National Home Infusion Association

COVID-19 VARIANTS, VACCINES AND MONOCLONALS

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Objectives

- Discuss available data on COVID-19 vaccine-induced immunity and vaccination timing in the context of use of COVID-19 monoclonal antibody therapies
- Describe COVID-19 variants and potential impacts on clinical course, therapeutic and vaccines
- Review frequent questions and educational points regarding COVID-19 based on our current knowledge

Outline

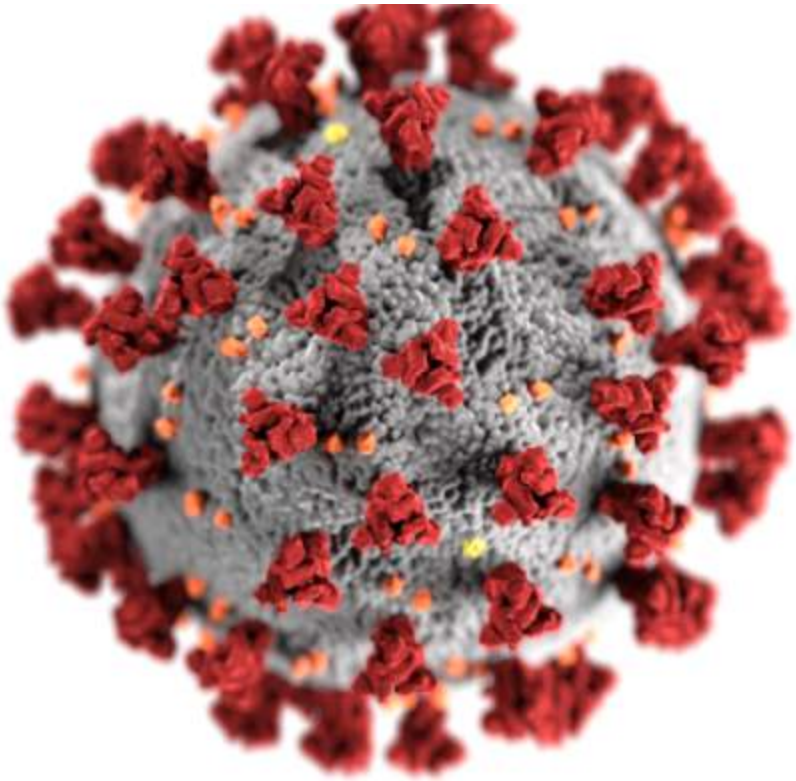
- Variants
- Vaccines
- Vaccines and variants
- Monoclonal antibody data
- Variants and monoclonals

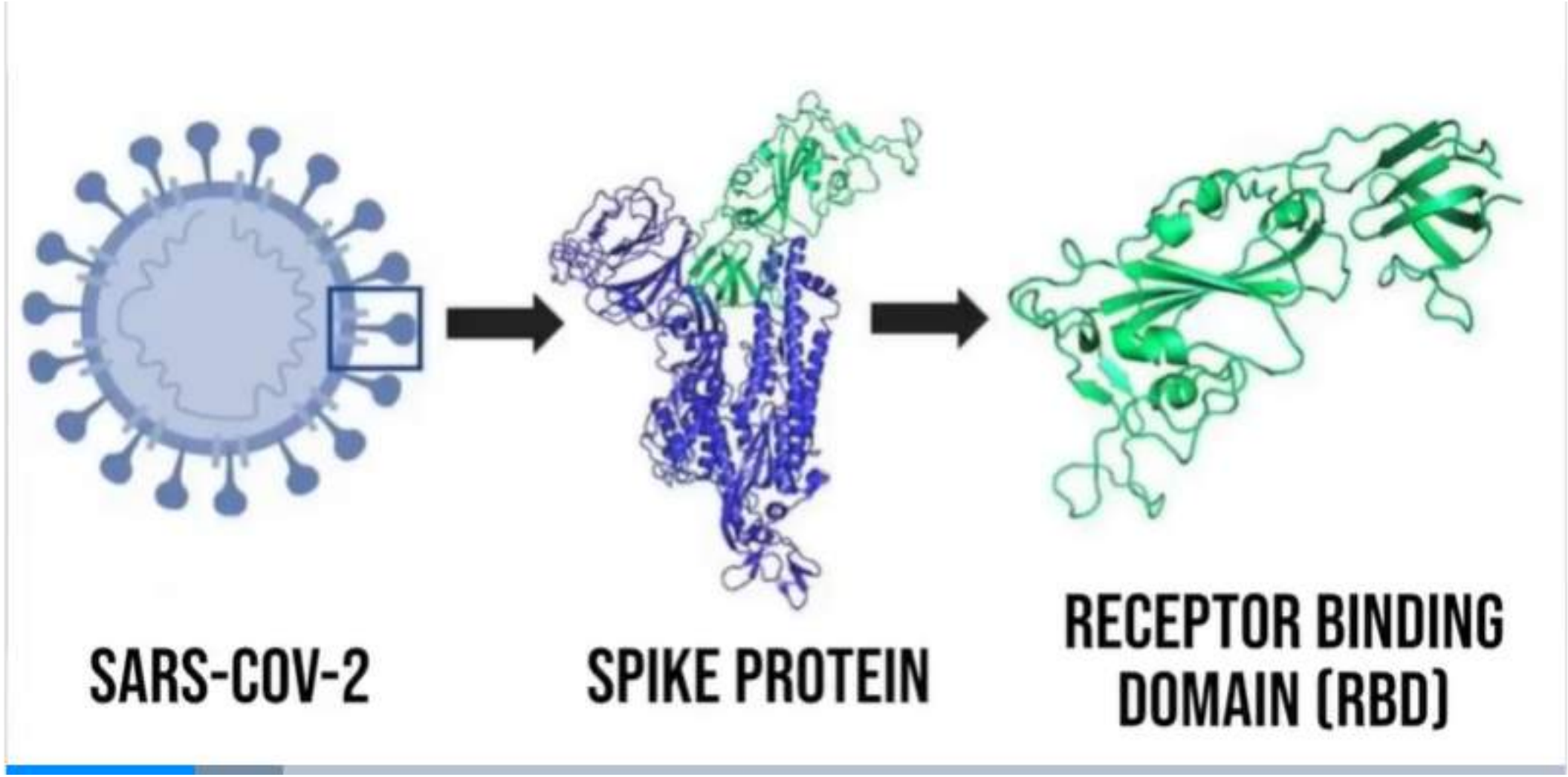
https://www.scientificamerican.com/article/the-most-worrying-mutations-in-five-emerging-coronavirus-variants/

‘Variants’

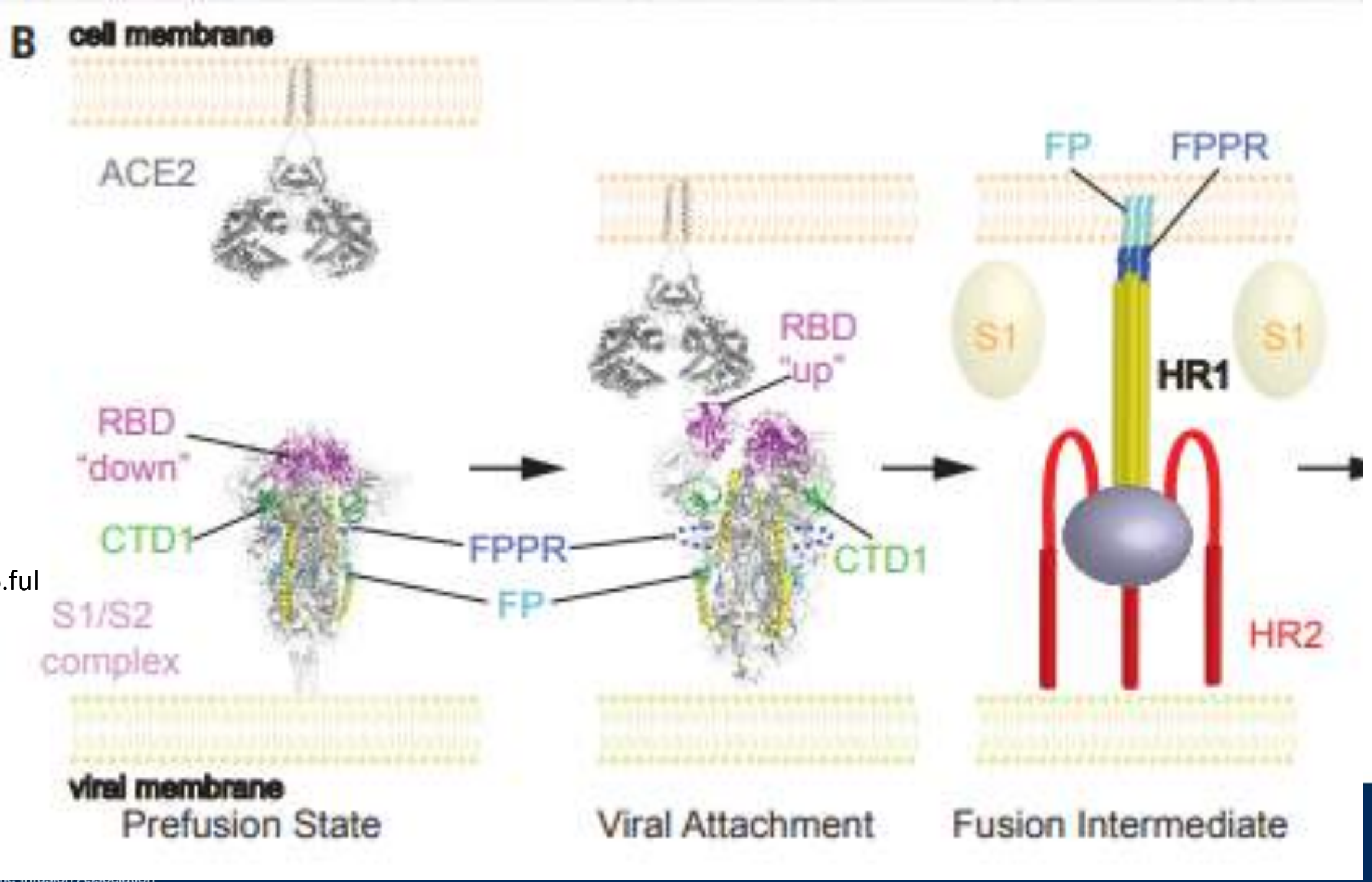
- mRNA viruses mutate
- Coronaviruses have ‘proofreading’ system unlike Influenza or HIV
- But due to HUGE NUMBERS, virus had lots of opportunities to change a little bit
- Continue to acquire random mutations now with changes in contagiousness and then outcompeting preexistent variants
- Similar mutations arising in multiple places
- Mutations occur randomly
  - Viruses that have mutations that evade the existing antibody immune response could be selected for by plasma or monoclonal antibodies
- Mutations that render a virus more ‘fit’ to cause infection can come to predominate over less infectious strains

Variants





Sean Crotty, Scripps


B
cell membrane
ACE2
RBD
"down"
CTD1
S1/S2
complex
FPPR
FP
RBD
"up"
CTD1
FP
FPPR
S1
S1
HR1
HR2
viral membrane
Prefusion State
Viral Attachment
Fusion Intermediate

511/1586.ful

Quick review of molecular biology

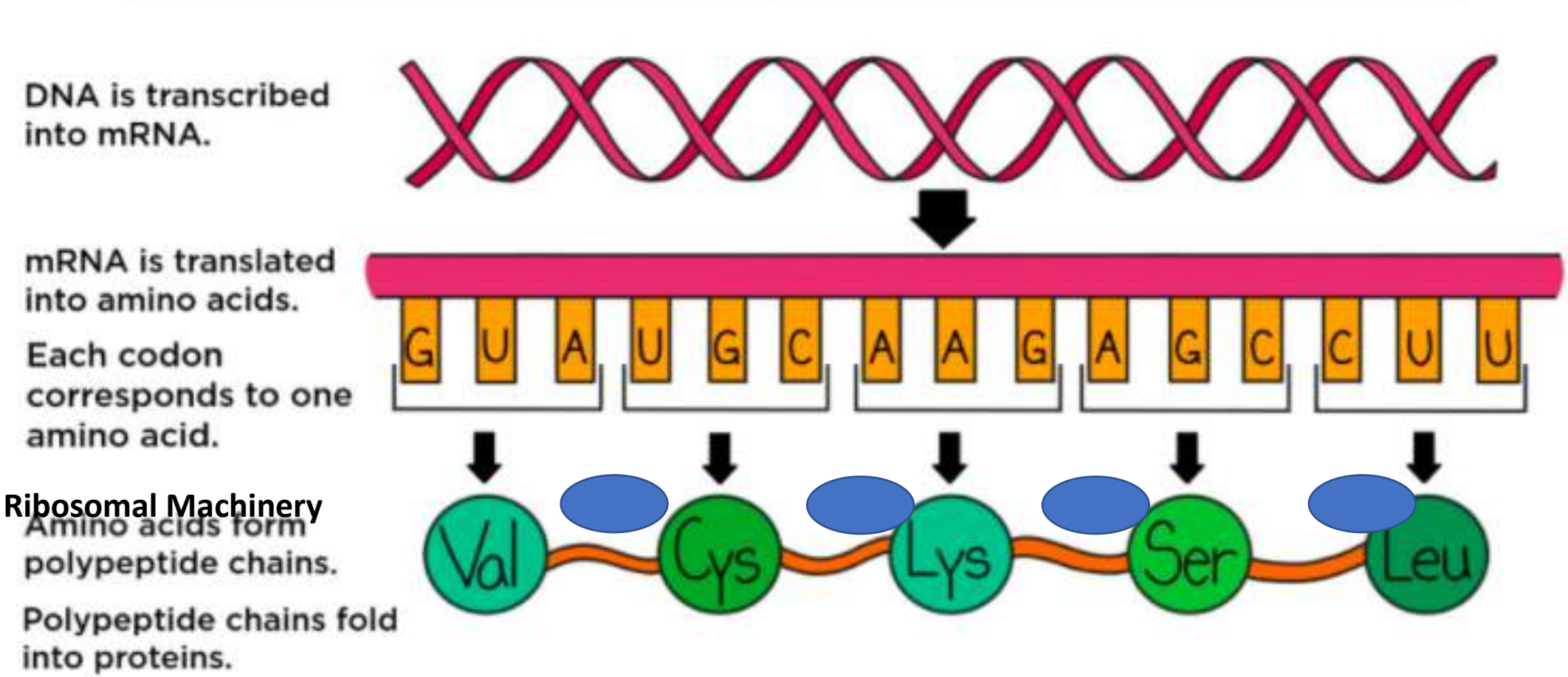


Image source: By Gabi Slizewska

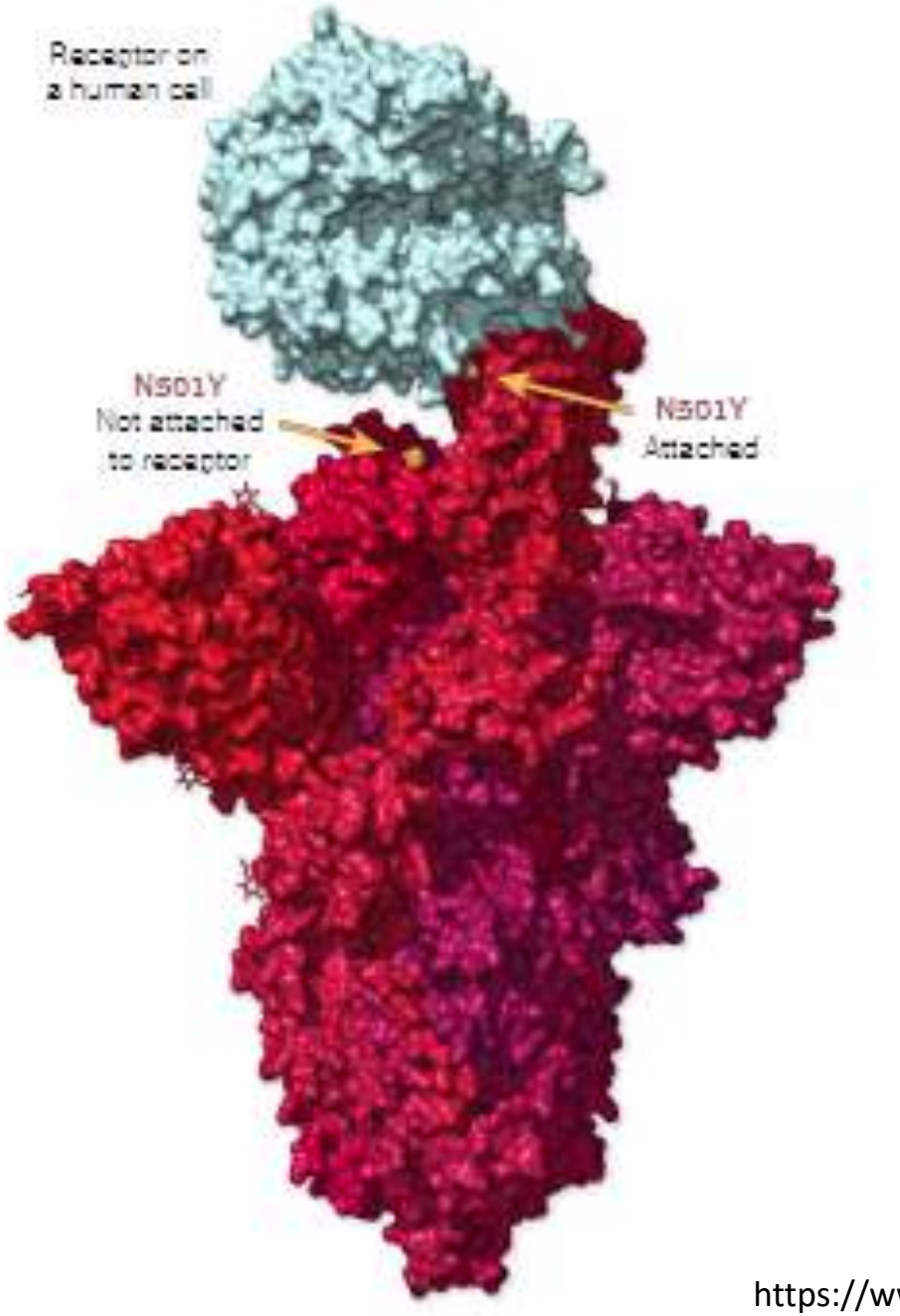
Variant Concerns – 'Variants of Concern'

- Most concentrated attention on the S protein. Mutations causing:
  - More infectious virus (R0 number)
  - Specific amino acid mutations that cause tighter binding to ACE-2 receptor
  - Clinical severity – unclear – and COMPLICATED*
  - Immune ESCAPE - Specific AA mutations that reduce antibody neutralization
    - Concern re: reinfection – escape from preexisting immunity
    - Escape from monoclonal antibodies
    - Vaccine ESCAPE – escape from vaccine induced immunity
- Mutations in certain areas beneficial to the virus's ability to attach, infect or evade the immune response can arise independently in different times/persons → can propagate when given the opportunity*
  - Key 'signature' mutations emerging that can lead to 'Variants of Concern'
  - increased infectivity, escape from natural immunity, escape from the monoclonal antibodies, escape from vaccine-induced antibody response

Some of the KEY mutations of note

Lineage	Mutation	Status
B.1	D614G	Appeared in early 2020 and spread around the world.
Several	N501Y	A defining mutation in several lineages, including B.1.1.7, B.1.351 and P.1. Helps the virus bind more tightly to human cells.
Several	E484K or "Eek"	Appears in several lineages. May help the virus avoid some kinds of antibodies.
Several	K417	Appears in several lineages, including B.1.351 and P.1. May help the virus bind more tightly to cells.
Several	L452R	Increasingly common in California, May be more infectious
Several	Q677	Found in seven U.S. lineages, but not yet shown to be more infectious.

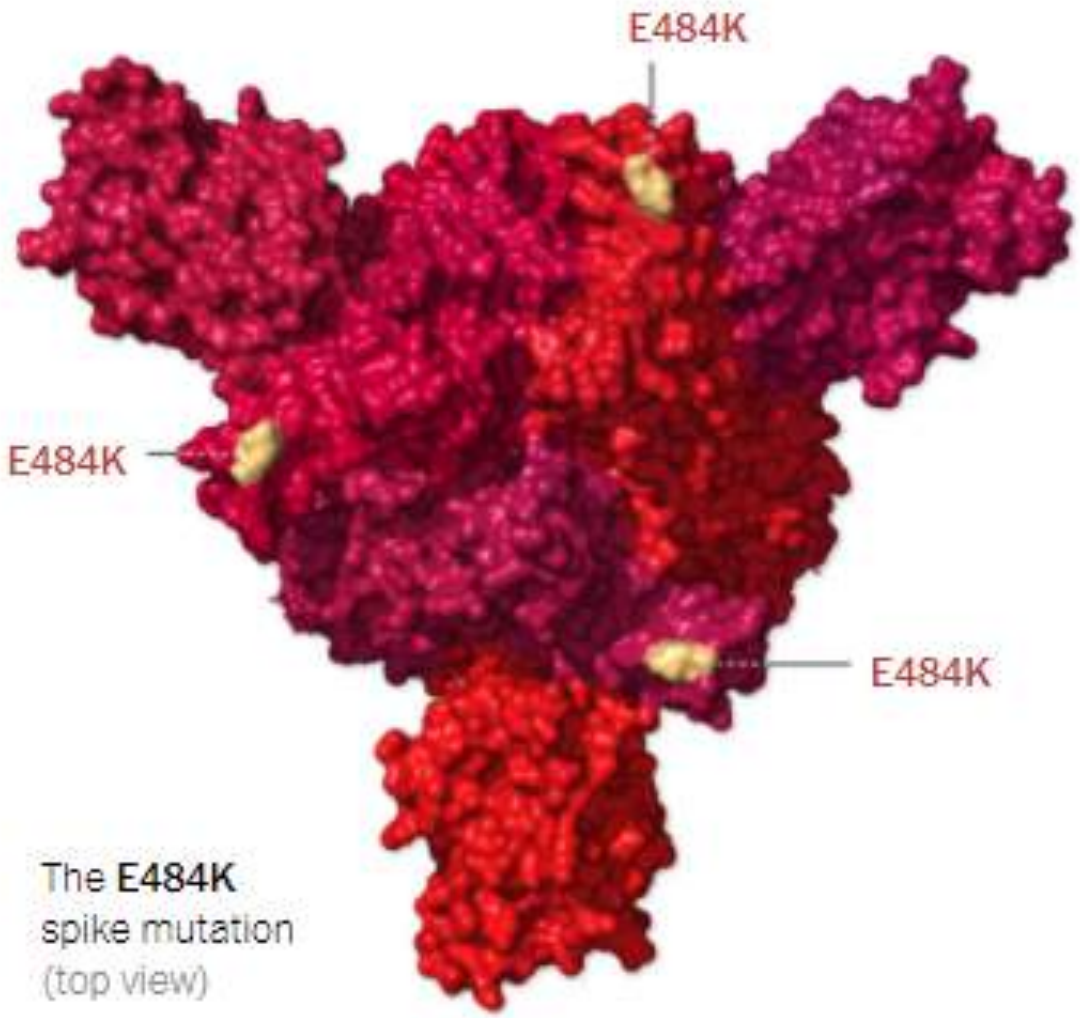
Coronavirus Variant Tracker - The New York Times (nytimes.com)



- N501Y mutation
- Refines the shape of attachment allowing tighter fit, increased chance of successful infection
- Binds MORE tightly to the ACE-2 receptor
- Has evolved INDEPENDENTLY in many lineages
  - Australia, Brazil, Denmark, Japan, Netherlands, South Africa, Wales, Illinois, Louisiana, Ohio, Texas

https://www.nytimes.com/interactive/2021/health/coronavirus-mutations-B117-variant.html

It takes three spike proteins to form one ‘spike’ so the mutations occur in three places

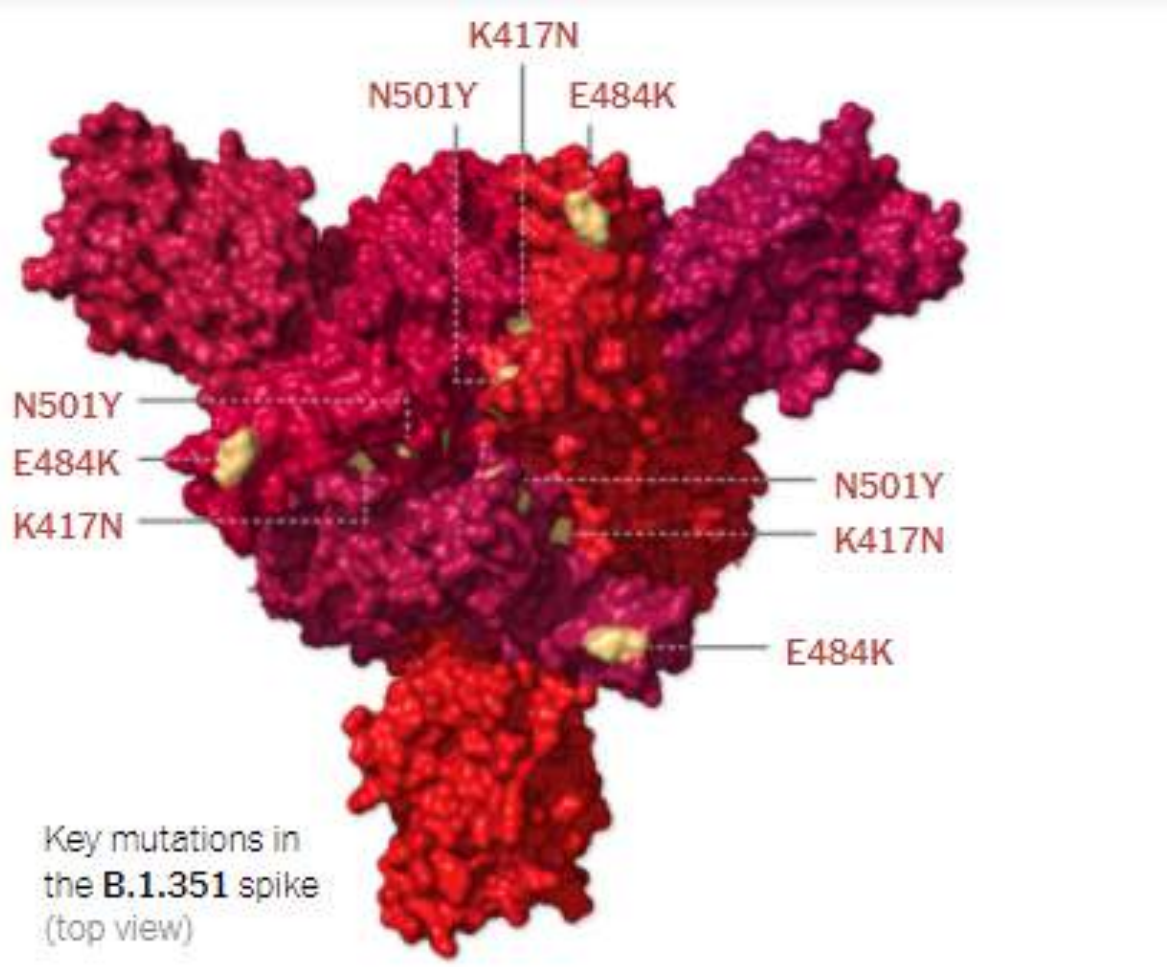


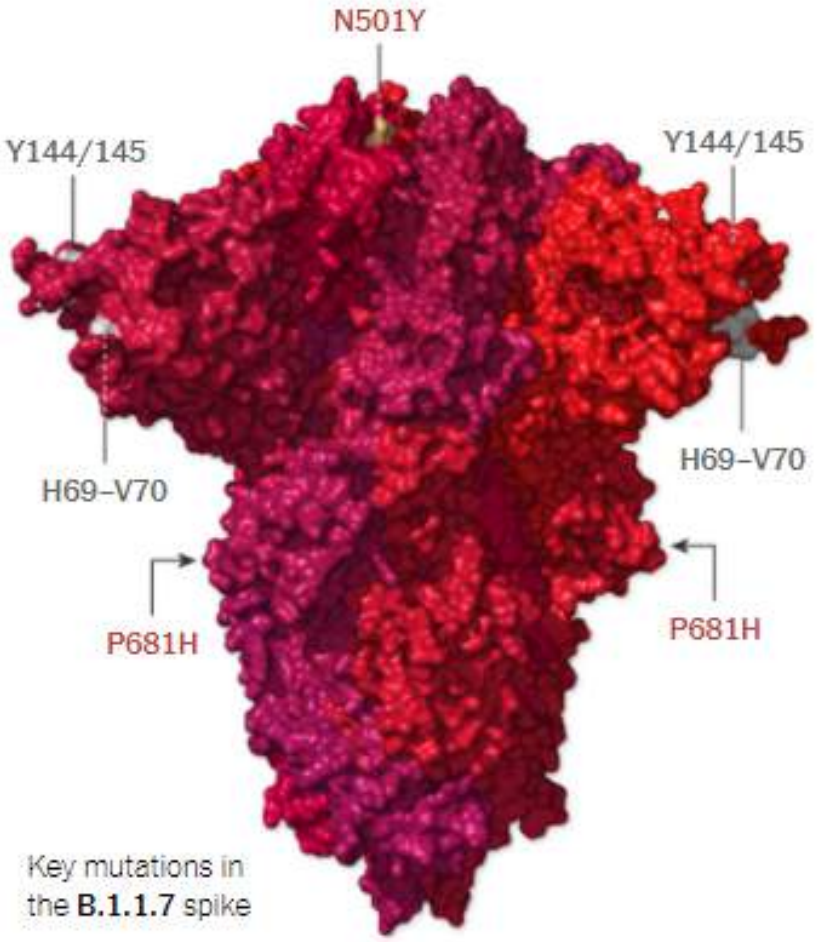
The **E484K** spike mutation (top view)

- E484K ‘eek’ mutation
- Mutation near top of the spike and alters shape of the protein.
- Helps it to evade some coronavirus antibodies
- Has evolved INDEPENDENTLY in many lineages
  - South Africa, UK, now Britain and Oregon (together with the N501Y in infectious variant), Canada, Japan, Argentina

https://www.nytimes.com/interactive/2021/health/coronavirus-variant-tracker.html?searchResultPosition=3#E484K

Other potentially important mutations:





Nomenclature

- ‘Variants’
- ‘Lineages’
- ‘Strains’
- ‘A bloody mess’
- Geopolitical issues ‘UK strain’, ‘South African strain’, ‘Brazil strain’
  - Could stigmatize and discourage aggressive surveillance for new variants
- Naming process May CHANGE –
- Major lineages named with a LETTER: A and B (two ‘roots’)
- Then new lineage: At least 5 genomes, has shared nucleotide differences from ancestor with attention to ongoing transmission
- Iterative procedure with max 3 sublevels: Once the iteration gets beyond 3 sublevels, the ROOT name changes: B.1.1.28.1 → P.1

https://www.nature.com/articles/s41564-020-0770-5

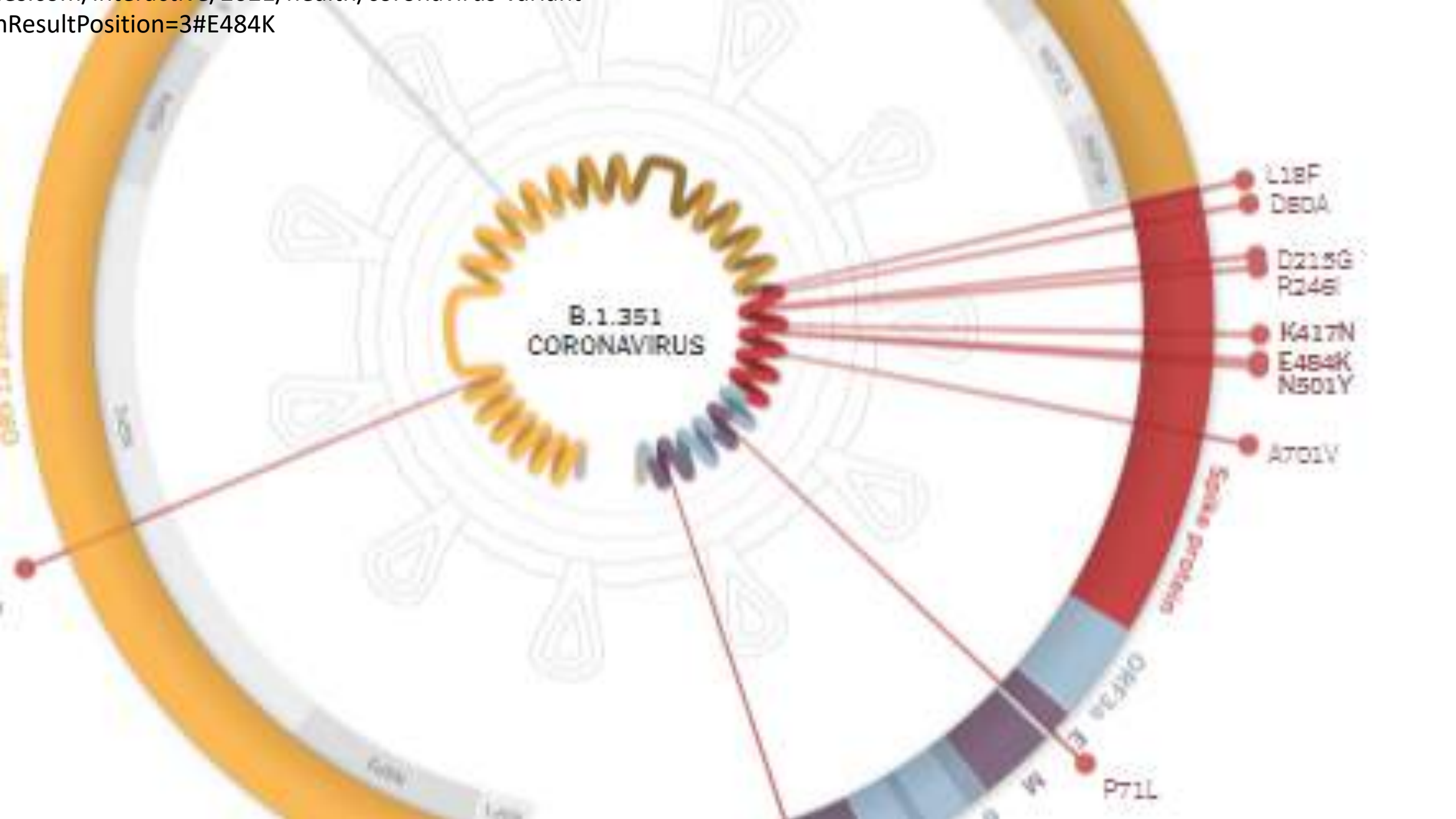
‘Variants of concern’

- B.1.1.7
  - 17 mutations, several in spike protein
  - Including N501Y
  - Deletion of the Δ69-70 codon
  - Many mutations → speculation evolved in immunocompromised patient over time
- B.1.1.28 → convergent variants of concern → B.1.1.28.1 → P.1 (more mutations than P.2)
  - BOTH have the E484K mutation
- ‘Variants of interest’
  - B.1.427
  - B.1.526

- B.1.351
  - Also has N501Y (independently) and E484K
  - More difficult for antibodies to bind to the spike
  - Some monoclonal antibodies - less effective binding to spike
  - Convalescent serum less effectively neutralizes
  - Antibodies from vaccinated less neutralizing

Coronavirus Variant Tracker - The New York Times (nytimes.com)

nResultPosition=3#E484K



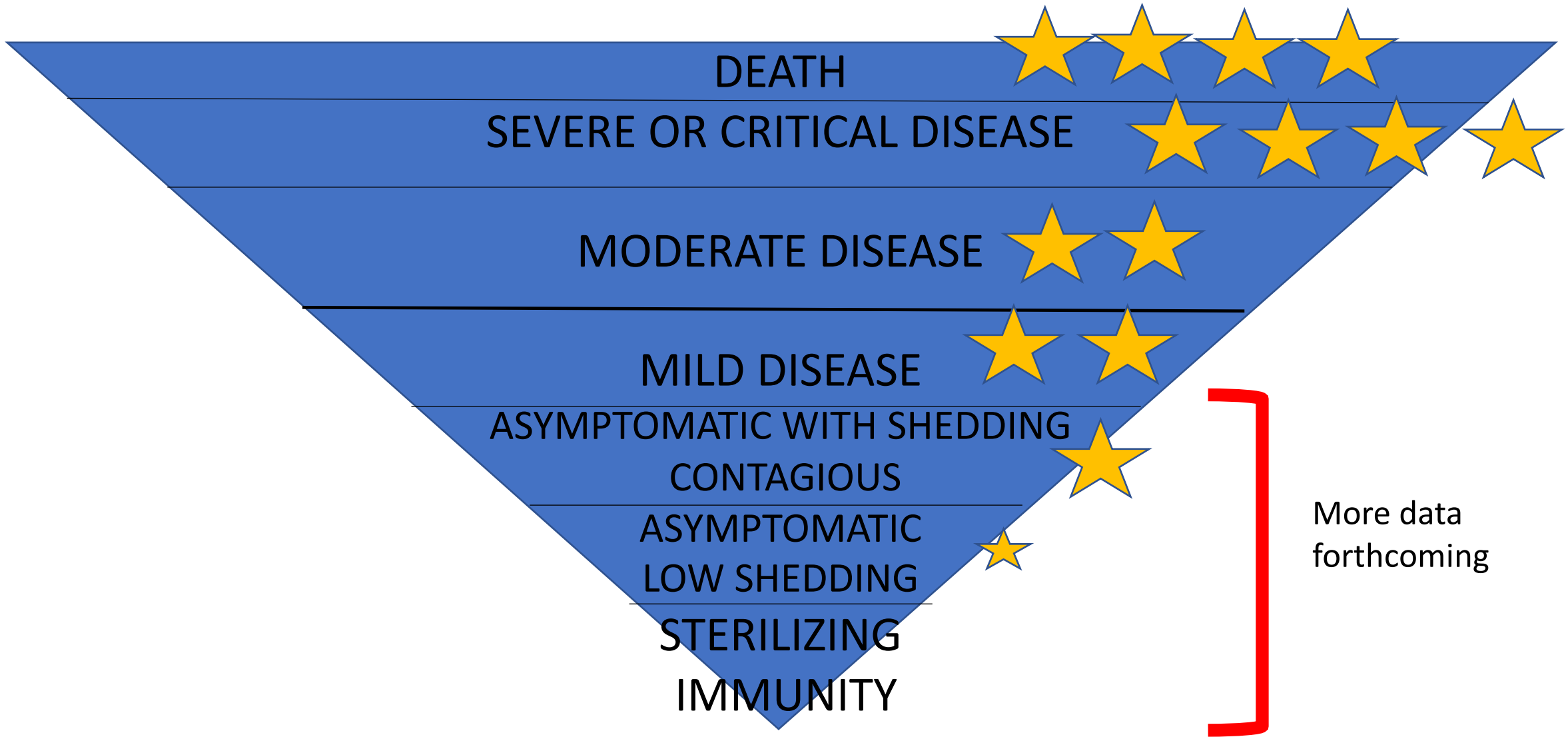
U.S. sequencing

- Many university, state labs have escalated sequencing
- Not in conjunction with a coordinating tracking system analogous to UK
- Lots of variants being seen
- But how many are actually ‘variants of interest’?
  - Eg, B.1.526 – isolated in NYC and up and down East coast
    - Contains the E484K mutation
    - Risk for immune evasion or decreased vaccine efficacy?
  - Significance?

Vaccines and Variants

- Vaccine efficacy and effectiveness
- Impact of variants

EFFICACY, EFFECTIVENESS, WHAT ARE OUTCOMES OF INTEREST?



Overall vaccine efficacy

COVID-19 Vaccines:

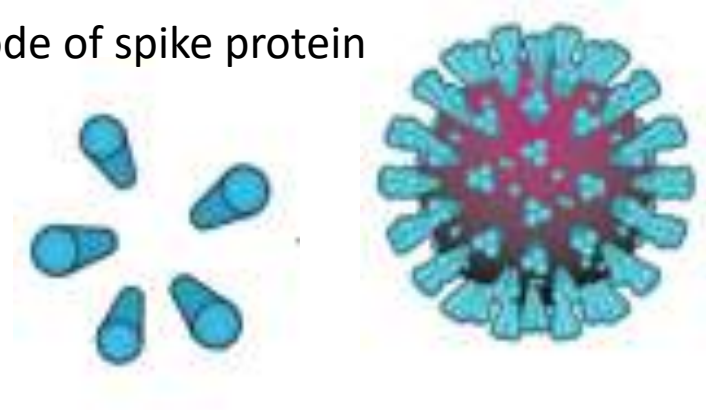
- mRNA
- First vaccines approved under emergency use authorization
  - Pfizer/BioNTech (12/11), Moderna (12/17)
- Adenoviral vector vaccine
  - J&J (Janssen) Ad26.COV2.S

Background of mRNA vaccine research

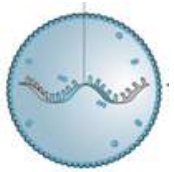
- mRNA is intermediary between our DNA and the ribosomes – the cell ‘machines’ that make protein
- Our cells correctly fold, modify and reproduce proteins
- Each cell can make 1000-100,000 proteins from the mRNA – more POTENT and safer than injecting protein
- 7 years ago identified lipid nanoparticles as best and safest way to deliver vaccine
- Have been used now for years to deliver therapeutic vaccines to patients - well tolerated

How mRNA vaccine works

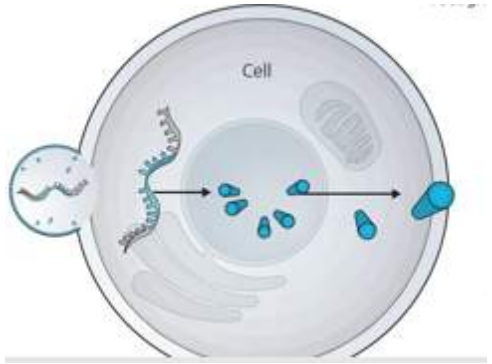
Identified genetic code of spike protein



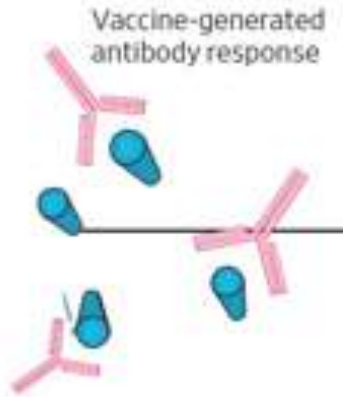
Modified it and made RNA from this genetic information
RNA is protected in a lipid coating (lipid nanoparticles)



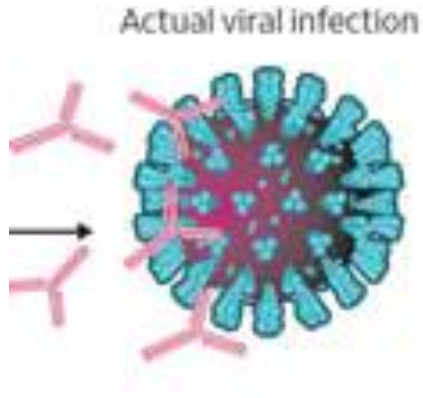
Inject into a patient
RNA enters healthy cells which then produce spike protein



Spike proteins trigger immune system and antibodies are produced



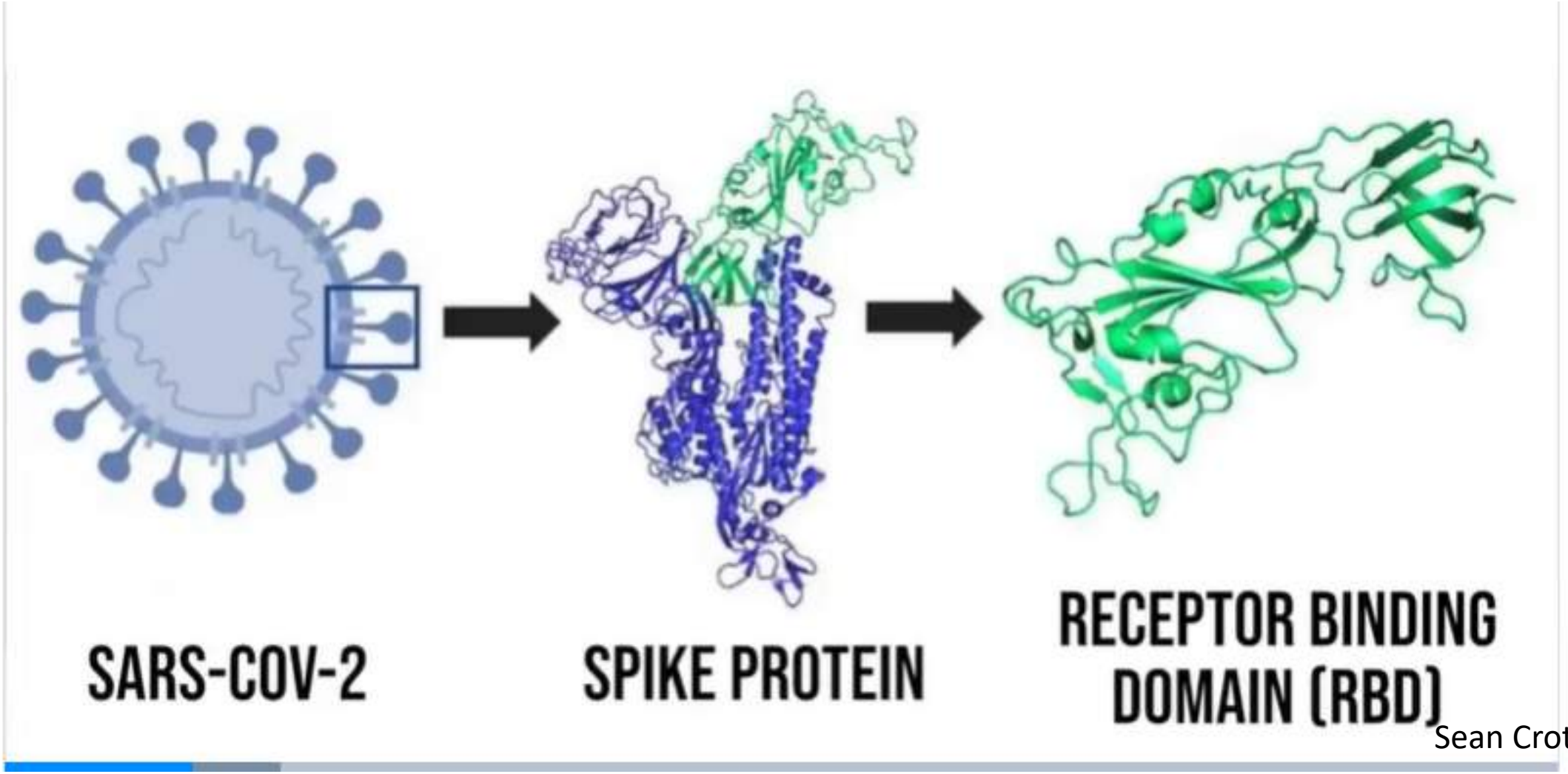
The antibodies remain in the body and if a person is exposed, the antibodies bind up the virus and help neutralize it.



WSJ

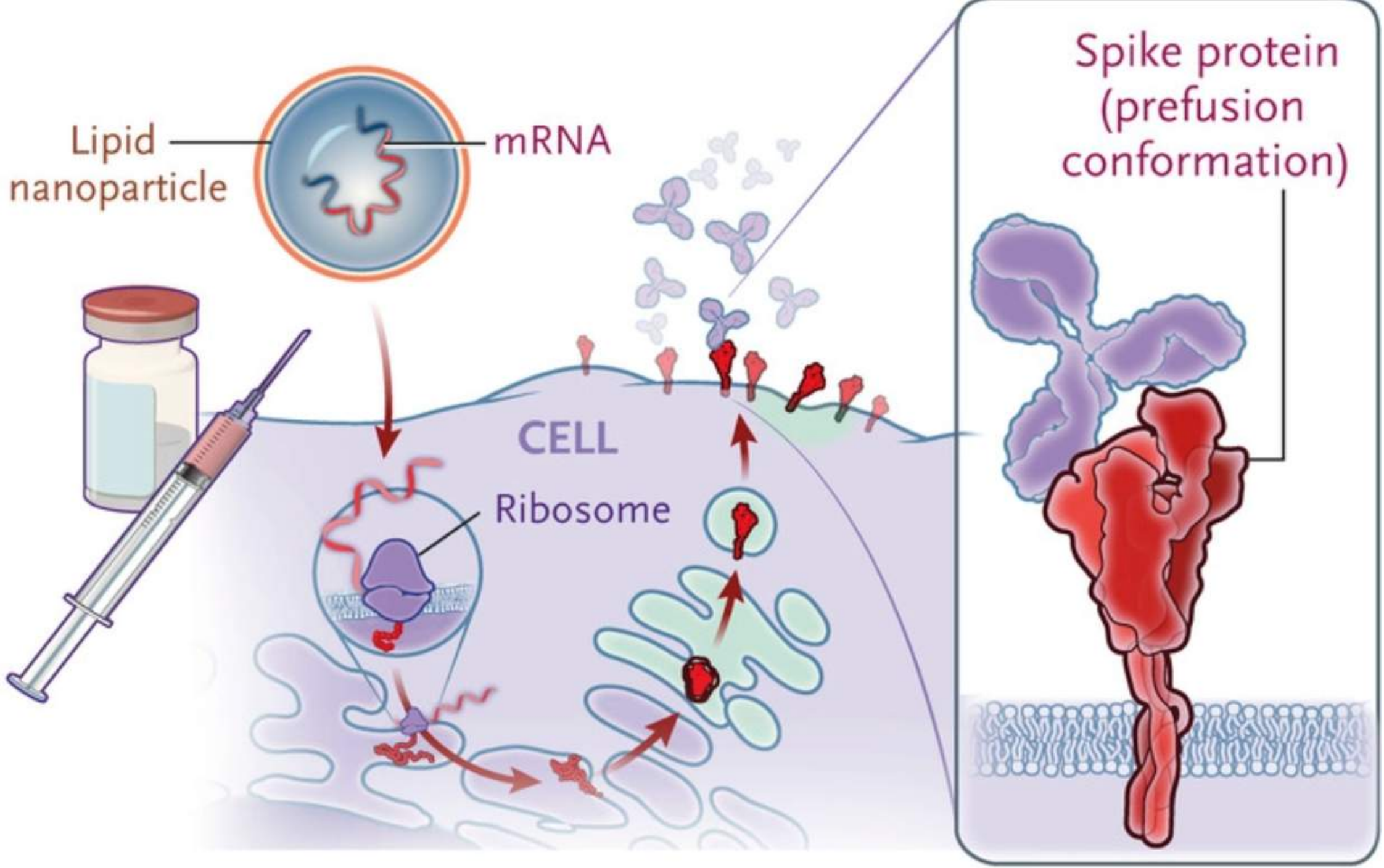
‘Previously Coronavirus SPIKE proteins were well characterized (including how best to stabilize as vaccine target)

- Allowed a **RAPID PIVOT** to developing a COVID-19 vaccine
  - YEARS of work creating right mutations to stabilize SPIKE protein from OTHER coronaviruses (cold viruses, SARS, MERS)
  - The 2 proline substitutions in SPIKE used in vaccine had already been recognized as able to stabilize the complex
  - → This work used to make SARS-CoV-2 spike sequence in the vaccines
    - SARS and MERS – other severe coronaviruses



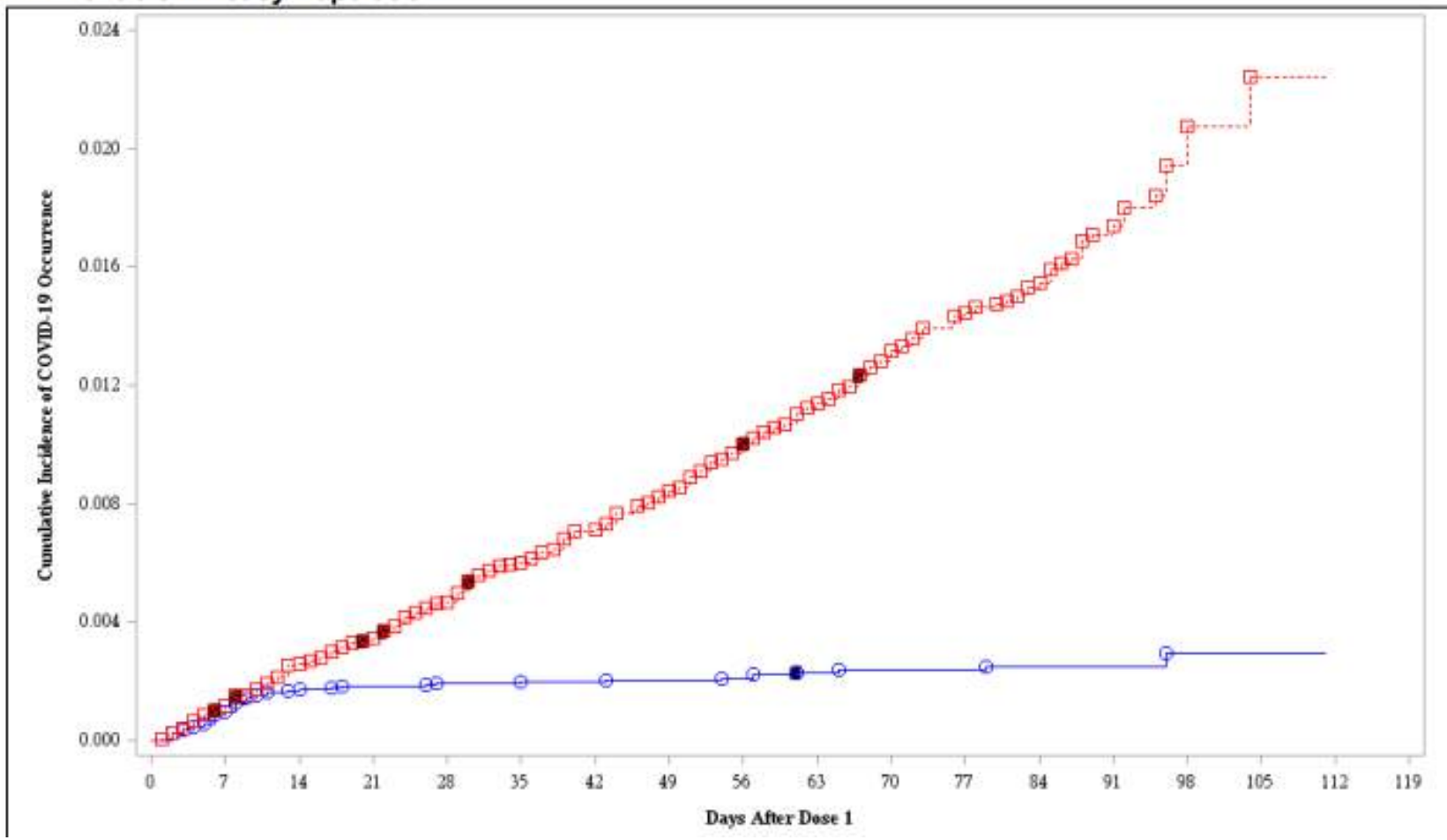
Sean Crotty, Scripps

- The mRNA in the vaccine is a modified sequence of mRNA that makes the amino acid sequence that folds together into the SPIKE protein.


Lipid nanoparticle
mRNA
CELL
Ribosome
Spike protein (prefusion conformation)

Pfizer/BioNTech vaccine

Figure 2. Cumulative Incidence Curves for the First COVID-19 Occurrence After Dose 1, Dose 1 All-Available Efficacy Population



- STUNNINGLY effective
- IN PREVENTING ANY CLINICAL DISEASE
- 95% effective overall

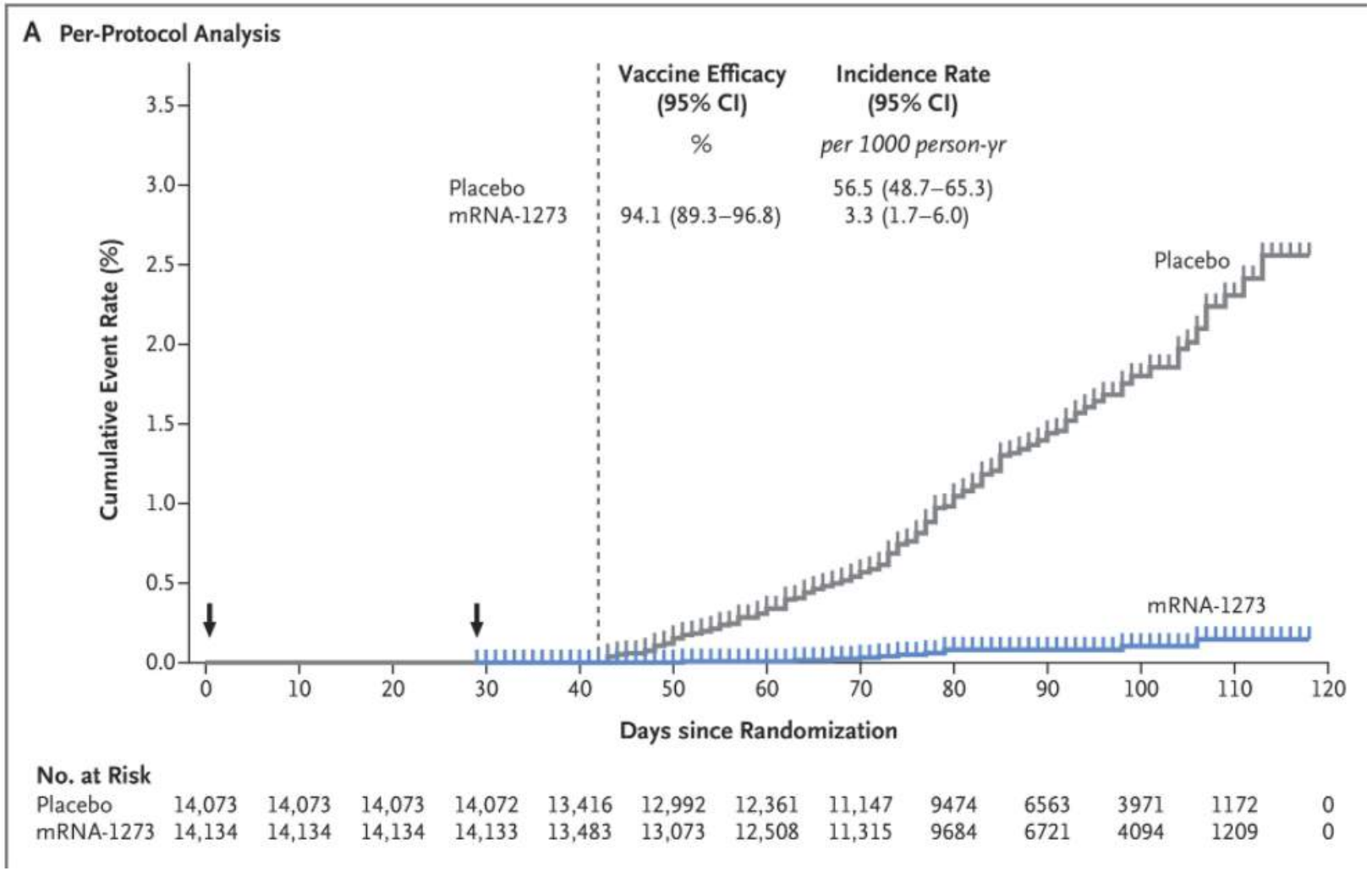
https://www.nejm.org/doi/full/10.1056/NEJMoa2034577

Efficacy subgroups

	BNT162b2	Placebo	Vaccine efficacy
Overall	8	162	95%
≥65	1	19	95%
≥75	0	5	100%
Black, Af Am	0	7	100%
LatinX	3	53	94%

Moderna Vaccine

	mRNA-1273	Placebo	Vaccine efficacy
Overall	11	185	94%
≥65	4	29	86%
Communities of Color	1	41	97.5%

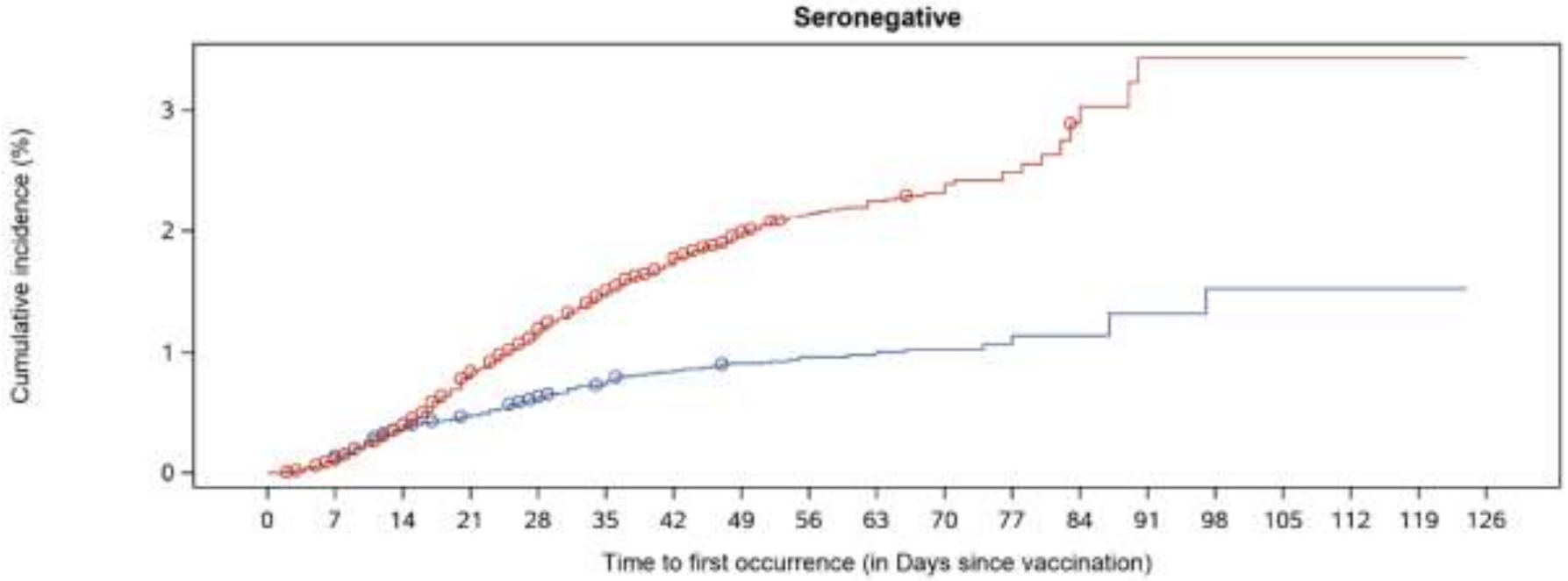


- 94% effective overall IN PREVENTING CLINICAL DISEASE

https://www.nejm.org/doi/full/10.1056/NEJMoa2035389?query=recirc_mostViewed_railB_article

Ad26.COV2.S Vaccine

- No deaths (vs. 5 placebo)
- By day 28, NO hospitalization in vaccine arm of trial (100%)
- 85% effective vs. severe/critical
- 66.7% effective vs. moderate/severe/critical
- ~70% effective against asymptomatic shedding (earlier data)
- Studied under different timeframe than Pfizer, Moderna



Ad26.COV2.S Vaccine efficacy day 28

	Ad26.COV2.S	Placebo	Vaccine efficacy
Overall	66	195	66.5%
≥60 (day 28)	14	43	67.9%
Black or Af Am	21 (3330)	66 (3300)	69%
LatinX/Hispanic	59 (8688)	153 (8741)	61.3%
DEATH (COVID-19)	0	8	100%

Vaccines practical considerations

- https://www.cdc.gov/vaccines/covid-19/vaccination-provider-support.html
- Vaccine storage and temperature monitoring equipment
- Vaccine inventory management
- Vaccine preparation
  - multidose vials
- Vaccine transport
  - Portable refrigerator
  - Containers, packouts
- Emergency vaccine storage and handling
- Vaccine storage and handling SOPs
- Proper storage conditions, monitor storage unit temperatures

FEW PRACTICAL POINTS RE: 3 CURRENT VACCINES

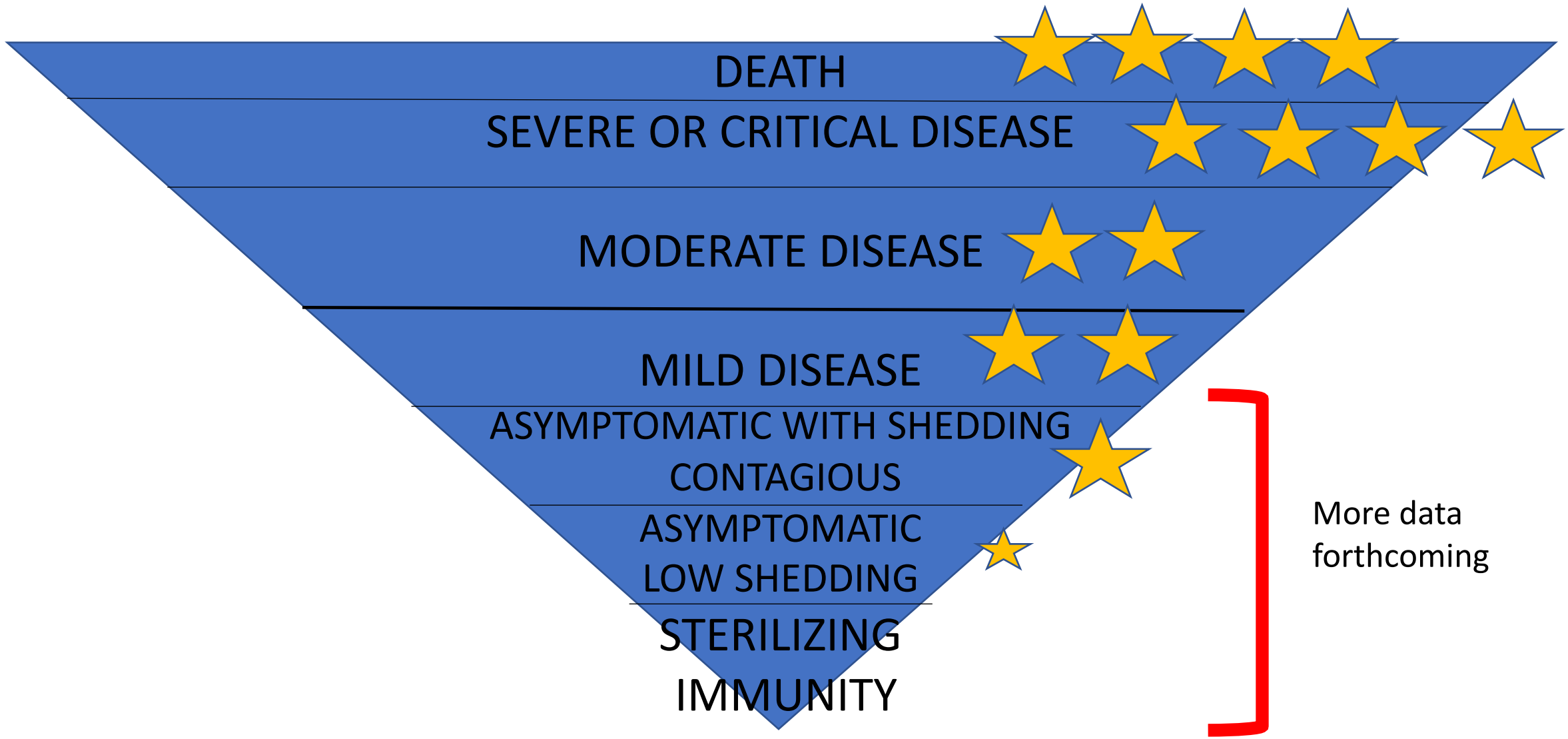
	PFIZER	MODERNA	JANSSEN
STORAGE	-80 - -60C UNTIL EXP. -25 - -15C (-13-5F) FOR TWO WEEKS REFRIGERATOR -2=8C FOR 5 (SUBSEQUENT) DAYS	REFRIGERATE 2-8C X 30 DAYS FREEZER UNTIL EXP.	REFRIGERATE 2-8C UNTIL EXP.
THAW			
TRANSPORT	CANNOT AGITATE	CANNOT AGITATE	
PREPARATION	ADD DILUENT 0.9% SALINE PRESERVATIVE FREE, MULTIUSE 6	NO DILUENT, MULTIUSE 10	NO DILUENT, MULTIUSE 5
ONCE PUNCTURED	6 HOURS REFRIGERATED	6 HOURS REFRIGERATED	6 HOURS REFRIGERATED, 2 HOURS ROOM TEMP
DOSING	2 DOSES AT LEAST 3 WEEKS APART	2 DOSES AT LEAST 4 WEEKS APART	SINGLE DOSE
OTHER	CANNOT SHAKE	CANNOT SHAKE	SHOULDN'T SHAKE

Home administration of COVID-19 vaccine

- CDC guidance
- https://www.cdc.gov/vaccines/covid-19/clinical-considerations/homebound-persons.html
- Assessing for allergies - determine if higher risk (duration monitoring, etc.)
  - Hx of allergy to any injectable or vaccine
  - Polyethylene glycol and polysorbate 80 allergies
- Developing script for staff to ascertain allergies prior to going out to house so don't waste doses or time
- Anaphylaxis is RARE with these vaccines
  - So far looking to be less than 0.002% (less than 1 in million)
- Anaphylaxis protocol/kit analogous to what use for home infusion with IM Benadryl, IM epinephrine and plan CPR, for contacting EMS

Vaccine effectiveness for the prevention of variant strains of COVID19

EFFICACY, EFFECTIVENESS, WHAT ARE OUTCOMES OF INTEREST?



Methods of assessing retention of vaccine efficacy against variants

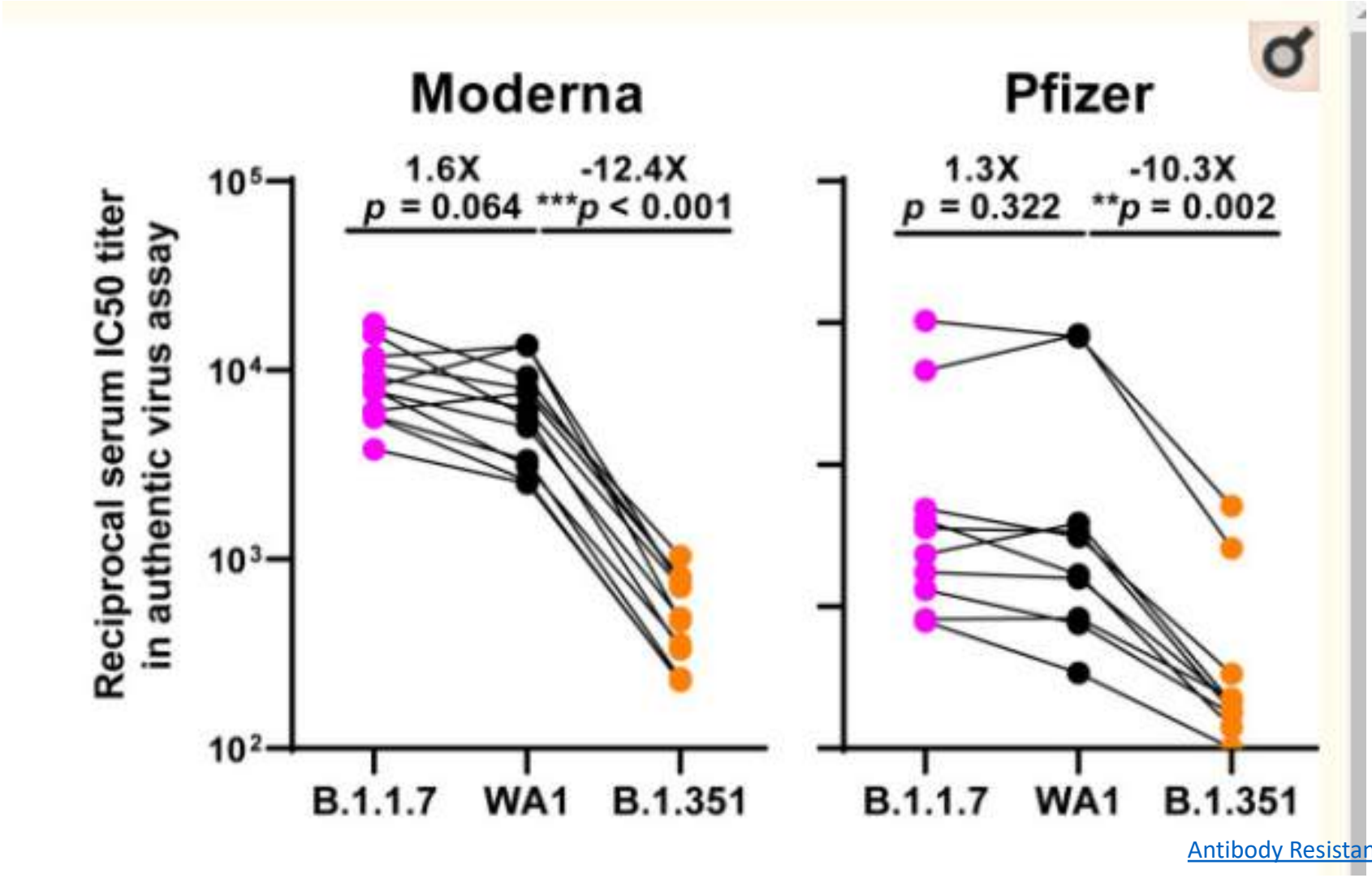
- In vitro antibody neutralization assays using serum from vaccinated people (or from people who have recovered from COVID-19)
- In vitro T-cell assays
- Clinical effectiveness and clinical trials data

- 'Variants of concern'
- B.1.1.7
- B.1.351
- P.1
- Other – 'variants of interest'
  - B.1.427/B.1.429 (20CL452R), B.1.526

Antibodies, B-cells, Adaptive immune response

- Includes **B-cells** and antibodies
- Humoral immunity or ‘antibody-mediated’ immunity
- BUT ALSO - **T-cells**
- Cell-mediated immunity
- Activation of B-cells with T-helper cells activation → effective immune response and goal of vaccines
- T cell mediated immunity to vaccine also develops by presentation of ‘epitopes’ and recognition based on our HLA makeup.

Variant impact on vaccine-induced antibody ability to neutralize virus



B.1.1.7
Vaccinee sera (2x)

B.1.351
6-8.6X more resistant to vaccinee sera

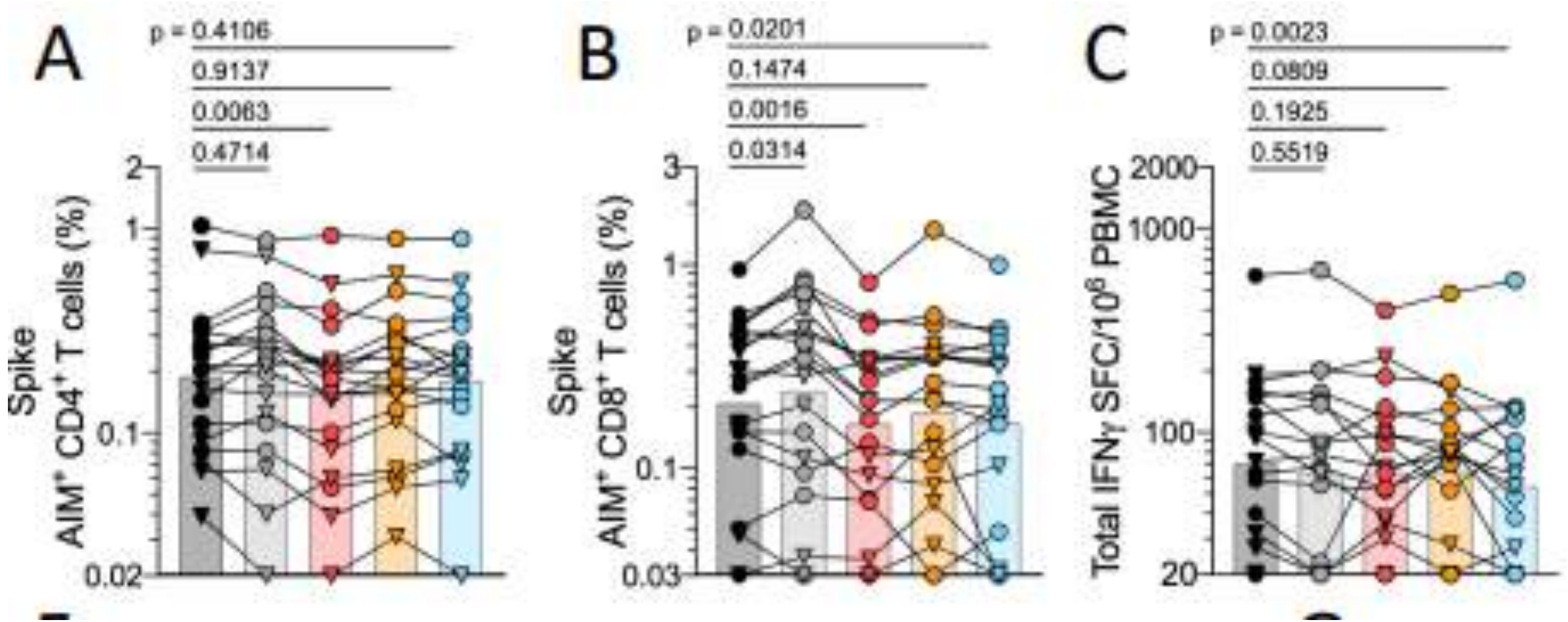
[Antibody Resistance of SARS-CoV-2 Variants B.1.351 and B.1.1.7 (nih.gov)]

CD4 and CD8 responses have role in resolution

- People with early and robust CD4, CD8 have milder disease
- CD4 and CD8 modulate disease severity
- T-cells don’t prevent infection but can modulate disease severity
- People with agammoglobulinemia or on rituximab can have uncomplicated disease
- Robust CD4+ and CD8+ T cell memory induced after COVID-19 AND these vaccines elicit CD4+ and CD8+ T-cell responses
- Variant that may escape antibody recognition, T-cells may still be able to modulate disease severity – for example associated with more severe severity or death

T cell responses of vaccinated against different Spike variants – NO decrements

- Black – wild type, grey B.1.1.7, red B.1.351, orange P.1., light blue Cal.20.C



Negligible impact of SARS-CoV-2 variants on CD4+ and CD8+ T cell reactivity in COVID-19 exposed donors and vaccinees (biorxiv.org)

Effects of these variants of concern on T cell responses

- T-cell responses largely unaffected in the variants thus far
- Possible vaccines inducing significant T-cell responses associated with protection from severe disease EVEN in face of escape from antibody response
- Future vaccines – could incorporate antigens to enhance T cell responses

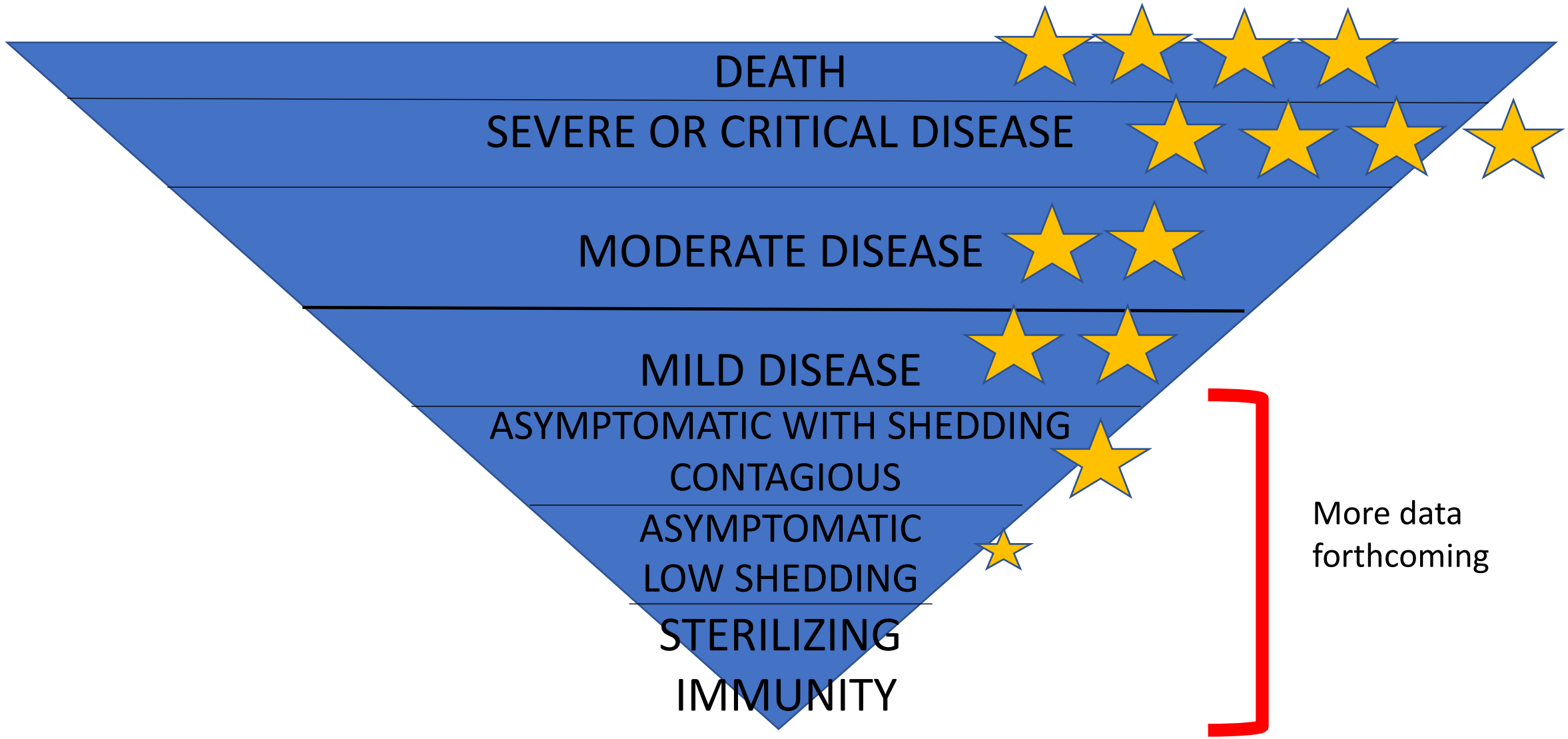
What about clinical efficacy against variants

- Parallel to in vitro data
- B.1.1.7 good data that vaccine efficacy remains
- Israel high prevalence B.1.1.7 and maintains efficacy
  - Pfizer vaccine being used there

Ad26.COV2.S Vaccine efficacy vs. variants

- At least 28 days after vaccination,
- Overall Efficacy US: 72.0% (58.2, 81.7)
- 68.1% (48.8, 80.7) in Brazil
- 64.0% (41.2, 78.7) in South Africa
- Appears OVERALL efficacy against B.1.351 variant decreased slightly (~8%)
- HOWEVER, MAINTAINS protection against DEATH and SEVERE disease
- May be a function of RETAINED cell mediated immunity
  - Preventing severe infection

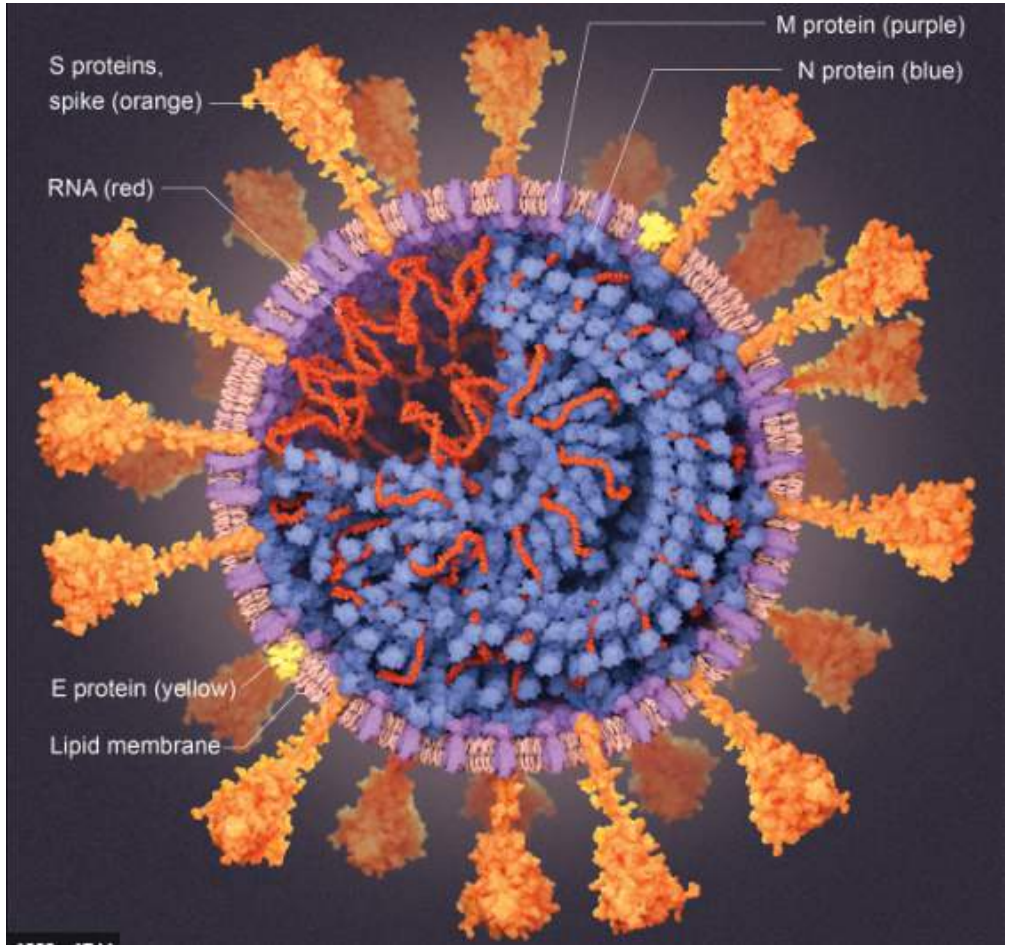
EFFICACY, EFFECTIVENESS, WHAT ARE OUTCOMES OF INTEREST?



More data continues to emerge

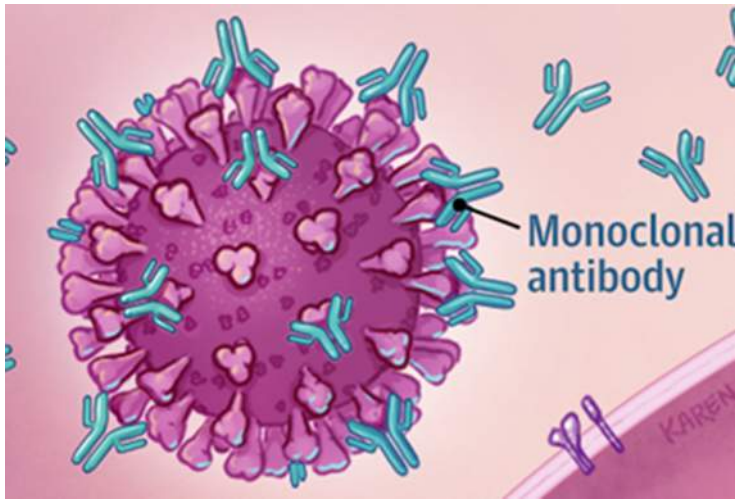
Anti-SARS-CoV-2 Antibody Therapy

- Bamlanivimab
- Bamlanivimab and etesivimab
- Casirivimab/Imdevimab



Monoclonal antibodies

- Block epitopes of the spike protein receptor-binding domain of SARS-CoV-2
- **Bamlanivimab**
- **Combination** bamlanivimab and etesevimab
- Combination of **casirivimab/imdevimab**



Chen P et al. NEJM Oct 28, 2020;
https://www.fda.gov/media/143892/download

Goals of monoclonal antibody therapy

- Prevent progression to severe disease
- Prevent hospitalization
- Prevent death
  - Emerging data
- Prevent CLINICAL disease when given prophylactically after high risk exposure
  - In unvaccinated individuals

Monoclonal Antibodies

- BLAZE-1 trial Bamlanivimab (interim analysis)
  - 452 outpts w/ mild to mod COVID-19 (SpO2 >93% RA) with first positive SARS-CoV-2 result ≤3d prior to infusion.
  - Randomized to one of three doses of mAb (700mg, 2800mg or 7000mg) vs placebo.
  - Randomization stratified by duration symptoms (≤8d vs >8d)

Chen P et al. NEJM Oct 28, 2020

Monoclonal Antibodies

- BLAZE-1 trial Bamlanivimab (Prelim data)
  - Symptom Score: modest benefit with BAM- better change in symptom score from baseline c/w placebo
  - **COVID-19- Related Hospitalization**
    - **BAM 1.6% (pooled doses) vs placebo 6.3%**
    - **Post-hoc analysis of pts ≥ 65yo or BMI ≥ 35: BAM 4% vs placebo 15%**

Table 3. Hospitalization.*

Key Secondary Outcome	LY-CoV555	Placebo	Incidence
	no. of patients/total no.		%
Hospitalization		9/143	6.3
	700 mg, 1/101		1.0
	2800 mg, 2/107		1.9
	7000 mg, 2/101		2.0
	Pooled doses, 5/309		1.6

Chen P et al. NEJM Oct 28, 2020

Monoclonal Antibodies

- Bamlanivimab + Etesevimab
  - 2800mg bamlanivimab + 2800mg etesevimab
  - Same inclusion and exclusion criteria
  - Hospitalization or ED visits by D29: 0.9% in combination therapy group
  - Pts 65yo+ or BMI of 35+ had hospitalization rate 13.5% w/ placebo (7/52pts) vs 0% with combination (0/31 high risk pts)
  - Immediate hypersensitivity reactions: 6 BAM, 2 combo, 1 placebo

Gottlieb RL et al. JAMA Jan 21,2021

BLAZE-1 (Phase 3)

- Additional phase 3 data
  - 518 additional subjects in combination therapy arm (2800 mg doses) versus 517 subjects in placebo arm (all high risk patients)
  - **Primary endpoint:** proportion of subjects with COVID-19 related hospitalization or death by any cause at day 29
    - **36/517 (7%) in placebo versus 11/518 (2%) in combination therapy arm (p<0.001) – 70% reduction**
    - 10 deaths in placebo group and no deaths in combination therapy group (p<0.001)
  - At Day 7, 29% of subjects treated with placebo and 10% of subjects treated with combination therapy had persistently high viral loads (p<0.000001), which was defined as SARS-CoV-2 viral load >5.27

https://www.fda.gov/media/145802/download

Casirivimab/Imdevimab

- Press Release 2/26/21 – HALTED enrollment in placebo arm of their casirivimab/imdevimab trials because the data monitoring committee found clear clinical efficacy on reducing the rate of hospitalization and death with both the 1,200 mg and 2,400 mg doses of REGEN-COV compared to placebo
- Detailed results expected in March 2021

https://newsroom.regeneron.com/news-releases/news-release-details/independent-data-monitoring-committee-finds-clear-efficacy-regen

Monoclonal Antibodies

- REGN-COV2 trial: casirivimab-imdevimab (interim analysis)
  - 275 symptomatic non-hospitalized mild pts < 7d of symptom and < 72hr of positive SARS-CoV-2 result.
  - Randomized 1:1:1 placebo, 2.4g REGN-COV2 or 8.0g REGN-COV2
  - Outcomes:
    - Viral load change from day 1 to day 7, quantitative RT-PCR of NP swab
    - ≥ 1 COVID-19 medical visit through day 29 (telemed, OV, urgent care, ED, hospitalization)
    - Pre-specified analysis by baseline serum antibody status

Weinreich DM et al. NEJM Jan 21, 2021

Monoclonal Antibodies

- REGN-COV2 trial: casirivimab-imdevimab (interim analysis)
- Results:
    - Lower VL in mAb group, esp in baseline seronegatives
    - 3% of REGN-COV2 pts vs 6% of placebo w/ medical visit
    - 2% vs 4% hospitalized/ED w/in 28d
    - Baseline serum Ab-negative group: 6% REGN-COV2 vs 15% placebo
    - Post-hoc analysis of more patients –pts at high risk for disease progression: hospitalization and ER visits in 3% of mAb pts vs 9% in placebo group.

    - 3 infusion rxn or hypersensitivity rxn in both groups
    - Estimated half-life 25 to 37d for both antibodies

Weinreich DM et al. NEJM Jan 21, 2021

Monoclonal Antibodies

- EUA –updated Feb 9, 2021
  - Bamlanivimab 700mg + etesevimab 1400mg OR casirivimab/imdevimab 2.4g (1,200mg of each)
  - Within 10d of symptom onset for non-hospitalized pts with mild to moderate COVID-19 at high risk for severe disease/hospitalization.
    - Body mass index (BMI) ≥35
    - Chronic kidney disease
    - Diabetes mellitus
    - Immunocompromising condition
    - Currently receiving immunosuppressive treatment
    - Aged ≥65 years
    - Aged ≥55 years, *and* Cardiovascular disease, *or* Hypertension, *or COPD or other chronic respiratory disease* .

Prophylaxis strategies

- Evolving story in the context of more widespread vaccination
- Bamlanivimab – prevented symptomatic COVID-19 in nursing home patients and staff
  - OR 0.43 for symptomatic COVID-19 in bamlan vs. placebo overall
  - OR 0.20 for the patients – 80% lower risk contracting COVID-19
- DATA at CROI March 9 – 10% of household contacts with placebo became infected. 5.3% receiving casirivimab and imdevimab did but NONE developed symptoms and NONE had viral loads >10^4 copies/mL in nose
  - 100% symptomatic infection prevented
  - CROI abstract 123LB, March 9, 2021

Monoclonal Antibodies

- Not for inpatients
  - Bamlanivimab trial halted in hospitalized pts because of futility
  - Casirivimab/indevimab stopped enrolling high flow and MV pts due to unfavorable risk/benefit. Ongoing enrollment of low flow and no O2 inpatients (can obtain compassionate use)
  - EXCEPTION – can used in high risk hospitalized persons if hospitalized for another reason

- Future:
  - Prophylaxis POST-Exposure
  - Long-acting antibody combination AZD7442 (Astra Zeneca) proposed duration 6-12mos

Wang P et al. bioRxiv 2021

Monoclonal antibodies

- **Earlier the better (in trials often <3 days from symptom onset, EUA – 10 days)**
- **Target patients at high risk for severe disease based on risks**
- **List:**
  - Within 10d of symptom onset for non-hospitalized pts with mild to moderate COVID-19 at high risk for severe disease/hospitalization.
    - Body mass index (BMI) ≥35
    - Chronic kidney disease
    - Diabetes mellitus
    - Immunocompromising condition
    - Currently receiving immunosuppressive treatment
    - Aged ≥65 years
    - Aged ≥55 years, *and* Cardiovascular disease, *or* Hypertension, *or COPD or other chronic respiratory disease* .

- **(eg age, BMI, DM, immunocompromise)**
- If you target them earlier enough, they are still feeling okay – challenging…

Monoclonal infusion

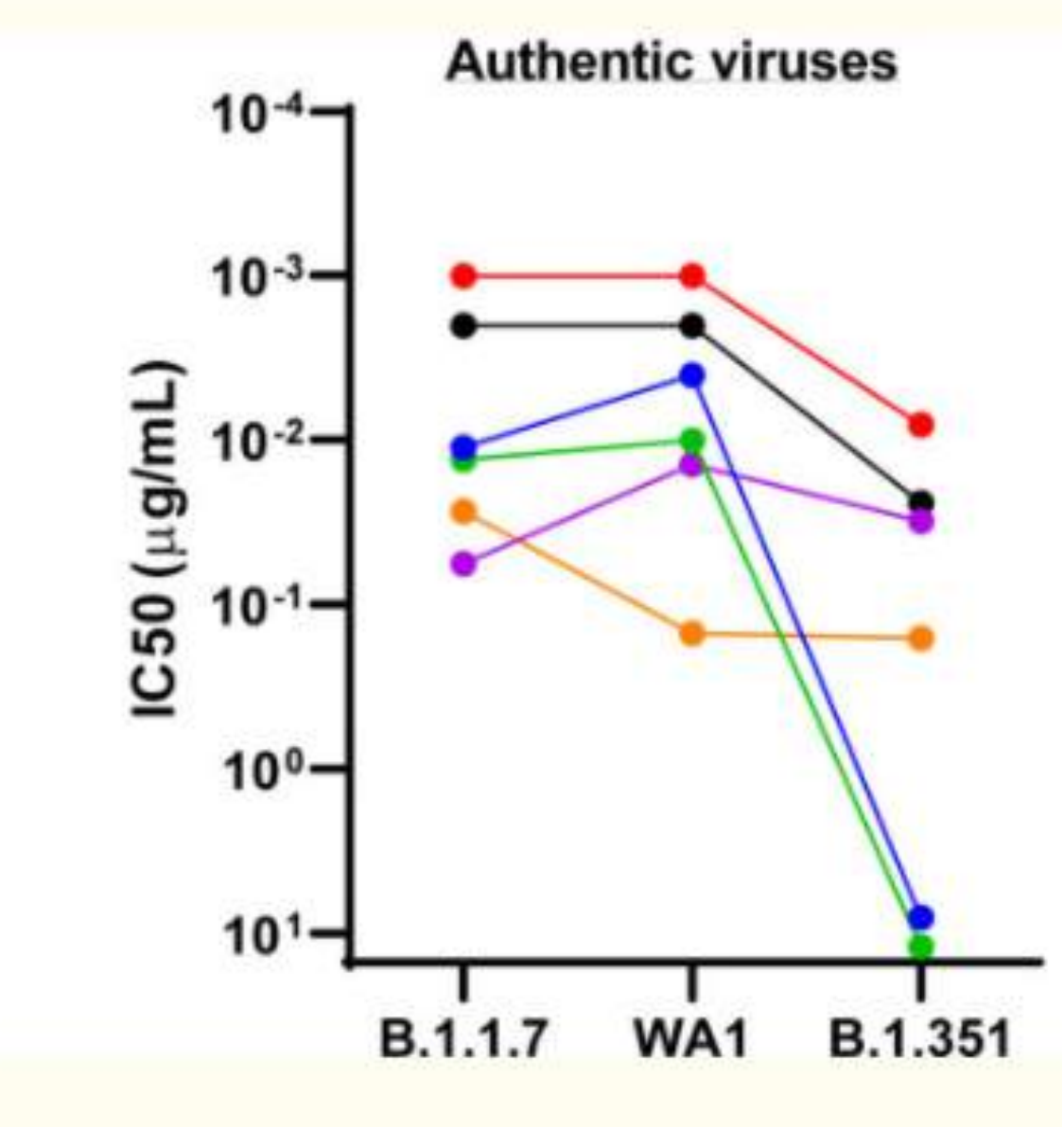
- Medication administered as single infusion
- ≥1 hour of subsequent observation

- **Side effects**
- Well tolerated
- Possible side effects include but are not limited to nausea, vomiting, diarrhea, itching, dizziness, headache, fatigue, fever, and chills.
- Has potential for anaphylaxis - severe allergic reactions in <1% of cases

- **Should still quarantine after receipt**
- **Should delay vaccination after receipt**
- **CDC guidelines**

Monoclonals and variants

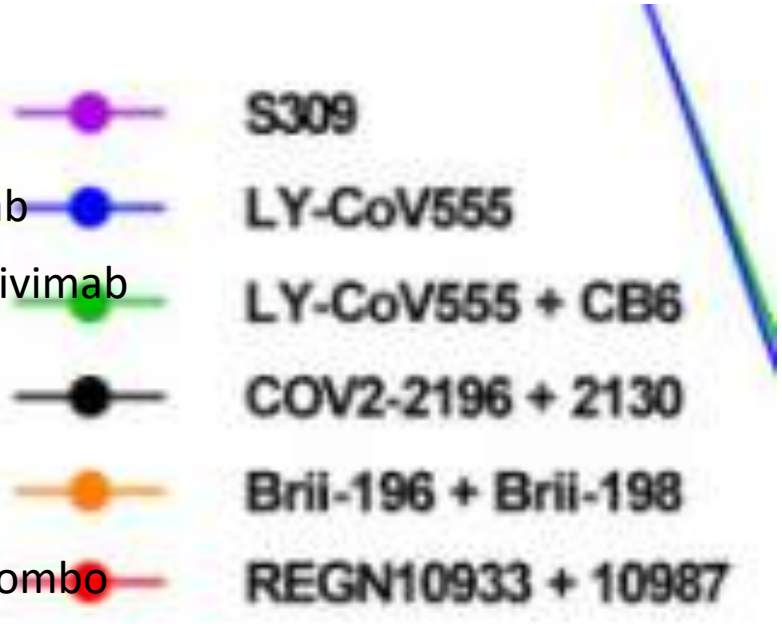
[Antibody Resistance of SARS-CoV-2 Variants B.1.351 and B.1 (nih.gov)]



Bamlanivimab

Bamlan/etesivimab

Regeneron combo



Monoclonal antibodies and variants – data evolving

- Viral variants with spike protein mutations
  - **B.1.1.7 (UK variant):** Bamlanivimab, bam/etesevimab and casirivimab/imdevimab retain significant neutralizing activity
  - **B.1.351 (South Africa Variant):** bamlanivimab and bamlanivimab/etesevimab unable to neutralize. Casirivimab has no activity.
  - Combination casirivimab/imdevimab still has activity but reduced

IDSA Guidelines (updated 3/2/21)

- Recommendation 13: Among ambulatory patients with mild to moderate COVID-19 at high risk for progression to severe disease, the IDSA guideline panel suggests bamlanivimab/etesevimab rather than no bamlanivimab/etesevimab. (Conditional recommendation, low certainty of evidence)
  - Remarks:
    - Patients with mild to moderate COVID-19 who are at high risk of progression to severe disease admitted to the hospital for reasons other than COVID-19 may also receive bamlanivimab/etesevimab.
    - For patients at high risk for progression to severe disease, the data are strongest for bamlanivimab/etesevimab. Bamlanivimab monotherapy or casirivimab/imdevimab may have similar clinical benefit, but data are more limited.
    - There are limited data on efficacy of bamlanivimab/etesevimab in high-risk patients between 12 and 18 years of age.
- Recommendation 14: Among hospitalized patients with severe COVID-19, the IDSA guideline panel recommends against bamlanivimab monotherapy. (Strong recommendation, Moderate certainty of evidence)

https://www.idsociety.org/practice-guideline/covid-19-guideline-treatment-and-management/

Timing regarding monoclonals and vaccination

- Not tons of data
- If <7 OR 14 OR 28 days after vaccine dose AND fulfills high risk criteria AND dx within COVID-19 within 10 days, consider
- IF fully vaccinated > 7 or 14 or 28 days ago, at this point in most people would not give monoclonal
- Likely some exceptions if profound defects in antibody formation (eg, rituximab) and handle case by case

- If receives monoclonal therapy, defer vaccination at least 90 days
- The COVID-19 infection itself is going to provide a duration of immunity
- To avoid interference of monoclonal antibody with vaccine-induced immune response

NEW THERAPIES…..

The Days are Just Packed, Bill Waterson

Thank you!