

Vermont Medical Society: Update on COVID-19 Vaccines

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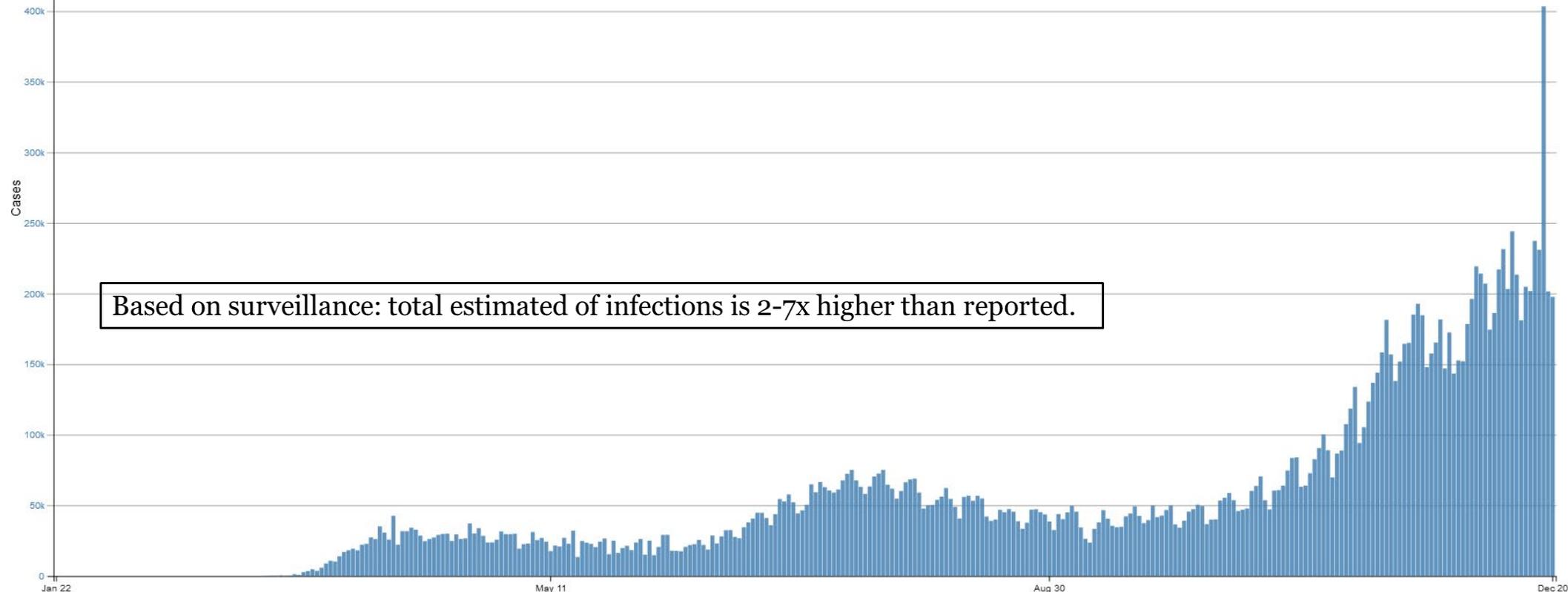
Trends in COVID-19 reported cases in the United States (Jan-Dec 2020)

TOTAL CASES
17,790,376
+197,616 New Cases

CASES PER 100,000 PEOPLE
5,438

TOTAL DEATHS
316,844
+1,584 New Deaths

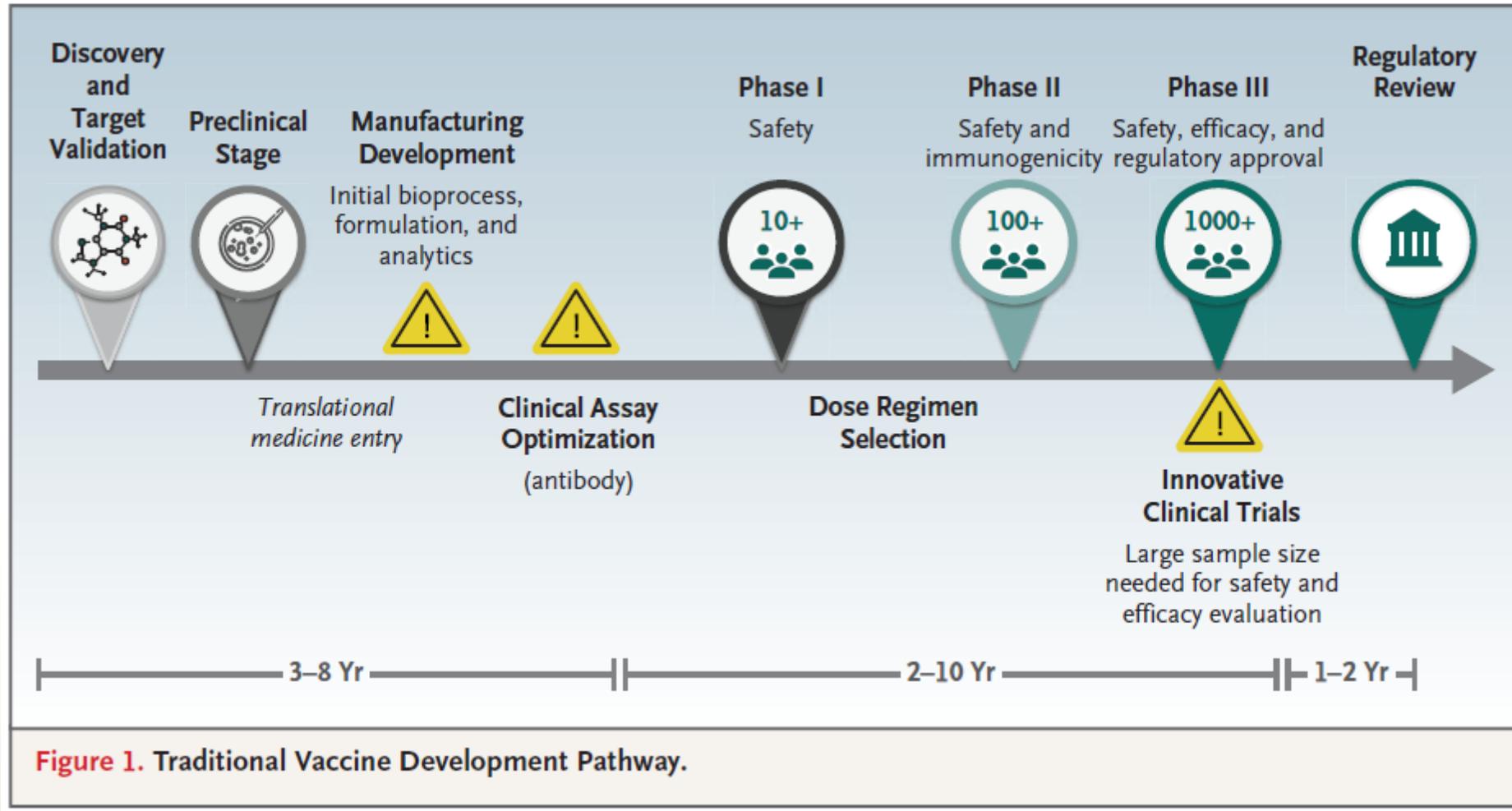
CDC | Updated: Dec 21 2020 12:16PM



<https://www.cdc.gov/covid-data-tracker/>

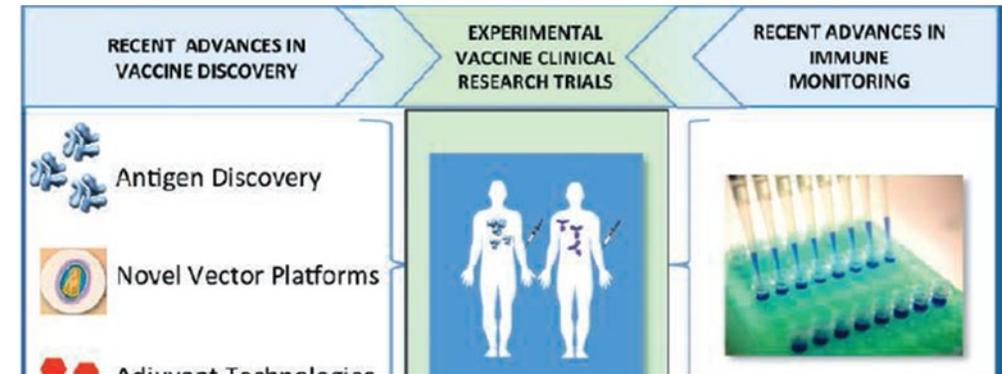


Human Vaccine Development



Safely accelerating vaccine development

- Massive financial investment (“at-risk” vaccine development).
~\$9 billion.



NO SAFETY or REGULATORY SHORTCUTS

- Harmonized and seamless trial designs
- Prioritized work

IMPROVED SUCCESS RATES IN VACCINE DEVELOPMENT

Accelerating next-generation vaccine development. Recent advances in vaccine discovery and immune monitoring will enable new human immunology–based clinical research studies to address major gaps in knowledge of vaccine-induced human immune responses and thereby accelerate development of next-generation vaccines. [Photo credit: IAVI]

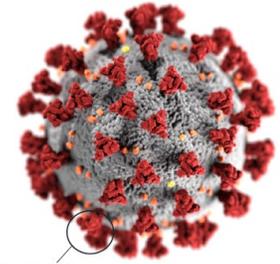


Pfizer and Moderna COVID-19 Vaccines

- Highly effective in preventing COVID-19 illness.
- No major safety issues have been identified.
- Short term side effects are similar to other licensed vaccines and include arm pain, chills, fatigue in the first 1-2 days after vaccination.



Snapshots of the mRNA vaccines (Pfizer and Moderna)



- Injectable (intramuscular, IM) vaccines.
- Contain the nucleic acid (mRNA) of the SARS-CoV2 spike protein in a lipid particle.
- Do **not** contain live virus. Do **not** enter the nucleus or modify the human genome.
- Two-dose vaccines, 21 (Pfizer) or 28 (Moderna) days apart.
- Broad racial/ethnic groups, co-morbidities and ages were included in the phase III studies.



Vaccine Efficacy: Protection against symptomatic COVID-19

Pfizer/BioNTech

95%

(CI: 90.3-97.6%)

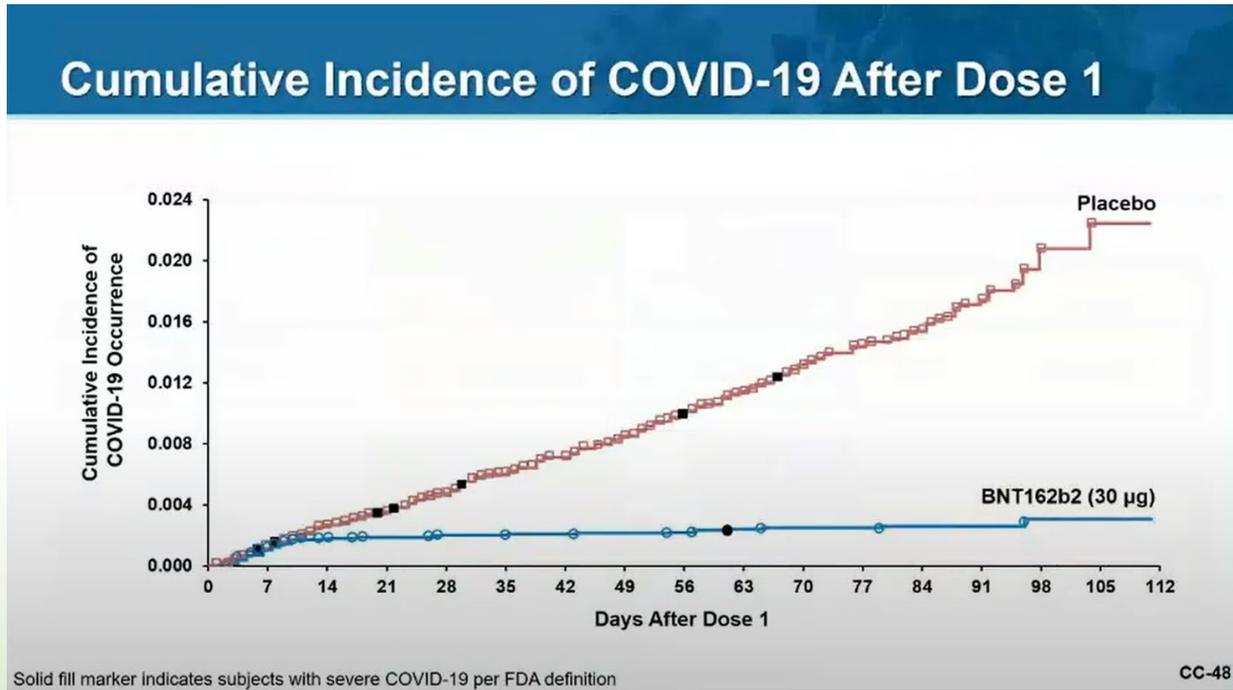
Moderna

94.1%

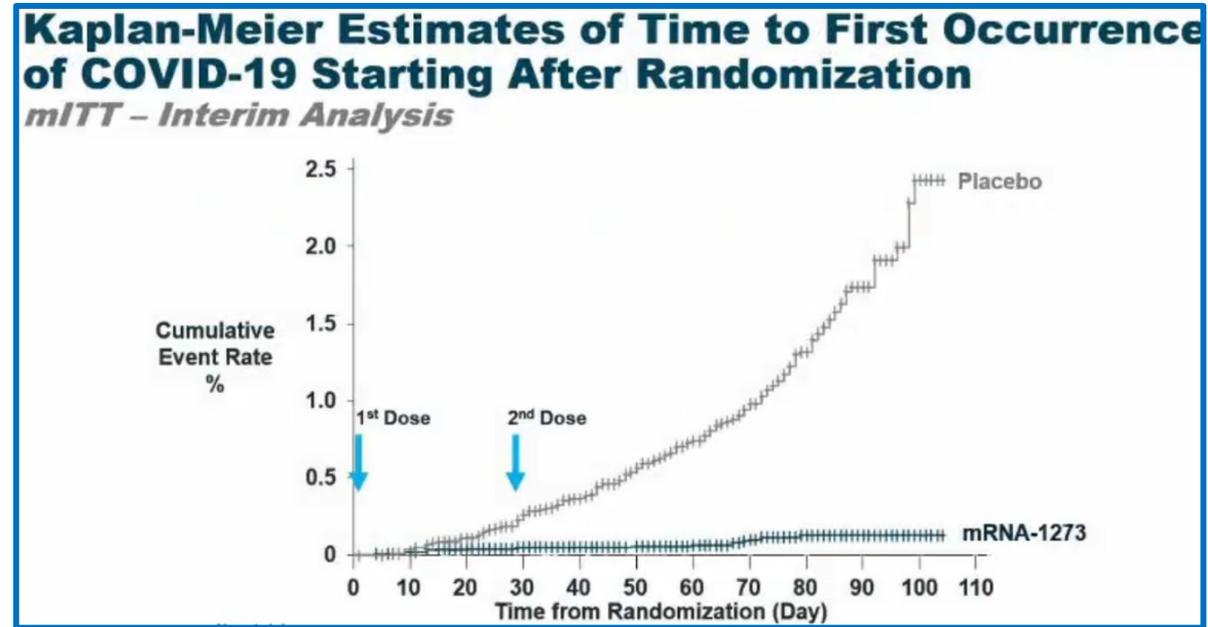
(CI: 89.3-96.8%)



After vaccination, most cases of COVID-19 are in subjects who received placebo.



Pfizer/BioNTech



Moderna



Interim data **suggest:** (although numbers are still small)

- Efficacy in **all age groups** is high and comparable
- Efficacy for African Americans and Latinx individuals is high and comparable.
- Efficacy is **not diminished** in individuals with obesity, malignancy, cardiovascular, chronic pulmonary disease, diabetes, hypertension.
- Early data suggest protection against severe disease (very small numbers).



First COVID-19 Occurrence From 7 Days After Dose 2 by Comorbidity Status – Evaluable Efficacy (7 Days) Population

Subjects WITHOUT Evidence of Infection Prior to 7 days after Dose 2

	BNT162b2 (30 µg) N=18,198		Placebo N=18,325		VE (%)	(95% CI)
	n	Surveillance Time (n)	n	Surveillance Time (n)		
Overall	8	2.214 (17,411)	162	2.222 (17,511)	95.0	(90.0, 97.9)
Comorbidity						
No comorbidity	4		76		94.7	(85.9, 98.6)
Any comorbidity	4		86		95.3	(87.7, 98.8)
Any malignancy	1		4		75.7	(-145.8, 99.5)
Cardiovascular	0		5		100.0	(-0.8, 100.0)
Chronic pulmonary disease	1		14		93.0	(54.1, 99.8)
Diabetes	1		19		94.7	(66.8, 99.9)
Obese (≥ 30.0 kg/m ²)	3		67		95.4	(86.0, 99.1)
Hypertension	2		44		95.4	(82.6, 99.5)
Diabetes (including gestational diabetes)	1		20		95.0	(68.7, 99.9)

Pfizer and Moderna COVID-19 vaccines: side effects

- Local and systemic side effects after both doses should be expected:
 - Injection site pain, fatigue, chills, muscle pain, headache are the most common.
 - Severity is mild-moderate in most patients.
- Side effects may be more frequent after second dose.
- Side effects may be more frequent/intense in younger patients > older patients.
- Almost all side effects abate by day 3.



Pfizer vs. Moderna

- Phase II/III trial of 43, 448 subjects.
- Emergency Use Authorization (12/11/2020): Use in all persons over 16 years of age.
- Ongoing studies for children, pregnant or lactating women or immunocompromised persons.
- Must be stored in -70C freezer
- Doses at day 1,21 (3 weeks)
- Insufficient data to show prevention vs. severe disease (n=9P/1V). Highly likely.
- Side effects higher in young, esp after 2nd dose

- Phase III trial of 30,351 subjects
- Emergency Use Authorization (12/18/2020): Use in all persons **over 18 years of age.**
- Ongoing studies for children, pregnant or lactating women or immunocompromised persons.
- **Can be stored in regular (-20C) freezer**
- Doses at **day 1, day 28 (4 weeks)**
- **More** data suggesting protection vs. severe disease (n=30P/OV)
- Similar, if not more pronounced side effects vs. Pfizer.



Other issues for your radar (Pfizer and Moderna)

- No long term side effects related to these vaccine have been found yet.
- Anaphylaxis (Pfizer): Seen in two UK volunteers (09DEC2020) with past history of significant allergies. Not seen in phase III trial.
 - Do not vaccinate if past anaphylactic response to any component of the Pfizer COVID vaccine
 - Precaution if known allergic reaction to other vaccines or injectable therapy.
- Facial swelling after Moderna vaccine (n=2): Subjects with dermal fillers.
- Bell's palsy, a few cases in both Pfizer and Moderna:
 - This frequency is consistent with background rate in general population.

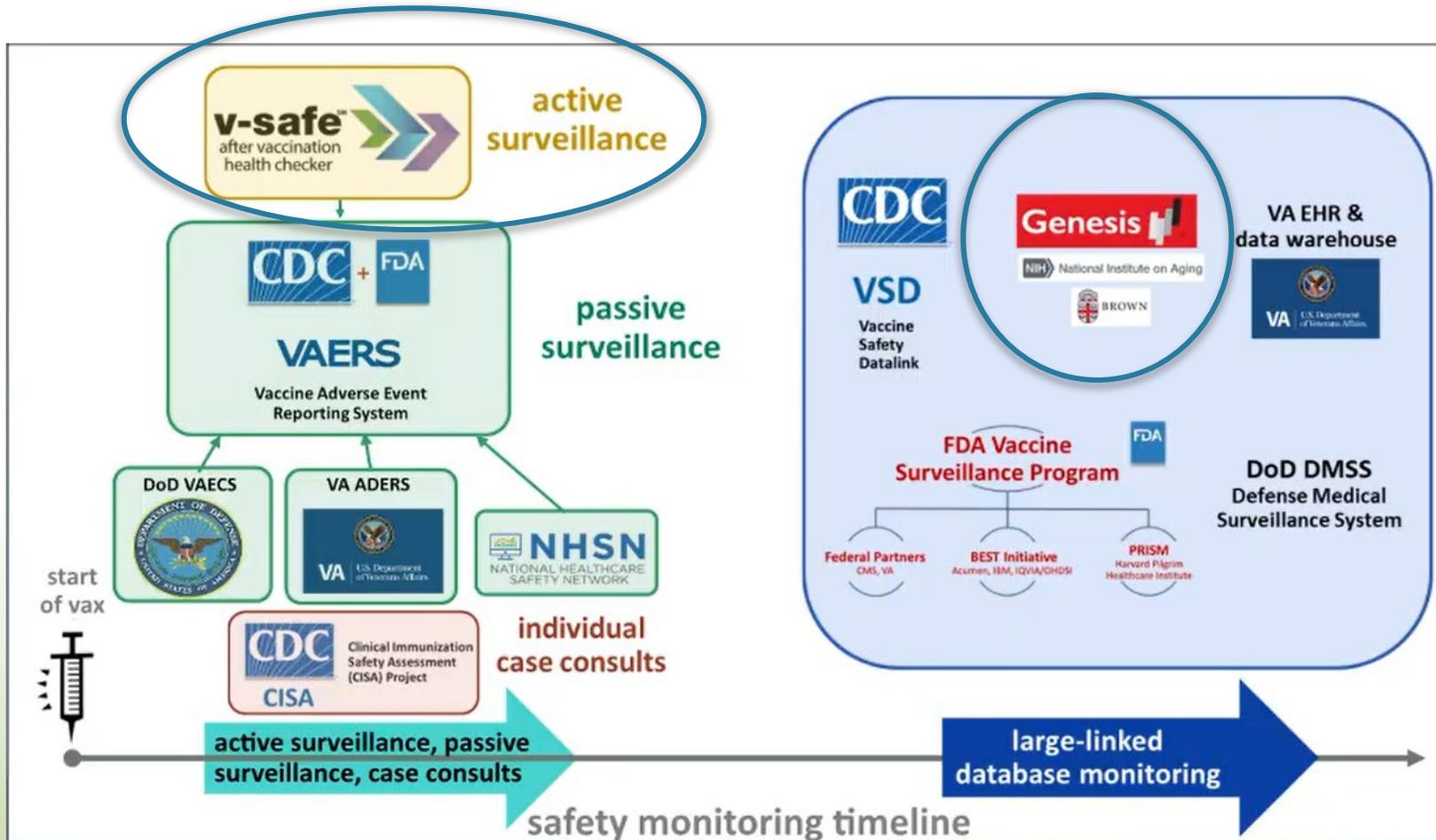


Many results are not yet known and are still under careful study:

- Durability of protection.
- Protection from infection-asymptomatic carriage-transmission (presumed based on animal data).
- Safety and efficacy in pregnant or lactating women, immunocompromised patients, and children.
- Co-administration with other vaccines, like influenza.
- Different COVID-19 vaccines, used together.
- How the vaccine works in real-life situations (effectiveness)



Safety Follow up: Usual and Expanded



VAERS: Required reporting

V-safe: Voluntary. Text-based

Genesis: for Long Term Care Facilities

Case Control Study: Health Care workers (safety and effectiveness)



What's next

- Focus on the roll out. Vermont and NYS Departments of health set priority groups and distribution plans.
 - Long term care facility residents and staff
 - High risk HCW
- Expect vaccine shortages AND vaccine hesitancy.
- Watch for news on other COVID-19 Vaccines in 2021:
 - Viral vectored: Janssen (J&J) and AstraZeneca: expect FDA review in the winter.
 - Recombinant Protein: Novavax starting Phase III trial. GSK/Sanofi and Merck-regrouping.



RESOURCES

- What clinicians need to know:
 - <https://www.cdc.gov/vaccines/covid-19/downloads/pfizer-biontech-vaccine-what-Clinicians-need-to-know.pdf>
 - https://emergency.cdc.gov/coca/ppt/2020/12.18.2020_COCA_Pfizer-BioNTech-and-Moderna_COMBINED-2.pdf
- Comprehensive COVID vaccine toolkit from the CDC:
<https://www.cdc.gov/vaccines/covid-19/health-systems-communication-toolkit.html>
- The FDA's Emergency Use Authorization for the Pfizer and Moderna COVID vaccines:
 - <https://www.fda.gov/emergency-preparedness-and-response/counterterrorism-and-emerging-threats/coronavirus-disease-2019-covid-19>
 - <https://www.fda.gov/advisory-committees/advisory-committee-calendar/vaccines-and-related-biological-products-advisory-committee-december-10-2020-meeting-announcement#event-information>
 - <https://www.fda.gov/advisory-committees/advisory-committee-calendar/vaccines-and-related-biological-products-advisory-committee-december-17-2020-meeting-announcement>

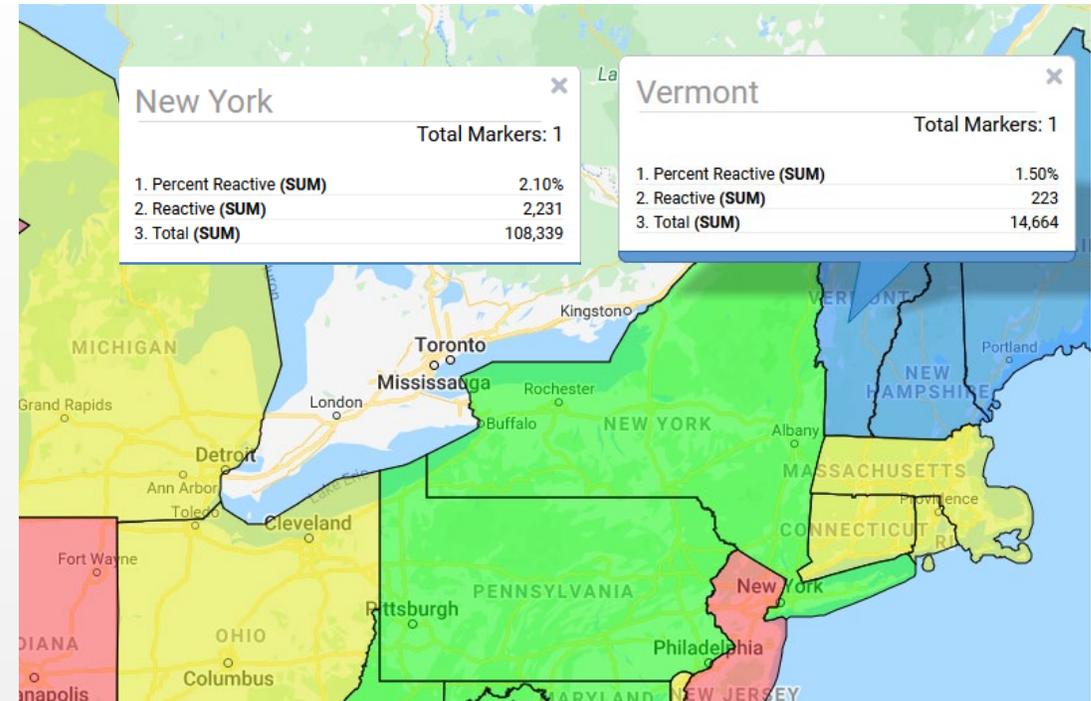
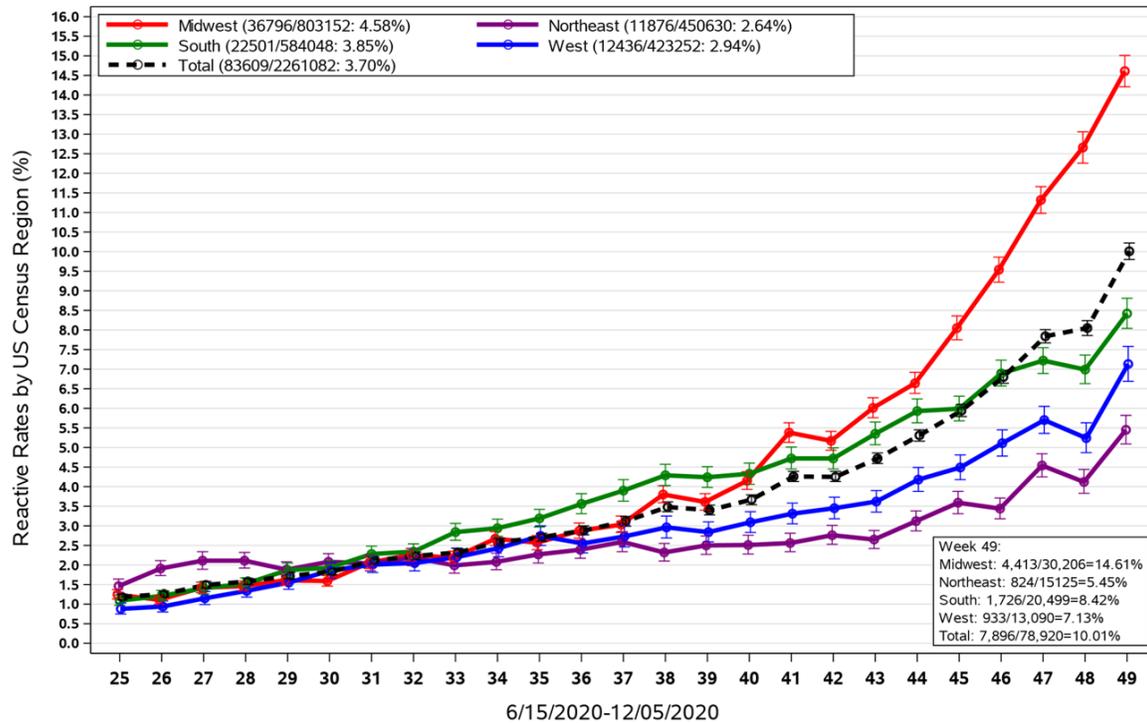


Extra slides

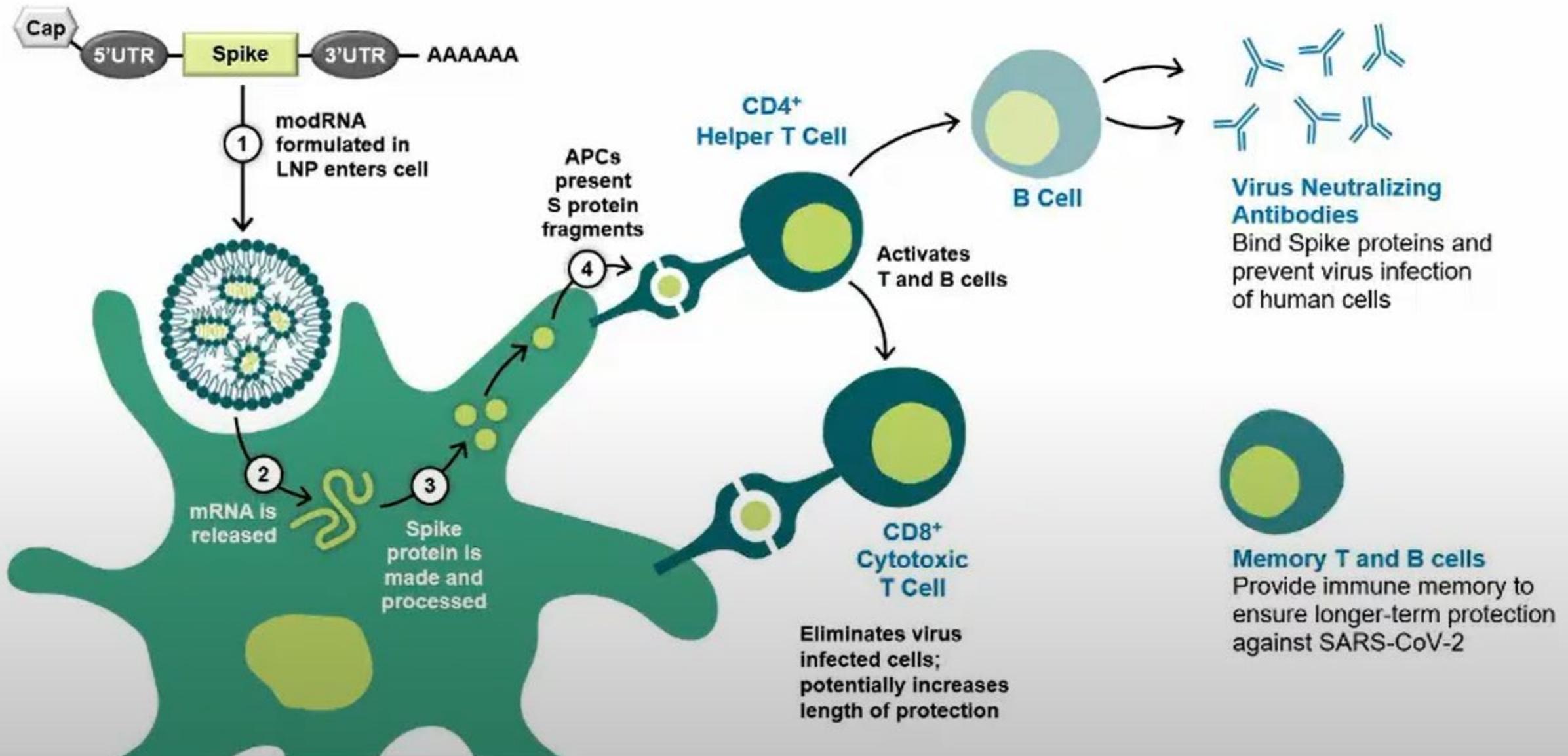


COVID-19 antibody data (Dec 8, 2020): VT and Northern NY are nowhere near 'herd immunity'

Percent Antibody Reactive by US Census Region



Mode of Action of the BNT162 Vaccine Candidates



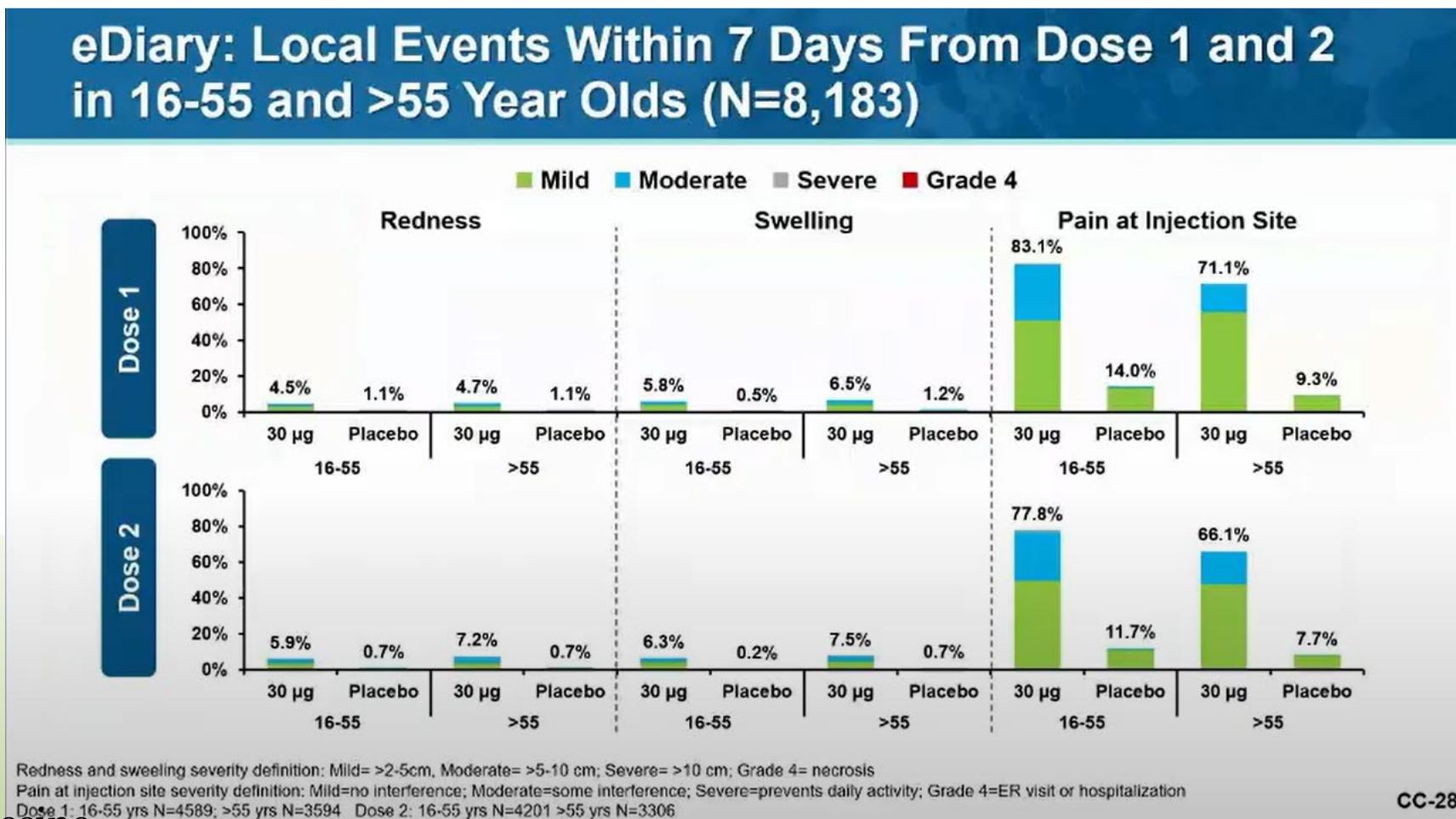
Ingredients* included in mRNA COVID-19 vaccines

Description	Pfizer-BioNTech COVID-19 vaccine	Moderna COVID-19 vaccine
mRNA	nucleoside-modified mRNA encoding the viral spike (S) glycoprotein of SARS-CoV-2	nucleoside-modified mRNA encoding the viral spike (S) glycoprotein of SARS-CoV-2
Lipids	2[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide	1 monomethoxypolyethyleneglycol-2,3-dimyristylglycerol with polyethylene glycol of average molecular weight 2000 (PEG2000-DMG)
	1,2-distearoyl-sn-glycero-3-phosphocholine	1,2-distearoyl-sn-glycero-3-phosphocholine
	cholesterol	cholesterol
	(4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate)	SM-102 (proprietary to Moderna)
Salts and Sugars	potassium chloride	Tris buffer containing sucrose and sodium acetate
	monobasic potassium phosphate	
	sodium chloride	
	dibasic sodium phosphate dihydrate	
	sucrose	

*As reported in the prescribing information

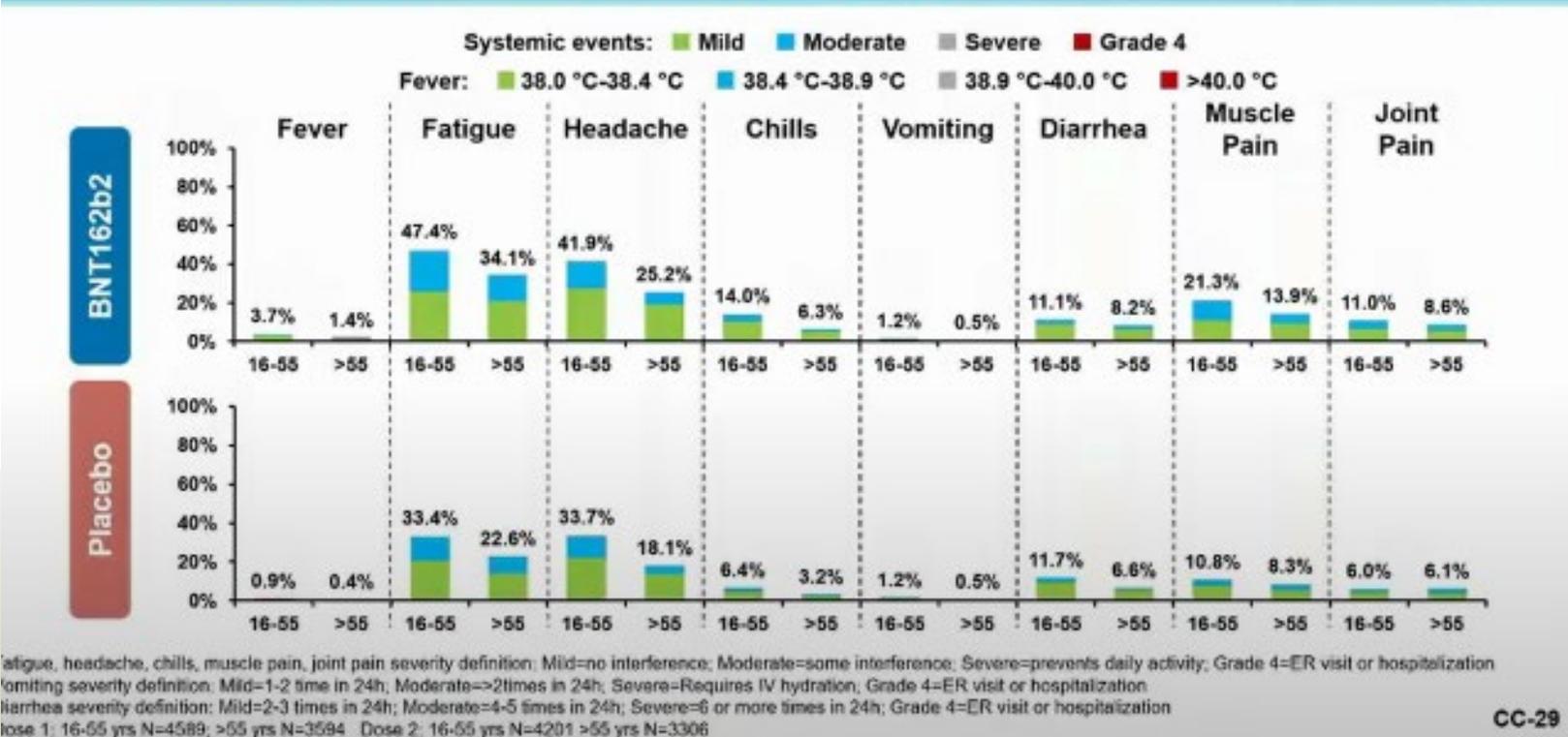


Pfizer: Local side effects in the first 2 days after vaccination are expected, mild-moderate.



Pfizer. Systemic side effects in the first 2 days after vaccination are expected, mild-moderate.

eDiary: Systemic Events Within 7 Days From Dose 1 in 16-55 and >55 Year Olds (N=8,183)

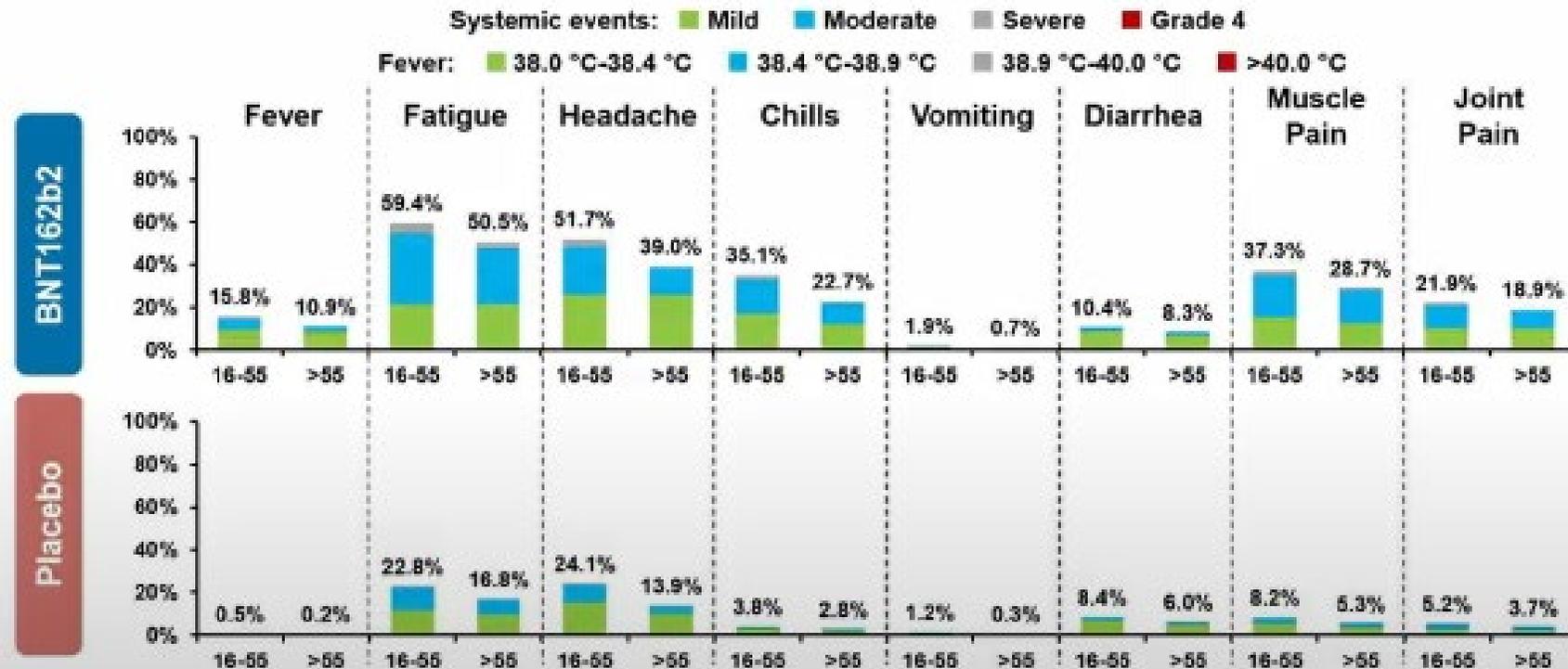


CC-29



Pfizer: Expect similar, even increased side effects, after the **second** dose.

eDiary: Systemic Events Within 7 Days From Dose 2 in 16-55 and >55 Year Olds (N=8,183)

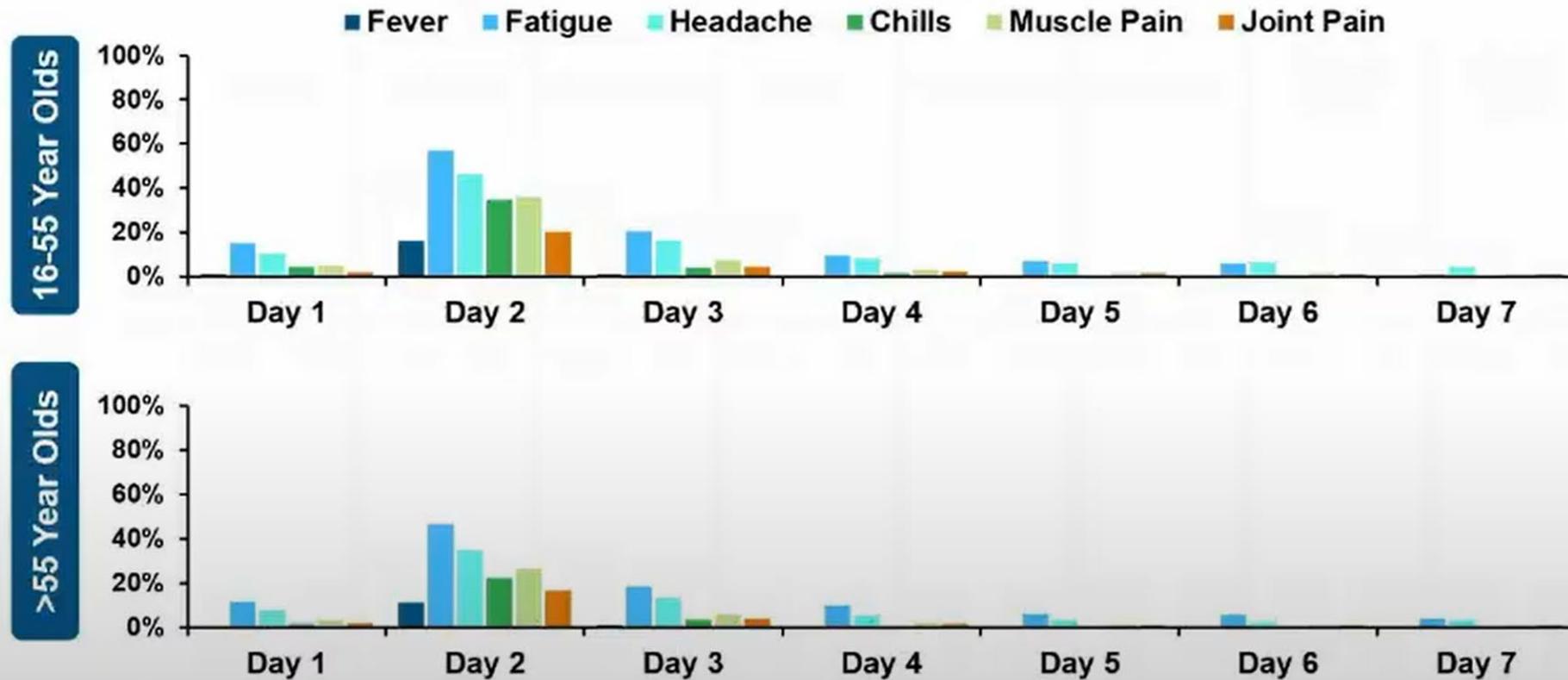


Fatigue, headache, chills, muscle pain, joint pain severity definition: Mild=no interference; Moderate=some interference; Severe=prevents daily activity; Grade 4=ER visit or hospitalization
 Vomiting severity definition: Mild=1-2 times in 24h; Moderate=>2times in 24h; Severe=Requires IV hydration; Grade 4=ER visit or hospitalization
 Diarrhea severity definition: Mild=2-3 times in 24h; Moderate=4-5 times in 24h; Severe=6 or more times in 24h; Grade 4=ER visit or hospitalization
 Dose 1: 16-55 yrs N=4589, >55 yrs N=3594 Dose 2: 16-55 yrs N=4201 >55 yrs N=3306



Pfizer: Most side effects abate by day 3

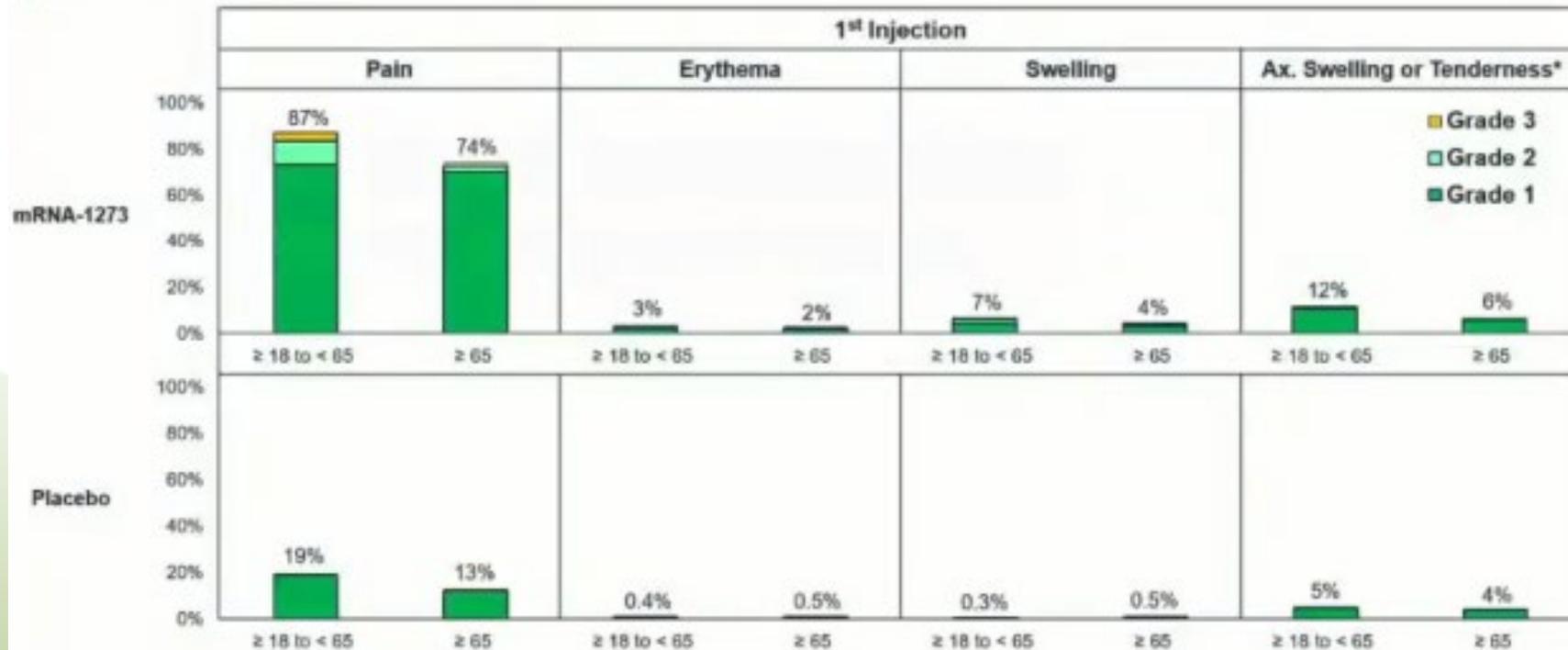
eDiary: Systemic Events Each Day From Dose 2 in 16-55 and >55 Year Olds (N=8,183) BNT162b2



Moderna: Local side effects in the first 2 days after 1st vaccination are expected, mild-moderate.

CO-54

Study 301: Most Solicited Local Adverse Reactions Were Mild-to-Moderate (1st Injection) Safety Set, 9-Week Median Follow-up



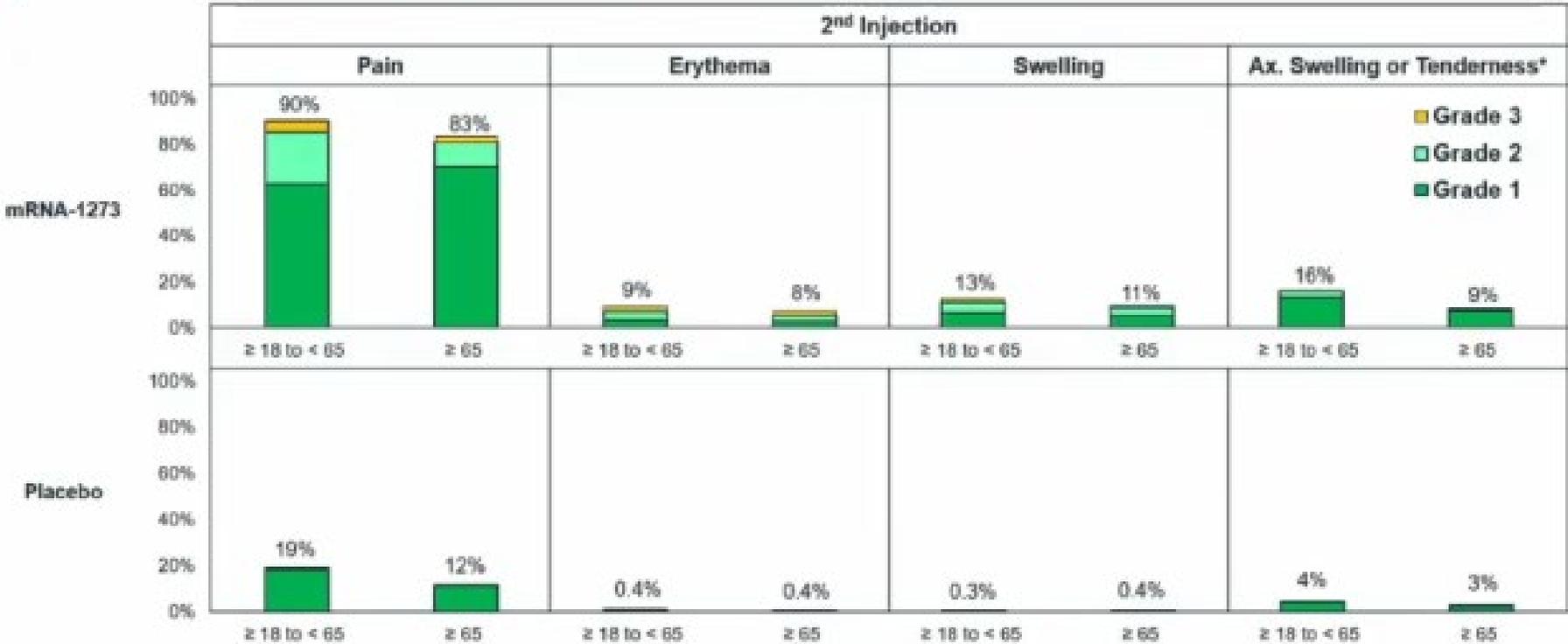
Note: Includes reports within 7 days of either injection. *Localized axillary swelling or tenderness ipsilateral to the vaccination arm.



Moderna: Expect similar, increased local side effects, after the **2nd** dose

CO-5!

Study 301: Most Solicited Local Adverse Reactions Were Mild-to-Moderate (2nd Injection) Safety Set, 9-Week Median Follow-up



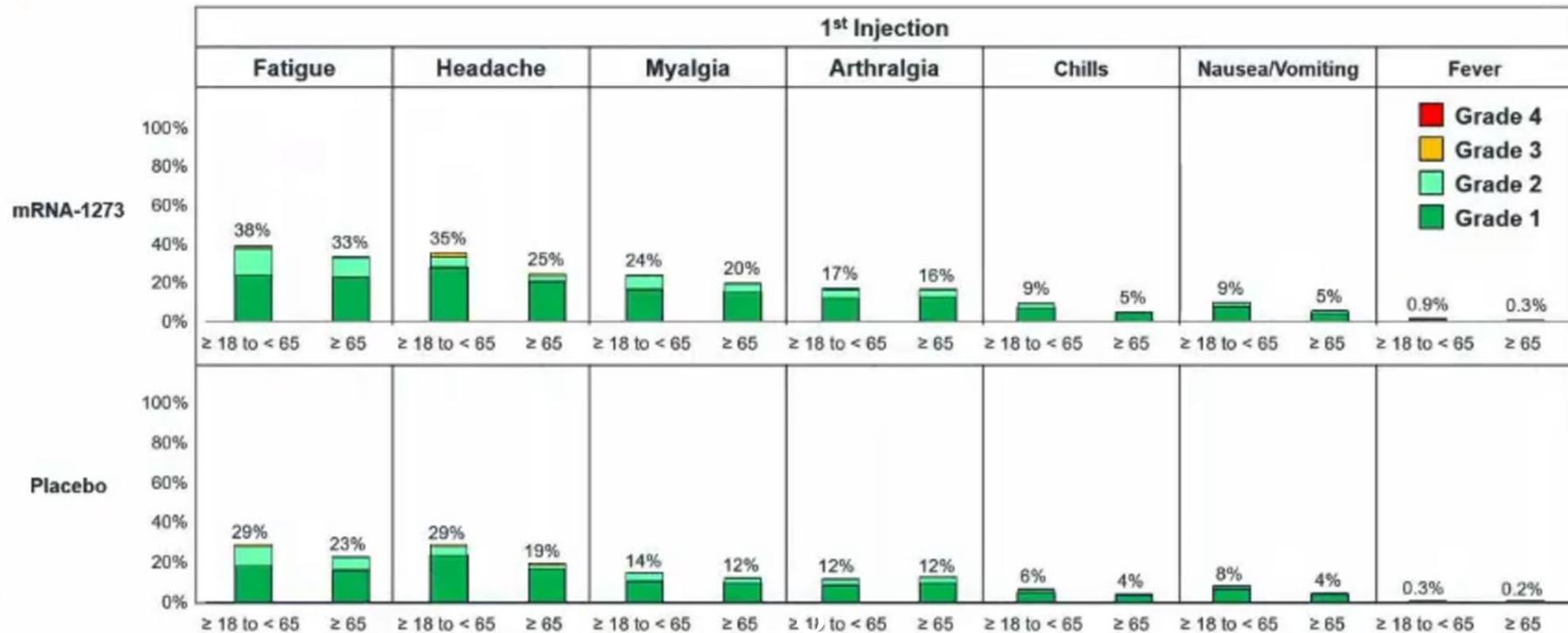
Note: Includes reports within 7 days of either injection. *Localized axillary swelling or tenderness ipsilateral to the vaccination arm.



Moderna. Systemic side effects in the first 2 days after vaccination are expected, mild-moderate

CO-56

Study 301: Most Solicited Systemic Adverse Reactions Were Mild-to-Moderate (1st Injection) Safety Set, 9-Week Median Follow-up



Note: Solicited Systemic ARs include reports within 7 days of either injection

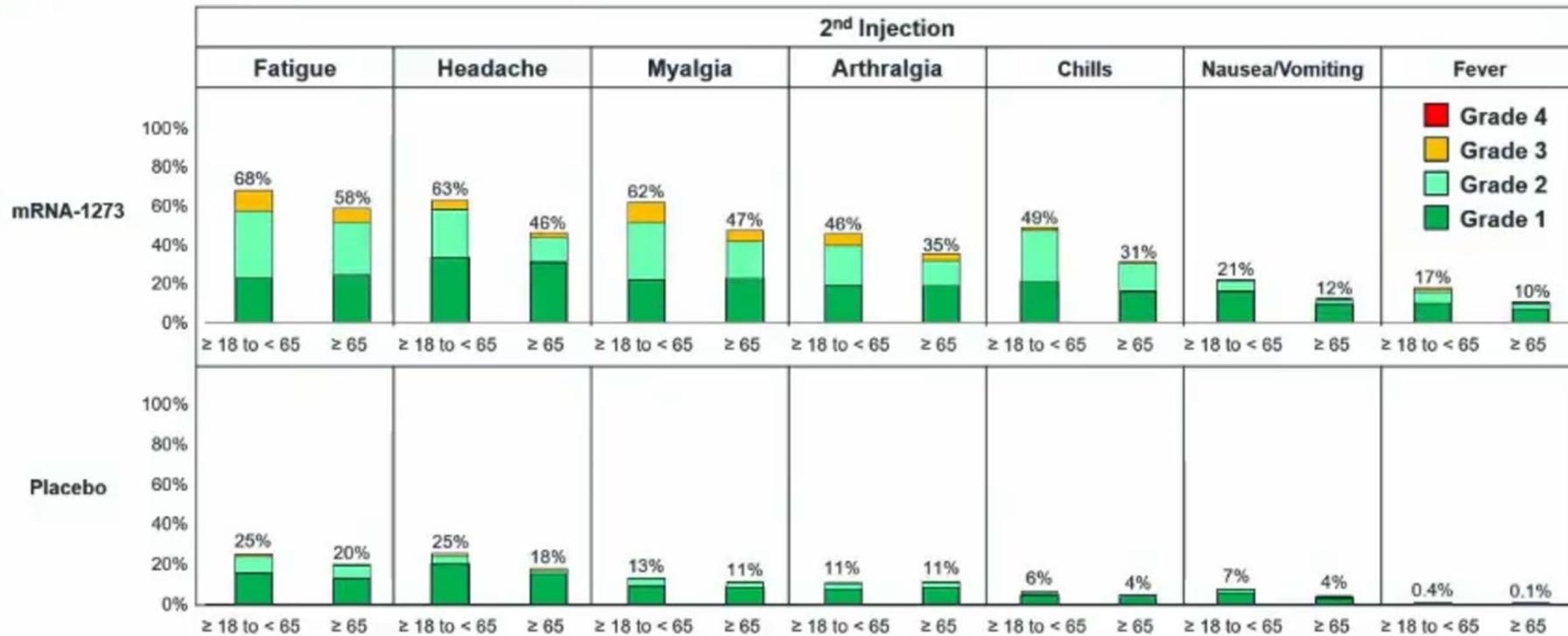
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Moderna: Expect similar, increased systemic side effects, after the **2nd** dose

CO-57

Study 301: Most Solicited Systemic Adverse Reactions Were Mild-to-Moderate (2nd Injection) Safety Set, 9-Week Median Follow-up



Ethical Values in Vaccine Allocation

- Maximize benefits
 - mortality, morbidity, societal function
- Fairness and equal concern for every person
 - Everyone considered using same criteria
 - Prioritization not equated with valuation
- Mitigation of health inequities
- Transparency
- Evidence-based

Four criteria for vaccine prioritization

1. Likelihood of exposure to SARS-CoV-2
2. Likelihood of developing severe COVID-19 if exposed
3. Likelihood of transmitting SARS-CoV-2
4. Importance to prevention of acute societal collapse

A few examples of how those criteria apply

Group	Exposure risk	Transmission risk	Severe disease risk	Essential to acute ability to keep people alive
High risk health care workers	High	High	Medium	High
Residents of long-term care facilities	High	Medium	High	Low
Adults >65 yo in the community	Low	Low	High	Low
College students	Medium	High	Low	Low
Schoolteachers	Medium	Medium	Medium	Low
General public	Low	Low	Medium	Low

HIGH RISK and shades of gray

- Seeing patients with COVID-19 > seeing many patients/people > little patient/public contact
- Airway instrumentation > face-to-face/lengthy contacts > video
- Congregational living vs living alone
- Socioeconomic marginalization

Overlapping prioritization



Key points

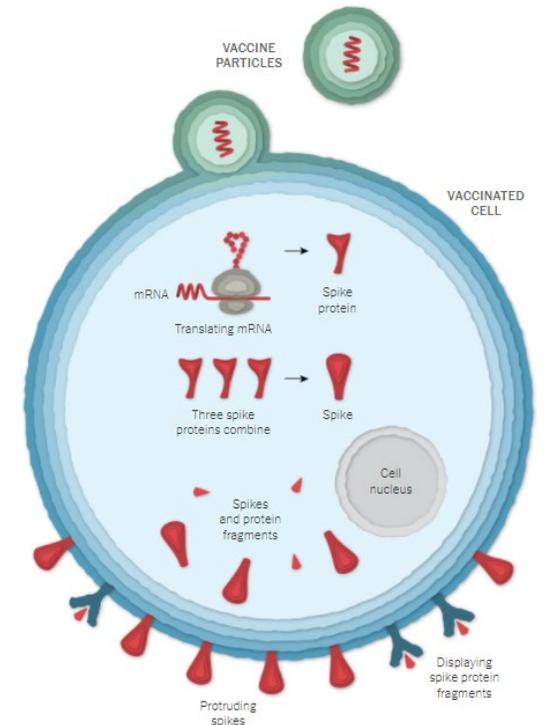
- We need to **save the most lives** possible
- We are prioritizing by (1) exposure risk, (2) transmission risk, (3) severe disease risk, and (4) lifesaving work
- **How** is harder than **what**
 - It's **multiple "lines"** not a single file line
 - Organizational **affiliations** and **distribution** dynamics determine a lot
- **Community partnerships** are critical, especially to marginalized groups
- It's **not a single-file line** – it's multiple lines

COVID-19 vaccination in special populations

William Raszka

COVID-19 vaccines and pregnant women

- There are no data on safety in pregnant women
 - Pregnant and lactating women excluded from trials
 - About 30 women became pregnant (equal number in both arms)
- Animal data:
 - Moderna vaccine:
 - No adverse effects on rat reproduction, fetal/embryonal development, or postnatal development
 - Ongoing studies in animals for both Moderna and Pfizer
- mRNA COVID-19 vaccines
 - Not live!
 - Degraded quickly
 - Do not enter nucleus



COVID-19 and pregnancy

- Increased risk of:
 - Severe illness (hospitalization, ICU admission, etc)
 - Preterm labor
- Not associated with:
 - Increased risk of spontaneous loss
 - Infertility

Recommendations for COVID vaccination in pregnant women

- If part of a group that is recommended to receive a COVID-19 vaccine (e.g., healthcare personnel), they may choose to be vaccinated
- A conversation between the patient and their clinical team may assist with the decision
 - Conversation with a healthcare provider is not required prior to vaccination
 - A pregnancy test before vaccination is not recommended

COVID-19 vaccination and pregnancy

- Considerations:
 - Level of COVID-19 community transmission
 - Patient's personal risk of contracting COVID-19
 - Risks of COVID-19 to the patient and potential risks to the fetus
 - Efficacy of the vaccine
 - Side effects of the vaccine
 - Lack of data about the vaccine during pregnancy

Managing information

- UK:
 - Pregnant women should defer vaccination
- Social media and some physicians
 - *People* planning fertility may be advised against receiving the vaccine
- Social media:
 - Vaccine leads to infertility
 - antibodies against the spike protein will also target a protein in the placenta of pregnant mothers



Management:

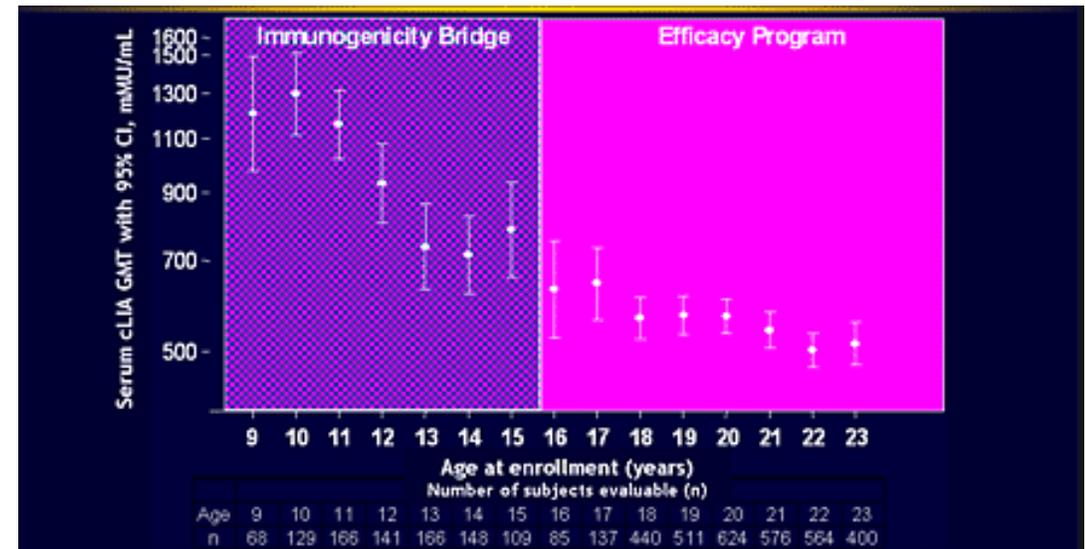
- Routine testing for pregnancy before vaccination not recommended
- Acetaminophen for fever in pregnant women
- Reassurance for those worried about fertility

COVID-19 vaccines and lactating women

- No data on the safety in lactating people, effects on the breastfed infant, or milk production/excretion
- mRNA vaccines are not thought to be a risk to the breastfeeding infant
- Long history of vaccinating lactating women without complication
- A lactating person who is part of a group recommended to receive a COVID-19 vaccine (e.g., healthcare personnel) may choose to be vaccinated

COVID-19 vaccination in children

- The following groups are authorized to receive vaccination:
 - Pfizer-BioNTech: ages ≥ 16 years
 - Moderna: ages ≥ 18 years
- Children outside of these age groups should not receive COVID-19 vaccination at this time
- Children in trials
 - Pfizer: have enrolled children ≥ 12 years
 - Moderna: plan to enroll children ≥ 12 years
 - Younger children?
- Efficacy vs. bridging data



Engaging in Effective COVID-19 Vaccine Conversations

- Start from a place of empathy and understanding
- Assume patients will want to be vaccinated but may not know when to expect It
 - Provide general information about the timeline for COVID-19 vaccines
- Give strong recommendation
 - Importance of vaccine to protect patients' health and the health of those around them
- Listen to and respond to patient questions
- Wrapping up the conversation
 - Let your patients know that you are open to continuing the conversation

COVID-19 Vaccine Hesitancy

- Safety

- Adverse events
- Long term follow up
- Speed

Safety huge priority at every step
Compression of time table

- Distrust

- People of color

Effort to recruit subjects representative of the US population