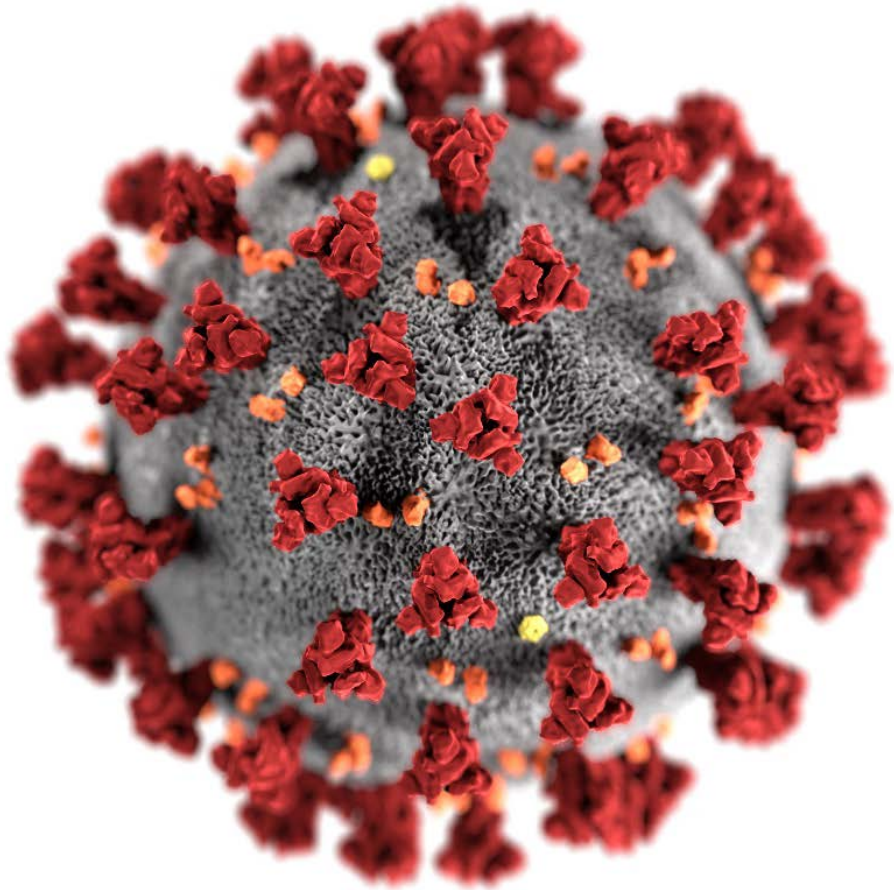
COVID 19
CORONAVIRUS DISEASE

ACIP Meeting: COVID-19 Vaccines



October 30, 2020

Today's agenda

Vaccine Development & Regulatory

- **Update from VRBPAC meeting:** Dr. Doran Fink (FDA)
- **NVX-CoV2373 Vaccine Candidate:** Dr. Filip Dubovsky (Novavax)
- **Janssen's SARS-CoV-2 Vaccine Program:** Dr. Jerry Sadoff (Janssen)

Implementation

- **Update on vaccine implementation planning:** Dr. Janell Routh (CDC)
- **Vaccinate with Confidence:** Dr. Amanda Cohn (CDC)

Safety

- **FDA safety surveillance systems:** Dr. Steven Anderson (FDA)
- **Post-authorization safety monitoring plans:** Dr. Tom Shimabukuro (CDC)

Allocation and Epidemiology

- **Modeling strategies for the initial allocation of COVID-19 vaccines:** Dr. Matthew Biggerstaff (CDC)
- **Updates to immunity and epidemiology to inform COVID-19 vaccine policy:** Dr. Megan Wallace (CDC)
- **Ethical principles for early vaccine allocation:** Dr. Mary Chamberland (CDC)

Work Group Interpretation

- **Work Group interpretation of data:** Dr. Sara Oliver (CDC)
- **Policy questions, Evidence to Recommendation Framework, and outcomes:** Dr. Kathleen Dooling (CDC)

Vaccine Update: Phase III clinical trials in the U.S.

- AZD1222 vaccine (AstraZeneca) announced removal of FDA hold 10/23, resuming Phase III trials

- Ad26.COV2.S vaccine (Janssen) announced lifting of safety pause 10/23, resuming Phase III trials

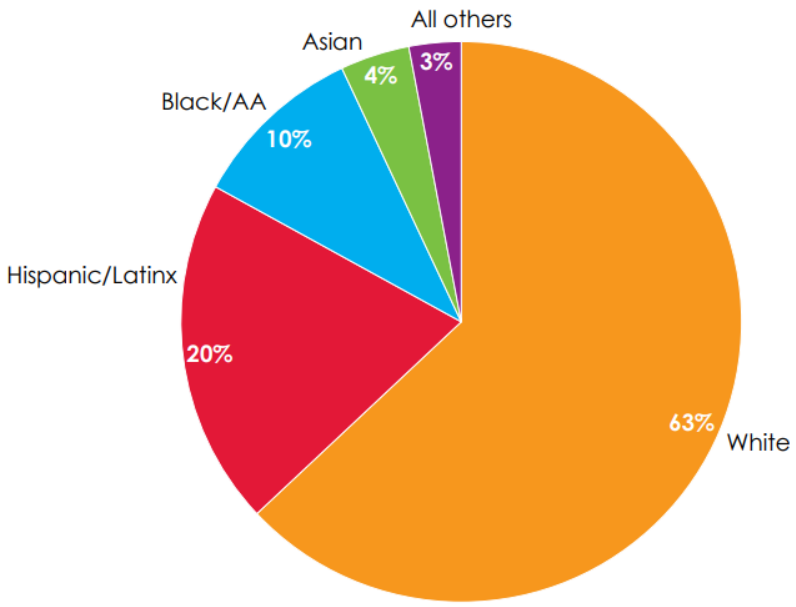
- BNT162b2 vaccine (Pfizer/BioNtech)
  - **42,133** participants enrolled as of 10/26/2020
  - 35,771 participants have received their second vaccination
  - 30% of U.S. participants enrolled have “diverse backgrounds”

- mRNA-1273 vaccine (Moderna): ***Enrollment Complete***
  - **30,000** participants enrolled as of 10/22/2020
  - 25,654 participants have received their second vaccination

Sources: https://www.modernatx.com/cove-study; https://www.pfizer.com/science/coronavirus/vaccine, https://connect.trialscope.com/studies/34986a8a-b779-4169-a35c-5d929149d426; https://www.reuters.com/article/us-health-coronavirus-pfizer/pfizer-says-coronavirus-vaccine-study-shows-mostly-mild-to-moderate-side-effects-idUSKBN26631T

Vaccine Update: Phase III clinical trials in the U.S.

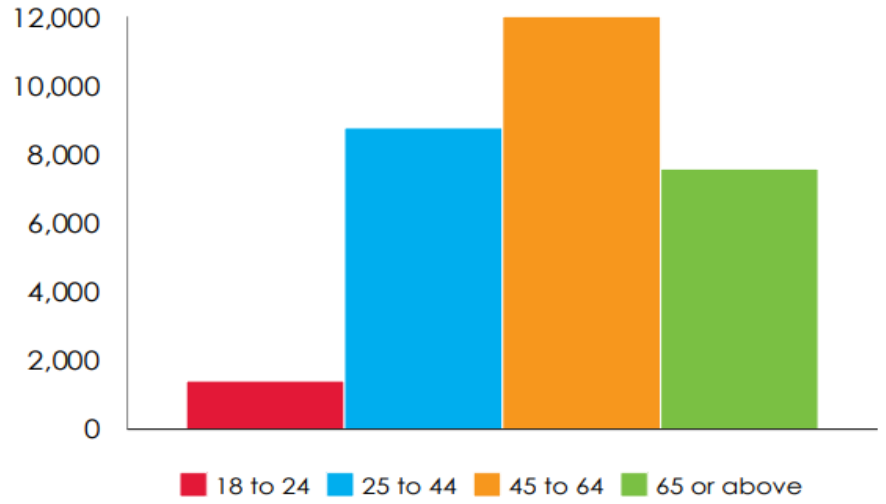
Race and ethnicity



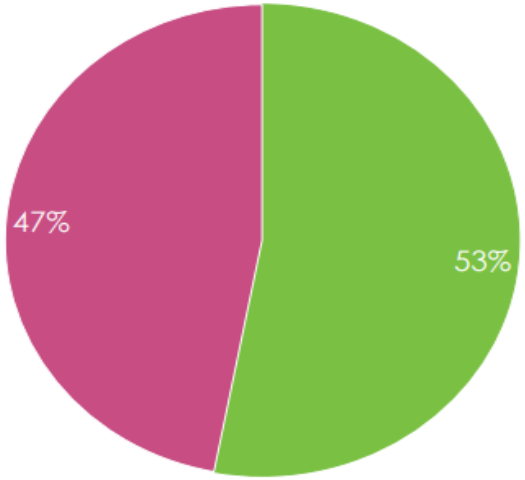
22% healthcare personnel

27% of participants living with comorbidities:
including diabetes, cardiac disease, lung disease, obesity

Cove Study age breakdown



Cove Study gender distribution



Age and gender

moderna

Sources: https://www.modernatx.com/sites/default/files/content_documents/2020-COVE-Study-Enrollment-Completion-10.22.20.pdf

Prior infection

Summary of Work Group interpretation:
COVID-19 vaccine and Prior infection

- Await data from Phase III trials for any possible vaccine-associated enhanced disease or reactogenicity after prior infection
- In the absence of concerning data from Phase III trials:
  - PCR +
  - Antigen +
  - Antibody +

  → Not a contraindication to receive COVID-19 vaccine
- Any vaccine recommendations that rely on knowledge of prior immunity/antibody testing would be difficult to implement

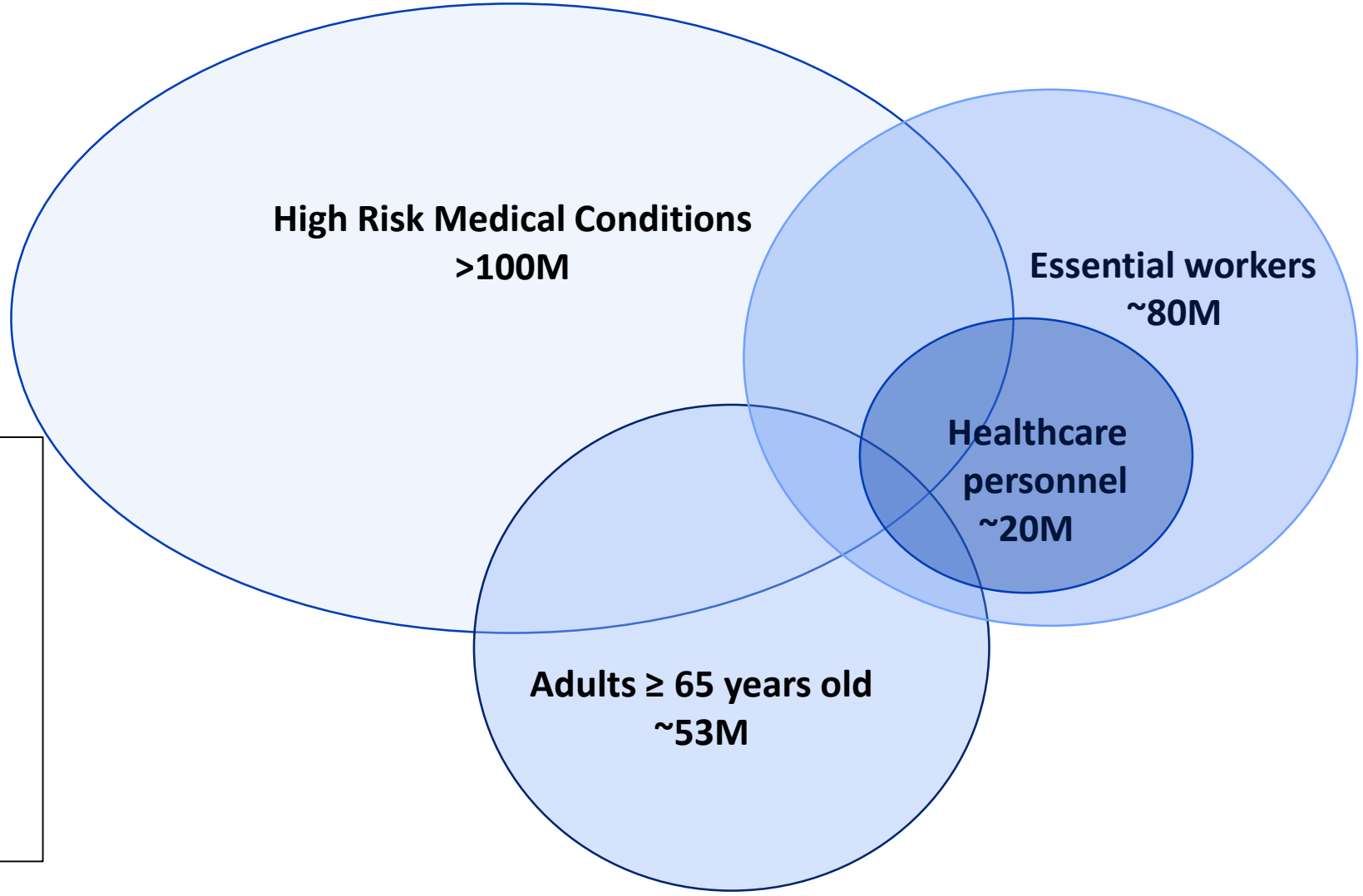
Pregnant and Breastfeeding Women

Possible groups for Phase 1 vaccination

From prior ACIP Discussions:

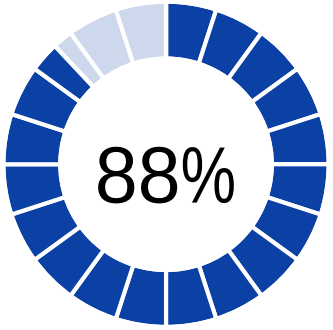
Phase 1a:
-HCP

Phase 1b:
-Essential Workers
-High Risk Med Conditions
-Adults ≥ 65 years old

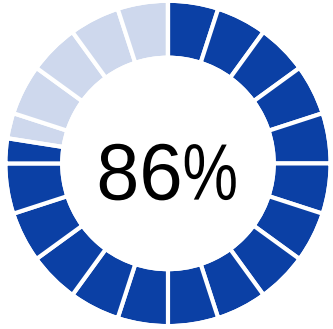


75% of the healthcare workforce are women.

Women are a majority among the largest healthcare personnel groups



Registered Nurses



Healthcare support workers: Nursing, psychiatric, and personal and home health aides

From 2019 Census Data

Increased risk for ICU admission, mechanical ventilation and death during pregnancy

Outcomes of Interest	No. (%)*		Crude RR (95% CI)	aRR (95% CI)†	Previously Published¶ aRR (95% CI)†
	Pregnant women (N = 24,558)	Nonpregnant women (N = 419,887)			
ICU Admission	225 (0.9)	1,551 (0.4)	**2.4 (2.2-2.9)**	**2.2 (1.9-2.5)**	**1.5 (1.2-1.8)**
Mechanical Ventilation	79 (0.3)	451 (0.1)	**3.0 (2.4-3.8)**	**2.5 (2.0-3.2)**	**1.7 (1.2-2.4)**
ECMO¶	17 (0.1)	121 (0.0)	**1.9 (1.1-3.4)**	**2.0 (1.2-3.4)**	--
Death	41 (0.2)	486 (0.1)	**1.4 (1.1-2.0)**	**1.6 (1.1-2.2)**	0.9 (0.5-1.5)

* Percentages calculated among total in pregnancy status group; those with missing data on outcomes were counted as not having the outcome

† Adjusted for age, race/ethnicity, and presence of underlying conditions. Nonpregnant women are the referent group.

§ Ellington S, Strid P, Tong VT, et al. Characteristics of Women of Reproductive Age with Laboratory-Confirmed SARS-CoV-2 Infection by Pregnancy Status — United States, January 22–June 7, 2020. MMWR Morb Mortal Wkly Rep 2020;69:769–775. DOI: http://dx.doi.org/10.15585/mmwr.mm6925a1

¶ Extracorporeal membrane oxygenation

Preliminary Unpublished Data

Summary of Work Group interpretation:
COVID-19 vaccine and Breastfeeding Women in Tier 1a

- Most Work Group members agreed that breastfeeding would not be a contraindication to receive a COVID-19 vaccine
  - Need to be evaluated for each vaccine, especially if any live virus/vector vaccines are authorized/licensed

Summary of Work Group interpretation:
COVID-19 vaccine and Pregnant Women in Tier 1a

- Limited data on pregnancy expected from Phase III trials
- Work Group did not reach a consensus
- Majority felt that if a woman is recommended to receive the vaccine in an early allocation phase, pregnancy should be a **precaution**, but not a contraindication to receive a COVID-19 vaccine
  - Emphasizing need to allow women to make an informed decision, providing all current knowledge of COVID-19 vaccines/platforms with pregnancy and risk of disease

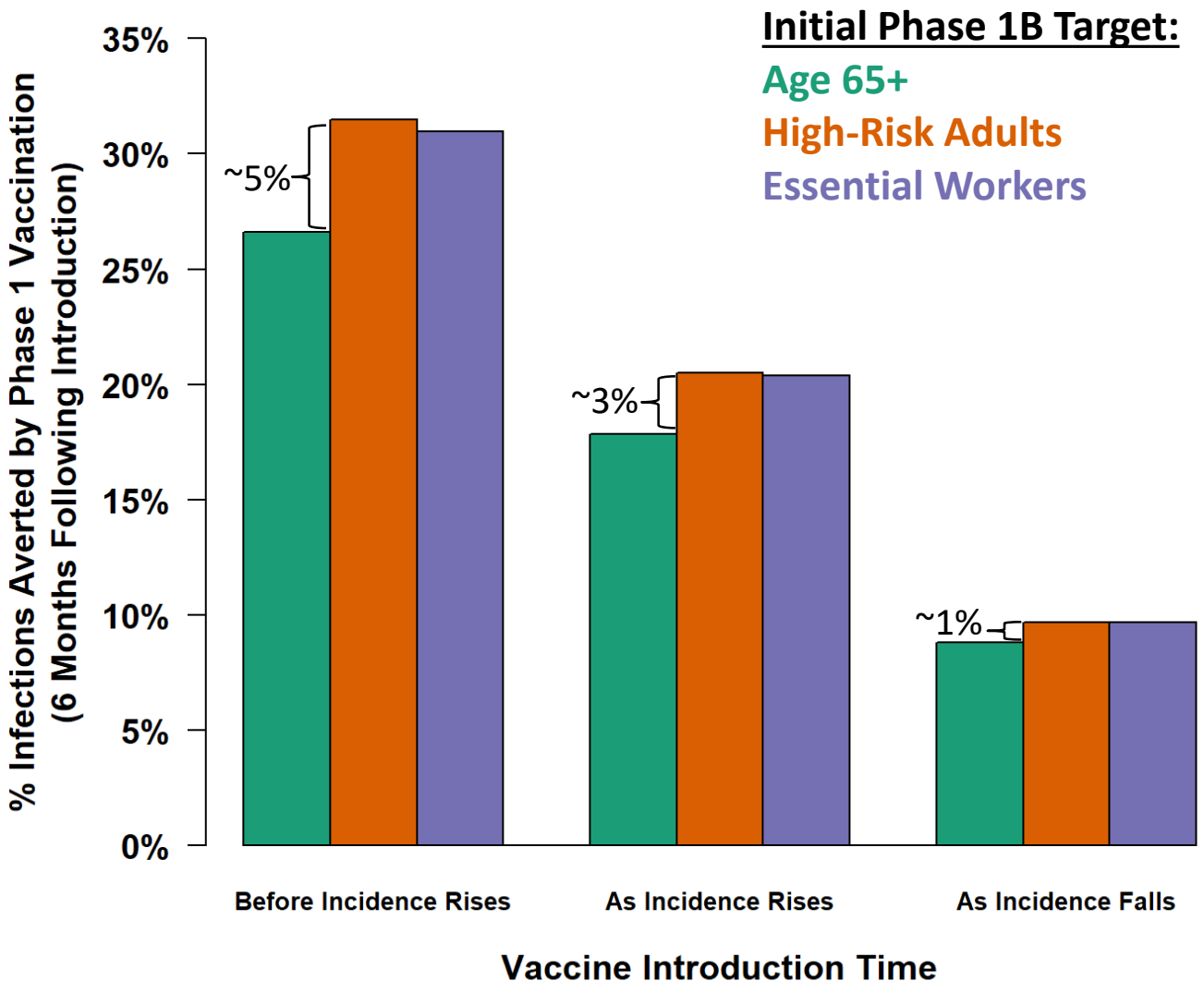
Summary of Work Group interpretation:
COVID-19 vaccine and Pregnant Women in Tier 1a

- Additional situation: Pregnancy diagnosed after receipt of first dose of COVID-19 vaccine

- Majority of Work Group felt that the second dose could be given at the recommended interval
  - Minority opinion: Postponing second dose until second trimester or until after pregnancy
  - Emphasizing need to allow women to make an informed decision

Modeling

Population-Wide Averted Infections:
Infection-Blocking Vaccine, Older Adults Receive Full Protection



- Initially vaccinating high-risk adults or essential workers in Phase 1B averts approximately 1–5% more infections, compared to targeting age 65+
  - This difference is greatest in the scenario where the vaccine is introduced before incidence rises
- Findings are robust to assumptions of reduced VE in older populations

Summary of Work Group interpretation:
Modeling data

- Differences among 3 strategies is minimal
  - Ethical principles and implementation considerations may greatly contribute to selecting the optimal sequence in Phase Ib
- Largest impact in averted deaths and infections is the timing of vaccine introduction in relation to increases in COVID-19 cases
  - Emphasizes the need to continue non-pharmaceutical interventions (e.g. wearing a mask, social distancing) while we await available vaccine
- Many factors will inform interpretation of modeling data and allocation decisions
  - VE in older adults
  - Vaccine's ability to prevent severe disease or transmission
  - If the goal is to prevent greatest number of infections or greatest number of deaths

Clinical Trial Data

Immunogenicity and Safety Information Reviewed by Work Group

NVX-CoV2373 (Novavax) N=131

- **Immunogenicity**
  - Neutralizing antibodies (wild-type neutralization assay titers) and binding antibodies (ELISA) measured 14 days post-dose 2
  - Responses similar to or exceeded convalescent sera comparison
  - Th1-biased CD4+ T-cell response
  - **5µg** dose + Matrix-M1 selected for Phase III clinical trials

- **Safety**
  - Local and systemic symptoms followed for 7 days post-vaccination
    - Headache, fatigue and myalgia most common symptoms reported
  - Reactogenicity symptoms higher after second dose
  - No vaccine-related serious adverse events (SAEs) reported

Protein Subunit Vaccine

Immunogenicity and Safety Information Reviewed by Work Group

Ad26.COV2.S (Janssen) N=775

- **Immunogenicity**
  - Neutralizing antibodies (wild-type virus neutralization antibody titers) and binding antibodies (ELISA) measured 28 days post-dose 1
  - Responses similar to human convalescent sera
  - CD4+ and CD8+ T cell response demonstrated
  - Th1-biased CD4+ T-cell response
  - **$5x10^{10}$** viral particle **single** dose of Ad26.COV2.S selected for Phase III clinical trials

- **Safety**
  - Local and systemic symptoms followed after administration
    - Fatigue, headache and pain most common
  - Reactogenicity symptoms lower in older population (≥65 years)

Nonreplicating Adenovirus Vector Vaccine

Work Group Interpretation

- Phase I/II data from the vaccines show induction of binding and neutralizing antibodies as well as T-cell responses, favorable safety/reactogenicity profile, supporting advance to Phase III trials
- Both platforms with prior experience from other vaccines
- Safety pauses are expected with large clinical trials, indicate the process is working appropriately

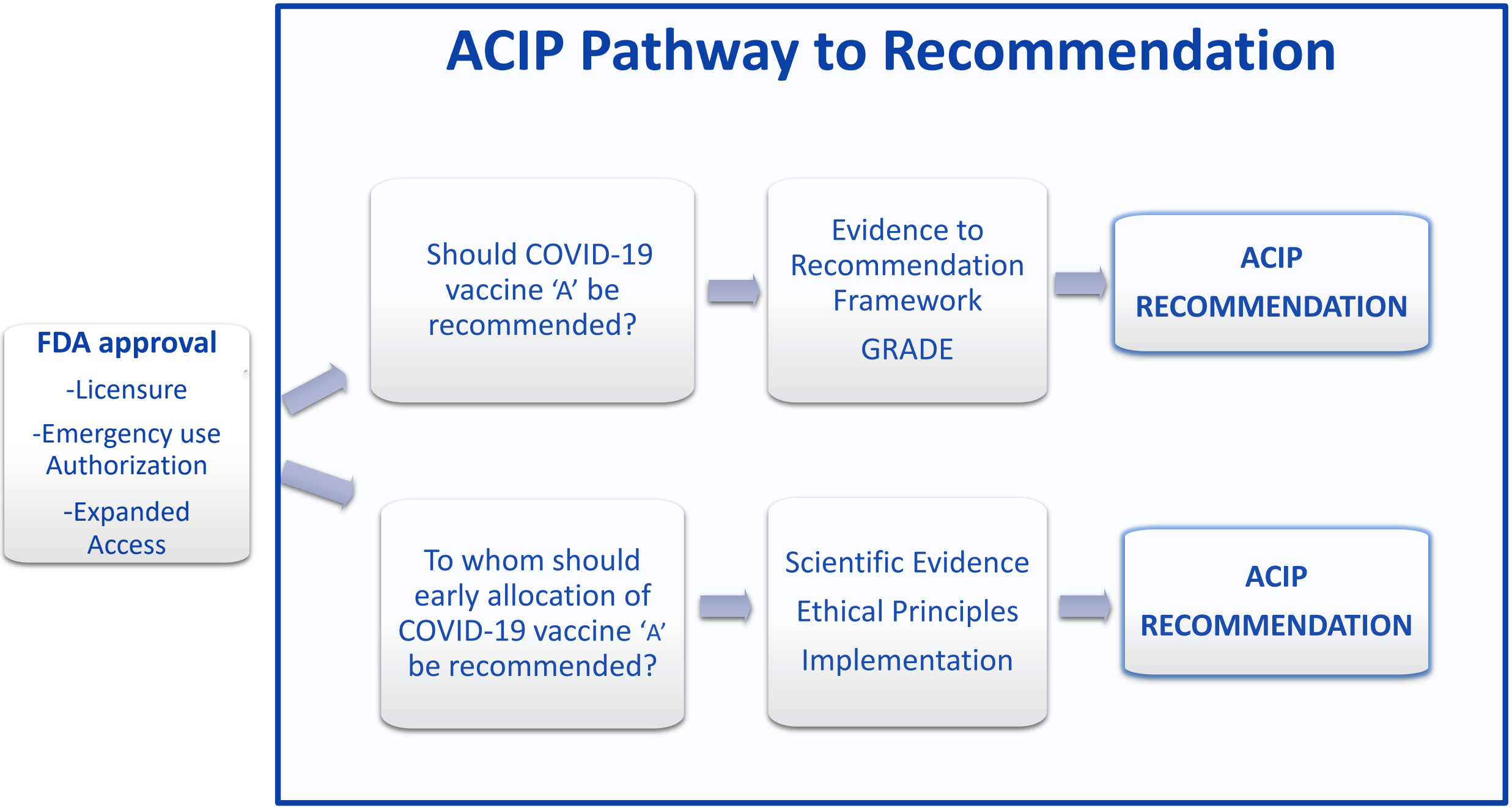
Work Group Interpretation:

Current Phase III Clinical Trials

- Importance of enrolling **diverse** study participants
- Importance of harmonizing safety and efficacy **endpoints** across all Phase III trials to the extent possible
- Need to report **maternal** and **fetal** outcomes for women who become pregnant during the clinical trials
- Support FDA's guidance for ensuring that Phase III trials conduct **ongoing** assessment of long-term safety and efficacy, and that issuance of an EUA is not grounds to unblind follow-up in an ongoing clinical trial

ACIP Policy Questions

ACIP Pathway to Recommendation



PICO for Vaccine Policy Question #1

Population	Adults		
Intervention	COVID-19 vaccine “A”		
Comparison	No vaccine (Placebo, including saline or non-COVID-19 vaccine)		
Outcomes		Benefits (*prevention of*)	Harms (*possible risks*)
	Critical	• Symptomatic COVID-19 (PCR* conf) • Hospitalization due to COVID-19	• Serious Adverse Events (including vaccine-associated enhanced disease)
	Important	• Death (all cause) • SARS-CoV-2 Seroconversion (non-spike) • Serial PCRs for asymptomatic infection	• Reactogenicity

PCR= Polymerase chain reaction

Outcomes under study in clinical trials

Outcome	In clinical Protocols?	Comments
Symptomatic COVID-19 (PCR+)	✓	Primary outcome, consistent definition
Hospitalization due to COVID-19	✓	Exploratory aim (or as adverse event)
Serious Adverse Events	✓	Unsolicited, consistent definition
Death (all cause)	✓	Exploratory aim (or as adverse event)
Reactogenicity	✓	Solicited symptoms 7d
SARS-CoV-2 Seroconversion (non-spike)	✓	Differences in timing & assay
Serial PCRs for asymptomatic infection	X	? Outside U.S.

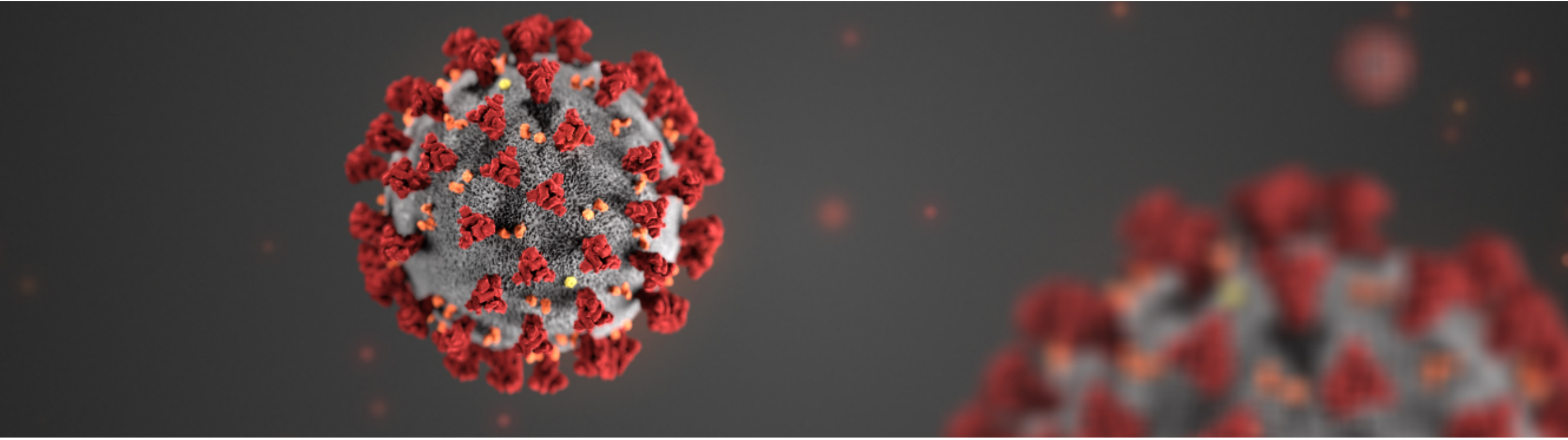
COVID-19 Vaccine Work Group next steps

Policy Question #1: **Vaccine Recommendations**

- Populate the Evidence to Recommendation Framework
- Start GRADEing vaccine evidence and incorporate Phase III data when available
- Discuss clinical guidance (special populations/concomitant administration/scheduling)

Policy Question #2: **Allocation Recommendations**

- Publish ethical principles manuscript
- Incorporate latest information regarding science, implementation, and ethics to further refine Phase 1 allocation



For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

Thank you

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.