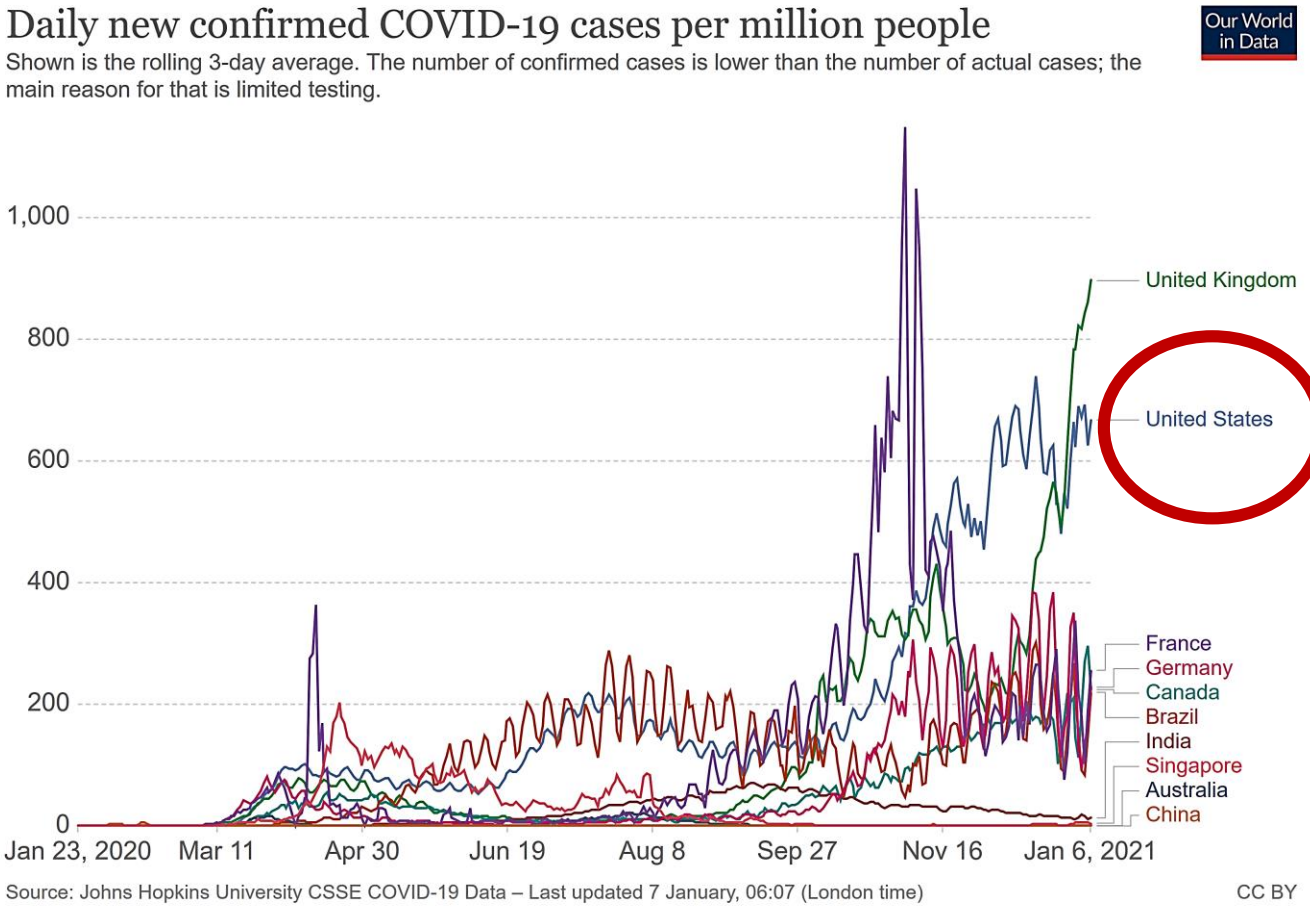
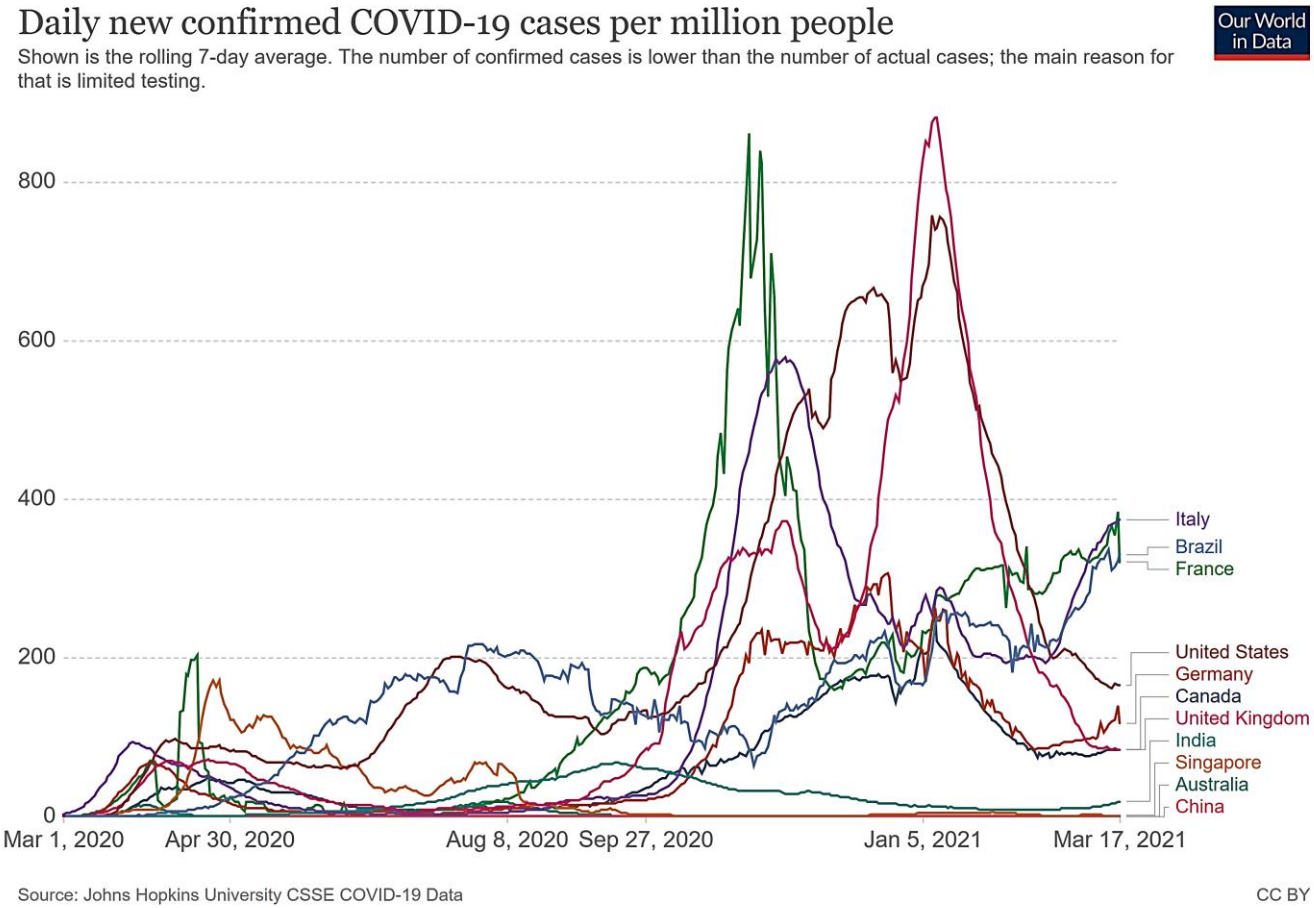
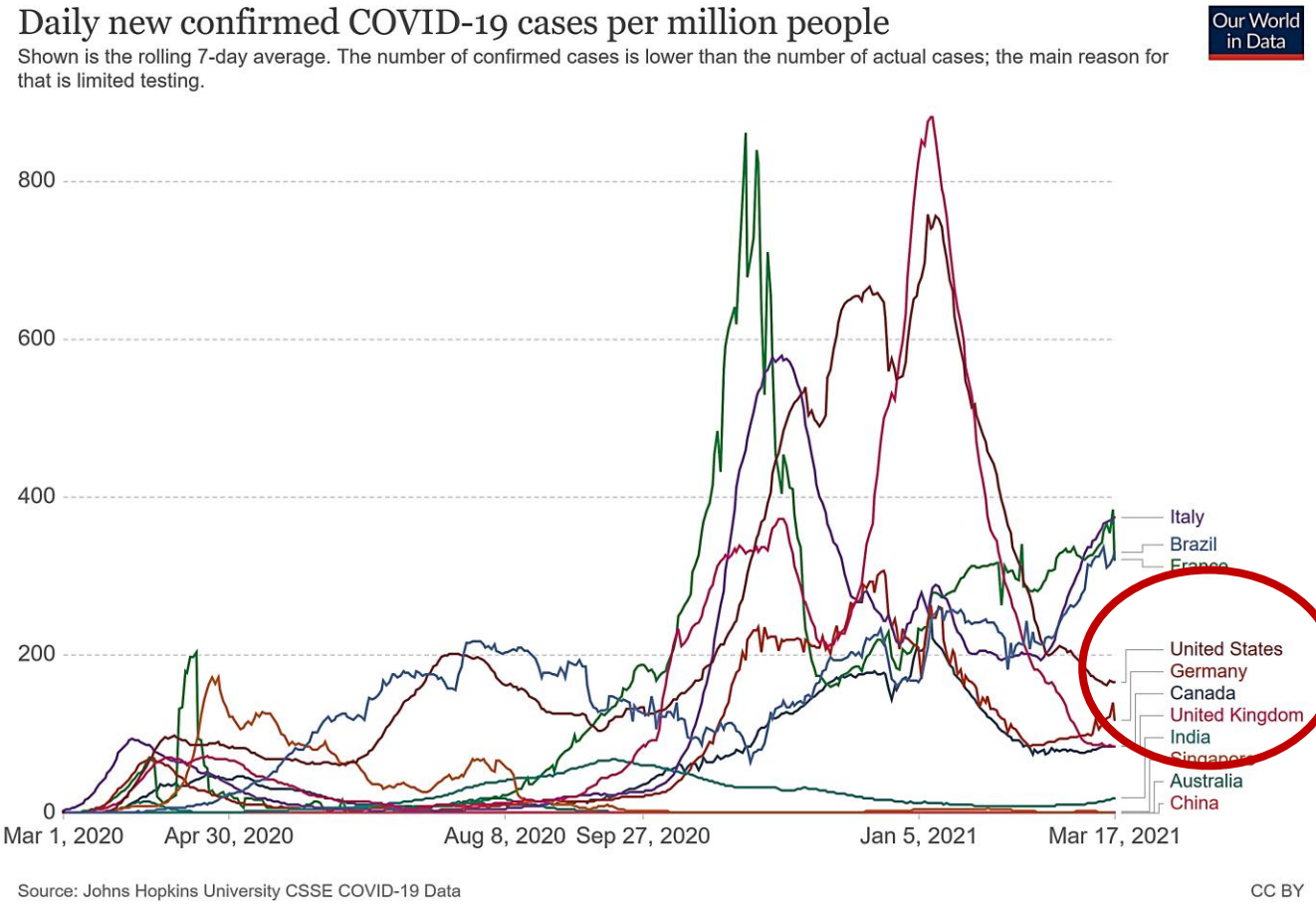


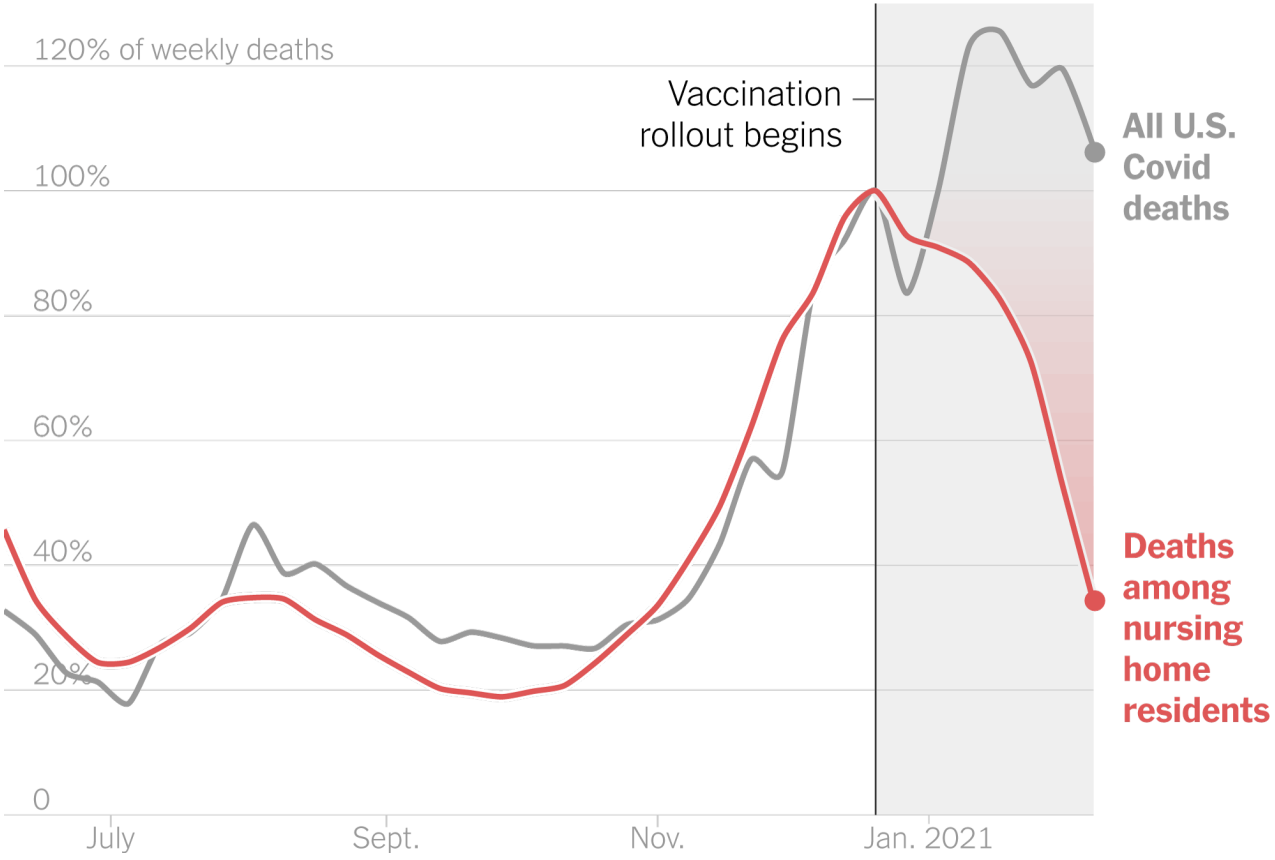
March 18, 2021 (yesterday)



March 18, 2021 (yesterday)



First, some good news



The Vaccine vs. Variant Race

Researchers find worrying new coronavirus variant in New York City

By Maggie Fox, CNN

Updated 6:21 AM ET, Thu February 25, 2021

"The virus is not going to stand still."

-Stephen Hoge

President, Moderna

Should we be worried about variants?

	B.1.1.7	B.1.351	P.1
Alternate name	501Y.V1	501Y.V2	501Y.V3
Country identified	United Kingdom	South Africa	Brazil
Mutations	23	21	17
Spike mutations	8	9	10
Key RBD, spike mutations beyond N501Y in all	E69/70 deletion, P681H 144Y deletion, A570D	E484K, K417N, orf1b deletion	E484K, K417T, orf1b deletion
Other mutations, including N-terminal	T7161, S982A, D1118H	L18F, D80A, D215G, Δ242-244, R264I, A701V	L18F, T20N, P26S, D138Y, R190S, H655Y, T10271
Transmissibility Δ	>50% increased	Not established	Not established
Lethality Δ	Likely increased >30%	?	?
Immune evasion	Unclear	Yes	Yes, less than B.1.351
Vaccine efficacy Clinical Trials	Minimal reduction <10% point decline in 2 trials (Novavax, AZ)	60% Efficacy Novavax 64% Efficacy J&J No AZ efficacy vs mild/mod infections	68% Efficacy J&J
Countries reported	94	48	26
US States reported	48	23	10

Source: @EricTopol, Twitter

One to watch: Poland

March 5

REUTERS

Poland's cases of British coronavirus variant rising: minister

March 17

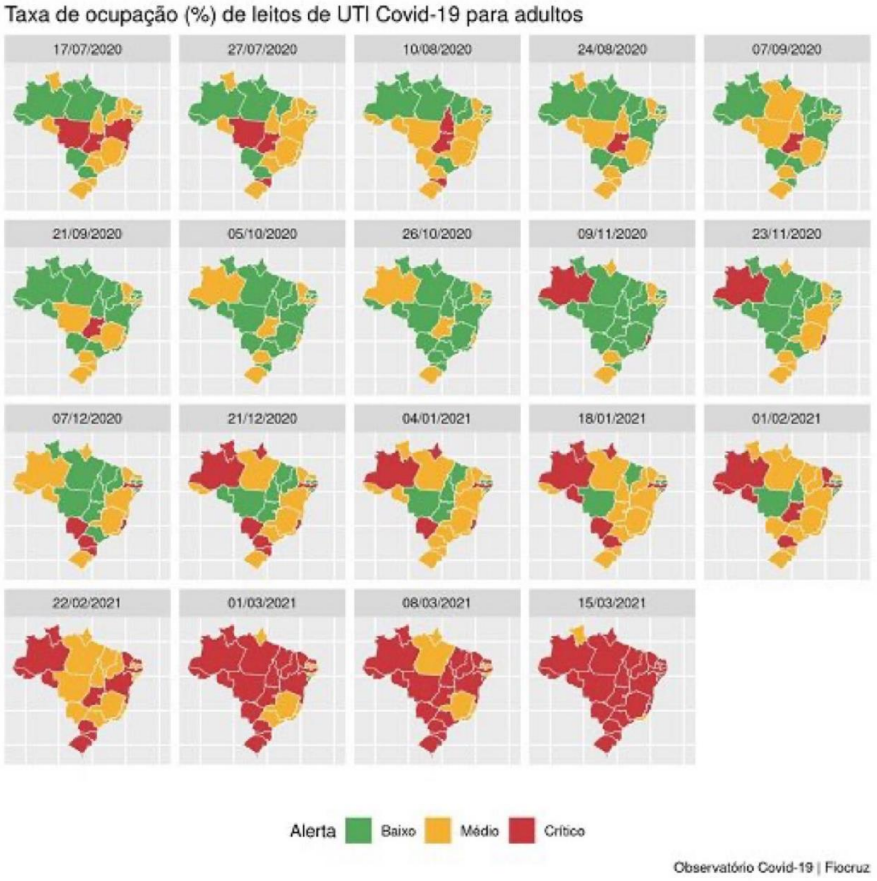
REUTERS

Poland announces lockdown; could toughen it if epidemic doesn't ease - minister

52% of cases are UK variant

Another to watch: Brazil

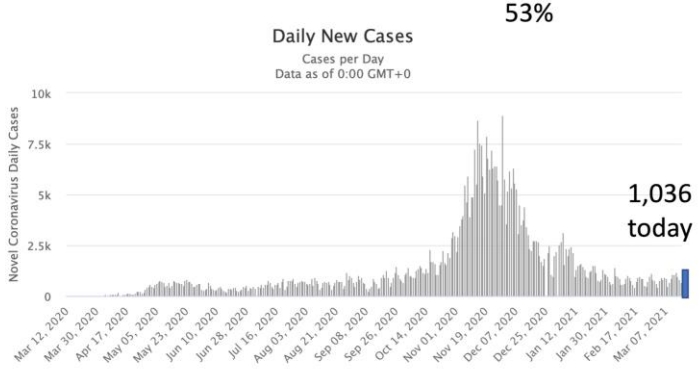
- Health service in “worse crisis in history”
- 19 of 27 state capitals are at 90% capacity
- Surging in areas even with high prior infection rates



And here at home…

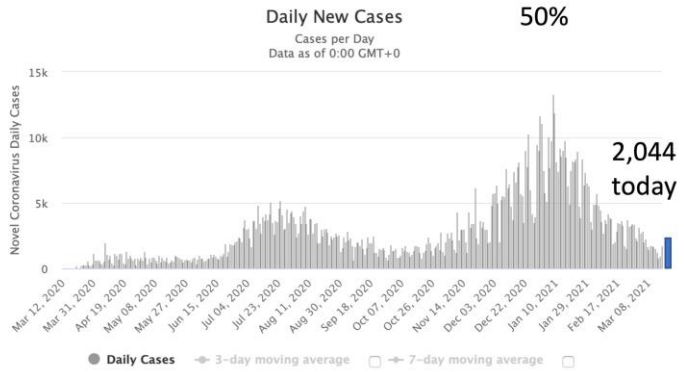
Daily New Cases in Minnesota

B.1.1.7
53%



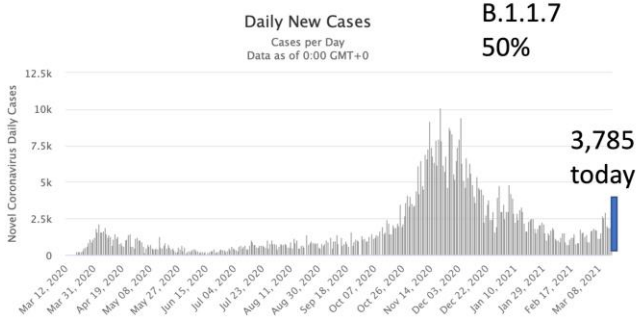
Daily New Cases in Georgia

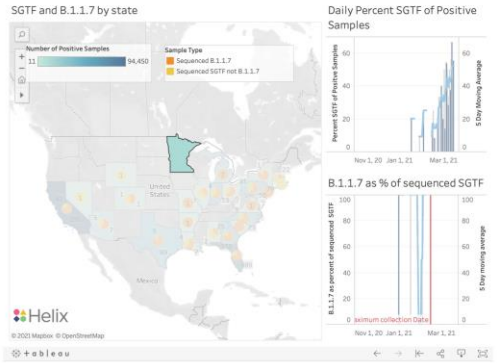
B.1.1.7
50%



Daily New Cases in Michigan

B.1.1.7
50%





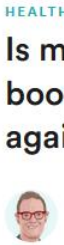
“Plug and play”

Moderna Announces First Participants Dosed in Study Evaluating COVID-19 Booster Vaccine Candidates

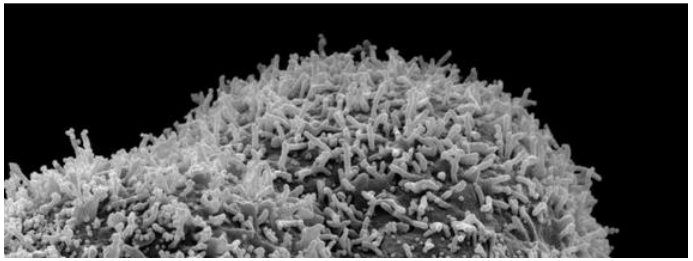
March 10, 2021 at 4:09 PM EST

HEALTH

Is more simply better? Why Pfizer thinks a booster of its Covid vaccine might work against new variants



By Matthew Herper Feb. 25, 2021

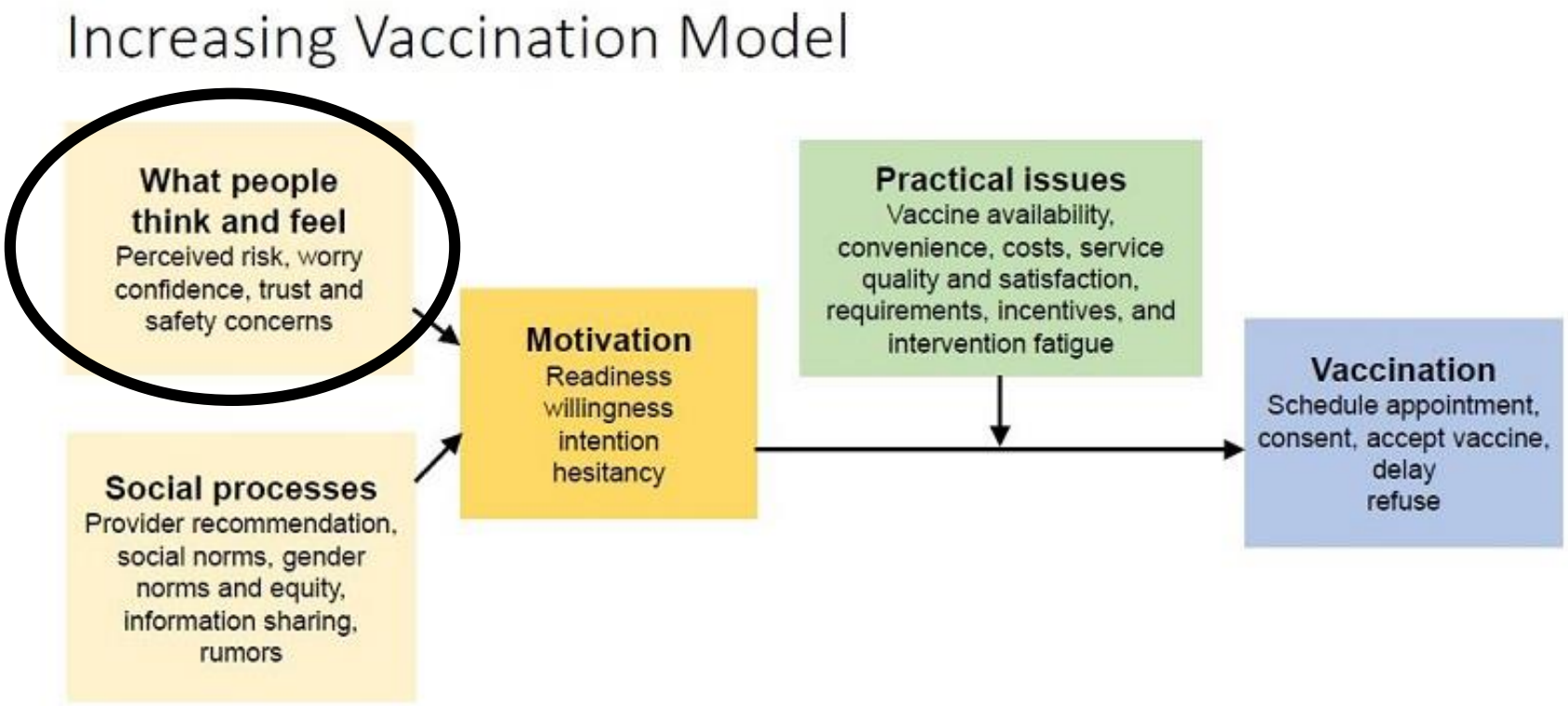


NIH U.S. National Library of Medicine

ClinicalTrials.gov

Safety and Immunogenicity Study of a SARS-CoV-2 (COVID-19) Variant Vaccine (mRNA-1273.351) in Naïve and Previously Vaccinated Adults

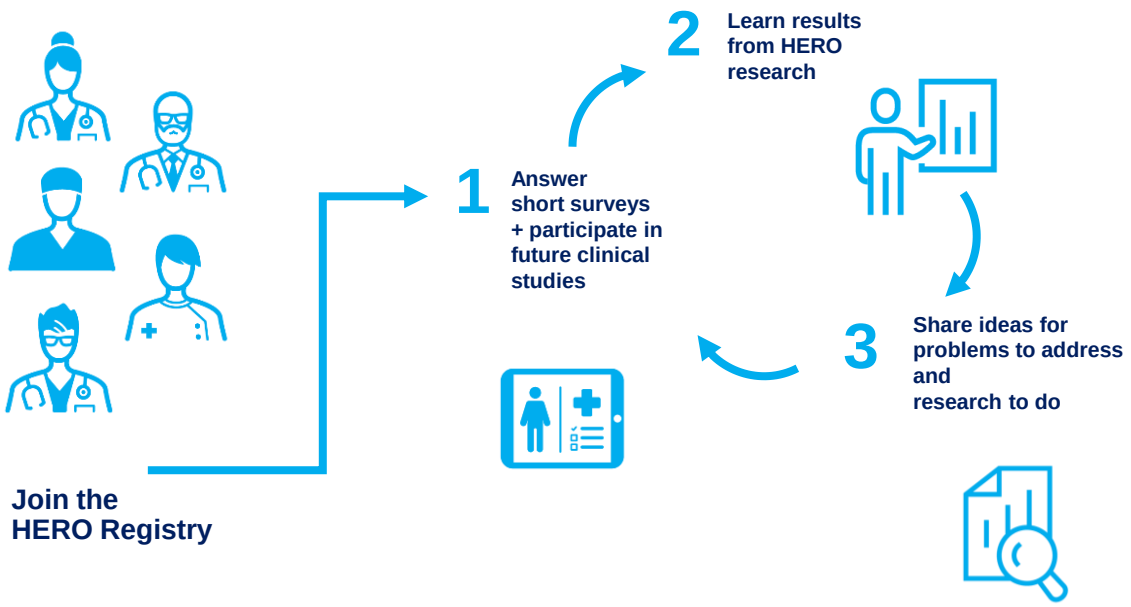
How do we increase vaccination?



Source: The BeSD expert working group. Based on: Brewer NT, Chapman GB, Rothman AJ, Leask J, and Kempe A (2017). Increasing vaccination: Putting psychological science into action. *Psychological Science for the Public Interest*. 18(3): 149-207

How does HERO work?

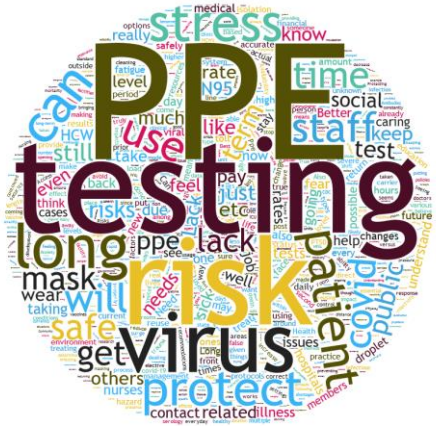
- Any healthcare worker across the US can join from anywhere
- To join, HERO Registry participants must be:
  - A U.S. healthcare worker of any profession
  - ≥ 18 years old



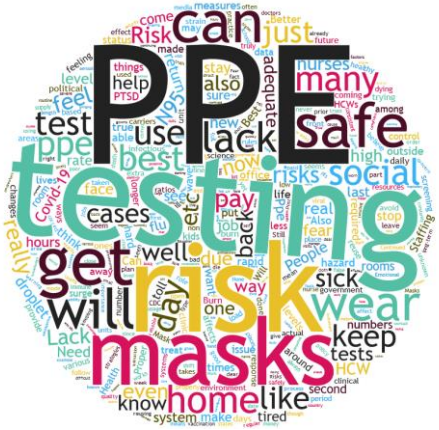
Healthcare worker priorities

The HERO Baseline Survey asked: “What are the most pressing or important issues today that you feel need to be better understood related to healthcare workers and COVID-19?

Spring 2020



Summer 2020

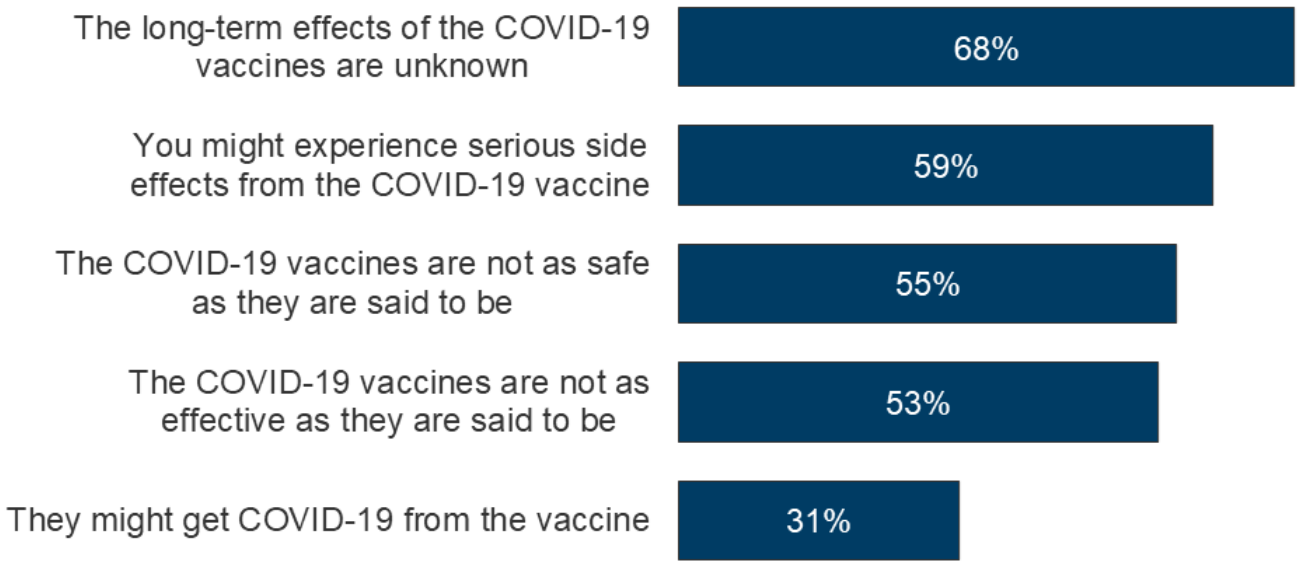


Fall 2020

Winter 2021

Many Express Concern About COVID-19 Vaccine's Long-Term Effects, Side Effects, Safety, and Effectiveness

Percent who say they are **very or somewhat concerned** about each of the following:



NOTE: Among those who have not been vaccinated against COVID-19
SOURCE: KFF COVID-19 Vaccine Monitor (conducted Jan. 11-18, 2021). See topline for full question wording.

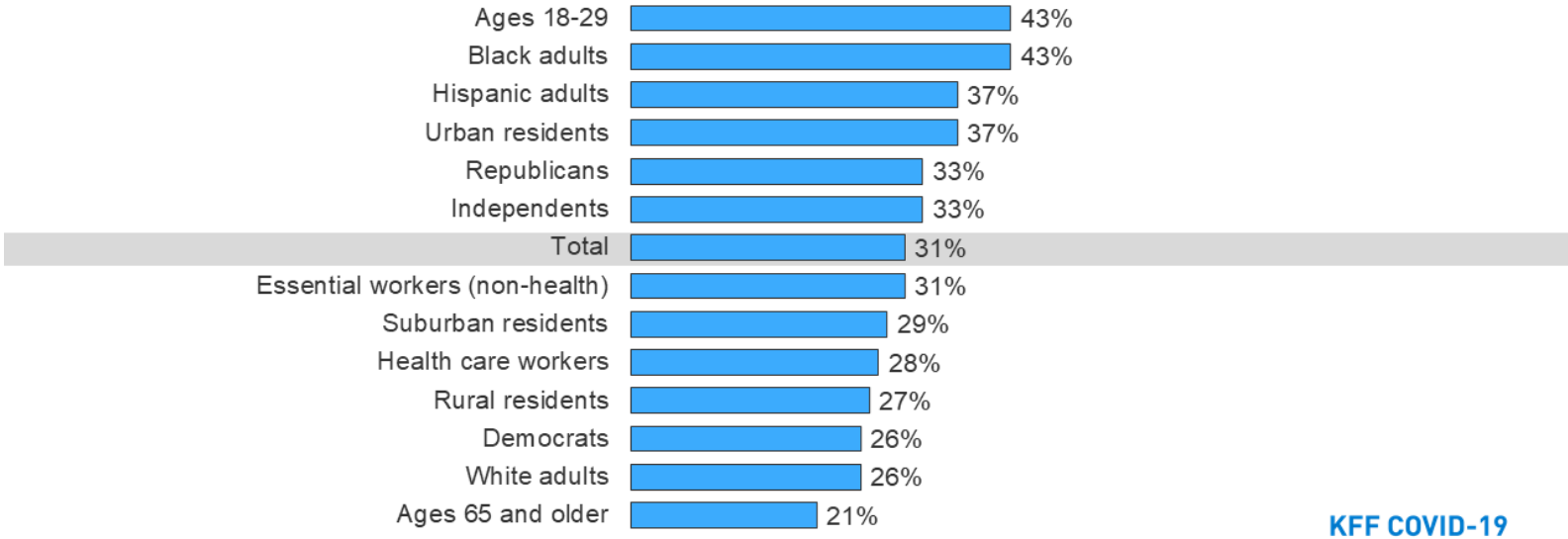
KFF COVID-19 Vaccine Monitor

Impact of age and race

Figure 6

Young Adults, Black Adults Most Likely To Want To “Wait And See”

Percent within each group who say, when an FDA approved vaccine for COVID-19 is available to them for free, they would **wait and see** how it is working for other people:



SOURCE: KFF COVID-19 Vaccine Monitor (conducted Jan. 11-18, 2021). See topline for full question wording.

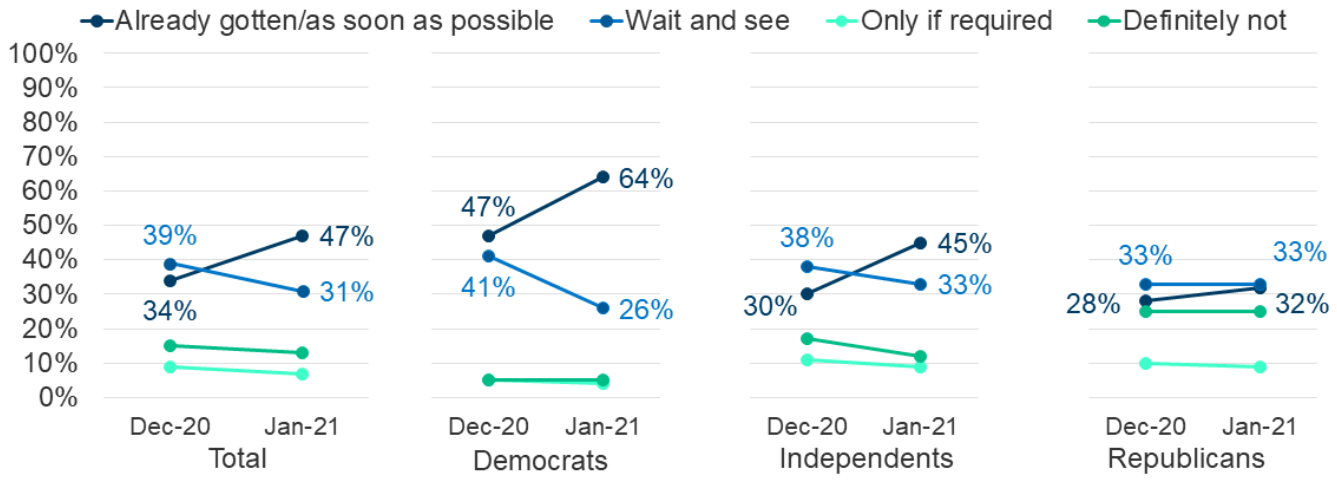
KFF COVID-19 Vaccine Monitor

Impact of political affiliation

Figure 4

Increase In Vaccine Enthusiasm Driven Entirely By Democrats And Independents; Republicans Remain Reluctant

Percent who say they will get a COVID-19 vaccine:



KFF COVID-19 Vaccine Monitor

SOURCE KFF COVID-19 Vaccine Monitor (Nov. 30-Dec. 8, 2020 and Jan. 11-18, 2021). See topline for full question wording.

Misinformation Superspreaders

CEO at amazon.com/viahart.

Replying to @nntaleb

mRNA is totally new in humans. While it may not be best for society if everyone follows suit, it's probably wise to wait before getting vaccinated with an mRNA vaccine.

Precautionary principle.

7:47 PM · Mar 15, 2021 · Twitter for iPhone

1 Retweet **4** Quote Tweets **72** Likes

Dr. Christiane Northrup
June 27 ·

This is absolutely correct. NO vaccine has been tested against an inert placebo. And vaccine manufacturers have complete immunity from any and all damages or liability for vaccine injuries as of 1986. In that year, Congress passed the legislation granting immunity. Since then the CDC vaccine schedule has tripled. And the CDC itself owns many vaccine patents. So the fox is guarding the hen house.

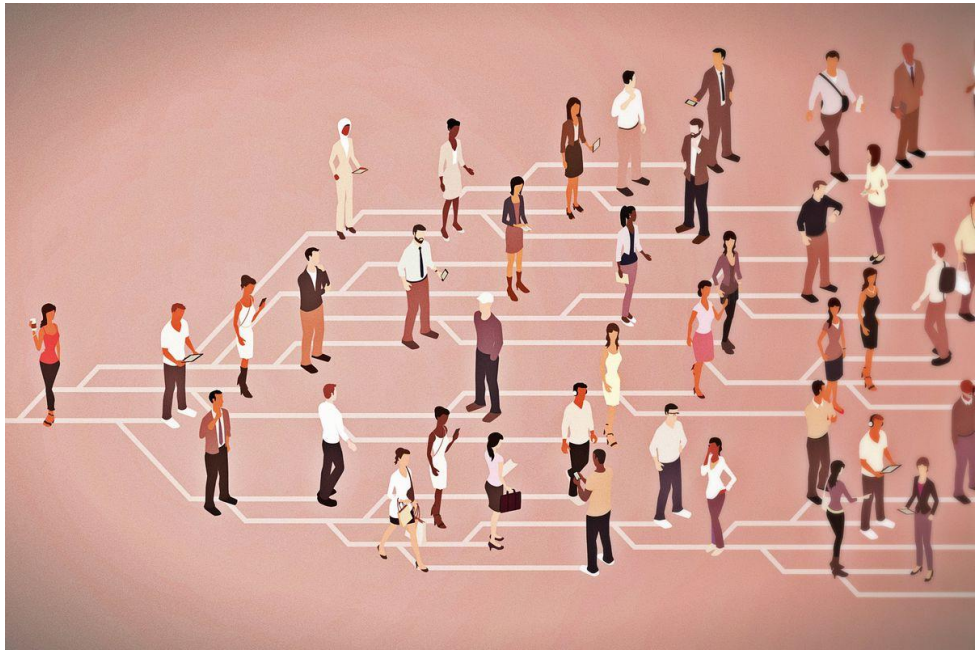
Head of Pfizer Research: Covid Vaccine is Female Sterilization

Health & Money News / December 2, 2020 / News

The vaccine contains a **spike protein (see image) called syncytin-1**, vital for the formation of human placenta in women. If the vaccine works so that we form an immune response AGAINST the spike protein, we are also **training the female body to attack syncytin-**

HERO TOGETHER

Combating an Infodemic



In an analysis of 4.5 million tweets from 2006-2017, “falsehood diffused significantly farther, faster, deeper, and more broadly than the truth in all categories of information.”

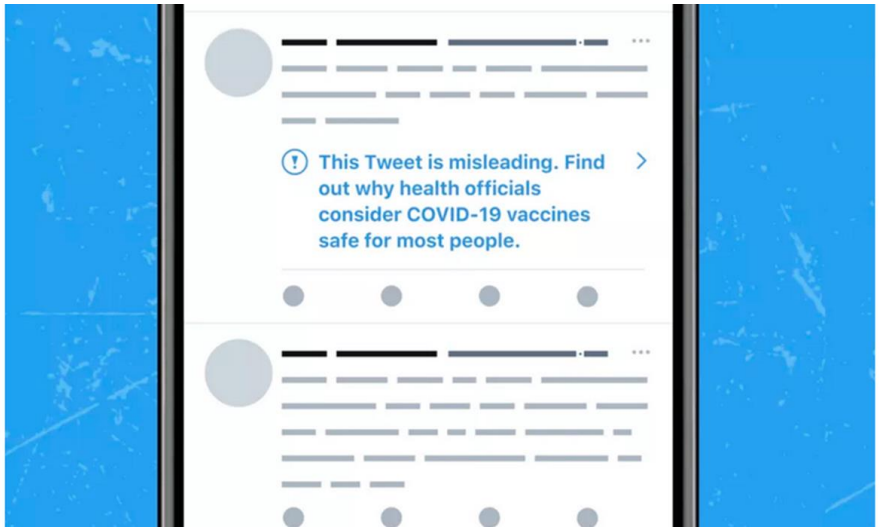
Vosoughi S, et al. Science 2018; 359; 1146-1151

Progress

Twitter will label COVID-19 vaccine misinformation and enforce a strike system

Repeatedly sharing misleading information can lead to your account being locked

By Ian Carlos Campbell | @soupsthename | Mar 1, 2021, 5:02pm EST



- One strike: no account-level action
- Two strikes: 12-hour lock
- Three strikes: 12-hour lock
- Four strikes: 7-day lock
- Five or more strikes: permanent suspension

White House Vaccine Confidence initiative

POLITICS

The White House is set to unveil a wide-reaching, billion-dollar campaign aimed at convincing every American to get vaccinated

By Lev Facher March 15, 2021

- ✓Multiple channels (television, radio, and digital advertising)
- ✓Tailor to the local environment
- ✓Use trusted messengers (including celebrities)

Can celebrities impact public health?

The New York Times

SUBSCRIBE FOR $1/WEEK

H.I.V. Tests Up 60% Since the Disclosure From Magic Johnson

By Calvin Sims

Dec. 7, 1991

CNN politics • LIVE TV

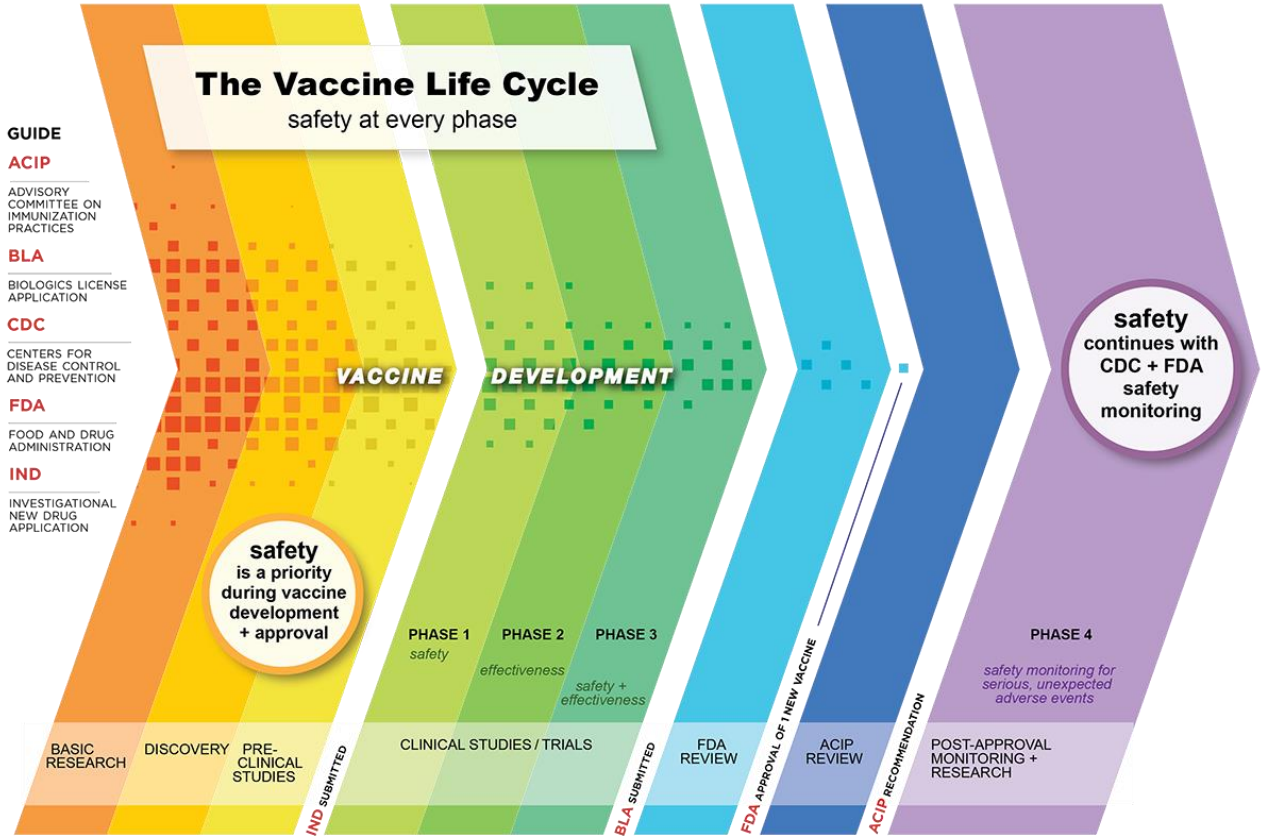
Trump urges Americans to get Covid-19 vaccine: 'I would recommend it'

By Paul LeBlanc, CNN

Updated 7:48 AM ET, Wed March 17, 2021

Where do we go from here?

Long-term safety studies are part of the life cycle

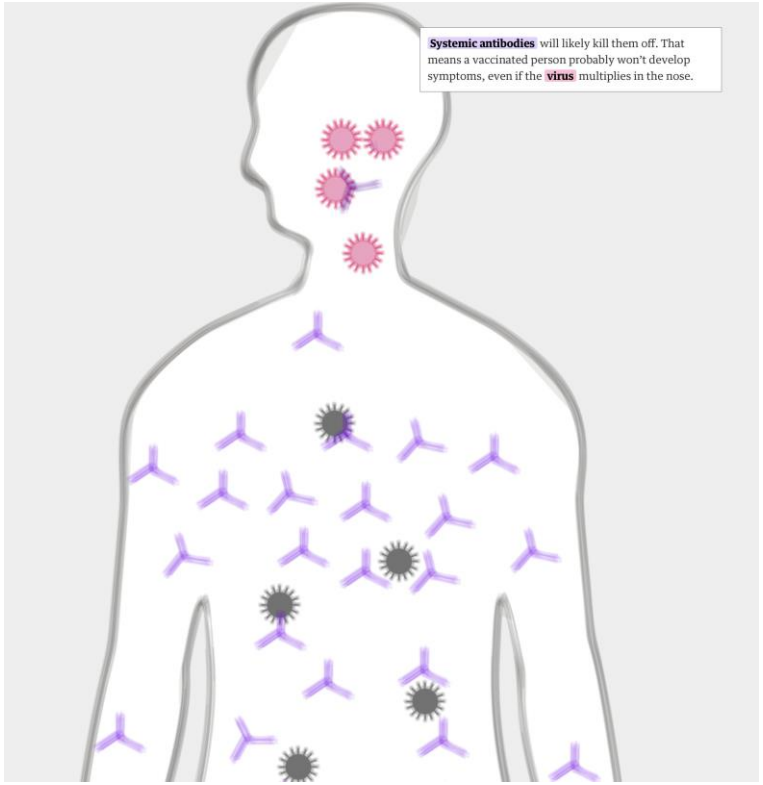


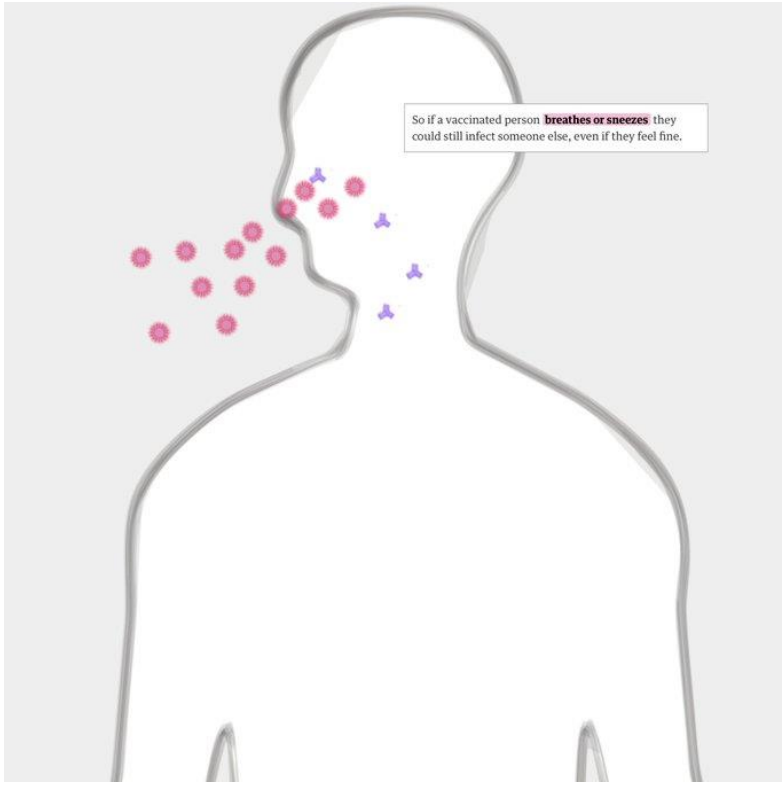
Why does Phase 4 matter for vaccines?

1. Ensures the benefits of vaccines approved in the U.S. outweigh the risks.
2. Evaluates groups not included in clinical trials
3. Describes side effects and adverse events reported after vaccination.
4. Evaluates whether adverse events can be directly linked to a vaccine

https://www.cdc.gov/vaccinesafety/research/index.html

Asymptomatic Transmission Post-Vaccination?





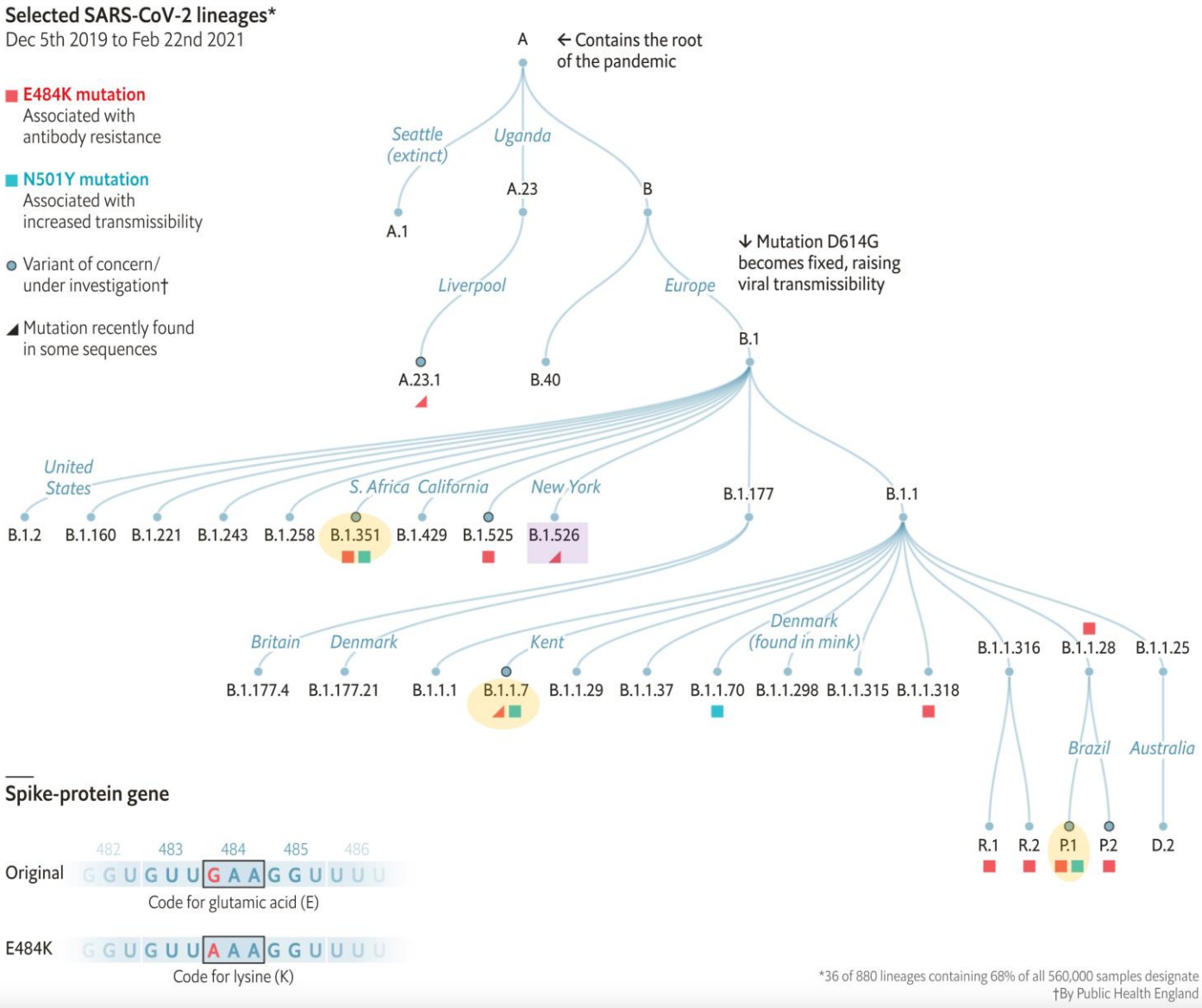


Table. SARS-CoV-2 Vaccines

Vaccine	Manufacturer	Vaccine type	Antigen	Dose	Dosage	Storage conditions	Efficacy against severe COVID-19[a]	Overall efficacy	Current approvals
mRNA-1273	Moderna (US)	mRNA	Full-length spike (S) protein with proline substitutions	100 µg	2 Doses 28 d apart	−25° to −15 °C; 2-8 °C for 30 d; room temperature ≤12 h	100% 14 d After second dose (95% CI, not estimable to 1.00)	92.1% 14 d After 1 dose (95% CI, 68.8%-99.1%); 94.1% 14 d after second dose (95% CI, 89.3%-96.8%)	EUA: the US, EU, and UK
BNT162b2	Pfizer-BioNTech (US)	mRNA	Full-length S protein with proline substitutions	30 µg	2 Doses 21 d apart	−80° to −60 °C; 2-8 °C for 5 d; room temperature ≤2 h	88.9% After 1 dose (95% CI, 20.1%-99.7%)	52% After 1 dose (95% CI, 29.5%-68.4%); 94.6% 7 d after second dose (95% CI, 89.9%-97.3%)	EUA: the US, EU, and UK
Ad26.CoV2.S	Johnson & Johnson (US)	Viral vector	Recombinant, replication-incompetent human adenovirus serotype 26 vector encoding a full-length, stabilized SARS-CoV-2 S protein	5×10^{10} Viral particles	1 Dose	−20 °C; 2-8 °C for 3 mo	85% After 28 d; 100% after 49 d	72% in the US; 66% in Latin America; 57% in South Africa (at 28 d)	EUA process initiated in the US
ChAdOx1 (AZS1222)	AstraZeneca/ Oxford (UK)	Viral vector	Replication-deficient chimpanzee adenoviral vector with the SARS-CoV-2 S protein	5×10^{10} Viral particles (standard dose)	2 Doses 28 d apart (intervals >12 wk studied)	2-8 °C for 6 mo	100% 21 d After first dose	64.1% After 1 dose (95% CI, 50.5%-73.9%); 70.4% 14 d after second dose (95% CI, 54.8%-80.6%)	EUA: WHO/Covax, the UK, India, and Mexico
NVX-CoV2373	Novavax, Inc (US)	Protein subunit	Recombinant full-length, prefusion S protein	5 µg of protein and 50 µg of Matrix-M adjuvant	2 Doses	2-8 °C for 6 mo	Unknown	89.3% in the UK after 2 doses (95% CI, 75.2%-95.4%); 60% in South Africa (95% CI, 19.9%-80.1%)	EUA application planned
CVnCoV	CureVac/ GlaxoSmithKline (Germany)	mRNA	Prefusion stabilized full-length S protein of the SARS-CoV-2 virus	12 µg	2 Doses 28 d apart	2-8 °C for 3 mo; room temperature for 24 h	Unknown	Phase 3 trial ongoing	
Gam-COVID-Vac (Sputnik V)	Gamaleya National Research Center for Epidemiology and Microbiology (Russia)	Viral vector	Full-length SARS-CoV-2 glycoprotein S carried by adenoviral vectors	10^{11} Viral particles per dose for each recombinant adenovirus	2 Doses (first, rAd26; second, rAd5) 21 d apart	−18 °C (Liquid form); 2-8 °C (freeze dried) for up to 6 mo	100% 21 d After first dose (95% CI, 94.4%-100%)	87.6% 14 d After first dose (95% CI, 81.1%-91.8%); 91.1% 7 d after second dose (95% CI, 83.8%-95.1%)	EUA: Russia, Belarus, Argentina, Serbia, UAE, Algeria, Palestine, and Egypt
CoronaVac	Sinovac Biotech (China)	Inactivated virus	Inactivated CN02 strain of SARS-CoV-2 created from Vero cells	3 µg With aluminum hydroxide adjuvant	2 Doses 14 d apart	2-8 °C; Lifespan unknown	Unknown	Phase 3 data not published; reported efficacy 14 d after dose 2: 50.38% (mild) and 78% (mild to severe) in Brazil, 65% in Indonesia, and 91.25% in Turkey	EUA: China, Brazil, Columbia, Bolivia, Brazil, Chile, Uruguay, Turkey, Indonesia, and Azerbaijan
BBIBP-CorV	Sinopharm 1/2 (China)	Inactivated virus	Inactivated HB02 strain of SARS-CoV-2 created from Vero cells	4 µg With aluminum hydroxide adjuvant	2 Doses 21 d apart	2-8 °C; Lifespan unknown	Unknown	Phase 3 data not published; unpublished reports of 79% and 86% efficacy	EUA: China, UAE, Bahrain, Serbia, Peru, and Zimbabwe

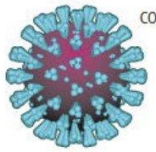
. Buddy Creech, MD, MPH[1]; Shannon C. Walker, MD[1]; Robert J. Samuels, MBChB[1]
Author Affiliations Article Information
JAMA. Published online February 26, 2021. doi:10.1001/jama.2021.3199

How Two Types of Covid-19 Vaccines Work

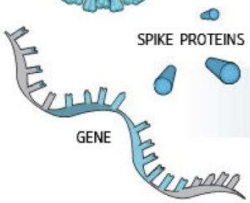
Like the ones from Pfizer and Moderna, Johnson & Johnson's vaccine delivers genetic instructions that help prime our immune systems to fight off coronavirus.

But J&J's vaccine delivers these instructions in a different way.

Unlike traditional vaccines, which use the whole virus to generate an immune response, these newer vaccines use coronavirus's outer spike proteins.



Scientists have isolated the genes in coronavirus responsible for producing these spike proteins



Vaccines' effectiveness

Results based on the companies' varying clinical trials and methodologies	Pfizer/ BioNTech	Moderna	Johnson & Johnson
Number of doses	2	2	1
Overall efficacy	95.0%	94.1%	66.1%
Efficacy against severe disease only	75.0*	100	85.4
Efficacy in people 65 and older	94.7	86.4	68.6
Efficacy in U.S.	94.9	94.1	72.0

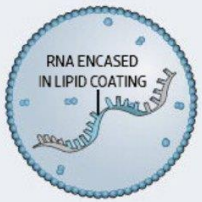
*Based on a small number of severe cases in study.

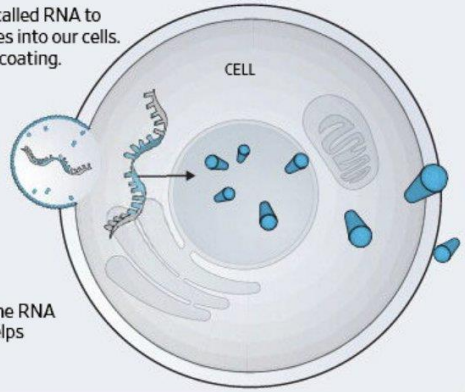
Source: Nature (process); the companies, the Food and Drug Administration and the New England Journal of Medicine (effectiveness)

Erik Brynildsen, Alberto Cervantes and Josh Ulick/THE WALL STREET JOURNAL

Pfizer and Moderna's mRNA vaccines

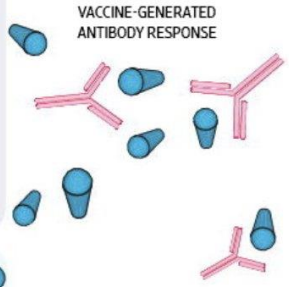
These vaccines use molecules called RNA to ferry information from the genes into our cells. The RNA is protected by a lipid coating.





When injected into a patient, the RNA enters healthy cells where it helps orchestrate the production of coronavirus spike proteins.

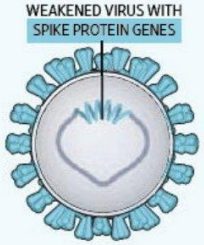
Once exported from the cells, the spike proteins trigger the immune system to produce specialized antibodies that are adapted to recognize the virus.

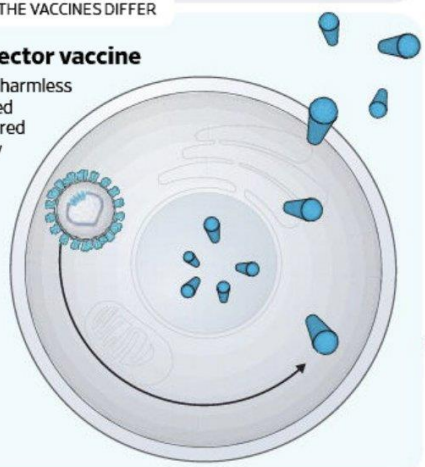


WHERE THE VACCINES DIFFER

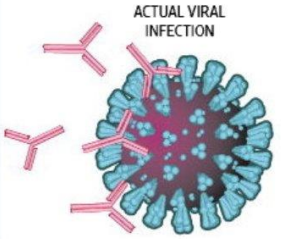
Johnson & Johnson's viral vector vaccine

The genes are spliced into weakened, harmless versions of other viruses. When injected into a patient, the genetically engineered viruses enter healthy cells where they produce coronavirus spike proteins.





After vaccination, the antibodies remain in the body. If the patient later becomes infected with the actual virus, the antibodies can identify and help neutralize it.



Data in Context

U.K.

Two in U.K. Suffer Allergic Reaction to Pfizer's Covid-19 Vaccine

Regulator says people with history of significant allergic reactions shouldn't get the shot

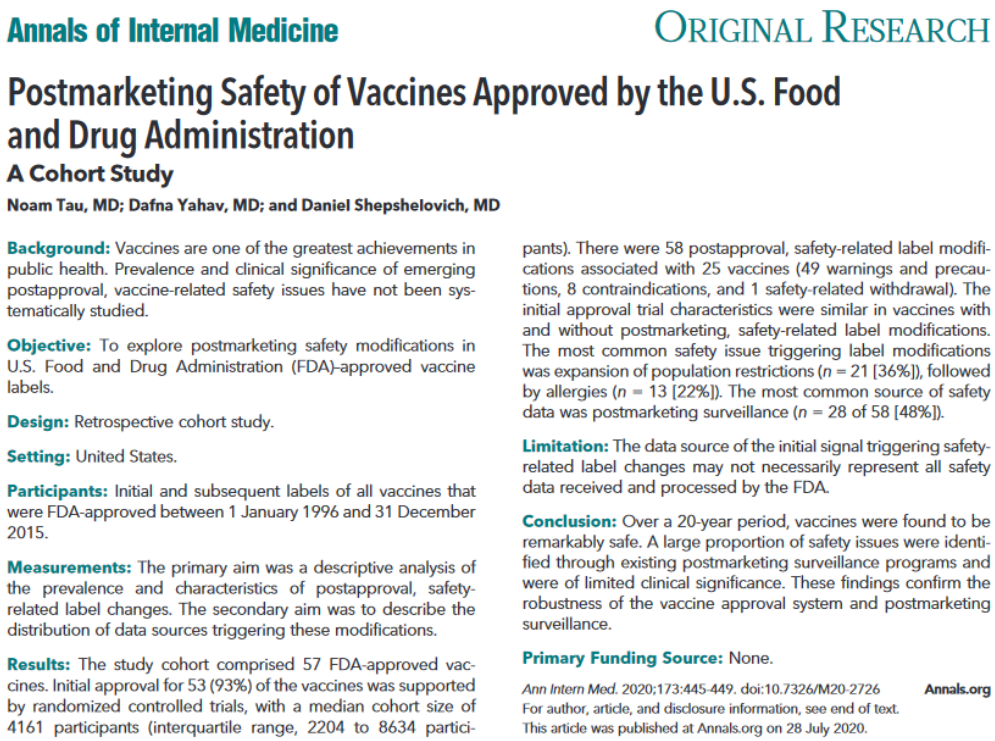
CDC: With nearly 5 million Americans vaccinated, just 29 have had confirmed allergic reactions

Hilary Brueck 22 hours ago

Availability Heuristic

Easy to recall	Hard to recall	Can lead to
Plane crashes	Safe flights	Fear of flying
Cold spell	Gradual warming	Ignoring climate change
Winning tickets	Normal tickets	Buying more
News reports of rare events	Millions vaccinated	Hesitancy

Post-marketing surveillance: an important contributor to safety-related label changes



Annals of Internal Medicine

ORIGINAL RESEARCH

Postmarketing Safety of Vaccines Approved by the U.S. Food and Drug Administration

A Cohort Study

Noam Tau, MD; Dafna Yahav, MD; and Daniel Shepshelovich, MD

Background: Vaccines are one of the greatest achievements in public health. Prevalence and clinical significance of emerging postapproval, vaccine-related safety issues have not been systematically studied.

Objective: To explore postmarketing safety modifications in U.S. Food and Drug Administration (FDA)-approved vaccine labels.

Design: Retrospective cohort study.

Setting: United States.

Participants: Initial and subsequent labels of all vaccines that were FDA-approved between 1 January 1996 and 31 December 2015.

Measurements: The primary aim was a descriptive analysis of the prevalence and characteristics of postapproval, safety-related label changes. The secondary aim was to describe the distribution of data sources triggering these modifications.

Results: The study cohort comprised 57 FDA-approved vaccines. Initial approval for 53 (93%) of the vaccines was supported by randomized controlled trials, with a median cohort size of 4161 participants (interquartile range, 2204 to 8634 participants). There were 58 postapproval, safety-related label modifications associated with 25 vaccines (49 warnings and precautions, 8 contraindications, and 1 safety-related withdrawal). The initial approval trial characteristics were similar in vaccines with and without postmarketing, safety-related label modifications. The most common safety issue triggering label modifications was expansion of population restrictions (n = 21 [36%]), followed by allergies (n = 13 [22%]). The most common source of safety data was postmarketing surveillance (n = 28 of 58 [48%]).

Limitation: The data source of the initial signal triggering safety-related label changes may not necessarily represent all safety data received and processed by the FDA.

Conclusion: Over a 20-year period, vaccines were found to be remarkably safe. A large proportion of safety issues were identified through existing postmarketing surveillance programs and were of limited clinical significance. These findings confirm the robustness of the vaccine approval system and postmarketing surveillance.

Primary Funding Source: None.

Ann Intern Med. 2020;173:445-449. doi:10.7326/M20-2726 Annals.org
For author, article, and disclosure information, see end of text.
This article was published at Annals.org on 28 July 2020.

- Over a 20-year period, vaccines were found to be remarkably safe
- A large proportion of safety issues were identified through post-marketing surveillance programs

Tau N, et al. Ann Intern Med. 2020; 173(6):445-449.

The AZ pause

"It's a very special picture [of symptoms]…Our leading hematologist said he had never seen anything quite like it."

-Steinar Madsen, medical director, Norwegian Medicines Agency

"The harm caused by depriving people of access to a vaccine will likely vastly outweigh even the worst case scenario if any link to the clotting disorders is eventually found."

-Stephen Griffin, University of Leeds virologist

EMA: “Safe and effective”

- Benefits of the AZ vaccine continue to outweigh risks
- Vaccine is not associated with ↑ in overall thromboembolic events
- No evidence of a batch-specific problem
- Vaccine may be associated with rare cases of blood clots associated with thrombocytopenia, including CVST

Statement from the European Medicine’s Agency Pharmacovigilance Risk Assessment Committee. March 18, 2021

How can healthcare workers help?

Filling evidence gaps

- Healthcare workers will be early SARS-CoV-2 vaccine recipients
- Emergency use-authorization will be based on limited follow-up data
- There is a need for long-term safety surveillance for SARS-CoV-2 vaccines

HERO-Together is…

- An **observational study of COVID-19 vaccines** in healthcare workers and their pod members (coming soon!)
- Open to people age 18+ who have **received any COVID-19 vaccine within the past 60 days**
- Monitoring short-and long-term safety of HCWs **vaccinated outside of clinical trials**
- Asking participants to complete brief surveys over 2 years about their **health and any unexpected medical care**

Who are Healthcare Workers?

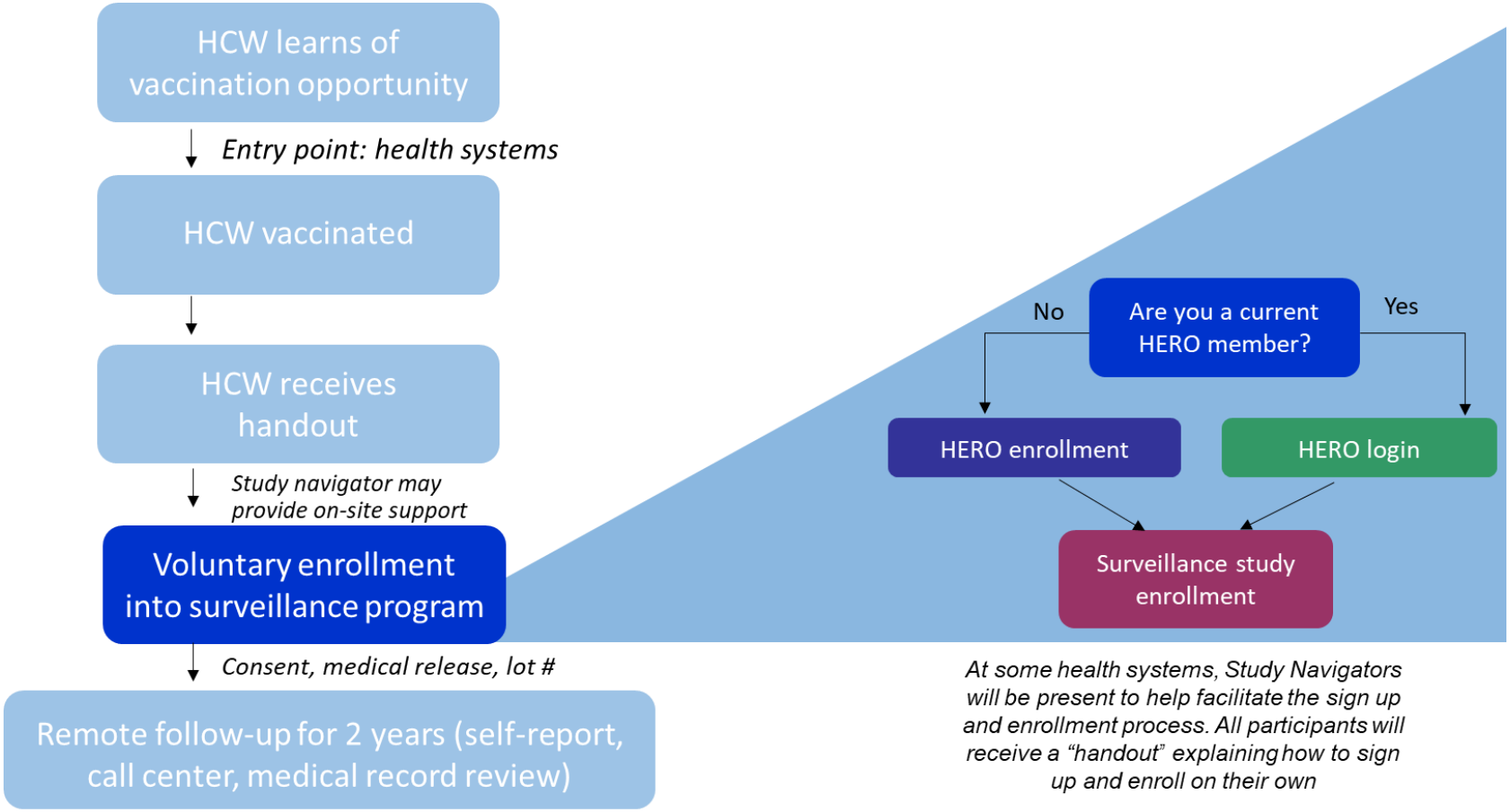
They are nurses, therapists, physicians, emergency responders, food service workers, dentists, environmental services workers, interpreters, and transporters.

A healthcare worker is anyone who works in a setting where people receive healthcare.

Who are pod members?

A “pod” is the group of people you live with or relate to as family and have regular household contact with at least once per week for the past 3 months.

HERO-Together enrollment pathway



At some health systems, Study Navigators will be present to help facilitate the sign up and enrollment process. All participants will receive a "handout" explaining how to sign up and enroll on their own

HERO TOGETHER

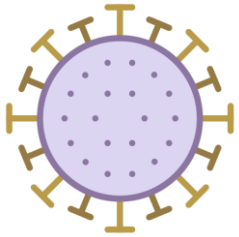
Data elements of interest

Vaccine info

Medical history

Unexpected medical care

Safety events



COVID-19 Info

Functional status

Top 5 Reasons to join HERO Together

1. Data on long-term safety is crucial for building vaccine confidence & studying non-trial populations
2. Return of results (e.g. What is the distribution of vaccinated healthcare workers by region?)
3. Early access to future study opportunities
4. Tell us your research priorities - make your voice heard!
5. Up to $200 compensation for time

Research in development

I was exposed to COVID. Am I protected?

I was just vaccinated. How long am I protected?

I received a vaccination, but I have ___. Am I protected?

I can get an antibody test. Does knowing my immune status lower my stress?

Creating a community

HERO TOGETHER

KEEPING COMMUNITIES HEALTHY WITH VACCINATION

COVID-19 mRNA Vaccines: How Did They Get Here So Fast?

January 7, 2021

Learning Together: What HERO Surveys Say

August 3, 2020

Some of us even like to rap.

Don’t miss your shot!

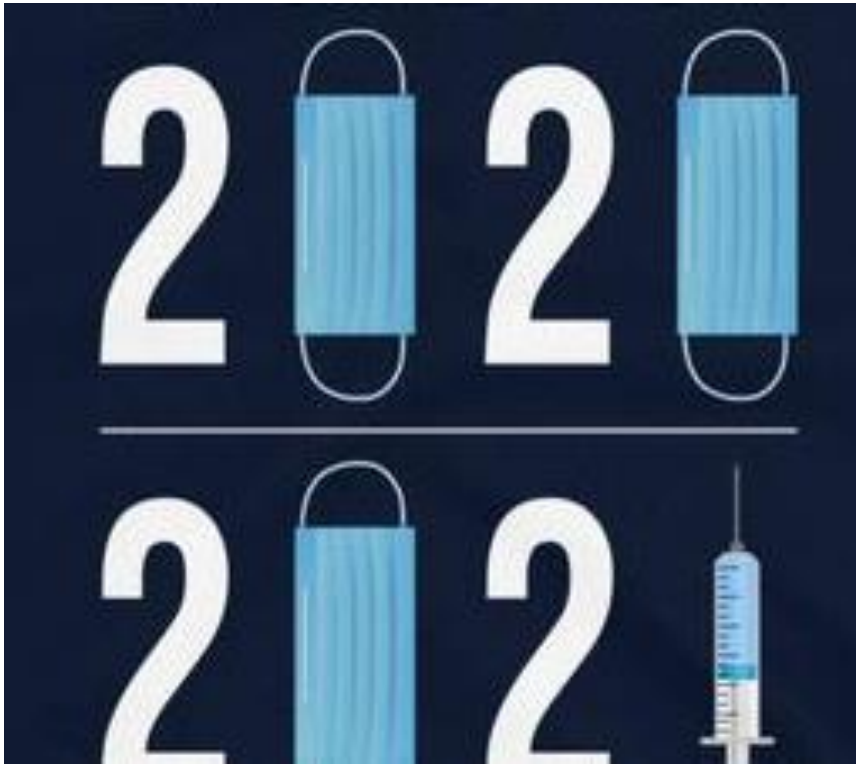
Sign-up is simple and easy at **heroesresearch.org/together.** Here are the steps:

1. Join the HERO Registry.
2. Complete the baseline survey.
3. Look out for additional survey invitations via email.
4. Help us spread the word on social media by tagging **@heroesresearch** and using the hashtag **#HEROTOGETHER**

Vaccinated?

Join us!

HeroesResearch.org


2020
2022