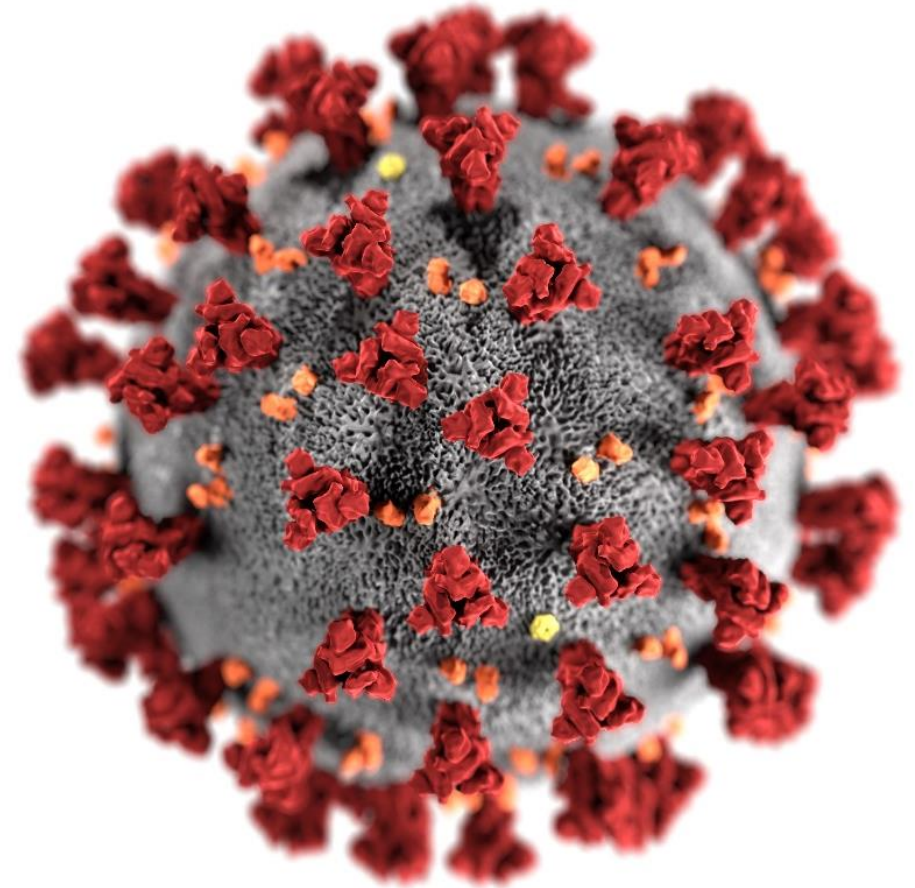


Implementation considerations for COVID-19 Vaccines

Dr. Kathleen Dooling, MD, MPH
ACIP Emergency Meeting, March 1, 2021



Outline- Implementation Considerations

- Janssen COVID-19 vaccine
- COVID-19 vaccine prioritization
- Dosing intervals for mRNA vaccines

Janssen COVID-19 vaccine

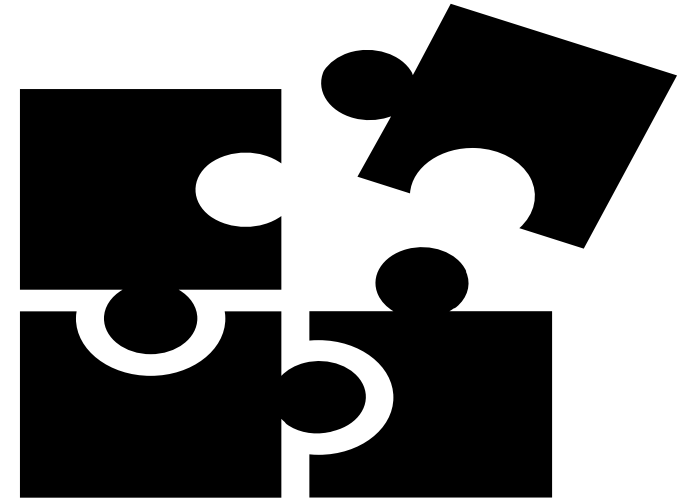
- ACIP states no preference for any of the three authorized vaccines
 - Results of Janssen Phase III trials not comparable with mRNA vaccines
 - Different calendar time
 - Different geography
- } Different circulating variants
Higher background incidence
- Strong protection against severe COVID-19
 - 93% VE against hospitalizations (2 cases in vaccinated vs. 29 in placebo)
 - No COVID-associated deaths in vaccinated vs. 7 in placebo

Janssen COVID-19 Vaccine

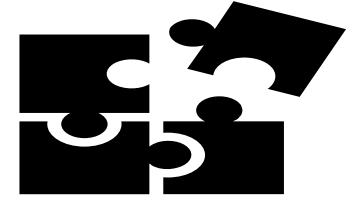
How does it best fit?

Characteristics of the vaccine

- 1 dose
- Transport, and storage (x3m) at 2-8°C
- No diluent/reconstitution necessary



Janssen COVID-19 Vaccine: Considerations for utilization



Where?

- Mobile/pop-up clinics
- Newly established vaccine administration sites
- Sites that do not have freezer capacity (e.g. adult HCP offices)

Who?

- People who want to be fully vaccinated quickly
- People who don't want to return or can't return for a second dose
- Mobile populations or homebound populations


COVID-19 Vaccine Work Group considerations

- During a pandemic, under EUA, offering Janssen COVID-19 vaccine to persons 18 years and older, according to established allocation and eligibility recommendations in a given jurisdiction, is an effective implementation strategy
 - Allows for jurisdictional flexibility
 - Supports rapid vaccination and increases in population immunity
 - Does not single out any group
 - Allows individuals to be vaccinated with the earliest vaccine available

COVID-19 vaccine prioritization



Work Group Considerations: Goals of the COVID-19 Vaccine Program

- **Ensure safety and effectiveness of COVID-19 vaccines**
 - **Reduce transmission, morbidity, mortality of COVID-19 disease**
 - **Help minimize disruption to society and the economy, including maintaining healthcare capacity**
 - **Ensure equity in vaccine allocation and distribution**
- 

COVID-19 Vaccination Program: Ongoing Roll-Out

Current status

- >72M doses administered, as of February 27
- Continued constrained COVID-19 vaccine supply
- Continued reliance on large vaccination centers
- Most jurisdictions are in Phase 1b or expanding into Phase 1c
- Most states have made modifications to the ACIP prioritization framework¹
 - Sub-prioritization or delay of essential workers
 - Adding age bands <65 years
 - Sub-prioritization of high-risk medical conditions or requiring ≥ 2 conditions

Estimated doses by the end of March 2021²

- Pfizer: 120M doses (>37M administered)
- Moderna: 100M doses (>35M already administered)
- Janssen: 20M doses

1. <https://energycommerce.house.gov/committee-activity/hearings/hearing-on-pathway-to-protection-expanding-availability-of-covid-19>

2. <https://www.kff.org/other/state-indicator/state-covid-19-vaccine-priority-populations>

Implementation Challenges and Considerations

- Challenge: difficulty adjudicating eligibility in large vaccination centers
 - E.g. Essential worker & High-risk conditions
 - **Verification of eligibility should not hamper throughput at large vaccination clinics**
 - **Medical care homes/Primary Care Providers may be better able to assess eligibility on the basis of underlying medical conditions**

- Challenge: implementing the list of high-risk conditions
 - CDC list relies on published studies and is not exhaustive
 - Certain conditions on the list encompass a wide range of severity
 - **Clinical judgement may determine if rare conditions not on the list confer increased risk of severe COVID-19.**

Implementation Challenges and Considerations

- Challenge: size of eligible groups in Phase 1c may exceed vaccine supply
 - **Consider addition of an eligibility age bands <65 yrs (e.g. 60-64 or 55-64 or 50-64)**
 - **Consider prioritizing persons with ≥ 2 high-risk conditions**
- Challenge: transmission in congregate settings (eg prisons, homeless shelter or LTCF)
 - **Consider offering vaccine to all unvaccinated staff and residents at the same time**

Implementation Challenges and Considerations

- Challenge: promoting health equity while ensuring efficient vaccine distribution and administration
- **Use Social Vulnerability Index (SVI) or other needs-based index to place vaccine clinics**
- **Partner with Federally Qualified Health Centers (FQHCs) to be vaccination hubs and help register eligible community members for vaccination**
- **Offer Janssen COVID-19 vaccine as an option for populations for whom returning for a second dose would be difficult**
- **Community engagement and education will be important as new COVID-19 vaccines are authorized and recommended for use**

Dosing intervals for mRNA vaccines



Dosing intervals for mRNA vaccines

Two issues:

1. Delay the second dose?
2. Single dose of mRNA vaccine for individuals with confirmed prior SARS-coV-2 infection?

Issue # 1:

Delay the second dose?

- **Background:** Extended inter-dose intervals have been adopted by other national vaccine advisory groups and proposed by individuals in the U.S. as a strategy to increase 1-dose coverage during a time when demand exceeds supply
- **Current guidance:** "The second dose should be administered as close to the recommended interval as possible. However, if it is not feasible to adhere to the recommended interval, the second dose of Pfizer-BioNTech and Moderna COVID-19 vaccines may be scheduled for administration up to **6 weeks (42 days)** after the first dose."

Issue # 1:

Delay the second dose?

- **Phase I/II clinical trials**: Neutralizing antibodies did not show large increases until after receipt of the 2nd dose (both Pfizer and Moderna).
- **Phase III trials**: 97-98% of recipients received both doses. Only studied out to 3 weeks (Pfizer) or 4 weeks (Moderna). VE estimated at 50-90% (higher when starting 2 weeks after 1st dose).

- **“Real world” effectiveness**:

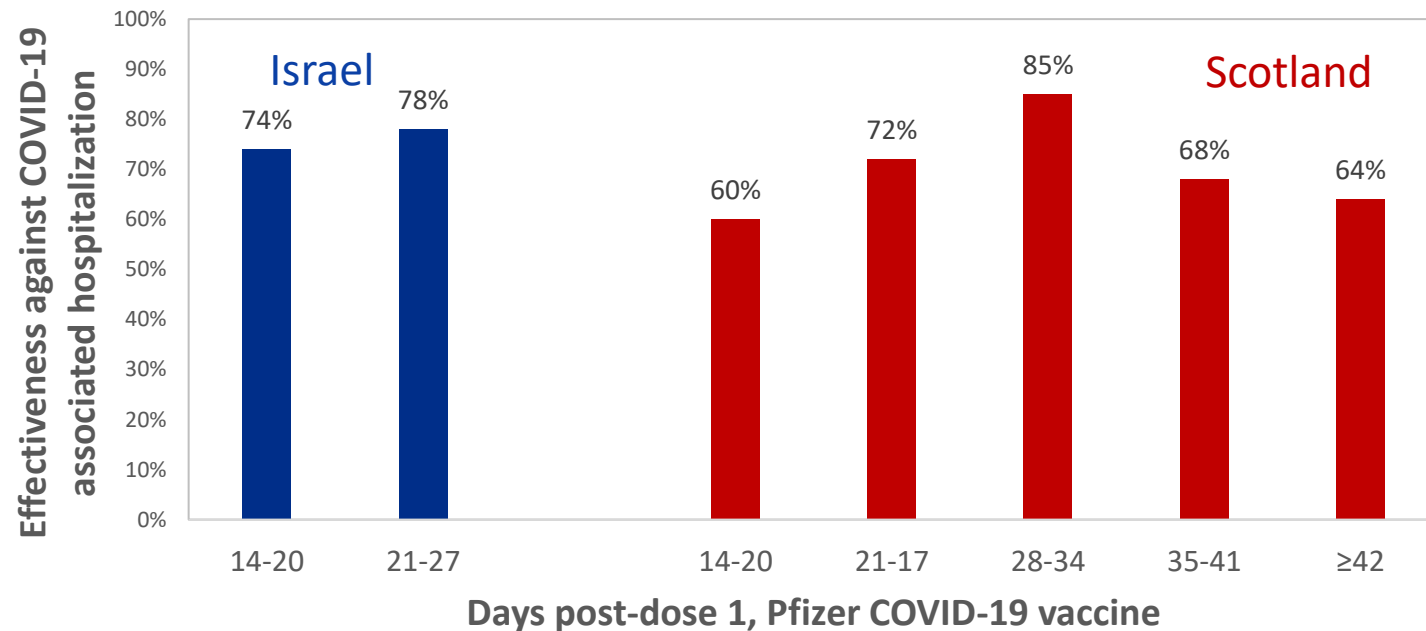
Recent studies evaluating effectiveness of 1-dose of Pfizer vaccine to prevent COVID-19 associated hospitalizations:

Matched case control study, Israel¹:

VE increased to **78%** 21-27 days post-dose 1

Prospective cohort study, Scotland²:

VE increased to **85%** 28-34 days post-dose 1, but then declined



¹Dagan N, et al. NEJM, 2021; ²Vasileiou E, et al. Lancet, preprint 2021

Issue #1:

Delay the second dose?

Pros	Cons
Could provide 1 dose protection to a larger number of people over the next several months. If 1 dose protection is high and persists, this could prevent more infections and deaths ¹ .	Lower neutralization antibodies could be protective against 'wild-type' COVID-19, but not novel variants ²⁻⁴ . 1-dose vaccination could leave individuals susceptible to variants, providing selective pressure and increase transmission of variants ⁵ .
Boosting still likely to be effective, even at longer interval	Estimates of effect for a single dose are imprecise and duration of protection after the 1 st dose is unknown.
	Would contradict FDA's Emergency Use Authorization (2-dose series, 3 or 4 weeks apart)

¹Accelerate COVID-19 Vaccine Rollout by Delaying the Second Dose of mRNA Vaccines <https://doi.org/10.1093/cid/ciab068>

¹The effectiveness of the first dose of BNT162b2 vaccine in reducing SARS-CoV-2 infection 13-24 days after immunization: real-world evidence | medRxiv

²Increased resistance of SARS-CoV-2 variants B.1.351 and B.1.1.7 to antibody neutralization. [2021.01.25.428137v2.full.pdf](https://doi.org/10.1101/2021.01.25.428137v2) (biorxiv.org)

³SARS-CoV-2 variant B.1.17 is susceptible to neutralizing antibodies elicited by ancestral Spike vaccines [Microsoft Word - Shen_B117_ver10.docx](https://doi.org/10.1101/2021.01.25.428137v2) (biorxiv.org)

⁴The E484K mutation in the SARS-CoV-2 spike protein reduces but does not abolish neutralizing activity of human convalescent and post-vaccination sera | medRxiv

⁵Epidemiological and evolutionary considerations of SARS-CoV-2 vaccine dosing regimes <https://doi.org/10.1101/2021.02.01.21250944>;

Issue # 1:

Delay the second dose?

■ **Summary of Work Group Discussions:**

- Currently, there are insufficient data to increase recommended intervals
- Important uncertainty regarding protection from the variants following 1 dose of mRNA COVID-19 vaccines

■ **Next Steps:**

- Continue to monitor post-authorization effectiveness studies
- Any updates to vaccine recommendations will be:
 - Evidence based
 - Discussed publicly
 - Made in collaboration with FDA

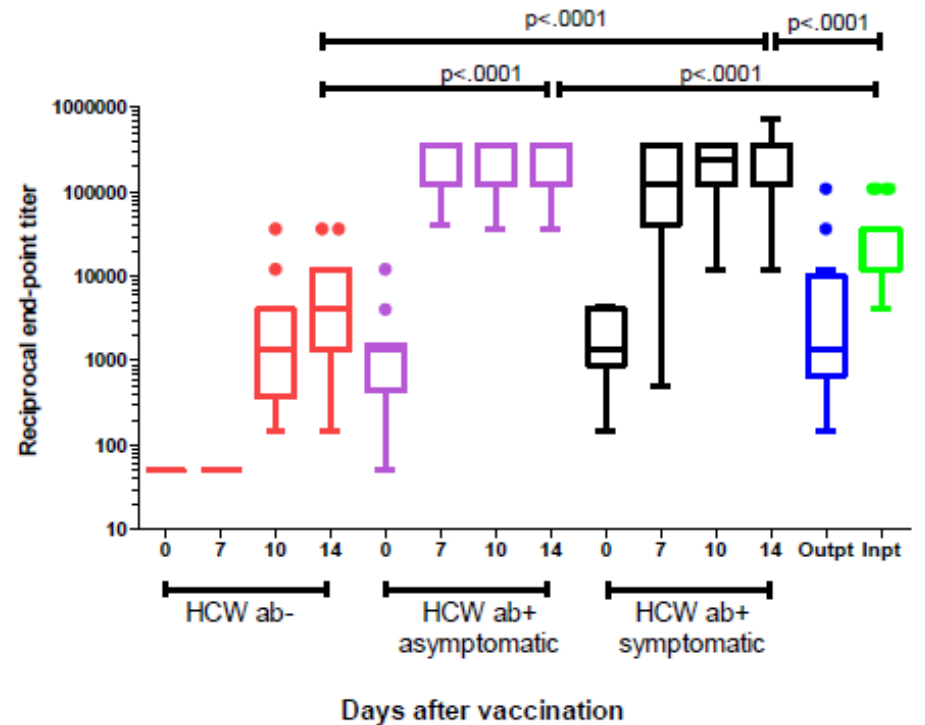
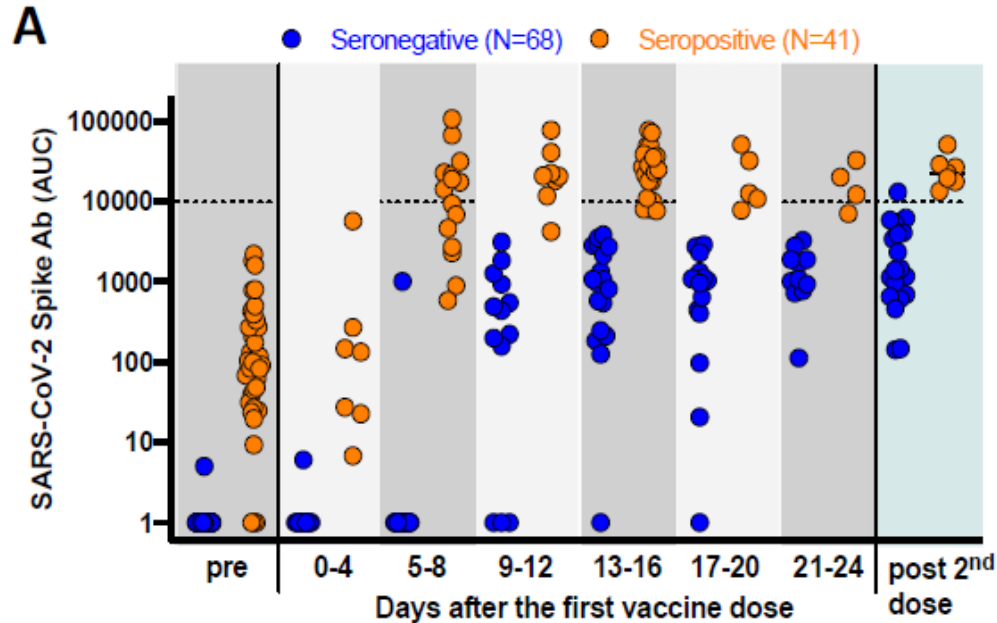
Issue # 2:

Single dose of mRNA vaccine for individuals with confirmed prior SARS-CoV-2 infection?

- **Background:** There have been anecdotal reports of increased reactogenicity following vaccination among people with prior COVID-19. Additionally, recently published reports suggest high antibody response after 1 dose for individuals with prior SARS-CoV-2 infection
- **Current guidance:** "...while vaccine supply remains limited, persons with recent documented acute SARS-CoV-2 infection may choose to temporarily delay vaccination, if desired, recognizing that the risk of reinfection, and therefore the need for vaccination, might increase with time following initial infection."

Issue # 2:

Single dose of mRNA vaccine for individuals with confirmed prior SARS-CoV-2 infection?



Immunogenicity evaluated in 2 pre-print studies^{1,2}:

Assessed antibody titers after 1 dose in seropositive compared to seronegative individuals
Both studies showed higher antibody titers in seropositive individuals after 1 dose

¹[Robust spike antibody responses and increased reactogenicity in seropositive individuals after a single dose of SARS-CoV-2 mRNA vaccine | medRxiv](#)

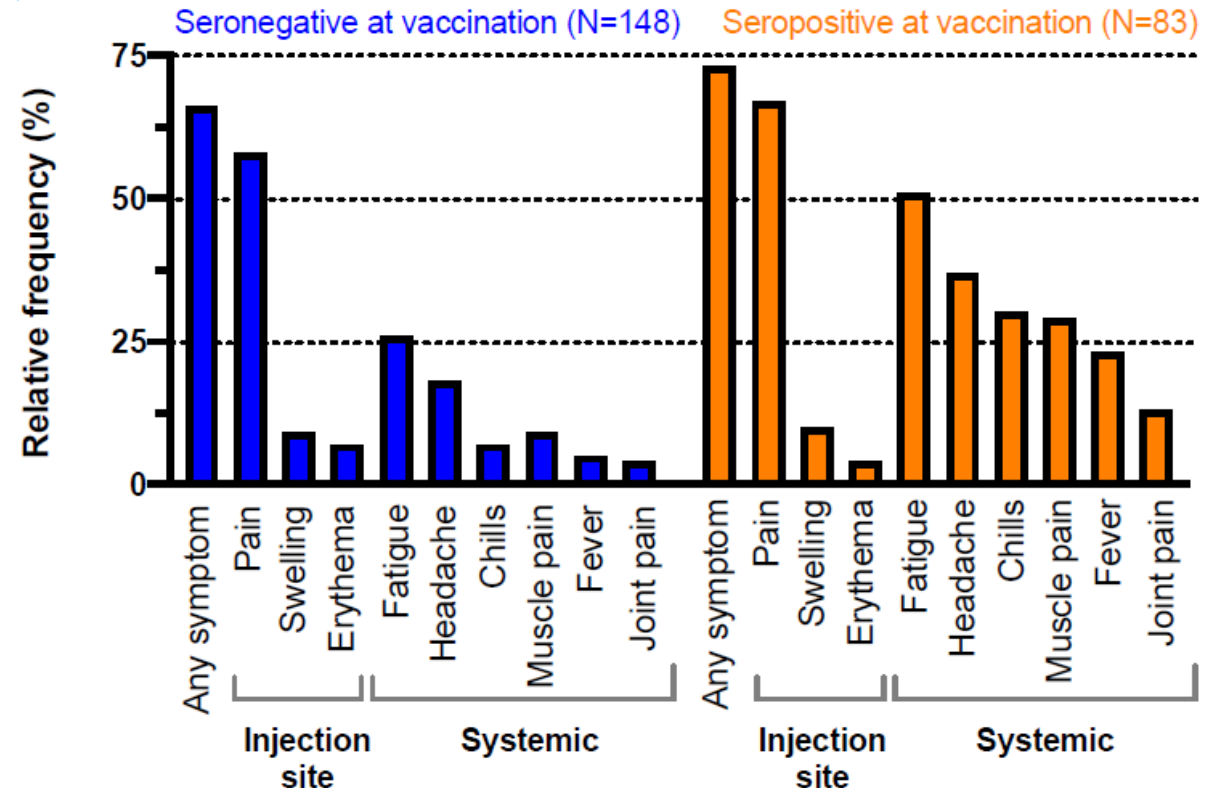
²[Single Dose Vaccination in Healthcare Workers Previously Infected with SARS-CoV-2 | medRxiv](#)

Issue # 2:

Single dose of mRNA vaccine for individuals with confirmed prior SARS-CoV-2 infection?

Reactogenicity evaluated in 1 preprint study¹:

- Localized injection site symptoms occurred with similar frequency.
- Systemic side effects occurred at higher frequency among individuals with pre-existing immunity:
 - Similar to symptoms reported for the second dose in the Phase 3 trials



¹[Robust spike antibody responses and increased reactogenicity in seropositive individuals after a single dose of SARS-CoV-2 mRNA vaccine | medRxiv](#)

Issue # 2:

Single dose of mRNA vaccine for individuals with confirmed prior SARS-CoV-2 infection?

Pros	Cons
Could 'free up' 2 nd doses for seropositive persons to be provided to seronegative persons	Current studies included individuals with confirmed antibodies to SARS-CoV-2. Performing large-scale antibody screening prior to vaccination is not feasible
Seropositive persons would not receive 2 doses of reactogenic vaccine	Correlate of protection currently unknown; unable to extrapolate antibody studies to vaccine effectiveness
	Limited data (small studies) currently
	Would contradict FDA Emergency Use Authorization (2-dose series, 3 or 4 weeks apart)

Issue # 2:

Single dose of mRNA vaccine for individuals with confirmed prior SARS-CoV-2 infection?

■ **Summary of Work Group Discussions:**

- Currently there are insufficient data to support changes to guidance or recommendations
- This is an area to pursue further data
- Consider promotion of existing guidance: those with prior infection may choose to temporarily delay vaccination for several months

■ **Next Steps:**

- Collect and review further data on safety and reactogenicity as well as immunogenicity and effectiveness of COVID-19 vaccines among individuals with prior infection
- Any updates to vaccine recommendations will be:
 - Evidence based
 - Discussed publicly
 - Made in collaboration with FDA

Questions for ACIP

Janssen COVID-19 vaccine

- Do you agree that offering Janssen COVID-19 vaccine to persons 18 years and older, according to established allocation and eligibility recommendations, is an effective implementation strategy?

Vaccination Prioritization

- What are the key challenges and opportunities of implementation guidance options for
 1. Additional age eligibility brackets <65 years
 2. Eligibility based on 2 or more high risk condition

mRNA vaccine dosing

- What additional data is needed to inform
 1. Delay the second dose?
 2. Single dose of mRNA vaccine for individuals with confirmed prior SARS-coV-2 infection?

Questions for ACIP

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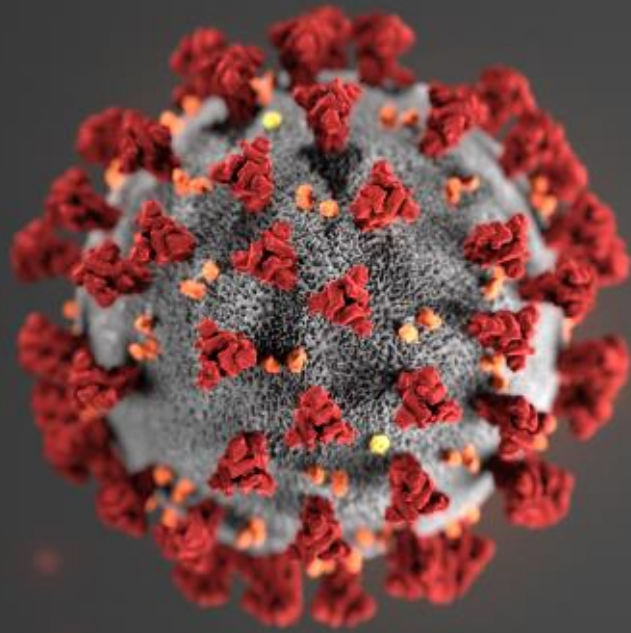
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For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

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.

