WESTERN STATES SCIENTIFIC REVIEW GROUP (WSSRG) COVID19 VACCINES

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WSSRG:BACKGROUND

- Concern that COVID 19 vaccine authorization would be influenced by political considerations because of Federal administration actions:

  - FDA granting Emergency Use Authorization hydroxychloroquine
  - Modification of CDC recommendations by political appointees
  - Requirement that CDC staff communications routed through VP Office

- Some state governors set up state committee to conduct independent reviews of vaccine safety, efficacy, review process, & recommendations.

Controversial: undercut CDC & FDA, lead to conflicting recommendations?

FEDERAL VACCINE ADVISORY COMMITTEES

VRBPAC - FDA Vaccines & Related Biologic Products Advisory Committee

Licensing & authorization of vaccines, biologicals, drugs

ACIP - CDC Advisory Committee on Immunization Practices

Recommendations for the use of FDA approved vaccines

NVAC - HHS National Vaccine Advisory Committee

- Immunization policy recommendations

Members: *diverse expertise, vetted for COI, independent, defined terms*.

Meetings: *public, agenda & presentations posted on-line.*

WSSRG: MEMBERS

CALIFORNIA

- Arthur Reingold, MD, Chair*
- Tomas J Aragon MD, DrPH
- Eric Gosby MD
- Rodney Hood, MD
- Nicola Klein MD, PhD
- Grace Lee MD, MPH*
- Bonnie Maldonado MD*
- Mark Sawyer MD*
- Robin Schecter MD*
- Matt Zahn MD*
- Peter Zilagyi MD, MPH*

NEVADA

- Ihsan Azzam MD, PhD
- Candice McDaniel MS

OREGON

- Laura Byerly MD
- Louis J. Picker MD

WASHINGTON

- John Dunn MD, MPH*
- Edgar K Marcuse MD, MPH*

*Past or current member of ACIP or VRBPAC

WSSRC: SCOPE, PERSPECTIVE

1. Assure safety & efficacy of COVID 19 vaccines that might be used in our states
2. Assess the transparency & objectivity of FDA VRPAC & CDC ACIP review process & the rigor validity and reliability of their data analysis
3. Ascertain whether equity has been considered appropriately in the design, implementation & analysis of clinical trials
4. Avoid undue delay in making available to our states' residents COVID-19 vaccines deemed by the FDA & CDC to be safe & effective

BIOLOGICAL LICENSE APPLICATION (BLA)
EMERGENCY USE AUTHORIZATION (EUA)

BLA

Usual process for licensing vaccine, biological or drug.

Requires data from $\geq$ 6 month follow-up.

FDA *approves* the vaccine for use as *safe & effective.*

EUA

Allows distribution of a new vaccine, biological or drug or its use “off label” during a public health emergency.

FDA *authorizes* distribution if the *benefits outweigh the risks.*

WSSRC: FINDINGS

- Endorsed the transparency, objectivity of VRPAC & ACIP review processes & the rigor, validity & reliability of their analyses.
- Concluded that equity had been considered appropriately in the clinical trials & that it continue to be a guiding principle in immunization, monitoring & communication.
- Unanimously recommended use of the Moderna &Pfizer mRNA vaccines in CA, NV, OR & WA.
- Avoid any undue delay in providing access to these vaccines.

EFFICACY AFTER 2nd DOSE PFIZER VACCINE

First COVID-19 Occurrence From 7 Days After Dose 2

Phase 2/3 Efficacy – Final Analysis

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

	BNT162b2 (30 µg) N=18,198		Placebo N=18,325				
Efficacy Endpoint	n	Surveillance Time (n)	n	Surveillance Time (n)	VE (%)	(95% CI)	Pr (VE >30%)
First COVID-19 occurrence ≥7 days after Dose 2	8	2.214 (17,411)	162	2.222 (17,511)	95.0	(90.3, 97.6)	>0.9999

Total surveillance time: 1000 person-years for all subjects within each group at risk for the endpoint..
Pr=Posterior probability

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EFFICACY AFTER 2nd DOSE MODERNA VACCINE

EP-11

Study 301: Consistent Reduction in Symptomatic, Confirmed COVID-19 Regardless of Age

Per Protocol – Primary Efficacy Analysis

	# Events / N		Vaccine Efficacy (95% CI)
	mRNA-1273	Placebo	
Overall	11 / 14,134	185 / 14,073	94.1% (89.3, 96.8)
≥ 18 to < 65	7 / 10,551	156 / 10,521	95.6% (90.6, 97.9)
≥ 65	4 / 3,583	29 / 3,552	86.4% (61.4, 95.2)
Breakdown of ≥ 65 group			
≥ 65 to < 75	4 / 2,953	22 / 2,864	82.4% (46.9, 93.9)
≥ 75	0 / 630	7 / 688	100% (NE, 100)

EFFICACY SEVERE DISEASE PFIZER VACCINE

BNT162b2 Protects Against Severe Disease

Phase 2/3 Efficacy – Post-Hoc Analysis (CDC Definition)

Severe illness – CDC Definition: hospitalization, admission to ICU, intubation or mechanical ventilation or death

	BNT162b2 (30 µg) N=18,198		Placebo N=18,325			
Efficacy Endpoint	n	Surveillance Time (n)	n	Surveillance Time (n)	VE (%)	(95% CI)
First Severe COVID-19 occurrence ≥7 days after Dose 2	0	2.213 (17,399)	5	2.229 (17,495)	100.0	(-9.9, 100.0)

	BNT162b2 (30 µg) N=21,669		Placebo N=21,686			
Efficacy Endpoint	n	Surveillance Time (n)	n	Surveillance Time (n)	VE (%)	(95% CI)
First Severe COVID-19 occurrence after Dose 1	1	4.018 (21,299)	14	4.001 (21,238)	92.9	(53.2, 99.8)

Total surveillance time: 1000 person-years for all subjects within each group at risk for the endpoint.
"Severe illness from COVID-19 is defined as hospitalization, admission to the ICU, intubation or mechanical ventilation, or death"
https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html

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EFFICACY SEVERE DISEASE MODERNA VACCINE

Study 301 Secondary Efficacy Endpoint: Cases of Confirmed Severe COVID-19

Per Protocol

Confirmed, Severe COVID-19 Cases	Interim Analysis		Primary Efficacy Analysis	
	mRNA-1273 N=13,934	Placebo N=13,883	mRNA-1273 N=14,134	Placebo N=14,073
Number of cases, n (%)	0 (0%)	11 (< 0.1%)	0 (0%)	30 (0.2%)
Vaccine efficacy based on hazard ratio (95% CI)	100% (NE, 100%)		100% (NE, 100%)	
Incidence rate per 1000 person-years	0	4.1	0	9.1

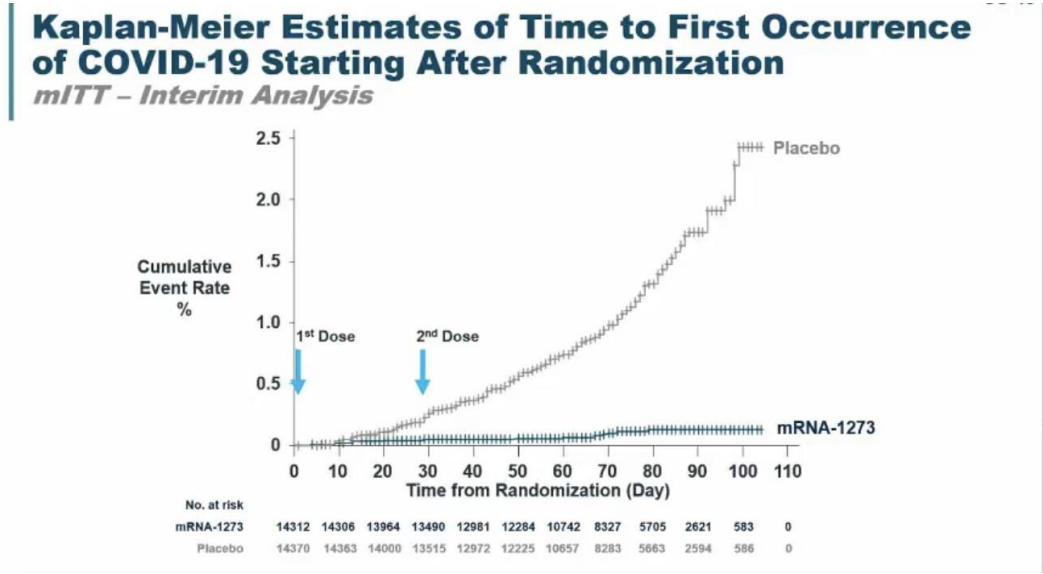
- One participant death due to COVID-19 in the placebo group
- Given the high efficacy against severe disease, no evidence for vaccine-associated enhanced disease was observed

One potential case of severe disease was reported in the mRNA-1273 group after data cut-off for the primary efficacy analysis, this case has yet to be adjudicated.

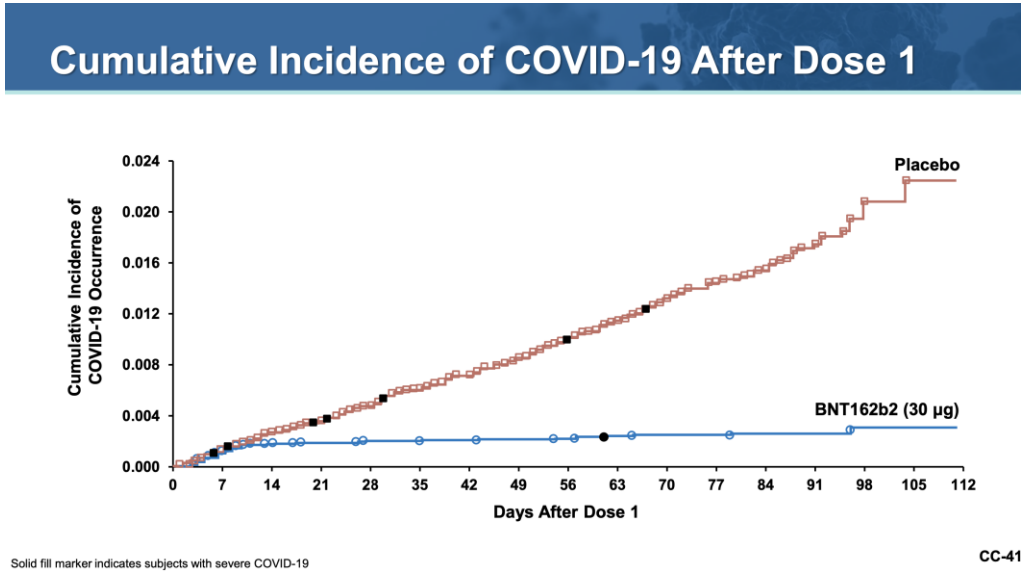
NE: not estimable

COVID 19 DISEASE AFTER DOSE 1

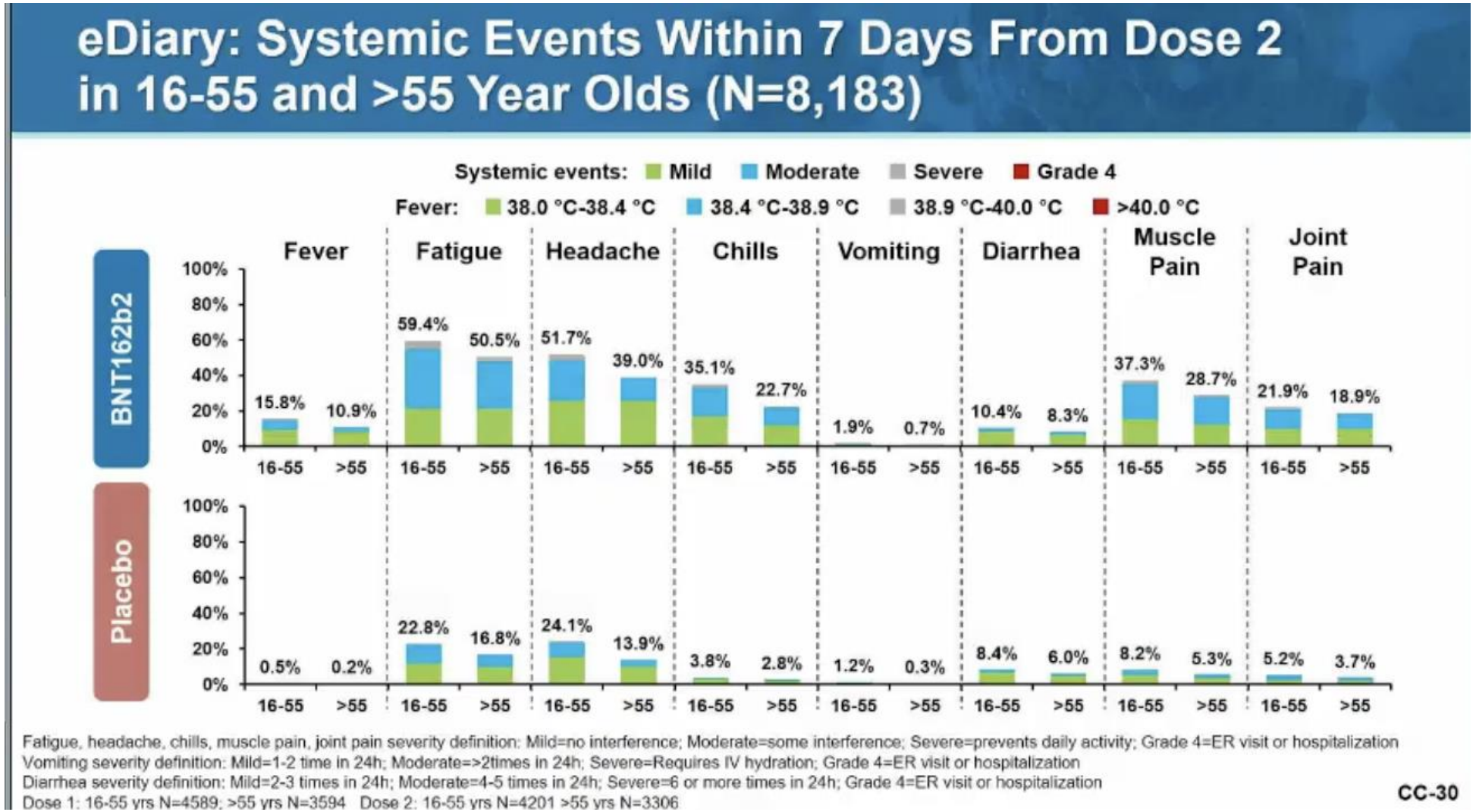
MODERNA VACCINE



PFIZER VACCINE



PFIZER mRNA VACCINE SAFETY



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 time 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

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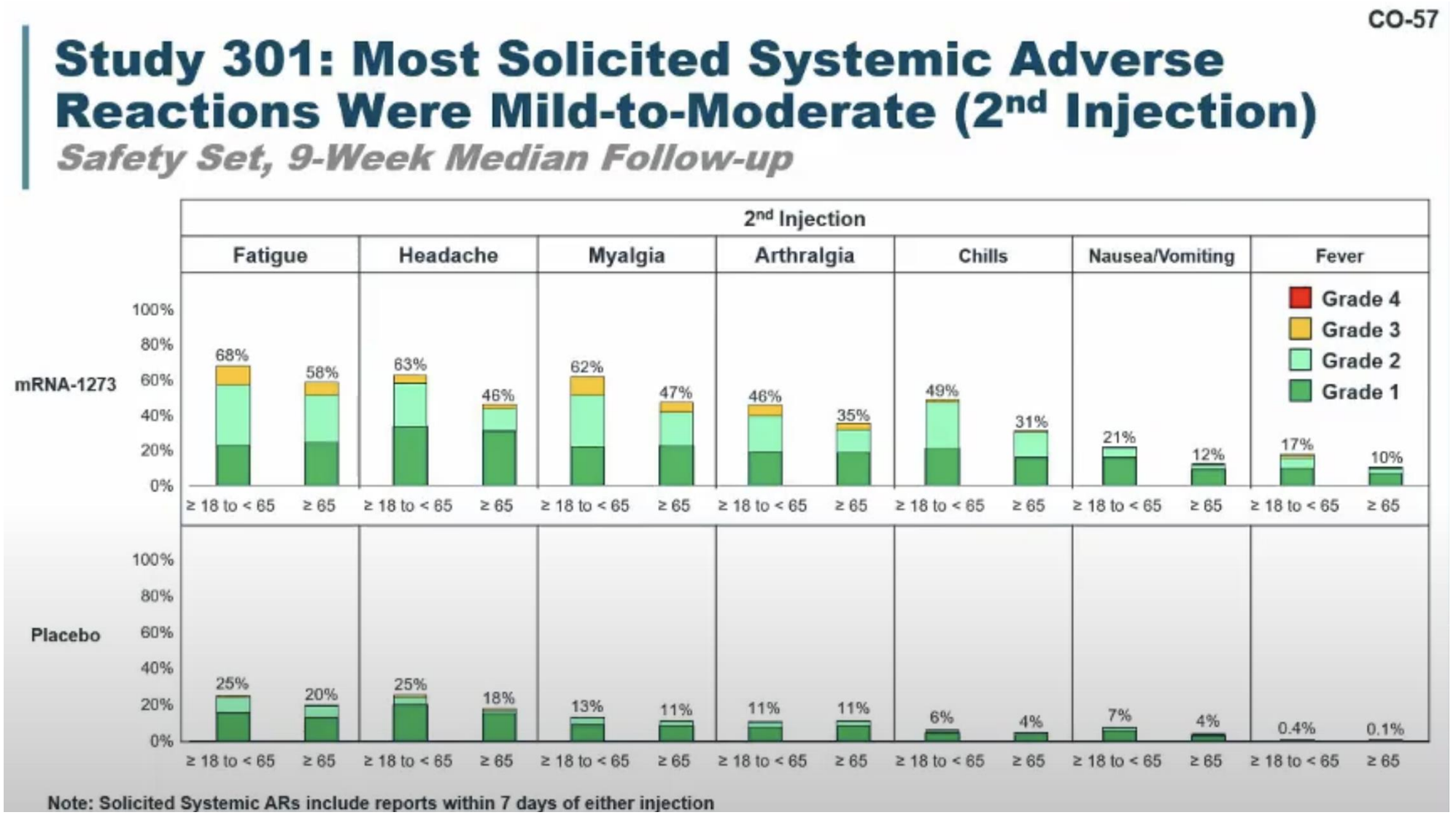
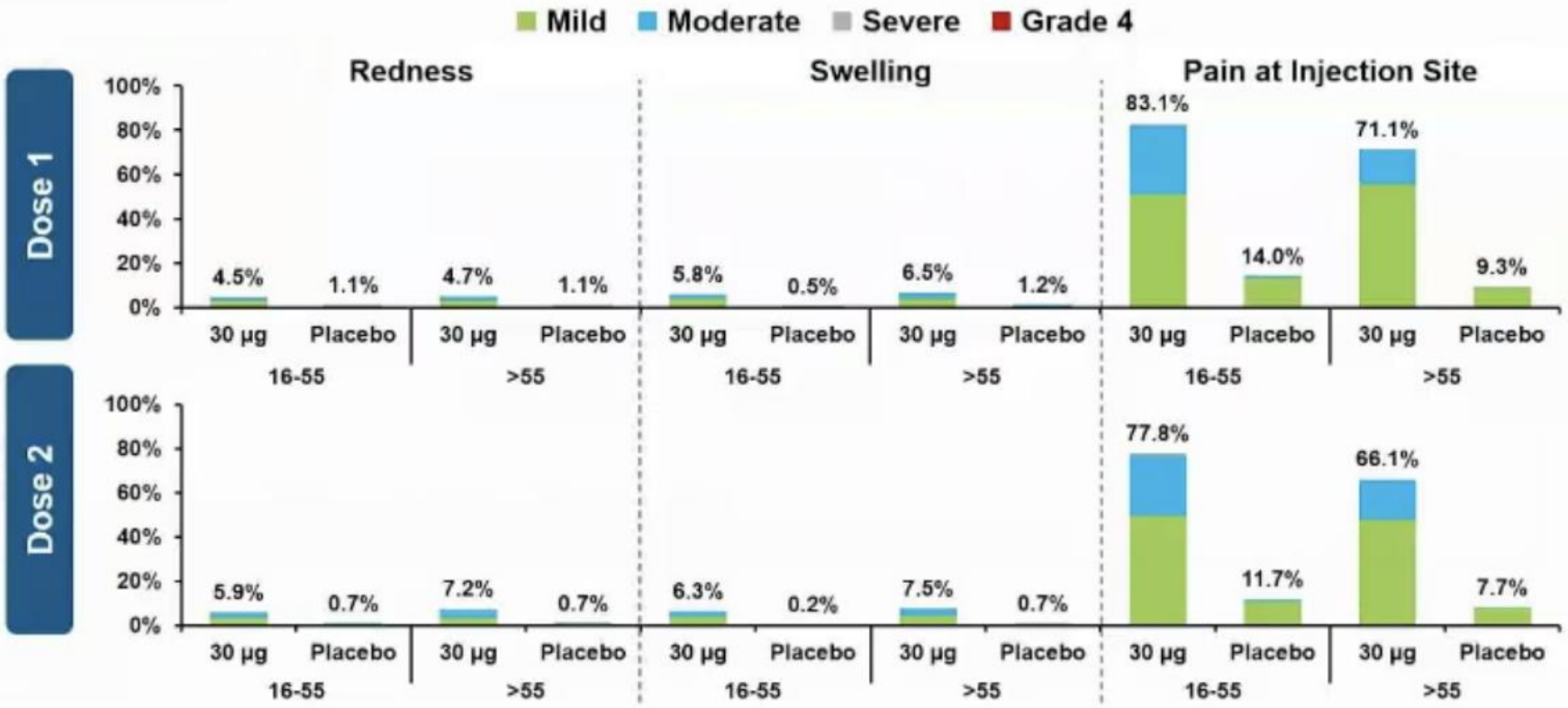
MODERNA mRNA VACCINE SAFETY



PFIZER mRNA VACCINE SAFETY

eDiary: Local Events Within 7 Days From Dose 1 and 2 in 16-55 and >55 Year Olds (N=8,183)



Redness and sweeling severity definition: Mild= >2-5cm, Moderate= >5-10 cm; Severe= >10 cm; Grade 4= necrosis
Pain at injection site severity definition: Mild=no interference; Moderate=some interference; Severe=prevents daily activity; 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

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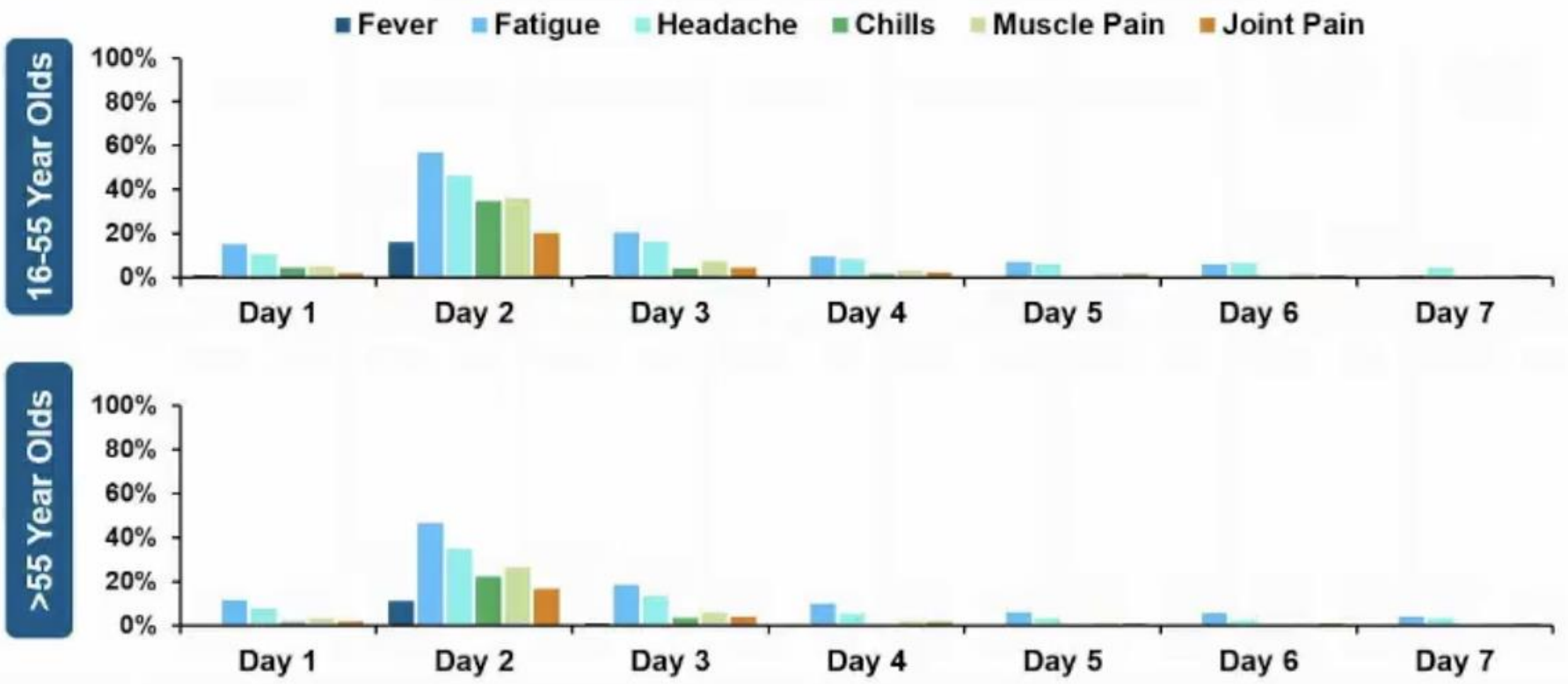
PFIZER mRNA VACCINE SAFETY

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



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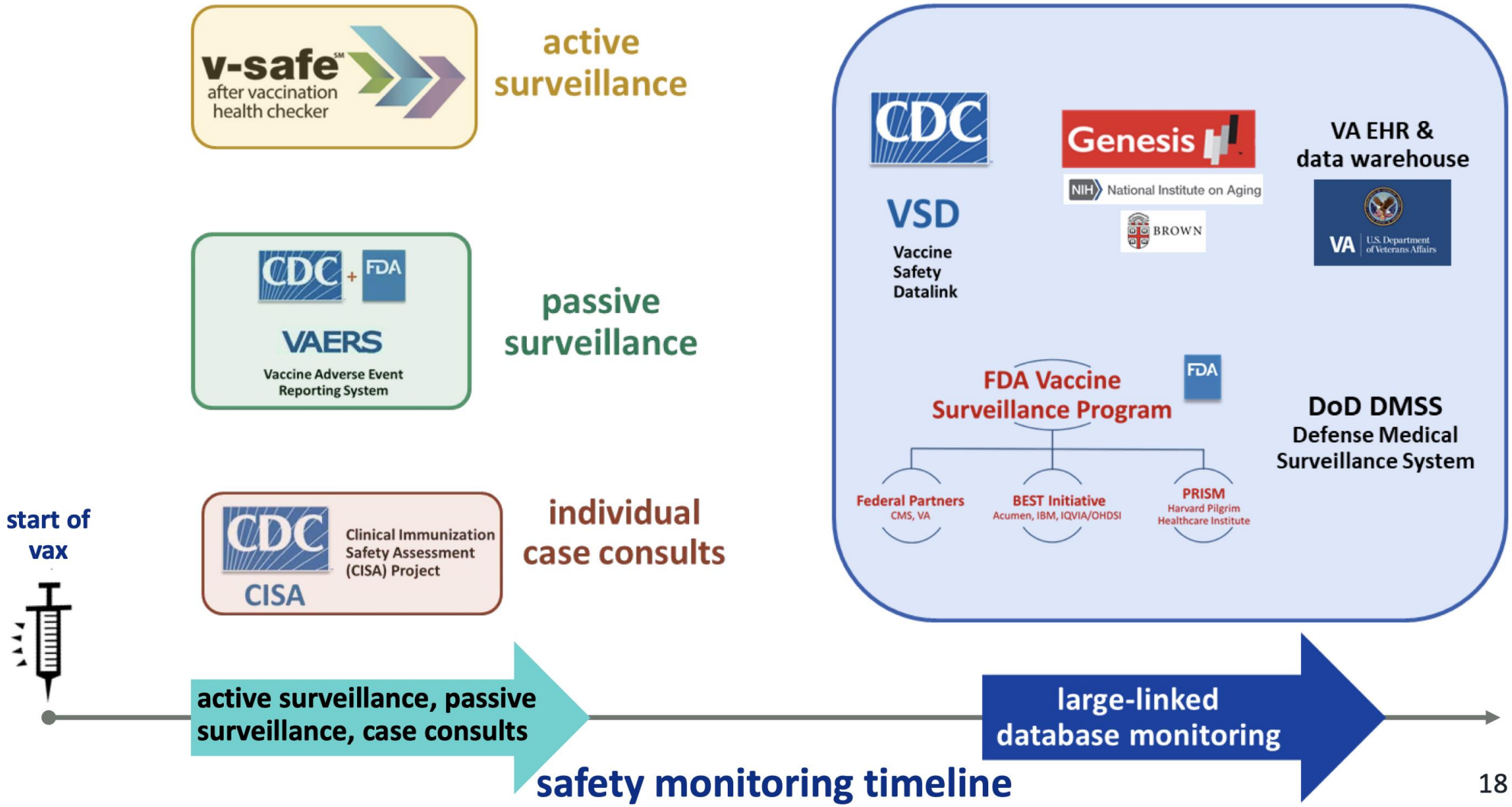
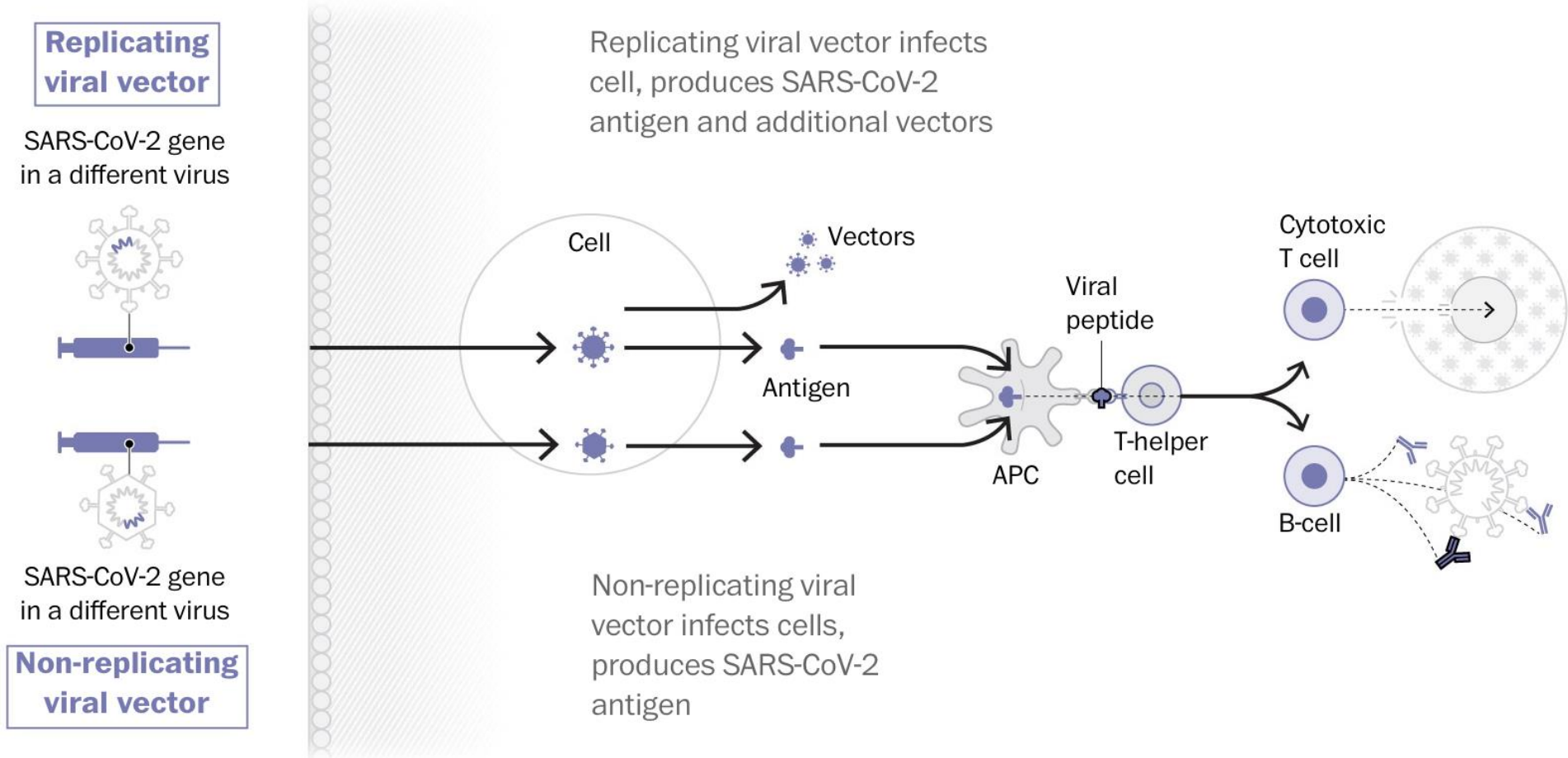
CONTINUED VACCINE SAFETY MONITORING



MODERNA VERSUS PFIZER VACCINE

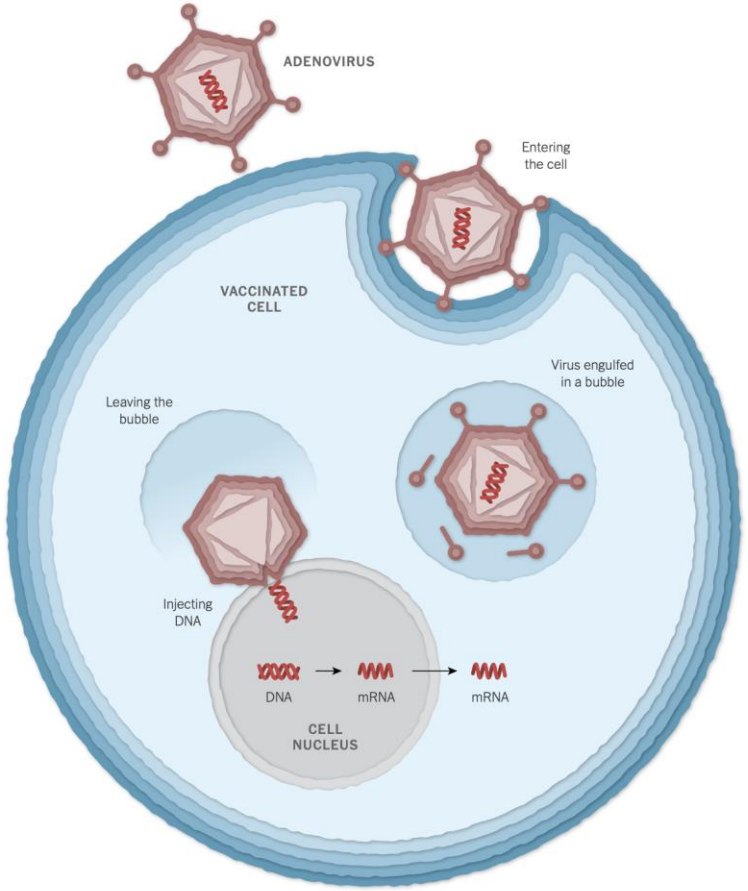
- Both vaccines are ~95% effective preventing COVID-19 illness after two doses.
- Both vaccines had no serious safety concerns identified in Phase 3 clinical trials.
- ~80% of people may develop a mild local symptom (pain at injection site).
- The Pfizer dose #2 is at 21 days (but 17-day minimum between doses).
- The Moderna is at 28 days (24-day minimum between doses).
- The Pfizer vaccine has a 16-year-old minimum age requirement.
- The Moderna vaccine’s minimum age requirement is 18 years).

NEXT COVID-19 VACCINES: Viral Vector Vaccines



Adapted from https://www.washingtonpost.com/graphics/2020/health/covid-vaccine-update-coronavirus/

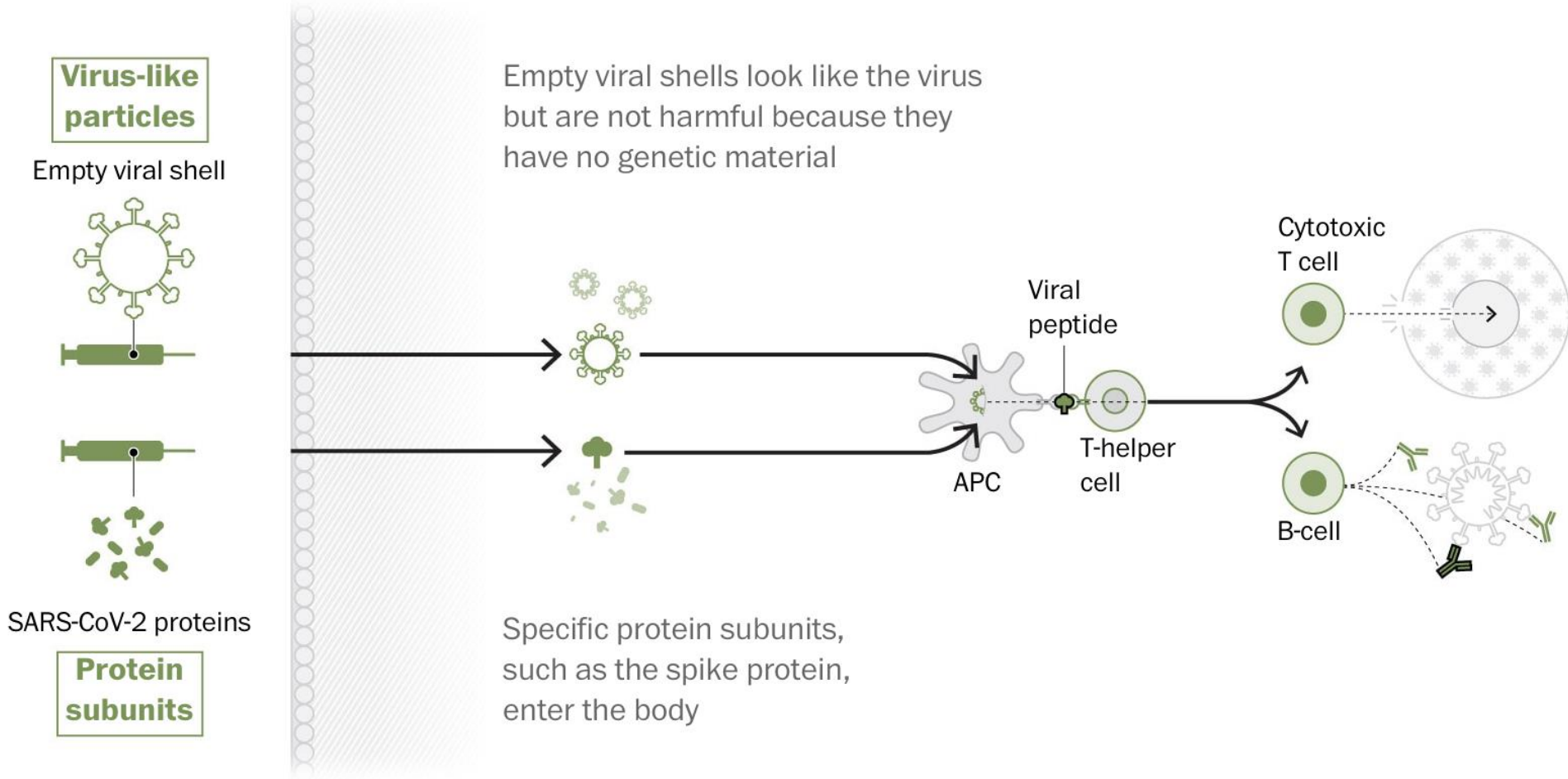
NEXT COVID-19 VACCINES:
Viral Vector Vaccines



The adenovirus pushes its DNA into the nucleus. The adenovirus is engineered so it can't make copies of itself, but the gene for the coronavirus spike protein can be read by the cell and copied into a molecule called messenger RNA, or mRNA.

Adapted from https://www.nytimes.com/interactive/2020/health/oxford-astrazeneca-covid-19-vaccine.html

NEXT COVID-19 VACCINES:
Viral Particle & Protein Subunit Vaccines



Adapted from https://www.washingtonpost.com/graphics/2020/health/covid-vaccine-update-coronavirus/

Q & A*

*RESOURCES
Websites of WA State DOH; Public Health Seattle-King; CDC –ACIP; FDA VRBPAC
UW Department of Global Health: https://globalhealth.washington.edu/subscribe
Washington Post: www.washingtonpost.com/graphics/2020/health/covid-vaccine-update-coronavirus/