ACG INSTITUTE RESEARCH GRANTS AND AWARDS 2022

EIGHT different award types; INCREASED Junior Faculty FUNDING;
NEW Health Equity Research Award; Med Resident and Student Awards

www.gi.org/research-awards

Grant System Opens: September 7, 2021

Deadline: December 3, 2021

Read the Grant Flyer, FAQs, or visit the webpage for the full RFAs.

1

2

ACG INSTITUTE RESEARCH GRANTS AND AWARDS 2022

ACG INSTITUTE FOR CLINICAL RESEARCH AND EDUCATION

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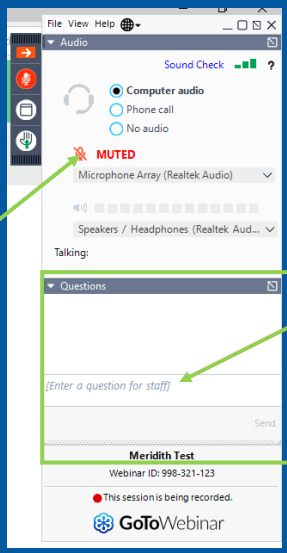
Participating in the Webinar



All attendees will be muted and will remain in Listen Only Mode.

Type your questions here so that the moderator can see them. Not all questions will be answered but we will get to as many as possible.

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How to Receive CME and MOC Points

LIVE VIRTUAL GRAND ROUNDS WEBINAR

ACG will send a link to a CME & MOC evaluation to all attendees on the live webinar.

ABIM Board Certified physicians need to complete their MOC activities by December 31, 2021 in order for the MOC points to count toward any MOC requirements that are due by the end of the year. No MOC credit may be awarded after March 1, 2022 for this activity.

5

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MOC QUESTION

If you plan to claim MOC Points for this activity, you will be asked to: Please list specific changes you will make in your practice as a result of the information you received from this activity.

Include specific strategies or changes that you plan to implement.
THESE ANSWERS WILL BE REVIEWED.

6


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Join us for upcoming Virtual Grand Rounds!
Week 34, 2021
ACG Clinical Guideline: Treatment of Helicobacter pylori Infection
William D. Chey, MD, FACG
September 2, 2021 at Noon Eastern
Week 35, 2021
Getting Ready for Artificial Intelligence in Gastroenterology
Tyler M. Berzin, MD, FACG
September 9, 2021 at Noon Eastern
Visit gi.org/ACGVGR to Register

7


Virtual Grand Rounds
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ACG VIRTUAL GRAND ROUNDS
Private Equity in GI: Looking Back and Moving Forward
THURSDAY, SEPTEMBER 9, 8:00-9:00 PM EDT
Daniel Pambianco, MD, FACG
Scott Fraser, MBA
Louis Wilson, MD, FACG
Ira Flax, MD, MACG
Register: gi.org/ACGVGR
#GIhomeschooling

8

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COVID-19: Where Are We Now?

Updates from the ACG COVID-19 Task Force

MONDAY, SEPTEMBER 20th, 8 to 9:30 pm EDT

Introduction
- David A. Greenwald, MD, FACG

Speakers
- Harish K. Gagneja, MD, FACG
- Francis A. Farraye, MD, MSc, MACG
- Melissa Latorre, MD, MS
- Samir Shah, MD, FACG
- Michael S. Morelli, MD, CPE, FACG

Co-hosts
- Costas H. Kefalas, MD, MMM, FACG
- Neil Stollman, MD, FACG

Register & Learn More: gi.org/ACGVGR

9

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Disclosures:

Moderator:
Samir Shah, MD, FACG
Dr. Shah, faculty for this educational event, has no relevant financial relationship(s) with ineligible companies to disclose.

Speaker:
Francis A. Farraye, MD, MSc, MACG
Consulting Fee: Arena, BMS, Braintree Labs, Gilead, GI Reviewers, GSK, IBD Educational Group, Iterative Scopes, Janssen, Pfizer, Sebela ; Ownership Interest: Innovation Pharmaceuticals; DSMB: Lilly, Theravance

Speaker:
Freddy Caldera, DO, MS
Dr. Caldera, faculty for this educational event, has no relevant financial relationship(s) with ineligible companies to disclose.

Speaker:
Rita German, MD
Dr. German, faculty for this educational event, has no relevant financial relationship(s) with ineligible companies to disclose.

Speaker:
David T. Rubin, MD, FACG
Consultant and/or Grant Support: AbbVie, Bristol-Myers Squibb, Janssen Pharmaceuticals, Lilly, Pfizer (GI), Takeda

*All of the relevant financial relationships listed for these individuals have been mitigated

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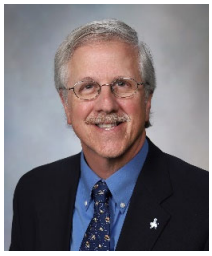
Covid 19 Delta Update



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Professor of Medicine
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Information up to date as of August 25, 2021
Lecture: August 31, 2021

11

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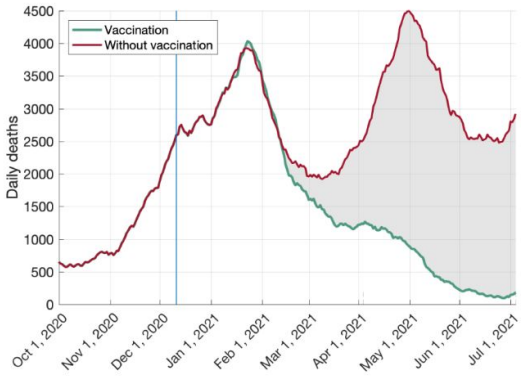
Effectiveness of Covid-19 Vaccines Prior to Spread of B.1.617.2 (Delta) Variant

Model developed by Commonwealth Fund prior to delta explosion

Without a vaccination program, by the end of June 2021 there would have been approximately 279,000 additional deaths and up to 1.25 million additional hospitalizations

Estimated U.S. seven-day rolling average of daily deaths with and without vaccination



https://www.commonwealthfund.org/publications/issue-briefs/2021/jul/deaths-and-hospitalizations-averted-rapid-us-vaccination-rollout

12

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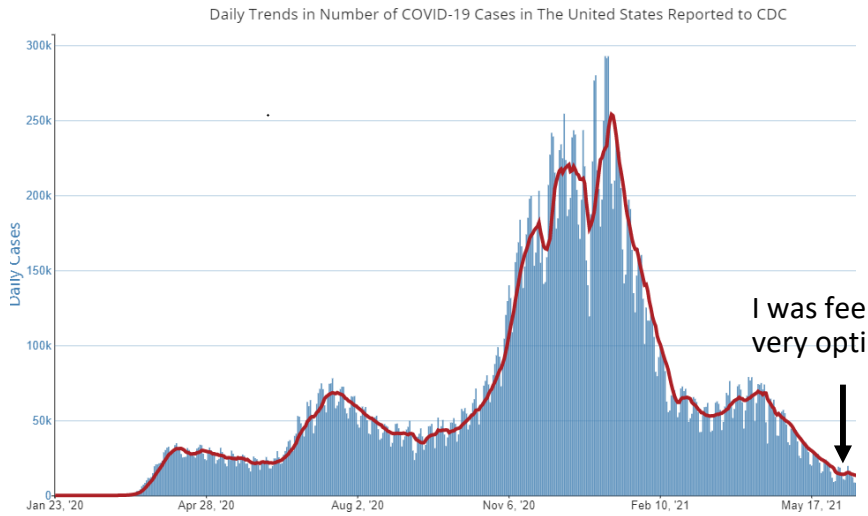
CDC Covid Tracker 8/23/21



CDC COVID Data Tracker

13

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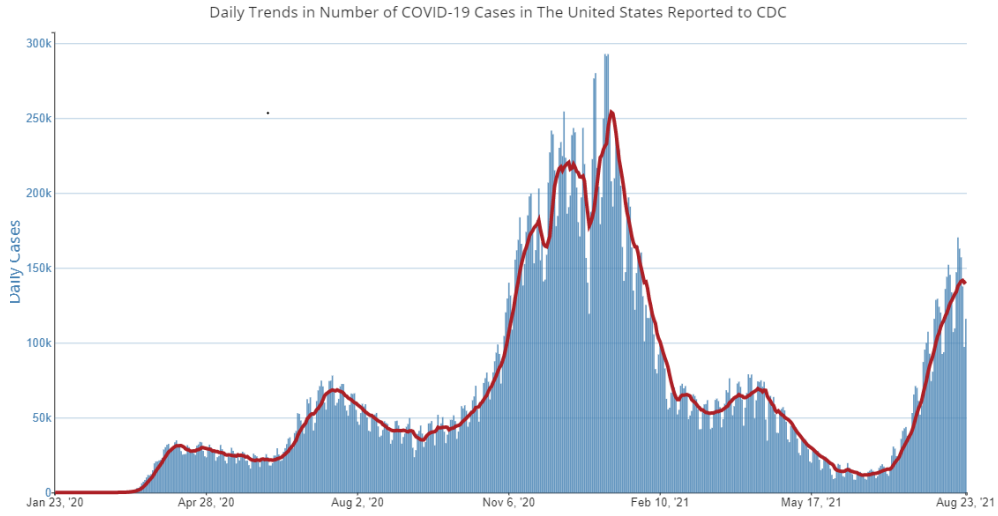
CDC Covid Tracker 8/23/21



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14

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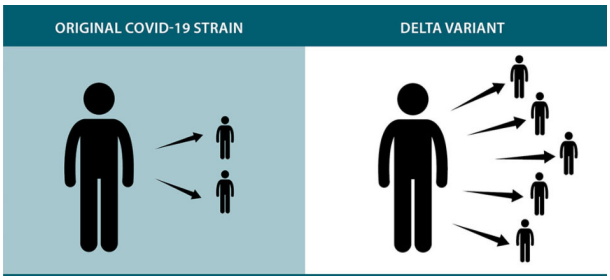
Delta Variant (B.1.617.2)

- Most common strain in the US since late June 2021
- Viral loads 1000-1200 times higher than original strain
- More than 2-fold more contagious than previous variants and as contagious as chicken pox



R_0 or the basic reproduction number is the average number of people to whom every infected person will spread the virus in a susceptible population

Delta R_0 of 6.4, is much higher than the R_0 of 2–4 estimated for the original version of SARS-CoV-2 virus

https://www.cdc.gov/coronavirus/2019-ncov/variants/delta-variant.html

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What Does The R_0 Mean?

- R_0 for original Covid Strain was 2 to 2.5
- One person spreads to 2.5 persons
  - After 10 cycles of transmission, you have about 9,500 infections
- R_0 for the Delta Covid Strain is 6.4
  - After 10 cycles of transmission, you have 60,500,000 infections

Gregory Poland, MD, Mayo Clinic Rochester

16

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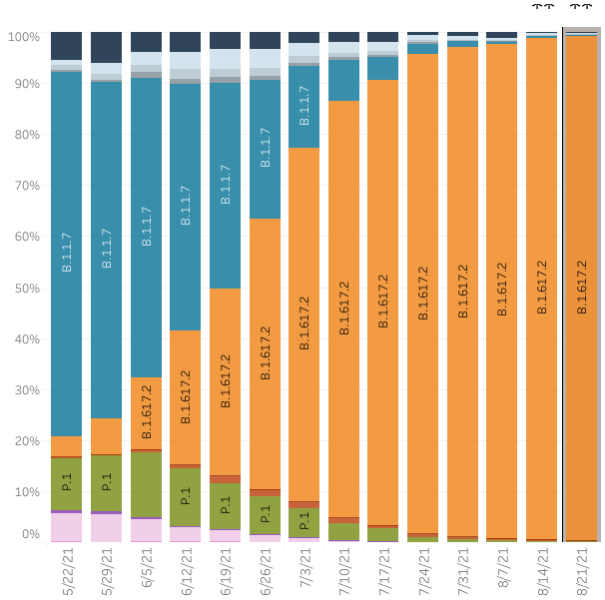
Covid Strains in the US as of 8/21/21



CDC COVID Data Tracker

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Delta Variant (B.1.617.2)

- Unvaccinated individuals remain greatest concern
- Some evidence that delta causes more severe disease in unvaccinated individuals
- People infected with the Delta variant of SARS-CoV-2 are more likely to spread the virus before developing symptoms than are people infected with earlier variants
- Vaccinated individuals appear to be infectious for shorter periods of time
- Fully vaccinated individuals with delta variant breakthrough infections can transmit to others

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Preprint Data from Israel

- Nationwide vaccination program with Pfizer vaccine since December 2020
- 2.3-fold increased risk for breakthrough infections among patients vaccinated with Pfizer vaccine in January 2021 vs April 2021
- Higher breakthrough infection rate (2.4% vs 1.1%, OR = 2.2) among those who received 2nd dose ≥ 5 months ago compared to < 5months
- Higher magnitude of difference with increasing age

Mizrah B, et al. medRxiv 2021.07.29.21261317; Israel A, et al. medRxiv 2021.08.03.21261496

19

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Effectiveness of Covid-19 vaccines against B.1.617.2 (Delta) Variant

- Study of 4000 health care workers in 6 US States from December 2020-August 2021
- Eight-three percent of healthcare workers in the study were vaccinated; 65% had received the Pfizer-BioNTech vaccine, 33% received the Moderna vaccine and 2% received the Johnson & Johnson vaccine
- Vaccine effectiveness against COVID-19 infections declined from 91% prior to the delta variant's emergence to 66% after the rise of the delta variant in the summer
- This might be related to increased prevalence of delta or waning immunity due to time from vaccination

https://www.cdc.gov/mmwr/volumes/70/wr/mm7034e5.htm?s_cid=mm7034e5_w

20

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Effectiveness of Covid-19 vaccines against B.1.617.2 (Delta) Variant

- During May 1–July 25, 2021, among 43,127 SARS-CoV-2 infections in residents of Los Angeles County, California, 10,895 (25.3%) were in fully vaccinated persons, 1,431 (3.3%) were in partially vaccinated persons, and 30,801 (71.4%) were in unvaccinated persons
- As of July 25, infection and hospitalization rates among unvaccinated persons were 4.9 and 29.2 times, respectively, those in fully vaccinated persons

https://www.cdc.gov/mmwr/volumes/70/wr/mm7034e5.htm?s_cid=mm7034e5_w

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Breakthrough Infections in the US

- As of 8/2/21, among more than 164 million fully vaccinated in US, there have been 7,101 hospitalizations & 1,507 deaths with vaccine breakthrough reported to passive surveillance
- Among hospitalized or fatal breakthrough cases, 74% in persons ≥ 65

https://www.cdc.gov/coronavirus/2019-ncov/covid-data/covid-net/purpose-methods.html

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22

What does this mean for you and your patients?

- Breakthrough infections are to be EXPECTED
- MUST continue prevention strategies
  - Vaccination
  - Masks
  - Distancing
- Mitigating activities of masking and distancing INCLUDES vaccinated individuals
- Recommendations will certainly and appropriately change as we learn more about SARS COV-2 variants

23

US Covid Vaccination Rates as of 8/24/21

Total Vaccine Doses

Delivered	428,529,385
Administered	363,915,792

Learn more about the distribution of vaccines.

171.4M
People fully vaccinated

People Vaccinated	At Least One Dose	Fully Vaccinated
Total	202,041,893	171,367,657
% of Total Population	60.9%	51.6%
Population ≥ 12 Years of Age	201,814,781	171,236,408
% of Population ≥ 12 Years of Age	71.2%	60.4%
Population ≥ 18 Years of Age	189,079,986	161,646,180
% of Population ≥ 18 Years of Age	73.2%	62.6%
Population ≥ 65 Years of Age	50,032,561	44,437,665
% of Population ≥ 65 Years of Age	91.5%	81.2%

About these data

CDC | Data as of: August 24, 2021 6:00am ET. Posted: Tuesday, August 24, 2021 3:10 PM ET

CDC COVID Data Tracker

24

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What risk do you want?

- COVID 19 vaccination
- Perpetual isolation
- Get COVID and hope for the best

Gregory Poland, MD, Mayo Clinic Rochester

25

Virtua

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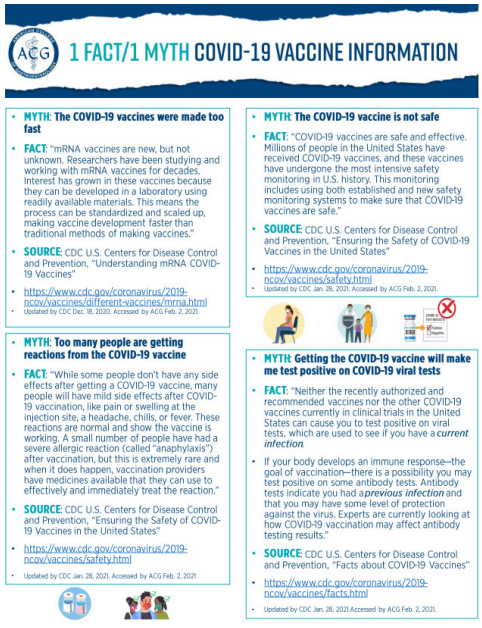

26

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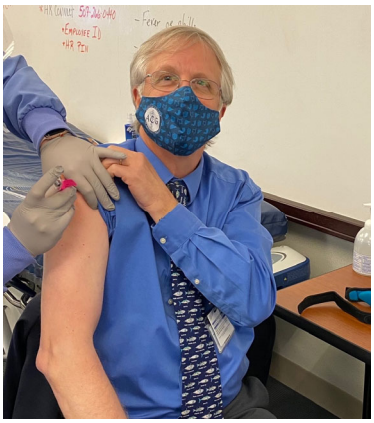
Set an Example for Your Patients and Staff and Get Vaccinated



Waiting for Vaccine Number 3

28

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Thank You
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29

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Additional COVID-19 Vaccine and Other Updates from Advisory Committee on Immunization Practice (ACIP)

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DEPARTMENT OF Medicine
UNIVERSITY OF WISCONSIN SCHOOL OF MEDICINE AND PUBLIC HEALTH

30

Objectives

- Explain why the ACIP recommended an additional dose
- Discuss the differences between an additional dose and booster
- Provide update on pregnancy recommendations
- Provide update on contraindications and precautions

31

ACIP and recommendations for immunosuppressed populations

- Immunocompromised people comprise 2.7% of US adults including
  - Solid tumor and hematologic malignancies
  - Receipt of solid-organ or hematopoietic stem cell transplant
  - Severe primary immunodeficiencies
  - Persons living with HIV
  - Treatment with immunosuppressive medications such as cancer chemotherapeutic agents, TNF blockers, certain biologic agents (e.g., rituximab), and high-dose corticosteroids
- ACIP has provided special recommendations regarding vaccine in the past
  - Pneumococcal 13 serotype vaccine
  - Zostavax vaccine

Harpaz et al. Prevalence of Immunosuppression Among U.S. Adults, 2013. JAMA 2016

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Immunocompromised people and SARS-CoV-2 infection

- More likely to get severely ill from COVID-19
  - Organ transplant OR 6.0 (4.37-7.61)
  - Rheumatoid arthritis 1.30 (1.21-1.38)
  - Other immunosuppressive condition 2.75 (2.1-3.62)
- Patients with IBD are NOT at increased risk
- Higher risk for
  - Prolonged SARS-CoV-2 infection and shedding
    - Case reports in oncology patients

Williamson et al. *Factors Associated with COVID-19-related Death Using Open SAFELY*. Nature 2020.
Truong et al. *Persistent SARS-CoV-2 Infection and Increasing Viral Variants in Children and Young Adults With Impaired Humoral Immunity*. medRxiv 2021.
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
Baang et al. *Prolonged Severe Acute Respiratory Syndrome Coronavirus 2 Replication in an immunocompromised Patient*. JID 2021
Choi et al. *Persistence and Evolution of SARS-CoV-2 in an Immunocompromised Host*. NEJM 2020
Helleberg et al. *Persistent COVID-19 in an Immunocompromised Patient Temporarily Responsive to Two Courses of Remdesivir Therapy*. JID 2020

33

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Immunocompromised people and SARS-CoV-2 infection in vaccinated individuals

- More likely to have breakthrough infection
  - 44% of hospitalized breakthrough cases are immunocompromised people in US study
    - These were solid organ transplant or hematologic malignancy
  - Out of 152 breakthrough cases, 40% were in immunocompromised people in
    - Common causes of immunosuppression were chronic corticosteroids treatment, chemotherapy, or anti-metabolite treatment, solid organ transplantation and anti-CD20 treatment.

Tenforde et al. Effectiveness of SARS-CoV-2 mRNA Vaccines for Preventing Covid-19 Hospitalizations in the United States (2021) DOI: https://doi.org/10.1101/2021.07.08.21259776

Brosh –Nissimiv et al. *BNT162b2 vaccine breakthrough: clinical characteristics of 152 fully-vaccinated hospitalized COVID-19 patients in Israel* (2021) https://doi.org/10.1016/j.cmi.2021.06.036

34

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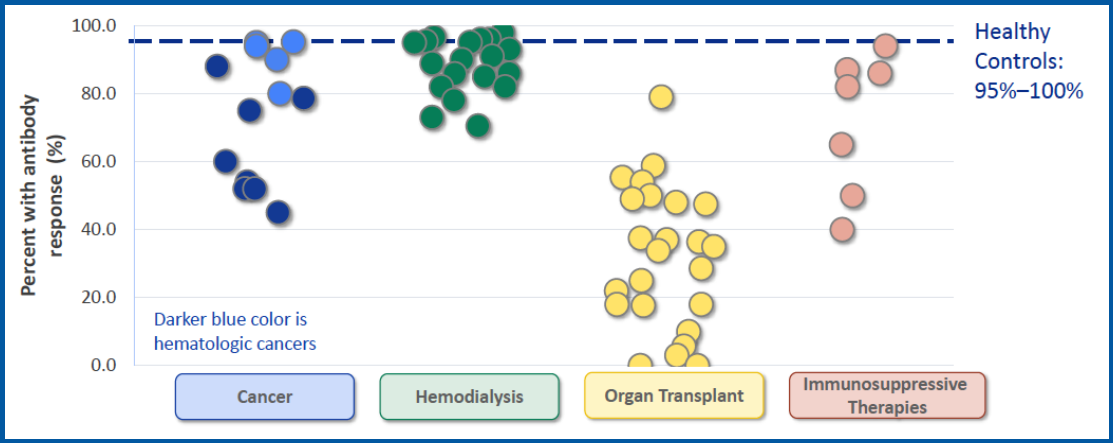
Percent of subject with antibody response after two mRNA vaccine doses by condition



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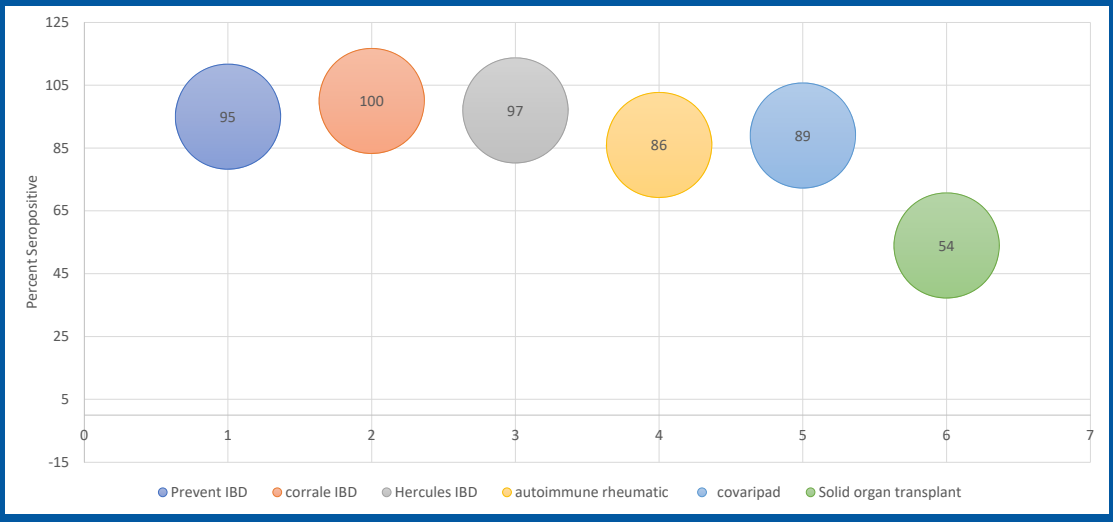
Subjects who were seropositive after two doses of mRNA vaccine on Immune-modifying therapy



Pozdnyakova V, et al. Gastroenterology 2021, Kappelman MD,. Gastroenterology. 2021, Caldera (under review), Boyarsky BJ, K, et al. Jama 2021;325:2204-2206, Deepak et al, Annual of Internal Medicine

36

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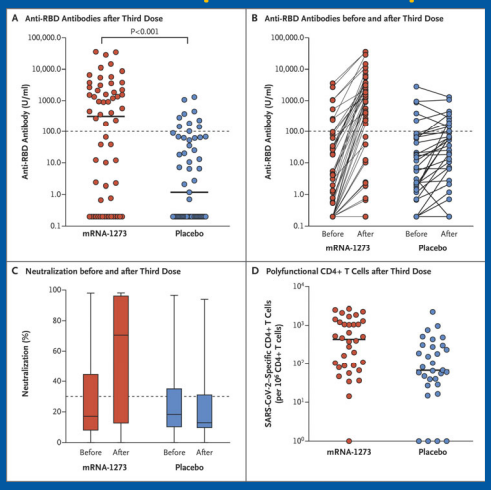
Randomized Trial of a 3rd Dose of Moderna Vaccine in Transplant Recipients (n=120)



- 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

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

37

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FDA: Emergency Use Authorization (EUA) Amendment

- August 12, 2021: FDA Authorizes Additional Vaccine Dose for Certain Immunocompromised Individual
  - ✓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 individuals who received Janssen COVID-19 as a primary series

38

ACIP Recommendation

On August 13, 2021

- ACIP made an interim recommendation for use of an additional dose of an mRNA vaccine for moderate to severely immunocompromised individuals.
- An additional dose of
  - Pfizer-BioNTech COVID-19 vaccine (BNT162b2) (≥12 years old)
  - Moderna COVID-19 vaccine (mRNA-1273) (≥18 years old)

39

Moderate to Severely Immunocompromised People

- Active treatment for solid tumor and hematologic malignancies
- Receipt of solid-organ transplant and taking immunosuppressive therapy
- Receipt of CAR-T-cell or hematopoietic stem cell transplant (within 2 years of transplantation or taking immunosuppression therapy)
- Moderate or severe primary immunodeficiency (e.g., DiGeorge, Wiskott-Aldrich syndromes)
- Advanced or untreated HIV infection
- Active treatment with high-dose corticosteroids (i.e., ≥20mg prednisone or equivalent per day), alkylating agents, antimetabolites, transplant-related immunosuppressive drugs, cancer chemotherapeutic agents classified as severely immunosuppressive, TNF blockers, and other biologic agents that are immunosuppressive or immunomodulatory

*General Best Practice Guidelines for Immunization, CDC Yellow Book, IDSA 2013 guidelines

40

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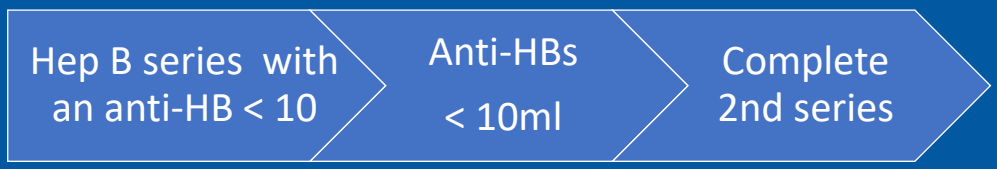
Role of an Additional Dose

Two roles of an additional dose

- **Additional dose after an initial primary vaccine series**:
  - administration of an additional dose when the initial immune response following a primary vaccine series is likely to be insufficient
  - E.g. Hepatitis B vaccine
    - In older adults or those on anti-TNF therapy



41

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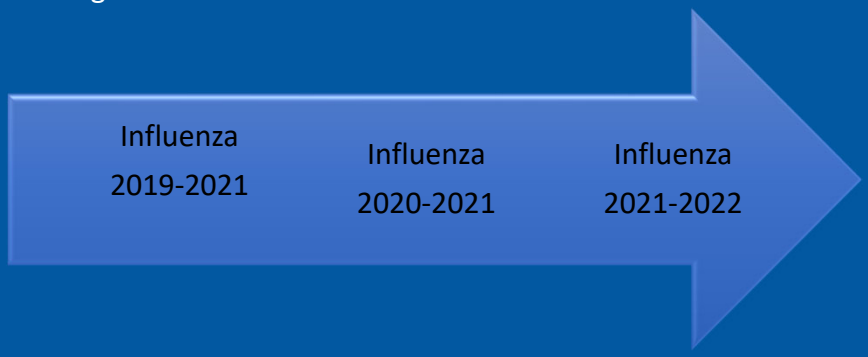
Booster dose: my thoughts

- **Booster dose:** a dose of vaccine administered when the initial sufficient immune response to a primary vaccine series is likely to have waned over time.
  - Need and timing of a COVID-19 booster have not been established
    - E.g. Influenza vaccine



42

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Booster dose: my thoughts

- Not uncommon for a vaccine series to require several doses
- Vaccines that require > 1 dose do not necessarily mean annual boosters needed
  - For many vaccines, the final dose is given at least 6 months after the initial dose

Vaccine	1st dose	2nd dose	3rd Dose
Herpes zoster (shingles)	Initial	2-6 months	
Hepatitis A	Initial	6 months	
Hepatitis B	Initial	1-2 months	6 months
Human papillomavirus (HPV)	Initial	1-2 months	6 months

43

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CDC update on Pregnancy

- Pregnancy is associated with increased risk of severe illness from COVID-19
  - COVID-19 associated with pregnancy complication and adverse pregnancy outcomes
- Vaccine uptake by pregnant people overall 23%
- Data from CDC v-safe COVID-19 vaccine registry
  - Included 2456 pregnant people enrolled in v-safe pregnancy registry
  - Risk of Spontaneous Abortion was not higher after mRNA immunization

Receipt of mRNA COVID-19 vaccines preconception and during pregnancy and risk of self-reported spontaneous abortions, CDC v-safe COVID-19 Vaccine Pregnancy Registry 2020-21 | Research Square

44

CDC Recommendation for Pregnant People

- COVID-19 vaccination is recommended for all people aged 12 years and older, including people who are pregnant, lactating, trying to get pregnant now or might become pregnant in the future
- Breast Feeding mothers
  - Antibodies developed from mRNA COVID-19 vaccines present in breast milk
- Fertility
  - No evidence that any COVID-19 vaccines cause fertility problems

45

Update on Considerations of mRNA COVID-19 vaccines

- People with a history of myocarditis or pericarditis
  - Occurred predominantly in males aged 12-29 days
    - If develop myocarditis after a first dose of an mRNA COVID-19 vaccine defer receiving the second dose.
- People with a history of Bell's palsy
  - Insufficient for FDA to conclude that these cases were related to vaccines

46

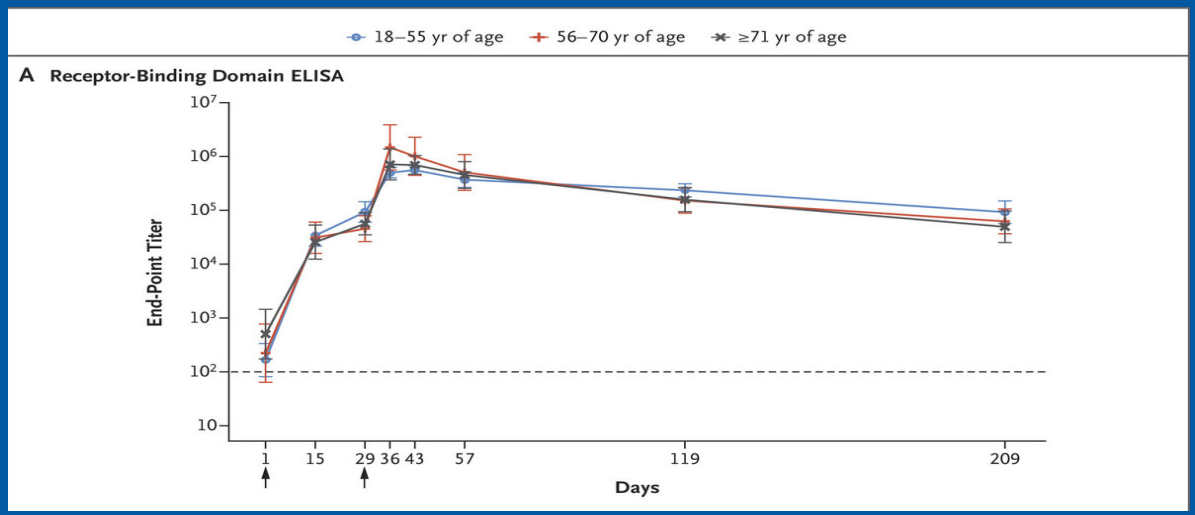
Special Considerations for J&J COVID-19 vaccines

- People with a history of Guillain-Barré syndrome
  - Increased risk of GBS during 42 days following Janssen vaccination
  - No risk with mRNA vaccines
- Women aged < 50 years
  - Any vaccine, but this group highest rate of TTS per vaccine doses administered

- People with a history of thrombosis or risk factors for thrombosis
  - Since etiology of TTS associated with Janssen COVID-19 vaccine is unclear
  - Should be offered an mRNA COVID-19 vaccine

47

Checking antibody post immunization



48

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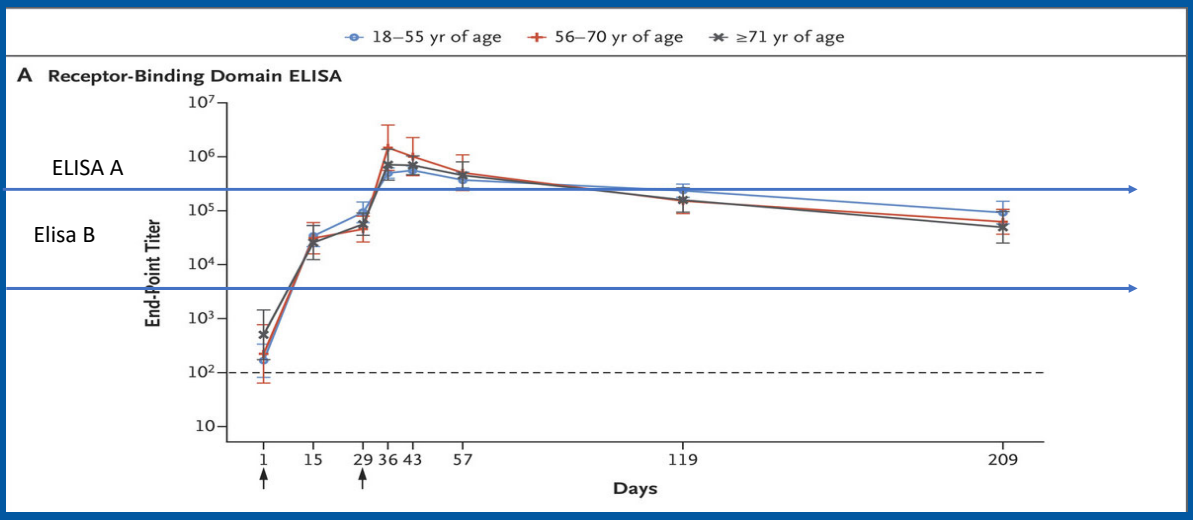
Checking antibody post immunization



N Doria-Rose et al. N Engl J Med 2021;384:2259-2261

49

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Conclusion

- ACIP decision on additional dose mostly based on data from solid organ transplant.
- New data shows vaccines are safe in pregnancy
- Few contraindications that prohibit COVID-19 immunization
- Do not use a commercial assay to evaluate for post immunization antibodies.

50

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Thank you

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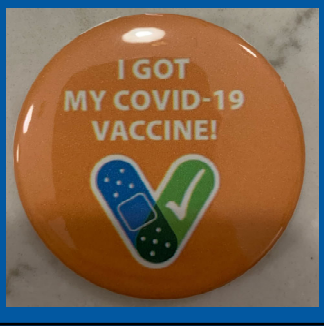

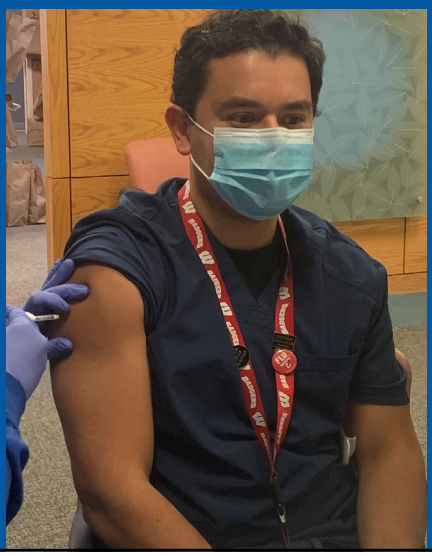

51

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ACG Virtual Grand Rounds 2021: Special COVID-19 Vaccine Update

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Medicine
UNIVERSITY OF WISCONSIN
SCHOOL OF MEDICINE
AND PUBLIC HEALTH

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Objectives

- Explain the impact of COVID-19 on solid organ transplant recipients (SOTr), particularly liver transplant recipients
- Discuss the immunogenicity of the mRNA COVID-19 vaccine in SOTr
- Provide an update on the ACIP recommended additional dose of the mRNA vaccine for SOTr

53

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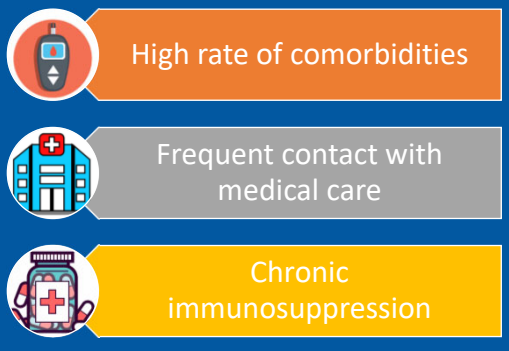
Impact of COVID-19 on Solid Organ Transplant Recipients (SOTr)

- COVID-19 infection in SOTr may be of greater severity than in non-immunosuppressed hosts[1,2]:



[1]AST FAQs for Organ Transplantation. Updated 8/9/21
[2]Akalin E et al. NEJM 2020
[3]Pereira MR et al. Am J Transplant 2020

54

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Impact of COVID-19 on SOTr

- **NYC Experience: March – April 2021[1,2]**
  - Pereira et al, Am J Transplant 2020
    - 90 SOTr analyzed
      - 76% of all pts were hospitalized
      - 30% with severe disease (ICU admission, intubation, death)
      - 18% of pts died overall while 52% of ICU pts died
  - Akalin et al, NEJM 2020
    - 36 kidney transplant pts
      - 78% hospitalized
      - 28% died, while 64% of intubated pts died

[1]Akalin E et al. NEJM 2020
[2]Pereira MR et al. Am J Transplant 2020

55

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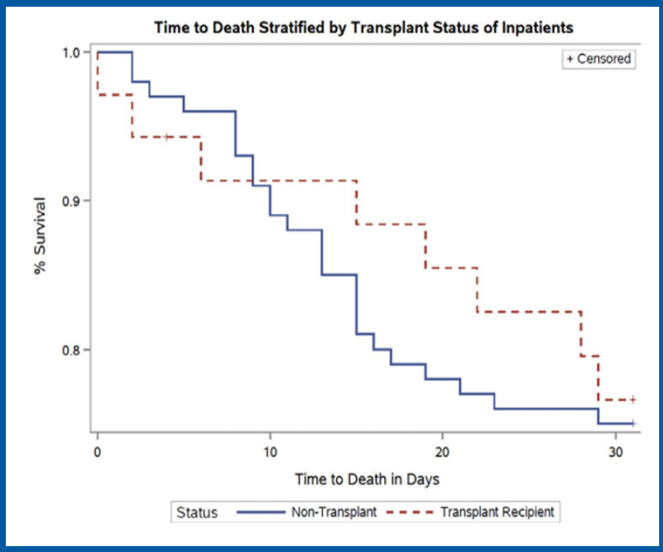
Impact of COVID-19 on SOTr

Chaudhry et al, Am J Transplant. Nov 2020

- 47 SOT recipients vs 100 controls
  - Higher % of comorbidities
  - 17% mortality overall
  - 58% of those requiring mechanical ventilation died
  - *Interestingly, transplant status was **not** associated with mortality*



Chaudhry et al, Am J Transplant. Nov 2020

56

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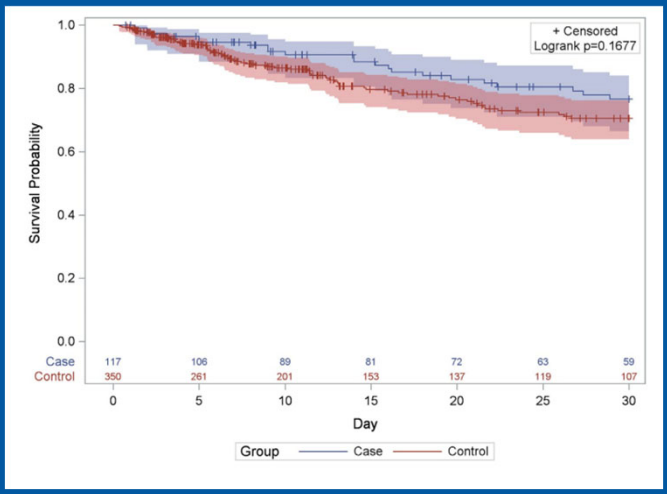
Impact of COVID-19 on SOTr

- **Periera et al, March 2020 – May 2020**
  - 117 SOTr vs 305 non-SOT pts
    - Higher rate of ICU admission (32.5% vs 27.7%)
  - Mortality was not different (23.08% in SOTr vs 23.14% in controls)
  - *Chronic immunosuppression may **not** be an independent risk factor for poor outcomes*



Periera et al. Transpl Infect Dis. 2021

57

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Impact of COVID-19 on SOTr

- Overall, 28-day mortality among hospitalized SOTr pts is high: 20.5%[1]
- Older age, lung disease, congestive heart failure, obesity are associated with mortality
- Immunosuppression does not seem to be the driver of mortality

[1]Kates et al. Clinical Infectious Dis. Aug 2020.

58

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Immunogenicity in SOTr with mRNA vaccination

- SOTr have generally been observed to have lower antibody responses to mRNA COVID vaccines than immunocompetent pts[1-7]
  - Ranging from ~30 – 58%
- Several different immunoassays are used between studies
- Antimetabolite-containing immunosuppression (i.e. mycophenolate mofetil) appears to negatively influence immune response[5,8]

[1]Chavarot et al, Transplantation 2021. [2]Holden et al, J Int Med 2021. [3]Benotmane et al, Kidney Intern 2021. [4]Mazzola et al, CID 2021. [5]Marinaki et al, Am J Transplant 2021. [6]Miele et al, Am J Transplant May 2021. [7]Olivier et al, Annals of Int Med 2021. [8]Rashidi-Alavijeh J et al. Vaccines (Basel). 2021 Jul

59

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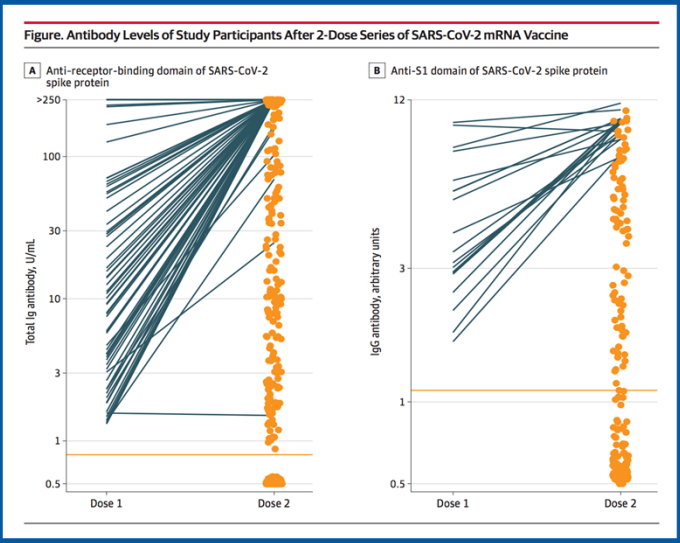
Immunogenicity in SOTr with mRNA vaccination

- 658 SOTr assessed
  - 1st dose: 15% antibody response
  - 2nd dose: 54% antibody response
  - Antimetabolite immunosuppression was associated with poor humoral response



Boyarsky BJ et al. *JAMA*. March 2021
Boyarsky BJ et al. *JAMA*. May 2021

60

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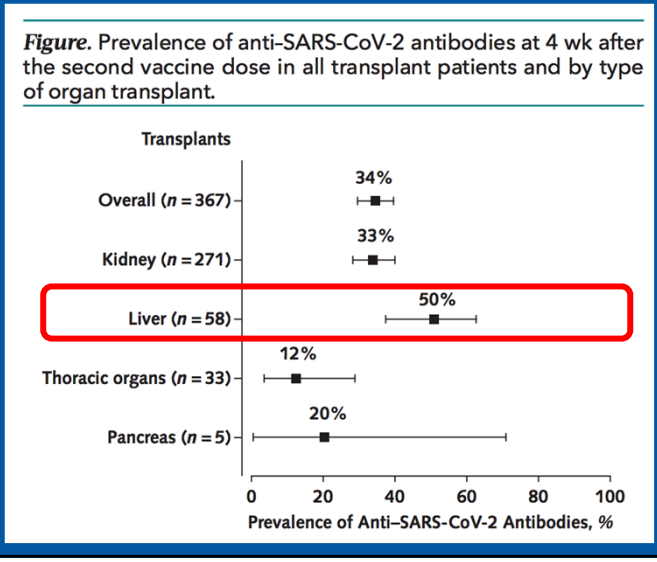
Immunogenicity in Liver Transplant Recipients (LTr) with mRNA vaccination



Olivier et al. Annals of Int Med. May 2021

61

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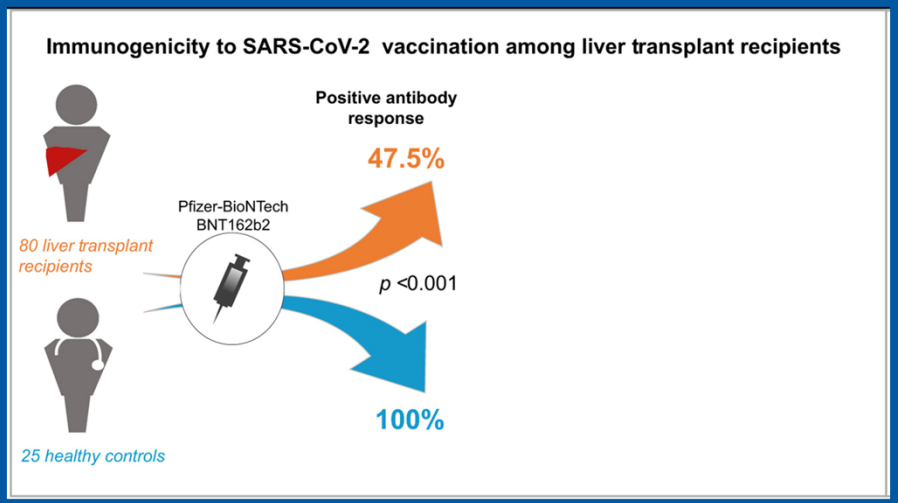
Immunogenicity in LTr with mRNA vaccination



Rabinowich et al. J Hepatology. Aug 2021

62

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Immunogenicity in LTr with mRNA vaccination

Predictors of vaccination failure in liver transplant recipients:

Age

OR 1.3 (1.17-1.95)

Rabinowich et al. J Hepatology. Aug 2021

63

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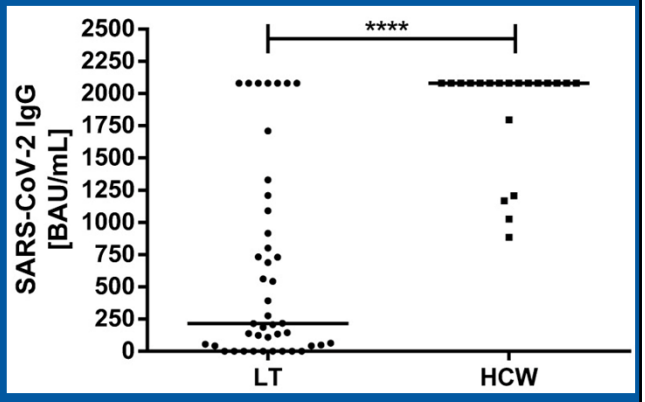
Immunogenicity in LTr with mRNA vaccination

- 43 LTr vs 20 healthcare workers (HCWs, controls)
  - 79% LTr vs 100% control developed antibodies (p=0.047)
  - IgG titer was significantly lower in LTr vs control: 215 vs >2080 BAU/mL, p=0.0001.
  - Pts receiving mycophenolate mofetil had reduced vaccination response



Rashidi-Alavijeh J et al. Vaccines (Basel). 2021 Jul

64

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Risk of Breakthrough COVID-19 Infection in SOTr

- **Qin et al, Transplantation 2021[1]**
  - 18,215 vaccinated SOTr[1]
    - 151 (0.83%) breakthrough infections
    - Mortality rate among breakthrough infections was 9.3%
      - vs 20.5% from de novo infection in unvaccinated SOTr[2]
  - Compared to general population, SOTr's have 82-fold higher risk of breakthrough infection

[1]Qin CX et al. Transplantation. July 2021
[2]Kates OS. CID Aug 2020

65

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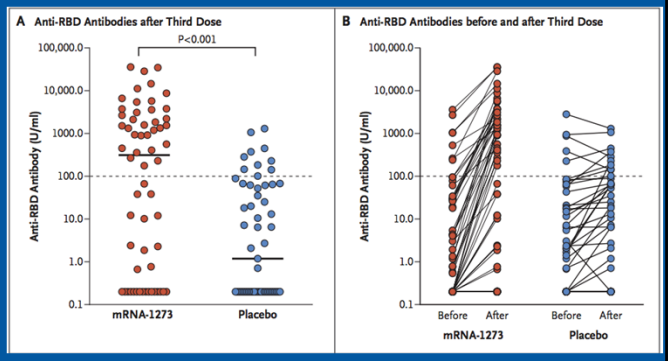
Randomized Trial of a 3rd dose of Moderna Vaccine in SOTr

- **Hall et al.**
  - N=120
  - Primary outcome = **anti-receptor binding domain (RBD) >100 U/mL**
    - 55% (33/60) of mRNA-1273 group
      vs
    - 18% (10/57) in placebo group
      - (RR 3.1, 95% CI 1.7 – 5.8, p<0.0001)
  - Adverse events:
    - Slightly more local and systemic events after 3rd dose.
    - No grade 3 or 4 events
    - No cases of acute rejection



Hall et al. NEJM. Aug 2021

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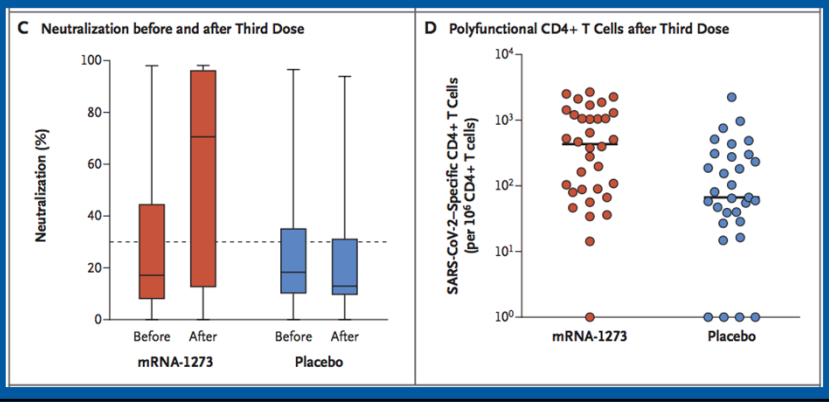
Randomized Trial of a 3rd dose of Moderna Vaccine in SOTr

- **Secondary outcomes:**
  - Enhanced viral percent neutralization (Figure 1C)
  - Increased SARS-CoV-2-specific polyfunctional CD4+ T cell response (Figure 1D)



Hall et al. NEJM. Aug 2021

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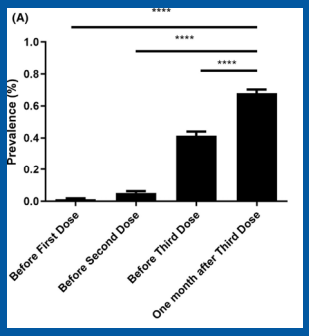
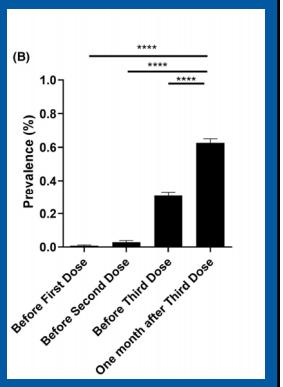
Three doses of mRNA COVID-19 Vaccine in SOTr

- 396 SOTr
  - 277 kidney transplant, 69 liver transplant and 50 other
  - 232 pts were seronegative before 3rd dose
    - 45.3% turned positive after 3rd dose
  - Higher seroconversion rate: Younger pts
  - Lower seroconversion rate:
    - Pts on mycophenolic acid, belatacept or triple immunosuppression





Del Bello et al. Am J Transplant. July 2021
Kamar et al. NEJM June 2021.

68

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Recommendations for a 3rd dose of mRNA Vaccine in SOTr

- Severe COVID-19 has been reported in vaccinated SOTr pts[1-3]
- Serologic response after 2 doses of mRNA vaccination is lower than immunocompetent controls
- Quantitative titers were typically below median titer in immunocompetent pts
  - (however, level of protective antibody is unknown)
- Breakthrough infections after vaccination in SOTr are higher than general population

Therefore, a third dose of the mRNA vaccine (Pfizer or Moderna) is recommended at least 28 days after the second dose.

[1]AASLD Expert Panel Consensus Statement. Aug 30, 2021.
[2]AST FAQs for Organ Transplantation. Updated 8/9/21
[3]Caillard et al. Kidney Int. 2021 Aug
[4]Werbel et al. Ann Intern Med. June 2021

69

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Summary

- SOTr, including, liver transplant recipients are likely at increased risk of severe COVID-19 infection
- All SOTr should be vaccinated against COVID-19
  - Priority should be to vaccinate pre-transplantation (ideally completing the series 2 wks prior to transplant).
- Immunogenicity is low after vaccination
  - Vaccinated SOTr remain at risk of COVID-19 infection. Masking is still recommended.
- Available data suggest that SOTr have an enhanced immune response to an additional dose of vaccine.
- Therefore, a third dose of the mRNA vaccine (Pfizer or Moderna) is recommended at least 28 days after the second dose in those that received the mRNA series.

70

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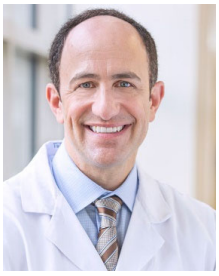
What an Additional Dose of the COVID-19 Vaccine Means for Patients with IBD



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71

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What an Additional Dose of the COVID-19 Vaccine Means for Patients with IBD

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Why this is so important to patients with Inflammatory Bowel Disease (and their providers!)

- IBD is a condition of an abnormal immune response
- Therapies for IBD are predominantly immune-based and immune-modifying or (less often) immune suppressive
- There has been increased concern and fear that the therapies for IBD are increasing risk of severe COVID-19 outcomes (but they don't!)
- CDC and FDA information is not specific to IBD and confusing (for all of us)

73

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What are the COVID-19 Outcomes in Patients with IBD?

74

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Patients With IBD Do Not Experience an Increased Risk of COVID-19 Infection or Severe COVID-19

- 2 retrospective studies evaluated infection rates in IBD compared with the general population
- No significant difference in infection, hospitalization, or death rates in IBD versus the general population

	U.S. Veterans Affairs Healthcare System	Dutch National Cohort
Number of Patients with IBD	38,378	34,763
Number of non-IBD Patients	67,433	General population of the Netherlands: ~17.2 million
Rate of COVID-19 Infection in IBD Cohort	87 (0.23%)	287.6 per 100,000 [95% CI 236.6–349.7]
Rate of COVID-19 Infection in non-IBD Cohort	132 (0.20%)	333.0 per 100,000 [95% CI 329.3–336.7]
P - value	0.29	0.15

Khan N, et al. *Am J Gastroenterol*. 2021 Apr;116(4):808-810.
Derikx LAAP, et al. *J. CRohn's Colitis*. 2021 Apr;15(4):529-539.

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What are the Risks of IBD Therapies and COVID-19?

76

Corticosteroids Associated with Increased Risk of Severe COVID-19

SECURE-IBD DATABASE
Surveillance Epidemiology of Coronavirus (COVID-19) Under Research Exclusion

- SECURE-IBD *update 31 Aug 2021:* n=6438
- Earlier analysis of n = 2,035 patients from up to Aug 2020
- Corticosteroids are associated with increased risk of severe COVID-19
- Biologic therapy (predominantly anti-TNF) is associated with decreased risk of severe COVID-19
- **No significant association with 5-ASAs and severe COVID-19** (contrary to earlier reports)

Table 3 Association of non-IBD comorbidities and adverse COVID-19 outcomes (hospitalization and death) in IBD patients with COVID-19 in the SECURE-IBD registry in a composite model

Variable[a]	aOR (95% CI)	*P* value
Asthma	1.96 (1.24–3.11)	0.004
Diabetes	1.95 (1.22–3.11)	0.005
Cancer	1.87 (0.94–3.75)	0.076
Cardiovascular disease	1.34 (0.87–2.06)	0.186
Chronic liver disease	1.97 (1.14–3.39)	0.015
Chronic kidney disease	3.02 (1.45–6.31)	0.003
COPD	2.92 (1.32–6.48)	0.008
Hypertension	1.50 (1.07–2.10)	0.018
Other chronic lung disease	2.38 (1.06–5.35)	0.035
Age	1.03 (1.02–1.04)	<0.001
Male sex	1.22 (0.97–1.53)	0.083
5-ASA	1.13 (0.88–1.45)	0.343
Corticosteroids	2.90 (2.09–4.03)	<0.001
Biologic therapy	0.51 (0.40–0.65)	<0.001

SECURE-IBD Surveillance Epidemiology of Coronavirus Under Research Exclusion for Inflammatory Bowel Disease, *COVID-19* coronavirus disease 2019, *COPD* chronic obstructive pulmonary disease, *5-ASA* 5-aminosalicylic acid, *aOR* adjusted odds ratio, *CI* confidence interval

Parekh R, et al. *Dig. Dis. Sci.* https://doi.org/10.1007/s10620-021-07104-0. 2021.

77

What are the Vaccine Recommendations for Patients with IBD?

78

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COVID-19 Vaccine Recommendations for People with IBD

IOIBD

SARS-CoV-2 vaccination for patients with inflammatory bowel diseases: recommendations from an international consensus meeting

Corey A Siegel ,[1] Gil Y Melmed,[2] Dermot PB McGovern,[2] Victoria Rai,[3,4] Florian Krammer,[5] David T Rubin ,[3] Maria T Abreu,[6] Marla C Dubinsky ,[7] on behalf of the International Organization for the Study of Inflammatory Bowel Disease (IOIBD)

Gut. 2021;70(4):635-640.

Box 1 Highlighted themes of accepted statements related to SARS-CoV-2 vaccination for patients with IBD by the International Organization for the Study of Inflammatory Bowel Disease (IOIBD)

- Patients with IBD should be vaccinated against SARS-CoV-2.
- The best time to administer SARS-CoV-2 vaccination in patients with IBD is at the earliest opportunity to do so.
- SARS-CoV-2 vaccines including messenger RNA vaccines, replication-incompetent vector vaccines, inactivated vaccines and recombinant vaccines are safe to administer to patients with IBD.
- SARS-CoV-2 vaccination should not be deferred because a patient with IBD is receiving immune-modifying therapies.
- Patients with IBD vaccinated with SARS-CoV-2 should be counselled that vaccine efficacy may be decreased when receiving systemic corticosteroids.

79

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How do Patients with IBD Respond to the Vaccine?

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How do Patients with IBD Respond to the Vaccine?

Study Name	Author	Number of IBD Patients	Journal	Main Finding
CLARITY-IBD	Kennedy et al. Lin et al.	2052 (2 doses mRNA on IFX) 925 (2 doses mRNA on VDX)	*Gut* Preprint	Patients on infliximab had lower seroconversion, defined as ≥15U/mL IgG spike protein, at week 16 after two doses of Pfizer-BioNTech or AstraZeneca vaccine than patients on vedolizumab.
CORALE	Botwin et al.	246 (2 doses mRNA)	*Am J Gastroenterol*	Adverse events due to COVID-19 infection were similar in patients with IBD compared to the general population. Adverse events were less common in patients with IBD receiving biologic or small molecule therapies.
PREVENT-COVID	Kappelman et al.	317 (2 doses mRNA)	*Gastroenterology*	300/317 patients (95%) with IBD after mRNA 2-dose vaccination had detectable antibodies 5 months post vaccination. *IBD therapy did not significantly decrease antibody titers.* Corticosteroids depressed antibody titers but did not have a significant effect on vaccine immunogenicity, measured as IgG spike protein titers 8-weeks post 2nd dose ≥ 10 μg/ml.
ICARUS	Wong et al.	15 (2-doses mRNA vaccine) 33 (1-dose mRNA vaccine)	*Gastroenterology*	No significant difference in seroconversion in patients with IBD versus healthy controls after 2 doses of mRNA vaccine.

CLARITY IBD https://www.clarityibd.org/

CORALE https://www.corale-study.org/

PREVENT COVID https://www.ibdpartners.org/preventcovid

ICARUS IBD https://www.icarusibd.org/

The University of Chicago Medicine Inflammatory Bowel Disease Center

Email: covidvaccine.ibd@lists.uchicago.edu

81

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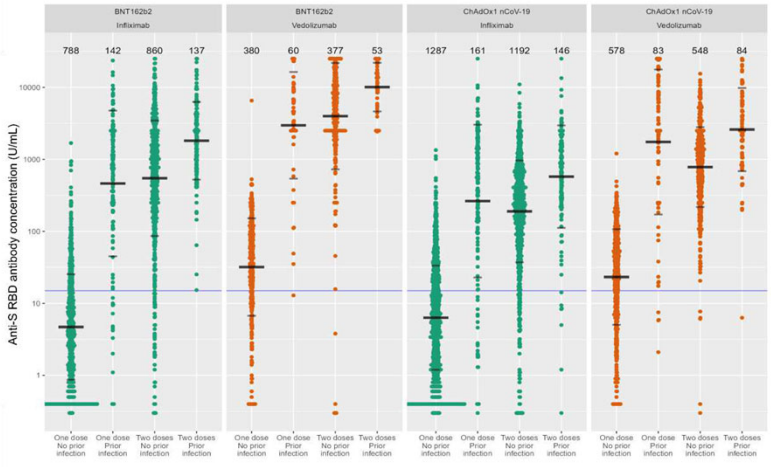
Anti-sars-cov-2 Antibody Responses are Attenuated in Patients with IBD Treated with Infliximab when Only One Dose Given



CLARITY IBD

n=6935

Kennedy NA, et al. *Gut*. 2021;70:865-875.
Lin S, et al. *Research Square*. 2021 July 30. Preprint.

82

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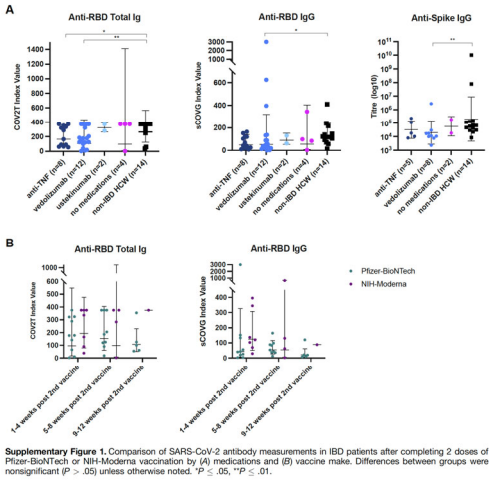
IBD Therapy Does Not Reduce Vaccine Immunogenicity

- IBD: n = 48 (CD = 23, UC = 25)
- Controls: n=43 (14 healthcare workers, 29 research controls)
- 100% seropositivity after 2 doses of either mRNA vaccine in patients with IBD, *regardless of therapy*



Supplementary Figure 1. Comparison of SARS-CoV-2 antibody measurements in IBD patients after completing 2 doses of Pfizer-BioNTech or NIH-Moderna vaccination by (*A*) medications and (*B*) vaccine make. Differences between groups were nonsignificant ($P > .05$) unless otherwise noted. $^{*}P \leq .05$, $^{**}P \leq .01$.

Wong SY, et al. *Gastroenterology*. 2021 Aug; 161(2):715-718.e4.

83

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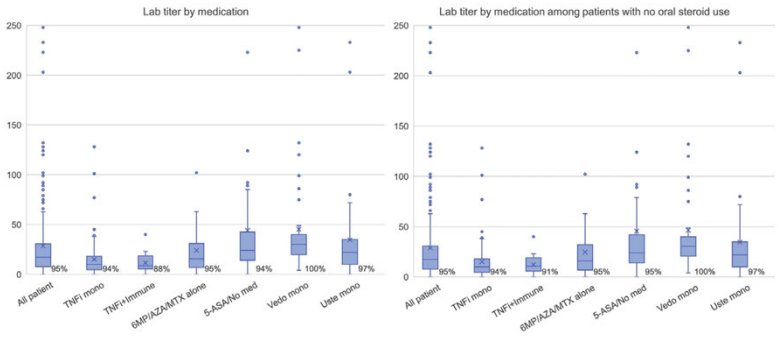
IBD Therapy Does Not Reduce Vaccine Immunogenicity

- All patients received two doses of an mRNA vaccine
  - Pfizer-BioNTech = 173
  - Moderna = 144
- No significant difference between spike protein IgG titer levels in patients on varying IBD therapies



Kappelman MD, et al. *Gastroenterology*. 2021 Jun 15:S0016-5085(21)03127-9.

84

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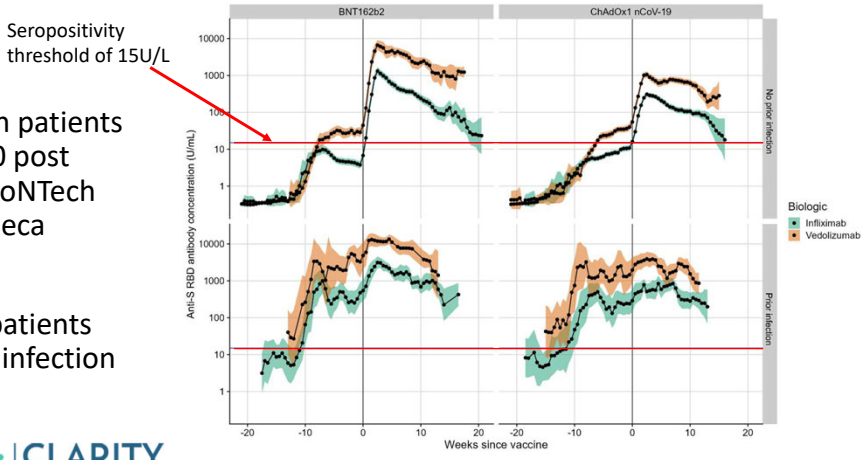
Patients on Infliximab Have Waning Antibodies After Second Dose of mRNA Vaccine

- Attenuated antibodies in patients on infliximab at week 20 post second dose of Pfizer-BioNTech (BNT162b2) or AstraZeneca (ChAdOx1 nCoV-19)
- Greater attenuation in patients without prior COVID-19 infection



CLARITY IBD

Lin S, et al. *Research Square*. 2021 July 30. Preprint.

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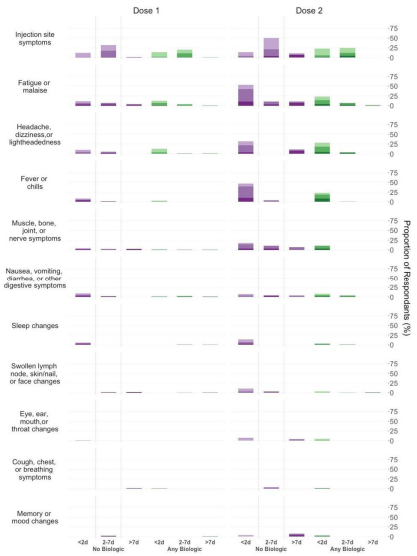
Anti-SARS-CoV-2 Vaccine Has Not Been Shown to Cause IBD Flares

- n=246 with IBD who received both doses of either the Pfizer-BioNTech or Moderna mRNA vaccines; similar adverse events as general population
- Sore arm, headache, and fatigue are the most common adverse effects of the vaccine
- **No increase in IBD flares was observed**



Botwin GJ, et al. *Am. J. Gastroenterol.* [E-pub ahead of print 2021].

87

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Are Vaccine Recommendations Different for Patients with Rheumatoid Arthritis on the Same Immunomodulators as Patients with IBD?

88

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American College of Rheumatology Does Not Recommend Altering Therapy Before or After Vaccination

- ACR consensus statement (4 August 2021) ultimately ***did not recommend*** adjustment in timing of immunomodulator therapies in relation to vaccination
- ACR task force considered modifying therapy timing in patients receiving methotrexate or JAK inhibitors based on data from studies of influenza and pneumococcal vaccinations in patients with RA
- No clinical or real-world evidence from COVID-19 vaccines to support withholding treatment

Curtis JR, et al. *Arthritis Rhematol.* 2021 Aug 4. E-pub.

89

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Should Patients with IBD get a Third Dose of the Vaccine?

90

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The Difference Between an Additional Dose and a Booster

- A **dose** is part of the primary series of vaccinations that is needed to produce an immune response that is protective against the virus
- A **booster** strengthens immune memory in people whose immune response may have weakened over time

91

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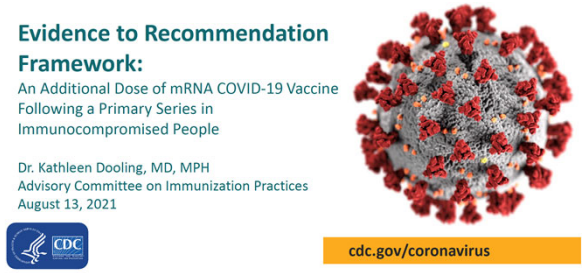
CDC Recommendations on Additional Vaccine Doses and Boosters

- CDC recommends individuals should get a third vaccine if:
  1. Previously received 2 doses of an mRNA vaccine
  2. Currently taking select therapies, including anti-TNF and anti-metabolites
  3. "Other biologic agents that are immunosuppressive or immunomodulatory"
  4. High dose steroids (prednisone ≥20 mg/d or equivalent for ≥2 weeks)
- All other individuals are recommended to get a booster 8 months after second mRNA vaccination



CDC Advisory Committee on Immunization Practices. "Evidence to Recommendation." 2021 Aug 13.

92

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Crohn's & Colitis Foundation Position Statement on Additional Vaccines

- The Crohn's & Colitis Foundation supports eligible IBD patients getting vaccinated
- The Foundation recognizes that most patients with IBD are not considered immunosuppressed and therefore *should not need an additional vaccine*
- Supports and encourages social distancing, mask wearing, and other strategies to mitigate the spread of the coronavirus

COVID-19 Vaccine Additional Dose

Position Statement

CROHN'S & COLITIS FOUNDATION

Crohn's & Colitis Foundation. "COVID-19 Vaccine Additional Dose Position Statement." 2021 Aug 26.

93

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Summary of 3rd Dose Recommendations for Patients with IBD from the CDC and Advisory Committee on Immunization Practices (as of 31 Aug 2021)

	Anti-TNF	Anti-Integrin and Anti-IL12/23	Immunomodulators (thiopurines and methotrexate)	Corticosteroids (prednisone ≥ 20mg or equivalent)	Targeted Synthetic Small Molecules (tofacitinib and ozanimod)
Pfizer-BioNTech and Moderna	eligible 28 days post second dose	eligible 28 days post second dose	eligible 28 days post second dose	eligible 28 days post second dose	No comment
Johnson & Johnson	No recommendation yet	No recommendation yet	No recommendation yet	No recommendation yet	No recommendation yet

(Notes: a 3rd dose is not the same as a booster and "eligible" doesn't mean it is needed in IBD. We will all likely need boosters.)

94

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Practical Considerations for Vaccines for Patients with IBD: What Should You Do? (my comments)

- **Patients with IBD should be vaccinated. Two dose vaccines are preferrable, especially if on anti-TNF based on data.**
- Reassure patients that they are not at increased risk of bad COVID outcomes (they are not at decreased risk either, e.g., age, obesity, DM, HTN). **There are NO DATA on breakthrough hospitalization or deaths in vaccinated individuals (yet).**
- Most patients with IBD on therapy beyond 5-ASA or budesonide are ***eligible*** to get a third dose now, but technically this is a booster, not a third dose (semantics, but reassuring to remind them that they are likely ok!)
  - For patients on combination therapy with anti-TNF and thiopurine or MTX or high dose steroids, reasonable to get the third dose/booster early.
- It is recommended to receive the same mRNA vaccine as the first two doses for the third dose, but mix and matching is probably ok (anecdote, expert opinion, early data).
  - If patients received the one dose Johnson & Johnson vaccine, and on anti-TNF +/- thiopurine or MTX or high dose steroids, reasonable to get another dose of any vaccine (anecdote, expert opinion, no data)
- Stay tuned for more information that will be coming…

95

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Questions?

Moderator:
Samir Shah, MD, FACG

Speaker:
Francis A. Farraye, MD, MSc, MACG

Speaker:
Freddy Caldera, DO, MS

Speaker:
Rita German, MD

Speaker:
David T. Rubin, MD, FACG

96