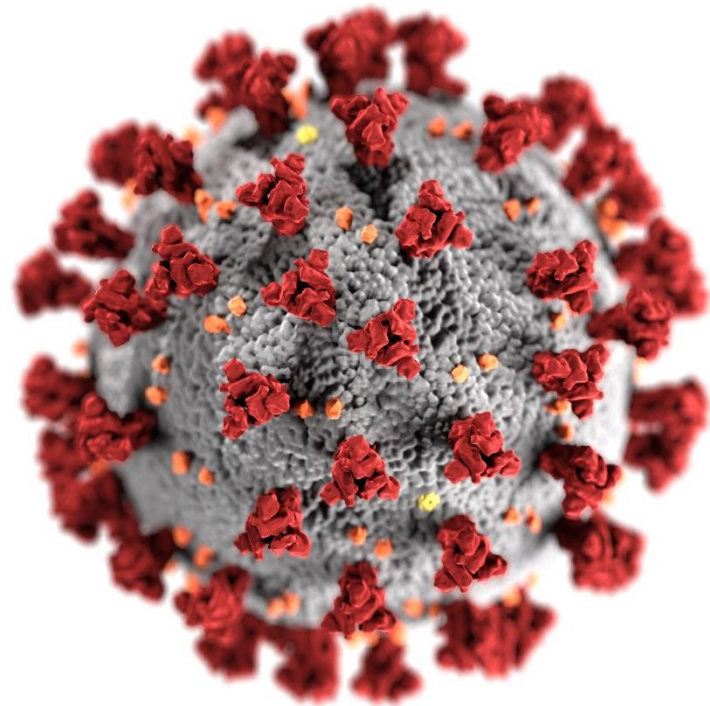


Evidence to Recommendation Framework:

An Additional Dose of mRNA COVID-19 Vaccine
Following a Primary Series in
Immunocompromised People

Dr. Kathleen Dooling, MD, MPH
Advisory Committee on Immunization Practices
August 13, 2021



cdc.gov/coronavirus

FDA: Emergency Use Authorization (EUA) Amendment

- **August 12, 2021:** FDA Authorizes Additional Vaccine Dose for Certain Immunocompromised Individuals*
 - Other fully vaccinated individuals do not need an additional dose right now
 - Amendment applies to:
 - **Pfizer-BioNTech** COVID-19 vaccine (BNT162b2) (≥ 12 years old)
 - **Moderna** COVID-19 vaccine (mRNA-1273) (≥ 18 years old)
- 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. CDC and FDA are actively engaged to ensure that immunocompromised recipients of Janssen COVID-19 vaccine have optimal vaccine protection

*<https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-additional-vaccine-dose-certain-immunocompromised>

Evidence to Recommendations Framework



Evidence to Recommendations (EtR) Framework

- Structure to describe information considered in moving from evidence to ACIP vaccine **recommendations**
- Provide **transparency** around the impact of additional factors on deliberations when considering a recommendation

Evidence to Recommendations (EtR) Framework

Policy Question

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

Population: Immunocompromised People

People with medical conditions or people receiving treatments that are associated with moderate to severe immune compromise.¹

- 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 may be associated with varying degrees of immune deficit

1. Additional information about the level of immune suppression associated with a range of medical conditions and treatments can be found in [general best practices for vaccination of people with altered immunocompetence, the CDC Yellow Book, and the Infectious Diseases Society of America policy statement, 2013 IDSA Clinical Practice Guideline for Vaccination of the Immunocompromised Host](#)

Intervention: An Additional Dose of mRNA COVID-19 Vaccine

- An additional dose of
 - **Pfizer-BioNTech** COVID-19 vaccine (BNT162b2) (≥ 18 years old)
 - **Moderna** COVID-19 vaccine (mRNA-1273) (≥ 18 years old)after an initial 2-dose primary series of mRNA COVID-19 vaccine, in immunocompromised people
- Attempts should be made to match the additional dose type to the mRNA primary series, however if that is not feasible, a **heterologous additional dose is permitted**
- The additional dose of mRNA COVID-19 vaccine should be administered **at least 28 days** after completion of the primary mRNA COVID-19 vaccine series

Importance of infection prevention measures

- Immunocompromised people, including those who receive an additional mRNA dose, should continue to follow prevention measures*
 - Wear a mask
 - Stay 6 feet apart from others they don't live with
 - Avoid crowds and poorly ventilated indoor spaces until advised otherwise by their healthcare provider
- Close contacts of immunocompromised people should be strongly encouraged to be vaccinated against COVID-19

* <https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/prevention.html>

Evidence to Recommendations (EtR) Framework

EtR Domain	Question
Public Health Problem	<ul style="list-style-type: none">• Is the problem of public health importance?
Benefits and Harms	<ul style="list-style-type: none">• How substantial are the desirable anticipated effects?• How substantial are the undesirable anticipated effects?• Do the desirable effects outweigh the undesirable effects?
Values	<ul style="list-style-type: none">• Does the target population feel the desirable effects are large relative to the undesirable effects?• Is there important variability in how patients value the outcome?
Acceptability	<ul style="list-style-type: none">• Is the intervention acceptable to key stakeholders?
Feasibility	<ul style="list-style-type: none">• Is the intervention feasible to implement?
Resource Use	<ul style="list-style-type: none">• Is the intervention a reasonable and efficient allocation of resources?
Equity	<ul style="list-style-type: none">• What would be the impact of the intervention on health equity?

Evidence to Recommendations (EtR) Framework

EtR Domain	Question
Public Health Problem	<ul style="list-style-type: none">• Is the problem of public health importance?
Benefits and Harms	<ul style="list-style-type: none">• How substantial are the desirable anticipated effects?• How substantial are the undesirable anticipated effects?• Do the desirable effects outweigh the undesirable effects?
Values	<ul style="list-style-type: none">• Does the target population feel the desirable effects are large relative to the undesirable effects?• Is there important variability in how patients value the outcome?
Acceptability	<ul style="list-style-type: none">• Is the intervention acceptable to key stakeholders?
Feasibility	<ul style="list-style-type: none">• Is the intervention feasible to implement?
Resource Use	<ul style="list-style-type: none">• Is the intervention a reasonable and efficient allocation of resources?
Equity	<ul style="list-style-type: none">• What would be the impact of the intervention on health equity?

“The problem” = COVID-19 among immunocompromised persons

“The intervention” = an additional dose of mRNA COVID-19 vaccine in immunocompromised people who have received a primary series of an mRNA COVID-19 vaccine

EtR Domain: Public Health Problem

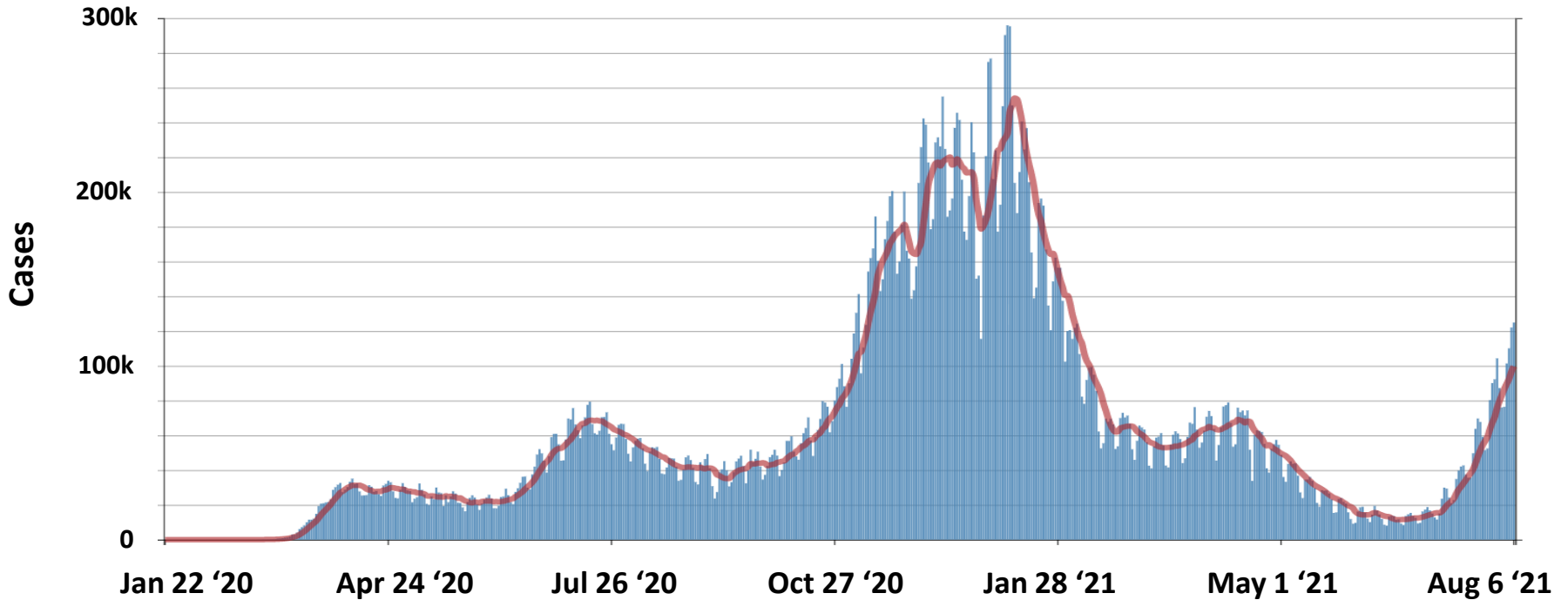


Daily Trends in Number of COVID-19 Cases in the US

January 22, 2020 – Aug 9, 2021

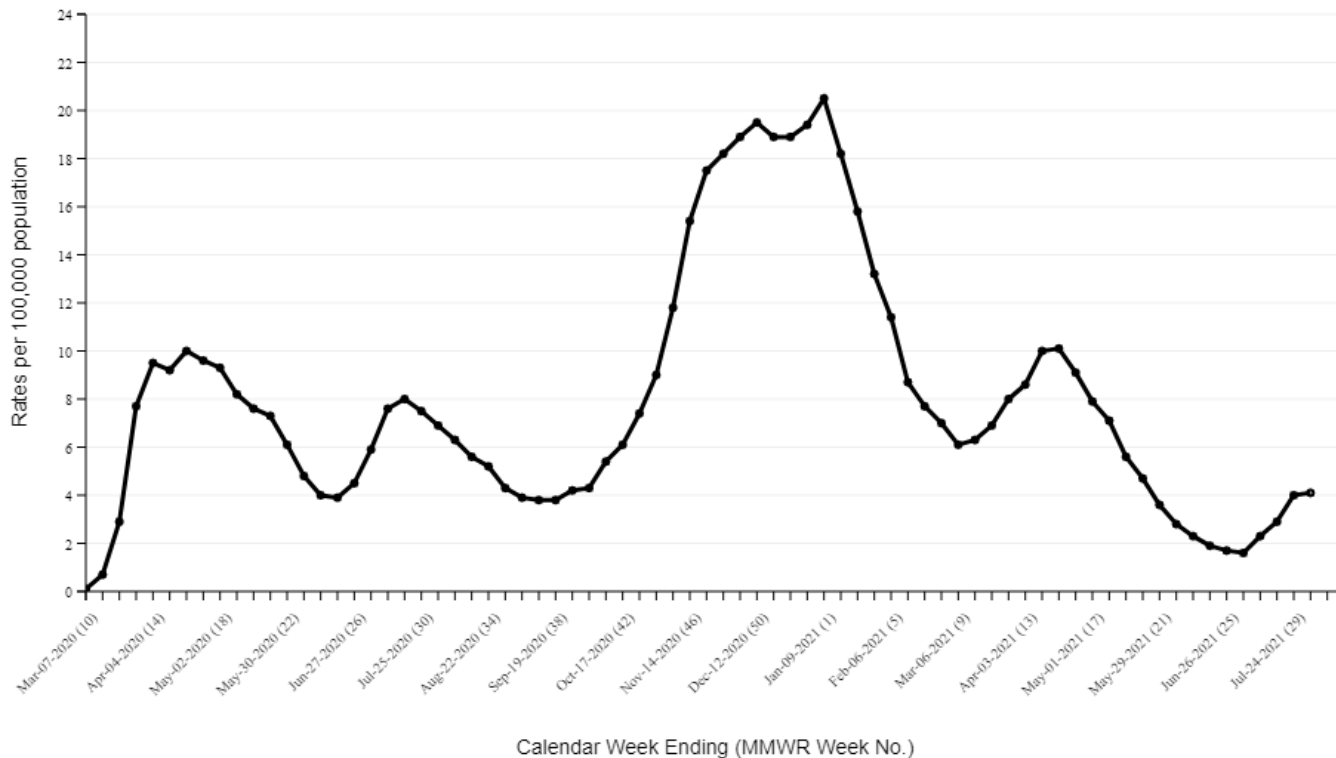
Cases Total

35,665,877



Weekly Trends in COVID-19 Associated Hospitalization Rates in the US

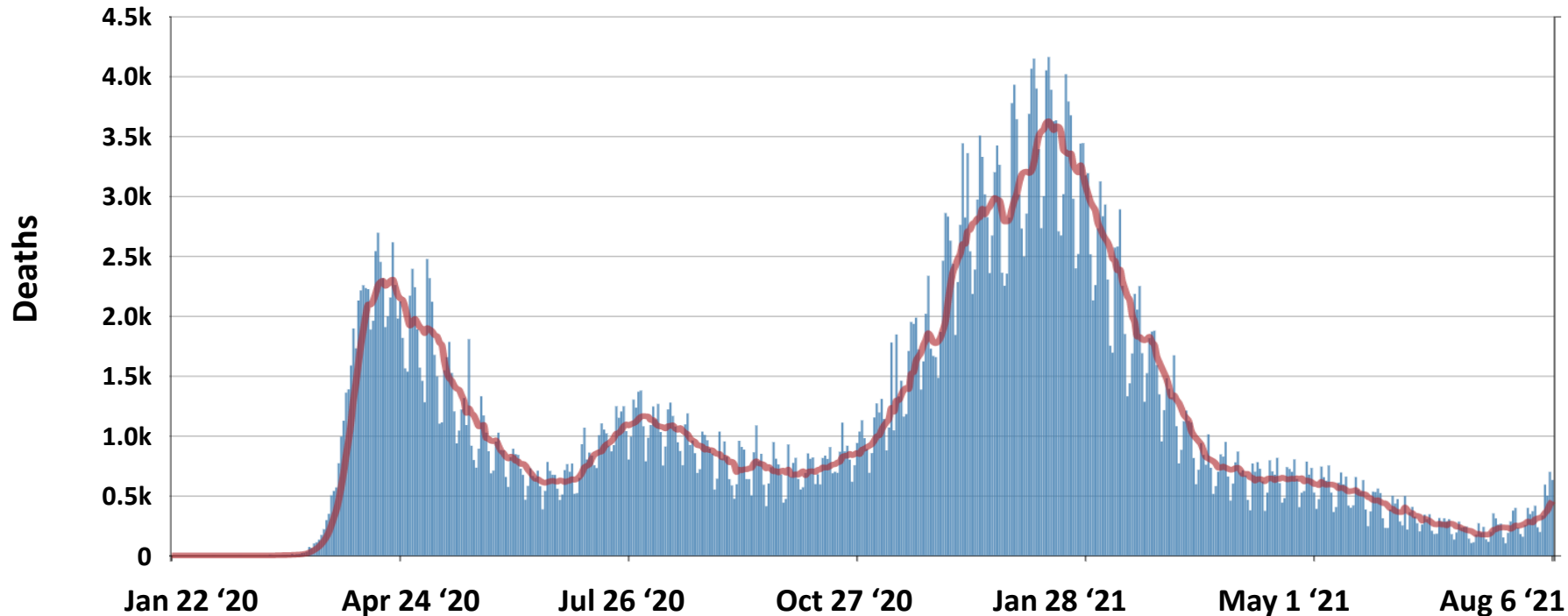
March 7, 2020 – Aug 7, 2021



Daily Trends in Number of COVID-19 Deaths in the US

January 22, 2020 – Aug 9, 2021

Deaths Total • 614,291



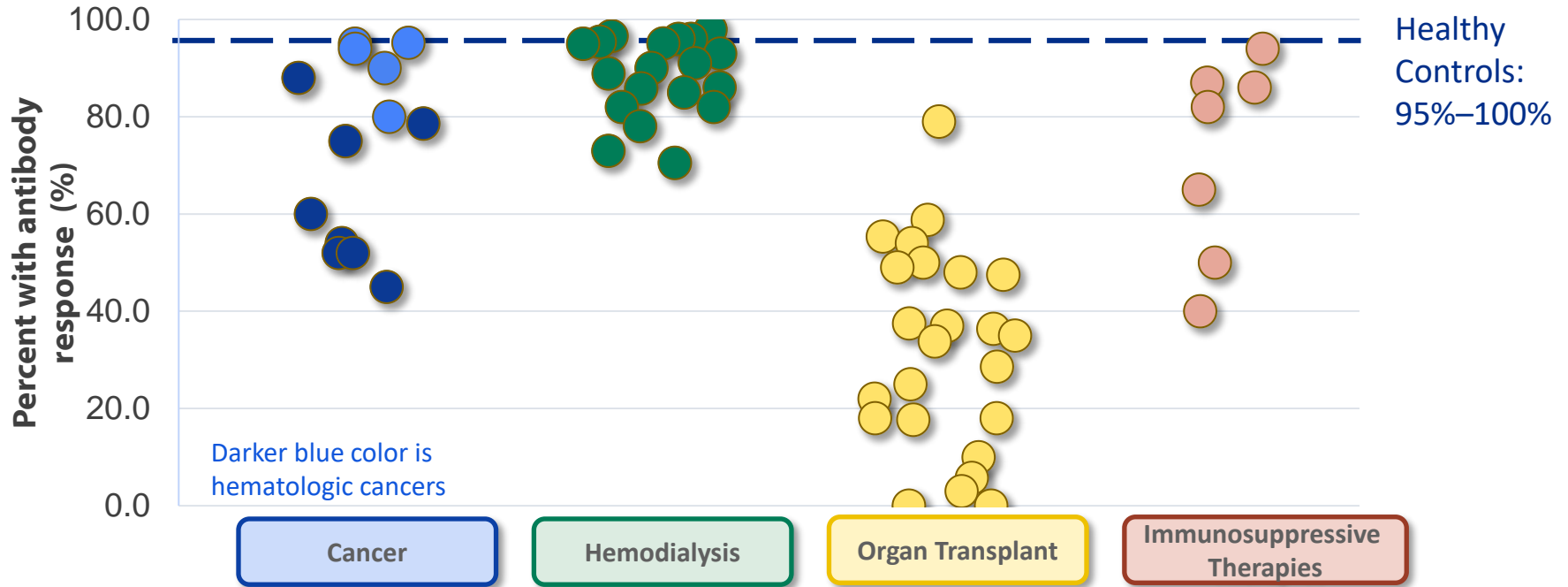
Immunocompromised People and SARS-CoV-2 Infection

- Immunocompromised people comprise ~2.7% of U.S. adults (~7 million adults)¹
- More likely to get severely ill from COVID-19^{1,2}
- Higher risk for:
 - Prolonged SARS-CoV-2 infection and shedding^{3-7, 14-16}
 - Viral evolution during infection and treatment (hospitalized patients)^{3,6,8-10,14,17}
- Lower antibody/neutralization titers to SARS-CoV-2 variants compared to non-immunocompromised people¹²
- More likely to transmit SARS-CoV-2 to household contacts¹¹

Immunocompromised People and Vaccine Breakthrough Infection

- More likely to have breakthrough infection
 - 40-44% of hospitalized breakthrough cases are immunocompromised people in US study¹⁻²
- Lower vaccine effectiveness
 - 59--72% VE among immunocompromised people vs. 90--94% among non-immunocompromised people after 2nd dose^{1, 3-5}

Percent of subjects with antibody response after two mRNA COVID-19 vaccine doses by immunocompromising condition and study (n=63)



- Studies that compared response after 1st and 2nd dose demonstrated less robust response after dose 1
- Antibody measurement and threshold levels vary by study protocol

International policies on additional doses for immunocompromised people

- **France**¹ (Announced April 11, 2021)
 - 3rd dose 4 weeks after the 2nd dose for patients who are “severely immunocompromised”
 - Could be extended at a later date to include a larger immunocompromised population
- **Israel**² (Announced July 11, 2021)
 - People living with organ or stem cell transplants, blood cancer, autoimmune disease and treatment with specific immunosuppressive medications
 - People with breast, lung, or colon cancer do not qualify
- **United Kingdom**³ (Announced July 1, 2021)
 - Additional dose for immunocompromised people ≥16 years (among others), to be implemented in September
- **Germany**⁴ (Announced August 2, 2021)
 - Immunocompromised persons (among others)

1. [dgs_urgent_n43_vaccination_modalites_d_administration_des_rappels.pdf](#) (solidarites-sante.gouv.fr),

2. <https://govextra.gov.il/media/30095/meeting-summary-15122020.pdf>

3. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1009174/COVID-19_vaccination_programme_guidance_for_healthcare_workers_6_August_2021_v3.10.pdf

4. <https://www.reuters.com/world/europe/french-president-macron-third-covid-vaccine-doses-likely-elderly-vulnerable-2021-08-05/>

Public Health Problem

Is COVID-19 disease among immunocompromised people of public health importance?

- Are the consequences of COVID-19 serious in this population?
- Is COVID-19 urgent?
- Are a large number of immunocompromised people affected by COVID-19?
- Are there populations disproportionately affected by COVID-19?

No Probably no Probably yes Yes Varies Don't know



EtR Domain: Benefits and Harms



Benefits and Harms

How substantial are the desirable anticipated effects?

- How substantial are the anticipated effect for each main outcome for which there is a desirable effect?

Minimal Small Moderate Large Varies Don't know



Benefits and Harms

How substantial are the undesirable anticipated effects?

- How substantial are the anticipated effect for each main outcome for which there is a undesirable effect?

Minimal Small Moderate Large Varies Don't know



Benefits and Harms

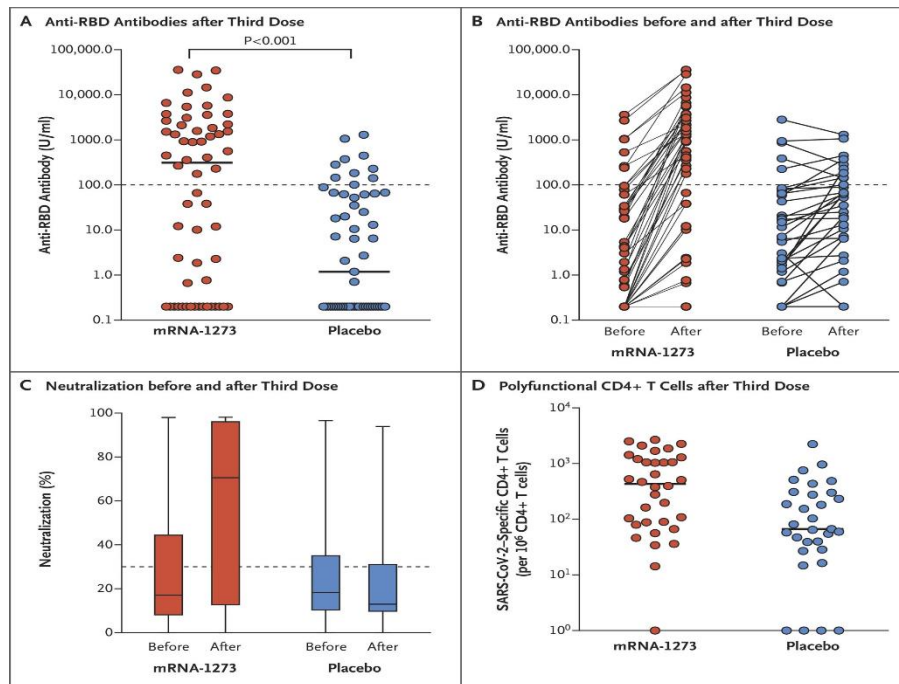
Do the desirable effects outweigh the undesirable effects?

- What is the balance between the desirable effects relative to the undesirable effects?
 - Favors intervention (An additional dose of mRNA vaccine in IC people)
 - Favors comparison (no additional COVID-19 vaccine doses)
 - Favors both
 - Favors neither
 - Unclear



Benefits:

Randomized Trial of a 3rd Dose of Moderna Vaccine in Transplant Recipients (n=120)



RBD antibody (≥ 100 U/ml)
1 month post dose 3:

33 of 60 patients
(55%) vaccine group

vs.

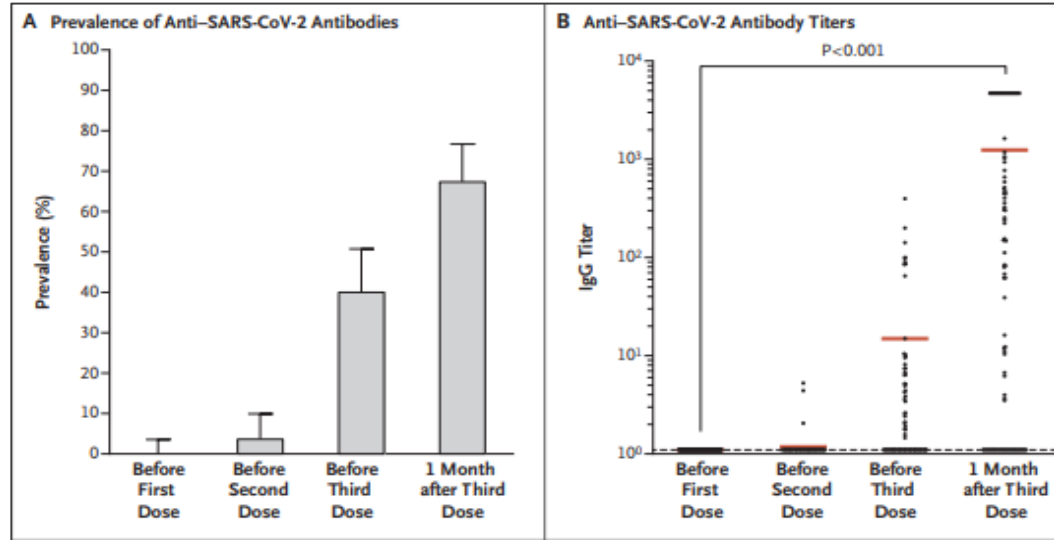
10 of 57 patients
(18%) placebo group

Benefits:

Study	Patient Population	2 nd Dose			3 rd Dose Seronegative after 2 nd dose		
		Sample Size	Seronegative N (%)	Seropositive N (%)	Sample Size	Seronegative N (%)	Seropositive N (%)
Kamar et al.	Recipients of solid-organ transplant	99	59 (60)	40 (40)	59	33 (56)	26 (44)
Werbelt et al.	Recipients of solid-organ transplant	30	24 (80)	6 (20)	24	16 (67)	8 (33)
Longlune et al.	Patients on hemodialysis	82	13 (16)	69 (84)	12	7 (58)	5 (42)
Epsi et al.	Patients on hemodialysis	106	66 (62)	40 (38)	12	6 (50)	6 (50)
Ducloux et al.	Patients on hemodialysis	45	5 (11)	40 (89)	5	3 (60)	2 (40)

- Among those who had **no detectable antibody** response to an initial mRNA vaccine series, **33-50% developed an antibody response to an additional dose**

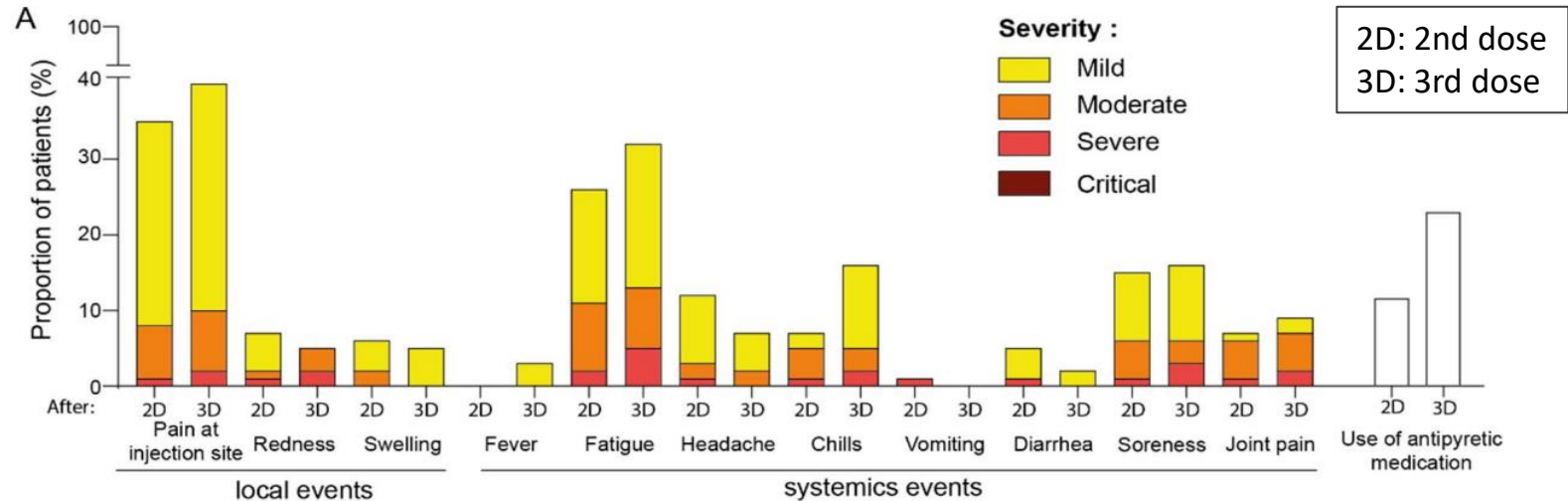
Benefits and Harms:



- The proportion of the group who are seropositive increase after each dose: **40%** post dose 2 and **68%** post dose 3
- Average antibody titre increased after each dose
- No serious adverse events were reported after administration of the 3rd dose, and no acute rejection episodes occurred (n=99 Solid Organ Transplant Patients)

Harms:

- No patients developed critical side effects which required hospitalization
- Symptoms reported were consistent with previous doses and the intensity of the symptoms was mostly mild or moderate



Benefits and Harms:

Summary of the Available Evidence

Benefits:

- Emerging experimental and observational data in adults suggest that an additional mRNA COVID-19 vaccine dose in immunocompromised people enhances antibody response and increases the proportion who respond to COVID-19 vaccine
- No efficacy or effectiveness studies of COVID-19 prevention following a 3rd dose

Harms:

- In small studies of an additional dose of mRNA vaccine
 - No serious adverse events were observed
 - Reactogenicity of the 3rd dose of mRNA vaccine was similar to prior doses
- 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

Benefits and Harms

How substantial are the desirable anticipated effects?

- How substantial are the anticipated effect for each main outcome for which there is a desirable effect?

Minimal Small Moderate Large Varies Don't know



Benefits and Harms

How substantial are the undesirable anticipated effects?

- How substantial are the anticipated effect for each main outcome for which there is an undesirable effect?

Minimal Small Moderate Large Varies Don't know



Benefits and Harms

Do the desirable effects outweigh the undesirable effects?

- What is the balance between the desirable effects relative to the undesirable effects?

- Favors intervention (an additional dose of mRNA COVID-19 vaccine in IC people)
- Favors comparison (no additional COVID-19 vaccine doses)
- Favors both
- Favors neither
- Unclear



EtR Domains: Values & Acceptability



Values

Criteria 1:

Does the target population feel that the desirable effects are large relative to undesirable effects?

- How does the target population view the balance of desirable versus undesirable effects?
- Would patients/caregivers feel that the benefits outweigh the harms and burden?
- Does the immunocompromised population appreciate and value an additional dose of mRNA COVID-19 vaccine?

Minimal Small Moderate Large Varies Don't know



Values

Criteria 2:

Is there important uncertainty about, or variability in, how much people value the main outcomes?

- How much do individuals value each outcome in relation to the other outcomes?
- Is there evidence to support those value judgements?
- Is there evidence that the variability is large enough to lead to different decisions?

- Important uncertainty or variability
- Probably important uncertainty or variability
- Probably not important uncertainty or variability
- No important uncertainty or variability
- No known undesirable outcomes



Acceptability

Is an additional dose of mRNA COVID-19 vaccines acceptable to key stakeholders?

- Are there key stakeholders that would not accept the distribution of benefits and harms?
- Are there key stakeholders that would not accept the undesirable effects in the short term for the desirable effects (benefits) in the future?

No Probably no Probably yes Yes Varies Don't know



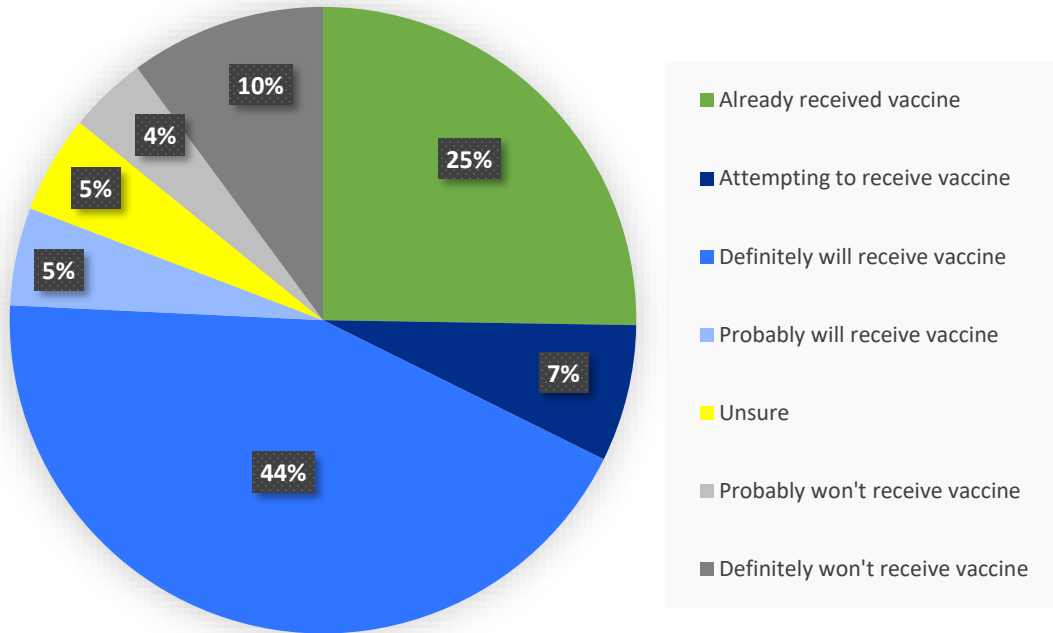
Additional doses of COVID-19 vaccines in the general U.S. population

- Approximately 139.5 million individuals completed a 2-dose series of Moderna or Pfizer-BioNTech COVID-19 vaccine
 - ~1.14 million (<1%) received 1 or more additional COVID-19 vaccine doses
- Approximately 12 million individuals received 1 dose of Janssen COVID-19 vaccine
 - ~90,979 (<1%) received 1 or more additional COVID-19 vaccine doses



Values:

Survey of individuals with cancer, autoimmune diseases, and other serious co-morbid conditions, January 15-February 22, 2021 (n=21,943)



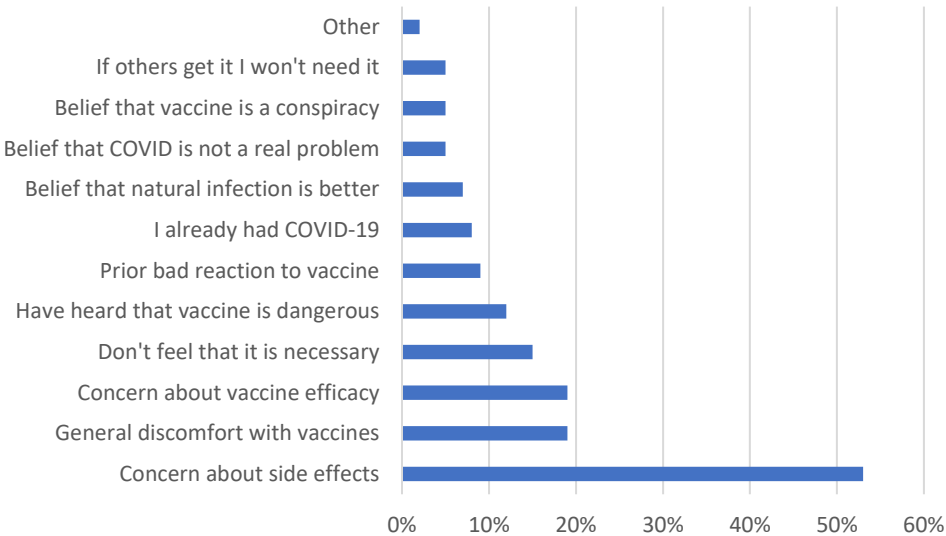
■ Factors associated with vaccine hesitancy

- Younger age
- Female gender
- Black, Pacific Island, Native American race/ethnicity
- Less formal education
- Anti-vaccine sentiment
- Distrust of media

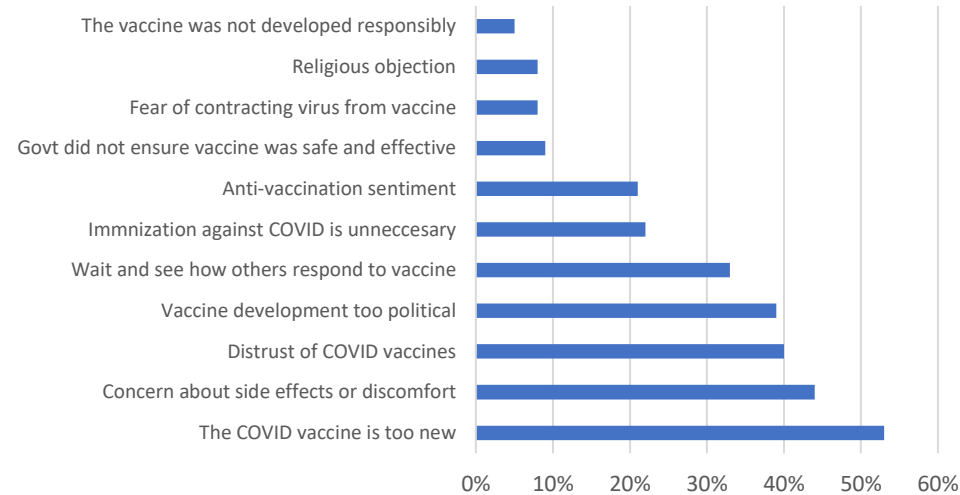
Values:

Stated reasons for vaccine refusal

Survey of patients on hemodialysis



Survey of patients with cancer, autoimmune disease, and other comorbid conditions



1. [COVID-19 vaccine hesitancy among individuals with cancer, autoimmune diseases, and other serious comorbid conditions \(medrxiv.org\)](https://www.medrxiv.org/content/10.1101/2020.08.14.20176101v1)
2. [SARS-CoV-2 Vaccine Acceptability in Patients on Hemodialysis: A Nationwide Survey | American Society of Nephrology \(asnjournal.org\)](https://asnjournal.org/2020/09/24/sars-cov-2-vaccine-acceptability-in-patients-on-hemodialysis-a-nationwide-survey/)

Acceptability:

Professional bodies strongly support COVID-19 vaccination and an additional dose

- 1) Encourage study of safety and efficacy/effectiveness of an additional dose of COVID-19 vaccine in immunocompromised people
 - 2) Support swift action on the part of ACIP to recommend use of an additional dose of COVID-19 vaccine in immunocompromised people
- 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

Acceptability:

Advocacy bodies strongly support COVID-19 vaccination and study of an additional dose

Leukemia and Lymphoma Society **supports:**

- Providing access to doses of COVID-19 vaccine for supplemental vaccination in immunosuppressed patients and urges that these patients have the opportunity to be among the first to receive these additional doses

Values:

Summary of the available evidence

- Overall, initial intent to vaccinate is high among immunocompromised populations
- Concerns about safety and possible side-effect are major reasons for vaccine hesitancy
- Vaccine hesitancy appears to be associated with younger age, female gender, racial/ethnic minorities, and less formal education
- Strong support for an additional dose was expressed by immunocompromised patients via written and oral comment to ACIP meeting July 22, 2021

Acceptability:

Summary of the available evidence

- Professionals who provide healthcare to immunocompromised people recognize their patients are at high risk for severe outcomes from COVID-19 and strongly support a recommendation for an additional dose of COVID vaccine
- Societies that advocate for access to the best quality care for patients with immunocompromising conditions support access to an additional dose of COVID-19 vaccine to increase the chances of vaccine protection

Values

Criteria 1:

Does the target population feel that the desirable effects are large relative to undesirable effects?

- How does the target population view the balance of desirable versus undesirable effects?
- Would patients/caregivers feel that the benefits outweigh the harms and burden?
- Does the immunocompromised population appreciate and value an additional dose of mRNA COVID-19 vaccine?

Minimal Small Moderate Large Varies Don't know



Values

Criteria 2:

Is there important uncertainty about, or variability in, how much people value the main outcomes?

- How much do individuals value each outcome in relation to the other outcomes?
- Is there evidence to support those value judgements?
- Is there evidence that the variability is large enough to lead to different decisions?

- Important uncertainty or variability
- Probably important uncertainty or variability
- Probably not important uncertainty or variability
- No important uncertainty or variability
- No known undesirable outcomes



Acceptability

Is an additional dose of mRNA COVID-19 vaccines acceptable to key stakeholders?

- Are there key stakeholders that would not accept the distribution of benefits and harms?
- Are there key stakeholders that would not accept the undesirable effects in the short term for the desirable effects (benefits) in the future?

No Probably no Probably yes Yes Varies Don't know



EtR Domain: Feasibility



Feasibility

Is an additional dose of mRNA COVID-19 vaccine feasible to implement among immunocompromised people?

- Is the additional dose of mRNA COVID-19 vaccine sustainable?
- Are there barriers that are likely to limit the feasibility of implementing the additional dose of mRNA COVID-19 vaccine or require considerations when implementing it?
- Is access to an additional dose of mRNA COVID-19 vaccine for immunocompromised people an important concern?

No Probably no Probably yes Yes Varies Don't know



Feasibility:

- High levels of interaction between immunocompromised populations and healthcare system provide opportunities for an additional dose to following the primary series
- mRNA COVID-19 vaccine supply in the United States is sufficient to make additional doses for immunocompromised people feasible
- Testing for antibodies following vaccination is not recommended, reducing the complexity of a recommendation for an additional dose

Feasibility

Is an additional dose of mRNA COVID-19 vaccine feasible to implement among immunocompromised people?

- Is the additional dose of mRNA COVID-19 vaccine program sustainable?
- Are there barriers that are likely to limit the feasibility of implementing the additional dose of mRNA COVID-19 vaccine or require considerations when implementing it?
- Is access to an additional dose of mRNA COVID-19 vaccine for immunocompromised people an important concern?

No Probably no Probably yes Yes Varies Don't know



EtR Domain: Resource Use



Resource Use

Is an additional dose of mRNA COVID-19 vaccine, given to immunocompromised people, a reasonable and efficient allocation of resources?

- What is the cost-effectiveness of the additional mRNA COVID-19 vaccine dose in this population?
- How does the cost-effectiveness of the additional dose change in response to changes in context, assumptions, etc?

No Probably no Probably yes Yes Varies Don't know



Resource Use:

Review of the available evidence

- U.S. Government has purchased 600 million doses of mRNA vaccines¹
- Vaccine is available at no cost to the recipient
- No studies evaluated cost-effectiveness around the use of COVID-19 vaccines among immunocompromised
 - Immunocompromised patients experience high medical costs at baseline and are at higher risk of hospitalization. The cost of an additional dose of COVID-19 vaccine is small relative to these costs.

¹ <https://www.hhs.gov/about/news/2021/02/11/biden-administration-purchases-additional-doses-covid-19-vaccines-from-pfizer-and-moderna.html>

Resource Use:

Work Group Interpretation

- Work Group concluded that cost-effectiveness may not be a primary driver for decision-making during a pandemic and for vaccine used under EUA

Resource Use

Is an additional dose of mRNA COVID-19 vaccine, given to immunocompromised people, a reasonable and efficient allocation of resources?

- What is the cost-effectiveness of the additional mRNA COVID-19 vaccine dose in this population?
- How does the cost-effectiveness of the additional dose change in response to changes in context, assumptions, etc?

No Probably no Probably yes Yes Varies Don't know



EtR Domain: Equity



Equity

What would be the impact of an additional dose of mRNA COVID-19 vaccine, given to immunocompromised people, on health equity?

- Are there groups or settings that might be disadvantaged in relation to COVID-19 disease burden or receipt of the additional dose?
- Are there considerations that should be made when implementing the additional mRNA COVID-19 vaccine dose program for immunocompromised people to ensure that inequities are reduced whenever possible, and that they are not increased?



Reduced

Probably reduced

Probably no impact

Probably increased

Increased

Varies

Don't know

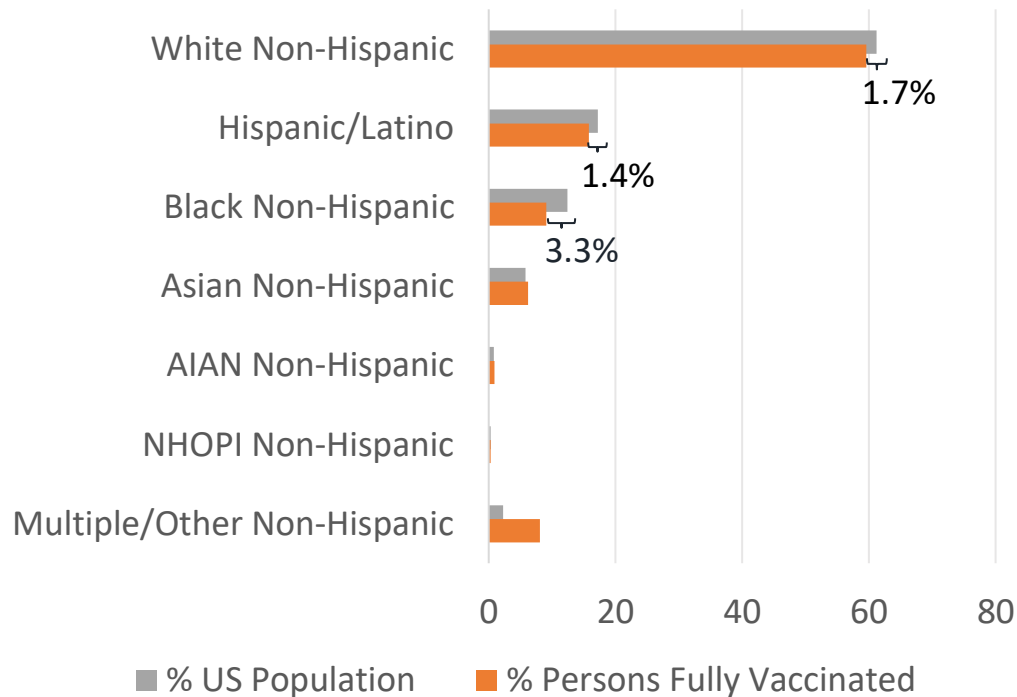
Which immunocompromised groups in the United States could be disadvantaged with respect to an additional mRNA COVID-19 vaccine dose?

- **Place of residence**
 - Living in rural/frontier areas
 - Living in congregate settings (long-term care facilities)
 - Experiencing homelessness
- **Racial and ethnic minority populations**
 - Black, Hispanic or Latino, and Alaskan Native/American Indian
 - Immigration status
- **Socioeconomic status**
 - Poverty
 - High social vulnerability
- **Personal characteristics associated with discrimination**
 - With disabilities
 - Substance use
- **Recipients of Janssen COVID-19 Vaccine**

Equity:

Data on equitable provision of COVID-19 vaccine in adults

- As of August 8, 2021, Black adults had the largest difference in the percentage of fully vaccinated persons compared with the percentage in the overall U.S. population
- May see similar patterns in immunocompromised



Equity:

Opportunities to increase equitable access of an additional dose of mRNA COVID-19 vaccine to immunocompromised people

- Multipronged approach to ensure access
 - Primary care providers and specialist clinics serving immunocompromised patients, FQHCs, rural health clinics, community health centers, hospitals, & pharmacies

Equity

What would be the impact of an additional dose of mRNA COVID-19 vaccine, given to immunocompromised people, on health equity?

- Are there groups or settings that might be disadvantaged in relation to COVID-19 disease burden or receipt of the additional dose?
- Are there considerations that should be made when implementing the additional mRNA COVID-19 vaccine dose program for immunocompromised people to ensure that inequities are reduced whenever possible, and that they are not increased?



- | | | |
|--|--|---|
| <input type="radio"/> Reduced | <input type="radio"/> Probably reduced | <input checked="" type="radio"/> Probably no impact |
| <input type="radio"/> Probably increased | <input type="radio"/> Increased | <input type="radio"/> Varies <input type="radio"/> Don't know |

Summary



EtR Domain	Question	Work Group Judgments
Public Health Problem	Is COVID-19 disease among immunocompromised people of public health importance?	Yes
Benefits and Harms	How substantial are the desirable anticipated effects?	Large
	How substantial are the undesirable anticipated effects?	Minimal
	Do the desirable effects outweigh the undesirable effects?	Favors additional dose of mRNA vaccine in immunocompromised people
	What is the overall certainty of the evidence for the critical outcomes?	Not GRADED
Values	Does the target population feel the desirable effects are large relative to the undesirable effects?	Large
	Is there important variability in how patients value the outcomes?	Probably not important variability
Acceptability	Is an additional dose of mRNA COVID-19 vaccines acceptable to key stakeholders?	Yes
Feasibility	Is an additional dose of mRNA COVID-19 vaccine feasible to implement among immunocompromised people?	Yes
Resource Use	Is an additional dose of mRNA COVID-19 vaccine, given to immunocompromised people, a reasonable and efficient allocation of resources?	Yes
Equity	What would be the impact of an additional dose of mRNA COVID-19 vaccine, given to immunocompromised people, on health equity?	Probably no impact

Evidence to Recommendations Framework

Summary: Work Group Interpretations

Balance of consequences	Undesirable consequences <i>clearly outweigh</i> desirable consequences in most settings	Undesirable consequences <i>probably outweigh</i> desirable consequences in most settings	The balance between desirable and undesirable consequences is <i>closely balanced</i> or <i>uncertain</i>	Desirable consequences <i>probably outweigh</i> undesirable consequences in most settings	Desirable consequences <i>clearly outweigh</i> undesirable consequences in most settings	There is insufficient evidence to determine the balance of consequences
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Evidence to Recommendations Framework

Summary: Work Group Interpretations

Type of recommendation	We do not recommend the intervention	We recommend the intervention for individuals based on shared clinical decision-making	We recommend the intervention
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Questions for ACIP discussion

- 1) **Intervention:** does ACIP support the intervention of an additional dose of mRNA COVID-19 vaccine following a primary series in immunocompromised people?
- 2) **Population:** balancing potential benefits and potential harms, what is the optimal lower age threshold for the additional dose intervention in immunocompromised people?

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- Jack Gersten
- Eddie Shanley
- Hannah Rosenblum
- Amanda Cohn
- Epi Task Force:
 - COVID-NET
 - DVD Enhanced Surveillance
 - Community Surveillance
 - Seroprevalance
- Data, Analytics and Visualization Task Force
- Respiratory Viruses Branch

References: Immunocompromised people and SARS-CoV-2 infection (Slides 14)

1. Harpaz et al. *Prevalence of Immunosuppression Among US Adults*, 2013. JAMA 2016.
2. Williamson et al. *Factors Associated with COVID-19-related Death Using Open SAFELY*. Nature 2020.
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References: Percent of subjects with antibody response after two mRNA vaccine doses (Slide 16 - 3)

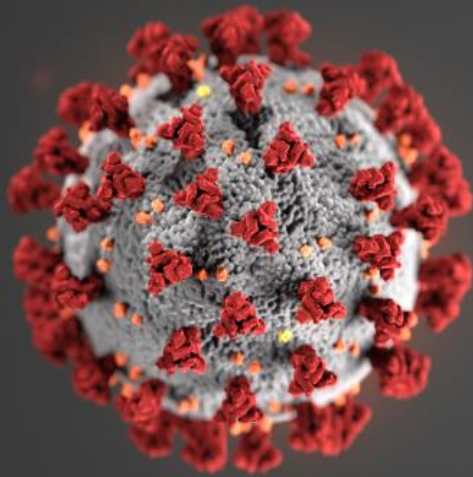
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