ACIP Evidence to Recommendations for Use of an Additional COVID-19 Vaccine Dose in Immunocompromised People

Question:

Should ACIP recommend vaccination with an additional dose of an mRNA COVID-19 vaccine (Pfizer-BioNTech, Moderna) following a primary series in immunocompromised people, under an Emergency Use Authorization?

Population:

People with medical conditions or people receiving treatments that are associated with moderate to severe immune compromise:

- Active or recent treatment for solid tumor and hematologic malignancies
- Receipt of solid-organ or recent hematopoietic stem cell transplants
- Severe primary immunodeficiency
- Advanced or untreated HIV infection
- Active treatment with high-dose corticosteroids, alkylating agents, antimetabolites, tumor-necrosis (TNF) blockers, and other biologic agents that are immunosuppressive or immunomodulatory
- Chronic medical conditions such as asplenia and chronic renal disease (degree of immune deficit varies)

Intervention:

An additional dose of Pfizer-BioNTech COVID-19 vaccine (≥12 years old) or Moderna COVID-19 vaccine (≥18 years old) at least 28 days after an initial 2-dose primary series of mRNA COVID-19 vaccine, in immunocompromised people.

Background: The emergence of SARS-CoV-2, the virus that causes coronavirus disease 2019 (COVID-19), has led to a global pandemic with substantial societal and economic impacts on individual persons and communities. In the United States, more than 45 million cases and more than 700,000 COVID-19-associated deaths have been reported as of October 20, 2021. Persons of all ages are at risk for infection and severe disease. However, the risk for severe illness from COVID-19 is higher in people who are immunocompromised.

Three COVID-19 vaccines are currently approved under a Biologics License Application or authorized under an Emergency Use Authorization (EUA) by the Food and Drug Administration (FDA) and recommended for primary vaccination by the Advisory Committee on Immunization Practices (ACIP): the two-dose mRNA-based Pfizer-BioNTech/Comirnaty and Moderna COVID-19 vaccines and the single-dose adenovirus vector-based Janssen (Johnson & Johnson) COVID-19 vaccine.

On August 12, 2021, the FDA amended the EUAs for Pfizer-BioNTech (persons aged ≥12 years) and Moderna (persons aged ≥18 years) COVID-19 vaccines to authorize an additional dose for certain immunocompromised persons. Due to insufficient data, the EUA amendment for an additional dose does not apply to Janssen COVID-19 vaccine or to individuals who received Janssen COVID-19 as a primary series.

Additional background information supporting the ACIP recommendation on the use of additional or booster doses of COVID-19 vaccine can be found in the relevant publication of the recommendation referenced on the ACIP website.

Problem

Criteria	Work Group Judgements	Evidence	Additional Information
Is the problem of public health importance?	Yes	**Immunocompromised people and SARS-CoV-2 infection** Immunocompromised people comprise approximately 2.7% of U.S. adults (~7 million adults).[1] Immunocompromised people are more likely to get severely ill from COVID-19[1,2] and have a higher risk for prolonged SARS-CoV-2 infection and shedding[3-7] as well as viral evolution during infection and treatment.[3,6,8-13] In addition, antibody neutralization titers to SARS-CoV-2 variants are lower in immunocompromised people compared to non-immunocompromised people.[14] Furthermore, immunocompromised people are more likely to transmit SARS-CoV-2 to household contacts.[15] Immunocompromised people have lower vaccine effectiveness compared to non-immunocompromised people (59-72% vs. 90-94%, respectively).[16-19] Immunocompromised people are also more likely to have serious breakthrough infections, with 40-44% of hospitalized breakthrough cases occurring among immunocompromised people.[16,20]	**Vaccination:** As of October 20, 2021, more than 189 million people in the United States are fully vaccinated against COVID-19, including over 104 million people who received Pfizer-BioNTech and 69 million who received Moderna.[21] **Variants of Concern:** As of October 20, 2021, the Delta variant is the dominant circulating variant in the United States and is more than twice as contagious as previous variants.[22]

Benefits and Harms

Criteria	Work Group Judgements	Evidence	Additional Information
How substantial are the desirable anticipated effects?	Large	In a series of small studies, 16–80% of solid organ transplant recipients and hemodialysis patients had no detectable antibody response following the 2nd dose of an mRNA COVID-19 vaccination series; among these, 33–55% developed antibodies after an additional dose.[1,2,3,4]	There are no efficacy or effectiveness studies of COVID-19 prevention following a 3rd dose in immunocompromised persons.

Criteria	Work Group Judgements	Evidence	Additional Information
How substantial are the undesirable anticipated effects?	Minimal	Symptoms reported after an additional dose in certain immunocompromised persons were mostly mild to moderate and similar to those observed with previous doses[2]; no severe adverse events were reported.[1]	mRNA COVID-19 vaccines are associated with rare but serious adverse events, including anaphylaxis as well as myocarditis and pericarditis in young adults. The impact of immunocompromising conditions on these rare events is unknown. There are no safety studies of an additional mRNA dose in immunocompromised adolescents.
Do the desirable effects outweigh the undesirable effects?	Favors the intervention	The Work Group concluded that the desirable effects of an additional mRNA COVID-19 vaccine dose outweigh the undesirable effects.	

Values

Criteria	Work Group Judgements	Evidence	Additional Information
Does the target population feel that the desirable effects are large relative to undesirable effects?	Large	Overall, intent to be vaccinated with a COVID-19 vaccine is high among immunocompromised populations. In a survey of individuals with cancer, autoimmune diseases, and other serious co-morbid conditions, 76% of respondents state they have either received, are trying to receive, or definitely will receive a COVID-19 vaccine.[1]	
Is there important uncertainty about, or variability in, how much people value the main outcomes?	Probably not important uncertainty or variability	COVID-19 vaccine hesitancy in immunocompromised individuals appears to be associated with younger age, female gender, racial/ethnic minorities, and less formal education.[1] Concerns about safety and possible side effects are major reasons for vaccine hesitancy.[1,2]	

Acceptability

Criteria	Work Group Judgements	Evidence	Additional Information

Criteria	Work Group Judgements	Evidence	Additional Information
Is the intervention acceptable to key stakeholders?	Yes	Professional societies that advocate for access to high quality care for patients with immunocompromising conditions have voiced support for an additional dose of COVID-19 vaccine in immunocompromised persons.[1] These include[1]: • Infectious Diseases Society of America • American College of Rheumatology • American Society of Transplantation • American Society of Transplant Surgeons • International Society for Heart and Lung Transplantation • Pediatric Infectious Diseases Society • Children's Oncology Group • Leukemia and Lymphoma Society	

Resource Use

Criteria	Work Group Judgements	Evidence	Additional Information
Is the intervention a reasonable and efficient allocation of resources?	Yes	The U.S. government has purchased 600 million doses of mRNA vaccines.[1] These doses are available at no cost to the recipient. Furthermore, immunocompromised patients experience high medical costs at baseline and are at higher risk for hospitalization. The cost of an additional dose of COVID-19 vaccine is small relative to these costs.	The Work Group concluded that cost-effectiveness may not be a primary driver for decision-making during a pandemic and for vaccine use under an Emergency Use Authorization.

Equity

Criteria	Work Group Judgements	Evidence	Additional Information
What would be the impact of the intervention on health equity?	Probably no impact	Several immunocompromised groups in the United States were identified by the Work Group as being potentially disadvantaged with respect to an additional mRNA COVID-19 vaccine dose: people living in rural/frontier areas, people in congregate settings, people experiencing homelessness, people belonging to certain racial and ethnic minority groups, people experiencing poverty, people with disabilities, people with substance use, and recipients of Janssen COVID-19 vaccine.	

Feasibility

Criteria	Work Group Judgements	Evidence	Additional Information

Criteria	Work Group Judgements	Evidence	Additional Information
Is the intervention feasible to implement?	Yes	There are high levels of interaction between immunocompromised populations and the healthcare system, which will help to provide opportunities for an additional dose following the primary series. In addition, the mRNA COVID-19 vaccine supply in the United States is sufficient to allow for additional doses of vaccine in immunocompromised persons.	

Balance of consequences

Desirable consequences *clearly outweigh* undesirable consequences in most settings.

Is there sufficient information to move forward with a recommendation? Yes.

Policy options for ACIP consideration

- ACIP recommends the intervention

Draft recommendation: ACIP and CDC recommendations

Moderately-to-severely immunocompromised persons aged ≥12 years (Pfizer-BioNTech) or ≥18 years (Moderna) should receive an additional COVID-19 vaccine dose at least 28 days after completion of primary vaccination.

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Acceptability:

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Resource Use

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Page last reviewed: October 29, 2021