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
**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

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
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

## Evidence to Recommendations (EtR) Framework

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“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

https://covid.cdc.gov/covid-data-tracker/#trends_dailytrendscases
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

https://covid.cdc.gov/covid-data-tracker/#trends_dailytrendscases
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 people\(^12\)
- More likely to transmit SARS-CoV-2 to household contacts\(^11\)
Immunocompromised People and Vaccine Breakthrough Infection

- More likely to have breakthrough infection
  - 40-44% of hospitalized breakthrough cases are immunocompromised people in US study\(^1-2\)

- Lower vaccine effectiveness
  - 59--72% VE among immunocompromised people vs. 90--94% among non-immunocompromised people after 2\(^{nd}\) dose\(^1,3-5\)

See reference slide at end
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

See reference slide at end
International policies on additional doses for immunocompromised people

- **France** (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** (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** (Announced July 1, 2021)
  - Additional dose for immunocompromised people ≥16 years (among others), to be implemented in September

- **Germany** (Announced August 2, 2021)
  - Immunocompromised persons (among others)

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1. dgs_urgent_n43_vaccination_modalites_d_administration_des_rappels.pdf (solidarites-sante.gouv.fr)
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

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

Benefits:

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

Hall et al. (2021) NEJM. Randomized Trial of a Third Dose of mRNA-1273 Vaccine in Transplant Recipients. DOI: 10.1056/NEJMc2111462
### Benefits:

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

See reference slide at end
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)

Kamar et al. (2021) NEJM Three Doses of an mRNA Covid-19 Vaccine in Solid-Organ Transplant Recipients (nejm.org)
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

Epsi et al. (2021) medRxiv doi: https://doi.org/10.1101/2021.07.02.21259913
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 3\textsuperscript{rd} 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

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Do the desirable effects outweigh the undesirable effects?

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- 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
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

COVID-19 vaccine hesitancy among individuals with cancer, autoimmune diseases, and other serious comorbid conditions (medrxiv.org)
Values:
Stated reasons for vaccine refusal

1. COVID-19 vaccine hesitancy among individuals with cancer, autoimmune diseases, and other serious comorbid conditions (medrxiv.org)
2. SARS-CoV-2 Vaccine Acceptability in Patients on Hemodialysis: A Nationwide Survey | American Society of Nephrology (asnjournals.org)
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
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?

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○ **Probably not important uncertainty or variability**
○ No important uncertainty or variability
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• 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
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 vaccines\(^1\)
- 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.

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

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## Evidence to Recommendations Framework
### Summary: Work Group Interpretations

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<th>Undesirable consequences</th>
<th>The balance between desirable and undesirable consequences</th>
<th>Desirable consequences</th>
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The table above outlines the interpretations of the balance of consequences based on evidence. Each cell describes the balance of consequences in different settings, with clear or probable outweigh for undesirable consequences, and close balance or uncertain for desirable consequences. If sufficient evidence is not present, the final cell notes that determination is not possible.
## Evidence to Recommendations Framework

**Summary: Work Group Interpretations**

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<th>Type of recommendation</th>
<th>We do not recommend the intervention</th>
<th>We recommend the intervention for individuals based on shared clinical decision-making</th>
<th>We recommend the intervention</th>
</tr>
</thead>
</table>
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?
Acknowledgements

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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)

4. Hensley et al. Intractable Coronavirus Disease 2019 (COVID-19) and Prolonged Severe Acute Respiratory Syndrome Coronavirus 2 (Sars-CoV-2) Replication in Chimeric Antigen Receptor-Modified T-Cell Therapy Recipient: A Case Study. CID 2021
5. Baang et al. Prolonged Severe Acute Respiratory Syndrome Coronavirus 2 Replication in an immunocompromised Patient. JID 2021
6. Choi et al. Persistence and Evolution of SARS-CoV-2 in an Immunocompromised Host. NEJM 2020
7. Helleberg et al. Persistent COVID-19 in an Immunocompromised Patient Temporarily Responsive to Two Courses of Remdesivir Therapy. JID 2020
10. Khatamzas et al. Emergence of Multiple SARS-CoV-2 Mutations in an Immunocompromised Host. medRxiv 2021
11. Lewis et al. Household Transmission of Severe Acute Respiratory Syndrome Coronavirus-2 in the United States. CID 2020
References: Immunocompromised people and SARS-CoV-2 infection (Slides 15)

5. Chemaitelly et al. SARS-CoV-2 vaccine effectiveness in immunosuppressed kidney transplant recipients. medRxiv 2021.08.07.21261578; doi: https://doi.org/10.1101/2021.08.07.21261578
References: Percent of subjects with antibody response after two mRNA vaccine doses (Slide 16 - 1)

References: Percent of subjects with antibody response after two mRNA vaccine doses (Slide 16 - 2)

- Longlune, Marie Béatrice Nogier, Marcel Miedougé, Charlotte Gabilan, Charles Cartou, Bruno Seigneuric, Arnaud Del Bello, Olivier Marion, Stanislas Faguer, Jacques Izopec, Nassim Kamar, High immunogenicity of a messenger RNA based vaccine against SARS-CoV-2 in chronic dialysis patients, Nephrology Dialysis Transplantation, 2021;, gfab193, https://doi.org/10.1093/ndt/gfab193
References: Percent of subjects with antibody response after two mRNA vaccine doses (Slide 16 - 3)

• Mounzer Agha, et al. Suboptimal response to COVID-19 mRNA vaccines in hematologic malignancies patients medRxiv 2021.04.06.21254949; doi: https://doi.org/10.1101/2021.04.06.21254949
References: Percent of subjects with antibody response after two mRNA vaccine doses (Slide 16 - 4)

References: Percent of subjects with antibody response after 3 mRNA vaccine doses (Slide 25)

- Epsi et al. (2021) medRxiv doi: https://doi.org/10.1101/2021.07.02.21259913
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