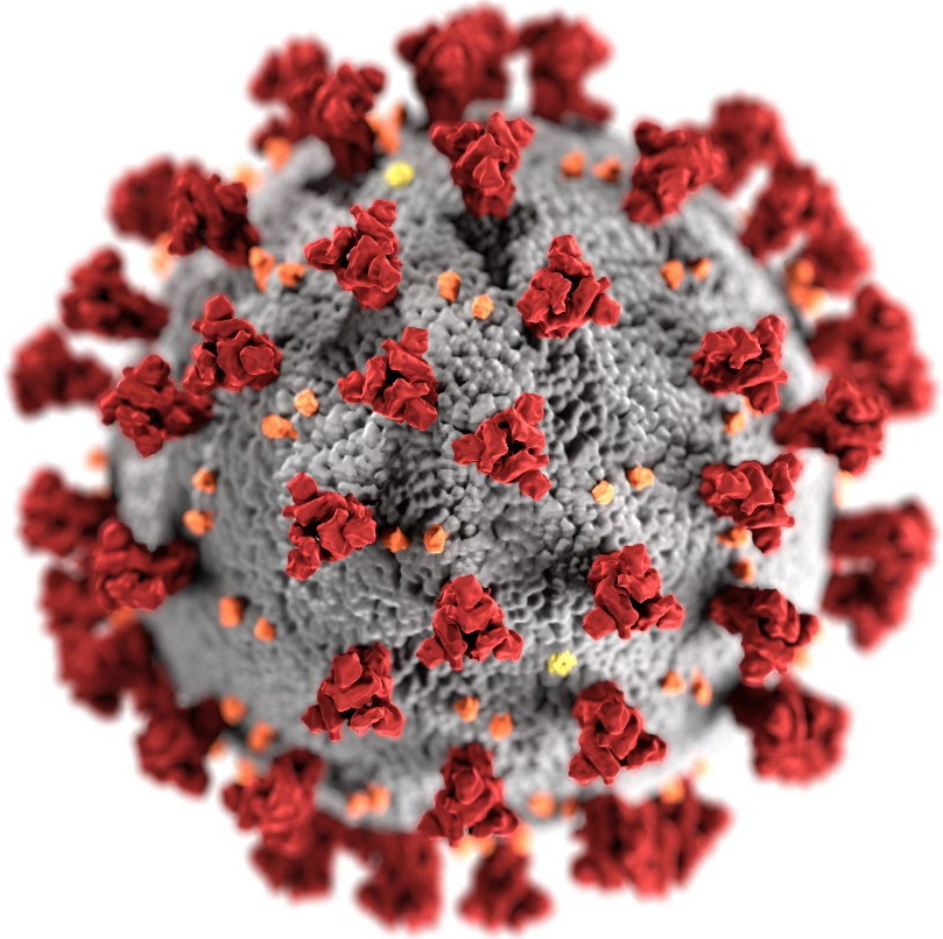
Updates to Interim Clinical Considerations for Use of COVID-19 Vaccines



Elisha Hall, PhD
Advisory Committee on Immunization Practices Meeting
February 4, 2022

cdc.gov/coronavirus

Anticipated Updates

- Clarification and updates on guidance for people who are moderately or severely immunocompromised
- Updates to recommendations on passive antibody products
- Reduction and reorganization for ease of use

Updated guidance for people who are moderately or severely immunocompromised

People Who Are Moderately or Severely Immunocompromised

- People with immunocompromising conditions or people who take immunosuppressive medications or therapies:
  - Are at increased risk for **severe COVID-19**
  - May **not mount a protective immune response** after initial vaccination
  - Have **waning protection** over time

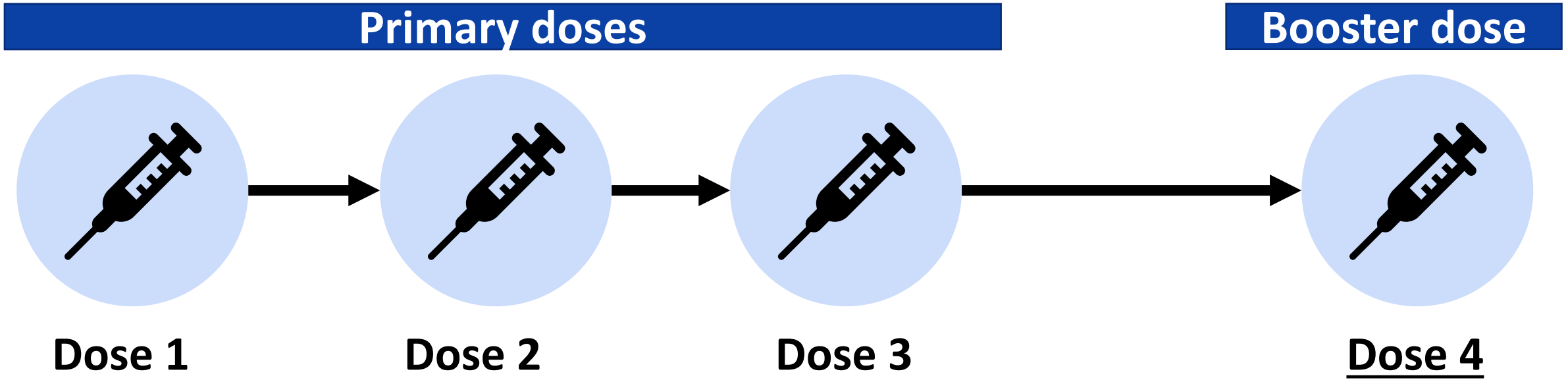
CURRENT COVID-19 Vaccination Schedule for People Who Are Moderately or Severely Immunocompromised

Vaccine	Vaccination Schedule			
Pfizer-BioNTech (ages 5 years and older)	**1st dose**	**2nd dose** (21 days after 1st dose)	**3rd dose** (at least 28 days after 2nd dose)	**Booster dose*** (at least 5 months after 3rd dose)
Moderna (ages 18 years and older)	**1st dose**	**2nd dose** (28 days after 1st dose)	**3rd dose** (at least 28 days after 2nd dose)	**Booster dose*** (at least 5 months after 3rd dose)
Janssen (ages 18 years and older)	**1st dose**		**Booster dose*** (at least 2 months after 1st dose)	

*Any COVID-19 vaccine can be used for the booster dose in people ages 18 years and older, though mRNA vaccines are preferred. For people ages 12–17 years, only Pfizer-BioNTech can be used. People ages 5–11 years should not receive a booster dose at this time.

Clarification of Existing Recommendation for mRNA COVID-19 Vaccine Primary Series

- People who are moderately or severely immunocompromised should receive:
  - 3-dose primary series
  - 1 booster dose

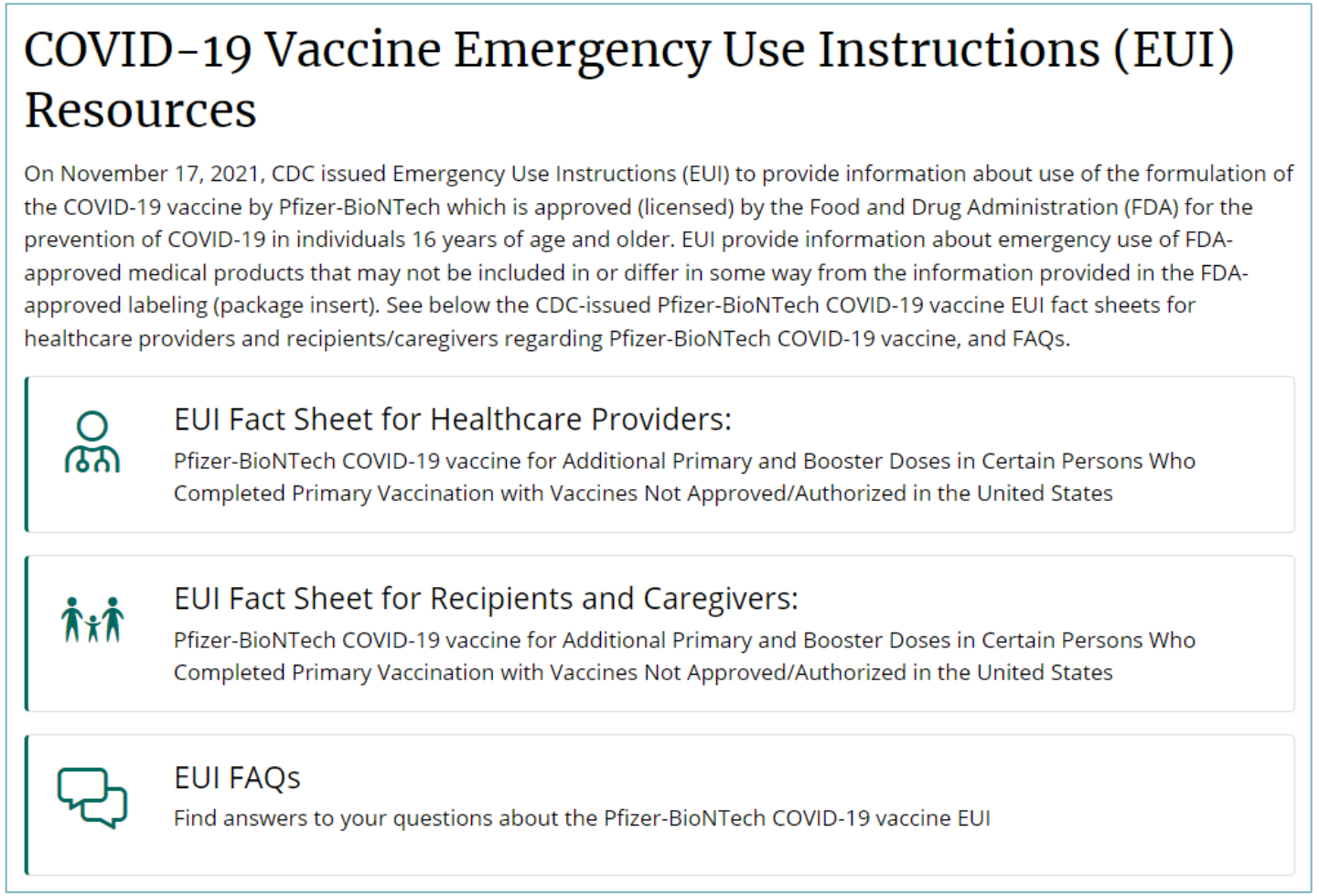


Emergency Use Instructions (EUI)

- Allowed under the Pandemic and All-Hazards Preparedness Reauthorization Act
- Provides information about emergency use of **FDA-approved medical products** that may **not be included or differ** from the information provided in the **FDA-approved labeling package insert.**
- Applies only to the use of:
  - Spikevax (Moderna) for people ages 18 years and older
  - Comirnaty (Pfizer-BioNTech) for people ages 12 years and older

https://www.cdc.gov/vaccines/covid-19/eui/index.html

Emergency Use Instructions (EUI)



COVID-19 Vaccine Emergency Use Instructions (EUI) Resources

On November 17, 2021, CDC issued Emergency Use Instructions (EUI) to provide information about use of the formulation of the COVID-19 vaccine by Pfizer-BioNTech which is approved (licensed) by the Food and Drug Administration (FDA) for the prevention of COVID-19 in individuals 16 years of age and older. EUI provide information about emergency use of FDA-approved medical products that may not be included in or differ in some way from the information provided in the FDA-approved labeling (package insert). See below the CDC-issued Pfizer-BioNTech COVID-19 vaccine EUI fact sheets for healthcare providers and recipients/caregivers regarding Pfizer-BioNTech COVID-19 vaccine, and FAQs.

EUI Fact Sheet for Healthcare Providers:

Pfizer-BioNTech COVID-19 vaccine for Additional Primary and Booster Doses in Certain Persons Who Completed Primary Vaccination with Vaccines Not Approved/Authorized in the United States

EUI Fact Sheet for Recipients and Caregivers:

Pfizer-BioNTech COVID-19 vaccine for Additional Primary and Booster Doses in Certain Persons Who Completed Primary Vaccination with Vaccines Not Approved/Authorized in the United States

EUI FAQs

Find answers to your questions about the Pfizer-BioNTech COVID-19 vaccine EUI

https://www.cdc.gov/vaccines/covid-19/eui/index.html

Updates for People Who Are Moderately or Severely Immunocompromised

- Shorter booster interval after an mRNA COVID-19 vaccine primary series
- An additional dose after a Janssen COVID-19 Vaccine primary series
- Revaccination for certain sub-groups
- Case-by-case clinical decision making

Revised Guidance for a 3-Month Booster Interval After an mRNA COVID-19 Vaccine Primary Series

Current guidance

People who are moderately or severely immunocompromised should receive a booster dose **at least 5 months** after the last (third) dose of an mRNA COVID-19 vaccine.

Revised guidance

People who are moderately or severely immunocompromised should receive a booster dose **at least 3 months** after the last (third) dose of an mRNA COVID-19 vaccine.

1. Kamar, N., Abravanel, F., Martion, O. (2021). Assessment of 4 Doses of SARS-CoV-2 Messenger RNA–Based Vaccine in Recipients of a Solid Organ Transplant. *Infectious Diseases, 4*(11), e2136030.
2. Benotmane, I., Bruel, T., Planas, D., et al. (2021). A fourth dose of the mRNA-1273 SARS-CoV-2 vaccine improves serum neutralization against the delta variant in kidney transplant recipients. *medRxiv*. Preprint. doi.org/10.1101/2021.11.25.21266704
3. Alejo, J.L., Mitchell, J., Chiang, T., et al. (2021). Antibody Response to a Fourth Dose of a SARS-CoV-2 Vaccine in Solid Organ Transplant Recipients: A Case Series. *Transplantation, 105*(12), e280-281.
4. Munro, A., Janani, L., Cornelius, V. (2021). Safety and immunogenicity of seven COVID-19 vaccines as a third dose (booster) following two doses of ChAdOx1 nCov-19 or BNT162b2 in the UK (COV-BOOST): a blinded, multicentre, randomised, controlled, phase 2 trial. *Lancet*, *398*, 2258-76.
5. Atmar, R.L., Lyke, K.E., Deming, M.E. (2021). Heterologous SARS-CoV-2 booster vaccinations-preliminary report. *medRxiv*. Preprint. doi: 10.1101/2021.10.10.21264827

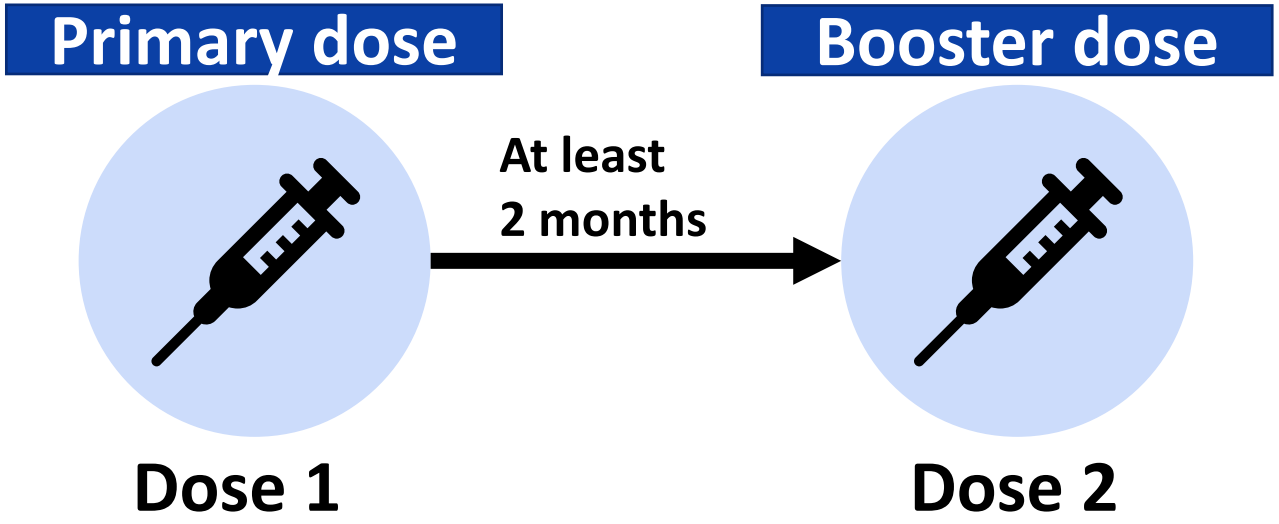
Rationale for 3-Month Booster Interval After an mRNA COVID-19 Vaccine Primary Series

- Concern about initial immune response and **loss of protection** over time, particularly during period of **high community transmission**.
- Small studies in people with immune compromise demonstrate **immunogenicity** of a 4th dose when administered **~1-3 months** after the 3rd dose.
- Multiple studies in the general population demonstrate **immunogenicity** of a booster as early as **3 months** following a 2-dose primary series.
- Multiple countries have **implemented booster doses as early as 3 months** in the general population following a 2-dose primary series.

1. Kamar, N., Abravanel, F., Martion, O. (2021). Assessment of 4 Doses of SARS-CoV-2 Messenger RNA–Based Vaccine in Recipients of a Solid Organ Transplant. *Infectious Diseases, 4*(11), e2136030.
2. Benotmane, I., Bruel, T., Planas, D., et al. (2021). A fourth dose of the mRNA-1273 SARS-CoV-2 vaccine improves serum neutralization against the delta variant in kidney transplant recipients. *medRxiv*. Preprint. doi.org/10.1101/2021.11.25.21266704
3. Alejo, J.L., Mitchell, J., Chiang, T., et al. (2021). Antibody Response to a Fourth Dose of a SARS-CoV-2 Vaccine in Solid Organ Transplant Recipients: A Case Series. *Transplantation, 105*(12), e280-281.
4. Munro, A., Janani, L., Cornelius, V. (2021). Safety and immunogenicity of seven COVID-19 vaccines as a third dose (booster) following two doses of ChAdOx1 nCov-19 or BNT162b2 in the UK (COV-BOOST): a blinded, multicentre, randomised, controlled, phase 2 trial. *Lancet*, *398*, 2258-76.
5. Atmar, R.L., Lyke, K.E., Deming, M.E. (2021). Heterologous SARS-CoV-2 booster vaccinations-preliminary report. *medRxiv*. Preprint. doi: 10.1101/2021.10.10.21264827

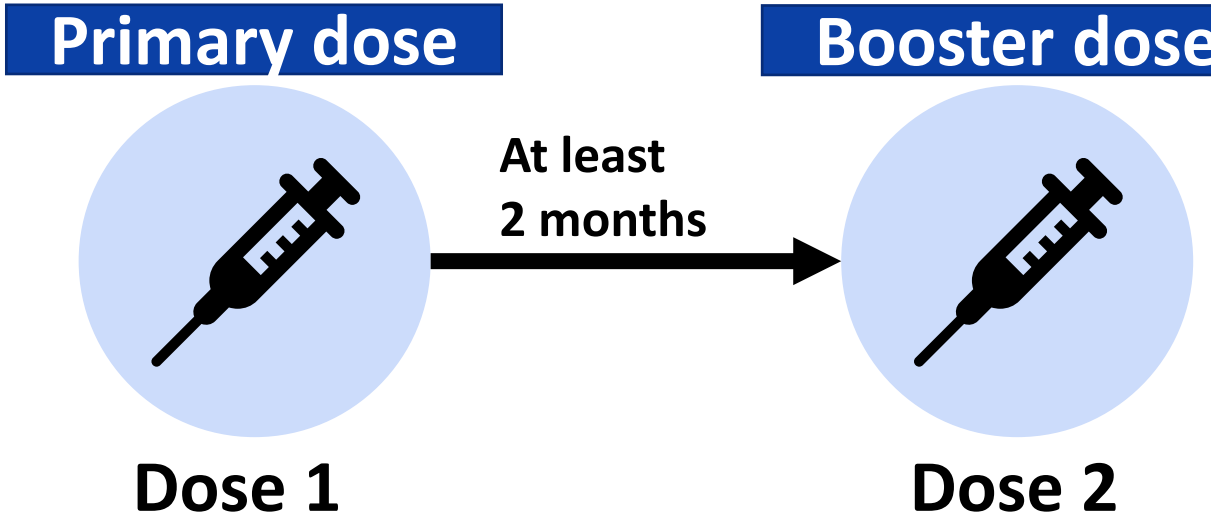
Schedule for People Who Received a Janssen COVID-19 Vaccine Primary Series

Current guidance

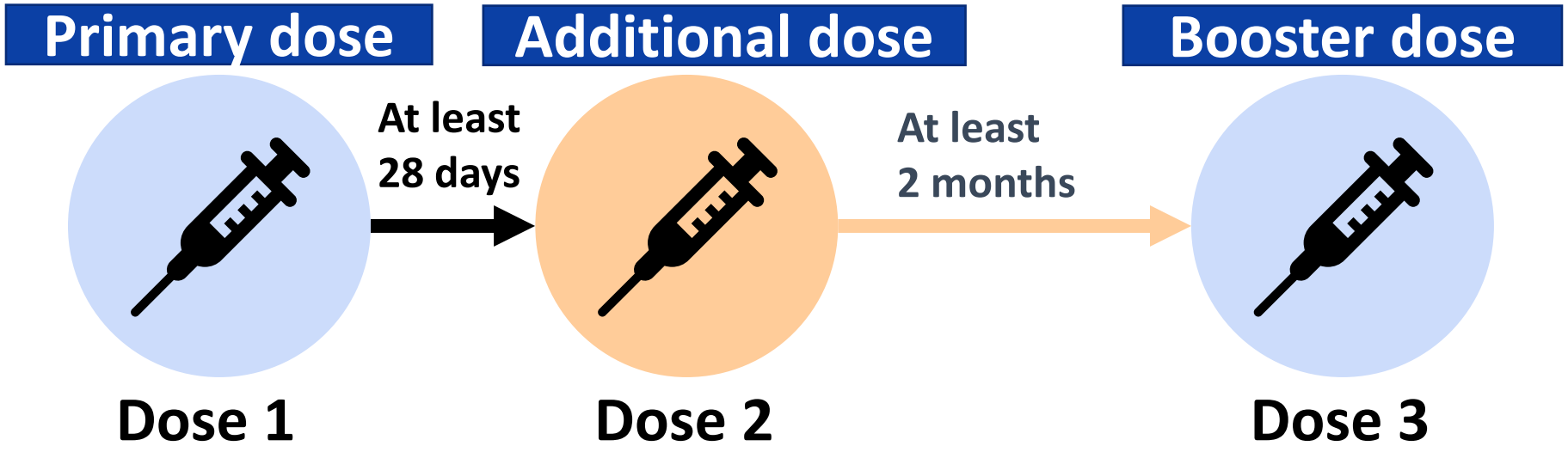


Schedule for People Who Received a Janssen COVID-19 Vaccine Primary Series

Current guidance



Revised guidance



Revaccination for Certain Sub-Groups

- **Current** guidance: Limited to recipients of hematopoietic cell transplant (HCT) and chimeric antigen receptor (CAR)-T-cell therapy.
- **Revised** guidance: Recipients of HCT, CAR-T-cell, **or other B-cell depleting therapies** who received doses of COVID-19 vaccine **prior to or during treatment** should be revaccinated for doses received before or during treatment.
- Based on clinical judgement, revaccination may also be considered once immune competence is regained for people who received COVID-19 vaccine doses during **chemotherapy or radiation treatment**.

Case-by-Case Decision Making Based on Clinical Judgement

- On a case-by-case basis, providers who care for moderately or severely immunocompromised patients may administer mRNA COVID-19 vaccines outside of the FDA and CDC dosing intervals **based on clinical judgement** when the benefits of vaccination are deemed to outweigh the potential and unknown risks.

REVISED COVID-19 Vaccination Schedule for People Who Are Moderately or Severely Immunocompromised

Vaccine	Vaccination Schedule				
Pfizer-BioNTech (ages 5 years and older)	**1st dose**	**2nd dose** (21 days after 1st dose)	**3rd dose** (at least 28 days after 2nd dose)		**Booster dose*** (at least 3 months after 3rd dose)
Moderna (ages 18 years and older)	**1st dose**	**2nd dose** (28 days after 1st dose)	**3rd dose** (at least 28 days after 2nd dose)		**Booster dose*** (at least 3 months after 3rd dose)
Janssen (ages 18 years and older)	**1st dose**	**Additional dose†** (at least 28 days after 1st dose)		**Booster dose*** (at least 2 months after additional dose)	

*Any COVID-19 vaccine can be used for the booster dose in people ages 18 years and older, though mRNA vaccines are preferred. For people ages 12–17 years, only Pfizer-BioNTech can be used. People ages 5–11 years should not receive a booster dose.

†Only Pfizer-BioNTech or Moderna COVID-19 Vaccine should be used

Passive antibody products

Passive Antibody Products

Current guidance

Defer COVID-19 vaccination for:

- 30 days if product used for post exposure prophylaxis
- 90 days if product used for treatment
- No guidance for pre-exposure prophylaxis

Revised guidance

- No recommended deferral period
- However, tixagevimab/cilgavimab (EVUSHELD™) should be deferred for at least two weeks after vaccination

Benschop, et al. (2021). The effect of anti-SARS-CoV-2 monoclonal antibody, bamlanivimab, on endogenous immune response to COVID-19 vaccination. *medRxiv*. Preprint.
doi: https://doi.org/10.1101/2021.12.15.21267605

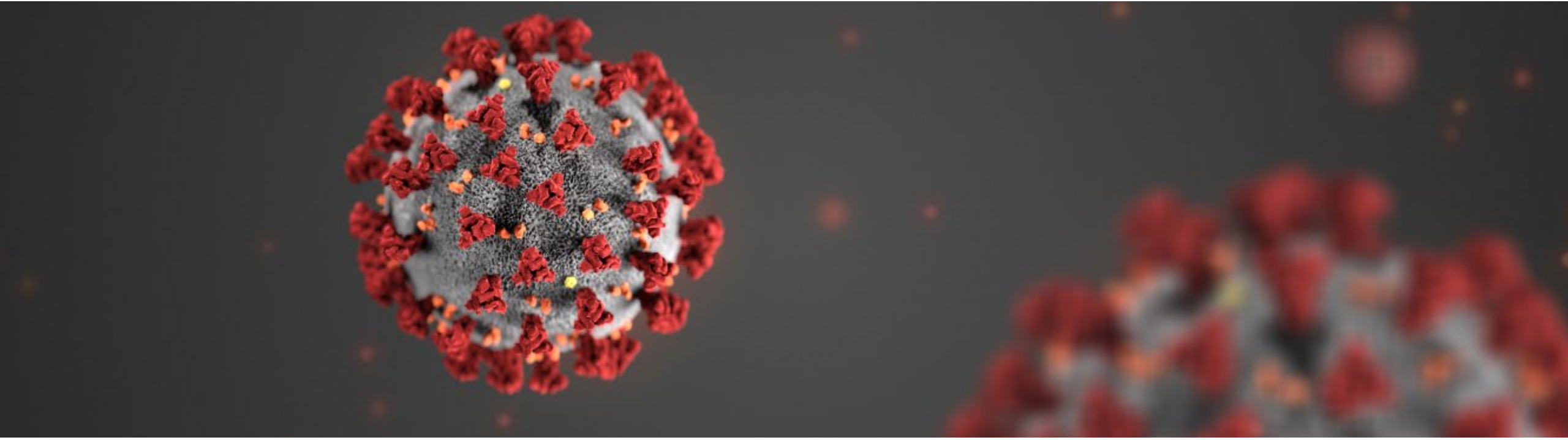
Passive Antibody Products

- Study among nursing home residents and staff demonstrated that recipients of bamlanivimab **mounted a robust immune response** to mRNA vaccination, regardless of age, risk category, or vaccine type.
- Although antibody response was **numerically lower** in people who received monoclonal antibodies, they were still considered to be **high** and the **clinical significance of the reduction is unknown**.
- There was **no correlation** between interval to COVID-19 vaccination and neutralizing titers in recent monoclonal antibody recipients.
- Programmatically, there are **challenges** to current intervals between receipt of monoclonal antibodies and COVID-19 vaccination.
- Getting vaccinated is a **priority**.

Benschop, et al. (2021). The effect of anti-SARS-CoV-2 monoclonal antibody, bamlanivimab, on endogenous immune response to COVID-19 vaccination. *medRxiv*. Preprint.
doi: https://doi.org/10.1101/2021.12.15.21267605

Interim Clinical Considerations

https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html#CoV-19-vaccination



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.