



# Defeating COVID-19

Harvard Business School,  
Section Presentation Series

## VACCINE UPDATE

Fred Brown  
November 15, 2020

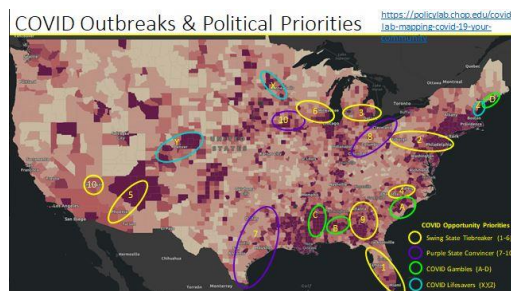
# HBS Series Session 3: Vaccine Update

This material is based on my experience developing 6 vaccines and managing prior pandemics

## Fred's Focus Since September 2020 Presentation

- Advising businesses on strategies for opening safely
- Advising manufacturers on process acceleration & regulatory dynamics
- Advising NGOs on best strategies
- Advising governments and candidates:
  - Countries, states, localities
  - U.S.

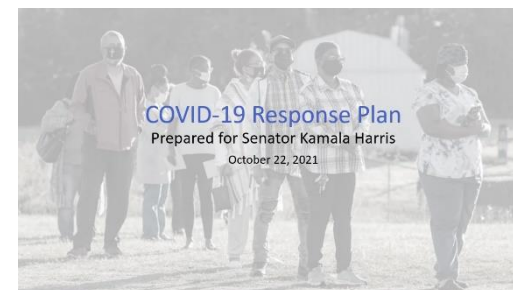
### Campaign priority areas



### Vaccine Distribution and Database Implementation



### COVID-19 Strategy *7 Transitions*



### Notes:

- This material is an extremely simplified discussion of a very complex topic.
- It is still early days in our knowledge of the virus, so expect changes in data.
- The opinions presented are mine alone.
- Please be a super spreader – use this material in context liberally.

# Vaccine Update Agenda

*Central Question: Will we get to herd immunity with the vaccine? When?*

- The Situation: Fred's predictions and new forecast
- The Science
  - Significance of the Pfizer vaccine
  - Vaccine 101: What you should know
  - What other vaccines are on the horizon and who has them?
- Production and Operations Management– challenges
- The Financial Implications for Big Pharma
- Getting to Normalcy: What to expect
  - U.S.
  - Global

# Fred's Predictions: Deaths/Day & Total

Deaths/Day

6,000

5,000

4,000

3,000

2,000

1,000

2,701 Maximum

March 23:  
773 Deaths

Fred's Projection for Sept, on 04/04:  
145,000 – 180,000

Fred's Projection For Nov, on 09/02:  
238,000 – 250,000

September 1:  
184,629 Deaths

November 14:  
245,040 Deaths

Fred's Projection For Dec 31 on 09/02:  
312,000 total, max ~3,000/day

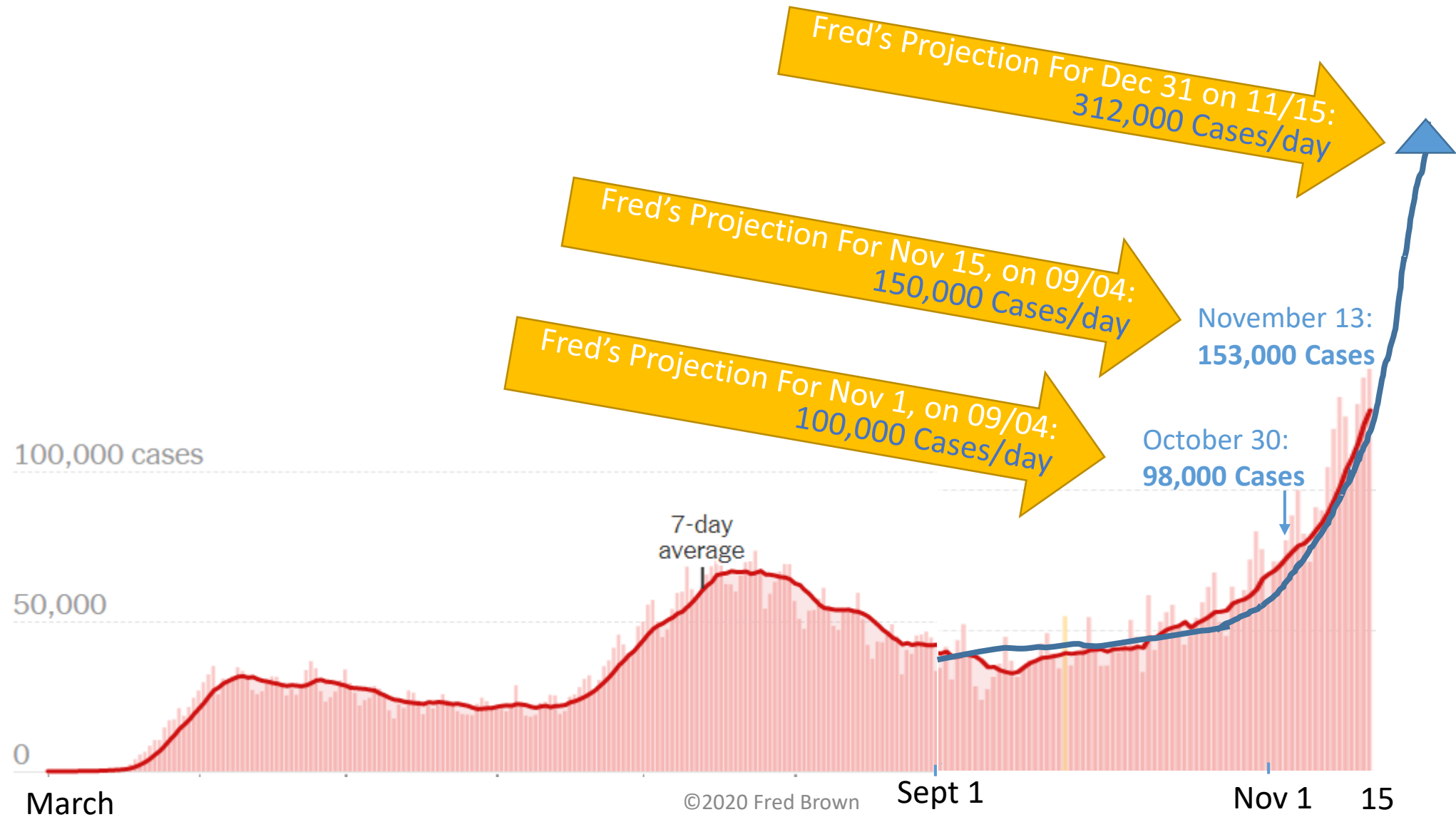
2020

Mar 22 Mar 31 Apr 09 Apr 18 Apr 27 May 06 May 15 May 24 Jun 02 Jun 11 Jun 20 Jun 29 Jul 08 Jul 17 Jul 26 Aug 04 Aug 13 Aug 22 Aug 31 Sep 09 Sep 18 Sep 27 Oct 06 Oct 15 Oct 24 Nov 02 Nov 11

Seven-day Average

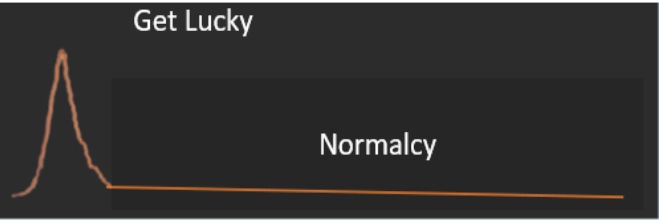
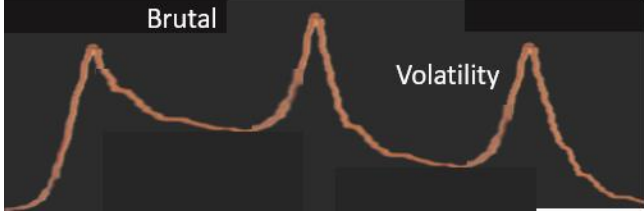
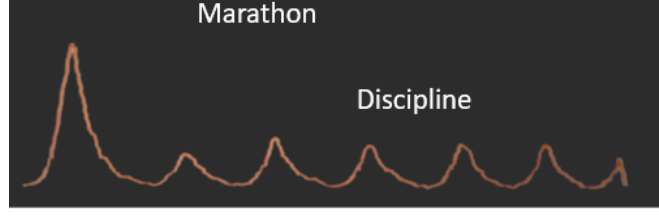
Cumulative Confirmed Deaths

# Fred's Predictions: Cases/Day & Total



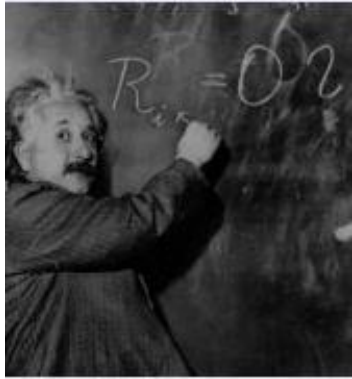
# The COVID Scenarios, Managing Uncertainty

September 2, 2020 advice, *“Play out the U.S. “Get Lucky” bet, but plan for a marathon.”*

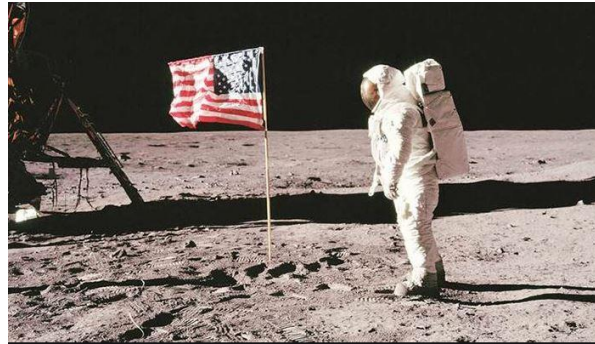
	“Get Lucky”	“Brutal”	“Marathon”
<i>Biologic Model</i>	“Silver Bullet” Vaccine	“Natural” Herd Immunity <i>Haphazard Decimation</i>	Partially effective Combo Controls
<i>Economy</i>	V-shaped recovery	L- shape downward	Sq Root if improve infrastructure & pandemic mgt
<i>Deaths</i>	500,000 U.S. until vaccine control	2.2M+ US deaths – depending on duration of immunity	650,000 deaths until control
<i>Best Moves</i>	Open fast. Restore Confidence	Survive! Build Hospital Infrastructure	Build Detect & Control Healthcare Infrastructure
<i>Viral Curve</i>			
Likelihood	Apr-20	20%	60%
	Sep-20	10%	55%
	Nov-20	10%	20%

# We are now witnessing a true revolution

- Synthetic vaccine capability vastly speeds our ability to respond to future pandemics
- This technology will become the basis for a new class of medicines impacting antibiotics, protein deficiency diseases & cancer



The Atom



Space



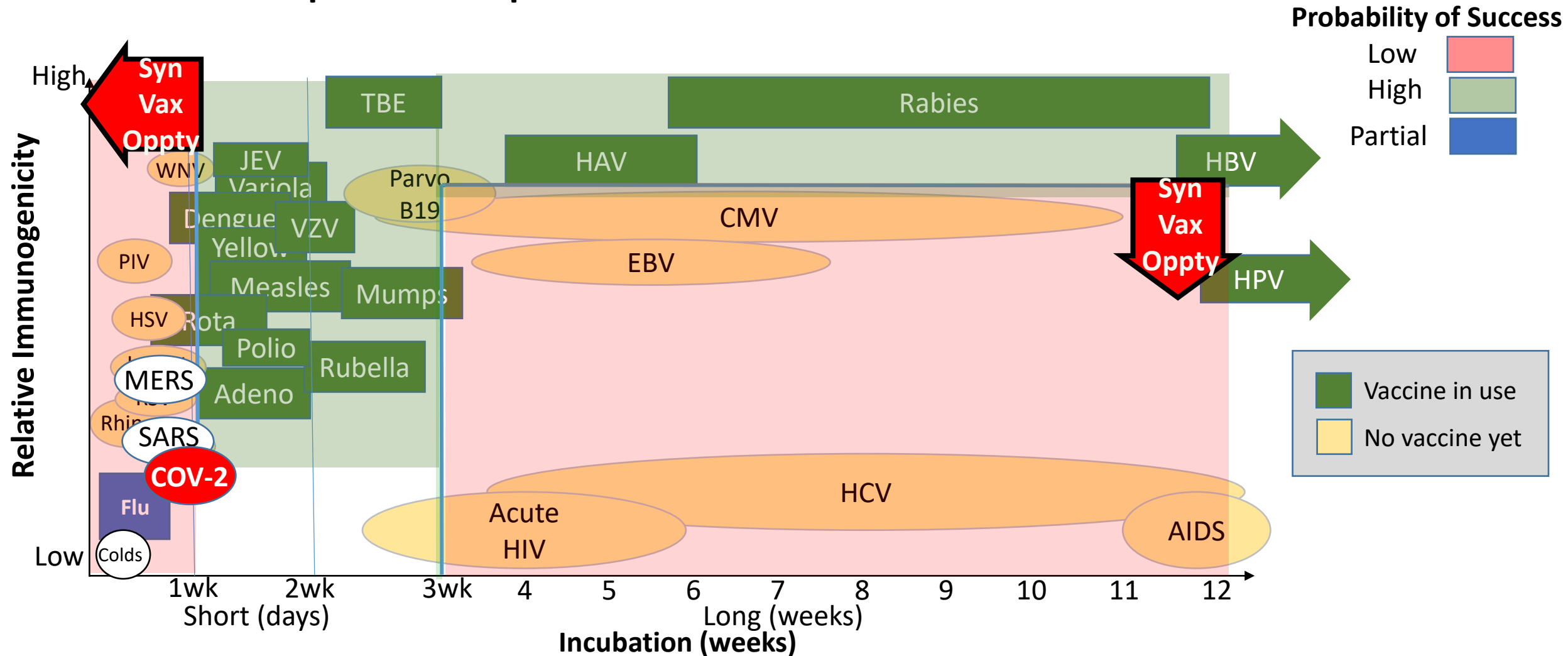
The Gene

- We bet that we could:
  - Vastly expand the vaccine “sweet spot”
  - Completely change the process by which we select lead compounds
  - Completely change the way we develop a product: parallel pathways

 **This U.S. high risk bet will save lives if logistics can catch up with vaccine development revolution**

# Synthetic Vaccines have increased the vaccine “sweet spot”

**Vaccine technology was limited for viruses that establish themselves too fast or hide**  
**Now we can replicate the speed of a virus**



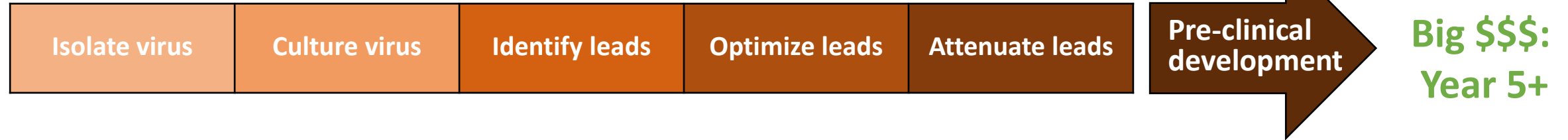
Relative Immunogenicity = virus genetic diversity x intensity of primary immune response x protective duration of primary immune response



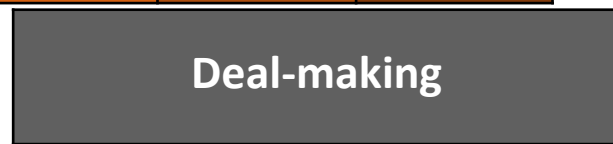
# Shrinking 45 Months to 45 Days

## The Revolution in Research & IP Licensing

4-10 Years (The old way)



1 day-3 Months (The new way)



Big \$\$\$:  
Week 5—Month 5

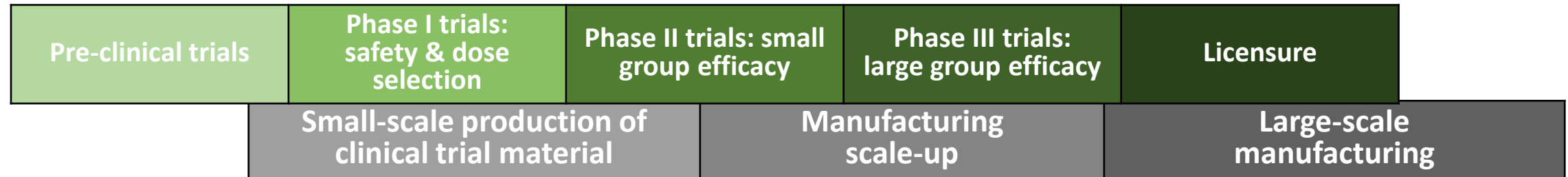
### First 6 OWS Deals (\$9.85B in 82 Days)

Days To Deal	Company	Deal (Billions)	# vaccinated w/ final mfg. dose
131	AstraZeneca	\$2.2	155
193	Pfizer	\$1.95	52
208	Johnson & Johnson	\$1.0	250
213	Moderna	\$1.0	155
202	Sanofi	\$2.1	956
178	Novavax	\$1.6	65

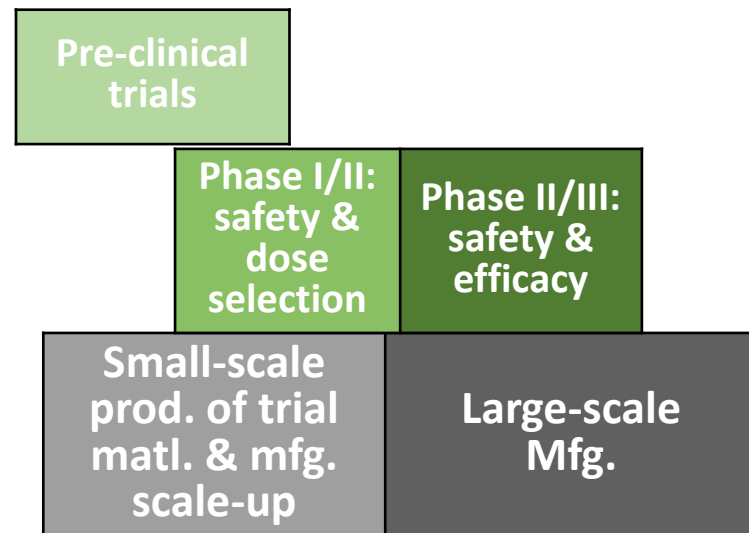
# Shrinking 9 Years to 9 Months

## The Revolution in Clinical Development

4-11+ Years



6-12 Months



### How?

#### FDA changed rules

- Disallowed higher-risk traditional approaches
- Allowed companies to overlap clinical phase testing
- Used Emergency Provisions/Authorization
- Fast tracked EUA and FDA approvals
- Limited liability

#### OWS offered R&D money, big pre-orders

#### Companies seized the opportunity

- Built on prior SARS and MERS vaccine work
- Scaled to Phase 3 clinical testing faster
- Scaled production manufacturing in advance of trial results
- Relied upon license-in product

### Huge Tradeoffs:

- Safety: We lose the chance to evaluate discrete populations over longer periods of time
- Efficacy: We resort to easier clinical endpoint

# Pfizer BNT 162b2 Vaccine

## **Pfizer Press Release:**

- <90% fewer self identified and diagnosed cases in vaccinated trial cohort (possible efficacy range: 47.5-100%)\*
- Pfizer did not release any scientific data sets

## **What we don't know**

- Transmission reduction?
- Durability
- Population differences
- Reduction of severity?
- Reduction in Long-Haul effects?

\*based on 94 infections in 44,000 participants

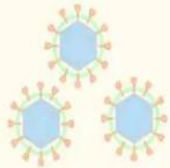
# 5 basic technologies

- U.S. is betting everything on genetic vaccines
- China's broader bet gives them better position

## Vaccine Types

CULTURE  
VIRUS

### Attenuated Live Virus

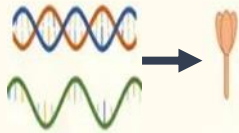


### Inactivated Virus

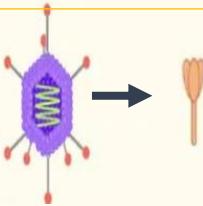


GENETIC  
VACCINES

### DNA/RNA – Spike Protein



### Viral Vector – Spike Protein



### Subunit Spike Protein



Adjuvants?  
Multiple doses?

Challenges	Leaders	EUA	Phase 1	Phase 2	Phase 3	U.S. Company
<b>Safety Risk:</b> Maintaining quality (too weak or too strong). Risk that the attenuated virus recombines with the attacking SARS CoV-2 virus and becomes virulent	India (pre-clinical)					
<b>Efficacy Risk:</b> Will it stimulate a strong enough response? Immunity fades over time. <b>Safety Risk:</b> Is inactivation complete?	China	3	1	1		
	India				1	
	Russia			1		
<b>Logistics Risk:</b> Extreme cold chain required. Unproven scalability.	USA		1	1	2	Moderna, Pfizer
	EU/UK			2	1	
	Japan, India			1 ea		
	China		1			
	Canada, Thailand & Korea		1 ea			
<b>Safety Risk:</b> Will the delivery vector be safe and not interfere with efficacy? Risk of reversion or genetic re-arrangement.	China	1 military use				
	Russia	1				
	USA		4		2	AZ, JnJ
	EU		1	1	1	
<b>Antigen Choice and Dosage Risk:</b> Choosing the right antigen and dose to stimulate a durable response. Maintaining Protein quality & consistency.	USA & EU		2		1	Novavax/T, Sanofi/GSK
	China		1	1		
	Russia, Japan, Cuba			1		
	India & Australia		2			
	Taiwan and Canada		1			

# Four Dimensions for Evaluating Vaccine Viability

## Safety

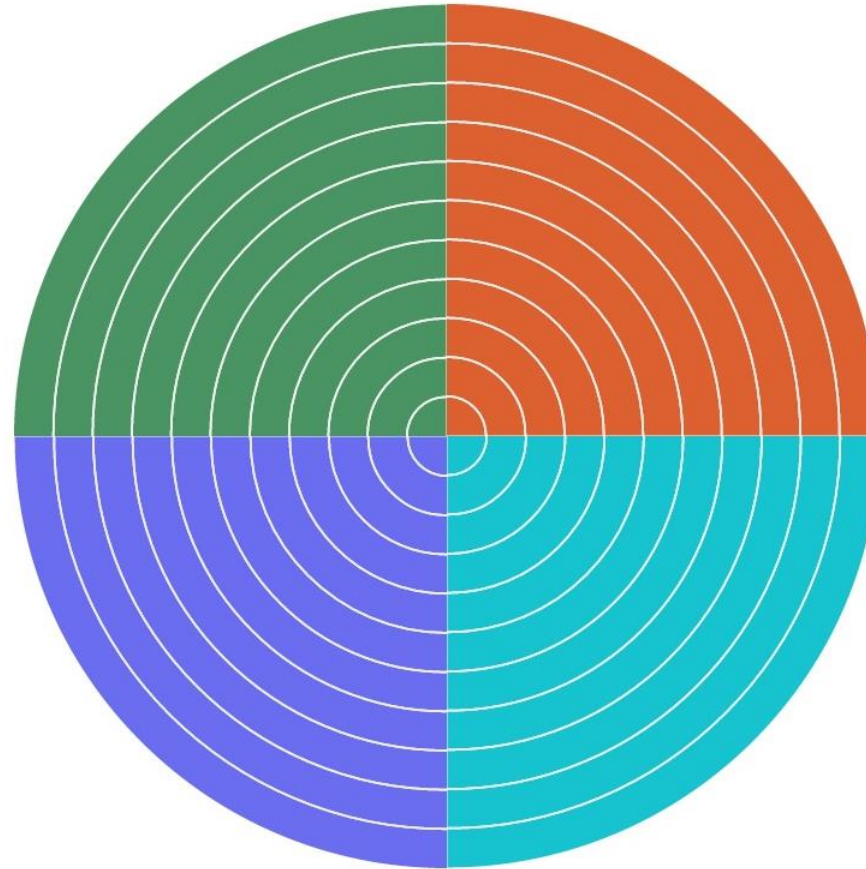
### *Clinical Measurements:*

- Low Serious Adverse Event Rates
- Broad Clinical Trial Inclusion
- Broad Demographic Eligibility
- Low Thresholds and Types of Adverse Events
- Long Study Length of Safety Data
- Large Numbers of Subjects

## Durability:

### *Clinical Data*

- Persistent High Titer levels of Neutralizing Antibodies
  - Polio: lifetime
  - Flu: 150 days
- Limited number and frequency of booster shots



## Effectiveness

### *Clinical Endpoints:*

- Reduction in transmission of the virus in populations (like Polio)
- Reduction in severity of symptoms (like flu)
- Reduction in duration of symptoms
- Improvements vs comparator medicines
- Double blind, placebo controlled trials

## Scalability

### *Stability and yield quality*

- Can it be produced in quantities that will make it widely available?
- Level of complexity of Administration—shelf life?
- Logistical challenges increase if the vaccine requires a booster shot
- No super-constrained ingredients



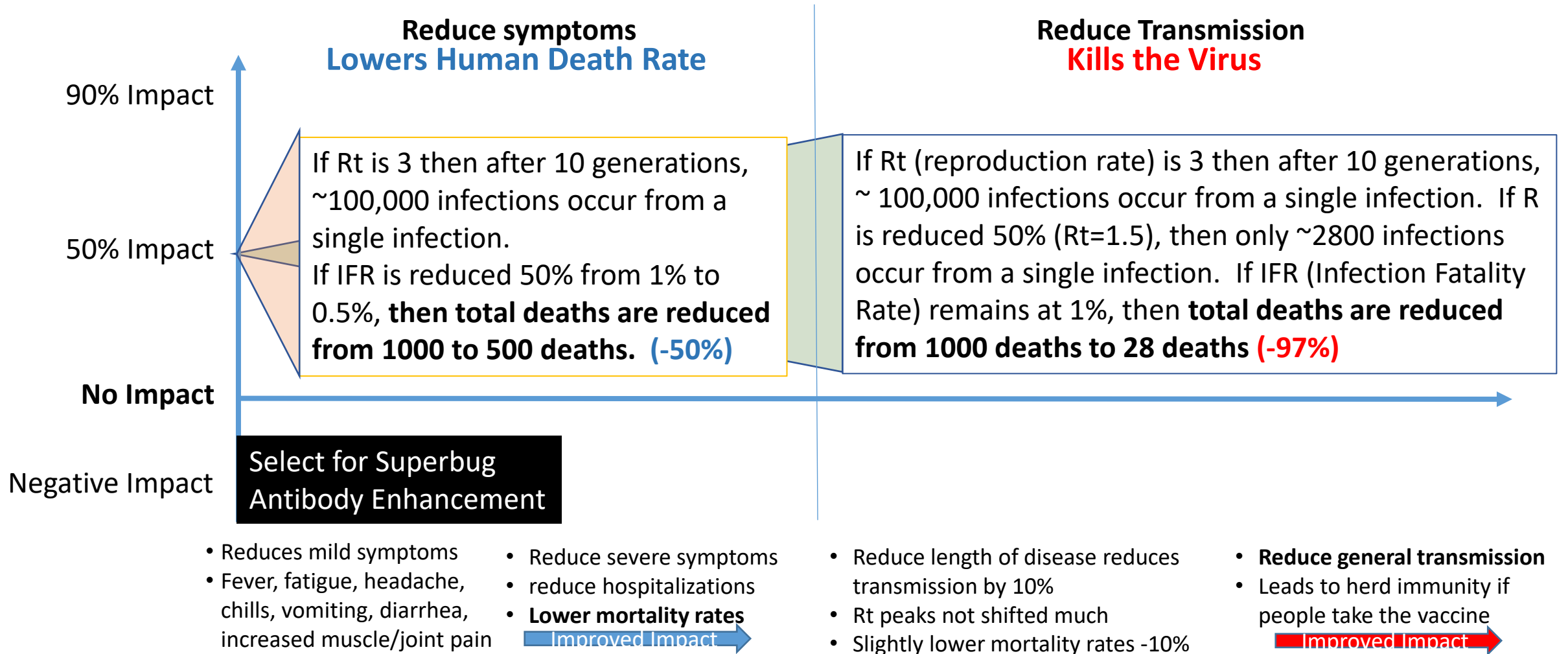
# Effectiveness Best case: "General" Vaccine Reducing Transmission

Selection of clinical endpoints matters! Today's trial end-points are impact on mild symptoms not severe symptoms or transmission because it is easier hurdle to detect and is faster. Critical issues: We can hit efficacy end points but

1. have no impact on transmission since we are not testing for transmission reduction, and
2. have no impact on severe symptoms which can reduce hospitalization and mortality

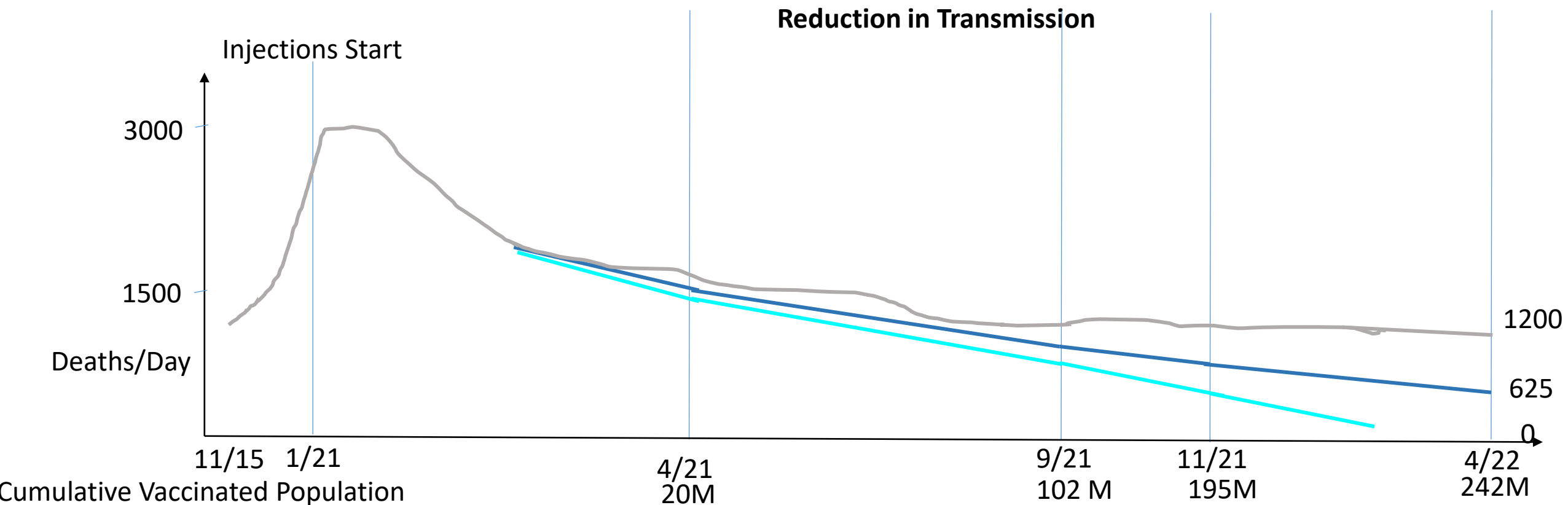
## Range of Effectiveness

## Vaccine Impact on COVID



# Transmission Efficacy – Population Scenario

Inflection point is in early November

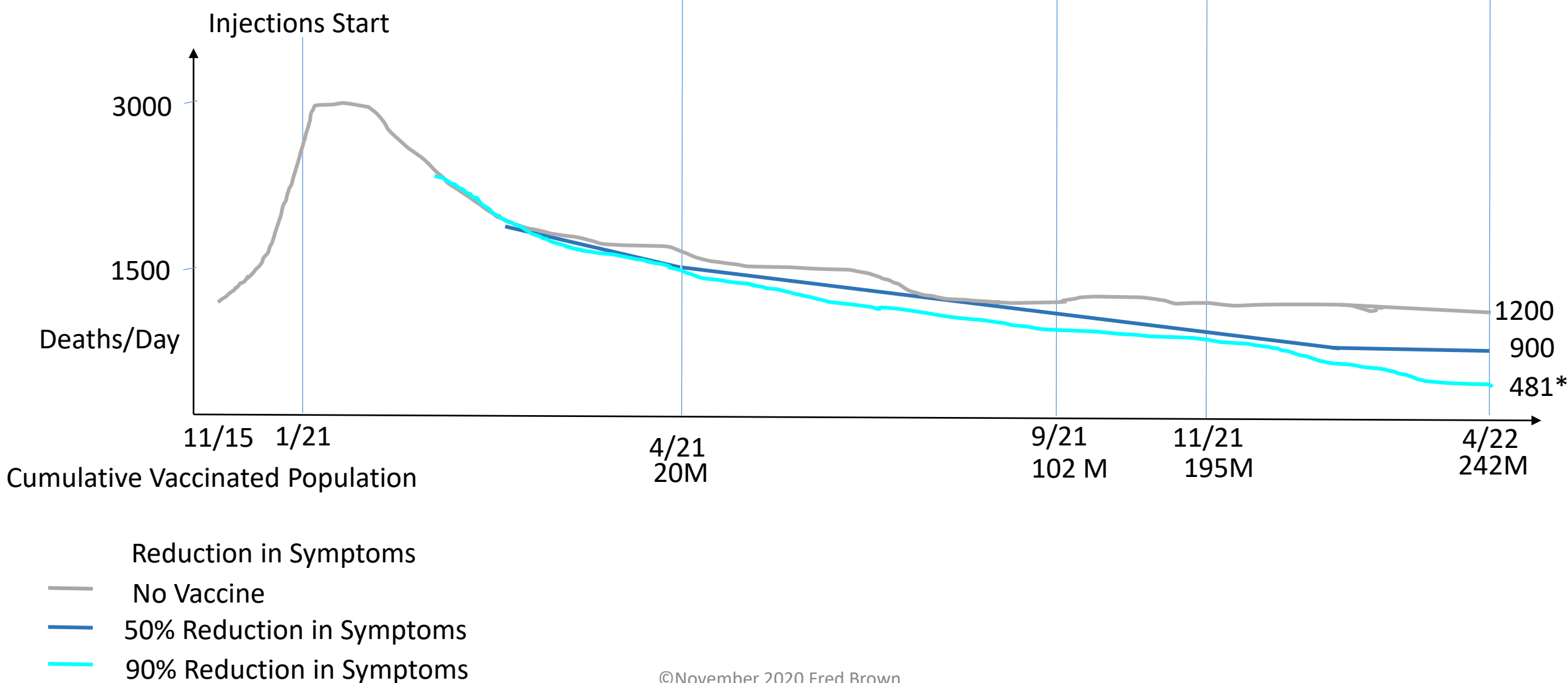


- No Vaccine Rt 1.2
- 50% Reduction in Rt dies out ~18mos at 75% of population innoculated ~3 months
- 90% Reduction in Rt herd immunity at 75% of population innoculated ~3 months

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# Symptomologic Efficacy – Population Scenario

Vaccines in trial may effect the length of time and the degree of COVID's infection severity. The clinical end-point of effecting disease severity in the most at risk patients is most impactful. Trials underway will not directly measure these endpoints, but in time we will see the effect. This is a model that considers just disease severity reductions that reduce infection mortality rate





# Dosing & Routes of Administration make a difference

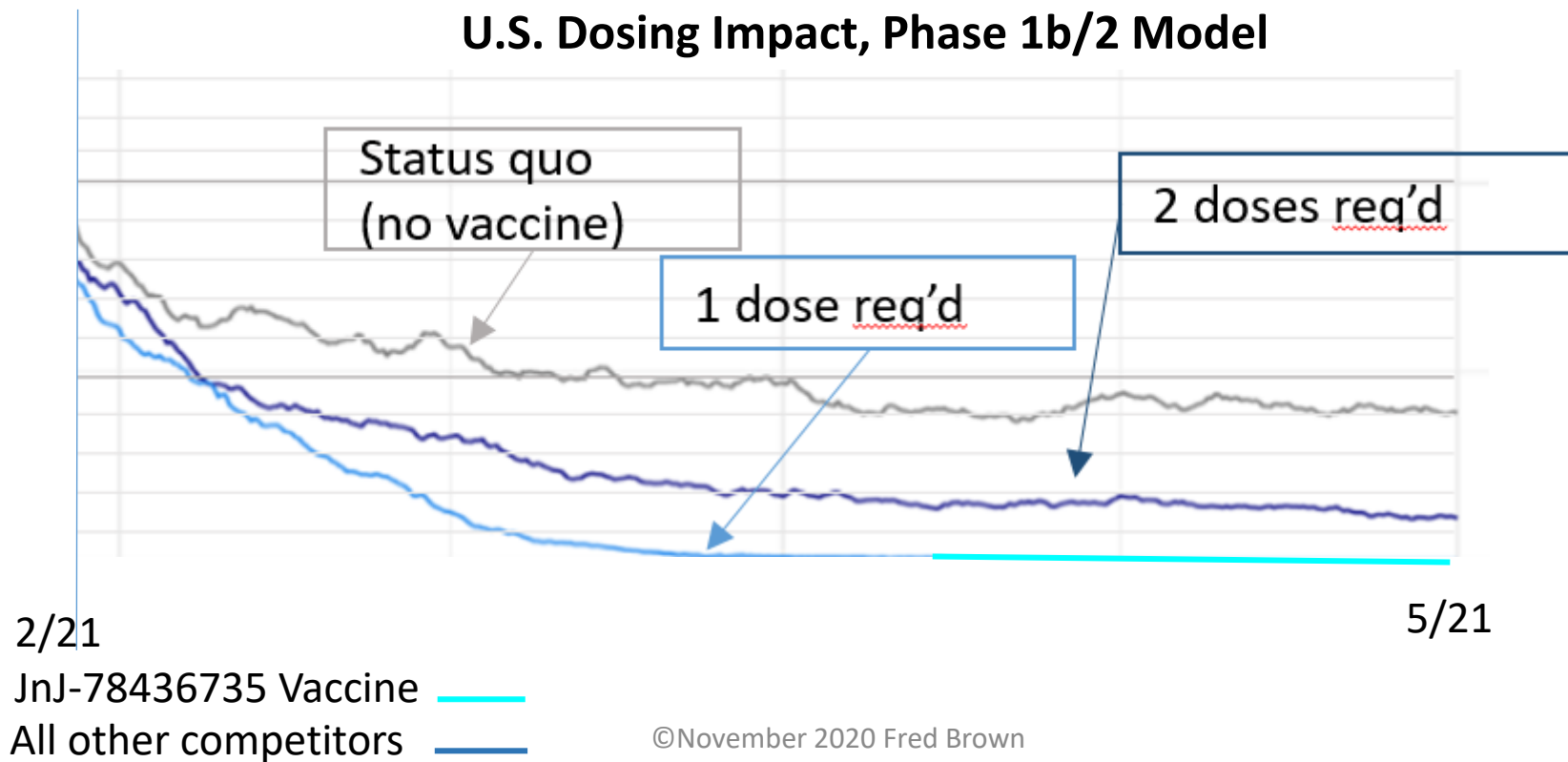
## Dosing

1. In periods of constrained supply single dose has double the supply impact vs double dose
2. Early in control phase, single dose vaccines increase speed to immunogenicity up to one month faster
  - For a symptom reducing vaccine this can reduce death rates by up to 20%
  - For a transmission blocking vaccine this can drive herd immunity speed by 10 – 20%

## Routes of Administration

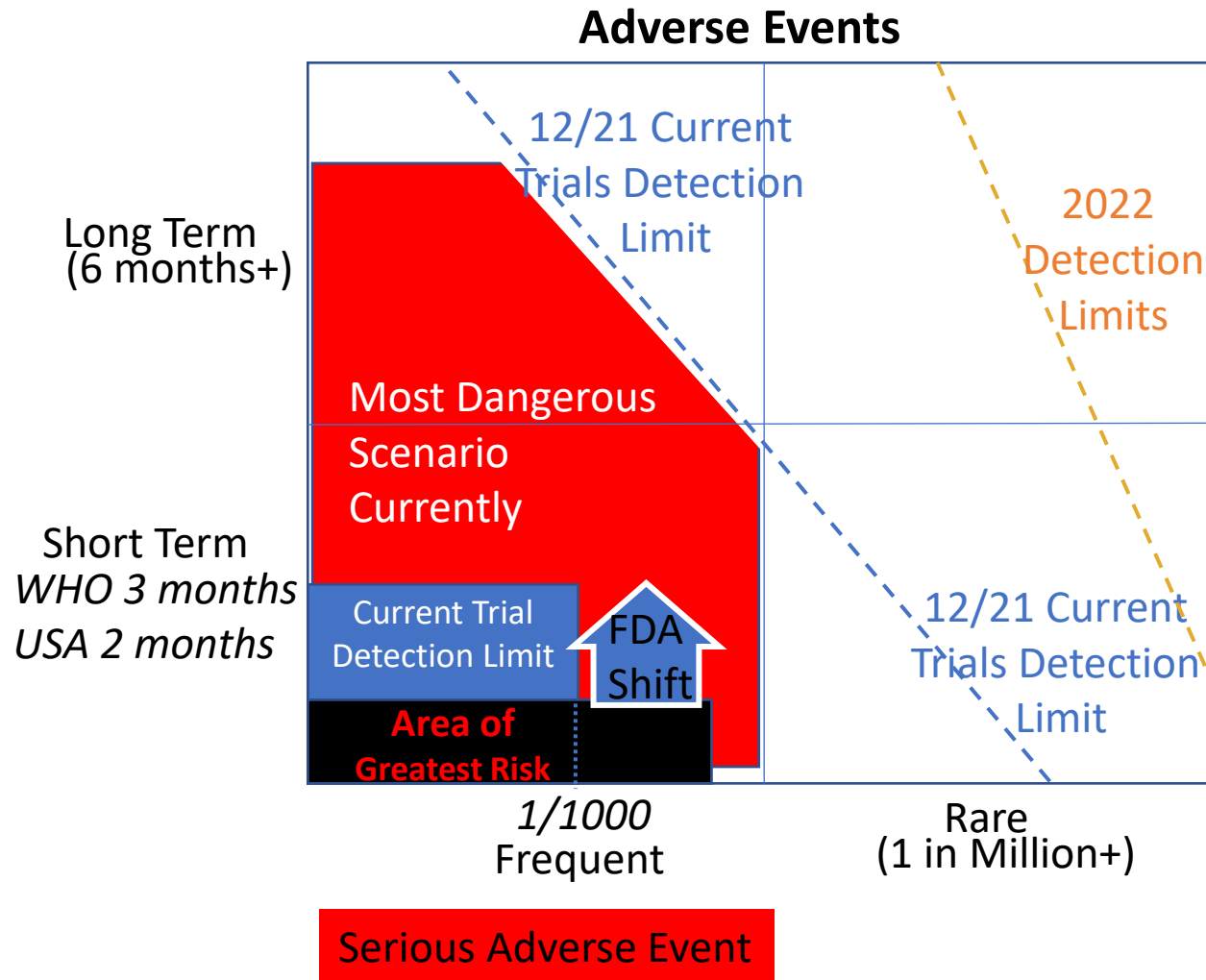
1. Nasal spray/mister administration may confer greater efficacy & durability of a COVID vaccine, especially in the upper respiratory tract
2. More flexibility can offer more options to more populations globally and avoid shortages in critical kitting supplies

### U.S. Dosing Impact, Phase 1b/2 Model



# Signal Detection is Too Shallow in Undersized, Fast trials

Large sample size needed to detect rare but serious adverse events in populations



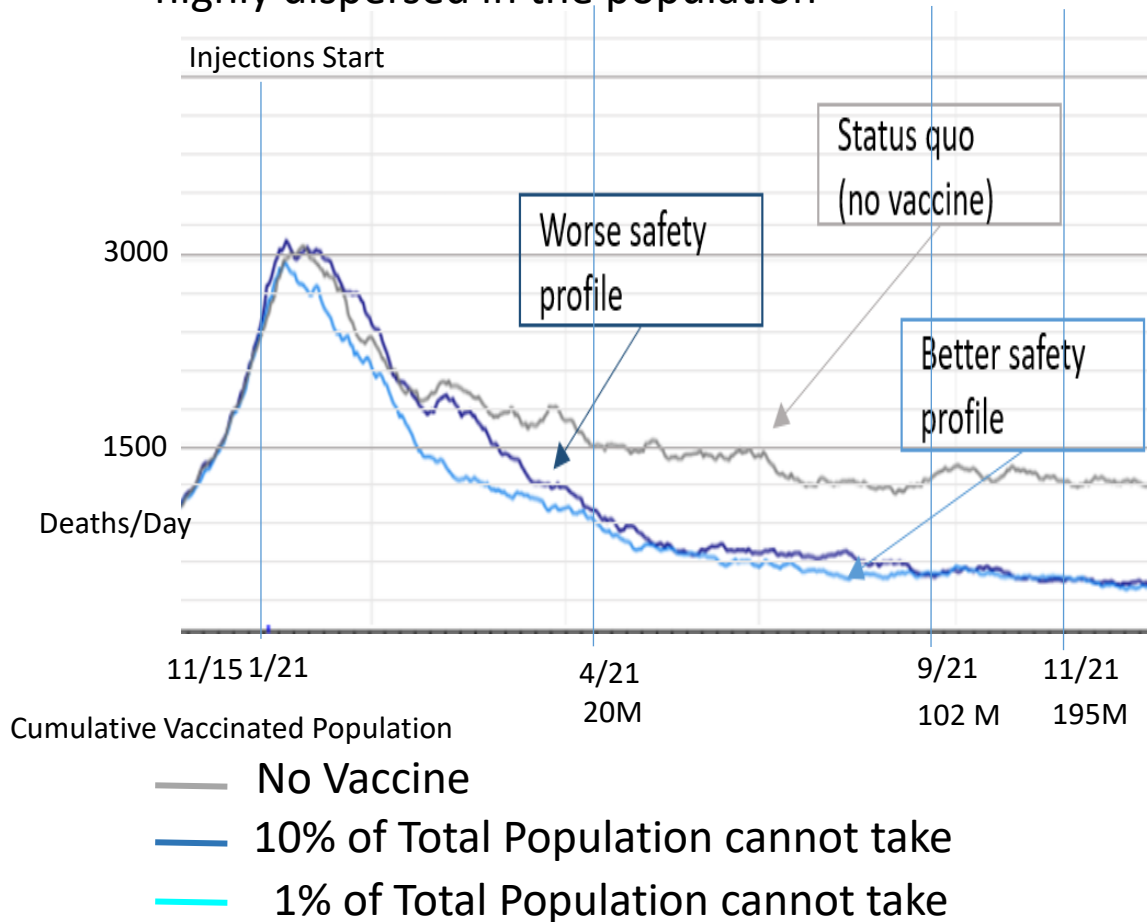
## Critical Unknowns

1. Population stratification of Serious Adverse Events (SAEs)
2. Risk of Antibody Dependent Enhancement (ADE)
3. Risk of late onset SAEs
4. Risks in excluded populations (pregnant, ethnic groups, under 12)
5. Contraindications based on prior diseases, health status, medications
6. Critical safety profile differences between vaccines (Opportunity for niche second generation vaccines)
7. Real world impact of expired or mis-administered vaccines in non-clinical trial setting

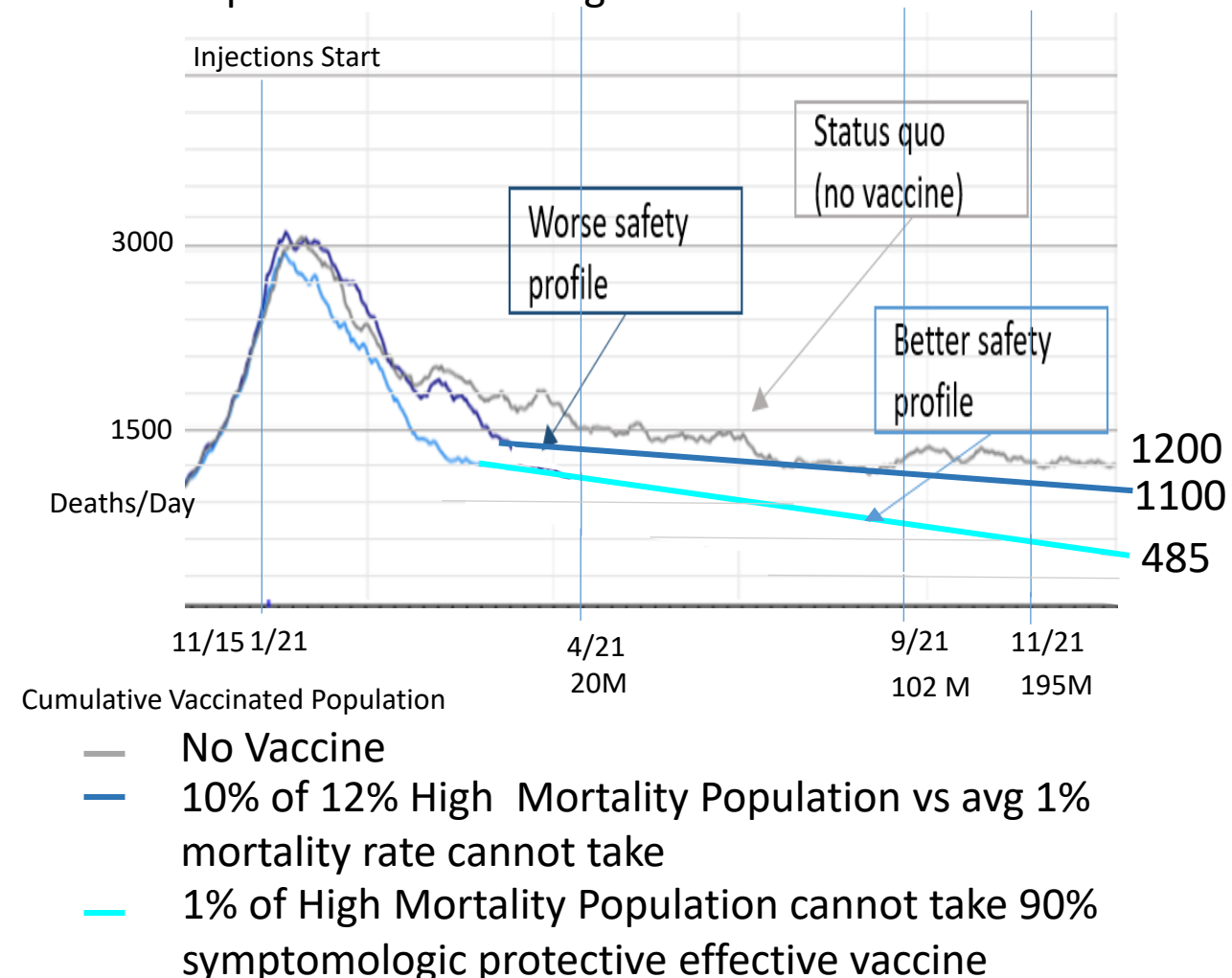
# Safety Best Scenario: No SAE's in High-Risk Populations

**Adverse Event Severity and Frequency matters! One serious adverse event can wreck a trial and your experience.**  
**Inclusion and Exclusion Criteria of a trial matters! It takes time. Watch numbers tested in stratified populations, the threshold for reporting a serious adverse event and see if you are at higher risk of an adverse events with selected vaccines.**

If Serious Adverse Events (e.g. allergy to drug) are highly dispersed in the population



If Serious Adverse Events exclude High Mortality Population from taking the vaccine

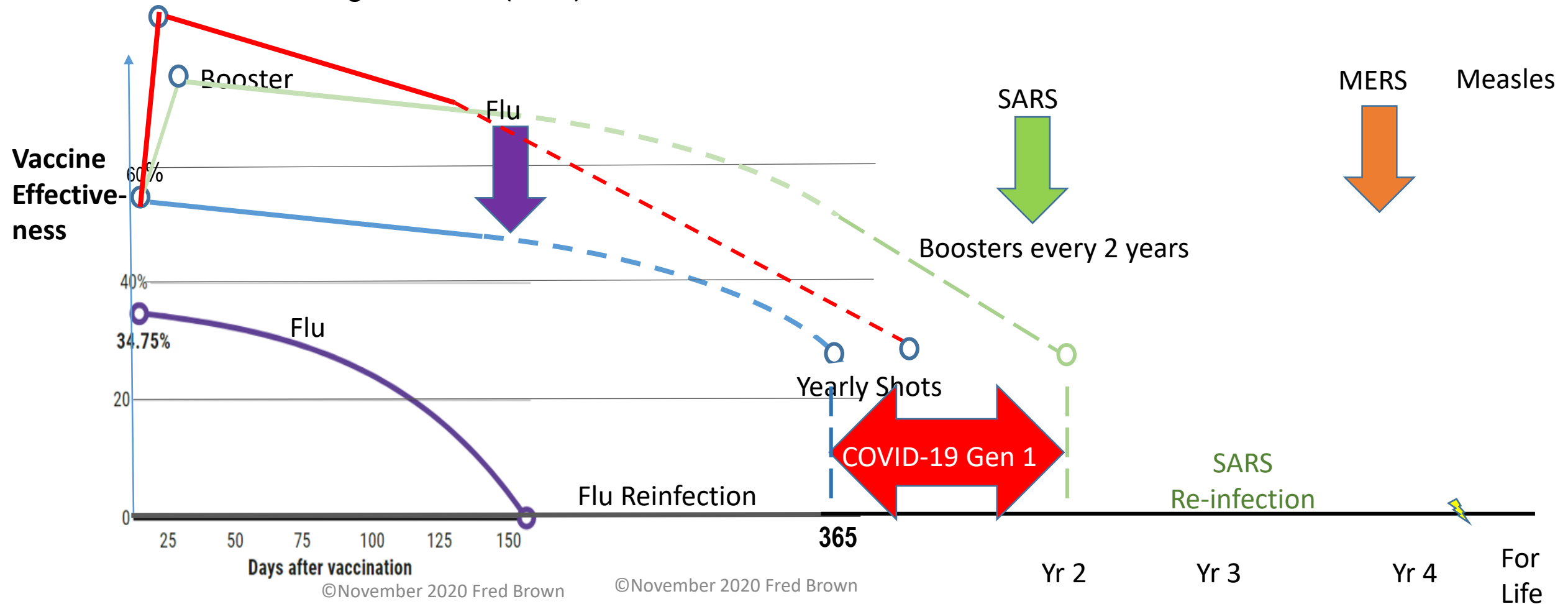


# Durability: only time will tell

COVID vaccines tested to date confer up to 9 months (IE, no waning in most participants) of effective immunity

Vaccine durability is not well understood. It can vary among populations and vaccines, so you may need to be tested regularly.

COVID clinical studies are measuring anti-body titers, but to determine durability time-series studies of neutralizing antibodies (Nabs) must be conducted



# Serology - dual pillars of population protection

- Longitudinal at-home blood testing may be required to ensure neutralizing anti-bodies are remaining
- Part of a kit that goes with the vaccine particularly for specific demographic groups/immunological profiles
- No centralized registry that is effective yet
- We may find that efficacy, safety and durability vary depending upon immunological profile
- The cost of going quickly...You will be part of the testing!

## Serologic Surveillance Testing

### *Improves Understanding and Policy*

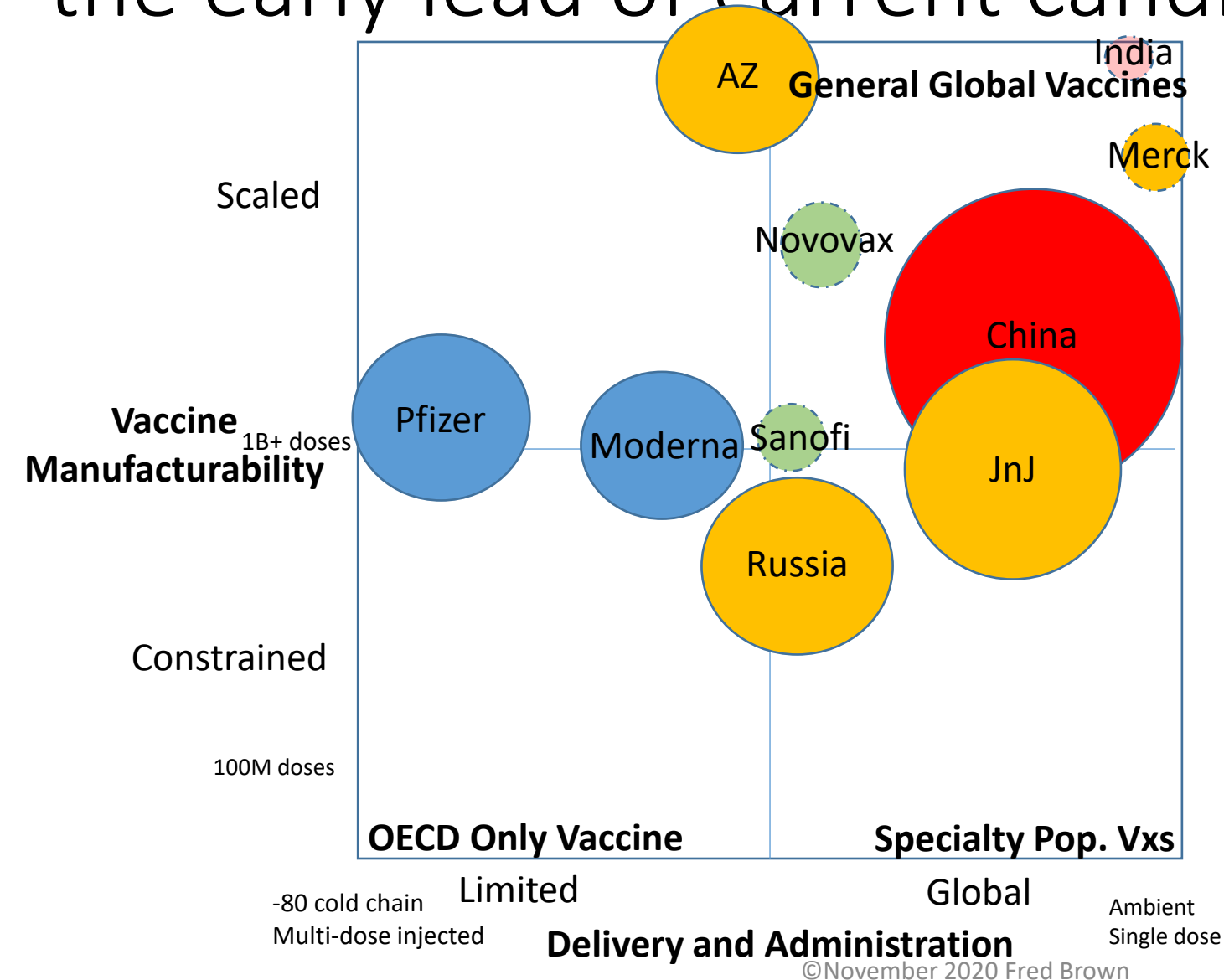
- Historic disease prevalence
- Infection Fatality Rates
- Disease spread patterns
- Modelling & predictive value
- Mutation tracking
- Post-Intervention tracking

## Neutralizing Ab Tracking

### *Optimizes Vaccine Management & Public Confidence*

- Herd immunity monitoring
- Population stratification & prioritization
- Vaccine comparative effectiveness
- Vaccine vs genotype & phenotypic responses
- Booster scheduling

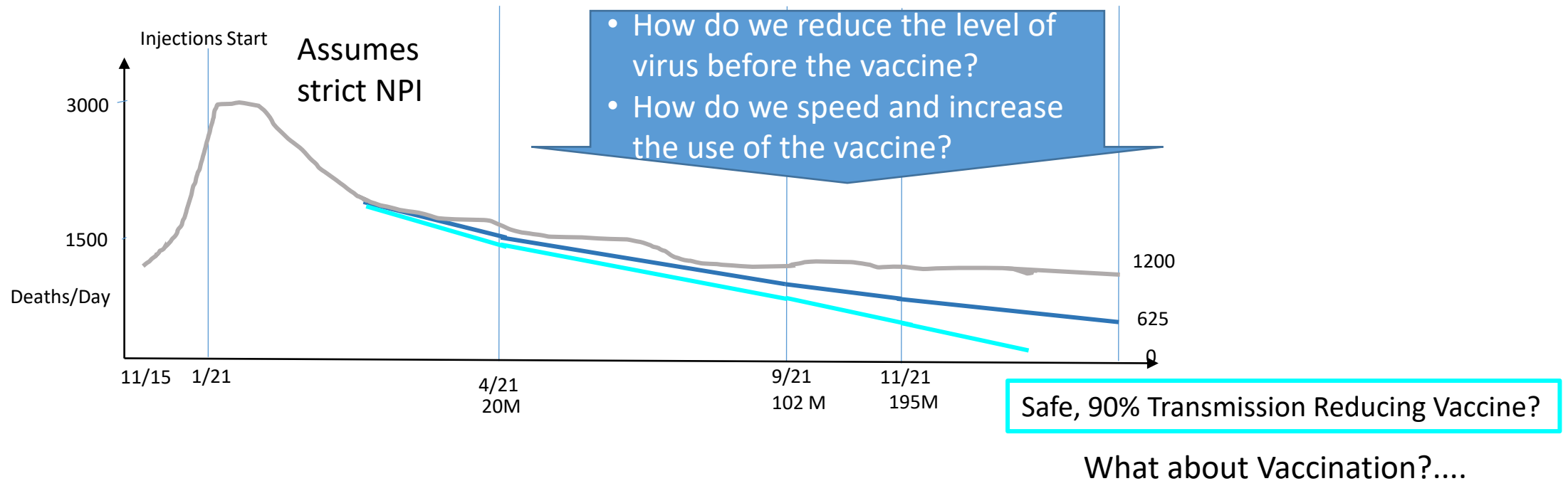
# Scalability: slower players are likely to catch the early lead of current candidates



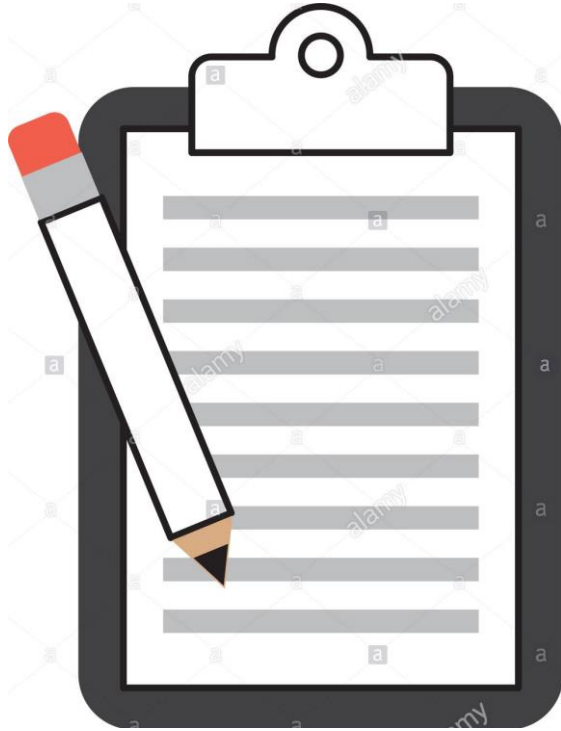
- J&J's vector vaccine will likely be the winner of the early movers— no ultra cold chain or double dose
- China is well positioned
- India is likely to remain the vaccine producer of the world
- Russia has little manufacturing capacity and a risky vaccine that requires complex administration

# Vaccine Recap

- Breath-taking speed and perfect execution. Three long-shot bets have paid off so far.
  - Genetic Revolution
  - Months to Days Research and Licensing
  - Years to Months Clinical Development
- The data matters– and we don't have it. *Phase 3 results have not been made available beyond interim regulatory reviews.*
- It is still very early days with many unknowns compounded by the accelerated efficacy and safety trial design
- Vigilant PPE use and testing is required until vaccines more significantly impact our health and lives: earliest November 2021
- Earliest path to herd immunity and normalcy is Q1 2022, and it may take much longer



# The Biden/Harris Administration Is Likely to Face a Bleak Situation on January 21<sup>st</sup>:



Virus Control	<i>Exponential growth</i>
Test Data	<i>Insufficient</i>
Economy	<i>Depressed</i>
Hospitals	<i>Overwhelmed</i>
PPE Supply	<i>Rationed</i>
PPE Compliance	<i>Polarized</i>
Vaccines	<i>Constrained deployment</i>

## **What should the new administration do?**

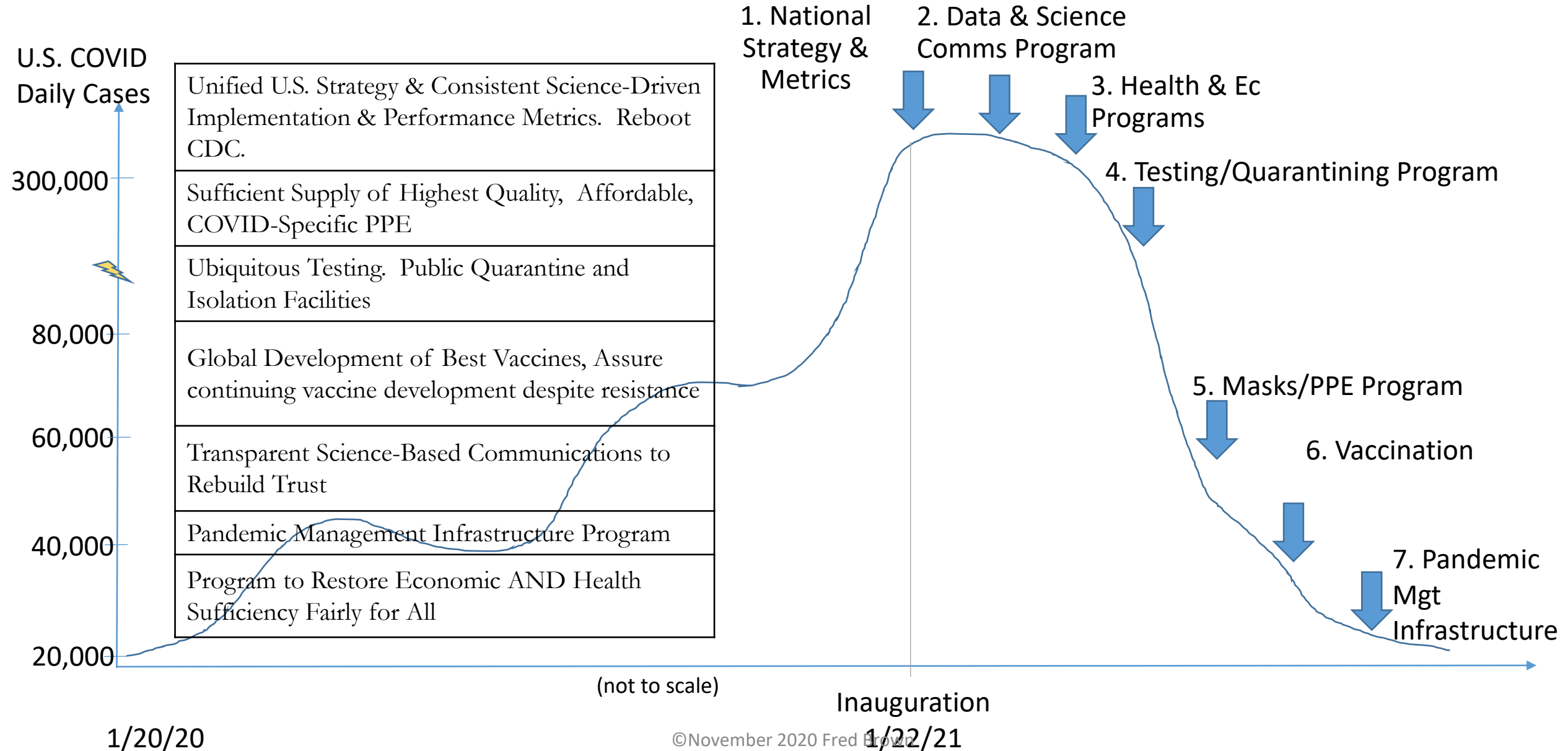
Option 1: rely entirely on largest weapon: vaccine

Option 2: close the economy: a different weapon

Option 3: redeploy traditional weapons: NPI and testing



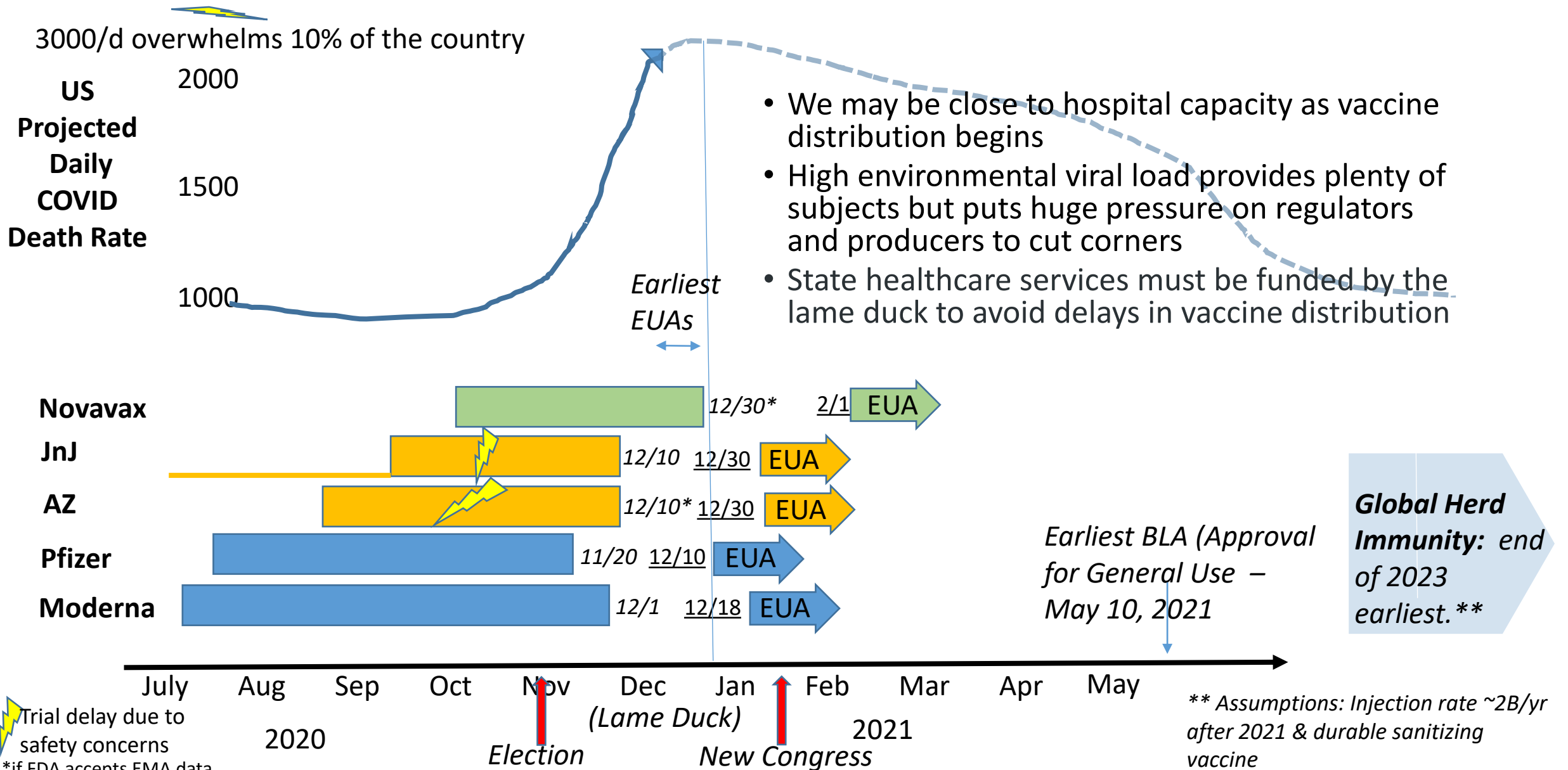
# 7 Essential Programs to Beat COVID-19



# Vaccine Rollout will be during high environmental viral load

Deaths/day: 7000 - 9000

Hospital Capacity Thresholds – CFR 2 – 14x Normal





Are you ready for the 4<sup>th</sup> bet?  
Deploying a logistics operation at Warpspeed

# From Vaccine to Vaccination: 4 Challenges Areas

1. Scale up of new technology antigen by 60 times

2. Speed required of old, fragmented supply chain



Raw Materials

Sub/Assembly

Finished Product

Distribution

Antigens

Adjuvants

- Preservatives
- Antibiotics
- Stabilizers
- Over 1,000 ingredients/dose

Injectors

Fill & Finish

Injectors & Needles

Medical Glass

3. Managing the complexity

4. Convincing the non-believers



*Lives are saved and harm is prevented only by the act of vaccination*



# 1. 60X Capacity Increase Needed To Meet Current U.S. Demand

Oct 2020

December 2020

June 2021

December 2021

EUA

HC Workers

US Public

Rest-of-World

## The Antigen

Available US capacity to produce antigen today is about 10% of COVID-19 vaccine demand for US alone, and about 1% of global demand.

Available Capacity Today: ~35M Doses

(Out of Total US Capacity of ~287M doses. The rest goes to flu vaccines, etc.)

+25-30M doses/mo/co

10X supply expansion demanded in 7 months

100M Doses+

Johnson & Johnson (1 dose)

100M Doses

Astra Zeneca (2 doses)

100M Doses+

Pfizer (2 doses)

100M Doses

Moderna (2 doses)

60X supply expansion demanded in 14 months

~2B Doses

add Novavax & Sanofi

~480M Doses for US

## 2. Real-time speed required across cobbled-together supply network

Oct 2020

December 2020

June 2021

December 2021

EUA

HC Workers

US Public

Rest-of-World

### Vaccine & Kit

#### Public-Private Partnership

##### 1. Unscaled, Fragmented Global Supply Chains

6 – 60x scale required at every network node  
Silos with no aggregate supply or demand control  
1000's of competitive decision makers

##### 2. Slow-moving Oligopolies

Highly Regulated, Health and National Security Interests  
Healthcare workforce is under pandemic duress  
State & local governments are under financial duress

##### 3. Changing Manufacturing

8 new product entrants may be approved & scaled in 2021  
Shifting business rules as scale-up continues  
New clinical trial results changes policy and demand function

##### 4. Challenging Logistics

20%+ wastage  
Novel, unaligned CDC & State allocation management  
Ultra-cold chain requirements & differing business rules

##### 5. Unintegrated Systems

Inaccurate, dated, inaccessible, unintegrated regulated data  
Antiquated, slow, closed, proprietary application systems  
Inflexible, unscaled, brittle uncoordinated IT operations

~2B  
Doses

add  
Novavax  
&  
Sanofi

~480M  
Doses for US

Available Capacity  
Today: ~35M Doses

Antigen

Adjuvants/  
Reagents  
Glass/Stoppers  
Injectors/Needles  
Serology Tests



~93%  
Constrained  
Supply



Vaccine

Kit

64 Jurisdictions

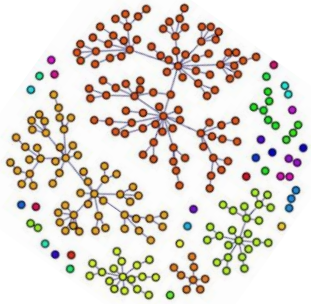
1000s of  
Vaccinator Sites

\*1-2 doses/person annually by ~75% of population



### 3. Complexity - Requires Agility With No Margin for Error

This is ~500,000 times more complicated than the flu vaccine

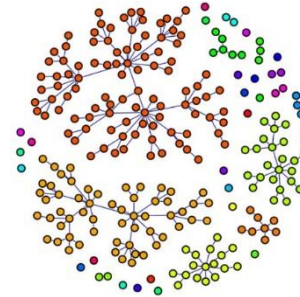


#### Static Complexity

Possible Network Fulfillment Configurations

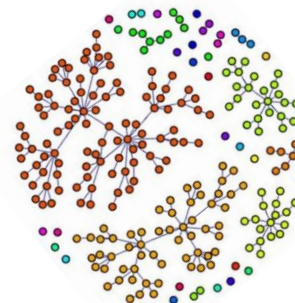
Supply Chain	Pfizer Today Trial Supply	COVID Vaccine Supply Chain 12/31/20
Manufacturer	1	8
Kit providers	1	3
Distributors	1	6
Airfreight providers	2	4
Trucking providers	21	1,000
Vaccinator sites	154	5,000
Patients	17,000	100,000,000
<b>System Nodes</b>	<b>109,956,000</b>	<b>288,600,000,000,000,000</b>

*2.6M x greater static complexity within 12 months*



#### Dynamic Complexity

- Number of network nodes
- Number of processes
- Degree of non-linearity of the processes
- Number of process control points
- Number of process measurements
- Frequency of process measurements
- Variability in process operations



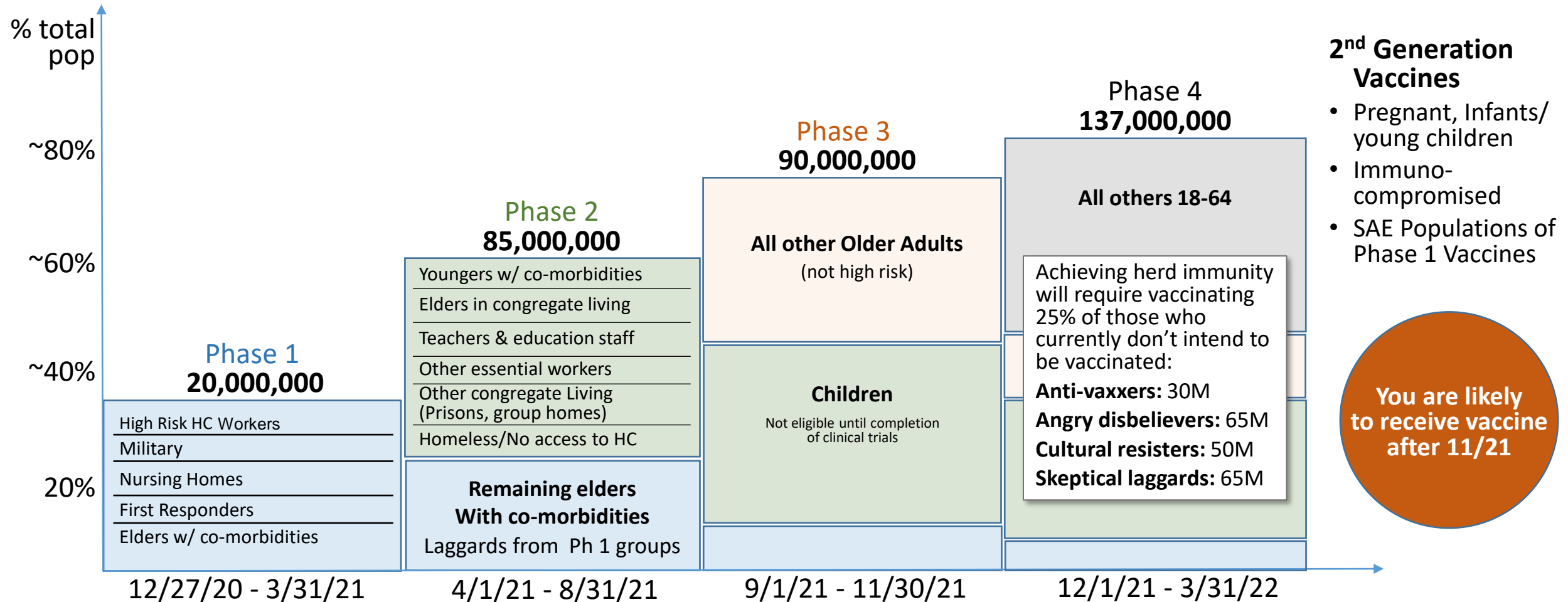
#### Decision Making Complexity

- Policy
- Politics
- Information Gaps
- Dependencies
- Sequencing/Hierarchies
- Degree of Non-Synchronization
- Automation
- Speed of Learning
- Customer Expectations

# NAM's Proposed Vaccine Distribution

## *Vaccine resisters balance supply constraints*

US population is ~332M. Need 75-85% compliance for functional herd immunity– might get there mid-2022.

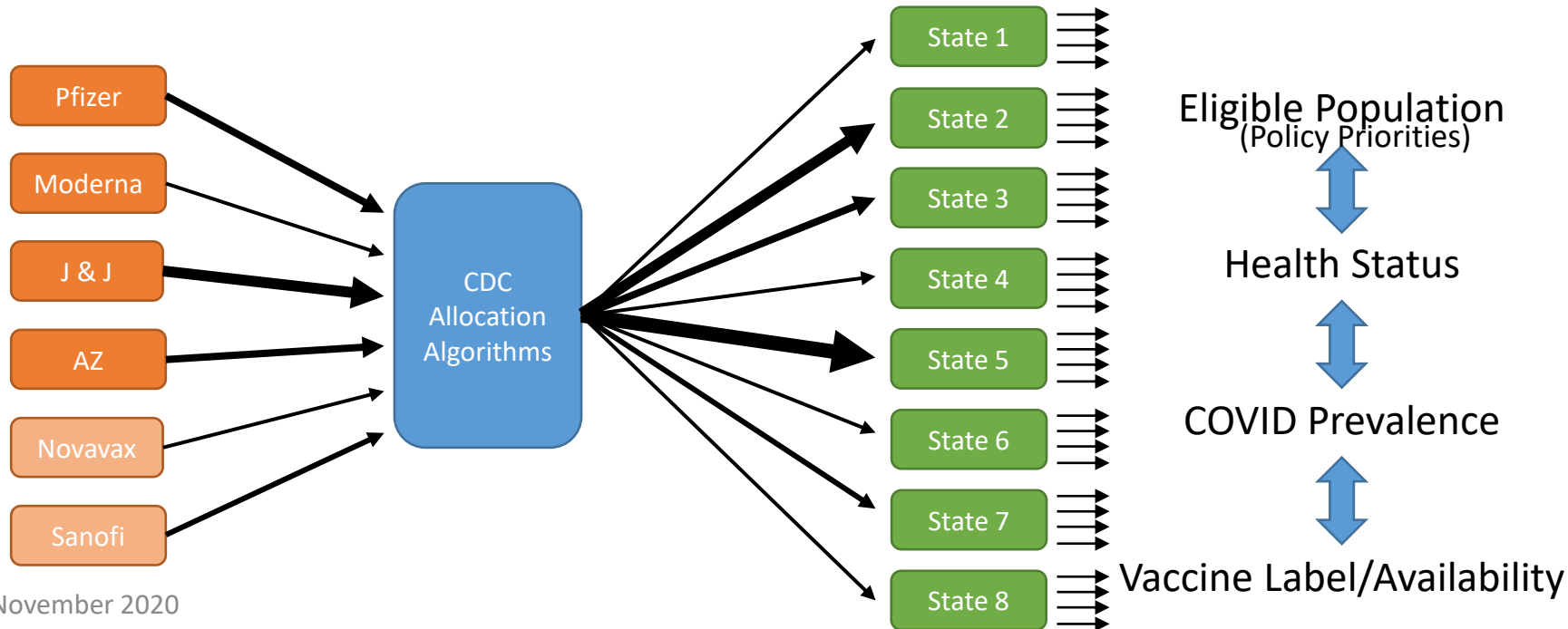




# Jurisdictional Demand Management – Highly Variable

1. Manufacturers release vaccine batches
2. CDC allocates supply to each jurisdiction
3. Jurisdictions are responsible for the last mile allocations to each patient

**64 jurisdictions**  
each have additional separate algorithms



## People come to vaccines

- Advertised locations prepared to deliver high throughput

## Vaccines go to people

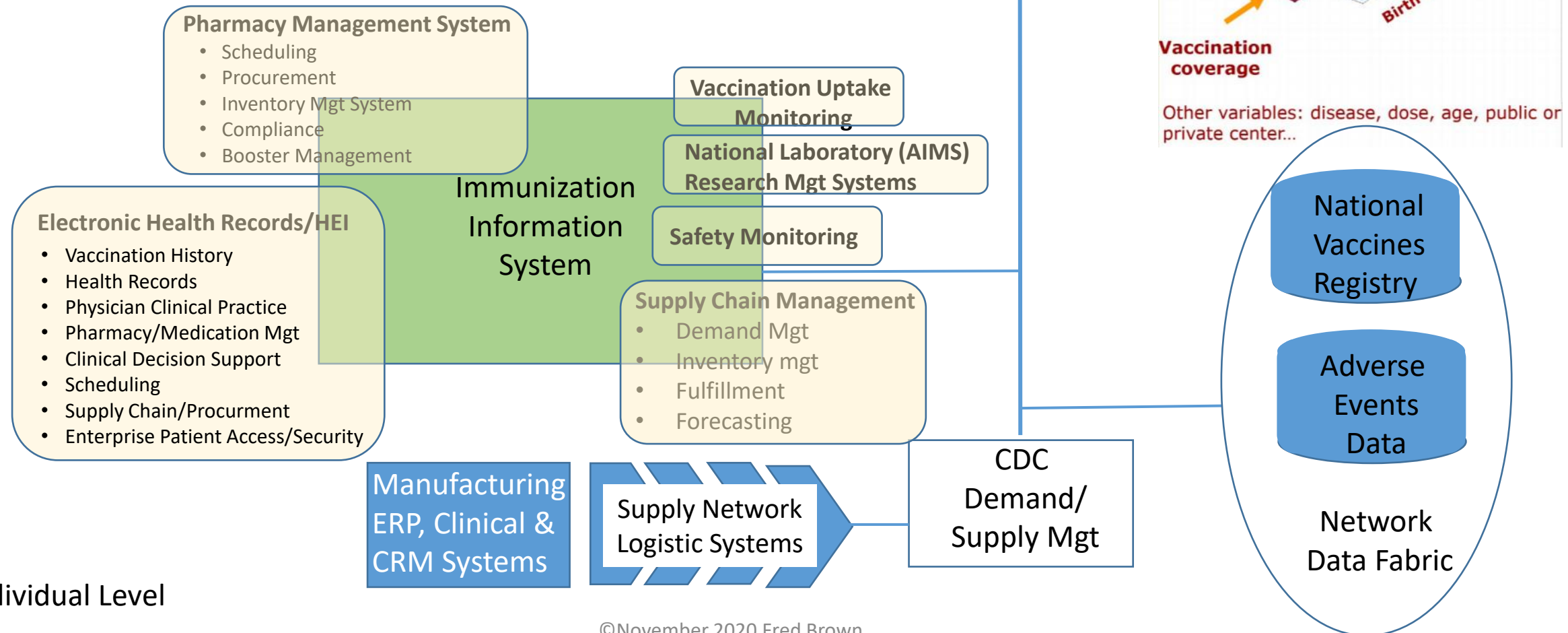
- Hospitals, nursing homes, military, police/fire, prisons, etc

# The Last Mile Challenge - Information

We are applying under-scaled, outdated, rigid, complex, unresponsive and custom built/proprietary information technologies to a new virus. Data has little real-time access is unreliable/insecure, with few machine readable data standards in use.

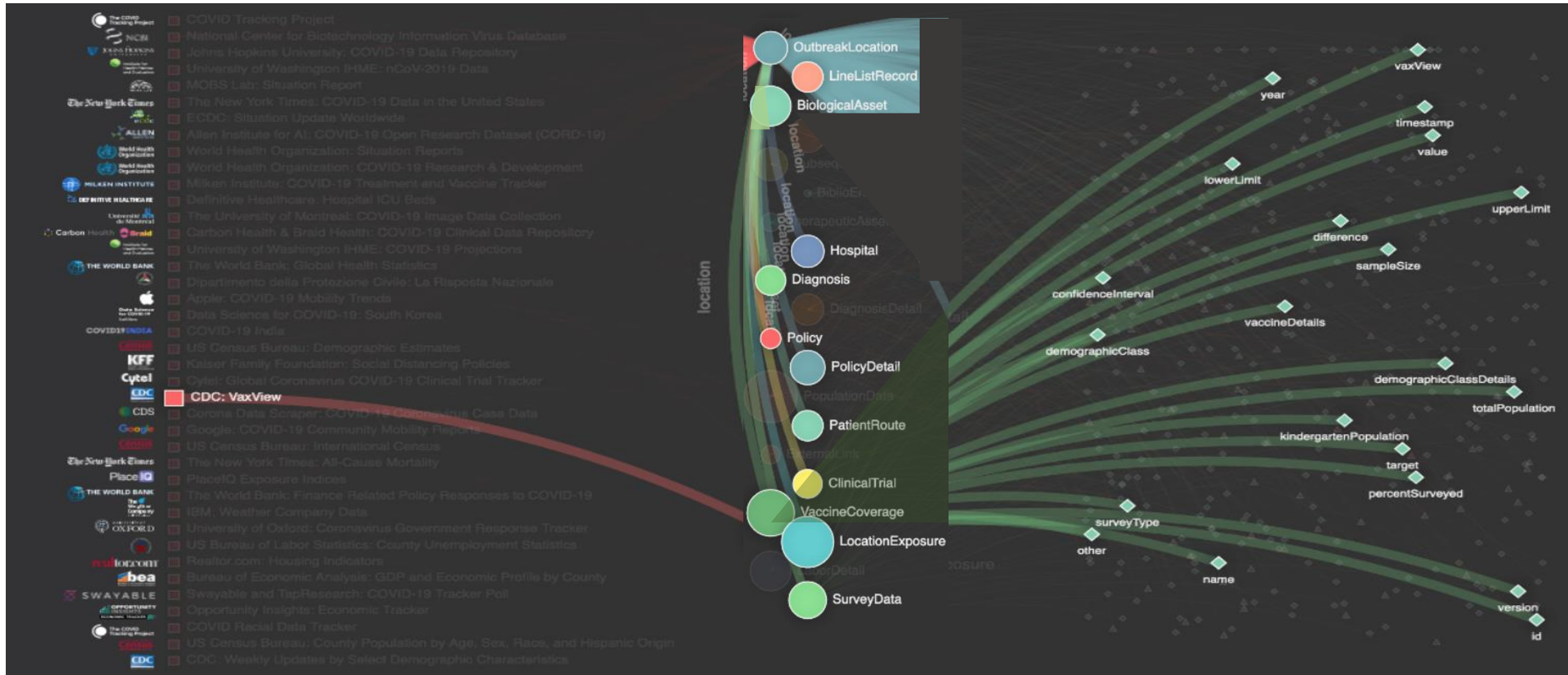
## Expect challenges in April

The System should look like this, but it does not ....



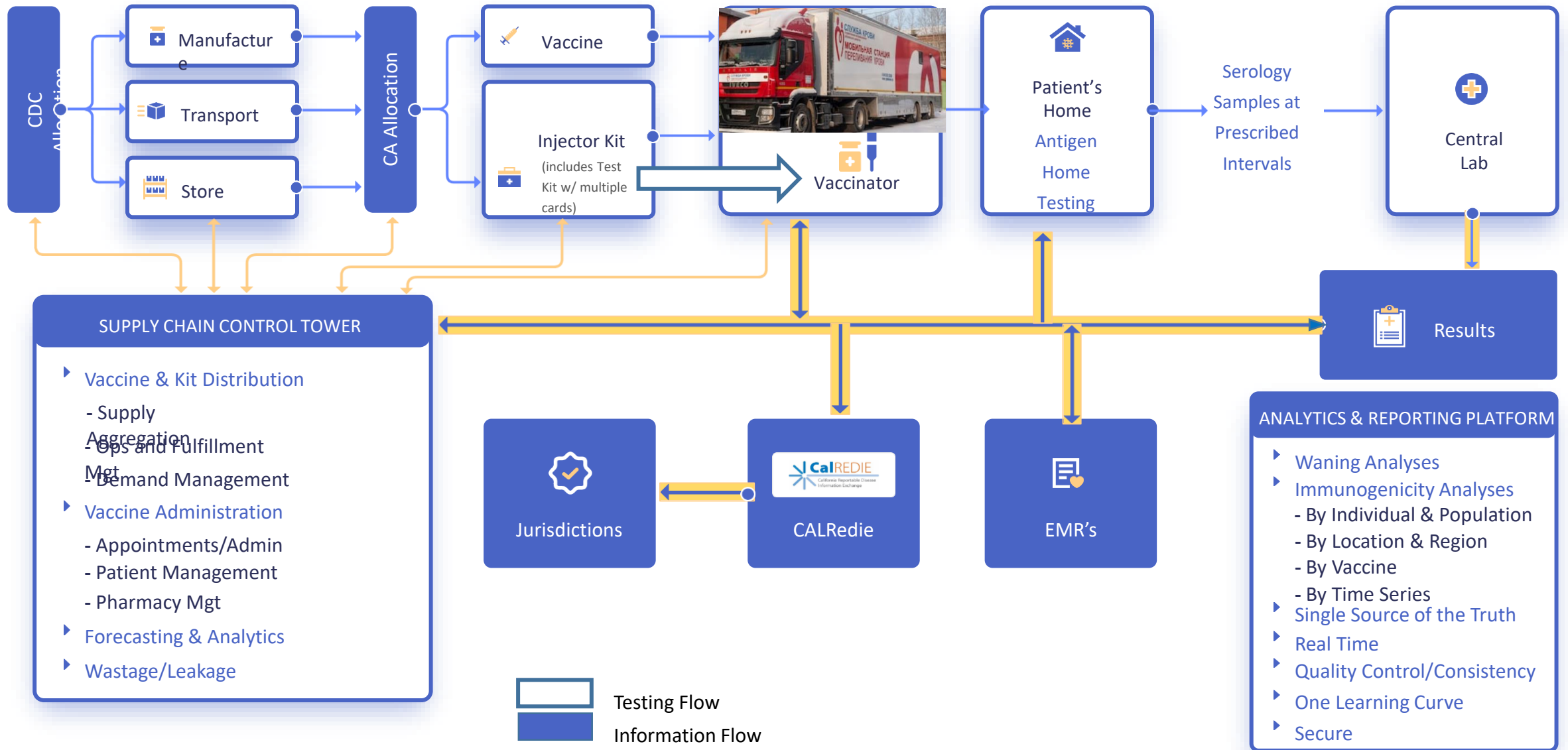
# We don't have the Data System Needed to control COVID

- Existing systems are designed to eventually document the epidemiology of diseases that are in control
- Real time systems to limit COVID's uncontrolled outbreaks, to provide patient and population level planning and decision support, and to automate prioritization and deployment of vaccine distribution and mitigation measures are not available. Real time data mash-up as diagramed below are needed



# Last Mile Challenge

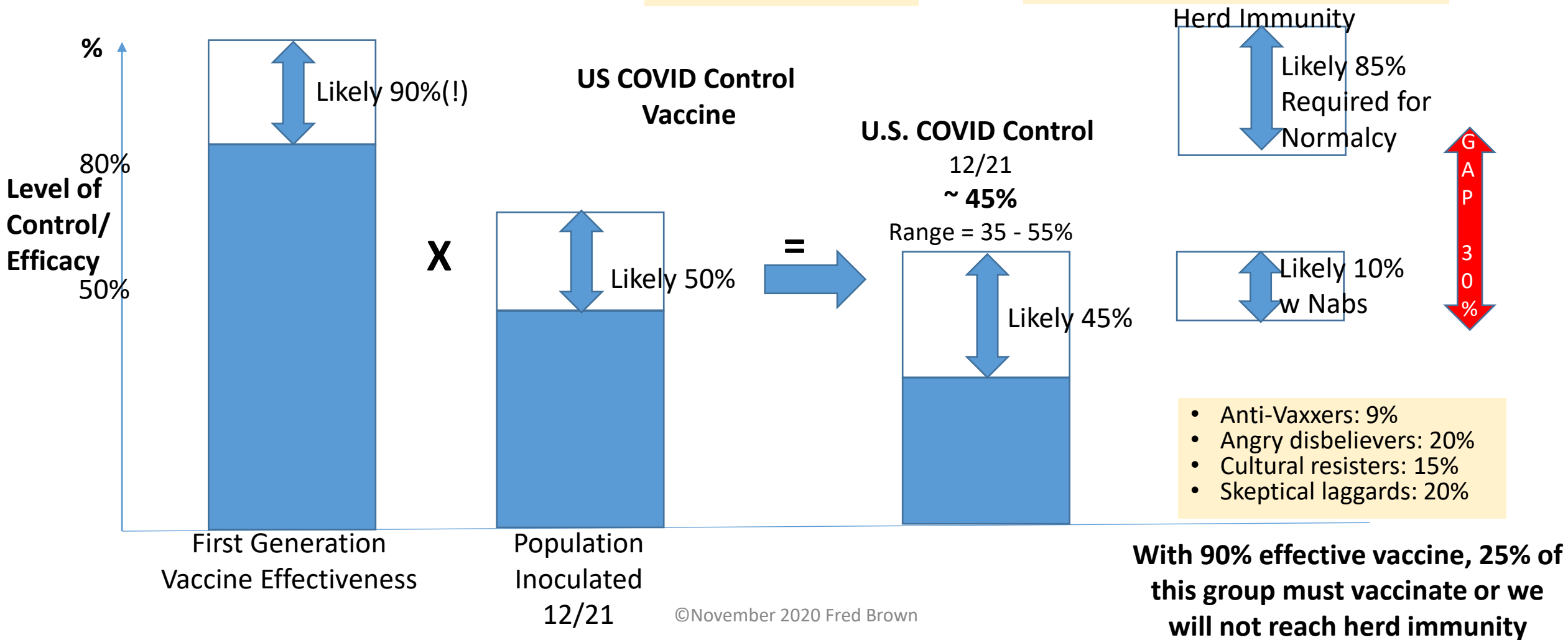
- Without adequate data flow, physical systems must become much more agile and resilient.
- Inflexibility of current health infrastructure compounds the issues arising from inadequate informatics



# 4. Herd Immunity = Effectiveness x Adoption Rate

Factors impacting adoption rate:

- ✓ Percent of population for whom the vaccine is safe & effective
- ✓ Availability in the geographic area
- ? Public confidence that available vaccines are safe and effective





# Political credibility needed for widescale adoption of vaccine has eroded

## Formerly Trustworthy Health Agencies have discredited themselves



Early over-reliance ILI flu data to project COVID spread.  
Lack of accurate, actionable information. Improper shut-down advice. Delayed, reversed, watered-down and discredited re-opening guidelines.

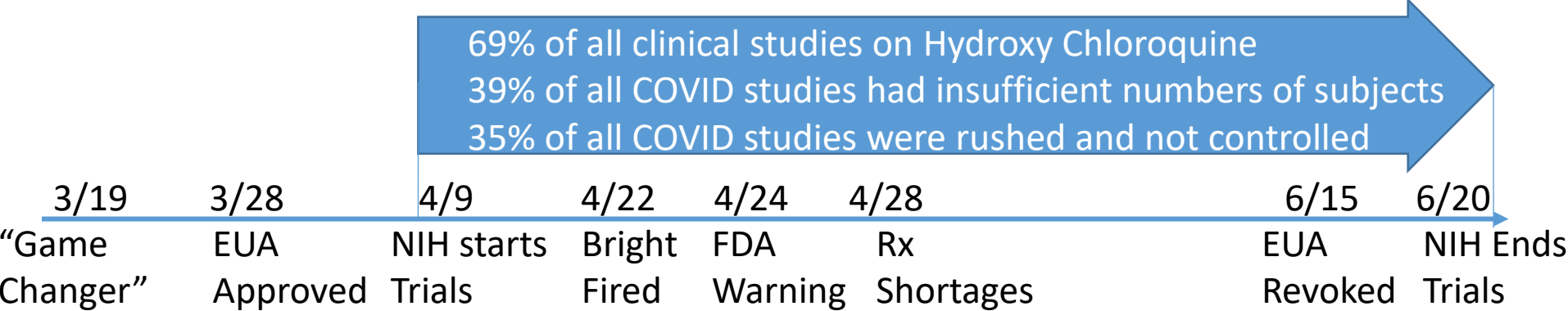


Directs all COVID hospital data to bi-pass the CDC. Federal contractor collects & analyzes COVID hospital statistics.

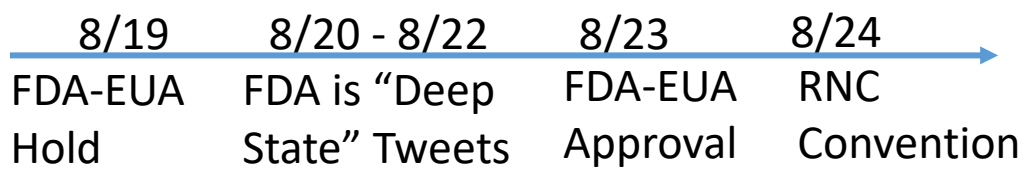


Halts on diagnostic test EUA's for gross inaccuracies. Reinstated EUA's for clinical testing labs.  
Recent hold/adverse event data of AZ is announced to investors, but data not released to public.

## Hydroxy Chloroquine Politics Diverted Attention from Scientifically more Promising Medicines



## Convalescent Plasma EUA decision reversed for political, not scientific, reasons



# To get to herd immunity we must rebuild trust

Mindset Segments	2021	2022	Message*	Delivery	Media
Skeptical laggards	20%	3%	Education: Safe, Effective Vaccine See your doctor & Social Norms Document successes Overcome fear Restoring what has been lost	Healthcare Pros PSAs Family/Friends	F2f Social Mass
Cultural resisters	15%	8%	Cite corrections of past mistakes New social contracts It is easy and for you	Celebrities Spiritual Leaders Trusted Ambassadors Healthcare Professional	Social Mass Events F2F
Angry disbelievers Anti-Vaxxers	20% 9%	20% 9%	Preventing the spread of mis-information by working with the platforms and structures in place Employ EO to eliminate 230 Protections for misinformation on matters pertaining to COVID as required for national emergency and national defense.		
<b>TOTAL</b>	<b>54%</b>	<b>40%</b>	* Much message testing to be done.		

**Mandates will likely be required to achieve herd immunity**

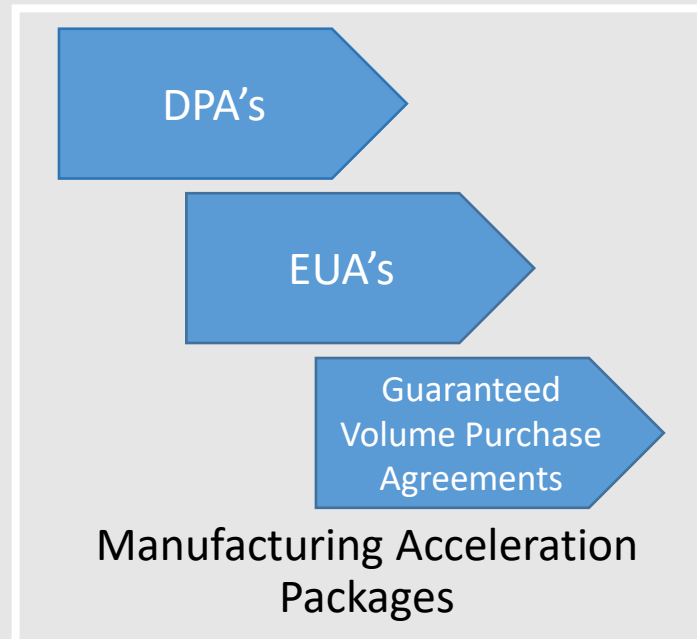
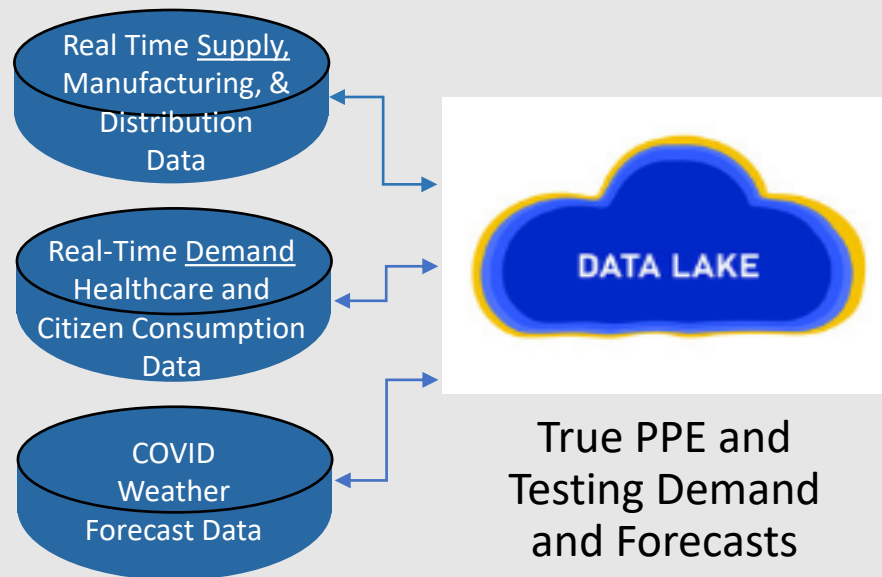
# Needed: Operation Warp Speed for PPE and Testing

## Goals:

1. Increase functional immunity by maximizing PPE.
2. Stop rationing N95 masks and best hygiene technologies.
3. Institute daily home testing for all.
4. Prevent monopolistic price gouging.

## A PPE & Testing “Apollo Program”

## Recommendations:



50x Supply



Every Healthcare Worker

Every Citizen

33x Supply



Every day

<\$0.50 per day per person



Timeframe: EUAs/DPA's and guaranteed purchase contracts. February 15, 2021



# Controlling the Virus Without/Before Vaccine



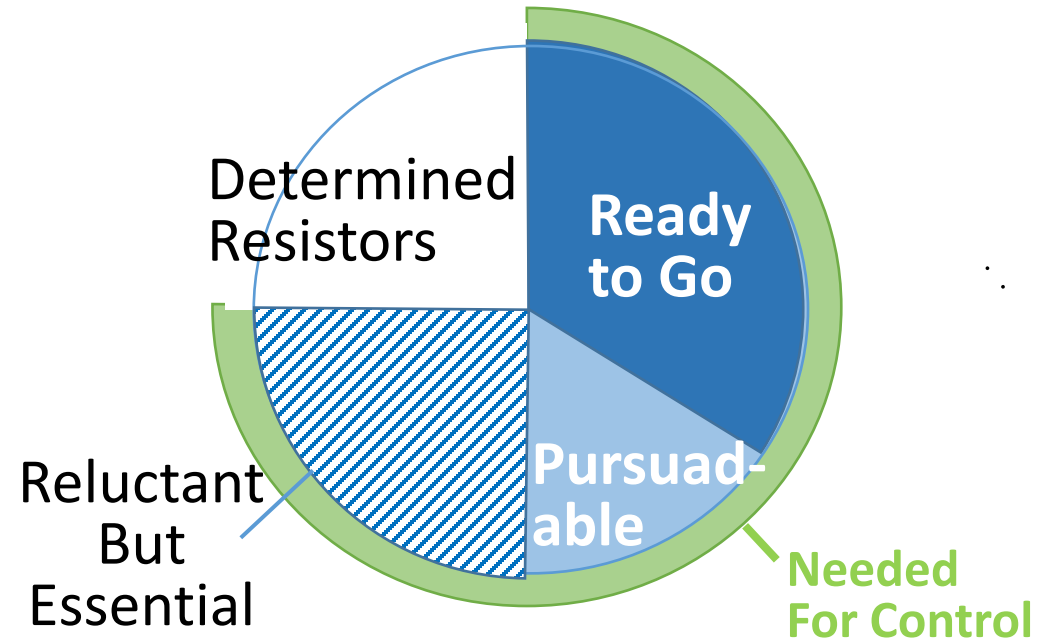
**70% control** possible with masking + hygiene alone



Increases to **90% control** if you add in ubiquitous testing



90% is good enough to achieve the functional equivalent of herd immunity—life resumes!



- By using the Defense Production Act, to scale up masking and testing, the U.S. could save many lives before widespread vaccine availability.
- But resistance to masking and testing is similar to vaccine resistance: eventually, to achieve herd immunity, we'll have to persuade enough resisters to accept either vaccines or masking/testing.
- Overlapping (NPI, testing & vaccine) mitigation measures are most effective, offer more options to different resistant segments and will help us gain control faster.

# The Leaders Will be Well-Rewarded

## *Privatized gain for socialized risk*

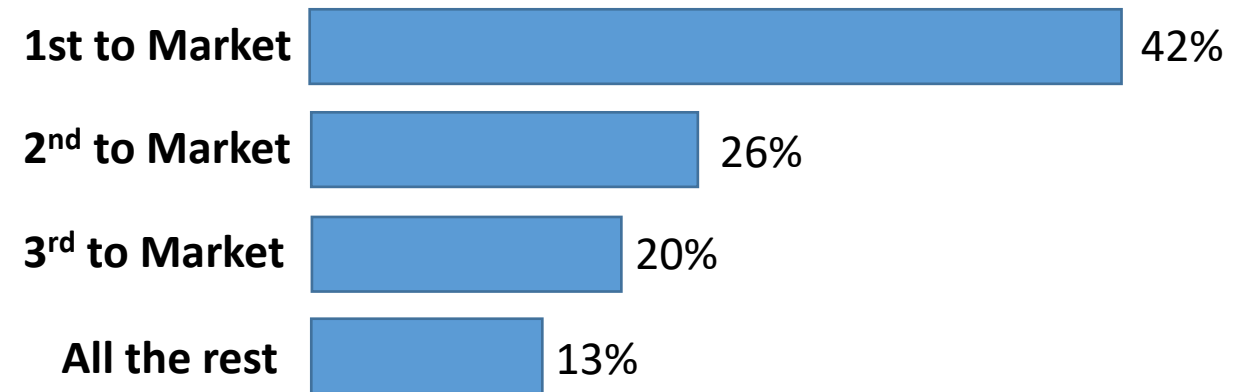
### **OWS Deals Secure:**

- Favored access to US market
- Accelerated path to market w/o regulatory hurdles
- Guaranteed sales of very large numbers of doses
- Taxpayer funds for R&D minimize corporate risk
- Early escape to free market
- Protection from liability



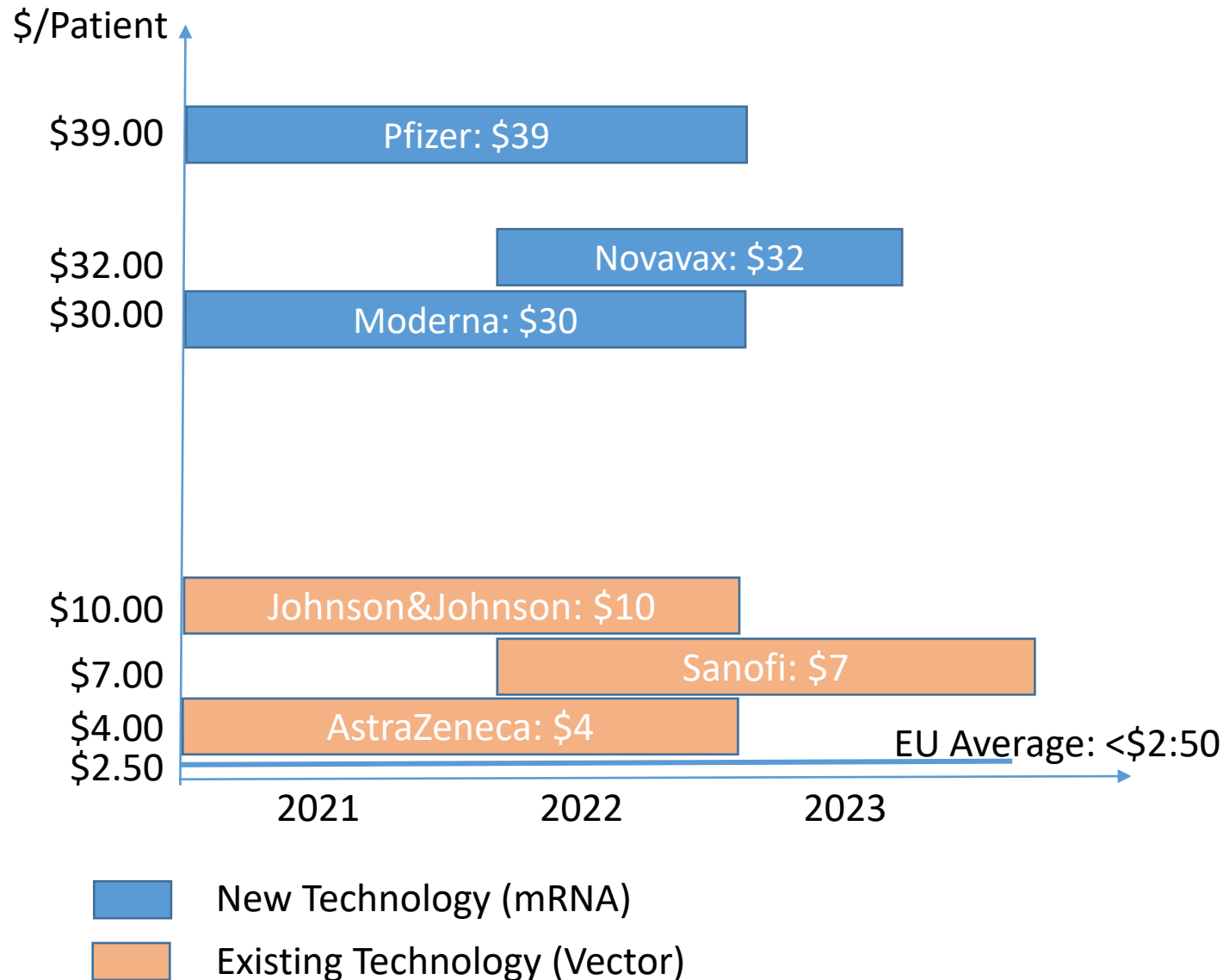
- COVID has unusually high profit potential for a vaccine
- First to market gets up to 60% market share

### **Projected Market Share in 10 Years**



- Establishes a beachhead vs competitors
  - Initial vaccines will dominate supply chains and distribution resources
  - Effectively eliminates opportunity to do further Phase 3 Studies in the US – no patients
  - Establish high performance benchmark for 2<sup>nd</sup> gen vaccines

# When Deals Run Out, Free Market Will Set Price



## Short term: OWS Vaccine Pricing & Terms

- After 2-year deal term, companies are free to decide who to sell to and at what price.
- Expect maximizing shareholder value to take precedence over maximizing pandemic control.

## Longer Term: Market driven in the US

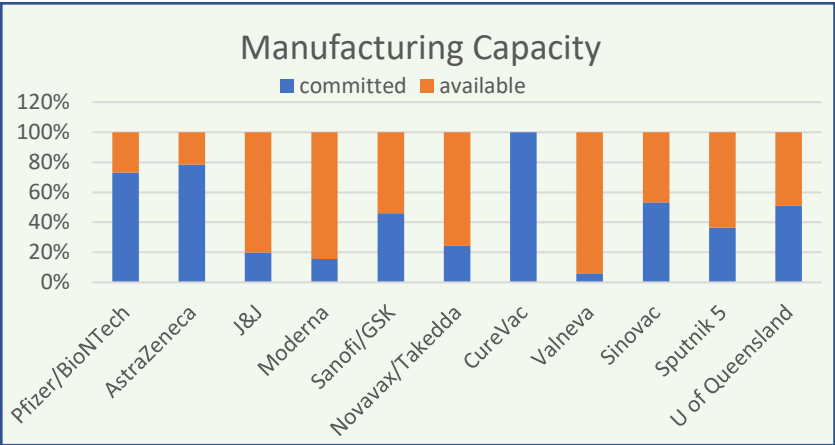
- **Prices may rise:**
  - for special populations with few options
  - due to global demand spikes
  - with materials shortages for
    - vaccines and adjuvants
    - injectors, glass, needles...
- **Prices may fall:**
  - Larger than typical number of competitors in pharma market
  - Potential for price controls among NGOs and certain countries
  - Vaccines may become currency of diplomacy

# Operation Warp Speed Deals To Date

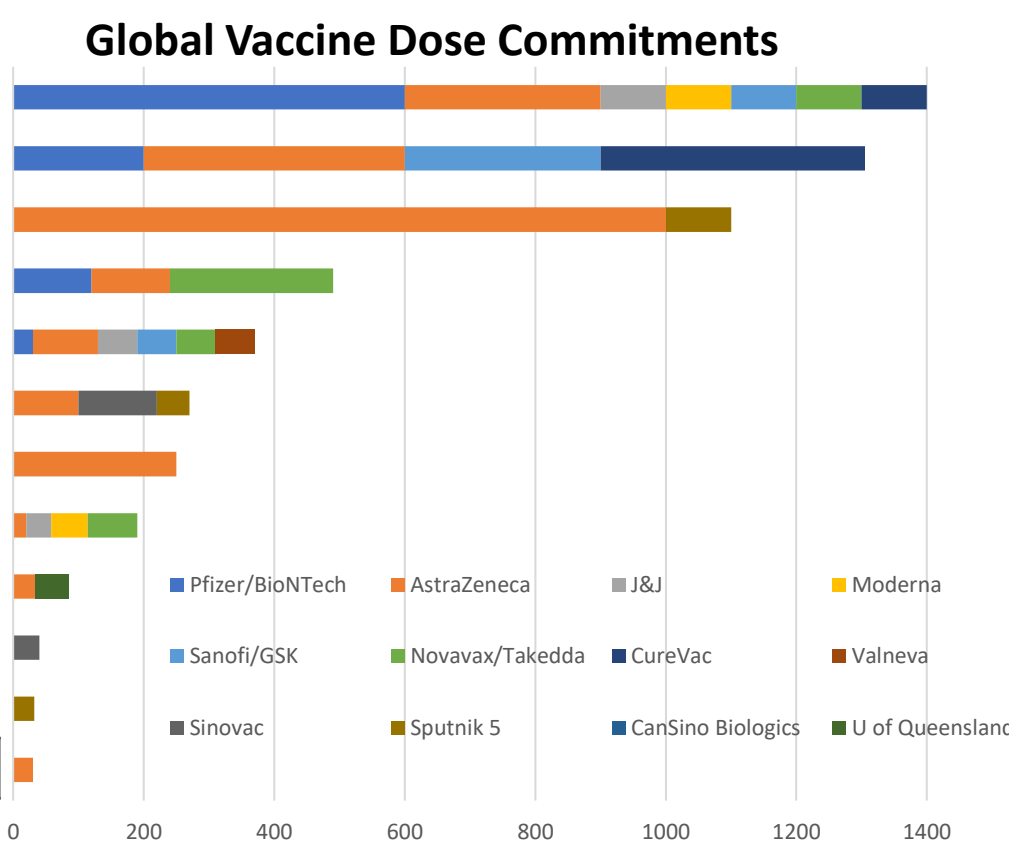
Company	Contract Price	Doses	Price/ Patient
AstraZeneca	\$1.3 B	300M	\$8
Johnson & J.	\$1.0 B	100M	\$10
Pfizer	\$1.95 B	100M + 500M option	\$39
Moderna	\$1.5 B	100M + 400M option	\$30
Sanofi	\$2.1 B	100M + 500M option	\$7
Novavax	\$1.6 B	100M	\$32

# U.S. Vaccine Deals are 25% of the Global Total

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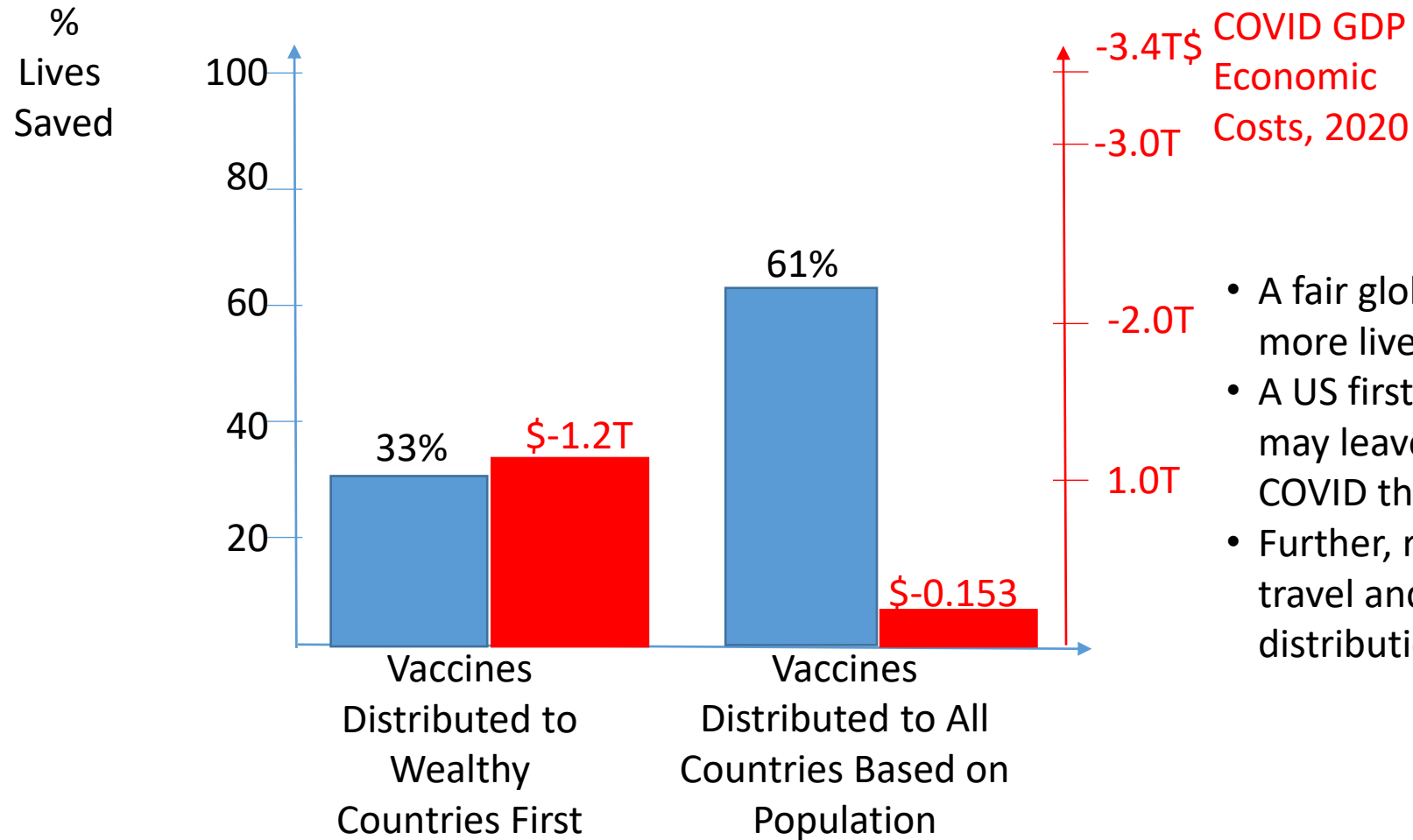


Country	Doses (mm)	% Pop Covered
USA	1,400	211.5%
EU	1,305	145.7%
India	1,100	39.9%
Japan	490	193.7%
UK	370	272.5%
Brazil	270	63.5%
L.Amer (excl Brazil)	250	21.4%
Canada	190	251.7%
Australia	85	166.3%
Indonesia	40	7.3%
Mexico	32	12.4%
Egypt	30	14.7%
<b>Total Commitments</b>	<b>5,562</b>	<b>~40.0%</b>



# Must think globally to achieve health normalcy

## Vaccine Distribution Modeling Health Impact



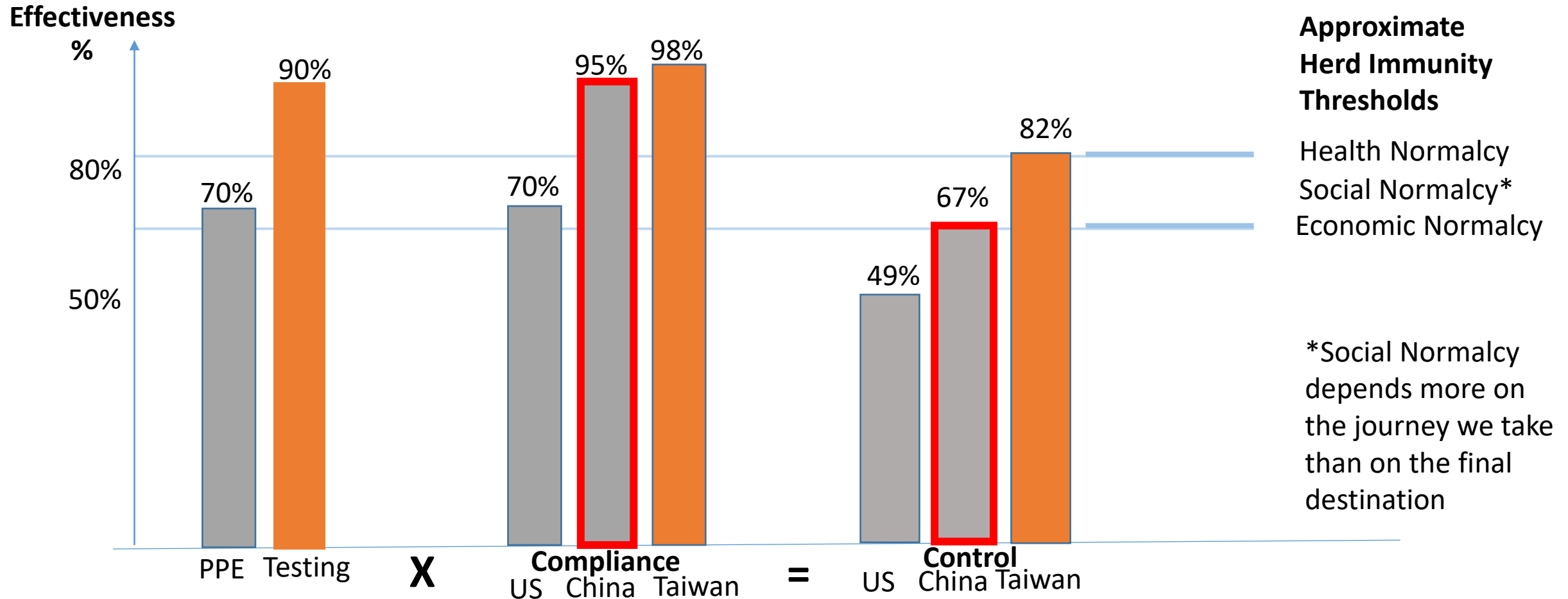
- A fair global distribution of vaccines save more lives
- A US first distribution of vaccines actually may leave more Americans vulnerable to COVID than a global distribution strategy
- Further, return to normal supply chains, travel and life would be faster with global distribution



# NPI successes in other countries provide normalcy targets

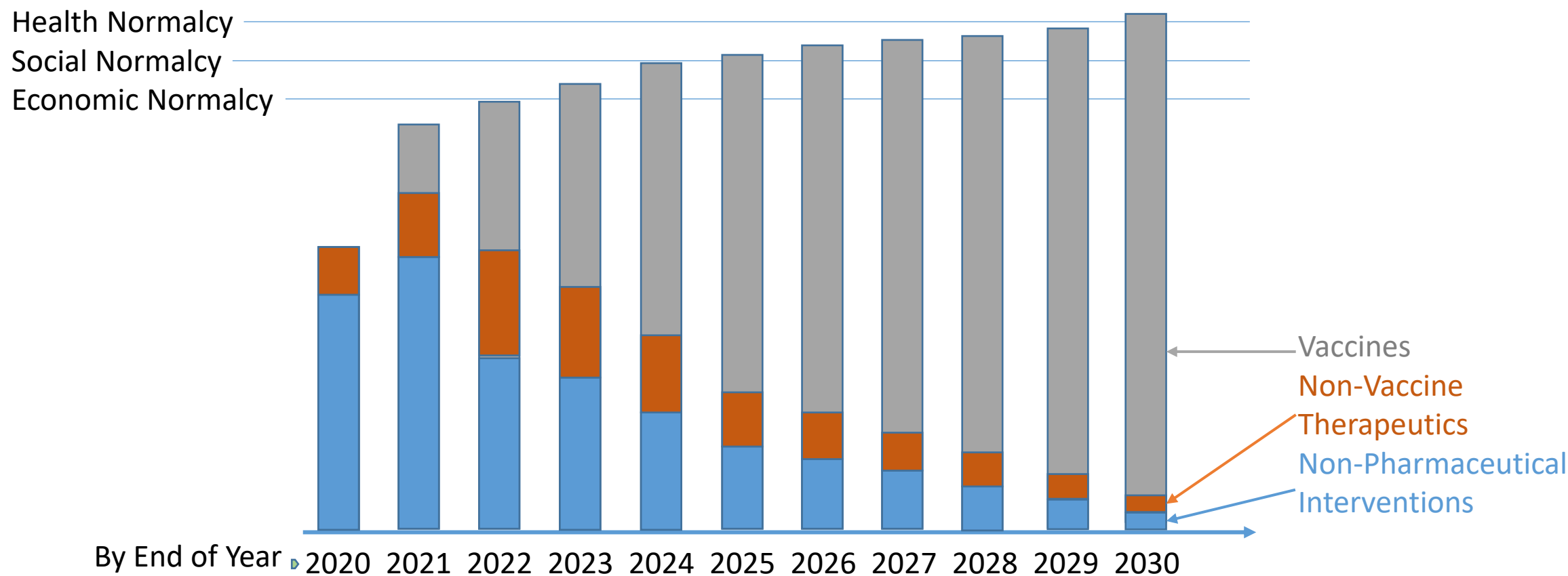
Just as with Vaccines, Effectiveness x Compliance = Control

## COVID Control: Impacts of PPE and Testing



# Achieving Degrees of Normalcy by Combining Weapons

(Illustrative Example)



Health Normalcy = <0.01% Deaths/Capita/Yr    Social Normalcy = Versions of Most Activities OK    Economic Normalcy = 99% Unimpaired Economy

©November 2020 Fred Brown

# Conclusions

Seven global trends	What they mean for you
Short term: the next four months will be the worst period in this pandemic. Lives will be saved (and improved) if we are able to upgrade our PPE/Test/Trace performance.	Assume you are at high risk and be very careful, using PPE and social distancing at full strength. Avoid ALL large indoor gatherings until PPE or vaccines provide much more control. Leading by personal example results in the best outcomes.
Longer term: there is suggestive evidence that vaccines will be good enough to lead us to normalcy as early as Q1 2022.	After reviewing data and consulting your physician, show up to your appointment and take your damned vaccine!
The scientific revolution accelerating vaccine development is making it harder for us to have faith in the results, and errors committed by healthcare institutions have damaged their credibility. As a result, public trust is low and vaccine acceptance could be impaired.	Listen to scientific experts discussing peer-reviewed data. Be cautious about the pronouncements of politicians and business people with vested interests. When evidence supports it, shift your mental model to adapt to the speed resulting from this scientific revolution.
The new vaccines are promising, but much remains unknown: we don't know how well they will prevent transmission, how long they will last, for whom they will be safe, or if they will achieve final approval. There are also major manufacturing and distribution challenges.	If you have no choice (if, for example, there's only one approved vaccine), take it if it available to you. If you have a choice among vaccines, know the scientific differentiation between them and make the effort to seek out the best match for your individual situation.
The U.S. will do a sufficient job of vaccinating the first 20 million high priority recipients. After that—for most of 2021--distribution in the U.S. may be chaotic.	Be prepared to continue masking, distancing, and testing as long as necessary—Some U.S. populations may not have access to a safe, effective vaccine until 2022.
Tragically, NPI could have spared us most of the losses we have endured to date, but we were unable to discipline ourselves to do it. Even now, better PPE use, testing, and distancing can save many lives before vaccines become widely available.	Advocate however you can for use of PPE and testing. This will save lives, drive us faster to herd immunity, and make the vaccination process safer. This tragedy is unequally shared. Do what you can to contribute to a safe and fair return to normalcy.
China leads the world right now in virus control and is among the leaders in vaccine development. It's important for the US to regain its leadership, for long-term geopolitical and economic reasons.	Prepare to manage and invest in a “post-war” world that will be extremely dynamic, with lots of opportunities and risks. Without a post-war dividend, expand your thinking to include the next generation and how we can invest to make the US more resilient as we face non-traditional foes in future battles.

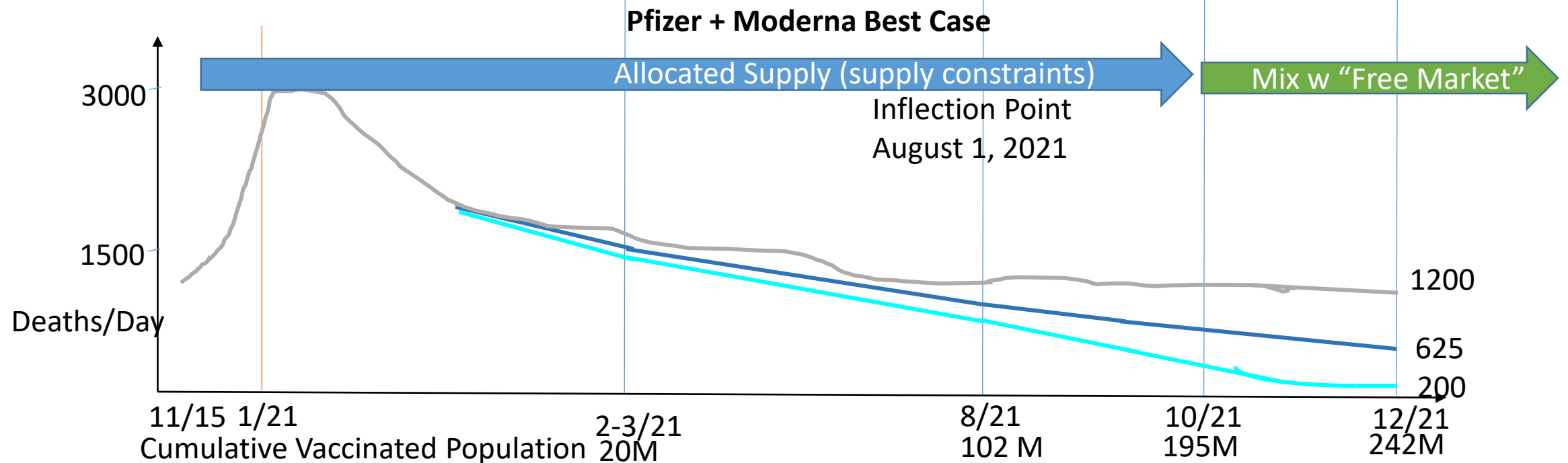
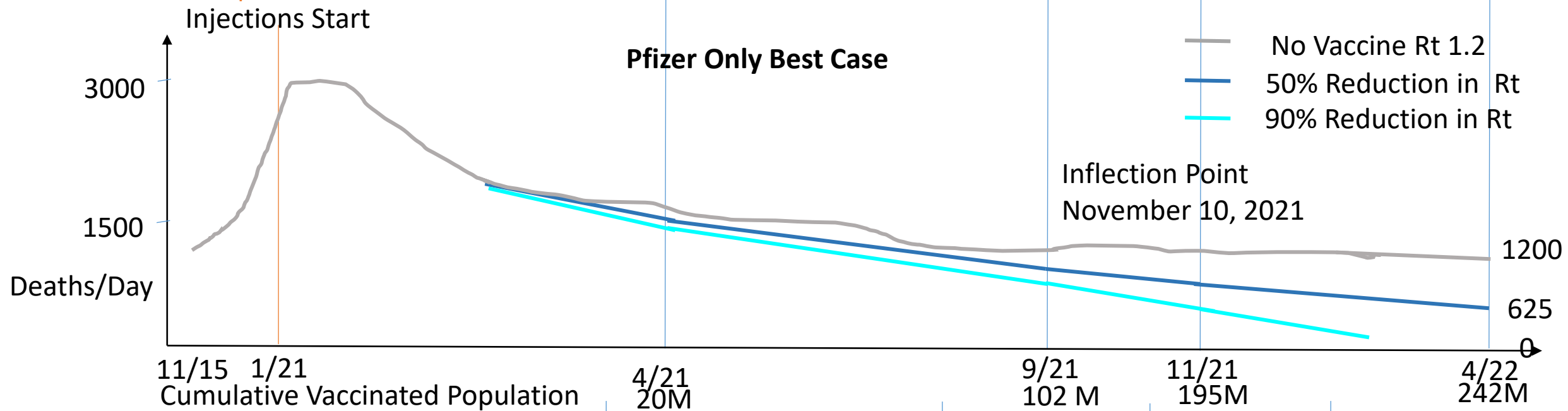
# UPDATE from 11/15 on 11/18/20

- November 16, Moderna: Preliminary data indicates mRNA 1273 vaccine is 94.5% effective serious symptoms. 95 subjects of 30,000+ tested were positive, 5 vaccinated, 90 placebo group. Eleven were severe cases, all from the placebo group. 37% of subjects are from racial and ethnic minorities. No reported Serious Adverse events. FDA EUA likely December 18. Cold chain – 20C and it can survive refrigerated after thawing for up to 30 days vs Pfizer - 70C and must be used within 5 days of thawing.
- November 16, CureVac: the EU announced a deal for 405 million doses from CureVac, a German maker of another mRNA vaccine, and signed a preliminary deal with Moderna for an additional 80M doses with an option for 80M more. The EU now has a portfolio of vaccine contracts totaling about 1.885 billion doses including options.
- November 18, Pfizer: BNT 162b2. 170 cases of COVID analyzed in 43185 trial subject. 162 in unvaccinated cohort, 8 in vaccinated = 95% efficacy that updated results from Phase III indicated 95% efficacy for its vaccine, and that it would be applying shortly for an EUA. 42% of global participants and 30% of U.S. participants have racially and ethnically diverse backgrounds, and 41% of global and 45% of U.S. participants are 56-85 years of age. No serious safety concerns observed; the only Grade 3 adverse event greater than 2% in frequency was fatigue at 3.8% and headache at 2.0%.

Participants	Overall Study	U.S. Only
Asian	4.5%	5.5%
Black	10.0%	10.1%
Hispanic/Latinx	26.1%	13.1%
Native American	0.8%	1.0%
Ages 56 to 85	40.9%	45.4%

IMPACT ON MODEL, pages 15, 16, 19, 23. The models assume launch on 12/20, 2020 with a single supplier (Pfizer) with cumulative patients documented over April, Sept, Nov, 2021. Latest indicates that we will likely launch 10 days earlier (~12/10/20) and that 2 manufactures will be supplying double doses. Moderna/Lonza uses a larger dose 100Mg/dose vs 30Mg/dose) and so best guess is that we will be achieving the goals stated on April 2022 in these slides on 12/31/21 and that the slopes on the curves will be 1/3 steeper.

# UPDATE - Impact on Model, Best Case U.S.



# Appendix



# PPE Mandates and Testing Have Controlled the Spread of COVID

- China (and Island Countries) are likely to achieve “normalcy” with First Gen Vaccine added to their successful PPE and comprehensive test, trace and quarantine programs
- Their economies will be held back due to lack of global control
- US will not achieve “normalcy” even with strong first-generation vaccine due to continued PPE and testing mismanagement
- ROW suffers as US isolationism prolongs economic and health challenges of COVID

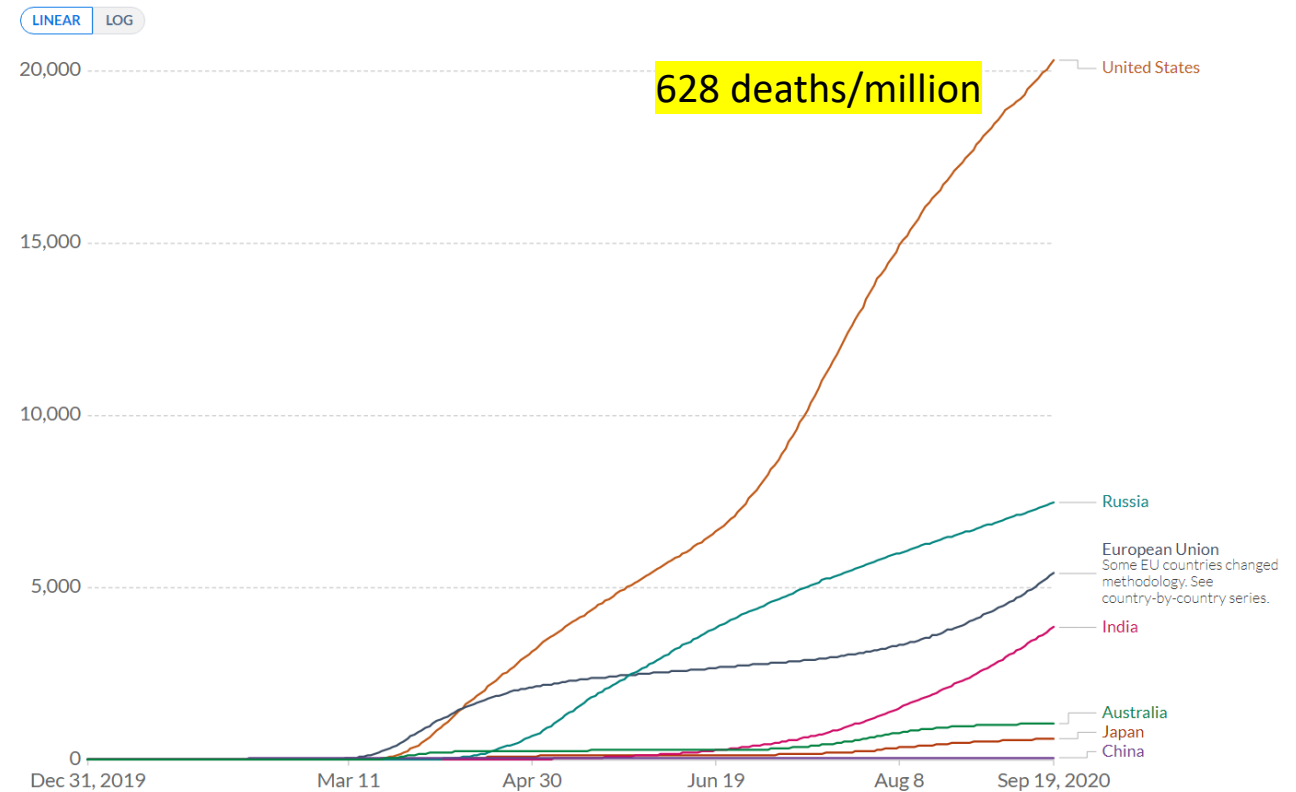


China is 150 times better than the U.S. at controlling the spread

Cumulative confirmed COVID-19 cases per million people

The number of confirmed cases is lower than the number of actual cases; the main reason for that is limited testing.

Our World in Data



Source: European CDC - Situation Update Worldwide - Last updated 19 September, 10:35 (London time)

CC BY

4 deaths/million

# Fred Prediction: Total Costs of COVID

One new case in the U.S. every 43 seconds...

Fred's March 23<sup>rd</sup> estimate through September 1, 2020 –

New unemployment claims filed: 44 M vs 45M Actual new claims actually filed.

Maximum Unemployment Trough: 26% vs 22.5% (Actual“joblessness” )

Projected U6 unemployment on November 15: (-12 to -14%) vs. (-12.1%) Actual

Total Net Economic Damage: \$2.5T Contraction in GDP (Actual: Q1+Q2 2020 lost \$2.45T)

Total Cumulative Economic Damage – \$17.3T vs Larry Summers analysis -\$16.1T Oct 12, 2020.

	Fred, March 23	Summers, On Oct 12	Calculation Basis
<b>Lost GDP</b>			
Health Loss	6200	7592	10M vs 7M Statistical Life Value
Premature Death	8500	4375	
Long Term Health Impairment	2600	2572	-35% QALY Dis-utility
Mental Health Impairment	_____	<u>1581</u>	
<b>Total</b>	<b>17,300B</b>	<b>16,121B</b>	

*“Increased investment in testing and contact tracing could have economic benefits that are at least 30 times greater than the estimated costs of the investment in these approaches.” Larry Summers, JAMA*

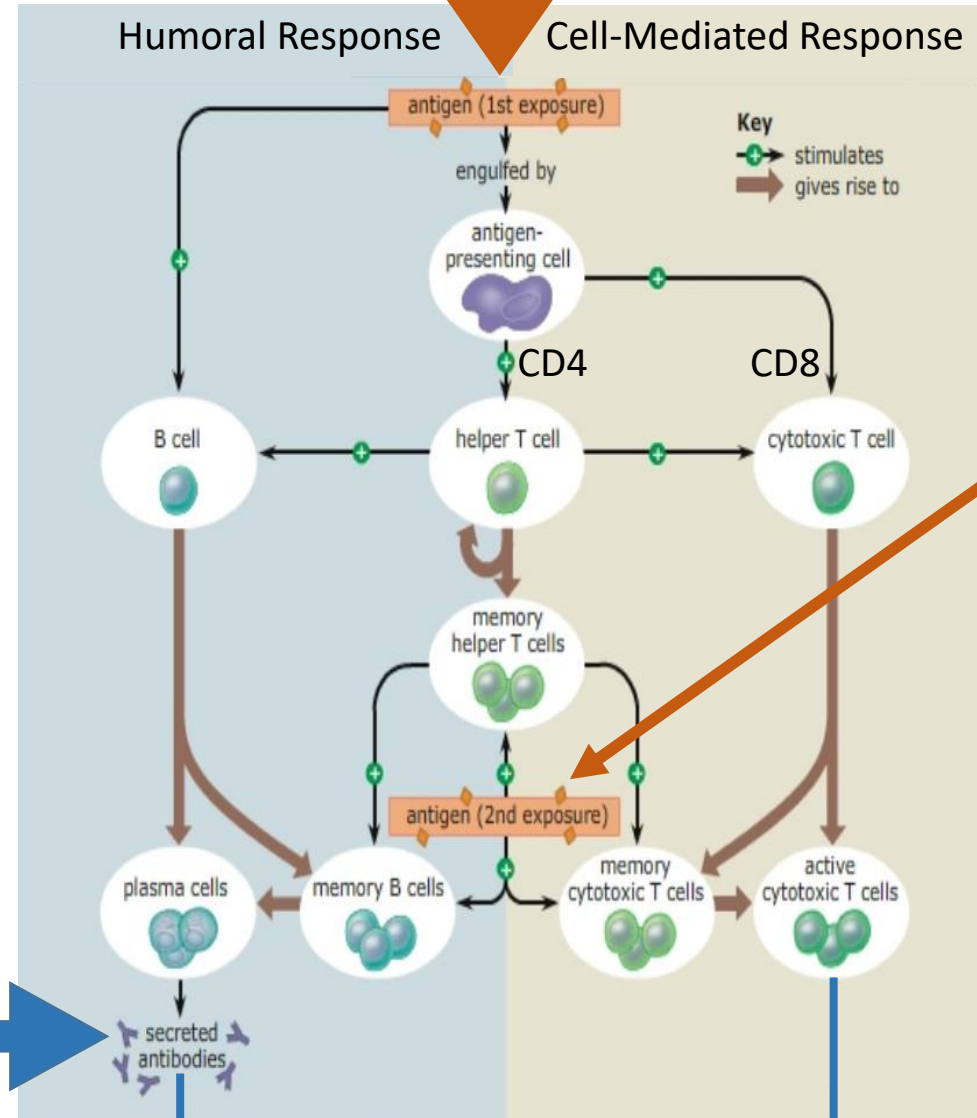
# Two Sources of Neutralizing Antibodies

2. **Vaccines** activate immune system without causing symptoms

1. **Monoclonal antibodies** provide a temporary instant boost in virus-fighting capability

## Temporary instant boost

- prophylactic control
- late stage disease control
- bridge to a vaccine
- immune system in a vial



## Permanent Machinery Activated

A sanitizing COVID vaccine will likely have to vigorously stimulate the production of both *B and T* cells.

Vaccines that do less than this can still be partially helpful.

## Vaccine Antigen Types

### Whole Virus

- Attenuated
- Dead

### Pieces of the Virus

- Spike protein subunits
- Other unique, conserved proteins

Extracellular Pathogen Neutralization    Intracellular Pathogen Neutralization