CDC/IDSA COVID-19 Clinician Call August 14, 2021

Welcome & Introduction

Dana Wollins, DrPH, MGC

Vice President, Clinical Affairs & Guidelines

IDSA

- 72nd in a series of weekly calls, initiated by CDC as a forum for information sharing among frontline clinicians caring for patients with COVID-19
- The views and opinions expressed here are those of the presenters and do not necessarily reflect the official policy or position of the CDC or IDSA. Involvement of CDC and IDSA should not be viewed as endorsement of any entity or individual involved.
- This webinar is being recorded and can be found online at www.idsociety.org/cliniciancalls.

TODAY'S TOPIC:

Additional Vaccine Doses in the Immune-Compromised; Plus the Latest on the Delta Variant and Vaccination in Pregnant Women



Delta Variant Update

CDR Heather Scobie, PhD, MPH Epi DVD Enhanced Surveillance **Epidemiology Task Force COVID-19 Emergency Response** Centers for Disease Control and Prevention

COVID-19 Vaccination in Pregnant Individuals

Dana M. Meaney-Delman, MD, MPH, FACOG Lead, Maternal Immunization Team Vaccine Task Force, COVID-19 Response Centers for Disease Control and Prevention

Additional Vaccine Doses for Immunocompromised Individuals



Peter Marks, MD, PhD Director Center for Biologics Evaluation and Research U.S. Food and Drug Administration



Grace M. Lee, MD Professor of Pediatrics, Infectious Diseases Stanford University School of Medicine Chair, Advisory Committee on Immunization Practices



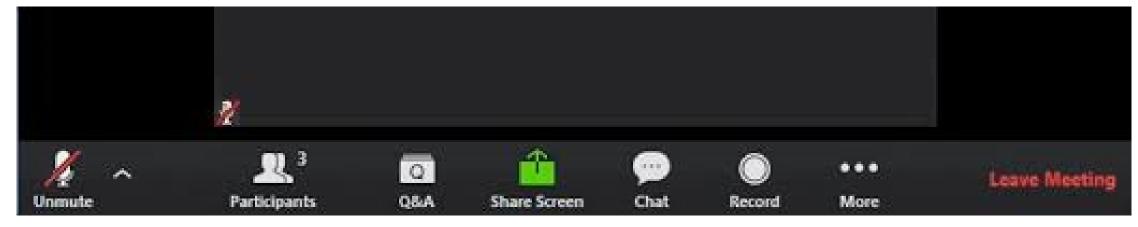
Kevin Chatham-Stephens, MD, MPH, FAAP CDR U.S. Public Health Service Chief Medical Officer, Vaccine Task Force **COVID-19 Response** Centers for Disease Control and Prevention

Question? Use the "Q&A" Button



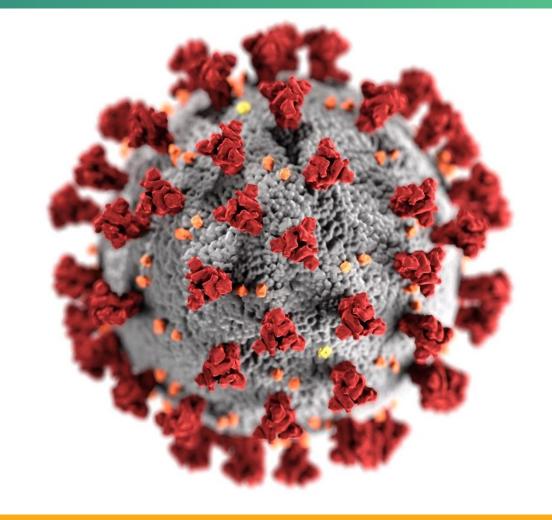


Comment?
Use the "Chat" Button



Delta Variant Update

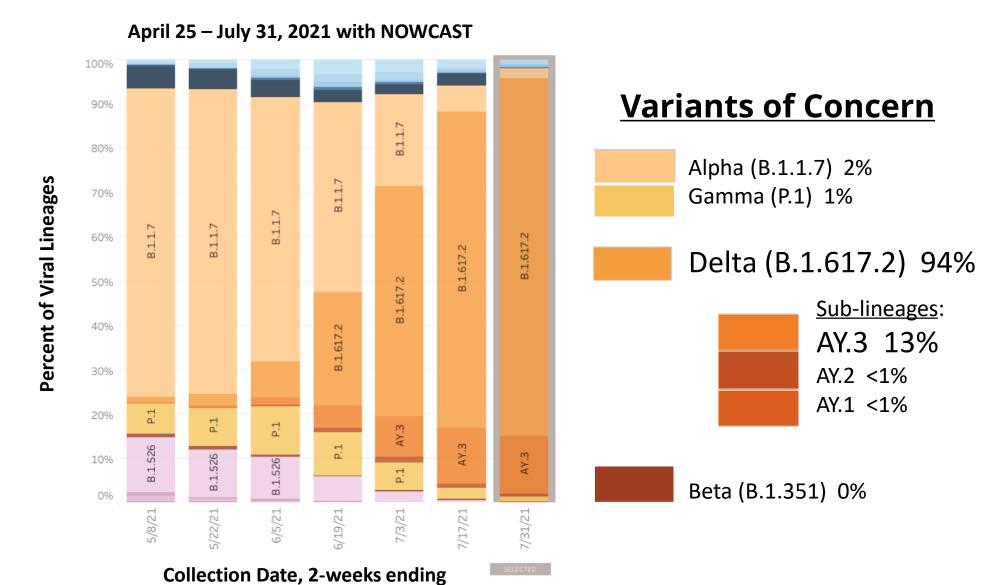
Heather Scobie, PhD, MPH IDSA August 14, 2021





cdc.gov/coronavirus

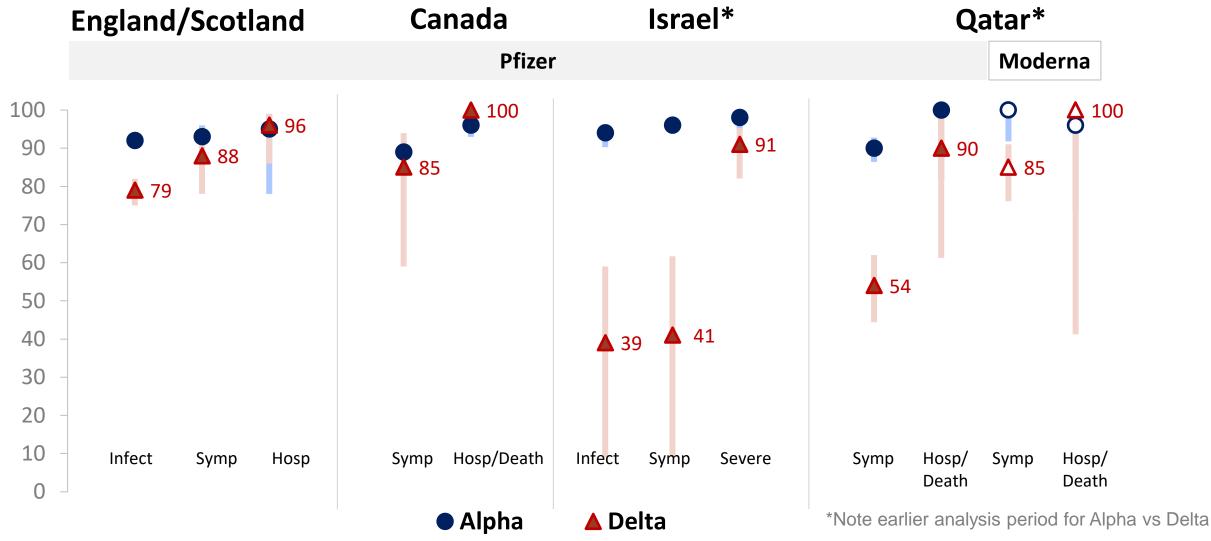
Estimated Proportions of SARS-CoV-2 lineages in the US



Delta variant: What we know

- Nearly twice as contagious as previous variants
- Some evidence of increased illness severity vs. previous strains in unvaccinated persons
- Greatest risk of transmission still among unvaccinated people
- Fully vaccinated people with Delta breakthrough infections can spread virus to others
 - However, vaccinated people with Delta appear to be infectious for a shorter period than unvaccinated persons with Delta

Pfizer & Moderna 2-Dose Effectiveness for Alpha vs. Delta



Sheikh et al. Lancet (2021): https://doi.org/10.1016/S0140-6736(21)01358-1; Lopez Bernal et al. medRxiv preprint; https://doi.org/10.1101/2021.05.22.21257658; Stowe et al. PHE preprint: https://doi.org/10.1101/2021.05.22.21257658; Stowe et al. PHE preprint: https://doi.org/10.1101/2021.05.22.21257658; Haas et al Lancet (2021): https://doi.org/10.1101/2021.06.28.21259420; Haas et al Lancet (2021): https://do

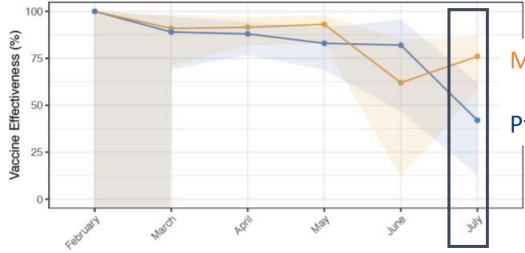
https://doi.org/10.1016/S0140-6736(21)00947-8; Israel MOH: https://www.gov.il/BlobFolder/reports/vaccine-efficacy-safety-follow-up-committee/he/files publications corona two-dose-vaccination-data.pdf
Abu-Radad and Butt. NEJM (2021); Chemaitelly et al. Nature Med (2021); Tang et al medRxiv

Declines in VE against infection Preprint and unpublished data from Israel

- Ministry of Health analysis higher breakthrough rates and lower Pfizer VE against infection for persons vaccinated in Jan–Feb 2021 compared with more recent months for persons aged 16–59 and ≥60 years
- Two retrospective cohort studies of persons vaccinated with Pfizer in large healthcare systems:
 - 2.3-fold increased risk for breakthrough infection among persons vaccinated with Pfizer in January vs. April 2021 (n=1.35 million)
 - Higher breakthrough infection rate (2.4% v. 1.1%, OR=2.2) among those who received 2nd dose ≥5 months ago compared with <5 months ago (n=33,993)
 - Higher magnitude of difference with increasing age

VE against Infection and Hospitalization July vs. Jan-MayMayo Clinic Health System, Minnesota, n=25,589

SARS-CoV-2
Infection

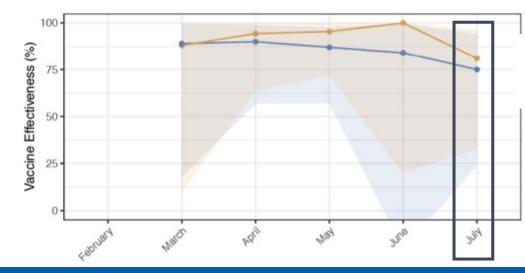


Moderna: 76% (95% CI: 58%-87%)

Pfizer: 42% (95% CI: 13%-62%)

Delta prevalence increased from 0.7% in May to >70% in July

COVID-19 Hospitalization



Moderna: 81% (95% CI: 33%-96%)

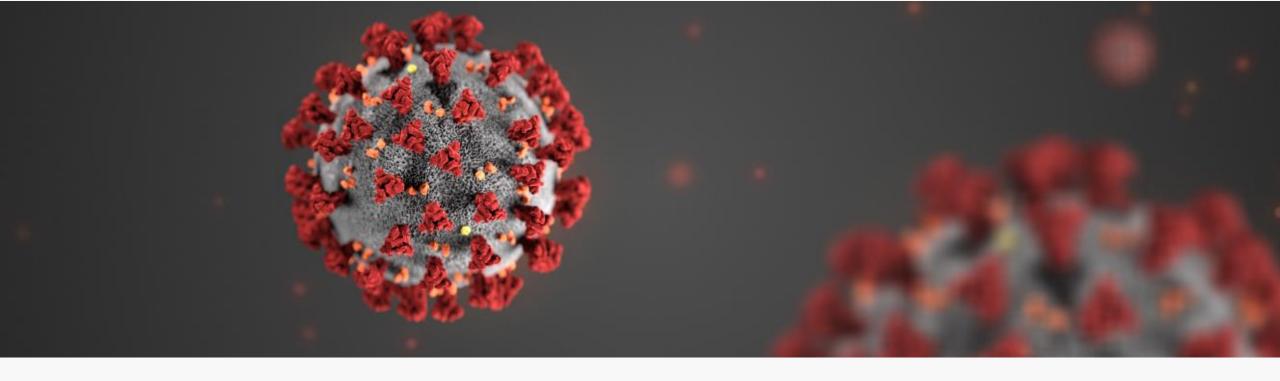
Pfizer: 75% (95% CI: 24%-94%)

Puranik et al. medRxiv:

https://www.medrxiv.org/content/10.1101/2021.08.06.21261707v2

Summary

- Currently authorized vaccines offer protection against known variants important to increase vaccine uptake in eligible populations
- CDC is closely monitoring real-world vaccine effectiveness and breakthrough infections using multiple methods, populations, and outcomes
- CDC continues to monitor emerging variants prevalence and impact on disease incidence, severity, and vaccine breakthrough
- ACIP will review evidence submitted for boosters and any next-generation vaccines
- Changing landscape CDC will communicate promptly about new evidence



For more information, contact CDC 1-800-CDC-INFO (232-4636)

TTY: 1-888-232-6348 www.cdc.gov

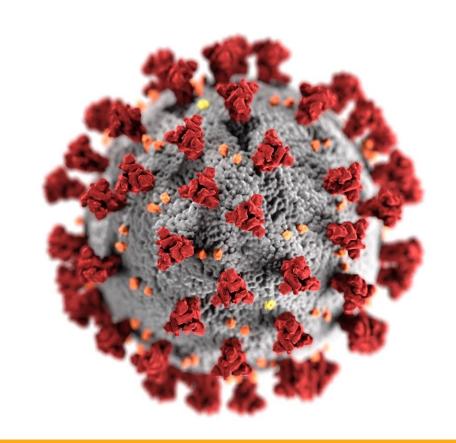
The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.



Update: COVID-19 Vaccination During Pregnancy

Dana Meaney-Delman, MD, MPH, FACOG Lead, Maternal Immunization CDC's COVID-19 Response

Infectious Diseases Society of America August 14, 2021





cdc.gov/coronavirus

COVID-19 vaccine and pregnancy



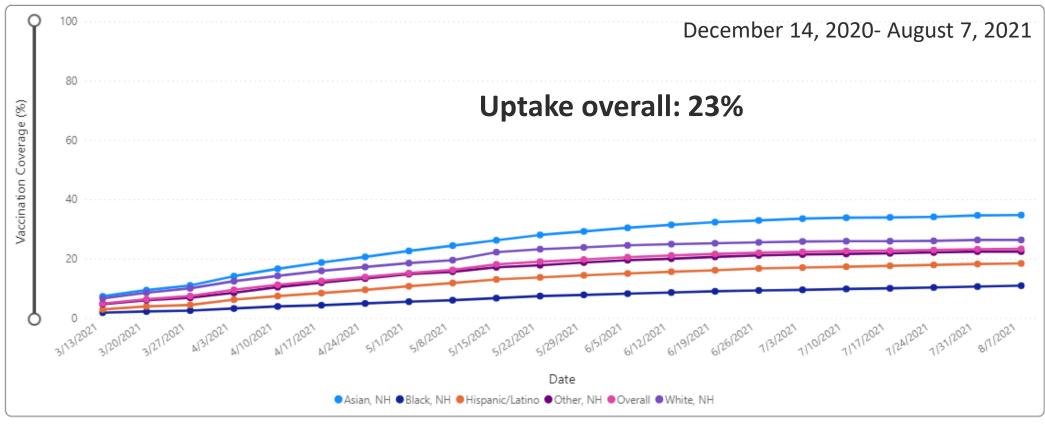
Pregnancy increases risk for severe illness from COVID-19

- Pregnancy is associated with increased risk of severe illness from COVID-19
 - ICU admission
 - Invasive ventilation
 - Death
- COVID-19 is associated with
 - Pregnancy complications (e.g., preeclampsia, coagulopathy, sepsis)
 - Adverse pregnancy outcomes (e.g., preterm birth, stillbirth)
- Perinatal transmission occurs but is rare



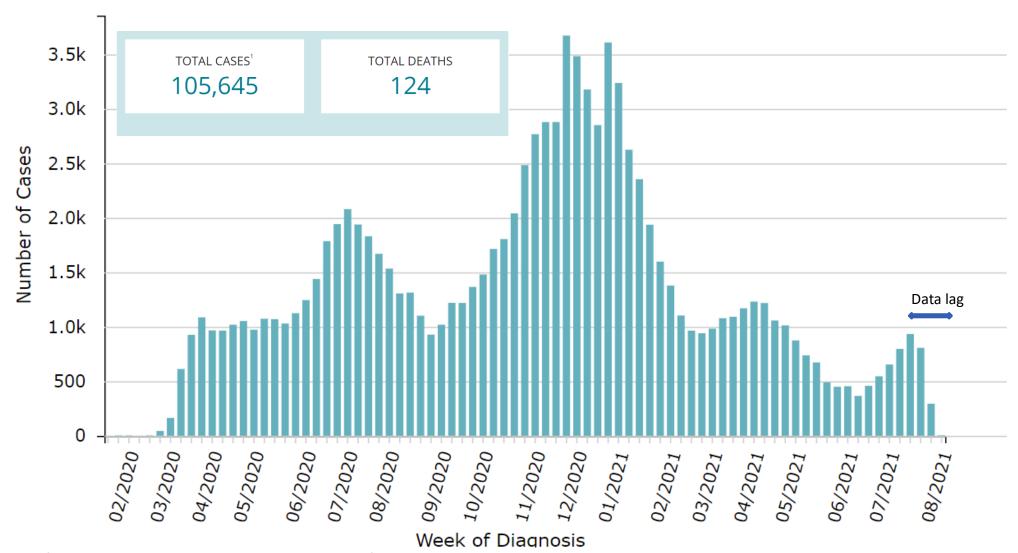
Low uptake of COVID-19 vaccine among pregnant people

Percent of Pregnant People aged 18-49 years receiving at least one dose of a COVID-19 vaccine during pregnancy overall, by race/ethnicity, and date reported to CDC - Vaccine Safety Datalink*, United States



NH = Non-Hispanic; "Other, NH" race includes American Indian or Alaska Native, Native Hawaiian or Pacific Islander, and Multiple or Other races; Vaccination coverage represents the total number of pregnant people (denominator as of August 7, 2021 = 174,744) who received at least one dose of a COVID-19 vaccine, including either first or second dose of the Pfizer-BioNTech or Moderna vaccines or a single dose of the Johnson & Johnson Janssen vaccine during pregnancy.

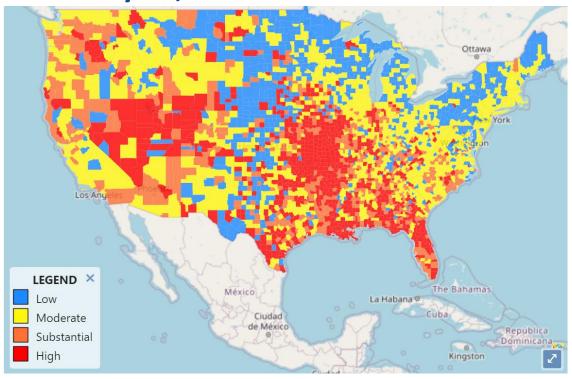
National COVID-19 Case Surveillance Data: Pregnant Women with Laboratory-Confirmed SARS-CoV-2 Infection*, Jan 22, 2020 – Aug 9, 2021



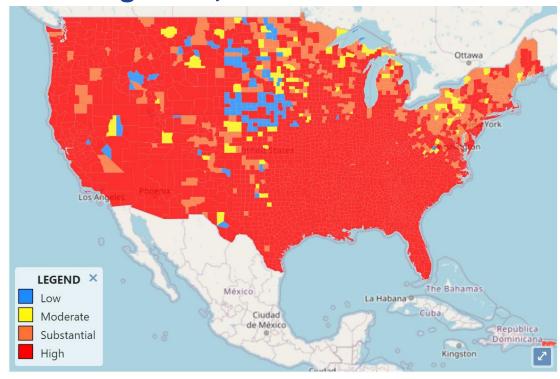
^{*} Based on detection of SARS-CoV-2 in a clinical specimen by molecular amplification techniques

Increased circulation of highly contagious Delta variant

SARS-CoV-2 Community Transmission as of July 12, 2021



SARS-CoV-2 Community Transmission as of August 11, 2021



Accumulating evidence indicates benefits of COVID-19 vaccination during pregnancy outweigh any potential risks



New Data Released



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

 Objective: Assess the cumulative risk of spontaneous abortion after mRNA COVID-19 vaccination among pregnant people

Methods:

- Included 2,456 pregnant people enrolled in v-safe pregnancy registry
 - Received at least one dose of an mRNA COVID-19 vaccine just before pregnancy or prior to 20 weeks of pregnancy
 - Still pregnant at 6 completed weeks of gestation
- Lifetable methods to look at cumulative risk



No Increased Risk of Spontaneous Abortion After COVID-19 Vaccination During Pregnancy

 Age-standardized cumulative risk of SAB after mRNA COVID-19 vaccination:

12.8% (95% CI: 10.8-14.8%)

- Similar to previously published baseline estimates of miscarriage (11-16%)
- Findings add to accumulating evidence that mRNA COVID-19 vaccines during pregnancy are safe

Risk of Spontaneous Abortion among v-safe Pregnancy Registry Participants, December 14, 2020—July 19, 2021

Gestational Age	Number at risk	Self-reported SAB*	Week-specific SAB* risk (%)	Cumulative SAB risk (%, 95% CI [¶])
6.0	904	15	1.66	1.66 (0.83-2.48)
7.0	982	18	1.83	3.46 (2.30-4.61)
8.0	1032	37	3.59	6.92 (5.36-8.46)
9.0	1087	39	3.59	10.26 (8.44-12.04)
10.0	1118	19	1.70	11.79 (9.87-13.66)
11.0	1184	12	1.01	12.68 (10.72-14.60)
12.0	1274	9	0.71	13.30 (11.31-15.24)
13.0	1394	5	0.36	13.61 (11.61-15.57)
14.0	1534	0		
15.0	1632	2	0.12	13.72 (11.71-15.68)
16.0	1742	2	0.11	13.81 (11.81-15.78)
17.0	1848	2	0.11	13.91 (11.90-15.87)
18.0	1941	3	0.15	14.04 (12.03-16.01)
19.0	2052	2	0.10	14.12 (12.11-16.09)

Early data suggest receiving an mRNA COVID-19 vaccine during pregnancy reduces the risk for infection



 Objective: Assess the association between receipt of mRNA COVID-19 vaccine and risk of SARS-CoV-2 infection among pregnant women

Methods:

- Retrospective cohort study included 15,060 pregnant women in Israel
- Received first dose from December 19, 2020, through
 February 28, 2021
- Vaccinated women were 1:1 matched to unvaccinated women by age, gestational age, residential area, population subgroup, parity, and influenza immunization status

https://jamanetwork.com/journals/jama/fullarticle/2782047

Early data suggest receiving an mRNA COVID-19 vaccine during pregnancy reduces the risk for infection

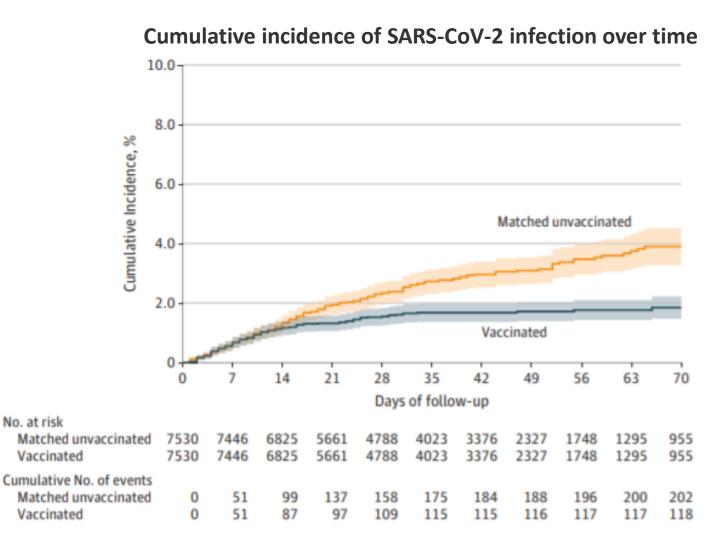
No. at risk

Vaccinated

Vaccinated

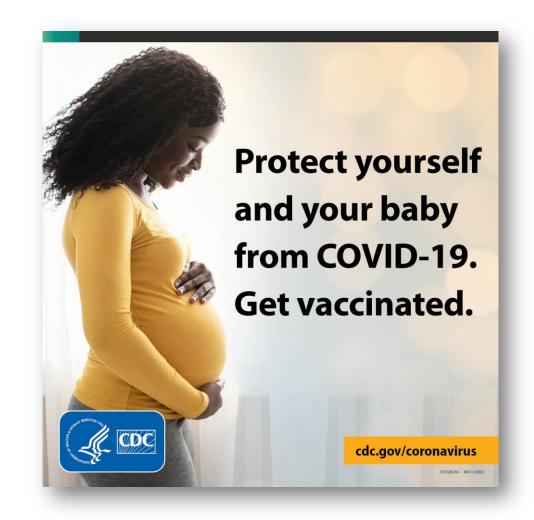
Results:

Vaccination with mRNA COVID-19 vaccines lowered the risk of infection from SARS-CoV-2 among pregnant people



Updated Clinical Considerations: COVID-19 Vaccination during Pregnancy and Lactation

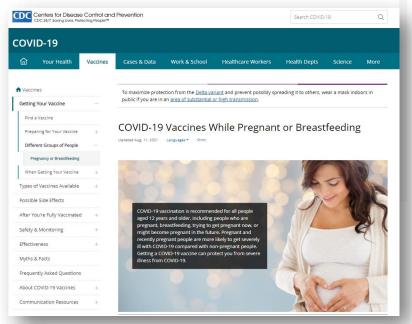
- COVID-19 vaccination is recommended for all people aged 12 years and older, including people who are pregnant, breastfeeding, trying to get pregnant now, or might become pregnant in the future.
- Consistent with recommendations from ACOG/SMFM

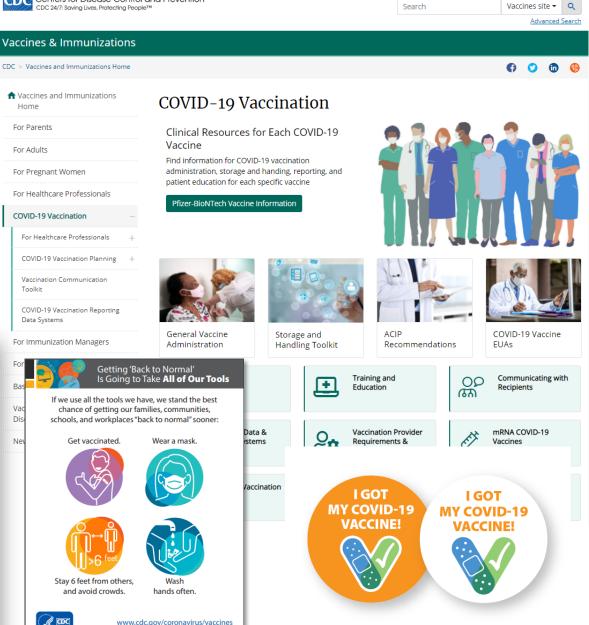


CDC Resources

CDC's COVID-19 vaccine tools and resources.

- COVID-19 Vaccination: <u>https://www.cdc.gov/vaccines/covid-19/index.html</u>
- For Healthcare Professionals:
 https://www.cdc.gov/vaccines/covid-19/hcp/index.html





(IIII) Centers for Disease Control and Prevention

Thank you



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For more information, contact CDC 1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov



COVID-19 Vaccines in Patients with Immunocompromise

Peter Marks, MD, PhD CDC/IDSA Clinician Call August 14, 2021

Top Line Messages



- The immunocompromised are a heterogenous group in their ability to respond to the authorized COVID-19 vaccines
- Individuals with some conditions that may be associated with immune impairment may respond well (diabetes mellitus)
- Other individuals may either not respond or respond poorly (solid organ transplant recipients, anti-CD20 antibody treatment)
- Third doses of the mRNA vaccines given at least 28 days after the second dose may increase response in certain individuals
 - Conventional COVID-19 precautions should be maintained





 Patients with diabetes mellitus were included in reasonably large numbers all the large randomized-controlled phase 3 trials for the Emergency Use Authorized COVID-19 vaccines

Vaccine	n (Vaccine)/ n (Placebo)	Overall Vaccine Efficacy (%)	Confidence Interval
Pfizer-BioNTech	1372/1374	95.4	66.8, 99.9
Moderna	1338/1309	100	N/A
Janssen	1399/1410	52.9	10.5, 76.3

https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization

Efficacy in Chronic Kidney Disease



- 17 studies in individuals on renal replacement therapy given a two-dose regimen of an mRNA vaccine
 - Efficacy found to be between 71% and 97% in producing an antibody response
- 13 studies in individuals after renal transplant or other solid organ transplants given a two-dose regimen of an mRNA vaccine
 - Efficacy found between 5% and 59% in producing an antibody response
 - Those also receiving the T-cell co-stimulation blocker belatacept found efficacy between 0 and 6% in producing an antibody response

Carr EJ et at. Kidney Int Rep 2021; https://doi.org/10.1016/j.ekir.2021.06.027





- 42 patients with multiple myeloma, 50 with myeloproliferative malignancies (MPN); 36 controls median age 81
- Serologic response rate in Multiple myeloma 33/42 (78.6%),
 MPN 44/50 (88%)
 Herishanu Y et al. Blood 2021; 137:3165-3173
- 167 patients with chronic lymphoid leukemia (CLL) versus 52 agematched controls (Median age 71)
- Serologic response rate 66/167 (39.5%) versus 100% in controls
- No patient exposed to anti-CD20 antibodies in the prior 12 months responded

 Pimpinelli F et al. J Hematol Oncol 2021; 14:81





- Single arm study in 101 individuals given 3rd dose 2 months after 2nd dose (99 treated)
- Transplants included heart, heart, kidney, liver, lung, pancreas a median of 97+8 months previously
- Levels of SARS-CoV-2 antibodies meeting pre-identified success criteria occurred four weeks after the third dose in 26/59 (44.0%) of those initially considered seronegative and 67/99 (68%) of the entire group
- The adverse event profile was similar to that after the second dose, and no grade 3 or grade 4 events were reported.

Kamar N et al. NEJM. 2021; DOI: 10.1056/NEJMc2108861





- Double-blind, randomized-controlled study in 120 individuals given 3rd dose 2 months after 2nd dose to 60 and placebo to 60
- Transplants included heart, kidney, kidney-pancreas, liver, lung, pancreas a median of 3.57 years earlier (range 1.99-6.75 years).
- Increased levels of SARS-CoV-2 antibodies occurred four weeks after the third dose in 33/60 (55.0%) of the vaccinated group and 10/57 (17.5%) of the placebo individuals
- Adverse event profile was similar to that after the second dose and no grade 3 or grade 4 adverse events were reported.

mRNA Vaccine Provider Information



- A third dose of COVID-19 Vaccine administered at least 28 days following the first two doses of this vaccine is authorized for administration to individuals at least 12 years of age (Pfizer-BioNTech) or 18 years of age (Moderna) who have undergone solid organ transplantation, or who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise
- Administration of third vaccine doses appears to be only moderately
 effective in increasing antibody titers, so patients should be
 counselled to maintain physical precautions to help prevent COVID19 and close contacts of immunocompromised persons should be
 vaccinated as appropriate for their health status





Updates from ACIP on COVID-19 Vaccines

*Slides from Aug 13, 2021 ACIP mtg



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

[&]quot;https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-additional-vaccine-dose-certain-immunocompromised

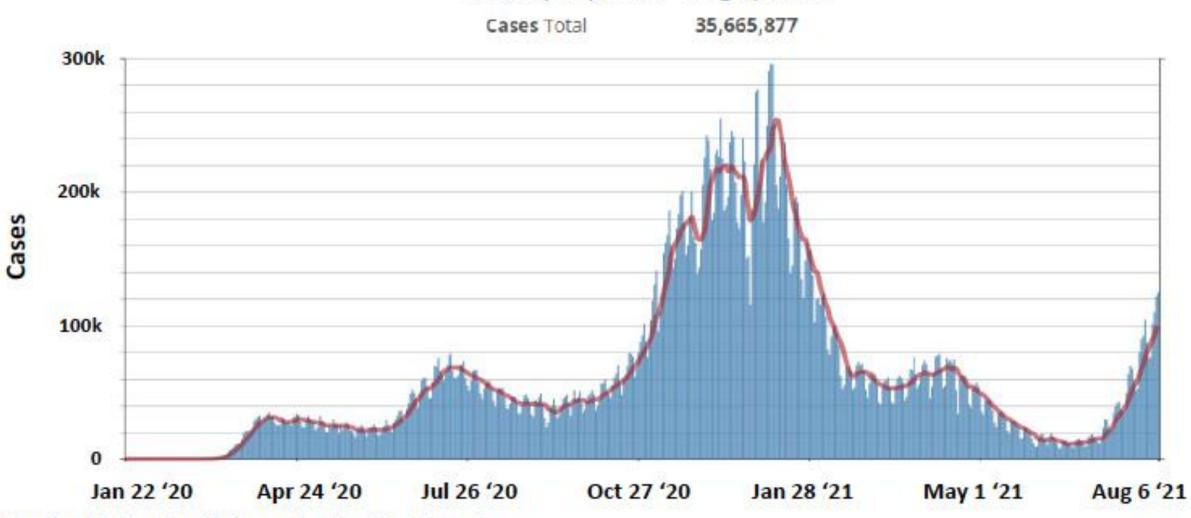
ACIP Recommendation

On August 13, 2021:

- ACIP made an interim recommendation for use of an additional dose of Pfizer-BioNTech COVID-19 vaccine (for persons aged ≥12 years) or Moderna COVID-19 vaccine (for persons aged ≥18 years) after an initial 2-dose primary mRNA COVID-19 vaccine series for moderately to severely immunocompromised people.
- The additional dose should be administered at least 28 days after the completion of the initial mRNA COVID-19 vaccine series.

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

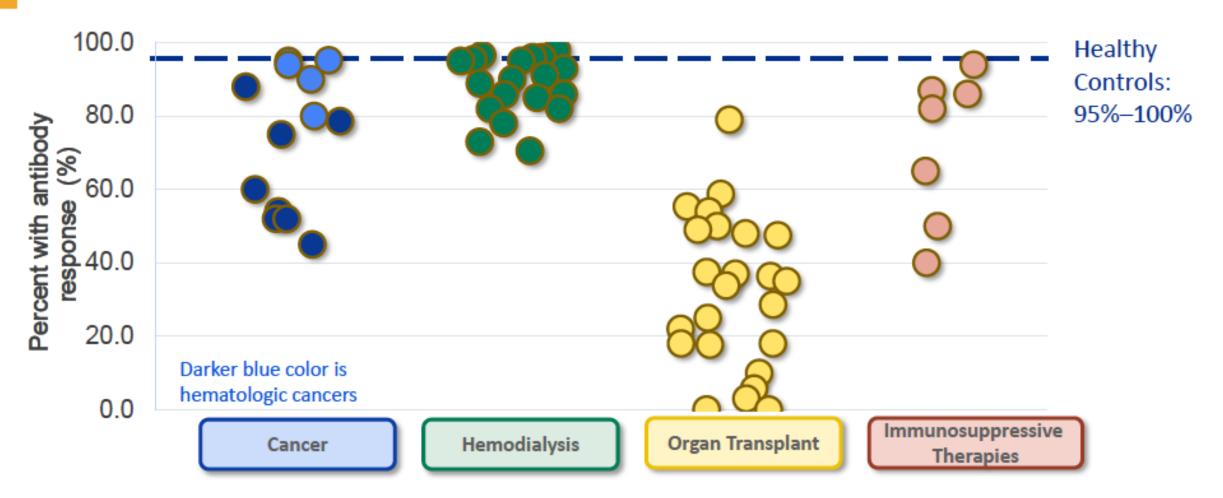
January 22, 2020 - Aug 9, 2021



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 nonimmunocompromised people after 2nd dose^{1, 3-5}

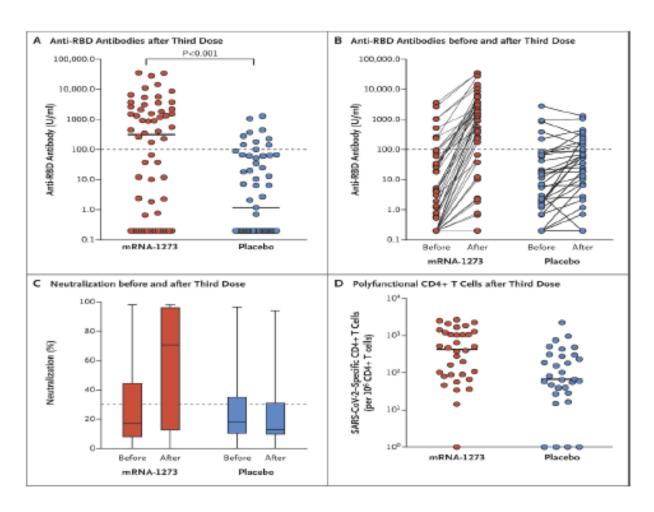
Percent of subjects with antibody response after two mRNA COVID-19 vaccine doses by immunocompromising condition and study (n=63)



- 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

Benefits:

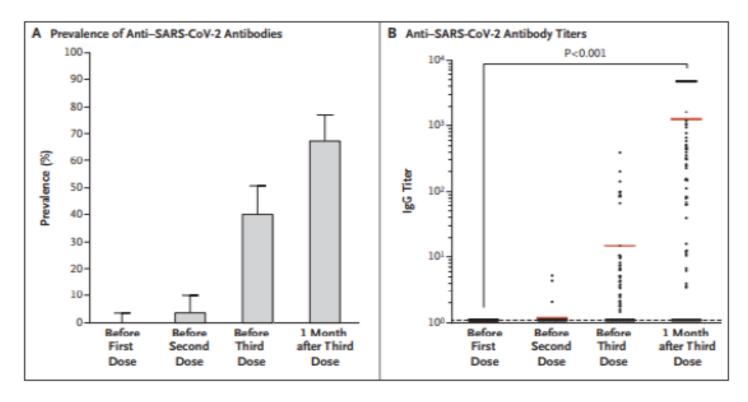
Randomized Trial of a 3rd Dose of Moderna Vaccine in Transplant Recipients (n=120)



RBD antibody (≥100 U/m1) 1 month post dose 3:

33 of 60 patients
(55%) vaccine group
vs.
10 of 57 patients
(18%) placebo group

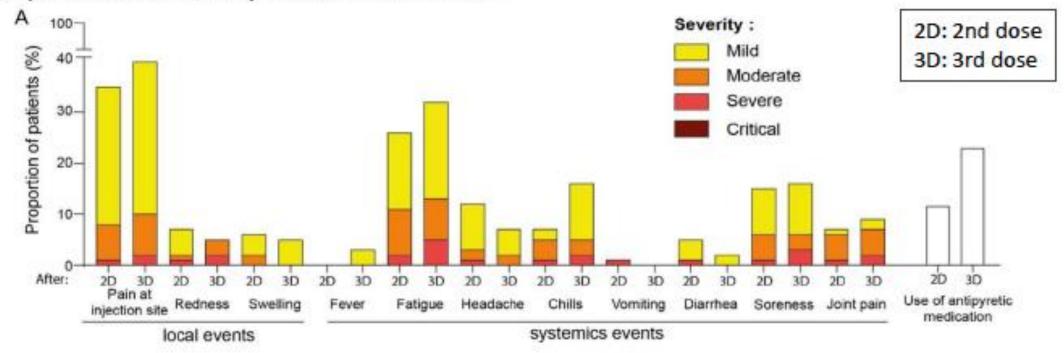
Benefits and Harms:



- 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



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

Moderately and 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

^{*}ACIP General Best Practice Guidelines for Immunization; CDC Yellow Book; 2013 IDSA Clinical Practice Guidelines for Vaccination of the Immunocompromised Host

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



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

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

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

Q&A and Discussion



An online community bringing together information and opportunities for discussion on latest research, guidelines, tools and resources from a variety of medical subspecialties around the world.



Specialty Society Collaborators

American Academy of Family Physicians
American Academy of Pediatrics
American College of Emergency Physicians
American College of Physicians
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Sept. 29 – Oct. 3, 2021 Virtual Conference



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CDC-IDSA Partnership: Clinical Management Call Support

FOR WHOM?

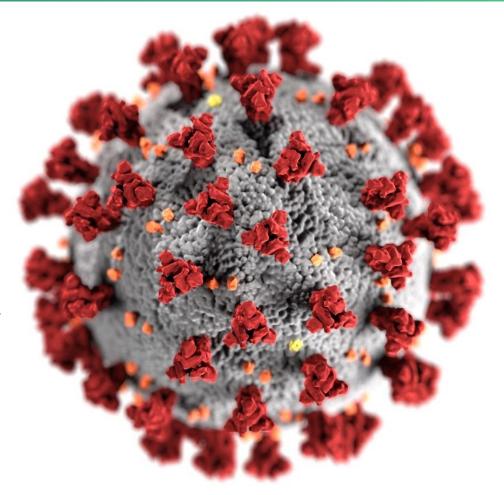
Clinicians who have questions about the clinical management of COVID-19

WHAT?

 Calls from clinicians will be triaged by CDC to a group of IDSA volunteer clinicians for peer-to-peer support

HOW?

- Clinicians may call the main CDC information line at 800-CDC-INFO (800-232-4636)
- To submit your question in writing, go to www.cdc.gov/cdc-info and click on Contact Form







Continue the conversation on Twitter

@RealTimeCOVID19
#RealTimeCOVID19



We want to hear from you!

Please complete the post-call survey.

Clinician calls are now twice a month:

Next Call: Saturday, August 28
Update on COVID-19 in the Pediatric
Population

A recording of this call will be posted Monday at www.idsociety.org/cliniciancalls

-- library of all past calls available --

Contact Us:

Dana Wollins (<u>dwollins@idsociety.org</u>)
Deirdre Lewis (<u>dlewis@idsociety.org</u>)