Let's Talk about Vaccines and Covid

Kathleen Beach MD MPH
Oct 26 2020

Objectives

A little about me and motivation for the talk

Vaccines and the immune system

Status of SARS COV2 vaccines

Data necessary to establish safety and efficacy

Review process

After “approval”

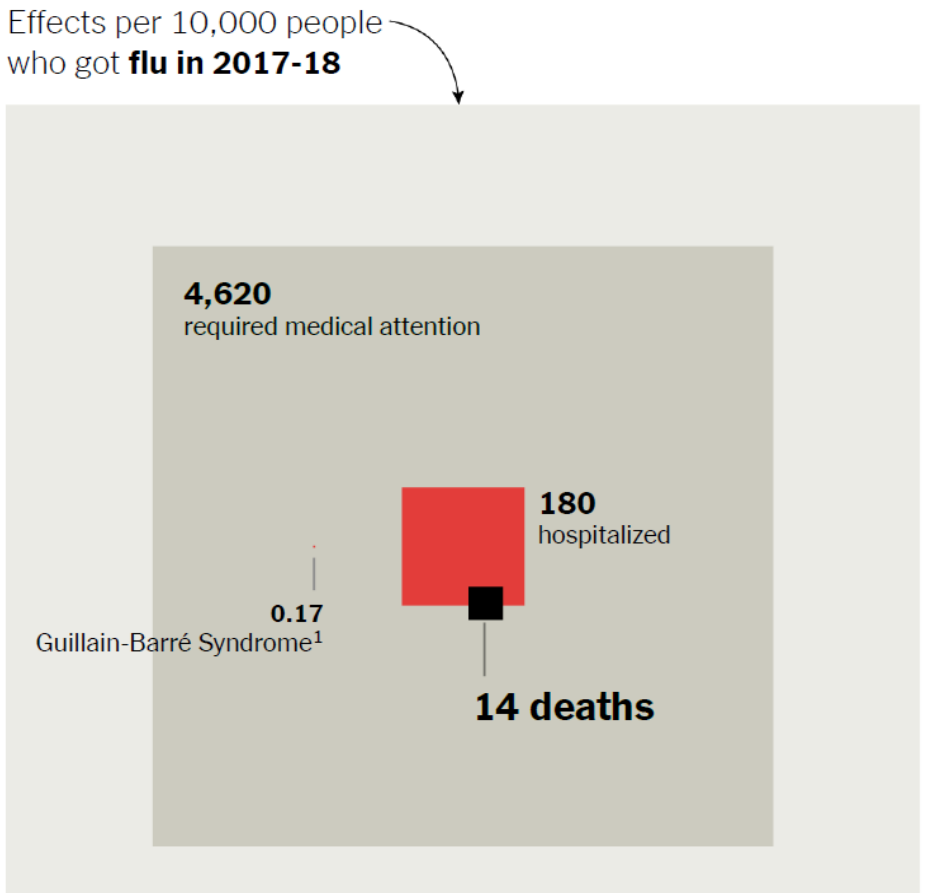
Distrust of vaccines goes back to the beginning

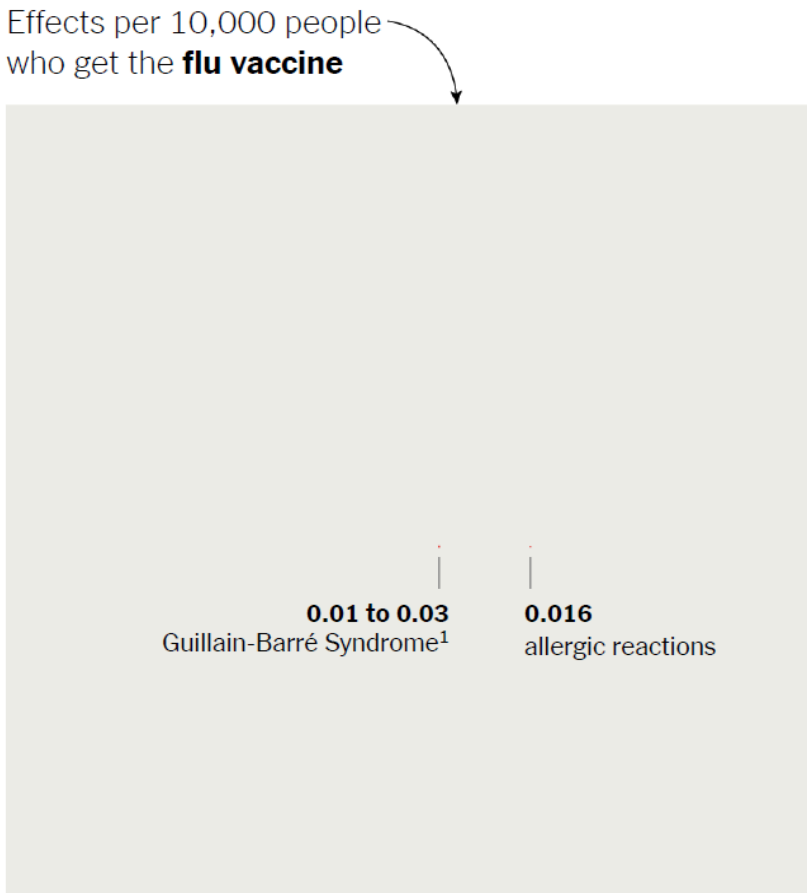
Intentions to Get Vaccinated

- Participants generally open to getting the COVID-19 vaccine *eventually*
- Many participants hesitant to get the COVID-19 vaccine when *first* available
- Concerns included:
  - Safety
  - Side effects (both short and long term)
  - Effectiveness
  - Sufficient testing in their group (age, race, ethnicity, underlying conditions)
  - Rapid development process
- Participants wanted more information and/or would "wait and see" before making a final decision (6 months commonly cited as a reasonable time frame)

You are unvaccinated and Got Sick: These are your odds

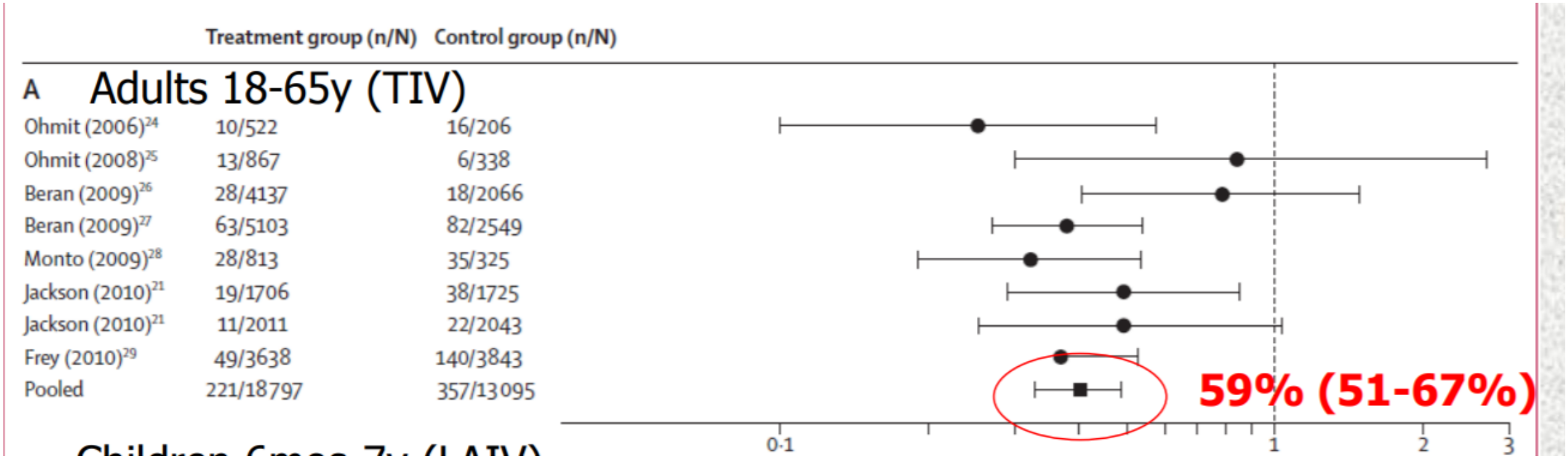
1.4/10 Americans got the flu 2017





Hotez PJ and Marsh B NYTimes Jan 2020

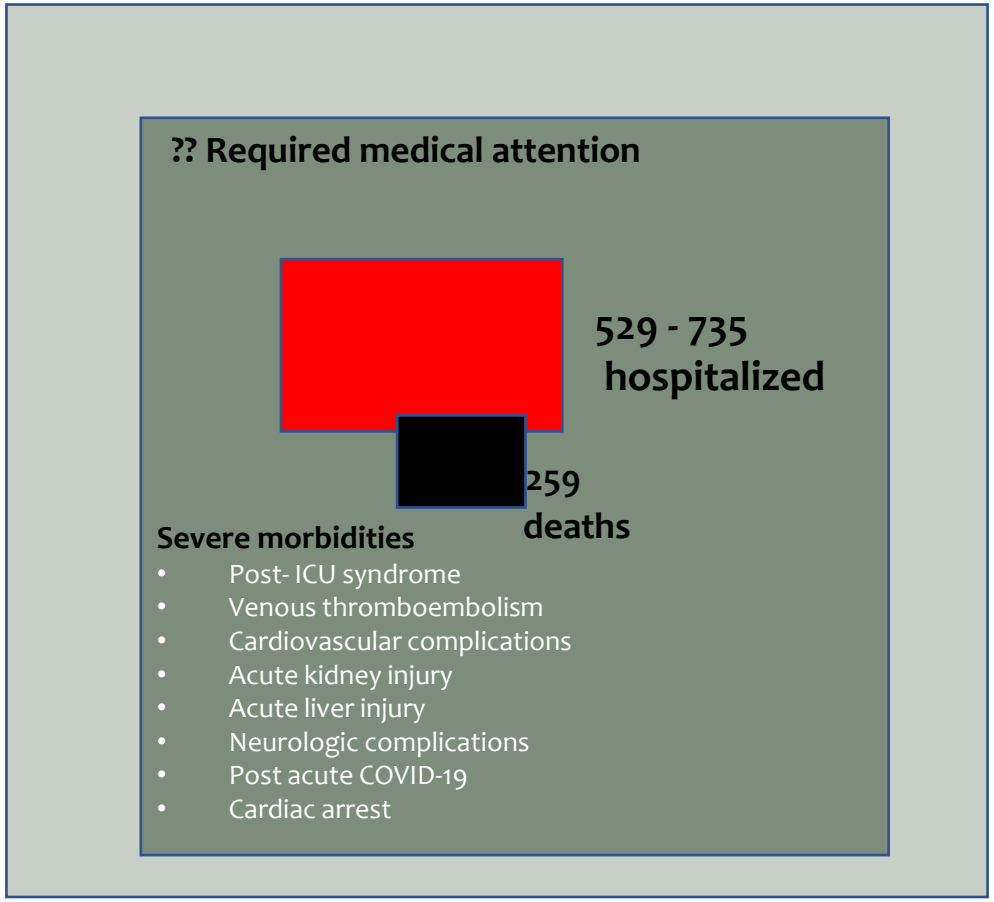
How effective are influenza vaccines?



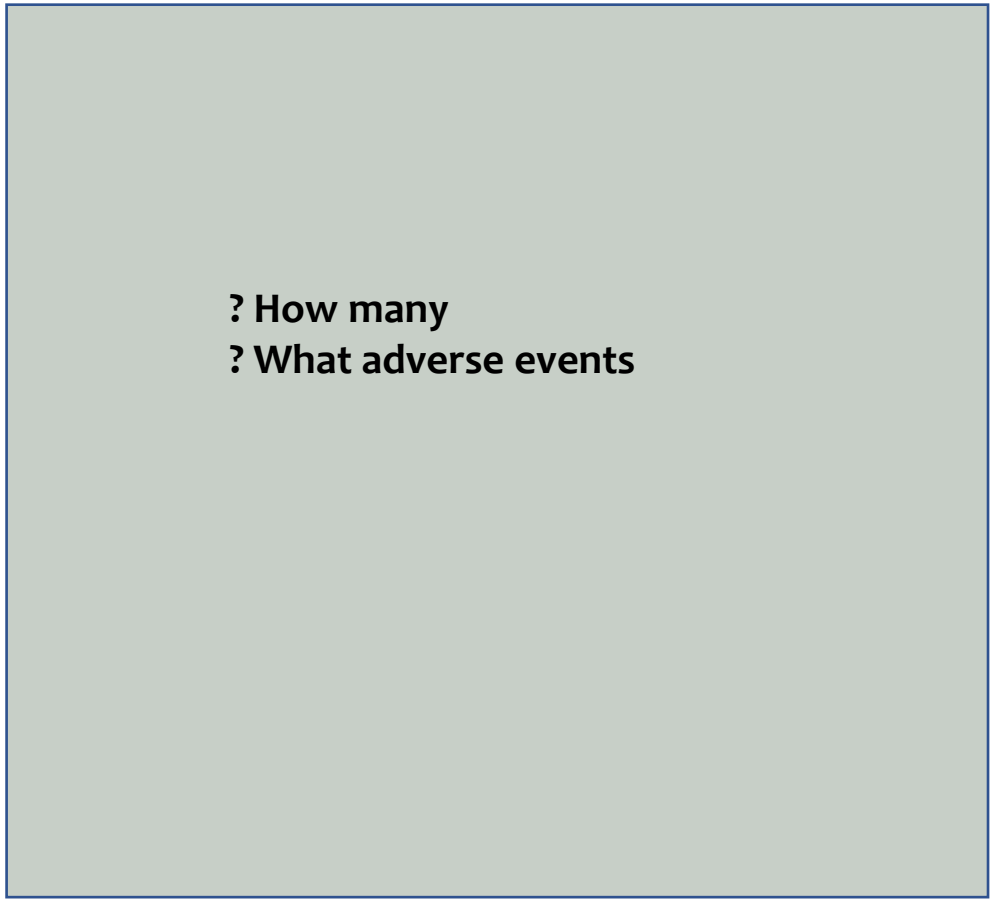
Osterholm Lancet ID 2012

So far 8.7million (2/10) and 225k deaths

Effects per 10000 with covid/SARS

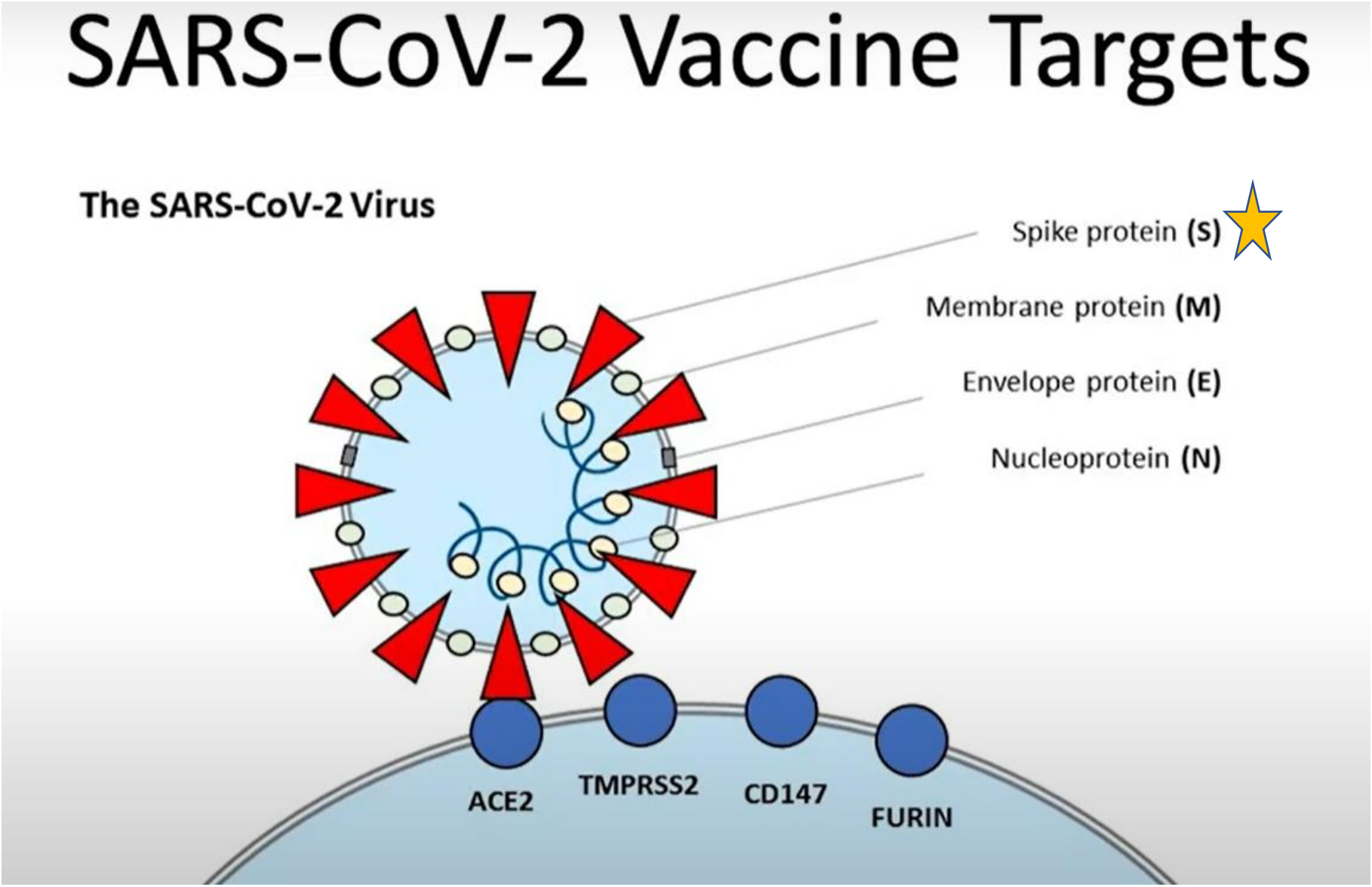


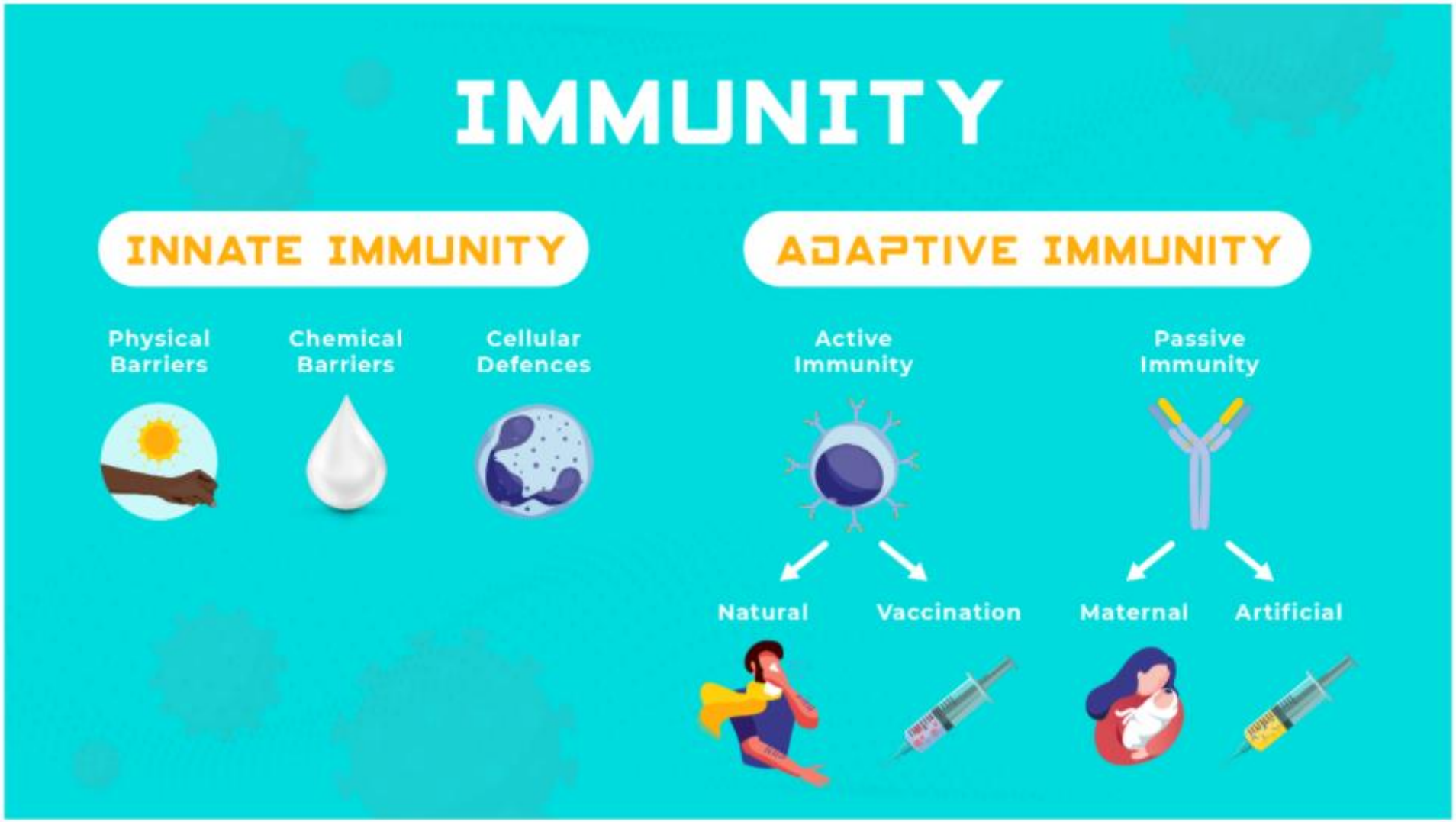
Effects per 10000 who get SARS vaccine



Assume 2000 additional asymptomatic yet infectious per symptomatic case

SARS-CoV-2 Vaccine Targets

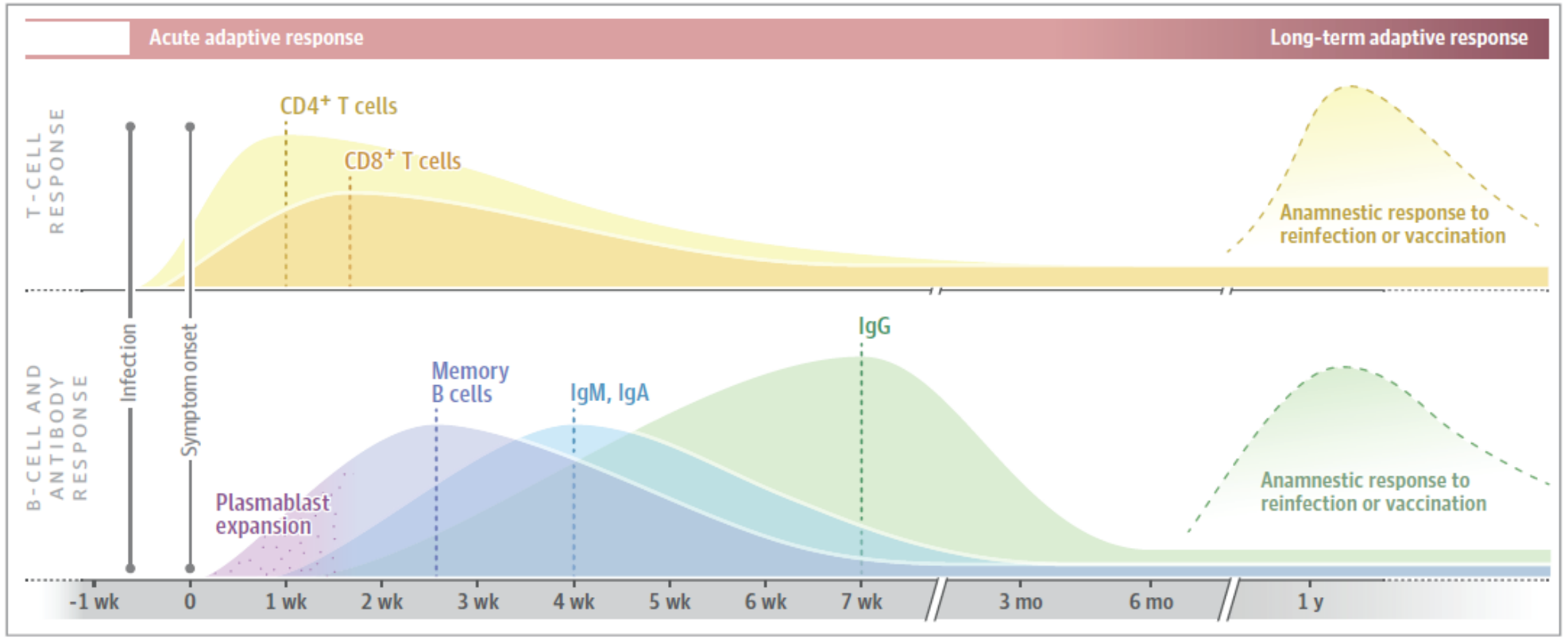




A comparison of innate and adaptive immunity

Gleichmann Immunology & Microbiology 2020

Figure. Adaptive Immunity to Coronavirus Disease 2019



Stephens JAMA 2020

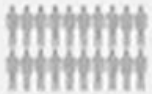
Vaccine "Platforms"

- DNA
- **RNA –Moderna, Pfizer/BioNTech (new technology)**
- Protein Subunit – close behind
- Inactivated virus – not in US. Old technology: Grow it, kill it
- **Non-Replicating Viral vector – J&J, Oxford/AZ (off hold)**
- Replicating viral vector
- Virus-like particle

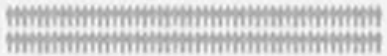
How a new vaccine is developed, approved and manufactured

The Food and Drug Administration (FDA) sets rules for the three phases of clinical trials to ensure the safety of the volunteers. Researchers test vaccines with adults first.

PHASE 1



20-100 healthy volunteers



- Is this vaccine safe?
- Does this vaccine seem to work?
- Are there any serious side effects?
- How is the size of the dose related to side effects?

PHASE 2

several hundred volunteers

- What are the most common short-term side effects?
- How are the volunteers' immune systems responding to the vaccine?

PHASE 3

hundreds or thousands of volunteers

- How do people who get the vaccine and people who do not get the vaccine compare?
- Is the vaccine safe?
- Is the vaccine effective?
- What are the most common side effects?

FDA licenses the vaccine only if:

- It's safe and effective
- Benefits outweigh risks

Vaccines are made in batches called lots.

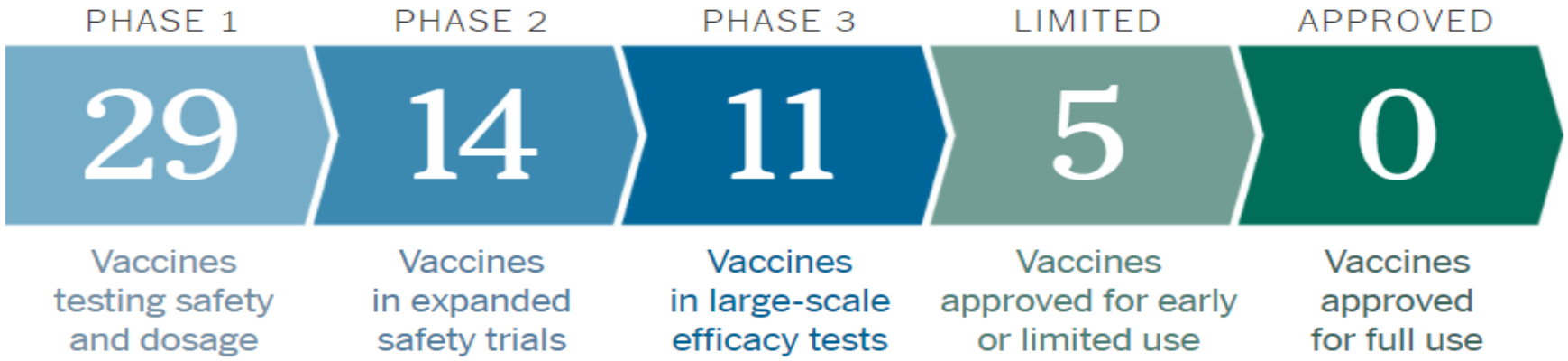
Manufacturers must test all lots to make sure they are safe, pure and potent. The lots can only be released once FDA reviews their safety and quality.

The FDA inspects manufacturing facilities regularly to ensure quality and safety.

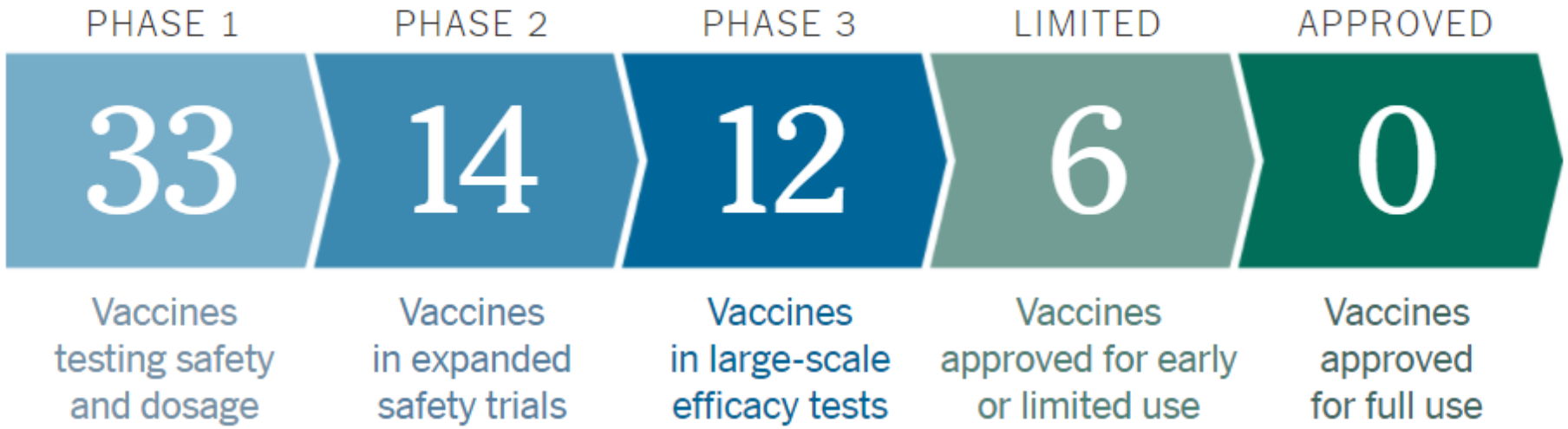
FOR MORE INFORMATION, VISIT HTTPS://WWW.FDA.GOV/CBER

Coronavirus Vaccine Tracker

By Jonathan Corum, Sui-Lee Wee and Carl Zimmer Updated October 12, 2020



By Jonathan Corum, Sui-Lee Wee and Carl Zimmer Updated October 24, 2020



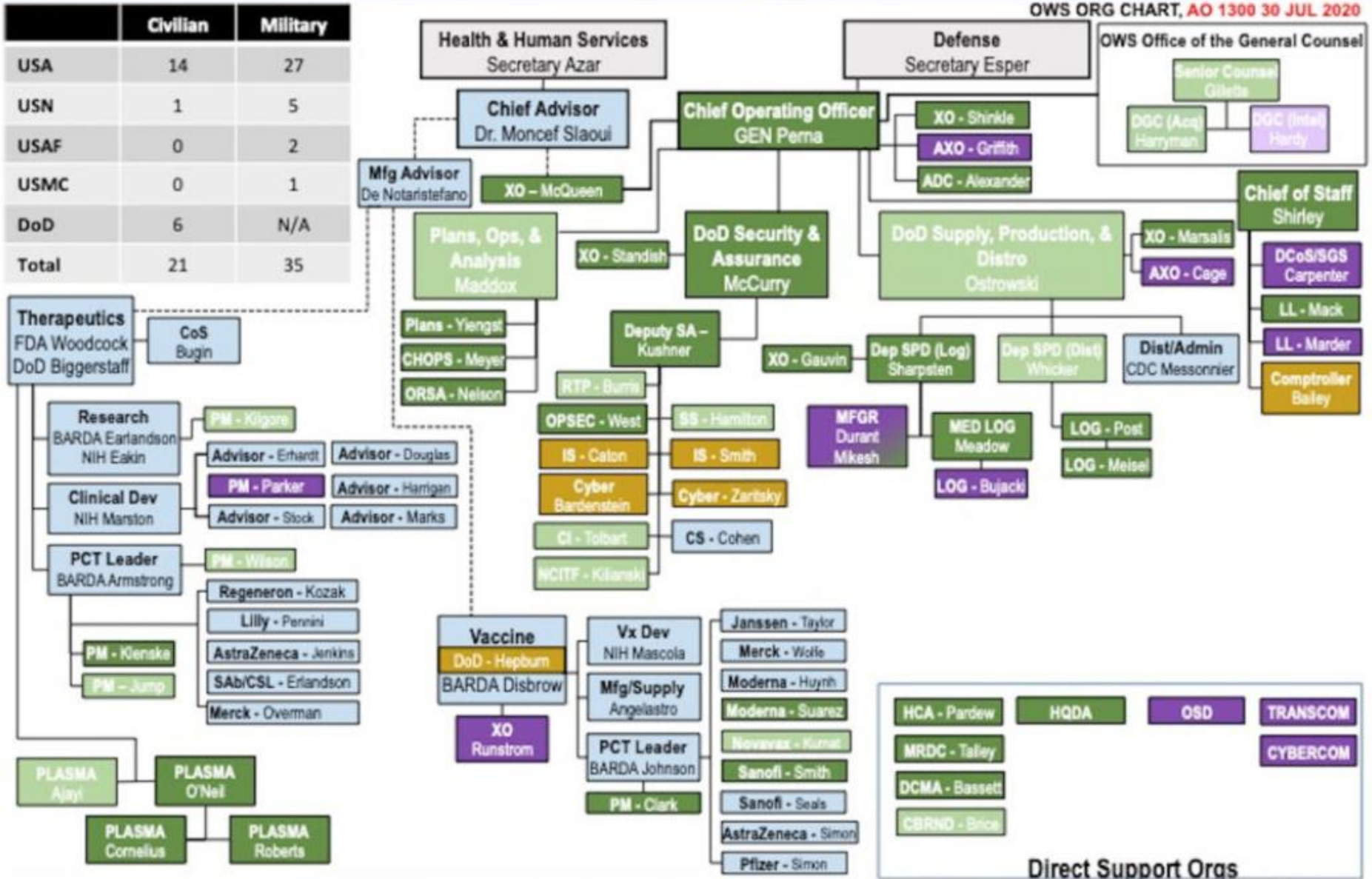
NYTimes

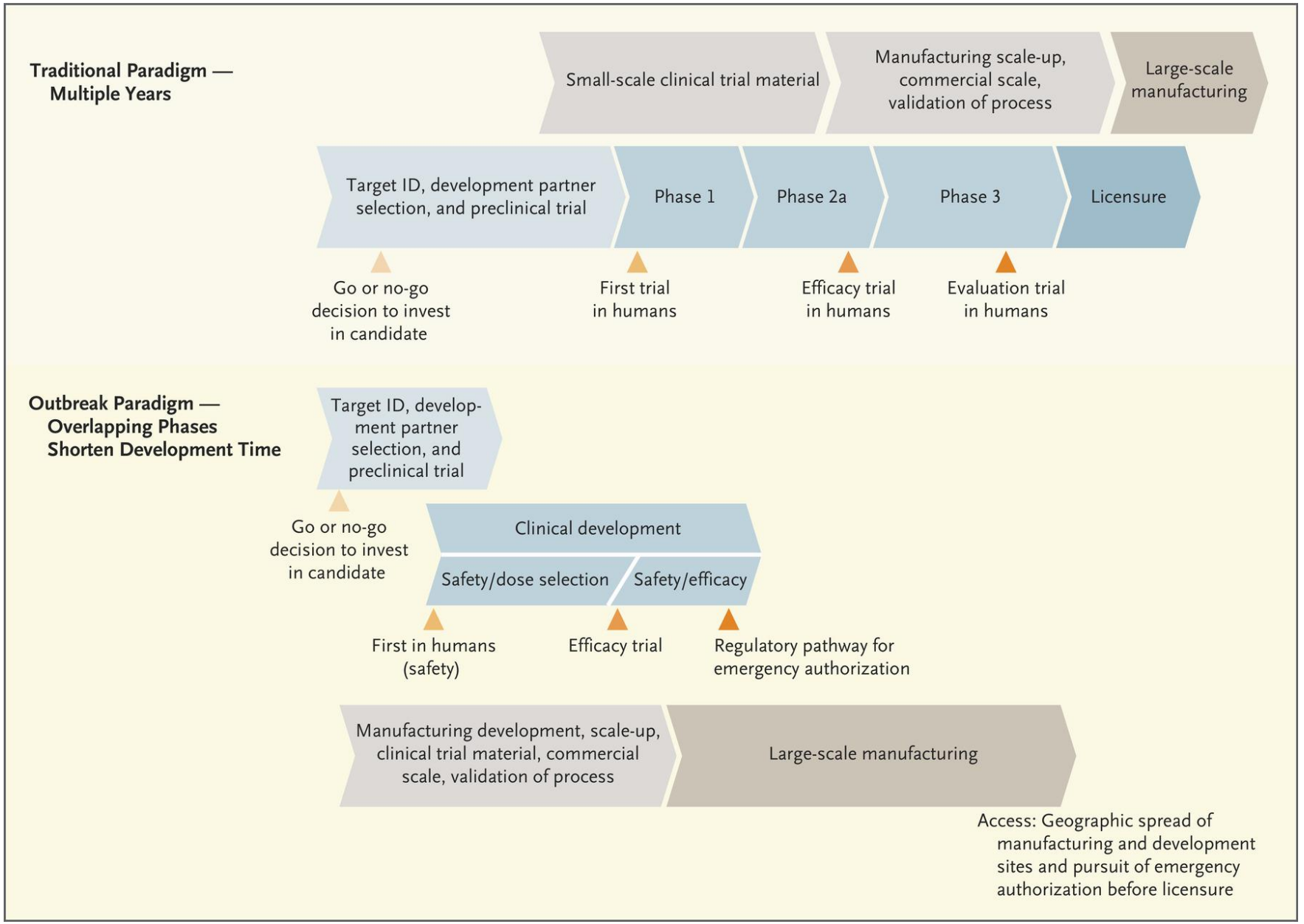
OPERATION WARP SPEED

Operation Warp Speed

OWS ORG CHART, AO 1300 30 JUL 2020

	Civilian	Military
USA	14	27
USN	1	5
USAF	0	2
USMC	0	1
DoD	6	N/A
Total	21	35





OPERATION WARP SPEED

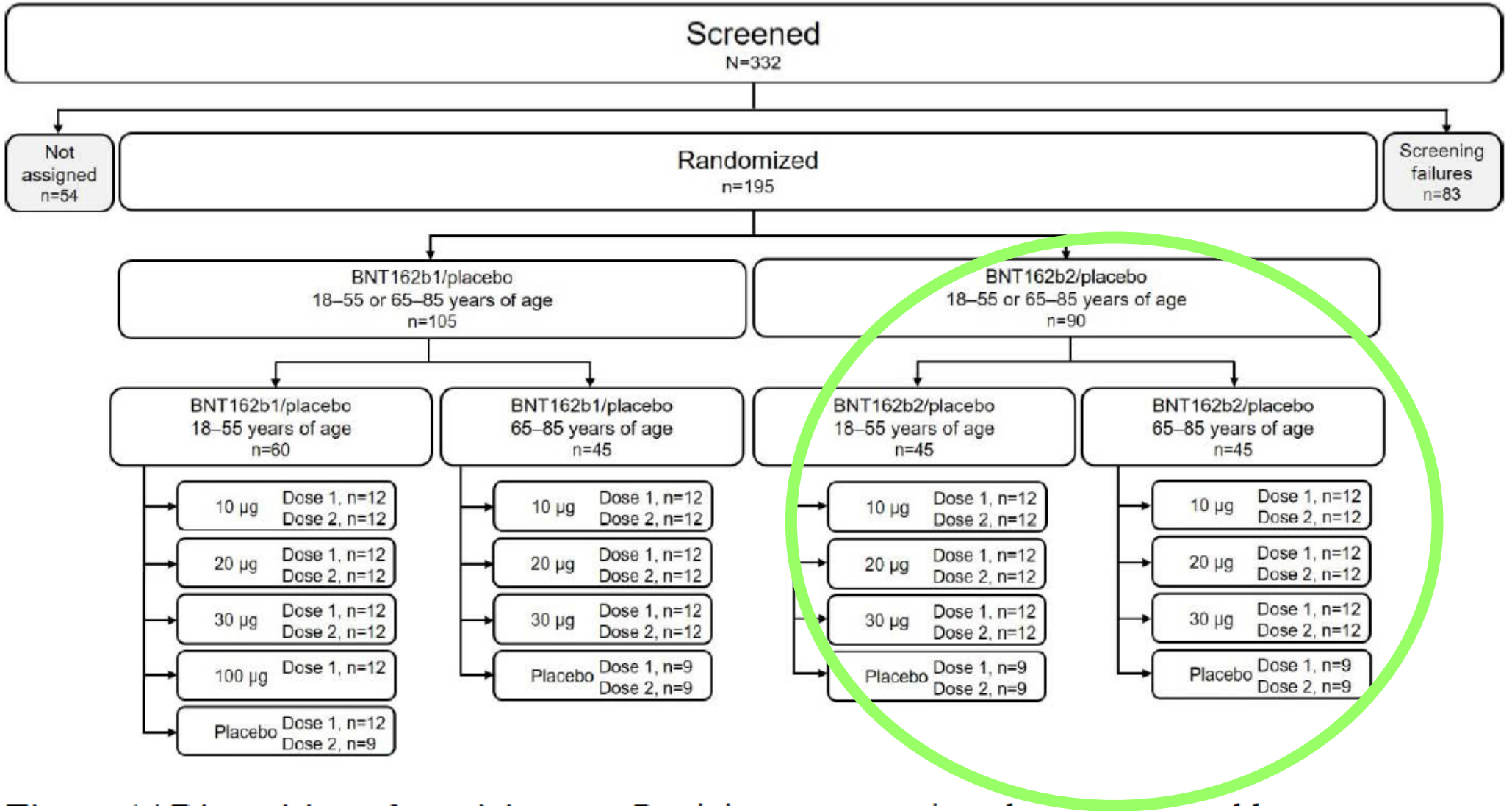
Multiple activities in parallel

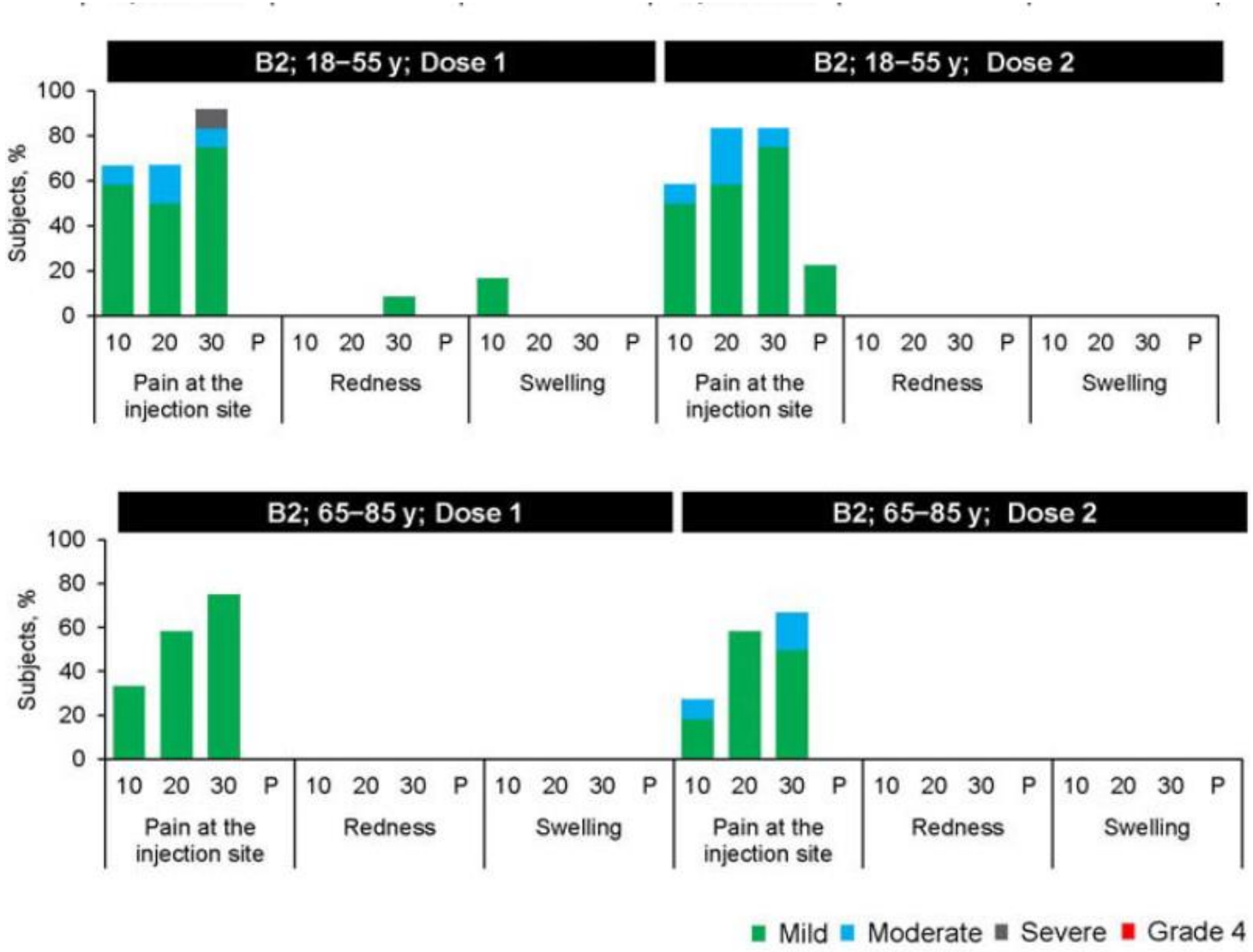
Financial risk – manufacturing investment

NEJM May 2020

Pfizer Phase 1 Trial to select Vaccine Candidate

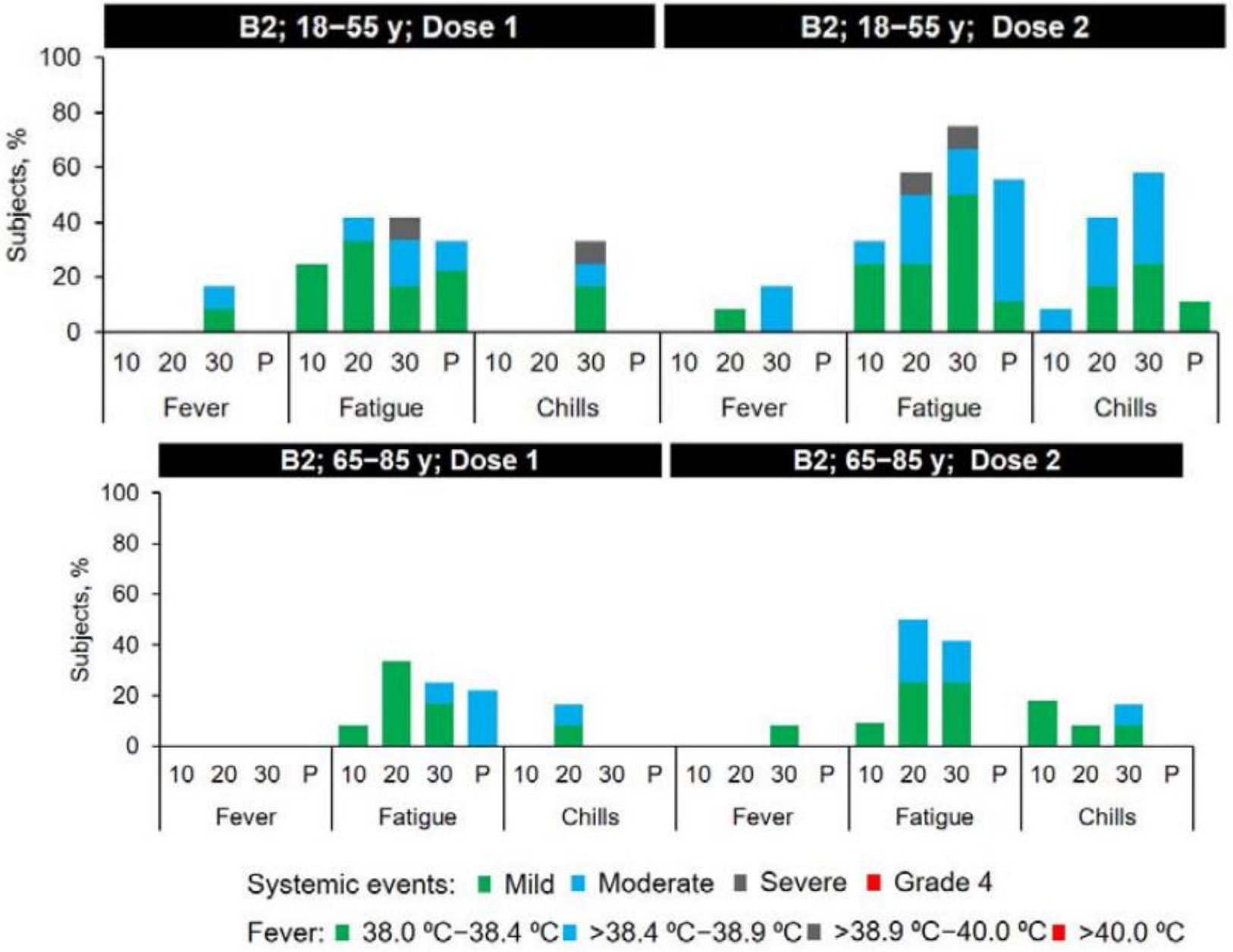
(medRxiv Walsh Aug 2020)





Local Injection Site Reactions

Walsh Aug 2020

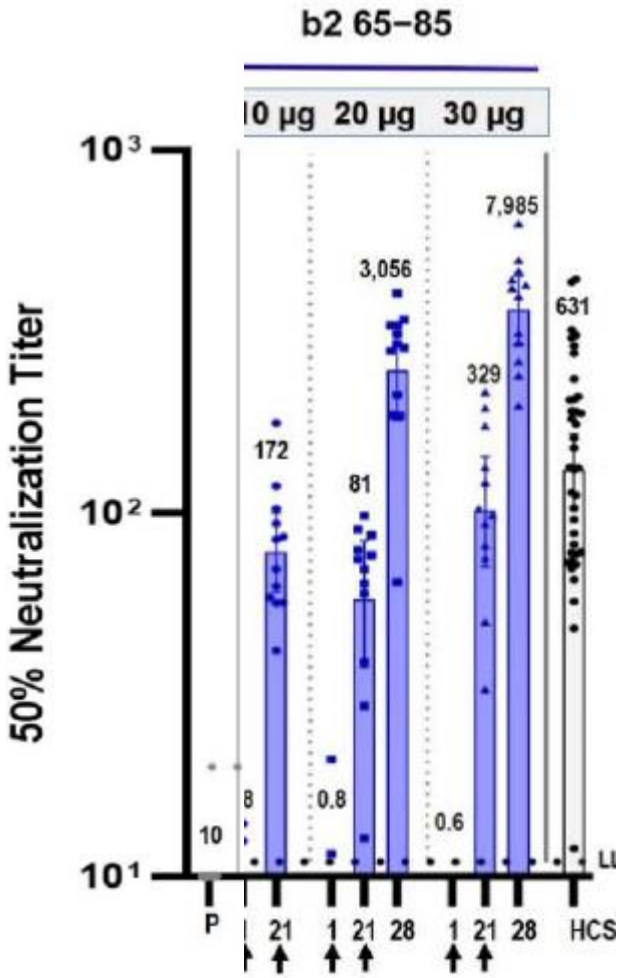


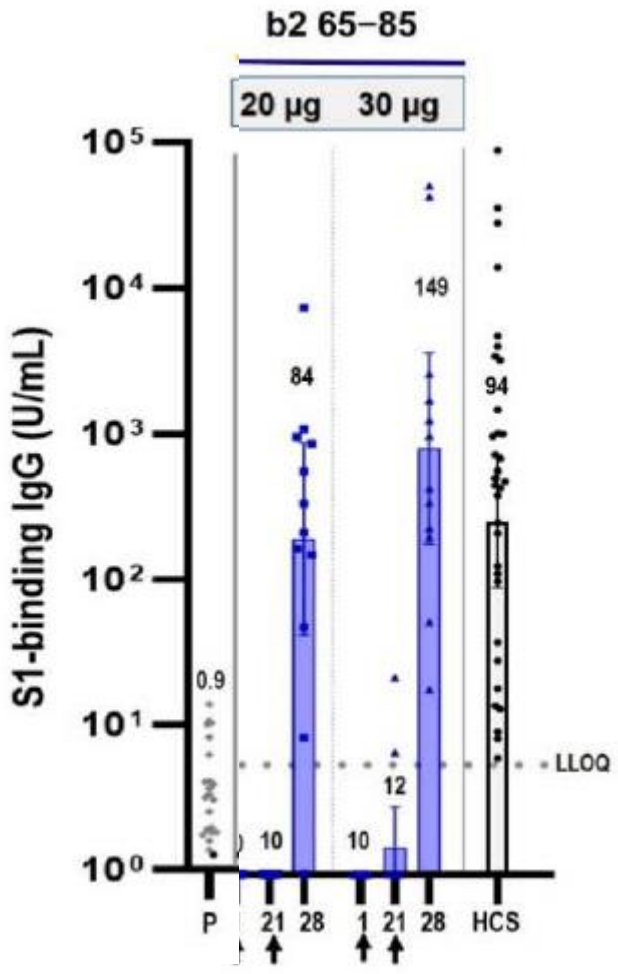
Systemic reactions

Walsh Aug 2020

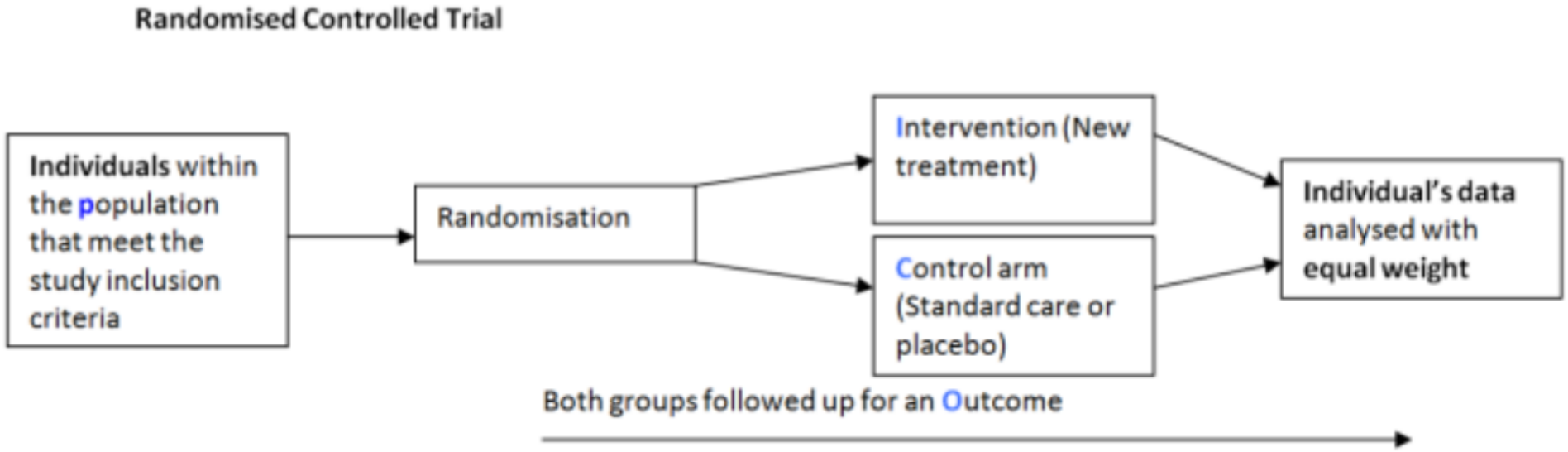
Immunogencity Profile in 65+ (IgG)

Walsh Aug 2020

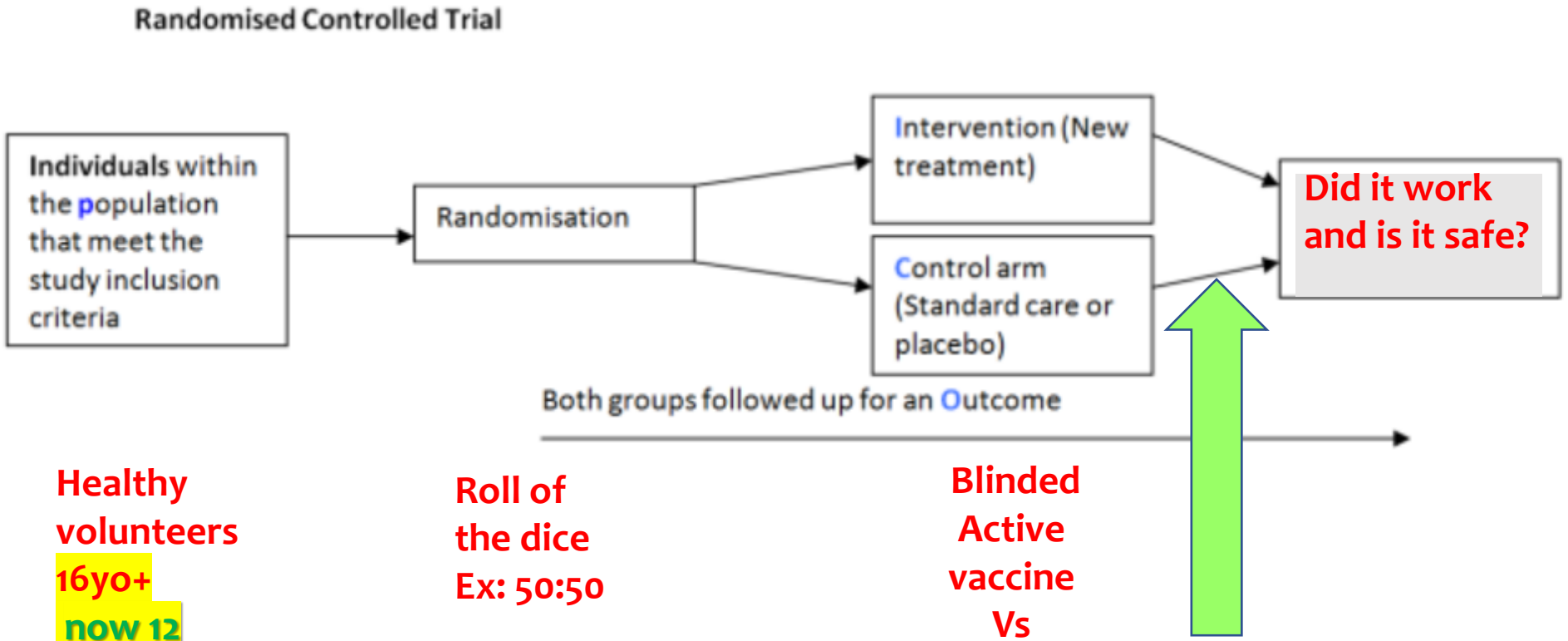




Phase 3 Design…….fairly standard



Prevention (not treatment) Studies



Healthy volunteers
16yo+
now 12

Roll of the dice
Ex: 50:50

Blinded
Active vaccine
Vs
Saline

Volunteers go about their lives as before – expect the risk of infection to be low in study population vs US

What counts as a COVID outcome?

First trials….

Infection

Vs

Infection + 1 symptom

Vs

Infection + severe disease

Under pressure, Transparency – Industry

A PHASE 1/2/3, PLACEBO-CONTROLLED, RANDOMIZED, OBSERVER-BLIND, DOSE-FINDING STUDY TO EVALUATE THE SAFETY, TOLERABILITY, IMMUNOGENICITY, AND EFFICACY OF SARS-COV-2 RNA VACCINE CANDIDATES AGAINST COVID-19 IN HEALTHY INDIVIDUALS

Study Sponsor:	BioNTech
Study Conducted By:	Pfizer
Study Intervention Number:	PF-07302048

Vaccine efficacy: reduction in % with Covid in vaccinated vs placebo

AND many of 2⁰ endpoints

Table 5. Interim Analysis Plan and Boundaries for Efficacy and Futility

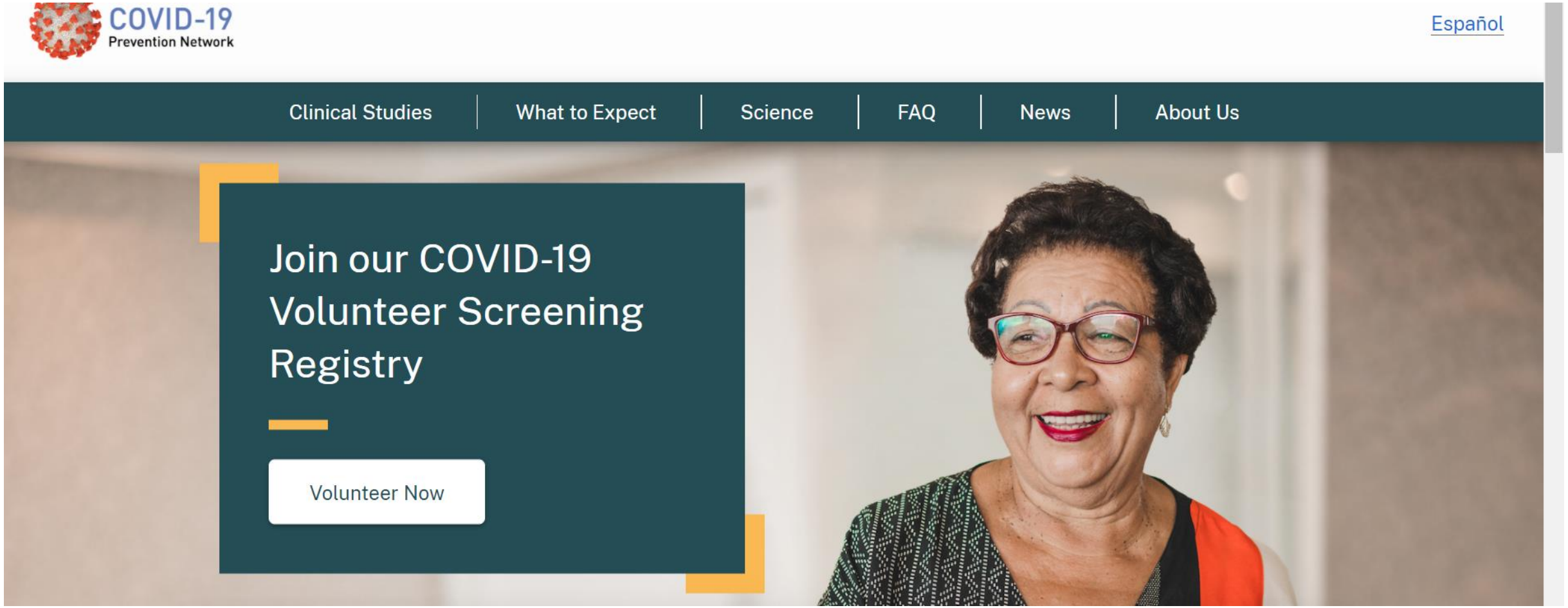
Analysis	Number of Cases	Success Criteria[a]	Futility Boundary
		VE Point Estimate (Case Split)	VE Point Estimate (Case Split)
IA1	32	76.9% (6:26)	11.8% (15:17)
IA2	62	68.1% (15:47)	27.8% (26:36)
IA3	92	62.7% (25:67)	38.6% (35:57)
IA4	120	58.8% (35:85)	N/A
Final	164	52.3% (53:111)	

Abbreviations: IA = interim analysis; N/A = not applicable; VE = vaccine efficacy.

Note: Case split = vaccine : placebo.

a. Interim efficacy claim: P(VE >30%|data) > 0.995; success at the final analysis: P(VE >30%|data) > 0.986.

So does the vaccine work (and is it safe)?
Role of the Data Safety/Monitoring Boards



https://coronaviruspreventionnetwork.org/

866-CVT-1919 (866-288-1919)

Pfizer Trial Status

Trial Locations

More than **130 clinical trial sites** in **5 countries,** including **39 U.S. states**

Trial Progress

The Phase 2/3 clinical trial is now enrolling participants 12 and over. **39,862 participants** are enrolled in the study, with **34,601** having received a **second vaccination**

Participant Diversity

Approximately **43%** of overall and **29%** of U.S. participants have diverse backgrounds

Participants	Overall Study	U.S. Only
Asian	4%	5%
Black	10%	10%
Hispanic/Latinx	28%	13%
Native American	0.7%	0.8%
Ages 56 to 85	42%	47%

Updated as of Monday, October 19, 2020 at 09:00am ET. Updates are made on a weekly basis.

Under pressure, Increased Transparency – FDA

Contains Nonbinding Recommendations

Development and Licensure of Vaccines to Prevent COVID-19

Guidance for Industry

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research
June 2020

Contains Nonbinding Recommendations

Emergency Use Authorization for Vaccines to Prevent COVID-19

Guidance for Industry

October 2020

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research

EUA for a SARS –COV-2 Vaccine

- Standard higher for vaccine VS therapeutic
- Must demonstrate clear and compelling efficacy in large, well designed Phase 3
- Provide safety data for a median of 2months
- Public meetings required for each vaccine applying for EUA/approval
  - RISK/BENEFIT assessment
- Enhanced post deployment safety surveillance (due to shorter in trial duration)

FDA Advisory Committee October 22 2020

- Vaccine and Related Biologics Products Ad Com
- External experts- nonbinding
- A general discussion; No specific application
- Open to the public via YOU TUBE

Now what?

FDA:

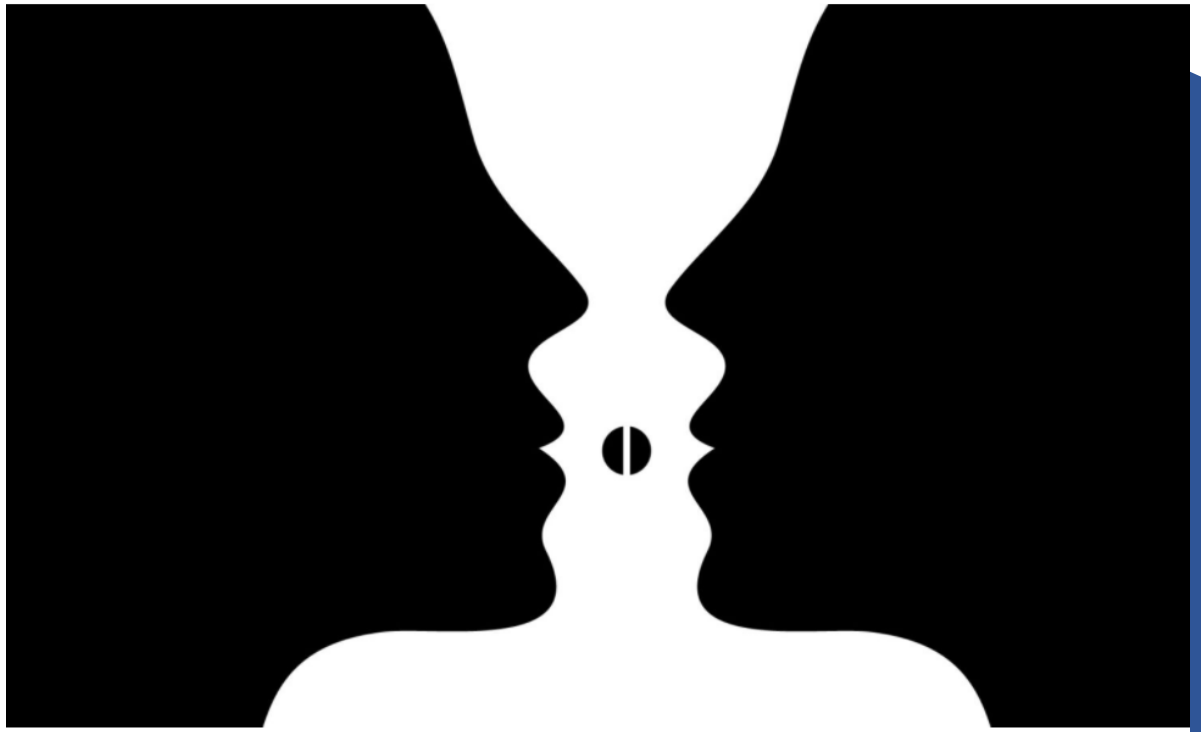
More internal discussions

Expanded access route instead?

Companies will submit data packages when ready

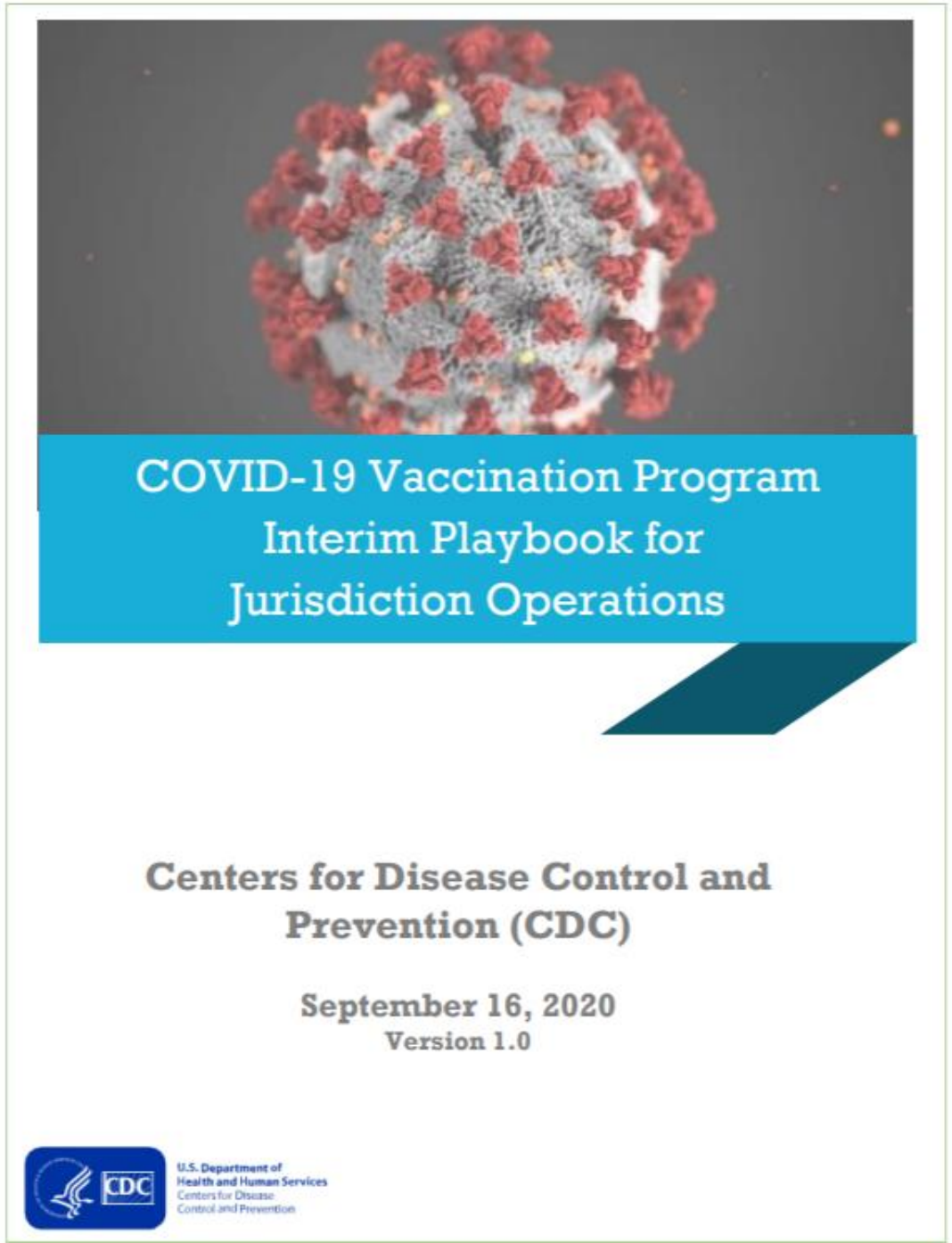
Trials continue to collect data (more longer term)!!

Public advisory committee meetings

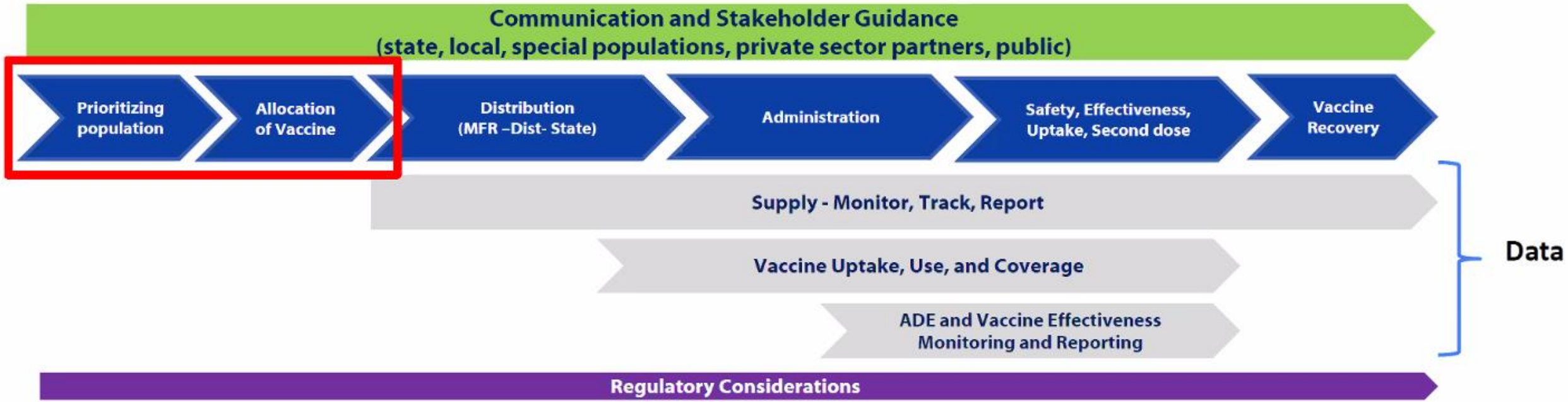


Weighing Benefits for Many vs Risks for a Few

Who gets a COVID vaccine first? Access plans are taking shape



Multiple Critical Components to Vaccine Implementation



Public health impact relies on rapid, efficient, and high uptake of complete vaccine series, with focus on high-risk groups

Appropriately paranoid… cybersecurity and physical security Mango HHS

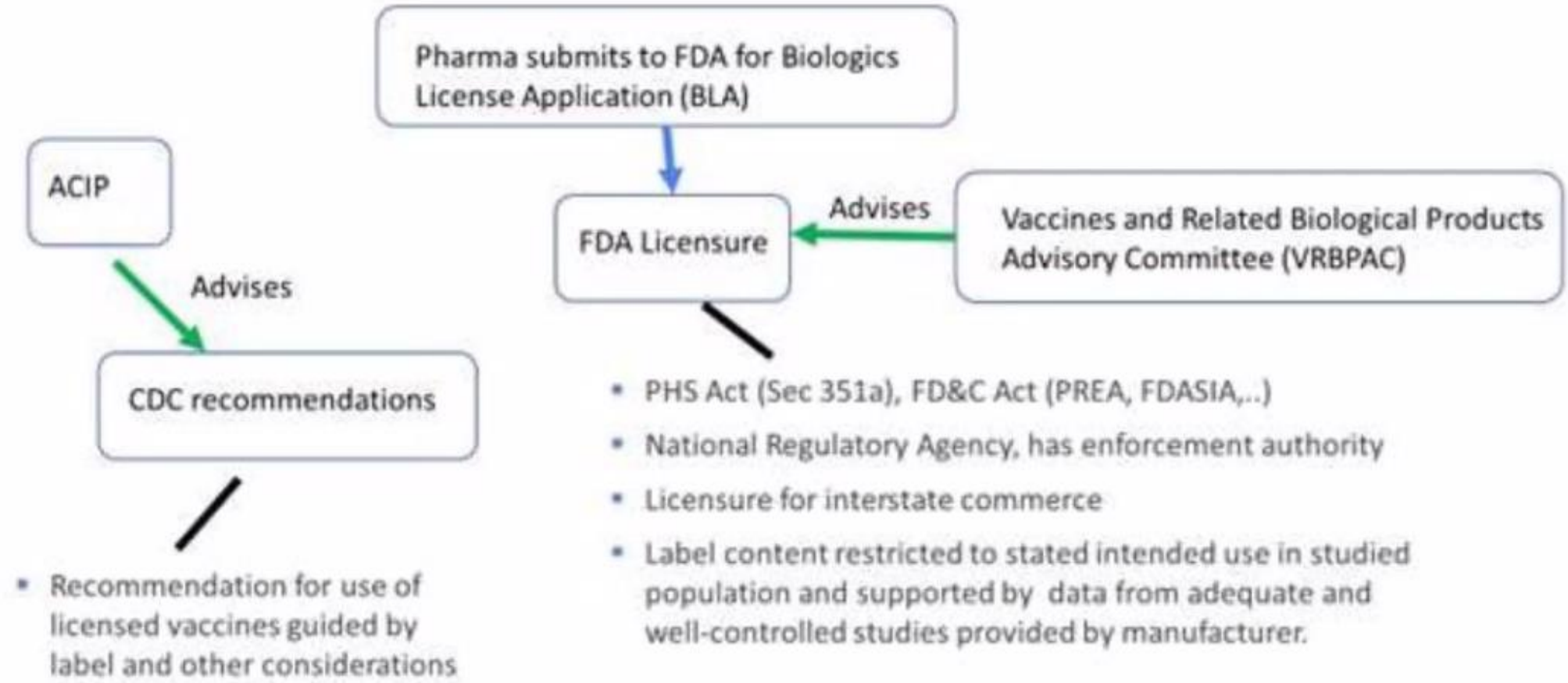
Wall Street Journal Oct 21 2020

HEALTH

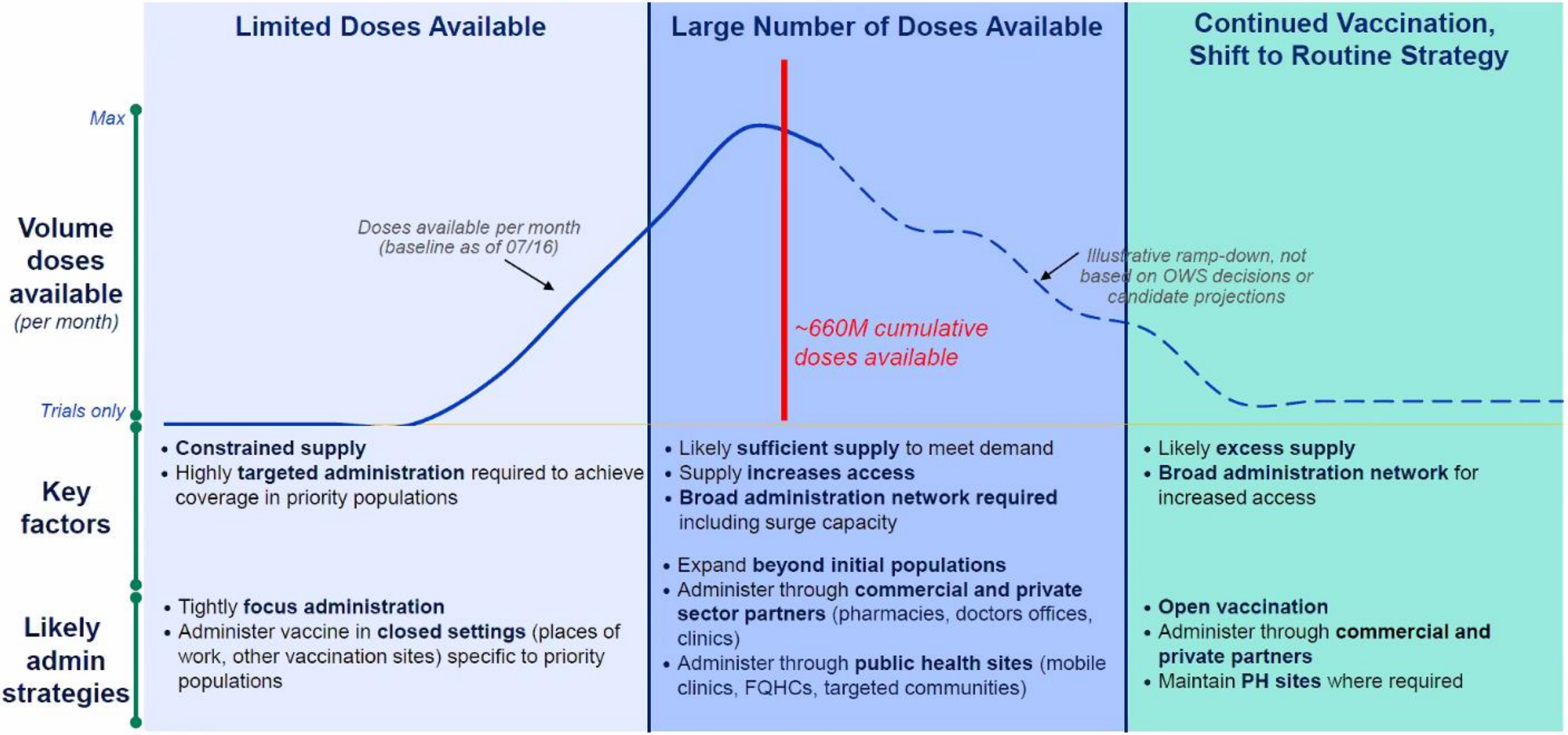
Covid-19 Vaccines to Be Stored Secretly Under Tight Security

Drugmakers and others plan to use fake shipments and GPS trackers to prevent potential thefts

Vaccine Licensure and Recommendations



Distribution will adjust as volume of vaccine doses increases



AF

NC vaccination plan outlines priorities for 4-phase rollout

BY LYNN BONNER
lbonner@newsobserver.com

There aren't going to be enough coronavirus shots for everyone who wants them when the first vaccines emerge from the

need to understand that there is only going to be a limited supply of those vaccines, so we're going to have to prioritize certain folks who will be able to get access to that vaccine at first," said Dr. Mandy Cohen, secretary of the

Dr. Anthony Fauci, director of the national Institute of Allergy and Infectious Diseases, told CBS News on Wednesday that he expects to know by the end of the year whether there's a safe and effective vaccine. A vaccine

Oct17 2020