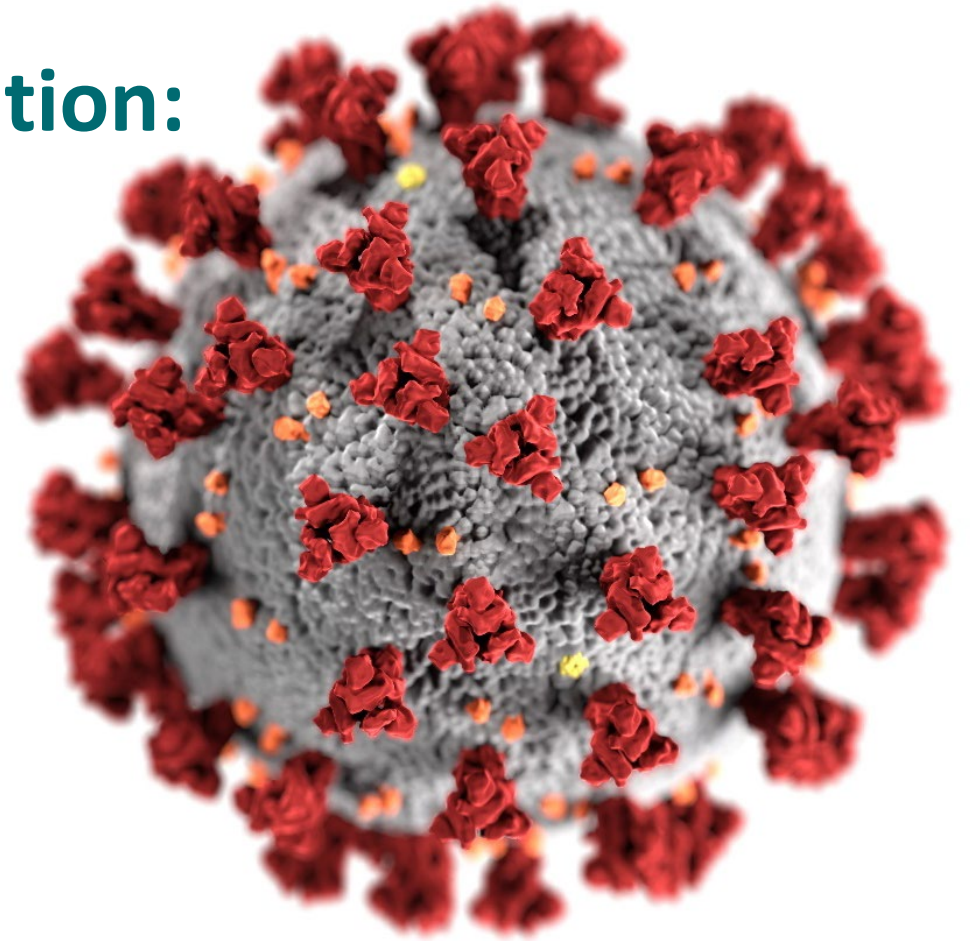


# Summary and Work Group Interpretation: Extended intervals for mRNA COVID-19 vaccines

Sara Oliver, MD, MSPH  
ACIP Meeting  
February 4, 2022



[cdc.gov/coronavirus](https://cdc.gov/coronavirus)

# Policy question for previous ACIP vote

- Should vaccination with the Moderna COVID-19 vaccine (Spikevax, 2-dose primary series) be recommended for persons 18 years of age and older?

Regulatory action, GRADE, Evidence to Recommendation Framework, Vote

**Moderna  
COVID-19 vaccine**

Compared to

**No  
COVID-19 vaccine**

# Question for discussion

- Based on new and emerging data, should CDC consider guidance around the interval between dose 1 and 2 for mRNA COVID-19 vaccines?

Implementation;  
Discussions around myocarditis and intervals

**Moderna  
COVID-19 vaccine**

And

**Pfizer-BioNTech  
COVID-19 vaccine**

# VaST assessment – Myocarditis/pericarditis following Moderna and Pfizer-BioNTech COVID-19 vaccination

- VaST reviewed the most recent data from three U.S. safety monitoring systems\*, and well as data from international partners
- Reported rates of myocarditis/pericarditis following mRNA COVID-19 vaccination are higher than background; rates are highest after dose 2 in adolescent and young adult males
- In most safety monitoring systems, myocarditis/pericarditis risk appears higher after dose 2 Moderna than dose 2 Pfizer-BioNTech COVID-19 vaccination
- Data are limited on myocarditis/pericarditis risk following different dose 1-dose 2 intervals<sup>+</sup>

VaST: Vaccine Safety Technical (VaST) Work Group \*VAERS, v-safe, VSD

<sup>+</sup>Source: Buchan S et al. Dec 2021, MedRxiv preprint.

# Summary: International data

## Myocarditis after mRNA COVID-19 vaccines

- Risk of myocarditis/pericarditis was higher for Moderna than Pfizer vaccine
  - The highest risk was seen after the second dose among younger males
- Rates of myocarditis/pericarditis were lower with extended interval ( $\geq 8$  weeks) between first and second dose of mRNA vaccine primary series

# Summary

## Extended primary series interval and mRNA COVID-19 vaccine effectiveness

- An extended primary series interval may improve immunogenicity and vaccine effectiveness
  - Antibody responses were higher following an extended interval (6–14 weeks) between the first and second doses of mRNA vaccine, compared to a standard interval (3–4 weeks)
  - mRNA vaccine effectiveness against infection and hospitalization was higher with an extended interval (6–8 weeks), compared to a standard interval (3–4 weeks)

# Benefits and risks balance for mRNA COVID-19 vaccines

## Adults ages 18–39 years

### Benefits

#### mRNA COVID-19 vaccines

Moderna COVID-19 vaccine

Pfizer-BioNTech COVID-19 vaccine



### Risks

#### mRNA COVID-19 vaccines

Moderna COVID-19 vaccine

Pfizer-BioNTech COVID-19 vaccine

# Methods for assessment of benefit-risk balance

## **Benefits** — Calculated per 1 million fully vaccinated people

- Age group: 18 – 39 years
  - Selected because this age group has the highest rates of myocarditis and lowest hospitalization rates among adults, and would therefore have the closest benefit/risk margin
- Age/sex specific hospitalization rates: COVID-NET (average of rates from Dec 11-Jan 1, 2022)<sup>1</sup>
- Pooled vaccine-specific VE estimates from two platforms<sup>2</sup>
- Time Horizon: 150-day period

## **Harms** — Calculated per 1 million fully vaccinated people

- Vaccine-specific myocarditis rates from Vaccine Safety Datalink (VSD)

VE: Vaccine Effectiveness

<sup>1</sup>[https://gis.cdc.gov/grasp/COVIDNet/COVID19\\_3.html](https://gis.cdc.gov/grasp/COVIDNet/COVID19_3.html)

<sup>2</sup><https://covid.cdc.gov/covid-data-tracker/#vaccine-effectiveness>



# Vaccine-specific estimates of effectiveness against COVID-19 hospitalization

VE against COVID-19 hospitalization <sup>1</sup>			
	IVY Network <sup>2</sup> , Oct – Nov, 2021 % (95% CI)	VISION <sup>2</sup> , Aug – Dec, 2021, % (95% CI)	Pooled VE Estimate
Moderna	91 (89-93)	92 (91-93)	92
Pfizer- BioNTech	86 (83-88)	87 (86-88)	87

VE= vaccine effectiveness; VE reported for 2 doses of mRNA COVID-19 vaccines

1. <https://covid.cdc.gov/covid-data-tracker/#vaccine-effectiveness>
2. VE estimate for 17-179 days after 2<sup>nd</sup> dose

# Reporting rates of myocarditis following mRNA COVID-19 vaccination (per million 2<sup>nd</sup> doses administered) among persons ages 18–39 years<sup>1</sup>

Vaccine	Sex	Rate per 1M 2 <sup>nd</sup> Doses in 7-day risk period among persons ages 18–39 years <sup>2</sup>
Moderna	Males	67.5
	All	33.0
Pfizer-BioNTech	Males	46.8
	All	24.1

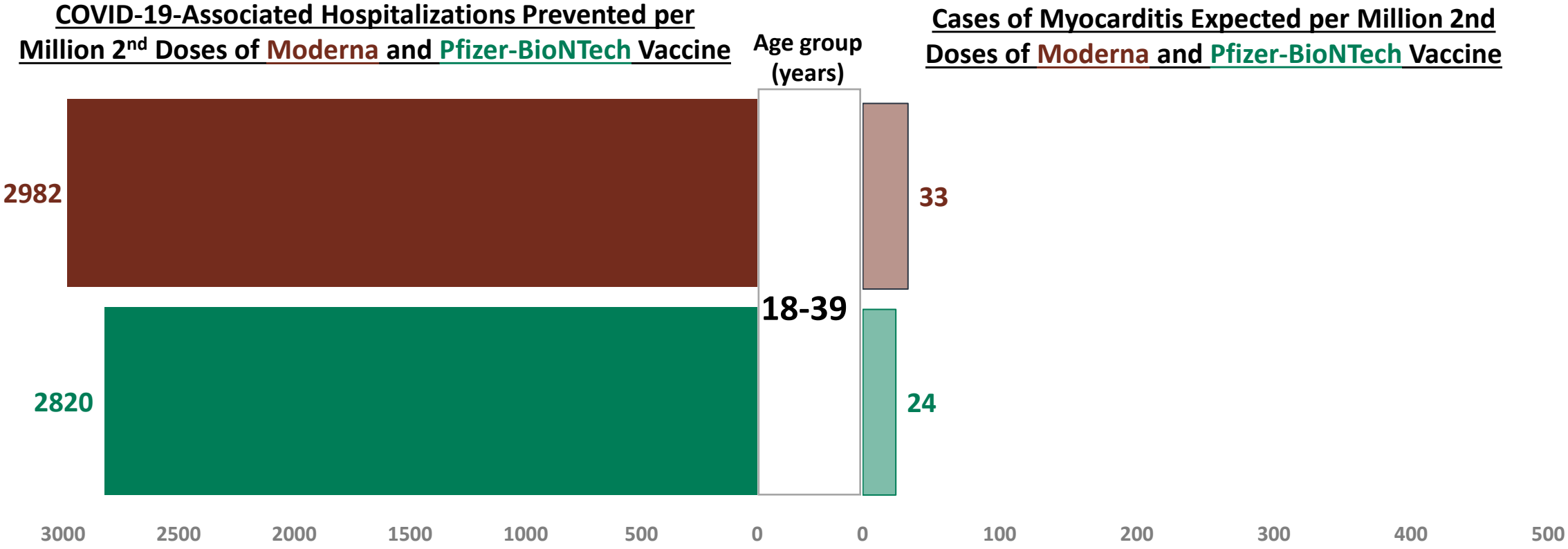
1. Data from the Vaccine Safety Datalink (VSD): <https://www.cdc.gov/vaccinesafety/ensuringsafety/monitoring/vsd/index.html>

2. Data through Jan 15, 2022

# Benefits and risks after mRNA COVID-19 vaccines among persons ages 18–39 years

*per million 2<sup>nd</sup> doses*

- COVID-19-associated hospitalizations prevented by mRNA COVID-19 vaccines compared with myocarditis cases expected
- Presented by vaccine product



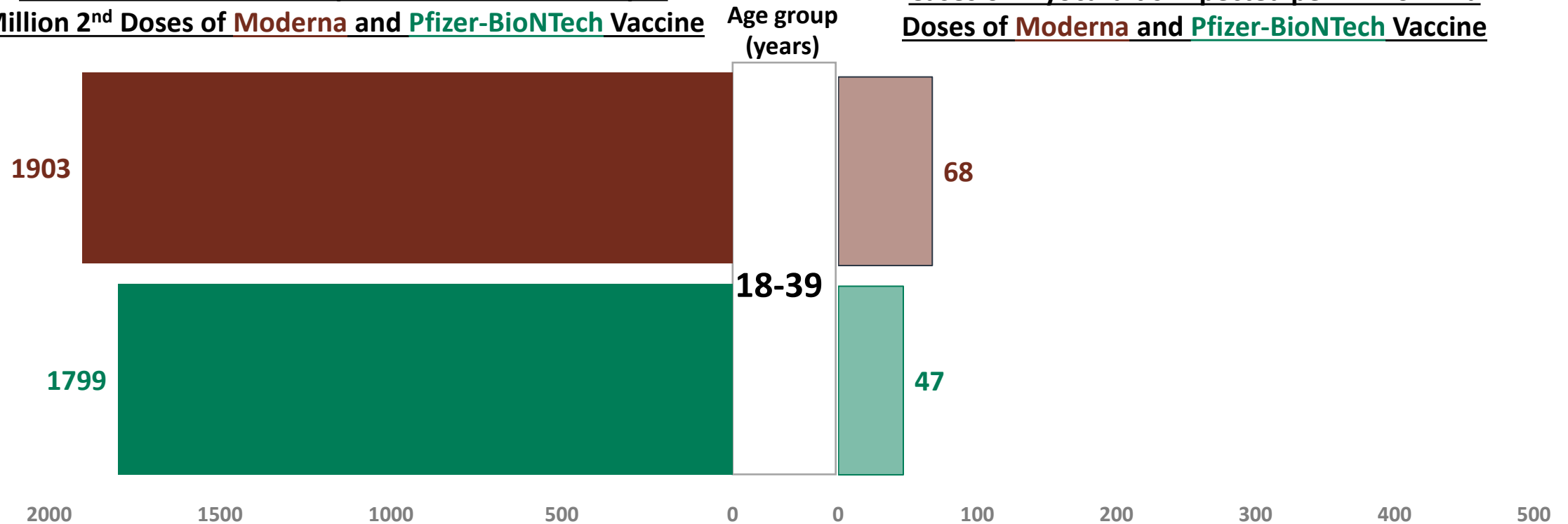
# Benefits and risks after mRNA COVID-19 vaccines among males ages 18–39 years

*per million 2<sup>nd</sup> doses*

- COVID-19-associated hospitalizations prevented by mRNA COVID-19 vaccines compared with myocarditis cases expected
- Presented by vaccine product

COVID-19-Associated Hospitalizations Prevented per Million 2<sup>nd</sup> Doses of Moderna and Pfizer-BioNTech Vaccine

Cases of Myocarditis Expected per Million 2<sup>nd</sup> Doses of Moderna and Pfizer-BioNTech Vaccine



# Limitations

- Benefit-risk analysis focuses on individuals 18–39 years of age, considers direct benefits and risk over a 150-day period, and compares vaccine vs. no vaccine
- VE assumptions used in the model do not yet include Omicron-specific VE estimates
- The model assumes static hospitalization rate over 5 months
  - Benefit/risk profile might change as hospitalization rates change
- Model does not account for booster doses or prior infection

# Benefits and risks balance for mRNA COVID-19 vaccines

## Benefits

COVID-19 hospitalizations averted by Moderna COVID-19 vaccine greater than Pfizer-BioNTech COVID-19 vaccine



## Risks

Myocarditis after Moderna COVID-19 vaccine likely greater than Pfizer-BioNTech COVID-19 vaccine

# Summary:

## Benefit/risk balance

- Benefits for both mRNA COVID-19 vaccines **far outweigh** risk of myocarditis, compared with no vaccine
- When compared to the benefit-risk balance for Pfizer-BioNTech COVID-19 vaccine, the Moderna vaccine prevents more COVID-19 hospitalizations, however more myocarditis cases would also be expected

# Summary:

## Myocarditis and Intervals

- When comparing the two mRNA COVID-19 vaccines, the risk of myocarditis/pericarditis was higher for Moderna than Pfizer vaccine
  - The highest risk was seen after the second dose among younger males
- Rates of myocarditis/pericarditis were **lower** with **extended interval** between first and second dose of mRNA vaccine primary series
- Extended primary series interval may **improve immunogenicity** and **vaccine effectiveness**



# Question for discussion

- Based on new and emerging data, should CDC consider guidance around the interval between dose 1 and 2 for mRNA COVID-19 vaccines?

Implementation; Discussions around myocarditis and intervals

**Moderna  
COVID-19 vaccine**


And

**Pfizer-BioNTech  
COVID-19 vaccine**

# Who would this apply to?

Number and percent of people with 0 doses administered, by age group

**~33 million**  
unvaccinated  
individuals ages  
12–39 years



Age Group	Number (M)	Percent
12–17 yrs	8.3	35
18–24 yrs	7.9	25
25–39 yrs	16.5	25
40–49 yrs	6.1	15
50–64 yrs	4.7	8
65–74 yrs	0.5	5
75+ yrs	0.5	5

# Considerations regarding extended intervals between first and second doses of mRNA vaccine (primary series)

## Possible Benefits

### ■ **Safety:**

- Extended interval appears to reduce the risk of myocarditis
- Lowest rates of myocarditis with interval at 8 weeks

### ■ **Effectiveness:**

- Extended interval appears to increase VE for primary series
- Benefit may 'level out' at  $\geq 8$  weeks

### ■ **Implementation:**

- Possibility that uptake for COVID-19 vaccine primary series could increase if individuals/parents desire action to lower risk for myocarditis

# Considerations regarding extended intervals between first and second doses of mRNA vaccine (primary series)

## Possible Risks

- **Effectiveness:**
  - Longer duration of time where individual only have the benefit of a single dose of mRNA vaccine
- **Implementation:**
  - For aspects that require being ‘fully vaccinated’ (shorter quarantine, travel or restaurants, etc), extending interval would extend the time before being ‘fully vaccinated’

# Work Group Interpretation

- An individual's **risk** of getting COVID-19 likely increases the longer they are only partially vaccinated with a single dose
- The risk would need to be balanced with the **benefits** of **lowering rates** of myocarditis and optimizing the **long-term vaccine effectiveness**
- This balance is influenced by trajectory of pandemic and recent epidemiology of COVID-19, and can change over time
- Early in the pandemic, the priority was for individuals to have **optimum protection** from the primary series as **quickly** as possible
  - Guidance around COVID-19 vaccines can be updated as **new data** become available and the focus expands to the **future** of the COVID-19 vaccine program

# Work Group Interpretation

- **Clear communication** for COVID-19 vaccines and preferred intervals is important
- May be populations where the benefits of earlier interval (3 or 4 weeks) would outweigh possible risks of myocarditis
  - Licensed intervals of 3 weeks (Pfizer-BioNTech) or 4 weeks (Moderna) continue to be recommended, especially in circumstances where early protection is desired
- The Work Group supported a preferred interval of **8 weeks** between the first and second dose of an mRNA COVID-19 vaccine primary series

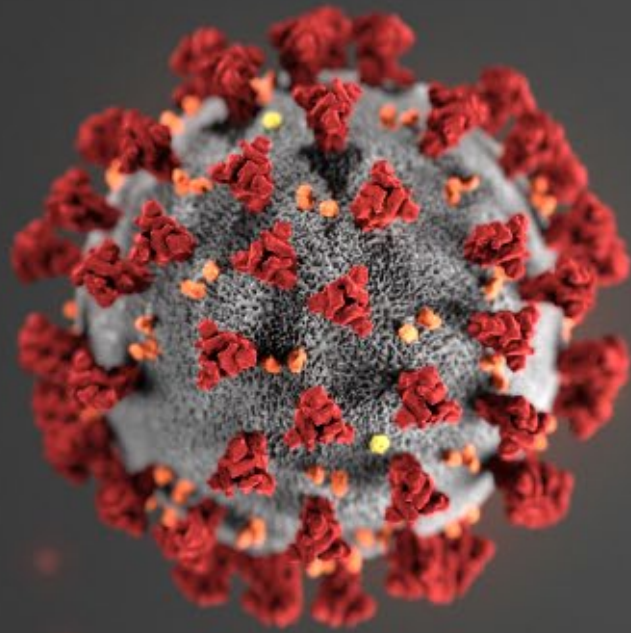
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- Vaccine Task Force
- Epi Task Force
- Data Analytics and Visualization Task Force
- Respiratory Viruses Branch

# Questions for ACIP

- What does ACIP think about an **extended interval** between the first and second doses of the mRNA COVID-19 vaccine primary series?
- What **time frame** does ACIP think would be preferred for the interval between first and second doses of the mRNA COVID-19 vaccine primary series?





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

