From: HHS COVID JIC <JIC@hhs.gov>
Sent: Fri, 5 Feb 2021 16:51:30 -0500
To: HHS COVID JIC
Subject: COVID-19 HHS Communications Coordination Group Report - February 5, 2021
Attachments: 2.5.21 HHS CCG COVID-19 Daily Communications Report.pdf

Senior Leaders:

Please find attached today's COVID-19 HHS Communications Coordination Group Report for February 5, 2021.

Kind regards,

COVID-19 Joint Information Center
U.S. Department of Health and Human Services (HHS)
General Inbox: JIC@hhs.gov

COVID-19 HHS COMMUNICATIONS COORDINATION GROUP

Daily Communications Report – February 5, 2021

Topline Messages

FDA Announces Advisory Committee Meeting to Discuss Janssen COVID-19 Vaccine Candidate: The FDA has scheduled a meeting of its Vaccines and Related Biological Products Advisory Committee (VRBPAC) on Feb. 26, to discuss the request for emergency use authorization (EUA) for a COVID-19 vaccine from Janssen Biotech Inc. The members of the VRBPAC are nationwide independent, scientific, and public health experts who provide advice. Final vaccine EUA decisions are made by the FDA, who intends to make background materials available to the public prior to the meeting. (FDA release)

Statewide Mask Mandates Lower Hospitalization Growth Rates in Younger Adults: CDC released a new study Feb. 5 that suggests statewide mask mandates have contributed to declines in COVID-19-associated hospitalization growth rates among adults aged 18 to 64 years. During March to October, data from 10 locations showed 2.9% decline in weekly hospitalization growth rates among adults aged 40-64 two weeks after mandates began; after three weeks, hospitalization growth rates dropped by 5.5% among adults 18-64. Feb. 5 MMWR.

High Rates of Mask Use at Universities with Mandates: A new CDC report on Feb. 5 shows that trained observers at universities with mask mandates in rural and suburban areas found high mask use (86%), September through November. More than 90% wore N95-type masks and cloth masks correctly; gaiters, scarves, and other face coverings were less likely to be worn correctly. Feb. 5 MMWR.

New CDC Resources for Health Departments on Reporting Cases: CDC posted worksheets and other new resources for health departments reporting COVID-19 cases to CDC on Feb. 5.

Guidance on Vaccinations for the Homeless: CDC provided Interim Guidance for Health Departments: COVID-19 Vaccination Implementation for People Experiencing Homelessness on Feb. 5.

Slow the Spread of COVID-19: We can each make a difference and protect ourselves and others by wearing a mask, staying at least 6 feet (about 2 arm lengths) from others who don't live with you, and avoiding crowds. The more people you are in contact with, the more likely you are to be exposed.

General Stats:

- U.S. Total Cases: 26,398,337 (+121,212)
- U.S. Total Deaths: 449,020 (+3,756)
- Tests Reported: 300,189,929 (+958,730)
- Vaccines:
  - Total Doses Distributed: 57,489,675 (+1,545,875)
  - Total Doses Administered: 35,203,710 (+1,325,456)
  - Number of People Receiving 1 or More Doses: 27,905,197 (+750,241)
  - Number of People Receiving 2 Doses: 6,926,050 (+489,119)

Sourced from the CDC COVID Data Tracker: Feb 04, 2021 5:20 PM

Trending: New deaths, cases, and hospitalizations remain high.

- **16.9% decrease in 7-day average of new cases**, as of Feb. 3: 134,524 daily average over past 7 days vs. 161,832 over 7 previous days. (CDC, 2/5)
- **6.7% decrease in 7-day average of new deaths**, as of Feb. 3: 3,056 daily average over past 7 days vs. 3,277 over 7 previous days. (CDC, 2/5)

- The **national percent positivity rate** in the past 7 days **is 8.1%**, based on data from 1/26 to 2/01.**Note: it takes on average 3 days for testing results to be reported to HHS. Number reported may be an underestimate due to delayed reporting*
- As of Feb. 5, the US government has **allocated 881,460** patient courses of Eli Lilly's bamlanivimab and Regeneron's casirivimab/imdevimab monoclonal antibodies in total.
- As of Feb. 4, there are **3,507 medical personnel** deployed for the COVID-19 Response, which includes 2,783 National Guard personnel. In total, there are 27,319 personnel deployed for the whole-of-government COVID-19 response.

Emerging SARS-CoV-2 Variants

Viruses constantly change through mutation, and new variants of a virus are expected to occur over time. Multiple variants of the virus that causes COVID-19 have been documented in the United States and globally during this pandemic.

- Many variants do not change how the virus behaves and many disappear.
- Infection by the variant that emerged in the UK (B.1.1.7), the variant that emerged in South Africa (B. 1.351), and the variant that emerged in Brazil (P.1) do not appear to cause more severe disease in infected individuals, although these variants may be more contagious.
- Scientists are working to better understand how easily these variants might be transmitted and whether currently authorized vaccines will protect people against them.
- Numbers of reported cases of variants in the U.S. as of February 4:
  - B.1.1.7. (first detected in the UK): 611 (33 states)
  - B. 1.351 (first detected in South Africa): 5 (SC, MD)
  - P.1 (first detected in Brazil): 2 (MN).
- For more information: New COVID-19 Variants, Emerging SARS-CoV-2 Variants.

Federal COVID Response for Vaccines

Operational Support

HHS-ASPR has deployed 100 vaccinators and logistical staff from the National Disaster Medical System to support COVID-19 vaccination sites in five Arizona counties.

Vaccine Confidence

- **Demographics of People Vaccinated:** On Feb. 1, CDC published the MMWR "Demographic Characteristics of Persons Vaccinated During the First Month of the COVID-19 Vaccination Program — United States, Dec. 14, 2020–Jan. 14, 2021."

- **Skilled Nursing Facilities Staff:** On Feb. 1, CDC published the MMWR: "Early COVID-19 First-Dose Vaccination Coverage Among Residents and Staff Members of Skilled Nursing Facilities Participating in the Pharmacy Partnership for Long-Term Care Program — United States, December 2020–January 2021."
- **CDC Offers Consultations**: The CDC Vaccine Task Force is rolling out vaccine confidence consultations for interested jurisdictions. To request this service, interested jurisdictions can reach out to confidenceconsults@cdc.gov. CDC also has online tips for building vaccine confidence.
- Resources: Strategy to Reinforce Confidence in COVID-19 Vaccines

Clinical Trials

AstraZeneca, Janssen (J&J), and Novavax remain in large Phase 3 clinical trials in the U.S.

- Participants are still needed in various trials to ensure adequate representation of various demographic categories.
- To volunteer for a COVID-19 vaccine trial, visit combatcovid.hhs.gov.

Vaccine Risk

Learn more about what to expect after getting vaccinated for COVID-19, including normal side effects and tips to reduce pain or discomfort.

- On Jan. 22, CDC released the MMWR "Allergic Reactions Including Anaphylaxis After Receipt of the First Dose of Moderna COVID-19 Vaccine."
- On Jan. 6, CDC released the MMWR "Allergic Reactions Including Anaphylaxis After Receipt of the First Dose of Pfizer-BioNTech COVID-19 Vaccine

Federal COVID Response for Therapeutics

Therapeutics focus on solutions that either attack the virus or help manage complications in people with severe cases of COVID-19 to reduce recovery time, prevent hospitalizations, and decrease mortality risk.

- Types of authorized or approved therapeutics currently in use: convalescent plasma, monoclonal antibodies, remdesivir, corticosteroids, or combinations of drugs as well as other types of drugs that are recognized as beneficial for treatment.
- FDA has issued 7 EUAs for therapeutics and approved one therapeutic (remdesivir). These therapeutics are being manufactured and administered, with many more in the pipeline.

Monoclonal Antibody Treatments:

Monoclonal antibodies directly neutralize the virus that causes COVID-19. In clinical trials, monoclonal antibodies decreased patients' viral load. Patients who received treatment soon after being diagnosed were less likely to require hospitalization.

- Treatments are currently given in outpatient settings as a one-time infusion.
- # of treatment courses distributed:
  - The federal response includes an agreement to purchase approximately 3 million treatment courses of the monoclonal antibody bamlanivimab.
  - Cases of bamlanivimab and the casirivimab/imdevimab monoclonal antibody cocktail are allocated weekly by ASPR to states, territories, and identified agencies. As of Feb. 3, **ASPR has**

allocated 738,482 bamlanivimab patient courses and 142,978 casirivimab/imdevimab patient courses.

Blood Thinners:

Blood Thinners for COVID-19 Patient Care: Full-dose blood thinners decreased need for life support and improved outcome in hospitalized COVID-19 patients, January 26 NIH news release.

Health Equity and Helping Populations at Risk

Mental Health Conditions Hit Hispanic/Latino Adults: A new CDC study of a survey conducted early in the COVID-19 pandemic finds that U.S. adults reported increased symptoms of depression; suicidal thoughts; stress and worry about the conditions where they live, learn, work, or play; and substance use or initiation in April and May 2020. Hispanic/Latino adults were especially affected. Feb. 4 MMWR

MMWR 2/5: Sexual Orientation Disparities in Risk Factors for Adverse COVID-19–Related Outcomes, by Race/Ethnicity — Behavioral Risk Factor Surveillance System, United States, 2017–2019

Diversity in Clinical Trials:

- Because clinical trials provide a crucial base of evidence for evaluating whether a medical product is safe and effective, enrollment in clinical trials should reflect the diversity of the population that is ultimately going to use the product.
- Ensuring meaningful representation of racial and ethnic minorities in clinical trials for regulated medical products is fundamental not only to the FDA's regulatory mission but also to public health.
- Participation by diverse volunteers helps researchers find better treatments and better ways to fight such diseases as cancer, diabetes, heart disease and HIV/AIDS.

American Indians and Alaska Natives:

To date, Indian Health Services (IHS) has completed **over 1.9 million tests** throughout Indian Country.

- As of Feb. 2, the Indian Health Service has reported:
  - 1,951,037 tests, of which 179,279 are positive and 1,629,768 are negative. 7-day average for positivity for all IHS Areas is **10.4%.**
    - Areas of concern with increasing 7-day positivity, over 10% are: Navajo (16.5%), Oklahoma City (15.2%), Phoenix (14.7%), Albuquerque (14.4%), California (12.4%), Tucson (11.3%), and Nashville (10.7%).
    - Total positivity rate for reporting I/T/U's is 9.9% (compared with US all races positivity rate of 9.2%).
- IHS areas exceeding U.S. positivity rate: Navajo (17.0%), Phoenix (14.6%), Oklahoma City (13.5%), Albuquerque (11.8%), Tucson (11.4%), California (11.0%), and Great Plains (10.6%).
- As of Feb. 3, 224,095 vaccine doses have been administered and 461,000 vaccine doses have been distributed. The Vaccine Task Force continues to provide onboarding support to I/T/U sites, develop a data reporting dashboard, and monitor vaccine adverse events.
- For information on the federal response in Indian Country: https://www.ihs.gov/coronavirus/.

Testing

Funding to Expand Production, Purchase At-Home OTC Test: On February 1, DoD and HHS awarded $231.8 million to Ellume USA LLC to increase production capacity and procure 8.5 million tests of the Ellume COVID-19 Home Test, a rapid antigen test that can be performed at home. DoD press release.

Overview:

- As of Feb. 5, **300 million tests** have been completed**.**
- The **national percent positivity rate** in the past 7 days **is 8.1%**, based on data from 1/26 to 2/01.**Note: it takes on average 3 days for testing results to be reported to HHS. Number reported may be an underestimate due to delayed reporting*
- As of today, more than 8.6 million tests have been completed by HRSA health centers (dashboard).
- In the past 7 days, **97.9%** of commercial lab tests were completed within 3 days and **98.5%** were completed within 5 days.
- Surge testing has been established in **23 states** with **4,500 locations** to date.
    - There are currently 85 active surge testing sites.
    - As of Feb. 5, more than 967,448 tests have been conducted at these sites. The turnaround times for current federal surge testing sites is less than 2 days.
- 13,985 rapid point-of-care instruments and 4.9 million tests have been delivered to 13,850 CLIA-certified nursing homes across the country.
- Retail and pharmacy partners in more than 4,000 locations in all 50 states, the District of Columbia, and Puerto Rico have conducted 7,114,460 tests to date. There are currently 3,586 active sites.

Risk and Prevention

Severe Symptoms and Pregnancy Complications: Pregnant women who had severe symptoms of COVID-19 have a higher risk of complications during and after pregnancy, according to early results announced Jan. 28. The NIH-supported study showed that the women with COVID-19 were at higher risk for cesarean delivery, postpartum hemorrhage, hypertensive disorders of pregnancy and preterm birth compared to pregnant women without symptoms.

MMWR reports published by the CDC:

- MMWR 2/4: Decreases in Young Children Who Received Blood Lead Level Testing During COVID-19 — 34 Jurisdictions, January – May 2020
- MMWR 1/26: COVID-19 Cases and Transmission in 17 K–12 Schools — Wood County, Wisconsin, Aug. 31– Nov. 29, 2020
- MMWR 1/26: SARS-CoV-2 Transmission Associated with High School Wrestling Tournaments — Florida, December 2020 – January 2021
- MMWR: 1/25 Implementation and Evolution of Mitigation Measures, Testing, and Contact Tracing in the National Football League, Aug. 9 – Nov. 21, 2020

Updated CDC guidance:

- On Feb. 2, CDC provided guidance to educators and school administrators, Operating schools during COVID-19: CDC's Considerations
- CDC recommends wearing masks with two or more layers of washable, breathable fabric. If wearing a cloth mask, the layers of fabric should be tightly woven and you should not be able to see light through it. If the mask is a single layer of fabric, another could be worn on top to achieve the recommended level of protection.

Additional Resources

COVID-19 Executive Orders and National Strategy

- **President Biden's National Strategy for COVID-19 and Pandemic Preparedness:** On Jan. 21, the Biden Administration released its national strategy to combat COVID-19, available publicly.
- **COVID-19 Executive Orders:**
- Executive Order on Establishing the COVID-19 Pandemic Testing Board and Ensuring a Sustainable Public Health Workforce for COVID-19 and Other Biological Threats
- Executive Order on Protecting Worker Health and Safety
- Executive Order on Supporting the Reopening and Continuing Operation of Schools and Early Childhood Education Providers
- Executive Order on Ensuring an Equitable Pandemic Response and Recovery
- Executive Order on a Sustainable Public Health Supply Chain
- Executive Order on Ensuring a Data-Driven Response to COVID-19 and Future High-Consequence Public Health Threats
- Executive Order on Improving and Expanding Access to Care and Treatments for COVID-19
- Executive Order on Promoting COVID-19 Safety in Domestic and International Travel
- Executive Order on Organizing and Mobilizing the United States Government to Provide a Unified and Effective Response to Combat COVID-19 and to Provide United States Leadership on Global Health and Security

Social Media Materials

- **COVID-19 Vaccine Communications:** Vaccination Communication Toolkit
- **Monoclonal Antibody Treatments:** Digital Toolkit
- **Flu Vaccine:** Use **#FightFlu** and **#SleeveUp** when receiving the flu vaccine.
    - Digital campaign resources: Digital Media Toolkit, Social Media Toolkit
    - For Medicare specific resources: Social Media Toolkit (English, Spanish)
- **Plasma Donation:** FDA Donate Plasma; Social Media Toolkit
- **Minority Risk:** CDC materials: Facebook @CDC

From: HHS COVID JIC <JIC@hhs.gov>
Sent: Mon, 8 Feb 2021 17:27:46 -0500
To: HHS COVID JIC
Subject: COVID-19 HHS Communications Coordination Group Report - February 8, 2021
Attachments: 2.8.21 HHS CCG COVID-19 Daily Communications Report.pdf

Senior Leaders:

Please find attached today's COVID-19 HHS Communications Coordination Group Report for February 8, 2021.

Kind regards,

COVID-19 Joint Information Center
U.S. Department of Health and Human Services (HHS)
General Inbox: JIC@hhs.gov

COVID-19 HHS COMMUNICATIONS COORDINATION GROUP

Daily Communications Report – February 8, 2021

Topline Messages

Virtual Presidential Visit: President Biden and Vice President Harris were provided a virtual tour of the vaccination center at State Farm Stadium in Glendale, Arizona, which is averaging between 8,000 and 9,000 vaccinations per day between first and second doses. The tour and remarks can be viewed here.

FEMA Releases Community Vaccination Playbook: As part of the national effort to speed the pace of COVID-19 vaccination campaigns, the president directed the federal government to establish new federally supported Community Vaccination Centers (CVCs). This playbook establishes guidance for providing federal support to existing and new CVCs including interagency coordination, resource support, facility setup, and other requirements that necessitate federal support

Monoclonal Antibody Administration: ASPR TRACIE has published Planning Considerations for Monoclonal Antibody Administration Tip Sheet, which provides information for healthcare providers on prescribing and administering COVID-19 monoclonal antibody therapeutics.

COVID-19 impact on the number of children tested for elevated blood lead levels: An estimated half million children may have missed screenings for elevated blood lead levels due to the pandemic. CDC data published Feb. 5 showed testing for elevated blood levels fell about one-third from January to May 2020 and by more than half from March to May 2020 compared to the same periods in 2019.

New CDC Resources for Health Departments on Reporting Cases: CDC posted worksheets and other new resources for health departments reporting COVID-19 cases to CDC on Feb. 5.

Guidance on Vaccinations for the Homeless: CDC provided Interim Guidance for Health Departments: COVID-19 Vaccination Implementation for People Experiencing Homelessness on Feb. 5.

Slow the Spread of COVID-19: We can each make a difference and protect ourselves and others by wearing a mask, staying at least 6 feet (about 2 arm lengths) from others who don't live with you, and avoiding crowds. The more people you are in contact with, the more likely you are to be exposed.

General Stats:

- U.S. Total Cases: 26,761,047
- U.S. Total Deaths: 460,582
- Tests Reported: 306,201,713
- Vaccines:
  - Total Doses Distributed: 59,307,800
  - Total Doses Administered: 41,210,937
  - Number of People Receiving 1 or More Doses: 31,579,100
  - Number of People Receiving 2 Doses: 9,147,185

Sourced from the CDC COVID Data Tracker: Feb 08, 2021 10:41AM

Trending: New deaths, cases, and hospitalizations remain high.

- **19.7% decrease in 7-day average of new cases**, as of Feb. 6: 119,906 daily average over past 7 days vs. 149,349 over 7 previous days. (CDC, 2/8)
- **2.4% increase in 7-day average of new deaths**, as of Feb. 6: 3,221 daily average over past 7 days vs. 3,146 over 7 previous days. (CDC, 2/8)

- The **national percent positivity rate** in the past 7 days **is 7.7%**, based on data from 1/29 to 2/04.**Note: it takes on average 3 days for testing results to be reported to HHS. Number reported may be an underestimate due to delayed reporting*
    - As of Feb. 8, the US government has **allocated 886,504** patient courses of Eli Lilly's bamlanivimab and Regeneron's casirivimab/imdevimab monoclonal antibodies in total.
- As of Feb. 8, there are **3,659 medical personnel** deployed for the COVID-19 Response, which includes 2,935 National Guard personnel. In total, there are 28,282 personnel deployed for the whole-of-government COVID-19 response.

Emerging SARS-CoV-2 Variants

Viruses constantly change through mutation, and new variants of a virus are expected to occur over time. Multiple variants of the virus that causes COVID-19 have been documented in the United States and globally during this pandemic.

- Many variants do not change how the virus behaves and many disappear.
- Infection by the variant that emerged in the UK (B.1.1.7), the variant that emerged in South Africa (B. 1.351), and the variant that emerged in Brazil (P.1) do not appear to cause more severe disease in infected individuals, although these variants may be more contagious.
- Scientists are working to better understand how easily these variants might be transmitted and whether currently authorized vaccines will protect people against them.
- Numbers of reported cases of variants in the U.S. as of February 7:
    - B.1.1.7. (first detected in the UK): 690 (33 states)
    - B. 1.351 (first detected in South Africa): 6 (MD, SC, VA)
    - P.1 (first detected in Brazil): 3 (MN, OK).
- For more information: New COVID-19 Variants, Emerging SARS-CoV-2 Variants.

Federal COVID Response for Vaccines

FDA Advisory Committee Meeting to Discuss Janssen COVID-19 Vaccine Candidate: The FDA Vaccines and Related Biological Products Advisory Committee (VRBPAC) will meet Feb. 26, to discuss the request for emergency use authorization (EUA) for a COVID-19 vaccine from Janssen Biotech Inc. (FDA release)

Operational Support

HHS-ASPR has deployed 100 vaccinators and logistical staff from the National Disaster Medical System to support COVID-19 vaccination sites in five Arizona counties. Additionally, ASPR is coordinating with DoD, the VA, and USDA to support vaccination efforts in California, Delaware, Louisiana, the Navajo Nation, New Jersey, Oklahoma, Texas, and the USVI.

Vaccine Confidence

- **Demographics of People Vaccinated:** On Feb. 1, CDC published the MMWR "Demographic Characteristics of Persons Vaccinated During the First Month of the COVID-19 Vaccination Program — United States, Dec. 14, 2020–Jan. 14, 2021."
- **Skilled Nursing Facilities Staff:** On Feb. 1, CDC published the MMWR: "Early COVID-19 First-Dose Vaccination Coverage Among Residents and Staff Members of Skilled Nursing Facilities Participating in the Pharmacy Partnership for Long-Term Care Program — United States, December 2020–January 2021."
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Clinical Trials

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- Participants are still needed in various trials to ensure adequate representation of various demographic categories.
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Learn more about what to expect after getting vaccinated for COVID-19, including normal side effects and tips to reduce pain or discomfort.

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Therapeutics focus on solutions that either attack the virus or help manage complications in people with severe cases of COVID-19 to reduce recovery time, prevent hospitalizations, and decrease mortality risk.

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- Treatments are currently given in outpatient settings as a one-time infusion.
- # of treatment courses distributed:

- The federal response includes an agreement to purchase approximately 3 million treatment courses of the monoclonal antibody bamlanivimab.
- Cases of bamlanivimab and the casirivimab/imdevimab monoclonal antibody cocktail are allocated weekly by ASPR to states, territories, and identified agencies. As of Feb. 8, **ASPR has allocated 738,482 bamlanivimab patient courses and 148,022 casirivimab/imdevimab patient courses.**

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Blood Thinners for COVID-19 Patient Care: Full-dose blood thinners decreased need for life support and improved outcome in hospitalized COVID-19 patients, January 26 NIH news release.

Health Equity and Helping Populations at Risk

Mental Health Conditions Hit Hispanic/Latino Adults: A new CDC study of a survey conducted early in the COVID-19 pandemic finds that U.S. adults reported increased symptoms of depression; suicidal thoughts; stress and worry about the conditions where they live, learn, work, or play; and substance use or initiation in April and May 2020. Hispanic/Latino adults were especially affected. Feb. 4 MMWR

MMWR 2/5: Sexual Orientation Disparities in Risk Factors for Adverse COVID-19–Related Outcomes, by Race/Ethnicity — Behavioral Risk Factor Surveillance System, United States, 2017–2019

Diversity in Clinical Trials:

- Because clinical trials provide a crucial base of evidence for evaluating whether a medical product is safe and effective, enrollment in clinical trials should reflect the diversity of the population that is ultimately going to use the product.
- Ensuring meaningful representation of racial and ethnic minorities in clinical trials for regulated medical products is fundamental not only to the FDA's regulatory mission but also to public health.
- Participation by diverse volunteers helps researchers find better treatments and better ways to fight such diseases as cancer, diabetes, heart disease and HIV/AIDS.

American Indians and Alaska Natives:

To date, Indian Health Services (IHS) has completed **over 1.9 million tests** throughout Indian Country.

- As of Feb. 3, the Indian Health Service has reported:
  - 1,960,619 tests, of which 180,057 are positive and 1,637,676 are negative.7-day average for positivity for all IHS Areas is **9.1%.**
    - Areas of concern with increasing 7-day positivity, over 10% are: : Navajo (14.9%), Oklahoma City (14.7%), Phoenix (13.9%), and California (11.9%).
    - Total positivity rate for reporting I/T/U's is 9.9% (compared with US all races positivity rate of 9.2%).
    - IHS areas exceeding U.S. positivity rate: Navajo (17.09%), Phoenix (14.6%), Oklahoma City (13.5%), Albuquerque (11.8%), Tucson (11.4%), California (11.1%), and Great Plains (10.6%).
- As of February 4, 238,594 vaccine doses have been administered and 477,275 vaccine doses have been distributed, a rate of 50.0%. The Vaccine Task Force continues to provide onboarding support to I/T/U sites, develop a data reporting dashboard, and monitor vaccine adverse events.
- For information on the federal response in Indian Country: https://www.ihs.gov/coronavirus/.

Testing

Funding to Expand Production, Purchase At-Home OTC Test: On February 1, DoD and HHS awarded $231.8 million to Ellume USA LLC to increase production capacity and procure 8.5 million tests of the Ellume COVID-19 Home Test, a rapid antigen test that can be performed at home. DoD press release.

Overview:

- As of Feb. 8, **306 million tests** have been completed**.**
- The **national percent positivity rate** in the past 7 days **is 7.7%**, based on data from 1/29 to 2/04.**Note: it takes on average 3 days for testing results to be reported to HHS. Number reported may be an underestimate due to delayed reporting*
- As of today, more than 8.6 million tests have been completed by HRSA health centers (dashboard).
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- Surge testing has been established in **23 states** with **4,500 locations** to date.
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- Retail and pharmacy partners in more than 4,400 locations in all 50 states, the District of Columbia, and Puerto Rico have conducted 7,151,526 tests to date. There are currently 3,586 active sites.

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Severe Symptoms and Pregnancy Complications: Pregnant women who had severe symptoms of COVID-19 have a higher risk of complications during and after pregnancy, according to early results announced Jan. 28. The NIH-supported study showed that the women with COVID-19 were at higher risk for cesarean delivery, postpartum hemorrhage, hypertensive disorders of pregnancy and preterm birth compared to pregnant women without symptoms.

MMWR reports published by the CDC:

- MMWR 2/5: Decline in COVID-19 Hospitalization Growth Rates Associated with Statewide Mask Mandates — 10 States, March–October 2020
- MMWR 2/5: Observed Face Mask Use at Six Universities — United States, September–November 2020
- MMWR 2/4: Decreases in Young Children Who Received Blood Lead Level Testing During COVID-19 — 34 Jurisdictions, January – May 2020

Updated CDC guidance:

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- CDC recommends wearing masks with two or more layers of washable, breathable fabric. If wearing a cloth mask, the layers of fabric should be tightly woven and you should not be able to see light through it. If the mask is a single layer of fabric, another could be worn on top to achieve the recommended level of protection.

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- **Monoclonal Antibody Treatments:** Digital Toolkit
- **Flu Vaccine:** Use **#FightFlu** and **#SleeveUp** when receiving the flu vaccine.
    - Digital campaign resources: Digital Media Toolkit, Social Media Toolkit
    - For Medicare specific resources: Social Media Toolkit (English, Spanish)
- **Plasma Donation:** FDA Donate Plasma; Social Media Toolkit
- **Minority Risk:** CDC materials: Facebook @CDC

From: HHS COVID JIC <JIC@hhs.gov>
Sent: Tue, 9 Feb 2021 19:42:24 -0500
To: HHS COVID JIC
Subject: COVID-19 HHS Communications Coordination Group Report - February 9, 2021
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Senior Leaders:

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Kind regards,

HHS COVID-19 Communications Coordination Group
U.S. Department of Health and Human Services (HHS)

COVID-19 HHS COMMUNICATIONS COORDINATION GROUP

Daily Communications Report – February 9, 2021

Topline Messages

Vaccine Intent Among Adults: At the launch of the national vaccination program, 40 percent of adults intended to receive the COVID-19 vaccine. Now, more adults (50 percent) intend to receive the vaccine, with the largest increase among those 65 and older. A new report from CDC published Feb. 9 describes results of internet survey panels to examine adults' perceptions toward COVID-19 vaccine.

New Study of Long-Acting Antibody Treatment: A new treatment study has begun to enroll participants hospitalized with COVID-19, NIH announced Feb. 8. This international, randomized, and controlled Phase 3 clinical trial will evaluate the safety and efficacy of AZD7442, an investigational long-acting antibody combination developed by AstraZeneca. The study is part of NIH's ACTIV-3 master protocol.

Virtual Presidential Visit: President Biden and Vice President Harris were provided a virtual tour of the vaccination center at State Farm Stadium in Glendale, Arizona, which is averaging between 8,000 and 9,000 vaccinations per day between first and second doses. The tour and remarks can be viewed here.

FEMA Releases Community Vaccination Playbook: As part of the national effort to speed the pace of COVID-19 vaccination campaigns, the president directed the federal government to establish new federally supported Community Vaccination Centers (CVCs). This playbook establishes guidance for providing federal support to existing and new CVCs including interagency coordination, resource support, facility setup, and other requirements that necessitate federal support

Monoclonal Antibody Administration: ASPR TRACIE has published Planning Considerations for Monoclonal Antibody Administration Tip Sheet, which provides information for healthcare providers on prescribing and administering COVID-19 monoclonal antibody therapeutics.

Slow the Spread of COVID-19: We can each make a difference and protect ourselves and others by wearing a mask, staying at least 6 feet (about 2 arm lengths) from others who don't live with you, and avoiding crowds. The more people you are in contact with, the more likely you are to be exposed.

General Stats:

- U.S. Total Cases: 26,852,809
- U.S. Total Deaths: 462,037
- Tests Reported: 307,726,596
- Vaccines:
  - Total Doses Distributed: 59,307,800
  - Total Doses Administered: 42,417,617
  - Number of People Receiving 1 or More Doses: 32,340,146
  - Number of People Receiving 2 Doses: 9,518,015

Sourced from the CDC COVID Data Tracker: Feb 8 2021 12:26PM ET

Trending: New deaths, cases, and hospitalizations remain high.

- **19.5% decrease in 7-day average of new cases**, as of Feb. 7: 116,905 daily average over past 7 days vs. 145,136 over 7 previous days. (CDC, 2/9)
- **0.3% increase in 7-day average of new deaths**, as of Feb. 7: 3,155 daily average over past 7 days vs. 3,146 over 7 previous days. (CDC, 2/9)

- The **national percent positivity rate** in the past 7 days **is 7.4%**, based on data from 1/30 to 2/05.**Note: it takes on average 3 days for testing results to be reported to HHS. Number reported may be an underestimate due to delayed reporting*
- As of Feb. 8, the US government has **allocated 886,504** patient courses of Eli Lilly's bamlanivimab and Regeneron's casirivimab/imdevimab monoclonal antibodies in total.
- As of Feb. 9, there are **3,653 medical personnel** deployed for the COVID-19 Response, which includes 2,935 National Guard personnel. In total, there are 28,674 personnel deployed for the whole-of-government COVID-19 response.

Emerging SARS-CoV-2 Variants

Viruses constantly change through mutation, and new variants of a virus are expected to occur over time. Multiple variants of the virus that causes COVID-19 have been documented in the United States and globally during this pandemic.

- Many variants do not change how the virus behaves and many disappear.
- Infection by the variant that emerged in the UK (B.1.1.7), the variant that emerged in South Africa (B. 1.351), and the variant that emerged in Brazil (P.1) do not appear to cause more severe disease in infected individuals, although these variants may be more contagious.
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- Numbers of reported cases of variants in the U.S. as of February 8:
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- For more information: New COVID-19 Variants, Emerging SARS-CoV-2 Variants.

Federal COVID Response for Vaccines

FDA Advisory Committee Meeting to Discuss Janssen COVID-19 Vaccine Candidate: The FDA Vaccines and Related Biological Products Advisory Committee (VRBPAC) will meet Feb. 26, to discuss the request for emergency use authorization (EUA) for a COVID-19 vaccine from Janssen Biotech Inc. (FDA release)

Guidance on Vaccinations for the Homeless: CDC provided Interim Guidance for Health Departments: COVID-19 Vaccination Implementation for People Experiencing Homelessness on Feb. 5.

Operational Support

On Feb. 12, HHS will deploy a 19-person NDMS vaccination team, plus support staff, to Oakland, California, to support a mass vaccination center at RingCentral Coliseum. The vaccination team will include 15 onsite supervisory medical providers (RN, NP or PA), and 4 providers for post-vaccination observation/allergic reaction response (EMTP or ED RN). In addition to administering vaccine, NDMS will provide oversight and train interagency partners, including 80 healthcare providers from the U.S. Forest Service, U.S Public Health Service, and other federal agencies. The team will be deployed for 14 days with a possible extension of an additional 14 days.

HHS-ASPR has deployed 100 vaccinators and logistical staff from the National Disaster Medical System to support COVID-19 vaccination sites in five Arizona counties. Additionally, ASPR is coordinating with DoD, the VA, and USDA to support vaccination efforts in California, Delaware, Louisiana, the Navajo Nation, New Jersey, Oklahoma, Texas, and the USVI.

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AstraZeneca, Janssen (J&J), and Novavax remain in large Phase 3 clinical trials in the U.S.

- Participants are still needed in various trials to ensure adequate representation of various demographic categories.
- To volunteer for a COVID-19 vaccine trial, visit combatcovid.hhs.gov.

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Learn more about what to expect after getting vaccinated for COVID-19, including normal side effects and tips to reduce pain or discomfort.

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Federal COVID Response for Therapeutics

Therapeutics focus on solutions that either attack the virus or help manage complications in people with severe cases of COVID-19 to reduce recovery time, prevent hospitalizations, and decrease mortality risk.

- Types of authorized or approved therapeutics currently in use: convalescent plasma, monoclonal antibodies, remdesivir, corticosteroids, or combinations of drugs as well as other types of drugs that are recognized as beneficial for treatment.
- FDA has issued 7 EUAs for therapeutics and approved one therapeutic (remdesivir). These therapeutics are being manufactured and administered, with many more in the pipeline.

Monoclonal Antibody Treatments:

Monoclonal antibodies directly neutralize the virus that causes COVID-19. In clinical trials, monoclonal antibodies decreased patients' viral load. Patients who received treatment soon after being diagnosed were less likely to require hospitalization.

- Treatments are currently given in outpatient settings as a one-time infusion.
- # of treatment courses distributed:
  - The federal response includes an agreement to purchase approximately 3 million treatment courses of the monoclonal antibody bamlanivimab.
  - Cases of bamlanivimab and the casirivimab/imdevimab monoclonal antibody cocktail are allocated weekly by ASPR to states, territories, and identified agencies. As of Feb. 9, **ASPR has allocated 738,482 bamlanivimab patient courses and 148,022 casirivimab/imdevimab patient courses.**
  - As of Feb. 8, up to 349,000 patient courses of monoclonal antibodies have been used to treat high-risk COVID-19 patients with mild-to-moderate symptoms, potentially **preventing over 16,000 hospitalizations and over 6,500 deaths** since November.

Blood Thinners:

Blood Thinners for COVID-19 Patient Care: Full-dose blood thinners decreased need for life support and improved outcome in hospitalized COVID-19 patients, January 26 NIH news release.

Health Equity and Helping Populations at Risk

Mental Health Conditions Hit Hispanic/Latino Adults: A new CDC study of a survey conducted early in the COVID-19 pandemic finds that U.S. adults reported increased symptoms of depression; suicidal thoughts; stress and worry about the conditions where they live, learn, work, or play; and substance use or initiation in April and May 2020. Hispanic/Latino adults were especially affected. Feb. 4 MMWR

MMWR 2/5: Sexual Orientation Disparities in Risk Factors for Adverse COVID-19–Related Outcomes, by Race/Ethnicity — Behavioral Risk Factor Surveillance System, United States, 2017–2019

Diversity in Clinical Trials:

Because clinical trials provide a crucial base of evidence for evaluating whether a regulated medical product is safe and effective, enrollment in clinical trials should reflect the racial and ethnic diversity of

the population that will ultimately use the product. Meaningful representation is fundamental to the FDA's regulatory mission and to public health.

American Indians and Alaska Natives:

To date, Indian Health Services (IHS) has completed **over 1.9 million tests** throughout Indian Country.

- As of Feb. 6, the Indian Health Service has reported:
  - 1,976,220 tests, of which 181,023 are positive and 1,650,546 are negative.7-day average for positivity for all IHS Areas is **7.6%.**
    - Areas of concern with increasing 7-day positivity, over 10% are: Oklahoma City (14.9%), Tucson (13.0%), Navajo (12.7%), California (12.6%), and Phoenix (11.6%).
    - Total positivity rate for reporting I/T/U's is 9.9% (compared with US all races positivity rate of 9.2%).
    - IHS areas exceeding U.S. positivity rate: Navajo (16.9%), Phoenix (14.6%), Oklahoma City (13.5%), Albuquerque (11.8%), Tucson (11.4%), California (11.1%), and Great Plains (10.6%).
- As of February 8, 291,338 vaccine doses have been administered and 492,875 vaccine doses have been distributed, a rate of 59.0%. The Vaccine Task Force continues to provide onboarding support to I/T/U sites, develop a data reporting dashboard, and monitor vaccine adverse events.
- For information on the federal response in Indian Country: https://www.ihs.gov/coronavirus/.

Testing

Funding to Expand Production, Purchase At-Home OTC Test: On February 1, DoD and HHS awarded $231.8 million to Ellume USA LLC to increase production capacity and procure 8.5 million tests of the Ellume COVID-19 Home Test, a rapid antigen test that can be performed at home. DoD press release.

Overview:

- As of Feb. 8, **308 million tests** have been completed**.**
- The **national percent positivity rate** in the past 7 days **is 7.4%**, based on data from 1/30 to 2/05.**Note: it takes on average 3 days for testing results to be reported to HHS. Number reported may be an underestimate due to delayed reporting*
- As of today, more than 8.6 million tests have been completed by HRSA health centers (dashboard).
- In the past 7 days, **98.7%** of commercial lab tests were completed within 3 days and **99.4%** were completed within 5 days.
- Surge testing has been established in **23 states** with **4,500 locations** to date.
  - There are currently 85 active surge testing sites.
  - As of Feb. 9, more than 978,157 tests have been conducted at these sites.
- 13,985 rapid point-of-care instruments and 4.9 million tests have been delivered to 13,850 CLIA-certified nursing homes across the country.
- Retail and pharmacy partners in more than 4,400 locations in all 50 states, the District of Columbia, and Puerto Rico have conducted 7,264,567 tests to date. There are currently 3,903 active sites.

Risk and Prevention

COVID-19 impact on the number of children tested for elevated blood lead levels: An estimated half million children may have missed screenings for elevated blood lead levels due to the pandemic. CDC data published Feb. 5 showed testing for elevated blood levels fell about one-third from January to May 2020 and by more than half from March to May 2020 compared to the same periods in 2019.

MMWR reports published by the CDC:

- MMWR 2/5: Decline in COVID-19 Hospitalization Growth Rates Associated with Statewide Mask Mandates — 10 States, March–October 2020
- MMWR 2/5: Observed Face Mask Use at Six Universities — United States, September–November 2020
- MMWR 2/4: Decreases in Young Children Who Received Blood Lead Level Testing During COVID-19 — 34 Jurisdictions, January – May 2020

Updated CDC guidance:

- On Feb. 2, CDC provided guidance to educators and school administrators, Operating schools during COVID-19: CDC's Considerations
- CDC recommends wearing masks with two or more layers of washable, breathable fabric. If wearing a cloth mask, the layers of fabric should be tightly woven and you should not be able to see light through it. If the mask is a single layer of fabric, another could be worn on top to achieve the recommended level of protection.

Additional Resources

COVID-19 Executive Orders and National Strategy

- **President Biden's National Strategy for COVID-19 and Pandemic Preparedness:** On Jan. 21, the Biden Administration released its national strategy to combat COVID-19, available publicly.
- **COVID-19 Executive Orders:** On Jan. 21, President Biden signed nine executive orders that directly impact the national response to COVID-19. All signed Executive Orders and administration priorities can be found on whitehouse.gov/priorities/covid-19.

Social Media Materials

- **COVID-19 Vaccine Communications:** Vaccination Communication Toolkit
- **Monoclonal Antibody Treatments:** Digital Toolkit
- **Flu Vaccine:** Use **#FightFlu** and **#SleeveUp** when receiving the flu vaccine.
    - Digital campaign resources: Digital Media Toolkit, Social Media Toolkit
    - For Medicare specific resources: Social Media Toolkit (English, Spanish)
- **Plasma Donation:** FDA Donate Plasma; Social Media Toolkit
- **Minority Risk:** CDC materials: Facebook @CDC

From: HHS COVID JIC <JIC@hhs.gov>
Sent: Wed, 10 Feb 2021 18:19:15 -0500
To: HHS COVID JIC
Subject: COVID-19 HHS Communications Coordination Group Report - February 10, 2021
Attachments: 2.10.21 HHS CCG COVID-19 Daily Communications Report.pdf

Senior Leaders:

Please find attached today's COVID-19 HHS Communications Coordination Group Report for February 10, 2021.

Kind regards,

HHS COVID-19 Communications Coordination Group
U.S. Department of Health and Human Services (HHS)

COVID-19 HHS COMMUNICATIONS COORDINATION GROUP

Daily Communications Report – February 10, 2021

Topline Messages

New PSA Campaign: Famous characters from films such as Austin Powers, Casablanca, Harry Potter, and The Lord of the Rings are encouraging Americans to "Mask Up" in a national PSA campaign launched Feb. 10 by CDC, the Ad Council, and WarnerMedia. The TV and digital video spot features key moments from these and other films with characters reimagined wearing face masks.

Improving Mask Effectiveness: Reports published in MMWR and JAMA Feb. 10 confirm that wearing masks is effective at slowing the spread of COVID-19, and the better a mask fits, the more protection it provides you and those around you. In lab tests, exposure to potentially infectious aerosols decreased by about 95% when the "source" and the "receiver" of the particles wore tightly fitted masks. CDC recommends masks with two or more layers and that fit snugly against your nose and sides of your face. CDC outlines ways to improve mask fit, such as wearing two masks (cloth mask over a medical mask).

EUA for Monoclonal Antibody Treatment: The FDA issued an emergency use authorization (EUA) for bamlanivimab and etesevimab administered together (Eli Lilly and Company) for the treatment of mild-to-moderate COVID-19 in adults and children over 12 years who are at high risk for progressing to severe COVID-19. In clinical studies, hospitalizations and emergency room visits occurred in 2% of those treated with the combination therapy compared to 7% in patients receiving placebo. The combination therapy also resulted in a lower risk of resistant viruses developing during treatment compared with bamlanivimab administered alone; however, both treatments are expected to benefit eligible patients. Bamlanivimab alone received an EUA Dec. 9; etesevimab is not authorized to be administered alone.

Vaccine Intent Among Adults: At the launch of the national vaccination program, 40 percent of adults intended to receive the COVID-19 vaccine. Now, more adults (50 percent) intend to receive the vaccine, with the largest increase among those 65 and older. A new report from CDC published Feb. 9 describes results of internet survey panels to examine adults' perceptions toward COVID-19 vaccine.

Monoclonal Antibody Administration: ASPR TRACIE has published Planning Considerations for Monoclonal Antibody Administration Tip Sheet, which provides information for healthcare providers on prescribing and administering COVID-19 monoclonal antibody therapeutics.

General Stats:

- U.S. Total Cases: 26,939,515
- U.S. Total Deaths: 463,659
- Tests Reported: 308,827,516
- Vaccines:
  - Total Doses Distributed: 65,972,575
  - Total Doses Administered: 44,769,970
  - Number of People Receiving 1 or More Doses: 33,783,384
  - Number of People Receiving 2 Doses: 10,469,514

Sourced from the CDC COVID Data Tracker: Feb 10 2021 1:26PM ET

Slow the Spread of COVID-19: We can each make a difference and protect ourselves and others by wearing a mask, staying at least 6 feet (about 2 arm lengths) from others who don't live with you, and avoiding crowds. The more people you are in contact with, the more likely you are to be exposed.

Trending: New deaths, cases, and hospitalizations remain high.

- **22.7% decrease in 7-day average of new cases**, as of Feb. 8: 111,329 daily average over past 7 days vs. 143,968 over 7 previous days. (CDC, 2/10)
- **0.8% decrease in 7-day average of new deaths**, as of Feb. 8: 3,118 daily average over past 7 days vs. 3,143 over 7 previous days. (CDC, 2/10)

- The **national percent positivity rate** in the past 7 days **is 7.2%**, based on data from 1/31 to 2/06.**Note: it takes on average 3 days for testing results to be reported to HHS. Number reported may be an underestimate due to delayed reporting*
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COVID-19 impact on the number of children tested for elevated blood lead levels: An estimated half million children may have missed screenings for elevated blood lead levels due to the pandemic. CDC data published Feb. 5 showed testing for elevated blood levels fell about one-third from January to May 2020 and by more than half from March to May 2020 compared to the same periods in 2019.

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- **Minority Risk:** CDC materials: Facebook @CDC

From: HHS COVID JIC <JIC@hhs.gov>
Sent: Thu, 4 Feb 2021 17:35:40 -0500
To: HHS COVID JIC
Subject: COVID-19 HHS Communications Coordination Group Report - February 4, 2021
Attachments: 2.4.21 HHS CCG COVID-19 Daily Communications Report.pdf

Senior Leaders:

Please find attached today's COVID-19 HHS Communications Coordination Group Report for February 4, 2021.

Kind regards,

COVID-19 Joint Information Center
U.S. Department of Health and Human Services (HHS)
General Inbox: JIC@hhs.gov

COVID-19 HHS COMMUNICATIONS COORDINATION GROUP

Daily Communications Report – February 4, 2021

Topline Messages

Severe Symptoms and Pregnancy Complications: Pregnant women who had severe symptoms of COVID-19 have a higher risk of complications during and after pregnancy, according to early results announced Jan. 28. The NIH-supported study showed that the women with COVID-19 were at higher risk for cesarean delivery, postpartum hemorrhage, hypertensive disorders of pregnancy and preterm birth compared to pregnant women without symptoms.

Mental Health Conditions Hit Hispanic/Latino Adults: A new CDC study of a survey conducted early in the COVID-19 pandemic finds that U.S. adults reported increased symptoms of depression; suicidal thoughts; stress and worry about the conditions where they live, learn, work, or play; and substance use or initiation in April and May 2020. Hispanic/Latino adults were especially affected, reporting higher rates of depressive symptoms, suicidal thoughts, and increased substance use than other racial/ethnic minority groups. Hispanic/Latino adults also reported feeling stress or worry about not having enough food or not having stable housing approximately twice as often as white adults. Feb. 4 MMWR

CDC Offers Vaccine Confidence Consultations: The CDC Vaccine Task Force is rolling out vaccine confidence consultations for interested jurisdictions. The program will match jurisdictions with CDC experts to answer questions around vaccine hesitancy and develop strategies to instill vaccine confidence for hesitant populations. To request this service, interested jurisdictions can reach out to confidenceconsults@cdc.gov. CDC also has online tips for building vaccine confidence.

Masks Required While on Public Transportation and at Transportation Hubs: Effective Feb. 2, all passengers and crew are required to wear face masks on planes, buses, trains, and other forms of public transportation and in U.S. transportation hubs such as airports and stations to help stop the spread of COVID-19. CDC Jan. 30 press release, guidance and FAQs, and order.

Slow the Spread of COVID-19: We can each make a difference and protect ourselves and others by wearing a mask, staying at least 6 feet (about 2 arm lengths) from others who don't live with you, and avoiding crowds. The more people you are in contact with, the more likely you are to be exposed.

General Stats:

- U.S. Total Cases: 26,277,125 (+116,915)
- U.S. Total Deaths: 445,264 (+3,433)
- Tests Reported: 299,231,199 (+1,244,442)
- Total Doses Distributed: 55,943,800 (+3,286,125)
- Total Doses Administered: 33,878,254 (+1,097,394)
- Number of People Receiving 1 or More Doses: 27,154,956 (714,120)
- Number of People Receiving 2 Doses: 6,436,931 (+372,139)

Sourced from the CDC COVID Data Tracker: Feb. 03, 2021 12:26 PM

Trending: New deaths, cases, and hospitalizations remain high.

- **16.3% decrease in 7-day average of new cases**, as of Feb. 2: 139,423 daily average over past 7 days vs. 166,497 over 7 previous days. (CDC, 2/4)
- **6.3% decrease in 7-day average of new deaths**, as of Feb. 2: 3,106 daily average over past 7 days vs. 3,316 over 7 previous days. (CDC, 2/4)

- The **national percent positivity rate** in the past 7 days **is 8.2%**, based on data from 1/25 to 1/31.**Note: it takes on average 3 days for testing results to be reported to HHS. Number reported may be an underestimate due to delayed reporting*
- As of Feb. 3, the US government has **allocated 881,460** patient courses of Eli Lilly's bamlanivimab and Regeneron's casirivimab/imdevimab monoclonal antibodies in total.
- As of Feb. 3, there are **3,404 medical personnel** deployed for the COVID-19 Response, which includes 2,783 National Guard personnel. In total, there are 27,388 personnel deployed for the whole-of-government COVID-19 response.

Emerging SARS-CoV-2 Variants

Viruses constantly change through mutation, and new variants of a virus are expected to occur over time. Multiple variants of the virus that causes COVID-19 have been documented in the United States and globally during this pandemic.

- Many variants do not change how the virus behaves and many disappear.
- Infection by the variant that emerged in the UK (B.1.1.7), the variant that emerged in South Africa (B. 1.351), and the variant that emerged in Brazil (P.1) do not appear to cause more severe disease in infected individuals, although these variants may be more contagious.
- Scientists are working to better understand how easily these variants might be transmitted and whether currently authorized vaccines will protect people against them.
- Numbers of reported cases of variants in the U.S. as of February 1:
  - B.1.1.7. (first detected in the UK): 541 (33 states)
  - B. 1.351 (first detected in South Africa): 3 (SC, MD)
  - P.1 (first detected in Brazil): 2 (MN).
- For more information: New COVID-19 Variants, Emerging SARS-CoV-2 Variants.

Federal COVID Response for Vaccines

Operational Support

HHS National Disaster Medical System (NDMS) personnel began administering vaccines at the Las Vegas Convention Center on Feb. 2. This is part of the federally supported, locally managed vaccination administration initiative announced by the Biden Administration. NDMS is working in partnership with the state of Nevada, the Southern Nevada Health District and FEMA to support second dose vaccines for the residents of the Las Vegas area.

ASPR is deploying 100 vaccinators and logistical staff from the National Disaster Medical System to support COVID-19 vaccination sites in five Arizona counties: Mohave, Pima, Maricopa, Coconino, Yavapai, and Pinal. All personnel will arrive in Arizona on Thursday, Feb. 4. Friday will be a training day. Vaccinations will start this weekend.

Vaccine Confidence

- **Demographics of People Vaccinated:** On Feb. 1, CDC published the MMWR "Demographic Characteristics of Persons Vaccinated During the First Month of the COVID-19 Vaccination Program — United States, Dec. 14, 2020–Jan. 14, 2021."
- **Skilled Nursing Facilities Staff:** On Feb. 1, CDC published the MMWR: "Early COVID-19 First-Dose Vaccination Coverage Among Residents and Staff Members of Skilled Nursing Facilities Participating in the Pharmacy Partnership for Long-Term Care Program — United States, December 2020–January 2021."
- Resources: Strategy to Reinforce Confidence in COVID-19 Vaccines

Clinical Trials

AstraZeneca, Janssen (J&J), and Novavax remain in large Phase 3 clinical trials in the U.S.

- Participants are still needed in various trials to ensure adequate representation of various demographic categories.
- To volunteer for a COVID-19 vaccine trial, visit combatcovid.hhs.gov.

Vaccine Risk

Learn more about what to expect after getting vaccinated for COVID-19, including normal side effects and tips to reduce pain or discomfort.

- On Jan. 22, CDC released the MMWR "Allergic Reactions Including Anaphylaxis After Receipt of the First Dose of Moderna COVID-19 Vaccine."
- On Jan. 6, CDC released the MMWR "Allergic Reactions Including Anaphylaxis After Receipt of the First Dose of Pfizer-BioNTech COVID-19 Vaccine

Federal COVID Response for Therapeutics

Therapeutics focus on solutions that either attack the virus or help manage complications in people with severe cases of COVID-19 to reduce recovery time, prevent hospitalizations, and decrease mortality risk.

- Types of authorized or approved therapeutics currently in use: convalescent plasma, monoclonal antibodies, remdesivir, corticosteroids, or combinations of drugs as well as other types of drugs that are recognized as beneficial for treatment.
- FDA has issued 7 EUAs for therapeutics and approved one therapeutic (remdesivir). These therapeutics are being manufactured and administered, with many more in the pipeline.

Monoclonal Antibody Treatments:

Monoclonal antibodies directly neutralize the virus that causes COVID-19. In clinical trials, monoclonal antibodies decreased patients' viral load. Patients who received treatment soon after being diagnosed were less likely to require hospitalization.

- Treatments are currently given in outpatient settings as a one-time infusion.
- # of treatment courses distributed:
  - The federal response includes an agreement to purchase approximately 3 million treatment courses of the monoclonal antibody bamlanivimab.
  - Cases of bamlanivimab and the casirivimab/imdevimab monoclonal antibody cocktail are allocated weekly by ASPR to states, territories, and identified agencies. As of Feb. 3, **ASPR**

has allocated 738,482 bamlanivimab patient courses and 142,978 casirivimab/imdevimab patient courses.

Blood Thinners:

Blood Thinners for COVID-19 Patient Care: Full-dose blood thinners decreased need for life support and improved outcome in hospitalized COVID-19 patients, January 26 NIH news release.

Health Equity and Helping Populations at Risk

- MMWR 2/5: Sexual Orientation Disparities in Risk Factors for Adverse COVID-19–Related Outcomes, by Race/Ethnicity — Behavioral Risk Factor Surveillance System, United States, 2017–2019

Diversity in Clinical Trials:

- Because clinical trials provide a crucial base of evidence for evaluating whether a medical product is safe and effective, enrollment in clinical trials should reflect the diversity of the population that is ultimately going to use the product.
- Ensuring meaningful representation of racial and ethnic minorities in clinical trials for regulated medical products is fundamental not only to the FDA's regulatory mission but also to public health.
- Participation by diverse volunteers helps researchers find better treatments and better ways to fight such diseases as cancer, diabetes, heart disease and HIV/AIDS.

American Indians and Alaska Natives:

To date, Indian Health Services (IHS) has completed **over 1.9million tests** throughout Indian Country.

- As of Jan. 30, the Indian Health Service has reported:
  - 1,928,584 tests, of which 177,196 are positive and 1,610,778 are negative.7-day average for positivity for all IHS Areas is **10.4%.**
    - Areas of concern with increasing 7-day positivity, over 10% are: Navajo (16.5%), Oklahoma City (15.2%), Phoenix (14.7%), Albuquerque (14.4%), California (12.4%), Tucson (11.3%), and Nashville (10.7%).
  - Total positivity rate for reporting I/T/U's is 9.9% (compared with US all races positivity rate of 9.2%).
    - IHS areas exceeding U.S. positivity rate: Navajo (16.9%), Phoenix (14.6%), Oklahoma City (13.5%), Albuquerque (11.8%), Tucson (11.4%), California (11.0%), and Great Plains (10.6%).
- As of Feb. 1, 210,664 vaccine doses have been administered and 423,600 vaccine doses have been distributed, a rate of 49.7% (per the CDC tracker).The Vaccine Task Force continues to provide onboarding support to I/T/U sites, develop a data reporting dashboard, and monitor vaccine adverse events.
- For information on the federal response in Indian Country: https://www.ihs.gov/coronavirus/.

Testing

Funding to Expand Production, Purchase At-Home OTC Test: On February 1, DoD and HHS awarded $231.8 million to Ellume USA LLC to increase production capacity and procure 8.5 million tests of the Ellume COVID-19 Home Test, a rapid antigen test that can be performed at home. This is the first

diagnostic test to receive FDA emergency use authorization for in-home use available without a prescription. DoD press release.

Overview:

- As of Feb. 4, **299 million tests** have been completed**.**
- The **national percent positivity rate** in the past 7 days **is 8.5%**, based on data from 1/24 to 1/30.**Note: it takes on average 3 days for testing results to be reported to HHS. Number reported may be an underestimate due to delayed reporting*
- As of today, more than 8.5 million tests have been completed by HRSA health centers (dashboard).
- In the past 7 days, **98.5%** of commercial lab tests were completed within 3 days and **99%** were completed within 5 days.
- Surge testing has been established in **23 states** with **4,500 locations** to date.
    - There are currently 85 active surge testing sites.
    - As of Feb. 4, more than 962,373 tests have been conducted at these sites. The turnaround times for current federal surge testing sites is less than 2 days.
- 13,985 rapid point-of-care instruments and 4.9 million tests have been delivered to 13,850 CLIA-certified nursing homes across the country.
- Retail and pharmacy partners in more than 4,000 locations in all 50 states, the District of Columbia, and Puerto Rico have conducted 7,072,390 tests to date. There are currently 3,586 active sites.

Risk and Prevention

Guidance for Workers and Employers: On February 2, CDC updated interim guidance documents for agricultural workers and employers, issued jointly with the Department of Labor; manufacturing workers and employers, issued jointly with the Occupational Safety and Health Administration (OSHA); and meat and poultry processers, issued with OSHA.

MMWR reports published by the CDC:

- MMWR 2/4: Decreases in Young Children Who Received Blood Lead Level Testing During COVID-19 — 34 Jurisdictions, January – May 2020
- MMWR 1/26: COVID-19 Cases and Transmission in 17 K–12 Schools — Wood County, Wisconsin, Aug. 31– Nov. 29, 2020
- MMWR 1/26: SARS-CoV-2 Transmission Associated with High School Wrestling Tournaments — Florida, December 2020 – January 2021
- MMWR: 1/25 Implementation and Evolution of Mitigation Measures, Testing, and Contact Tracing in the National Football League, Aug. 9 – Nov. 21, 2020

Updated CDC guidance:

- On Feb. 2, CDC provided guidance to educators and school administrators, Operating schools during COVID-19: CDC's Considerations

- CDC recommends wearing masks with two or more layers of washable, breathable fabric. If wearing a cloth mask, the layers of fabric should be tightly woven and you should not be able to see light through it. If the mask is a single layer of fabric, another could be worn on top to achieve the recommended level of protection.

Additional Resources

COVID-19 Executive Orders and National Strategy

- **President Biden's National Strategy for COVID-19 and Pandemic Preparedness:** On Jan. 21, the Biden Administration released its national strategy to combat COVID-19, available publicly.
- **COVID-19 Executive Orders:**
- Executive Order on Establishing the COVID-19 Pandemic Testing Board and Ensuring a Sustainable Public Health Workforce for COVID-19 and Other Biological Threats
- Executive Order on Protecting Worker Health and Safety
- Executive Order on Supporting the Reopening and Continuing Operation of Schools and Early Childhood Education Providers
- Executive Order on Ensuring an Equitable Pandemic Response and Recovery
- Executive Order on a Sustainable Public Health Supply Chain
- Executive Order on Ensuring a Data-Driven Response to COVID-19 and Future High-Consequence Public Health Threats
- Executive Order on Improving and Expanding Access to Care and Treatments for COVID-19
- Executive Order on Promoting COVID-19 Safety in Domestic and International Travel
- Executive Order on Organizing and Mobilizing the United States Government to Provide a Unified and Effective Response to Combat COVID-19 and to Provide United States Leadership on Global Health and Security

Social Media Materials

- **COVID-19 Vaccine Communications:** Vaccination Communication Toolkit
- **Monoclonal Antibody Treatments:** Digital Toolkit
- **Flu Vaccine:** Use **#FightFlu** and **#SleeveUp** when receiving the flu vaccine.
    - Digital campaign resources: Digital Media Toolkit, Social Media Toolkit
    - For Medicare specific resources: Social Media Toolkit (English, Spanish)
- **Plasma Donation:** FDA Donate Plasma; Social Media Toolkit
- **Minority Risk:** CDC materials: Facebook @CDC

From: HHS COVID JIC <JIC@hhs.gov>
Sent: Thu, 11 Feb 2021 18:59:31 -0500
To: HHS COVID JIC
Subject: COVID-19 HHS Communications Coordination Group Report - February 11, 2021
Attachments: 2.11.21 HHS CCG COVID-19 Daily Communications Report.pdf

Senior Leaders:

Please find attached today's COVID-19 HHS Communications Coordination Group Report for February 11, 2021.

Kind regards,

HHS COVID-19 Communications Coordination Group
U.S. Department of Health and Human Services (HHS)

COVID-19 HHS COMMUNICATIONS COORDINATION GROUP

Daily Communications Report – February 11, 2021

Topline Messages

First FQHCs to Receive Vaccine Directly: As part of the administration's efforts to ensure that the nation's hardest hit populations receive the vaccine, Federally Qualified Community Health Centers (FQHCs) will begin directly receiving vaccine supply starting the week of Feb. 15.

Mask Use by Students: Most middle and high school students (65%) attending school in-person report that other students wear a mask "all the time" in classrooms, hallways and stairs, but less frequently on the bus or in the bathroom and cafeteria, according to a Feb. 11 CDC analysis. The report said the lowest mask usage observed were during sports (28%) and outside on school property (25%).

New PSA Campaign: Famous characters from films such as Austin Powers, Casablanca, Harry Potter, and The Lord of the Rings are encouraging Americans to "Mask Up" in a national PSA campaign launched Feb. 10 by CDC, the Ad Council, and WarnerMedia. The TV and digital video spot features key moments from these and other films with characters reimagined wearing face masks.

Improving Mask Effectiveness: MMWR and JAMA reports Feb. 10 confirm that wearing masks is effective at slowing the spread of COVID-19, and the better a mask fits, the more protection it provides you and those around you. In lab tests, exposure to potentially infectious aerosols decreased by about 95% when the "source" and the "receiver" of the particles wore tightly fitted masks. CDC recommends masks with two or more layers and that fit snugly against your nose and sides of your face. CDC outlines ways to improve mask effectiveness, such as "double masking" (cloth mask over a medical mask).

EUA for Monoclonal Antibody Treatment: The FDA issued an emergency use authorization (EUA) for bamlanivimab and etesevimab administered together (Eli Lilly and Company) for the treatment of mild-to-moderate COVID-19 in adults and children over 12 years who are at high risk for progressing to severe COVID-19. In clinical studies, hospitalizations and emergency room visits occurred in 2% of those treated with the combination therapy compared to 7% in patients receiving placebo. Bamlanivimab alone received an EUA Dec. 9; etesevimab is not authorized to be administered alone.

Updates on Ventilator Splitters: The FDA issued a Letter to Health Care Providers Feb. 9 on Using Ventilator Splitters During the COVID-19 Pandemic to provide updated information based on real-world use. FDA indicates that the devices should be used only when no alternatives for invasive ventilatory support are available and describes certain features that improve performance of the devices.

Vaccine Intent Among Adults: At the launch of the national vaccination program, 40 percent of adults intended to receive the COVID-19 vaccine. Now, more adults (50 percent) intend to receive the vaccine, with the largest increase among those 65 and older. A new report from CDC published Feb. 9 describes results of internet survey panels to examine adults' perceptions toward COVID-19 vaccine.

Slow the Spread of COVID-19: We can each make a difference and protect ourselves and others by wearing a mask, staying at least 6 feet (about 2 arm lengths) from others who don't live with you, and avoiding crowds. The more people you are in contact with, the more likely you are to be exposed.

General Stats:

- U.S. Total Cases: 27,030,549
- U.S. Total Deaths: 46,465
- Tests Reported: 310,985,681
- Vaccines:
  - Total Doses Distributed: 65,972,575
  - Total Doses Administered: 44,769,970
  - Number of People Receiving 1 or More Doses: 33,783,384
  - Number of People Receiving 2 Doses: 10,469,514
    - *Sourced from the CDC COVID Data Tracker: Feb 10 2021 1:26PM ET*

Trending: New deaths, cases, and hospitalizations remain high.

- **22.8% decrease in 7-day average of new cases**, as of Feb. 9: 107,632 daily average over past 7 days vs. 139,423 over 7 previous days. (CDC, 2/11)
- **9.8% decrease in 7-day average of new deaths**, as of Feb. 9: 3,029 daily average over past 7 days vs. 3,106 over 7 previous days. (CDC, 2/11)

- The **national percent positivity rate** in the past 7 days **is 7.0%**, based on data from 2/01 to 2/07.**Note: it takes on average 3 days for testing results to be reported to HHS. Number reported may be an underestimate due to delayed reporting*
- As of Feb. 10, the US government has **allocated 897,291** patient courses of Eli Lilly's bamlanivimab and Regeneron's casirivimab/imdevimab monoclonal antibodies in total.
- As of Feb. 11, there are **3,674 medical personnel** deployed for the COVID-19 Response, which includes 2,935 National Guard personnel. In total, there are 29,370 personnel deployed for the whole-of-government COVID-19 response.

Emerging SARS-CoV-2 Variants

Viruses constantly change through mutation, and new variants of a virus are expected to occur over time. Multiple variants of the virus that causes COVID-19 have been documented in the United States and globally during this pandemic.

- Many variants do not change how the virus behaves and many disappear.
- Infection by the variant that emerged in the UK (B.1.1.7), the variant that emerged in South Africa (B. 1.351), and the variant that emerged in Brazil (P.1) do not appear to cause more severe disease in infected individuals, although these variants may be more contagious.
- Scientists are working to better understand how easily these variants might be transmitted and whether currently authorized vaccines will protect people against them.
- Numbers of reported cases of variants in the U.S. as of February 9:
  - B.1.1.7. (first detected in the UK): 932 (34 states)
  - B. 1.351 (first detected in South Africa): 9 (MD, SC, VA)
  - P.1 (first detected in Brazil): 3 (MN, OK).
- For more information: New COVID-19 Variants, Emerging SARS-CoV-2 Variants.

Federal COVID Response for Vaccines

FEMA Releases Community Vaccination Playbook: As part of the national effort to speed the pace of COVID-19 vaccination campaigns, the president directed the federal government to establish new federally supported Community Vaccination Centers (CVCs). This playbook establishes guidance for providing federal support to existing and new CVCs.

FDA Advisory Committee Meeting to Discuss Janssen COVID-19 Vaccine Candidate: The FDA Vaccines and Related Biological Products Advisory Committee (VRBPAC) will meet Feb. 26, to discuss the request for emergency use authorization (EUA) for a COVID-19 vaccine from Janssen Biotech Inc. (FDA release)

Operational Support

On Feb. 12, HHS will deploy a 19-person National Disaster Medical System (NDMS) vaccination team, plus support staff, to Oakland, California, to support a mass vaccination center at RingCentral Coliseum. The vaccination team will include 15 onsite supervisory medical providers (RN, NP or PA), and 4 providers for post-vaccination observation/allergic reaction response (EMTP or ED RN). In addition to administering vaccine, NDMS will provide oversight and train interagency partners, including 80 healthcare providers from the U.S. Forest Service, U.S Public Health Service, and other federal agencies. The team will be deployed for 14 days with a possible extension of an additional 14 days.

HHS-ASPR has deployed 100 vaccinators and logistical staff from the NDMS to support COVID-19 vaccination sites in five Arizona counties. Additionally, ASPR is coordinating with DoD, the VA, and USDA to support vaccination efforts in California, Delaware, Louisiana, the Navajo Nation, New Jersey, Oklahoma, Texas, and the USVI.

Vaccine Confidence

- **Demographics of People Vaccinated:** On Feb. 1, CDC published the MMWR "Demographic Characteristics of Persons Vaccinated During the First Month of the COVID-19 Vaccination Program — United States, Dec. 14, 2020–Jan. 14, 2021."
- **Skilled Nursing Facilities Staff:** On Feb. 1, CDC published the MMWR: "Early COVID-19 First-Dose Vaccination Coverage Among Residents and Staff Members of Skilled Nursing Facilities Participating in the Pharmacy Partnership for Long-Term Care Program — United States, December 2020–January 2021."
- **CDC Offers Consultations**: The CDC Vaccine Task Force is rolling out vaccine confidence consultations for interested jurisdictions. To request this service, interested jurisdictions can reach out to confidenceconsults@cdc.gov. CDC also has online tips for building vaccine confidence.
- Resources: Strategy to Reinforce Confidence in COVID-19 Vaccines

Clinical Trials

AstraZeneca, Janssen (J&J), and Novavax remain in large Phase 3 clinical trials in the U.S.

- Participants are still needed in various trials to ensure adequate representation of various demographic categories.
- To volunteer for a COVID-19 vaccine trial, visit combatcovid.hhs.gov.

Vaccine Risk

Learn more about what to expect after getting vaccinated for COVID-19, including normal side effects and tips to reduce pain or discomfort.

- On Jan. 22, CDC released the MMWR "Allergic Reactions Including Anaphylaxis After Receipt of the First Dose of Moderna COVID-19 Vaccine."
- On Jan. 6, CDC released the MMWR "Allergic Reactions Including Anaphylaxis After Receipt of the First Dose of Pfizer-BioNTech COVID-19 Vaccine

Federal COVID Response for Therapeutics

Therapeutics focus on solutions that either attack the virus or help manage complications in people with severe cases of COVID-19 to reduce recovery time, prevent hospitalizations, and decrease mortality risk.

- Types of authorized or approved therapeutics currently in use: convalescent plasma, monoclonal antibodies, remdesivir, corticosteroids, or combinations of drugs as well as other types of drugs that are recognized as beneficial for treatment.
- FDA has issued 8 EUAs for therapeutics and approved one therapeutic (remdesivir). These therapeutics are being manufactured and administered, with many more in the pipeline.

Monoclonal Antibody Treatments:

Monoclonal antibodies directly neutralize the virus that causes COVID-19. In clinical trials, monoclonal antibodies decreased patients' viral load. Patients who received treatment soon after diagnosis were less likely to require hospitalization. Treatments are given in outpatient settings as a one-time infusion.

- FDA has issued 3 EUAs for monoclonal antibody treatments as of February 9.
- ASPR TRACIE has published Planning Considerations for Monoclonal Antibody Administration Tip Sheet, which provides information for healthcare providers on prescribing and administering COVID-19 monoclonal antibody therapeutics.
- # of treatment courses distributed:
  - The federal response includes an agreement to purchase approximately 3 million treatment courses of the monoclonal antibody bamlanivimab.
  - Cases of bamlanivimab and the casirivimab/imdevimab monoclonal antibody cocktail are allocated weekly by ASPR to states, territories, and identified agencies. As of Feb. 10, **ASPR has allocated 748,231 bamlanivimab patient courses and 148,060 casirivimab/imdevimab patient courses.**
  - As of Feb. 8, up to 349,000 patient courses of monoclonal antibodies have been used to treat high-risk COVID-19 patients with mild-to-moderate symptoms, potentially **preventing over 16,000 hospitalizations and over 6,500 deaths** since November.

Health Equity and Helping Populations at Risk

Biden-Harris Administration COVID-19 Health Equity Task Force: To help ensure an equitable response to the pandemic, the administration announced their task force to address COVID-19 related health and social inequities.

Mental Health Conditions Hit Hispanic/Latino Adults: A new CDC study of a survey conducted early in the COVID-19 pandemic finds that U.S. adults reported increased symptoms of depression; suicidal thoughts; stress and worry about the conditions where they live, learn, work, or play; and substance use or initiation in April and May 2020. Hispanic/Latino adults were especially affected. Feb. 4 MMWR

MMWR 2/5: Sexual Orientation Disparities in Risk Factors for Adverse COVID-19–Related Outcomes, by Race/Ethnicity — Behavioral Risk Factor Surveillance System, United States, 2017–2019

Diversity in Clinical Trials:
Because clinical trials provide a crucial base of evidence for evaluating whether a regulated medical product is safe and effective, enrollment in clinical trials should reflect the racial and ethnic diversity of the population that will ultimately use the product. Meaningful representation is fundamental to the FDA's regulatory mission and to public health.

American Indians and Alaska Natives:
To date, Indian Health Services (IHS) has completed **over 1.9 million tests** throughout Indian Country.

- As of Feb. 7, the Indian Health Service has reported:
  - 1,981,436 tests, of which 181,576 are positive and 1,655,877 are negative. 7-day average for positivity for all IHS Areas is **7.6%.**
    - Areas of concern with increasing 7-day positivity, over 10% are: Oklahoma City (14.9%), Tucson (13.0%), Navajo (12.7%), California (12.6%), and Phoenix (11.6%).
    - Total positivity rate for reporting I/T/U's is 9.9% (compared with US all races positivity rate of 9.2%).
    - IHS areas exceeding U.S. positivity rate: Navajo (16.9%), Phoenix (14.6%), Oklahoma City (13.5%), Albuquerque (11.9%), Tucson (11.4%), California (11.1%), and Great Plains (10.6%).
- As of Feb. 9, 297,375 vaccine doses have been administered and 492,875 vaccine doses have been distributed, a rate of 60.0%. The Vaccine Task Force continues to provide onboarding support to I/T/U sites, develop a data reporting dashboard, and monitor vaccine adverse events.
- For information on the federal response in Indian Country: https://www.ihs.gov/coronavirus/.

Testing

Overview:

- As of Feb. 11, **311 million tests** have been completed**.**
- The **national percent positivity rate** in the past 7 days **is 7.0%**, based on data from 2/0 to 2/07.**Note: it takes on average 3 days for testing results to be reported to HHS. Number reported may be an underestimate due to delayed reporting*
- As of today, more than 8.6 million tests have been completed by HRSA health centers (dashboard).
- In the past 7 days, **99.2%** of commercial lab tests were completed within 3 days and **99.6%** were completed within 5 days
- Surge testing has been established in **23 states** with **4,500 locations** to date.
  - There are currently 86 active surge testing sites.
  - As of Feb. 11, more than 987,561 tests have been conducted at these sites.

- 13,985 rapid point-of-care instruments and 4.9 million tests have been delivered to 13,850 CLIA-certified nursing homes across the country.
- Retail and pharmacy partners in more than 4,400 locations in all 50 states, the District of Columbia, and Puerto Rico have conducted 7,341,586 tests to date. There are currently 3,910 active sites.

Risk and Prevention

MMWR reports published by the CDC:

- MMWR 2/5: Decline in COVID-19 Hospitalization Growth Rates Associated with Statewide Mask Mandates — 10 States, March–October 2020
- MMWR 2/5: Observed Face Mask Use at Six Universities — United States, September–November 2020
- MMWR 2/4: Decreases in Young Children Who Received Blood Lead Level Testing During COVID-19 — 34 Jurisdictions, January – May 2020

Additional Resources

COVID-19 Executive Orders and National Strategy

- **President Biden's National Strategy for COVID-19 and Pandemic Preparedness:** On Jan. 21, the Biden Administration released its national strategy to combat COVID-19, available publicly.
- **COVID-19 Executive Orders:** On Jan. 21, President Biden signed nine executive orders that directly impact the national response to COVID-19. All signed Executive Orders and administration priorities can be found on whitehouse.gov/priorities/covid-19.

Social Media Materials

- **COVID-19 Vaccine Communications:** Vaccination Communication Toolkit
- **Monoclonal Antibody Treatments:** Digital Toolkit
- **Flu Vaccine:** Use **#FightFlu** and **#SleeveUp** when receiving the flu vaccine.
    - Digital campaign resources: Digital Media Toolkit, Social Media Toolkit
    - For Medicare specific resources: Social Media Toolkit (English, Spanish)
- **Plasma Donation:** FDA Donate Plasma; Social Media Toolkit
- **Minority Risk:** CDC materials: Facebook @CDC

Risk of Reinfection from SARS-CoV-2 – An Update of Antibody Response Following SARS-CoV-2 Infection and Implications for Immunity: A Living Rapid Review

Version 2 (July 2021)

Questions for this Update

Key Question 2. What is the risk of reinfection from SARS-CoV-2 among adults with prior SARS-CoV-2 infection?

a) Does the risk of reinfection vary by patient characteristics (e.g., age, sex, race/ethnicity, and comorbidities), severity of the initial infection, initial antibody levels, SARS-CoV-2 variants, or vaccination status?
b) Is there a threshold level of detectable anti–SARS-CoV-2 antibodies necessary to confer natural immunity, and if so, does this threshold vary by patient characteristics (for example, age, sex, race/ethnicity, and comorbidities)?

Key Question 3. What is the duration of protection against reinfection among adults with prior SARS-CoV-2 infection?

a) Does the duration of protection vary by patient characteristics (e.g., age, sex, race/ethnicity, and comorbidities), severity of the initial infection, initial antibody levels, SARS-CoV-2 variants, or case identification method (e.g., surveillance, symptomatic testing only)?

What Did We Know?

Our original rapid review described the humoral (antibody) response after infection with the SARS-CoV-2 virus, but found little information on the duration of the response beyond 6 months or on antibody formation in asymptomatic patients or in those who are immunocompromised. At that time, only one study had measured the effect of natural immunity on the risk of reinfection and the relationship between features of the antibody response and the risk of reinfection.

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What Is New?

Updated: 07/14/2021

Search current as of 7/1/2021

This update adds 18 cohort studies that compared the risk of reinfection in adults with prior SARS-CoV-2 infection to the risk of infection in adults without a prior infection. Our main findings are that:

- Prior infection from SARS-CoV-2 reduced the risk of another infection by 80-90% compared with uninfected individuals in studies with a median follow-up 8 months (range 4-13 months). Protection remains >80% for at least 7 months. (High strength of evidence for effect size and duration up to 7 months, low SOE for protection from 7-10 months, and insufficient evidence for longer periods of time.)
- There are also several gaps in the evidence (all low or insufficient strength of evidence):
    - Data on reinfection risk in people who have asymptomatic primary infections is sparse and conflicting. Protection may be lower than for symptomatic primary infections.
    - Results for reinfection in the elderly were mixed. Overall, it seems more likely that protection for elderly individuals and younger adults is similar, but data are conflicting and additional evidence is needed.
    - There are no data about differences in protection from prior infection in immunocompromised individuals and people with other comorbidities, or among different race/ethnicity groups.
    - The studies were performed before vaccines became available. Additional data are needed to determine how vaccination increases the magnitude or duration of protection after infection, especially in people with asymptomatic or mildly symptomatic primary infections, elderly individuals, and people who are immunocompromised.
    - While evidence about the Alpha variant is reassuring, there are no data on reinfection risk with the Delta variant or other variants of concern.

Background and Purpose

The strength and expected duration of immunity, both from infection and from vaccination, are important for public health planning and clinical practice. Understanding the nature and duration of natural immunity to SARS-CoV-2 is a critical component of modeling the course of the pandemic and formulating public health policy.[1, 2] Better data on the risk for reinfection and on the relationship of antibody status to protection from reinfection can help guide practice policies regarding antibody testing and vaccination timing, particularly in immunocompromised patients and those with other comorbidities who have a higher risk of worse outcomes with COVID-19.

Over the past few months, several epidemiological studies have been published comparing infection risks between previously infected and uninfected adults, permitting analysis of

protection against reinfection from SARS-CoV-2 in the general population and of factors that might be associated with symptomatic reinfection. The findings from this review will be used by the American College of Physicians (ACP) to update clinical practice pointers on the topic.[3]

Methods

The protocol for this living rapid review was registered at PROSPERO (CRD42020207098), and posted to the Agency for Healthcare Research and Quality (AHRQ) Effective Healthcare Site.[4, 5] Detailed methods can be found in Appendix A.

Data sources, searches, and planned updates

For this update, we modified our search strategies to focus on identifying longitudinal controlled studies of risk of reinfection. To find systematic reviews, we searched www.covid19reviews.org, a website that catalogs results of bibliographic database searches for systematic reviews related to SARS-CoV-2. To find relevant research studies, we searched (1) Ovid MEDLINE ALL, WHO COVID, and ClinicalTrials.gov roughly every two weeks on average—4/6/2021, 4/13/2021, 04/26/2021, 5/14/2021, 6/1/2021, and 7/1/2021, (2) reference lists of pertinent systematic reviews, and (3) publications from prospective cohort studies identified from ClinicalTrials.gov, other registries, and news items. A complete description of the search strategy can be found in Appendix A.

This is the first update of this living rapid review.[6] For each update, in consultation with the ACP and AHRQ, we prioritize questions for current and future updates based on whether evidence identified in bi-weekly searches will likely substantially change the conclusions or certainty of evidence of our last review.[7, 8]

As noted above, this update focuses on estimating the risk of reinfection among adults in the general population and on the duration of protection against reinfection (Key Questions 2 and 3). The next update, which is currently underway and is expected to be completed in Fall of 2021, will review new evidence about the antibody response to SARS-CoV-2 exposure (Key Question 1) and about behavior and beliefs regarding SARS-CoV-2 antibody testing (Key Question 4). For the complete set of Key Questions, see our protocol[4] and Appendix A.

Study selection

We selected longitudinal studies that compared the risk of reinfection for individuals who had a documented infection with SARS-CoV-2 (the "positive" cohort) with the risk of new infections in individuals with no prior infection (the "negative" cohort).[9] Studies in the general population, health care workers, college students, and long-term care facilities were eligible, as were registry-based studies of patients with a specific condition. Studies that reported risk of reinfection but lacked an uninfected comparison cohort were ineligible, but we examined them to see whether they addressed populations or predictors of reinfection not adequately addressed in included studies. We used the Joanna Briggs Institute (JBI) cohort study checklist[10] to screen for methodological limitations that would almost certainly invalidate the study findings. Using this tool, we excluded two studies[11, 12] that used invalid criteria to allocate individuals to the positive

or negative cohorts or did not follow participants an adequate length of time for reinfections to occur. As described below, for the remaining (included) studies, we performed a second risk of bias assessment designed to identify limitations specific to this topic.

While we originally planned to exclude preprints, we decided to include those that passed the methodological (JBI) screen because monitoring indicated a very high chance of acceptance to a journal. Preprints are marked in plots, and their impact on pooled measures of effect was examined in sensitivity analyses. (Appendix C)

Data extraction and study quality

We used a spreadsheet to extract the following information by study: study design, population, data sources, study inclusion/exclusion criteria, age, race, gender, comorbidities, immunoassay type and brand (when applicable), definition of reinfection, follow-up test type and frequency of follow-up testing, primary infection symptom status, waiting period (if applicable), counts for all infection events/non-events, and main findings.

To assess study quality, we began by enumerating methodological challenges in studies of natural immunity that might bias effect sizes.[13] We then identified potential biases in four areas: sampling, cohort assignment, case definition, and ascertainment of cases during the follow up period. We abstracted information relevant to these methodological features from each study, recording variations in methods that could have an impact on the observed effect. Some of the considerations for each of these areas are described below:

- *Sampling.* We assessed whether selection bias could arise from the data sources used to identify eligible individuals or the ways participants were selected. Selection bias could spuriously drive effect size up or down if some groups in the target population were less likely to be recruited, if the cohorts were differentially enriched with individuals having unusual risk profiles, or if cohort inception was poorly delineated.
- *Cohort assignment*. Within a given sample, the "positive" (infected) or "negative" (not infected) cohorts form the denominators for follow-up and analyses. We considered which tests were used (serologic, virologic, and clinical assessment), when they were performed in relation to illness onset, and whether they were applied to all participants. Misclassification can occur if, for example, the tests used to diagnose infection had poor sensitivity or if cohorts included individuals with incomplete testing.
- *Outcome ascertainment.* We assessed the methods used to ascertain new infections during the follow-up period, such as scheduled surveillance with PCR tests, clinical surveillance, or identification of cases in clinical care without surveillance. In assessing ascertainment, we also considered, when applicable, whether surveillance for symptoms or access to medical evaluation differed among cohorts, as well as the frequency of, and adherence to, scheduled testing. Bias could also occur if the follow-up period was too short.
- *Classification of potential cases of reinfection during the follow-up period.* Ideally, a case is considered symptomatic reinfection only when a patient confirmed to have an infection has a negative PCR test during the follow-up period and, later, presents with symptoms and a positive PCR test or genetic typing. In most studies, however, reinfection was diagnosed when an individual had a positive PCR test following a

"waiting period" intended to give time for the initial episode to resolve clinically and virologically. Bias can occur if a positive PCR due to persistent viral shedding is counted as a reinfection, if the assay(s) used to confirm reinfection are not sensitive or specific, or if adjudication of reinfections in the positive was more or less rigorous than adjudication of incident infections in the negative cohort.

In each of these four categories, we identified methodological variations that are likely to be associated with higher or lower quality (risk of bias). In rating the quality of each study, we used only the study characteristics for which we could reasonably anticipate the direction of bias. For example, in most studies, only individuals who had a negative evaluation for SARS-CoV-2 infection—serology, PCR, or both—were assigned to the uninfected (negative) group. In one study, however, untested individuals were included in the uninfected group, increasing the chance of misclassification. This type of misclassification would be expected to bias the estimate of protection to the null.

In many cases, however, the magnitude or direction of bias associated with the features of a particular protocol may be unknown, often because knowledge of the course of disease is still developing. For example, as noted above, investigators must decide how long after cohort inception to count a positive PCR test as a reinfection. Different cut-offs for the waiting period between first and second positive tests influence the apparent rate of re-infection.[14] Starting the follow-up period too soon could misclassify persistent viral shedding as reinfection,[15] but waiting too long can exclude incident infections in the negative (previously uninfected) control group during a time when prior infection confers protection. In our judgment, all included studies employed reasonable time separations between assessments and adequate follow-up time. In this situation, *a priori* judgments about the risk of bias are suspect due to the novel nature of SARS-CoV-2 and lack of evidence to determine which decisions at the level of study design and methods could influence results.

We performed sensitivity analyses to assess whether the overall estimate of efficacy would change because of study-level factors. Such factors include study duration, the waiting period between cohort inception and the first reinfection assessment, median participant age, underlying prevalence (proxied by the proportion of new infections in the negative cohort), whether criteria for diagnosis of the initial infection would include only symptomatic infections, and whether serology, PCR, or both were used for cohort allocation (see Appendix C & Supplemental Appendix Table B-1). We examined the relationship between these factors and efficacy estimates but lacked sufficient data to evaluate them in a meta-regression. We also repeated our main analysis excluding preprint studies.

Data synthesis and strength of evidence

For Key Question 2, the main outcomes of interest were the effect of previous infection on the risk of symptomatic reinfection, any reinfection, and severity of reinfection. These outcome metrics, termed "efficacy" or "protection," are analogous to the those used in studies of vaccine efficacy.[16, 17] Here, however, incident infections detected during the follow up period in the positive cohort are reinfections and those in the negative cohort are primary infections; in vaccine studies all incident infections are considered primary infections. The category "any reinfection" includes individuals in whom virus is present, whether or not symptoms have been

detected. For Key Question 3, the outcome of interest was the duration of protection as indicated by the length of follow-up and, in some cases, by within-study analyses of efficacy by follow-up time period.

While many studies reported hazard ratios or relative rates of infection per person-time (often adjusted for various factors), our meta-analysis used absolute counts of events in both groups to obtain a relative risk estimate. We subsequently found a high degree of concordance between our calculated risk estimates and the rates reported in studies (see Appendix A).

The primary analyses focused on the magnitude of protection against reinfection, quantified as the proportion or percentage of prevented infections (another analogue to vaccine studies). Each included study provided counts of reinfected individuals from the positive cohort and newly infected individuals from the negative cohort, which together yield an estimate of "efficacy" of protection from reinfection—the difference in proportion of incident infections between the negative and positive cohorts relative to the proportion observed in the negative cohort. We pooled these estimates via meta-analysis, both unstratified and stratified by population composition (whether general population, health care workers only, young adult individuals only, or elderly individuals only), to obtain combined effect estimates and corresponding 95% confidence intervals. The empirical Bayes random-effects meta-analysis model[18] was chosen for its robustness properties and low bias in small-sample settings.[19] Study heterogeneity within strata was assessed using the I^2 statistic.[20] We assessed heterogeneity across strata using Cochran's Q_b statistic.[21] Analysis was performed using Stata version 16.1 (*Stata Statistical Software: Release 16*; StataCorp LLC, College Station, TX), in particular the *meta* family of commands for meta-analysis. See Appendix A for further details.

For some factors that varied within studies, or were specific to certain studies (including demographic variables, symptom status, health behaviors, vaccination, and genetic variants), we were unable to examine their quantitative impact on effect sizes within a meta-analytic framework due to inconsistent reporting among studies. We abstracted information from study-specific sensitivity analyses and regression analyses when available and summarize these findings qualitatively.

We graded the strength of evidence (SOE) to describe our confidence in effect estimates as high, moderate, low, and insufficient evidence. The assessment is based on our analysis of the study limitations, directness, consistency, precision, dose-response, plausible confounding, and strength of association (see Appendix B for more details).[22] We used the same domains to grade the strength of evidence for age, baseline comorbidities, and other factors listed in Key Questions 2a and 3a that may influence effect estimates.

Results

Overview of studies

The updated literature search identified 400 citations (Appendix B – Figure B-1). We identified 18 eligible cohort studies (including two preprints) that provided estimates of the risk of reinfection relative to uninfected individuals. Two other included preprints[23, 24] are synthesized only narratively because they lacked the data needed for our meta-analysis. No studies included in our original review were eligible for this update. The total positive cohort

n=465,206 and the total negative cohort n=12,505,204. Most included studies were of moderate to high quality. (Appendix B – Table B-3).

Four studies were conducted in the United States,[23, 25-27] five in the United Kingdom,[9, 28-31] two in Italy,[32, 33] and one each in Austria,[34] Denmark,[35] France,[36] Qatar,[37] Switzerland,[38] Israel,[24] and Scotland.[39] The studies were methodologically diverse. For example, four studies only used PCR to assign patients to the "positive" cohort,[27, 32, 34, 35] four used PCR or serology testing,[9, 25, 29, 36] and nine used serology only. Similarly, during the follow-up period, diagnostic method variations included scheduled PCR testing according to a protocol (versus detection in usual care); confirmation of PCR results by seroconversion and clinical adjudication (versus PCR alone); and classification of cases as "likely," "probable," and "suspected" (versus no classification). (Appendix B – Supplemental Excel Table B.1)

Risk of reinfection (Key Question 2)

Symptomatic and all reinfections

In our meta-analysis, prior infection reduced the risk of infection by 87% (95% confidence interval 84%-90%) compared with uninfected individuals (High SOE – Appendix Table B-4). The protection for health care workers was similar to that of general populations (87% vs. 88%, respectively, Figure 1). Overall, there was no compelling evidence that population characteristics—whether the cohort was comprised of mostly young or old individuals, or enriched with health care-setting exposures or not—influenced the degree of protection afforded by prior infection ($Q_b(3) = 5.63$; $p = 0.13$), which was substantial in all settings (87% estimated efficacy overall). Across studies, estimates for young (median age ~20) and older adults (median age ~85) were also qualitatively similar (82% for young vs. 92% for old), although for both estimates there were few studies and sample sizes for the available studies were not large. Study-level heterogeneity in effect size was substantial (I^2 = ~85%), but this value should be interpreted in the context of the very large sample sizes and low overall absolute counts of reinfection. The effect sizes all fall within a narrow and high range, varying between 80% protection at minimum to ~100% at maximum, and are always indicative of very high protection, comparable to what has been reported for the vaccines currently in use in similar populations.[9, 24, 40] There may be substantial heterogeneity of effect sizes *within* this range, but the practical takeaway is that protection is always high in our included studies, regardless of variation in study methods and populations. Figure 1 summarizes these findings. (An alternative version excluding preprints is available in Appendix C).

All included studies found that reinfection was an uncommon event (range 0 to 2.2%). The highest reinfection proportion, 2.2%, was in a college student population; the control group risk of infection was also very high (12.1%).[25] In settings with high proportions of control group infection (10% or above), reinfection rates were also relatively high (approximately 1% to 2%). When control group incidence of infection was below 5%, reinfection incidence was relatively low (about 0.7% at most). The anomaly was in long-term care facilities, where despite very high control group incidence (20.4% and 37.5%), reinfection rates were low (1.8% and 0, respectively). This anomaly may be partially explained by increased adherence to preventative measures for previously infected individuals.

Asymptomatic reinfections

Twelve studies reported the proportion of asymptomatic reinfections.[9, 23, 25, 27, 28, 30, 32, 33, 36-39] Prior infection clearly protects against asymptomatic reinfection. This proportion ranged from 0%-100%, but absolute counts were often low (range 1-155 cases), and study follow-up methods were not always adequate to accurately detect symptoms that were present at the time of, or in the weeks after, a positive PCR test. The SARS-CoV-2 Immunity and Reinfection Evaluation (SIREN) study, a well-designed study of health care workers in the U.K., had the highest number of reinfections (155) as well as the most reliable method to detect asymptomatic ones.[9] It found that 49% of reinfections were asymptomatic, versus 20% of incident infections in the negative cohort.

Across studies, prior infection clearly protected against asymptomatic reinfections, but whether this protection is as strong as it is for symptomatic reinfection is unclear. In the SIREN study, primary infection protected against both symptomatic and asymptomatic infections, but the degree of protection was different (93% lower risk of symptomatic COVID-19 reinfection versus 52% lower risk of asymptomatic reinfection.)[9] In contrast, in a US-based retrospective cohort study (Sheehan et al), protection against symptomatic infections was 84.5% for symptomatic infections vs. 81.8% when asymptomatic infections were included.[27]

Severity of symptomatic reinfection

Six studies provided information about the severity of symptomatic reinfections, but four of them described five or fewer cases.[28, 32, 33, 38] In the largest series, Sheehan et al, 31 patients had symptomatic reinfection.[27] While 18 of them were hospitalized within 30 days of the positive PCR test, only five had COVID-19 symptoms at the time of hospitalization and none of them required intensive care. In the other relatively large series, a study from Austria, five cases were described as moderate and 27 as mild.[34] The scarcity of data reflects the fact that, because prior infection prevented 80% or more symptomatic reinfections, severe reinfection is a rare event.

Figure 1. Risk of reinfection after primary infection from SARS-CoV-2 with a median follow-up time of 8 months (range 4-13 months)

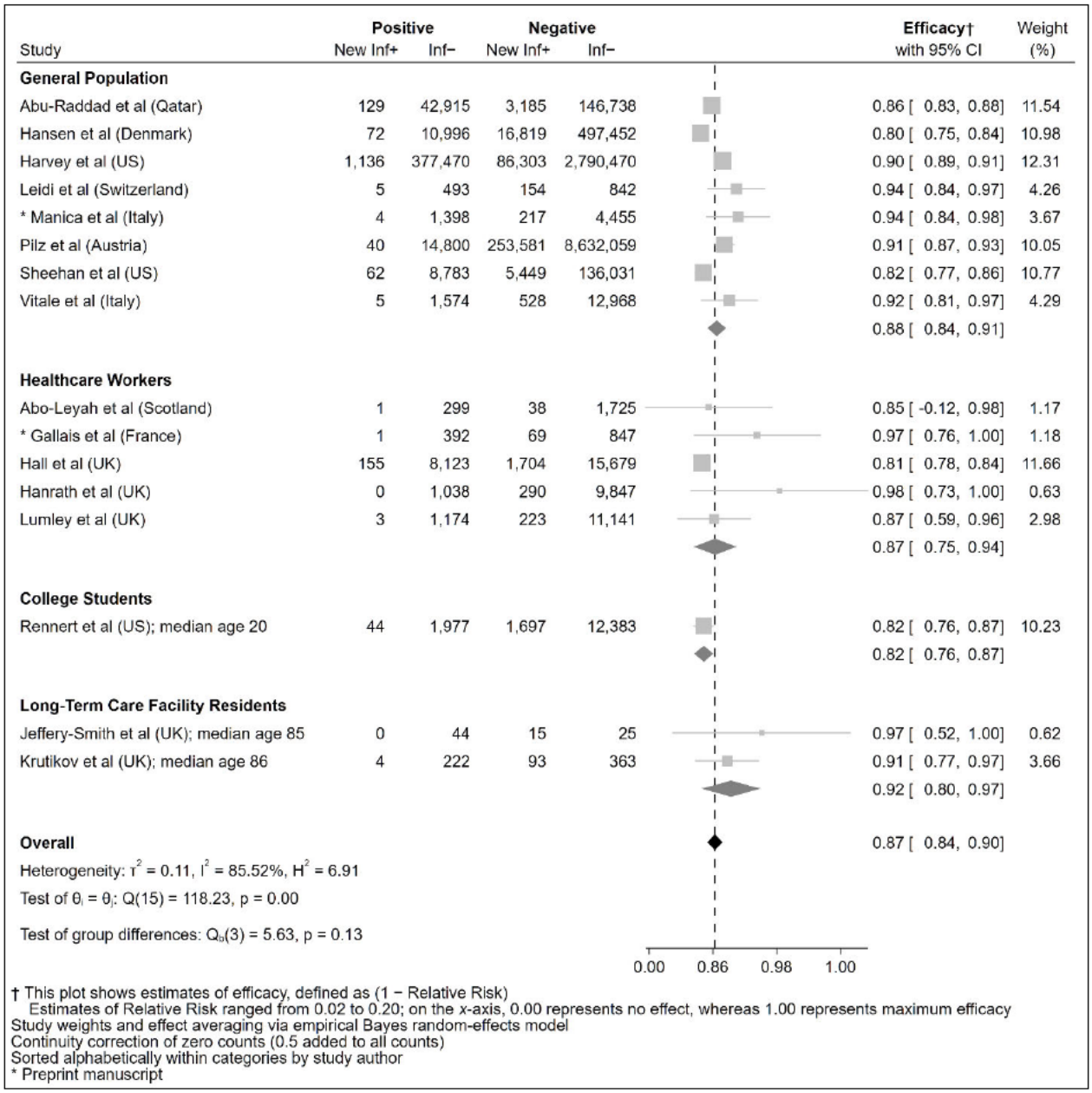

***Figure legend**: Positive indicates the group within a study where participants were PCR positive or seropositive at baseline. Negative indicates those within a study who were PCR negative and/or seronegative at baseline. Efficacy (1 – RR) can be interpreted as the proportion or percentage of infections that are prevented by the exposure. Median follow-up time was 8 months (range 4 to 13 months).*

Population and methodological factors affecting the risk of reinfection

We conducted analyses of six additional factors that might affect reinfection risk, but which vary among studies because best practices for studying SARS-CoV-2 reinfection are not

established. Study duration, waiting interval, median age of participants, underlying prevalence, inclusion of asymptomatic people in the positive cohort, and tests used to allocate people to the two cohorts did not appear to have a strong relationship with the estimated effect size (see Appendix C – Figure C-2). In our judgment, variation in these features of study design and conduct did not have a substantive influence on the estimates of efficacy. Protection against reinfection was only slightly lower in studies that used the most reliable methods to ascertain and characterize reinfections.[9, 35]

Some studies reported their own sensitivity analyses or mathematical modeling of the impact of these methodological factors.[9, 23, 28, 30, 35, 38] Overall, protection against reinfection was not correlated with the asymptomatic testing rate, cohort assignment criteria, or method for assessment of infection during the follow-up period.[9, 30, 38] Appendix Table B-5 summarizes findings and overall confidence rating for additional factors that may affect reinfection.

Baseline Factors

Age, sex, and race

In the Denmark study, there was no difference in the estimates of protection against repeat infection by sex, but there was a striking difference in protection against repeat infection in the elderly.[35] Among individuals aged 0 to 64 years, estimated protection was 80% to 82%, whereas in individuals over age 65, it was 47.1% (CI 24.7%-62.8%). Among those over age 65 who had a previous infection, the infection rate was 8.01 per 100,000 person-days of follow-up compared with 4.25 to 5.92 per 100,000 person-days in the younger age groups. However, in the negative control cohort, the infection rate in the elderly was much lower than it was in the younger groups (16.92 per 100,000 person-days versus 27.42 to 38.13 in the younger groups.) The low infection rate in the elderly controls relative to other controls could be related to public health approaches to opening up after lockdown (perhaps, selective isolation of more vulnerable groups), but this explanation does not account for the relatively high rate of reinfection in the positive cohort. Another study in Switzerland found a higher risk of reinfection among those older than 60 years old compared with those younger (>60 years old hazard ratio=0.44, 95% CI:0.14-1.4; <60 years old hazard ratio=0.05, 95% CI:0.01-0.20).[38] The study in Israel compared protection among age groups and found a slight decrease in the protection conferred by natural immunity for those greater than 80 years of age (overall protection: 94.8%, 95% CI 94.4-95.1; over 80 protection: 91.4%, 95% CI 85.5-94.9).[24]

These findings on age are in conflict with studies of presumably frail elderly patients in long-term care facilities, where rates of infection in the control groups were far higher, and rates of reinfection in the positive groups were as low as, or lower than, other populations (see Figure 1).[30, 31]

Studies offered very little information about the effect of race and ethnicity on protection from reinfection. Of the four U.S.-based studies, two did not mention race.[25, 27] A third stated that race and ethnicity had been deleted from the aggregated health system dataset before analysis to prevent Health Insurance Portability and Accountability Act (HIPAA) violations.[26] The fourth, a preprint, reported adjustment for race but has not yet reported the regression results.[23] The European studies had low proportions of individuals identified as Black, Hispanic, or Asian, whereas the largest US studies did not report results by race or ethnicity.

Immunocompromised patients and other comorbidities

While some studies adjusted for immunosuppression or other comorbidities, none reported on the incidence of reinfections in these subgroups. We expected to find registry studies of risk of reinfection in immunosuppressed patients but did not.

Initial antibody levels

Eleven studies provided information about the antibody response to the initial infection.[9, 23, 26, 28-31, 36-39] Additional analyses from these cohorts may shed light on the relationship of the initial antibody response or the persistence of antibodies to protection against reinfection. Seven studies did not include analyses of the antibody response.[25, 27, 30, 32-35]

Severity of initial infection

Assessments of the relationship between the severity of the initial infection and protection against reinfection were limited. In most studies, initial infections were not detected until antibodies had formed, and information about symptoms were either not recorded or were subject to recall bias. Hospitalization during the initial infection could also be a proxy for severity, but in most studies the number of hospitalized patients was too small for analysis. Comparing studies that used sampling methods that detected people with no or mild symptoms[28, 32, 36, 38, 39] with those that recruited only symptomatic people[26, 27, 29, 34] did not reveal a clear relationship between the recruitment method and protection against reinfection.

Variants

Currently, the U.S. Centers for Disease Control and Prevention (CDC) identifies six "variants of concern," defined as "variants for which there is evidence of an increase in transmissibility, more severe disease (e.g., increased hospitalizations or deaths), significant reduction in neutralization by antibodies generated during previous infection or vaccination, reduced effectiveness of treatments or vaccines, or diagnostic detection failures."[41] In July, 2021, the Delta variant became the dominant strain among new infections in the US.

The Alpha variant was studied in some of the studies we reviewed. While evidence is sparse, there is no indication of increased risk of reinfection for this variant. In the SIREN study, a cohort study of health care workers in the U.K., an increased prevalence of the Alpha variant, which accounted for most infections during the follow-up period, did not affect risk of reinfection.[9] Of two additional studies that reported on the Alpha variant, neither indicated an effect of the variant on reinfection.[24, 30] In an ecologic study among 36,920 U.K. users of the COVID-19 Symptom Study app, the rate of "possible reinfection" was 0.7 and did not change after the Alpha variant became prevalent.[42] The remaining fifteen studies included within our review did not include analyses of variants.[23, 25-36, 38, 39]

These results do not, of course, rule out the possibility that another variant of concern could evade natural immunity. None of the studies evaluated the Delta variant. In this regard, the rapidly changing variant causing outbreaks in Brazil is considered to be the most concerning.[43] A study from Brazil suggested higher reinfection risks due to variants, but was not included in our review because it reported increasing antibody levels instead of seroconversion or a positive PCR test as a possible signal for reinfection.[11]

Vaccination

An important clinical question is whether vaccination reduces risk of reinfection in those who have had an infection. No studies addressed this question. Only four studies reported on vaccinations in their sample populations, and none reported the impact of vaccination on risk of reinfection.[9, 24, 30, 36] In the SIREN study, 13,401 participants were vaccinated during the follow-up period, but follow-up after vaccination was too short to assess the protective effect of previous infection and vaccination separately.[9] The remaining 14 studies did not include vaccinated individuals within their study population.[23, 25-29, 31-35, 37-39] Because prior infection and vaccination both provide strong protection against infection, large sample sizes would be needed to determine whether vaccination augments protection from prior infection.

Concordance with risk of reinfection in uncontrolled studies

Studies that followed a group of infected patients but did not compare their outcomes with those of a control group (Appendix Table B-5) used large databases to make crude estimates of reinfection risk. For example, an abstract of an analysis from the Epic Health Research Center found that 4 per 1,000 individuals who had an initially positive PCR had another positive PCR 90 or more days later.[38] In an analysis using a dataset from 62 U.S. health systems that use a Cerner EHR, the criteria for reinfection were a positive PCR test followed by at least two negative PCRs, and then a positive PCR test at least 90 days after the initial positive PCR test.[14] A large proportion of patients in the dataset were excluded from the analysis due to lack of serial tests. A total of 63 (0.7%) of 9,119 patients had a reinfection. In this analysis, reinfection was associated with pre-existing asthma (odds ratio [OR] 1.9, 95% CI 1.1-3.2) and nicotine dependence/tobacco use (OR 2.7, 95% CI 1.6-4.5), but not with age. Among reinfected individuals, 37% were white, 16% were African American, and 25% were Hispanic, versus 36.1%, 17.7%, and 34.3%, respectively, among patients without reinfection.

Duration of protection (Key Question 3)

Eight studies[27, 30, 34-39] that included over 9 million participants in total (80,206 exposed, 9,696,466 control) examined whether the risk of reinfection varies over time. All eight found no evidence of waning protection during 6 to 13 months of follow-up. Further, two of the studies noted that the protection against reinfection may have increased over time.[27, 37] Sheehan et al. found that 6 months after primary infection, protection against symptomatic disease increased from 84.5% for all time points to over 90% for events at >6 months.[27] Abu-Raddad et al. saw incidence rates of reinfection slightly decreasing over time, implying increased protection over time, though this may alternately be explained by national population-level decreases in infection incidence rates during that time period.[37] Appendix Table B-7 summarizes findings for duration of protection against reinfection findings by study.

At present, these studies have not reported extensively on factors that could affect the duration of protection, partly because, within the range of follow-up durations that have been studied, late reinfection is a rare event. These results could change dramatically as the studies report longer follow-up times.

Statements From Public Health Organizations

The CDC states that, based on experience with other human coronaviruses,

> "*...the probability of SARS-CoV-2 reinfection is expected to increase with time after recovery from initial infection because of waning immunity and the possibility of exposure to virus variants.... The risk of reinfection may be increased in the future with exposure to SARS-CoV-2 variant virus strains that are not neutralized by immune antisera, such as one recently described in South Africa.... The risk of reinfection also depends on the likelihood of re-exposure to infectious cases of COVID-19. Continued widespread transmission makes it more likely that reinfections will occur.*"[15]

The World Health Organization (WHO) does not have a recent statement about reinfection.

Future Research, and Ongoing Studies

Longer follow-up from the included studies should assess whether protection lasts for periods longer than 7 to 10 months, whether variants that were not prevalent in current studies can evade natural immunity, and whether vaccination adds significant protection among individuals who have been infected. Additional studies are needed to address protection against reinfection is in the young, in the elderly, in patients who tested positive for SARS-CoV-2 but had no symptoms, and in immunocompromised patients and those with other comorbidities.

The populations studied to date are also relatively homogenous racially, ethnically, and geographically. Analysis of larger, more diverse cohorts of previously infected individuals could help verify whether the estimates of reinfection rates we found are applicable in other populations, social circumstances, and settings.

Ongoing studies of immune responses and risk of reinfection (Appendix D) may address some of these gaps. Three of these studies are examining COVID-19 survivors under the age of 18, contributing to the substantial knowledge gap in pediatric populations. Additionally, three studies will include groups of vaccinated individuals in their cohorts.

Discussion

The findings provide strong evidence that the natural immunity afforded by previous infection reduces the risk of both symptomatic and asymptomatic SARS-CoV-2 infections for at least 7 months (see Appendix Table B-4 for SOE assessment). The evidence for an overall effect is consistent and the effect sizes are too large to be accounted for by biases. In the evidence we reviewed, most investigators described their decision-making regarding study methods, and many conducted sensitivity analyses or alternative cohort analyses to minimize error and detect biases that are inherent in studying natural immunity.

Nevertheless, it is not clear that they overcame every challenge. With respect to cohort composition, no feasible study design can ensure that—within the target population—all infected individuals, regardless of symptoms, are identified and allocated appropriately, or that exclusions of individuals who lacked required tests for allocation would not bias the results. Most studies did not perform protocolized follow-up testing designed to capture all incident infections and

reinfections. While widely used in the literature, the term "asymptomatic infection" and "asymptomatic reinfection" are poorly defined, and methods to distinguish symptomatic reinfections from virological recurrence without clinical evidence for infection were problematic.[44] Study methods and knowledge of SARS-CoV-19 are not sufficiently developed to distinguish which people with "asymptomatic infections" are "presymptomatic" on the one hand, or "colonized" on the other.

None of the studies could account directly for the behavioral and occupational variables that affect infection risk and might well be unevenly distributed between the positive and negative cohorts. It is also possible that a group of people at higher reinfection risk, perhaps because they engaged in much riskier behavior than most people, were less likely to be recruited, perhaps because they avoided the testing that would make them eligible and countable in these studies. While possible, this and other scenarios that can be imagined seem unlikely and would require that all of the studies suffered from large, undetected confounding.

Of less concern, but worth noting, results do not address protection conferred by a first infection that occurred between or after high incidence surges. Many of the studies measured reinfections as new cases happening within the second pandemic wave in a particular geographic location. This approach avoids the time confounding that might exist should cases have been considered continuously. That is, because public health restrictions, variants, and other potential confounders changed frequently over time, no study could reasonably account for these changes analytically in continuous time. This means that the degree of protection afforded by natural immunity between waves has not been thoroughly studied.

The results may also be difficult to apply when there is uncertainty about how much time has elapsed since initial infection, as is often the case in clinical practice. Also, as the vast majority of timepoints included in studies were prior to the Emergency Use Authorization of any vaccines in late 2020, the results may also be less applicable in populations with high vaccination rates.

All the included studies were conducted in highly developed countries and our findings may not be as applicable to less developed countries where exposures may differ due to preventative public health measures not being as widespread or feasible. It is reassuring that the results apply to frail individuals residing in long-term care facilities, but results may also be less applicable to groups that were not well-represented in the studies, especially immunocompromised patients.

Despite these concerns, the findings provide strong evidence that the natural immunity afforded by previous infection confers strong protection against reinfection for at least 7 months.

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Abbreviations

ACP	American College of Physicians
AHRQ	Agency for Healthcare Research and Quality
CDC	Centers for Disease Control and Prevention
EHR	Electronic health records
HIPPA	Health Insurance Portability and Accountability Act
JBI	Joanna Briggs Institute
PCR	Polymerase Chain Reaction
RT-PCR	Reverse transcription polymerase chain reaction
SIREN	SARS-CoV-2 Immunity and Reinfection Evaluation
SOE	Strength of Evidence
WHO	World Health Organization

Appendices

APPENDIX A: Methods

Deferred Key Questions

Key Question 1. What are the prevalence, levels, and durability of anti-SARS-CoV-2 antibodies among adults infected with or recovered from SARS-CoV-2 infection confirmed by RT-PCR or by clinical presentation plus serologic testing?

> a) Do the levels and durability of detectable antibodies vary by patient characteristics (e.g., age, sex, race/ethnicity, and comorbidities), presence of symptoms, or as measured by different types of immunoassays?

Key Question 4. What are the consequences of conducting clinically indicated testing for anti-SARS-CoV-2 antibodies? (e.g., abandoning public health safety practices due to misconception that detectable antibodies are indicative of immunity against reinfection)

Search Strategy

The searches included free-text words related to COVID-19, SARS-COV-2, reinfection, and immunity. This updated review's search strategy changed from its previous iteration to mirror the strategy described in Hansen et al's SARS-Cov-2 publication.[35]

The reference lists of relevant existing systematic reviews were scanned to identify additional eligible studies. We also monitored the University of Washington's Alliance for Pandemic Preparedness COVID-19 Literature report weekly.[45] Additional articles suggested to us from any source, including peer and public review, were screened applying identical eligibility criteria.

Ovid MEDLINE ALL 1946 to July 1st, 2021

Date searched: July 1st, 2021

1 ("SARS-CoV-2" or "COVID-19" or "COVID" or "coronavirus").mp. (137407)

2 reinfection.mp. (8500)

3 immunity.mp. (306602)

4 and/1-3 (142)

Ovid Medline Syntax
.mp = Multi-purpose field (searches title, original title, abstract, subject heading, name of substance, and registry word fields)

WHO COVID (https://search.bvsalud.org/global-literature-on-novel-coronavirus-2019-ncov/)

Date searched: July 1st, 2021

tw:((tw:("SARS-CoV-2" OR "COVID-19" OR "COVID" OR coronavirus)) AND (tw:(reinfection)) AND (tw:(immunity))) AND db:("COVIDWHO") (36)

ClinicalTrials.org (https://clinicaltrials.gov/ct2/results?show_xprt=Y&xprt=reinfection+AND+immunity+AND+AREA%5BConditionSearch%5D+%28+SARS-CoV-2+OR+COVID-19+OR+COVID+OR+coronavirus+%29)

Date searched: July 1st , 2021

reinfection AND immunity AND AREA[ConditionSearch] (SARS-CoV-2 OR COVID-19 OR COVID OR coronavirus) (16)

COVID19reviews.org (https://www.covid19reviews.org/)

Date searched: July 1st, 2021

reinfection OR immunity (1)

Study Selection

Title and abstract screening was completed by a single screener and exclusion decisions confirmed by a second screener. Full-text screening was completed by two reviewers and any conflicts resolved by a third independent reviewer. The JBI Checklist for cohort studies was used as an additional level of screening. Consensus was required for exclusion reasons and any conflicts were resolved by a third independent reviewer.

Table A-1. Study selection criteria

PICOTS	Inclusion and Exclusion Criteria
Population	**Include**: **KQs 1-4**: Adults with documented COVID-19 infection compared with a concurrent control group. Index infection can be determined by RT-PCR or serologic testing for SARS-CoV-2 in the setting of a wave or outbreak of COVID-19. **Exclude**: Children less than 18 years of age.
Outcomes	**Include:** **KQ 1:** • Length of time anti-SARS-CoV-2 antibodies remain detectable. **KQ 2:** • Incidence of re-infection. Primary outcome is clinical re-infection; secondary outcomes are any reinfection and severity of reinfection. Re-infection is determined through either: o Genomic sequencing; o A repeat positive RT-PCR test result 45 or more days following negative RT-PCR testing; or o Positive RT-PCR test result 45 or more days following detection of anti-SARS-CoV-2 antibodies **KQ 3:** • Duration of immunity (i.e. length of time between an initial RT-PCR-confirmed or clinically diagnosed SARS-CoV-2 infection following documented clinical recovery to a repeat SARS-CoV-2 infection) **KQ 4:** • Unintended consequences of antibody testing after SARS-CoV-2 infection (*e.g.,* discontinuation of recommended safety practices such as wearing masks or social distancing due to misinterpretation of positive antibody test results as indicative of immunity) We will stratify outcomes by the following factors: • Patient characteristics (i.e. age, gender, race/ethnicity, comorbidities) • Severity of COVID-19 infection (i.e. mild, moderate, severe, and critical as defined in NIH COVID-19 treatment guidelines)[46] • Presence of symptoms (asymptomatic or symptomatic) • How reinfection or suspected reinfection was defined (genetic testing, repeat positive RT PCR, serologic testing)
Eligible study designs	**Include:** **KQs 1-3**: Large, population-based observational (cohort or case-control) studies. Systematic reviews that meet criteria for timeliness, relevance, and quality. **KQ4:** None at present. **Exclude:** Observational studies without an uninfected comparison group; case series, case reports, editorials, non-systematic reviews. For KQ1 we excluded non-peer reviewed articles. For KQ2-3, we excluded non-peer reviewed articles that failed pass a methodological screen.
Study settings	**Include**: Studies in the general population and settings of increased exposure rates (health care workers, communal living situations such as college dormitories or military barracks) **Exclude**: Studies in specific settings that don't have increased exposure rates

Data Abstraction

Data was abstracted by a single reviewer and verified by a second reviewer. Any discrepancies were resolved verbally, and any conflicts were resolved by a third independent reviewer. We classified studies into two groups based on whether primary infection status at group assignment included symptomatic people only or any infection event. Those classified as 'symptomatic only' included studies where people were only able to be recruited if they presented to a clinic with symptoms seeking a test. Those classified as 'any infection event' included studies where recruitment was done with some sort of surveillance screening not based on symptoms.

Statistical Analysis

Each included study provided counts of reinfected individuals from the positive cohort and newly infected individuals from the negative cohort, which together yield an estimate of "efficacy" of protection from reinfection — the difference in proportion of incident infections between the negative and positive cohorts relative to the proportion observed in the negative cohort. This estimate is formally one minus the relative risk (RR); i.e., efficacy = 1 – RR. We pooled these estimates via meta-analysis, both unstratified and stratified by population composition (whether general population, health care workers only, young adult individuals only, or elderly individuals only), to obtain combined effect estimates and corresponding 95% confidence intervals both for each population type and overall.

As a sensitivity analysis, we fitted the meta-analytic model with preprint studies excluded. We also performed a version of the meta-analyses stratified by cohort type, beginning with healthcare worker status, to assess the influence this characteristic may have had. We performed similar stratifications over studies observing very young (college-age) and very old (elderly-care facility resident) cohorts. We identified several other study-level factors that might influence estimates of efficacy, including study duration, length of waiting interval between reinfection assessments, median age of participant, underlying prevalence (proxied by the proportion of new infections in the negative cohort), and rigor in assessing positivity of infection (whether asymptomatic infections were identified by surveillance, whether validation testing was performed, etc.). We were unable to incorporate these in the meta-analytic model but plotted each factor against the effect sizes to visually assess association. Smooth regression lines were calculated using mean smoothing via nonparametric kernel regression (default Epanechnikov kernel) with bandwidth chosen empirically (see Appendix C).

Control for demographic characteristics and other confounders varied across studies, and studies additionally differed by whether they reported rates adjusted for person-time under observation or simply reported infection proportions. In the interest of robustness and simplicity of interpretation, we opted to ignore study-level adjustments and instead meta-analyze the crude proportions observed over the study period, however long or short, for each study. In a similar vein, we did not consider person-time to be a coherent normalization for this question because of its strong assumption of constant hazard and its population-level rather than person-level orientation. Rates of infection by unit person-time are appropriate for predicting the number of events showing up in a population registry but not directly predictive of individual risk in this context because a first exposure changes the nature of subsequent observation and the probability

of subsequent exposure. Our interest is primarily in how many of the previously infected are spared subsequent infection, on average across unknown and varying levels of exposure over sufficiently long durations to be relevant for public health policy. Ratios of crude proportions are the best fit for addressing this question. Note, however, that most of the studies considered in this report published efficacy rates that were both weighted by person-time and adjusted for individual-level and cohort-level factors that may affect infection risk (such as age, socioeconomic conditions, seasonal changes in prevalence, changes to public policy, and so on). Results were reported variously as hazard ratios, odds ratios, relative rates, or adjusted incidence rate ratios. Despite the variety of metrics and adjustment models chosen to quantify the degree of protection afforded, the concordance between our crude proportions and the corresponding adjusted efficacy rates variously reported by the studies was >0.85 by Lin's concordance coefficient,[47] suggesting a broad-based robustness to these adjustments.

A random effects meta-analysis model was chosen because it explicitly estimates a between-study component of variance in addition to pooling the within-study estimates of variance provided by each study, and we employed the empirical Bayes (aka Paule-Mandel) estimator for between-study variance. (An exhaustive recent comparative review[19] of the performance of alternative estimators of between-study variance in the meta-analytic context concluded that the empirical Bayes estimator has lower bias on average than the other alternatives, particularly the popular DerSimonian-Laird and REML estimators, while maintaining good properties such as robustness of estimation under small sample sizes and violations of distributional assumptions, and also has less variance than many alternative estimators.) Study heterogeneity within strata was assessed using the I2 statistic, which estimates the fraction of total outcome variance that can be attributed to fundamental differences in effect estimates between studies as opposed to within-study sampling variance. Study heterogeneity across strata was assessed using Cochran's Qb statistic, which follows a chi-squared distribution (degrees of freedom = #subgroups – 1) and uses a null hypothesis that stratum-specific estimates do not differ. Some additional measures of heterogeneity ($\tau 2$,[21] the model-based estimate of between-study variance, and H2, the ratio of total variance to pooled within-study variance[48]) and a standard test (Cochran's Q) of overall homogeneity are provided on forest plots.[49] Cochran's Q has a chi-squared distribution (degrees of freedom = #studies – 1) under the null hypothesis that all study-specific effect sizes are equal to the mean effect size across studies.

Analysis was performed using Stata version 16.1 (Stata Statistical Software: Release 16; StataCorp LLC, College Station, TX), in particular the meta family of commands for meta-analysis.

APPENDIX B: Results

See supplemental Excel files:

Table B.1 – Observational studies examining reinfection for those with SARS-CoV-2

Figure B-1. PRISMA flow diagram

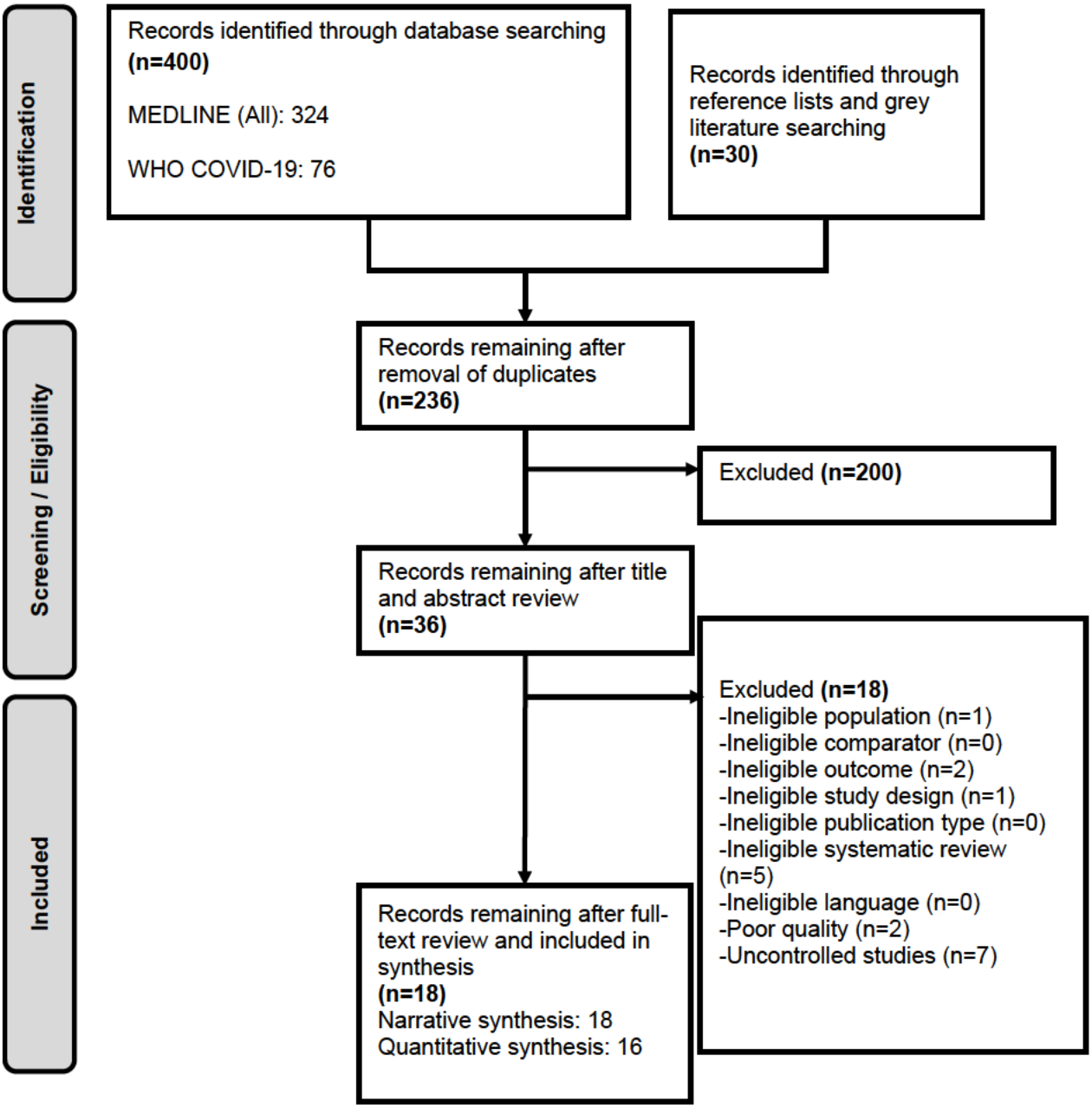


Table B-2. Joanna Briggs Institute cohort checklist used in study screening

Author, Year	1	2	3	4	5	6	7	8	9	10	11
Abo-Leyah, 2021[14]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Abu-Raddad, 2021[37]	Y	Y	Y	Y	Y	Y	Y	Y	U	U	Y
Finch, 2021[23]	Y	Y	Y	Y	Y	Y	Y	Y	Y	U	Y
Gallais, 2021[36]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Goldberg, 2021[24]	Y	Y	Y	Y	Y	Y	Y	Y	Y	U	Y
Hall, 2021[9]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Hanrath, 2021[29]	Y	N	Y	Y	N	Y	Y	Y	N	Y	U
Hansen, 2021[35]	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y
Harvey, 2020[26]	Y	N	Y	Y	N	Y	Y	Y	Y	N	Y
Jeffery-Smith, 2021[31]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Krutikov, 2021[30]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Leidi, 2021[38]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Letizia, 2021[12]	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	Y
Lumley, 2021[28]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Manica, 2021[33]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Pilz, 2021[34]	Y	N	Y	N	N	Y	Y	Y	Y	NA	Y
Prete, 2021[11]	U	N	N	Y	Y	Y	N	Y	Y	NA	Y
Rennert, 2021[25]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Sheehan, 2021[3]	Y	N	Y	Y	Y	Y	Y	Y	Y	U	Y
Vitale, 2021[32]	Y	U	Y	Y	Y	Y	Y	Y	Y	Y	Y

Abbreviations: N= no; NA= not applicable; U= unclear; Y= yes. Shaded rows=excluded.

Criteria (From the Joanna Briggs Institute Checklist for Cohort Studies[10]):

1. Were the two groups similar and recruited from the same population?
2. Were the exposures measured similarly to assign people to both exposed and unexposed groups?
3. Was the exposure measured in a valid and reliable way?
4. Were confounding factors identified?
5. Were strategies to deal with confounding factors stated?
6. Were the groups/participants free of the outcome at the start of the study (or at the moment of exposure)?
7. Were the outcomes measured in a valid and reliable way?
8. Was the follow up time reported and sufficient to be long enough for outcomes to occur?
9. Was follow up complete, and if not, were the reasons to loss to follow up described and explored?
10. Were strategies to address incomplete follow up utilized?
11. Was appropriate statistical analysis used?

Table B-3. Risk of bias and overall study quality ratings

Author	Sampling risk of bias	Cohort allocation risk of bias	Outcome ascertainment risk of bias	Outcome classification risk of bias	Risk of Bias overall rating	Study Quality Rating
Abo-Leyah[39]	Low	Low	Moderate	Moderate	Low	High quality
Abu-Raddad[37]	Low	Moderate	Moderate	Moderate	Moderate	Moderate quality
Finch[23]	Low	Moderate	Moderate	Moderate	Moderate	Moderate quality
Gallais[36]	Low	Low	Low	Moderate	Low	High quality
Goldberg[24]	Low	Low	Low	Moderate	Low	High quality
Hall[9]	Low	Low	Low	Moderate	Low	High quality
Hanrath[29]	Moderate	Low	Moderate	Moderate	Moderate	Moderate quality
Hansen[35]	Low	Low	Moderate	Moderate	Low	High quality
Harvey[26]	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate quality
Jeffery-Smith[31]	Low	Low	Low	Moderate	Low	High quality
Krutikov[30]	Low	Moderate	Low	Low	Low	High quality
Leidi[38]	Low	Moderate	Moderate	Low	Low	High quality
Lumley[28]	Low	Moderate	Low	Moderate	Low	High quality
Manica [33]	Low	Moderate	Moderate	Moderate	Low	High quality
Pilz[34]	Moderate	Serious	Moderate	Moderate	High	Poor quality
Rennert[25]	Low	Low	Low	Low	Low	High quality
Sheehan[27]	Moderate	Low	Moderate	Moderate	Moderate	Moderate quality
Vitale[32]	Low	Low	Moderate	Low	Low	High quality

Table B-4. Strength of evidence assessments for the statement "prior infection reduces the risk of both symptomatic and asymptomatic reinfections for at least 7 months" (KQ2 and KQ3) *

Outcome	N Studies, N total cohort	Study Limitations	Directness	Precision	Consistency	Dose Response	Plausible confounding	Strength of Association	Strength of Evidence
Risk of reinfection	**18 studies; N= 12,968,006** Abo-Leyah 2021,[39] Abu-Raddad 2021,[37] Finch 2021,[23] Gallais 2021,[36] Goldberg 2021,[24] Hall 2021,[9] Hanrath 2021,[29] Hansen 2021,[35] Harvey 2021,[26] Jeffery-Smith 2021,[31] Krutikov 2021,[30] Leidi, 2021,[38] Lumley 2020,[28] Manica, 2021,[33] Pilz 2021,[34] Rennert 2021,[25] Sheehan 2021,[27] Vitale 2021[32]	Moderate	Direct	Precise	Consistent	Undetected	Present	Strong	**High**

*This statement refers to the pooled estimate of efficacy of 87% (95% confidence interval 84%-90%). For this estimate, strength of evidence is low for 7-10 months and insufficient for >10 months.

Table B-5. Overall confidence assessments and narrative summary statements for additional factors that may impact the risk of reinfection

Additional factors that may impact risk of reinfection	N Studies, N total cohort	Narrative summary statement	Overall confidence rating
Initial antibody levels	**11 studies; N= 3,241,686** Abo-Leyah 2021,[39] Abu-Raddad 2021,[37] Finch 2021,[23] Gallais 2021,[36] Hall 2021,[9] Hanrath 2021,[29] Harvey 2021,[26] Leidi 2021,[38] Lumley 2020,[28] Krutikov 2021,[30] Jeffery-Smith 2021,[31]	Very uncertain about how initial antibody levels could impact reinfection. Subsequent update will aim to fill this gap.	**Insufficient**
Age	**5 studies; N= 529,105** Hansen 2021,[35] Krutikov 2021,[30] Jeffery-Smith 2021,[31] Leidi 2021,[38] Goldberg 2021,[24]	Overall, it is more likely that protection for elderly individuals and younger adults is similar, but additional evidence is needed to resolve the issue.	**Low**
Gender	**18 studies; N= 12,968,006** Abo-Leyah 2021,[39] Abu-Raddad 2021,[37] Finch 2021,[23] Gallais 2021,[36] Goldberg 2021,[24] Hall 2021,[9] Hanrath 2021,[29] Hansen 2021,[35] Harvey 2021,[26] Jeffery-Smith 2021,[31] Krutikov 2021,[30] Leidi, 2021,[38] Lumley 2020,[28] Manica, 2021,[33] Pilz 2021,[34] Rennert 2021,[25] Sheehan 2021,[27] Vitale 2021[32]	Both males and females were adequately represented in the cohorts, and effects for both were large and consistent.	**High**
Race/Ethnicity	**1 study; N= 4,411** Finch 2021[23]	Blacks were under-represented in the cohorts, and the impact of race on risk of reinfection is uncertain.	**Insufficient**
Comorbidities	**0 studies**	There is little evidence on how comorbidities may impact risk of reinfection.	**Insufficient**
Severity of primary infection	**10 studies; N= 12,345,502** Lumley 2020,[28]Leidi 2021, [38]Gallais 2021,[36] Vitale 2021,[32]Abo-Leyah 2021,[39] Pilz 2021,[34] Sheehan 2021,[27]Harvey 2021,[26]Hanrath 2021, [29]Hall 2021[9]	Mild or asymptomatic initial infections may be associated with a higher risk of reinfection, but evidence is inconsistent and incomplete.	**Low**
Variants	**3 studies; N= 27,772** Hall 2021,[9] Goldberg 2021,[24]; Krutikov 2021,[30]	The Alpha variant did not affect the protection against reinfection, but this result does not apply to variants not represented in the studies (such as the Delta variant).	**Low**
Vaccination	**4 studies; N= 29,081** Gallais 2021,[36] Hall 2021,[9] Goldberg 2021,[24]; Krutikov 2021,[30]	It is uncertain how vaccination may impact risk of reinfection.	**Insufficient**

Table B-6. Uncontrolled studies of reinfection from SARS-CoV-2

Author	Title	Country	Population
Graham, 2021[42]	Changes in symptomatology, reinfection, and transmissibility associated with the SARS-CoV-2 variant B.1.1.7: an ecological study	UK	General population
Qureshi, 2021[14]	Re-infection with SARS-CoV-2 in Patients Undergoing Serial Laboratory Testing	US	General population
Brouqui, 2021[50]	COVID-19 re-infection	France	General population
Thompson, 2021[51]	Rapid Emergence and Epidemiologic Characteristics of the SARS-CoV-2 B.1.526 Variant — New York City, New York, January 1–April 5, 2021 | MMWR (cdc.gov)	US	General population
Murillo-Zamora, 2021[52]	Predictors of severe symptomatic laboratory-confirmed SARS-CoV-2 reinfection - ScienceDirect	Mexico	General population

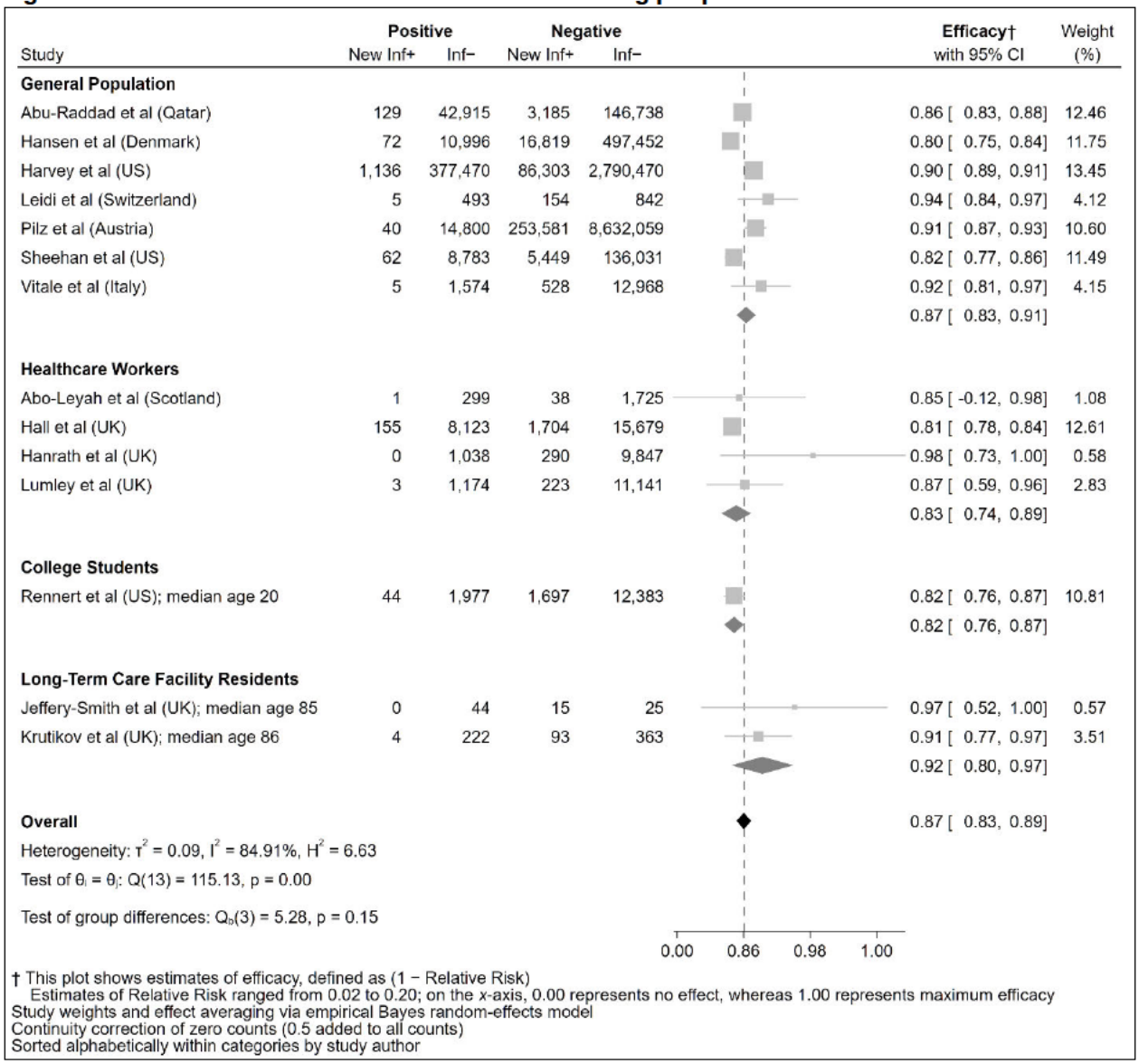
Table B-7. Duration of protection against reinfection findings by study

Finding	Study	Overall follow-up time (months)	Duration of protection finding
Evidence of no change in protection over time	Abo-Leyah, 2021[39]	6 months	No variation in protection estimate over time.
	Gallais, 2021[36]	13 months	"Altogether, our findings indicate that although anti-SARS-CoV-2 antibody titers do indeed decline, the risk of reinfection within a year post-infection remains low."
	Hansen, 2021[35]	10 months	No difference in protection estimate over time (3–6 months of follow-up 79·3% [74·4–83·3] vs ≥7 months of follow-up 77·7% [70·9–82·9]).
	Leidi, 2021[38]	9 months	No variation in protection estimate over time.
	Pilz, 2021[34]	10 months	Descriptive analyses found "no clear sign" reinfection odds changed over time.
	Krutikov, 2021 [30]	10 months	No variation in the protection estimate over time.

Finding	Study	Overall follow-up time (months)	Duration of protection finding
Suggests potential increase of protection over time	Abu-Raddad, 2021[37]	7 months	Reinfection rate decreased over time, implying a potential increase in protection.
	Sheehan, 2021[27]	10 months	Reinfection rate decreased over time, implying a potential increase in protection.

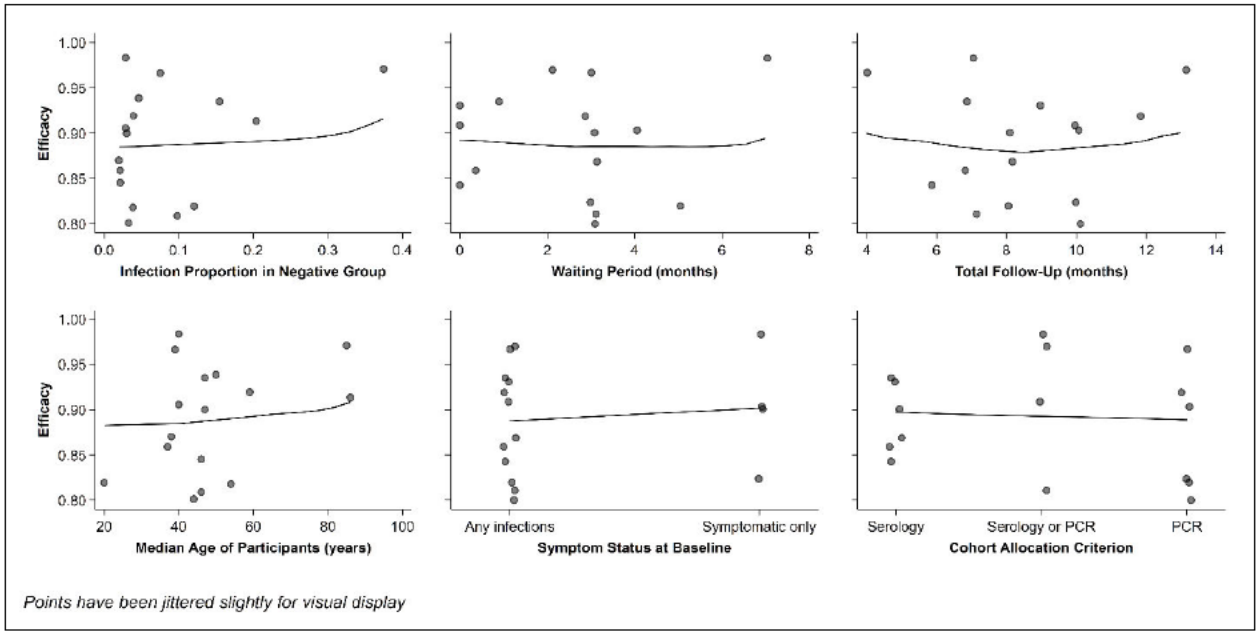
APPENDIX C: Sensitivity analyses

Figure C-1. Estimates of the risk of reinfection excluding pre-print studies



† This plot shows estimates of efficacy, defined as (1 − Relative Risk)
Estimates of Relative Risk ranged from 0.02 to 0.20; on the *x*-axis, 0.00 represents no effect, whereas 1.00 represents maximum efficacy
Study weights and effect averaging via empirical Bayes random-effects model
Continuity correction of zero counts (0.5 added to all counts)
Sorted alphabetically within categories by study author

Figure C-2. Methodological and other factors and their influence on protective effect of prior SARS-CoV-2 infection estimates



APPENDIX D: Ongoing Studies

Study Title ClinicalTrials.gov NCT Number	Study Design Country	Population Description	Expected Outcomes	Status per Last Update on Clinical Trials.gov	Anticipated Primary Completion Date
Humoral Immunity Against SARS-CoV-2 in Liver Transplanted Patients After COVID-19 in Comparison With Immunocompetent Patients NCT04410471	Case-control Spain	Liver transplant and control patients	Incidence of IgG against SARS-CoV-2; titration and evolution of humoral response (IgG) along first 12 months after having Covid-19; Reinfection of Covid-19; mortality	Recruiting as of June 2, 2020	May 29, 2020
Immune Response to Covid-19 in 300 Health Care Workers With Mild Symptoms NCT04356586	Observational Cohort Belgium	HCW previous tested for Covid-19 with mild symptoms in Jessa Ziekenhuis, Belgium	Percentage of serological positive healthcare workers; Percentage of HCW with positive Saliva-sabs	Completed as of September 7, 2020	August 21, 2020
COVID-19: Investigation of Transmission and Immunisation Among Hospital Staff NCT04346186	Observational Cohort Denmark	*Group 1:* hospital staff in the capital region of Denmark *Group 2*: healthy volunteer blood donors	Positive IgM/IgG tests at baseline, 1 month, 5 month; comparison of the point of care test and Elisa at baseline, 1 month, 5 months; reinfection rate at 180 and 360 days; IgM/IgG positive participants on follow-up test at 1 month and 5 months	Enrolling by invitation as of September 25, 2020	October 1, 2020
Validating an ELISpot for Early Detection of an Active Immune Response Against COVID-19 NCT04418206	Cohort France	COVID-19 patients will be selected in the 4 participating centers. Contact subjects and healthy volunteers will be selected only in the coordinating center (Centre Hospitalier Universitaire de Nice)	Proportion of subjects with IgA-specific cells of SARS-CoV-2's Spike 1 protein at inclusion and 7 +/-2 days later	Recruiting as of November 9, 2020	December 1, 2020

Study Title ClinicalTrials.gov NCT Number	Study Design Country	Population Description	Expected Outcomes	Status per Last Update on Clinical Trials.gov	Anticipated Primary Completion Date
Clinical and Immunological Evolution of Covid-19 Occurring in a Context of Non-Hodgkin Lymphoma NCT04641806	Observational case-control France	*Lymphoma cases*: Adults aged at least 18 years, with a Covid-19 confirmed by PCR, diagnosed between February and May 2020. Past history of B-cell NHL in remission, active surveillance or during first-line or second-line treatment Affiliated with a social security, consenting to the study *Control group*: Adults aged at least 18 years, with a Covid-19 confirmed by PCR, diagnosed between February and May 2020. No past history of lymphoma. Affiliated with a social security, consenting to the study	Immunological response to SARS Cov2 (Quantification of IgG anti-SARS-Cov-2 by ELISA.); Clinical evolution 6 months after Covid-19 diagnosis (length(s) of stay(s) for Covid-19 in hospitalization and intensive care)	Not yet recruiting as of November 24, 2020	April 16, 2021
Evaluation and Longitudinal Follow-up of Biomarkers Predictive of Severe Forms of COVID-19 NCT04648709	Observational Cohort France	Patients with COVID infection documented by PCR and/or antigenic testing will be included. *Group 1:* asymptomatic patients with PCR-positive PCR *Group 2:* patients with mild symptoms and PCR positive *Group 3*: seriously symptomatic patients with PCR positive *Group 4*: patients in resuscitation with positive PCR *Group 5*: heathy volunteer as control	*T cell immune response*: Characterize T-cell immune response in patient with COVID 19 infection *B cell immune response*: Characterize B-cell immune response in patient with COVID 19 infection *Platelet immune response*: Characterize platelet immune response in patient with COVID 19 infection *Immune response and chronic forms*: Immune response and chronic forms	Recruiting as of April 20, 2021	June 2021

Study Title ClinicalTrials.gov NCT Number	Study Design Country	Population Description	Expected Outcomes	Status per Last Update on Clinical Trials.gov	Anticipated Primary Completion Date
Cellular-Mediated Immunity in COVID-19 (DEMETRA) NCT04746521	Cross-sectional Italy	*Group 1*: Patients with previous Sars-CoV-2 infection who did not undergo vaccination *Group 2*: Patients with previous Sars-CoV-2 infection who undergone vaccination *Group 3*: Subjects without previous Sars-CoV-2 infection who undergone vaccination	Detection of Cellular-Mediated Immune Response; detection of T cell subpopulation maturation	Completed as of July 14, 2021	June 14, 2021
Convalescent Plasma as Therapy for Covid-19 Severe SARS-CoV-2 Disease (CONCOVID Study) NCT04342182	Randomized Comparative Trial Netherlands	Patients with PCR confirmed COVID disease, age >18 years. Donors will be included with a known history of COVID who have been asymptomatic for at least 14 days.	Overall mortality until discharge from the hospital or a maximum of 60 days after admission whichever comes first—the mortality in the 300ml convP group will be compared with the control arm	Active, not recruiting as of November 16, 2020	July 1, 2021
COVID-19 IgG Antibodies in the Serum of Recovered Patients NCT04470414	Observational Cohort Egypt	Patients recovered from COVID-19 infection within three months before the start of the study.	Levels of IgG in the serum of recovered COVID-19 patients (at 3, 6, 12 months post infection); Factors related to IgG level at 1 year	Not yet recruiting as of July 16, 2020	July 1, 2021
Post Covid-19 Cardiopulmonary and Immunological Changes NCT04388436	Observational Cohort Egypt	COVID-19 PCR positive survivors	Measurement of pulmonary function changes either obstructive or restrictive also lung diffusion and if there is remaining interstitial fibrosis; measurement for cardiac function and ejection fraction changes and if there is changes in pulmonary artery pressure; assessment of IGM and IGG level and if there is immunological changes	Active, not recruiting as of May 19, 2020	July 10, 2021

Study Title ClinicalTrials.gov NCT Number	Study Design Country	Population Description	Expected Outcomes	Status per Last Update on Clinical Trials.gov	Anticipated Primary Completion Date
BNT162b2 Vaccination With Two Doses in COVID-19 Negative Adult Volunteers and With a Single Dose in COVID-19 Positive Adult Volunteers NCT04824638	Non-Randomized interventional trial France	*Group 1*: SARS-CoV-2 naive participants (participants without antecedent of SARS-CoV-2 infection) *Group 2:* Previously SARS CoV-2 infected participants (participants with antecedent of SARS-CoV-2 infection [more than 6 months])	IgG humoral response to vaccine 28 days post vaccination; humoral response to vaccine; T cells response to vaccine; Mucosal response to vaccine; B cell response to vaccine; predictive determinants of vaccine response; Safety of BNT162b2 vaccine; SARS-CoV-2 infection	Recruiting as of April 1, 2021	August 8, 2021
Study of Kinetics and Efficacy of the Immune Response Against COVID-19 Among Hospital Staff NCT04408001	Observational Cohort France	Percy hospital staff having (symptomatic individuals group) or not (asymptomatic individuals group) presented COVID-19 infection symptoms *Group 1*: Hospital staff identified by the COVID-19 case census cell who have been infected, confirmed by positive PT-PCR; or who show clinical signs of COOVID-19 despite negative PT-PCR *Group 2*: Hospital staff who have not been identified by the COVID-19 case census cell (asymptomatic)	Induced SARS-CoV2 immunity Long-term protection of induced SARS-CoV2 immunity at 6 months; long-term protection of induced SARS-CoV2 immunity at 1 year; anti-SARS-CoV2 antibodies kinetics in blood throughout the study; anti-SARS-CoV2 antibodies kinetics in saliva throughout the study; kinetics of serum neutralization in blood throughout the study	Active, not recruiting as of July 7, 2021	September 30, 2021
DCI COVID-19 Surveillance Project NCT04780698	Cohort United States	Patients who receive in-center chronic dialysis (>3 months) at DCI Henry Avenue (Philadelphia, PA)	Incidence of COVID-19 infection in the cohort; Link the presence of COVID-19 infection to COVID-19 antibody formation (seroconversion) from quantitative and qualitative testing; Incidence of COVID-19 reinfection; presence of antibodies in cases of reinfection	Recruiting as of June 23, 2021	October 2021

Study Title ClinicalTrials.gov NCT Number	Study Design Country	Population Description	Expected Outcomes	Status per Last Update on Clinical Trials.gov	Anticipated Primary Completion Date
Immunity Against Severe Acute Respiratory Syndrome Coronavirus 2 Disease (COVID-19) in the Oncology Outpatient Setting NCT04779346	Observational Cohort Germany	Outpatient cancer patients: Cancer patients who are regularly treated in the Oncology Outpatient Clinic of the University Medical Center Hamburg-Eppendorf (UKE)	Rate of SARS-CoV-2 antibody positive patients; Rate of SARS-CoV-2 antibody positivity after 3, 6, 9, 12 months in previously SARS-CoV-2 antibody positive patients; Rate of SARS-CoV-2 antibody positivity after 3, 6, 9, 12 months in previously SARS-CoV-2 vaccinated patients	Recruiting as of March 22, 2021	December 31, 2021
Medical and Serological Follow-up of the Staff of the Paris Saint-Joseph Hospital Group Infected With Severe Acute Respiratory Syndrome Coronavirus 2 NCT04488484	Nonrandomized prospective cohort France	The Paris Saint- Joseph Hospital Group staff	Immune Response description and evolution of the SARS-CoV2 over time	Active, not recruiting as of August 12, 2020	December 31, 2021

Study Title ClinicalTrials.gov NCT Number	Study Design Country	Population Description	Expected Outcomes	Status per Last Update on Clinical Trials.gov	Anticipated Primary Completion Date
Study of COVID-19 Outbreak in Hospital Departments of Bamako, Mali NCT04710316	Non-Randomized interventional trial Mali	*Group 1:* Hospitalized patients in one of the four centers in Bamako, with clinical signs of infection of the upper or lower respiratory tracts with fever or feeling of fever or any other signs of SARS-Cov-2 infection or who have been in close contact with a SARS-CoV-2 infected person without effective protective measures *Group 2:* Caregivers of one of the four centers in Bamako. Serological screening: all. Molecular screening: with clinical signs of infection of the upper or lower respiratory tracts with fever or feeling of fever or any other signs of SARS-Cov-2 infection or who have seroconverted to SARS-CoV-2 or who have been in close contact with a SARS-CoV-2 infected person without effective protective measures	Incidence rate of positive SARS-Cov-2 RT-PCR in Bamako hospital departments during the study (and up to 15 months after study start date) – positive SARS-Cov-2 RT-PCRs are defined by the detection of SARS-Cov-2 genome after amplification using a test targeting 2 regions of the genome.	Not yet recruiting as of January 14, 2021	April 30, 2022
Patients and Health Staff of Cancer Centres During the Covid-19 Pandemic NCT04421625	Cohort France	Population in Cancer centers responding to one of these 3 definitions: patients having a treatment in process, patients under surveillance (having completed their treatment for more than a year), health staff.	Establishment of a clinical (12 months) and biological (15 days) basis for to describe the number and severity of Covid-19 infections in Cancer centers staff and patients. Establishment of a biological basis for to describe the number and severity of Covid-19 infections in Cancer centers staff and patients (3, 6, 9, and 12 months.	Recruiting as of May 5, 2021	June 15, 2022

Study Title ClinicalTrials.gov NCT Number	Study Design Country	Population Description	Expected Outcomes	Status per Last Update on Clinical Trials.gov	Anticipated Primary Completion Date
Longitudinal Follow-up of a Population Cohort in a French City With High SARS-CoV-2 Circulation, in Early 2020 COVID-19 NCT04644159	Observational Cohort France	Residents of a city in Northern France *Group 1*: Pupils, teachers and non-teaching staff who attended schools of the city during the 2019-2020 school year and members of their households *Group 2*: Residents and patients from retirement homes and long-term care units *Group 3*: Staff of health care institutions	Presence of specific anti-SARS-CoV-2 antibodies in the different study groups.	Recruiting as of November 27, 2020	June 30, 2022
Immunity Against SARS-CoV2 in Children and Their Parents COVID-19 NCT04355533	Nonrandomized interventional France	*Group 1:* hospitalized children or consulting at hospital *Group 2:* parents of included child *Group 3*: children with potential COVID during first wave *Group 4:* SARS-cov2 positive school children *Group 5*: person living under same room as children included in study	Seroconversion against SARS-CoV2	Recruiting as of March 26, 2021	July 2022
Workforce Serosurveillance to Track Long-term Modifications to COVID-19 Exposure Due to Factors in the Built Environment NCT04542200	Observational Cohort United States	Working population of Northwell Health	COVID-19 antibodies via serology testing	Enrolling by invitation as of February 8, 2021	December 31, 2022

Study Title ClinicalTrials.gov NCT Number	Study Design Country	Population Description	Expected Outcomes	Status per Last Update on Clinical Trials.gov	Anticipated Primary Completion Date
Pediatric SARS-CoV-2 and MIS-C Long-term Follow-up NCT04830852	Observational cohort United States	*Recovery*: Participants aged 21 years and younger and enrolled within 12 weeks after acute infection or positive test. *Convalescent:* Participants aged 21 years and younger and enrolled more than 12 weeks after acute infection or positive test. *Household contact of infected patients*: Household contacts of the infected patients will serve as a control group *Parents/guardians of participants:* Parents or guardians of participants in all cohorts will also be enrolled for limited participation to complete questionnaires about how the family is impacted by the participant's health and SARS-CoV-2.	Incidence and prevalence of medical sequelae among symptomatic SARS-CoV-2 infection survivors, asymptomatic SARS CoV 2 infection survivors, and MIS-C survivors over 6 years. Risk factors for medical sequelae among symptomatic SARS CoV 2 infection survivors, asymptomatic SARS-CoV-2 infection survivors, and MIS-C survivors over 6 years.	Recruiting as of July 19, 2021	July 1, 2027
A Longitudinal Study of COVID-19 Sequelae and Immunity NCT04411147	Longitudinal, observational cohort United States	People age 18 and older who have recovered from documented COVID-19 or were in close contact with someone who had COVID-19 but did not get the infection *Group 1*: Close contacts—individuals without COVID-19 diagnosis, lived in same home as a survivor during illness, were within 6 feet of a COVID-19 case for a prolonged period of time or had direct contact with secretions *Group 2:* COVID-19 Survivor—individuals with documented prior COVID-19 infection and who have recovered	Medical Sequelae in COVID- 19 Survivors; Risk Factors for Medical Sequelae in COVID-19 Survivors; Antibody and cell-mediated immune responses to SARSCoV-2; Antibody and cell-mediated immune responses to SARSCoV-2 over time; Incidence of reinfection with COVID-19; Incidence of clinical silent infection; Mental health status in COVID-19 survivors and contacts	Recruiting as of May 28, 2021	December 31, 2027

APPENDIX E: Version History

Version 2 – Provides an update for findings on Key Questions 2 and 3.

Version 1- Synthesizes available evidence (through December 2020) on prevalence of anti-SARS-CoV-2 antibodies following COVID-19.

Appendix Table B-1. Observational studies of reinfection from SARS-CoV-2

Author	Publication Year	Title	PMID	Publication Status at Time of Report Publication	Link/URL
Abo-Leyah	2021	The protective effect of SARS-COV-2 antibodies in Scottish healthcare workers	34104643	Fully published	https://doi.org/10.1183/23120541.00080-2021
Abu-Raddad	2021	SARS-CoV-2 antibody-positivity protects against reinfection for at least seven months with 95% efficacy	33937733	Fully published	https://doi.org/10.1016/j.eclinm.2021.100861
Finch	2021	SARS-CoV-2 infection and reinfection in a seroepidemiological workplace cohort in the United States	TBD	Preprint	https://doi.org/10.1101/2021.05.04.21256609
Gallais	2021	Anti-SARS-CoV-2 Antibodies Persist for up to 13 Months and Reduce Risk of Reinfection	TBD	Preprint	https://doi.org/10.1101/2021.05.07.21256823
Goldberg	2021	Protection of previous SARS-CoV-2 infection is similar to that of BNT162b2 vaccine protection: A three-month nationwide experience from Israel	TBD	Preprint	https://doi.org/10.1101/2021.04.20.21255670

Hall	2021	SARS-CoV-2 infection rates of antibody-positive compared with antibody-negative health-care workers in England: a large, multicentre, prospective cohort study (SIREN)	33844963	Fully published	https://dx.doi.org/10.1016/s0140-6736(21)00675-9
Hanrath	2021	Prior SARS-CoV-2 infection is associated with protection against symptomatic reinfection	33373652	Fully published	https://doi.org/10.1016/j.jinf.2020.12.023
Hansen	2021	Assessment of protection against reinfection with SARS-CoV-2 among 4 million PCR-tested individuals in Denmark in 2020: a population-level observational study	33743221	Fully published	https://doi.org/10.1016/S0140-6736(21)00575-4

Harvey	2021	Association of SARS-CoV-2 Seropositive Antibody Test With Risk of Future Infection	33625463	Fully published	https://doi.org/10.1001/jamainternmed.2021.0366
Jeffery-Smith	2021	Antibodies to SARS-CoV-2 protect against re-infection during outbreaks in care homes, September and October 2020	33541486	Fully published	https://doi.org/10.2807/1560-7917.ES.2021.26.5.2100092
Krutikov	2021	Incidence of SARS-CoV-2 infection according to baseline antibody status in staff and residents of 100 long-term care facilities (VIVALDI): a prospective cohort study	34104901	Fully published	https://doi.org/10.1016/S2666-7568(21)00093-3

Leidi	2021	Risk of reinfection after seroconversion to SARS-CoV-2: A population-based propensity-score matched cohort study	34043763	Fully published	https://doi.org/10.1093/cid/ciab495
Lumley	2020	Antibody Status and Incidence of SARS-CoV-2 Infection in Healthcare Workers.	33369366	Fully published	https://doi.org/10.1056/NEJMoa2034545

Manica	2021	The risk of symptomatic reinfection during the second COVID-19 wave in individuals previously exposed to SARS-CoV-2	TBD	Preprint	https://doi.org/10.1101/2021.04.14.21255502 \
Pilz	2021	SARS-CoV-2 re-infection risk in Austria	33583018	Fully published	https://dx.doi.org/10.1111/eci.13520
Rennert	2021	Risk of SARS-CoV-2 reinfection in a university student population	33993225	Fully published	https://doi.org/10.1093/cid/ciab454
Sheehan	2021	Reinfection Rates among Patients who Previously Tested Positive for COVID-19: a Retrospective Cohort Study	33718968	Fully published	https://dx.doi.org/10.1093/cid/ciab234
Vitale	2021	Assessment of SARS-CoV-2 Reinfection 1 year after primary infection in a population in Lombardy, Italy	34048531	Fully published	https://doi.org/10.1001/jamainternmed.2021.2959

Country	Study Design	Length of follow-up (Months)	Population category	Population Description	Data Source
Scotland	Prospective cohort	6	Healthcare workers	HCWs employed within the NHS in Tayside (Eastern Scotland)	Community health index (linkage to healthcare records & testing data)
Qatar	Retrospective cohort	7	General	Population of Qatar with serological test results	Centralized and standardized national anti-SARS-CoV-2 serological testing database complied at Hamad Medical Corportion (the main public healthcare provider and nationally designated provider for COVID-19 healthcare). Database was linked to the HMC national PCR testing and COVID-
US	Prospective cohort	9	General	U.S. SpaceX employees in California, Florida, Texas, and Washington state.	Data obtained as part of the study
France	Prospective cohort	13	Healthcare workers	HCWs at Strasbourg University Hospital	Data obtained as part of the study
Israel	Retrospective cohort	12	General	Every adult (age >/= 16) in Israel	Israel Ministry of Health and the Israel Central Bureau of Statistics

U.K.	Prospective cohort	7	Healthcare workers	Staff working in NHS publicly funded hospitals across the U.K.	Public Health England national laboratory testing surveillance system
U.K.	Retrospective cohort	7	Healthcare workers	Asymptomatic and symptomatic staff working at the Newcastle-upon-Tyne Hospital system	Regional virology diagnostic laboratory database
Denmark	Prospective cohort	10	General	General population of Denmark, with an additional sensitivity analysis in a subgroup of people routinely tested as part of their profession.	Danish Microbiology Database, which captures electronic records of bookins and results in a person-identifiable format with enriched data from the civil registry ssytem and other registries by the automated national surveillance system.

U.S.	Retrospective cohort/RWE	8	General	Data on individuals from across the U.S., predominatory in the Northeast, with an antibody test on or after Jan 2020 from a commercial health data aggregator	HealthVerity, a for-profit data aggregator with data from 70 different commercial health data sources. Demographic and geographic characterisitcs from EHR, administrative claims, and hospital records.
U.K.	Prospective cohort	4	Long-term Care Facility Residents	Residents and staff at two nursing homes in London	Data obtained as part of the study
U.K.	Prospective cohort	10	Long-term Care Facility Residents	Staff and residents in 100 long-term care facilities in England	Data obtained as part of the study (PCR results stored in the COVID-19 Datastore, established as part of the UK's pandemic response)

Switzerland	Retrospective cohort	9	General	Adults in Geneva and their households	Population-based representative sample of adults in Geneva and their households for seroprevalence study. PCR data from a centralized registry
U.K.	Prospective cohort	8	Healthcare workers	All symptomatic and asymptomatic staff working at four teaching hospitals in Oxfordshire, UK	Staff of Oxford Univerity Hospitals, whose data was obtained from the Infections in Oxfordshire Research Database

Italy	Retrospective cohort	7	General	All adults in five Italian municipalities within the Autonomous Province of Trento, Italy	Data obtained as part of the study
Austria	Retrospective cohort	10	General	All residents of Austria	Austrian epidemiological reporting system (ERS), provided by the Austrian Agency for Health and Food Safety (AGES)
US	Retrospective cohort	8	College Students	Students at Clemson University in South Carolina during the Fall 2020 semester	Data was collected during the study
U.S.	Retrospective cohort	10	General	Patients of one health system in Ohio and one in Florida tested for COVID-19 via PCR from March 12, 2020 to February 24, 2021	One health system in Ohio and Florida
Italy	Prospective cohort	12	General	People in Italy of all ages recruited from screening and contact tracing programs who underwent PCR testing during the first infection wave	Data obtained as part of the study

Inclusion criteria	Exclusion criteria	Positive Cohort definition	Negative Cohort definition
HCWs or social care workers over the age of 16 yrs	Participants with any contraindication to venepuncture and symptoms consistent with curent SARS-CoV-2 infection at the time of enrollment, or positive test in the preceding 14 days	Ab+	HCWs without a positive Ab test
All individuals for whom serological testing data was collected in Qatar	Deceased persons tested for Abs post-mortem	Ab+ persons in Qatar	Ab- persons in Qatar
Any employee of SpaceX	None	Ab+	Negative serology
HCW with at least one follow-up timepoint (M3-6 and/or M7-9 and/or M11-13)	HCW with no serum collected at follow-up timepoints	Positive serology or PCR	Negative serology without history of positive PCR
Adults (age >/= 16) in Israel whose first infection was diagnosed between June 1 and September 30, 2020	Individuals under age 16; individuals infected before June 1, 2020 or between October 1, 2020 and December 20, 2020	Frequency by age group, total pop., in thousands: 16-39: 2,997 40-49: 1,073 50-59: 827 60-69: 731 70-79: 456 80+: 267	NR

All health-care workers, support staff, and administrative staff working at hospital sites participating in SIREN, who could provide written informed consent and anticipated remaining engaged in follow-up for 12 months	Participants were excluded from this analysis if they had no PCR tests after enrolment, enrolled after Dec 31, 2020, or had insufficient PCR and antibody data to complete cohort assignment.	Ab+ on enrollment or Ab+ from previous clinical lab samples, with or w/o a previous PCR+; Ab- on enrollment with a PCR+ result before enrollment	Ab- test and no documented previous positive PCR or Ab test. Participants with negative PCR test but no Ab data were excluded.
Staff who worked at participating hospitals and had baseline infection status data	NR	Ab+ or prior positive PCR	Ab- or with negative PCR
All individuals who had a PCR test for SARS-Cov-2 between Feb 26 and Dec 31, 2020, in Denmark.	People who tested positive for the first time between the two surges (610 people) and those who died before the second surge (7,432 poeple).	All people in Denmark with a PCR+ before June 1, 2020	All people in Denmark with a PCR- before June 1, 2020

Individuals with an antibody test on or after January 2020	Individuals with more than one antibody test with discordant results	Ab+ on or after Jan 2020	Ab- on or after Jan 2020
NR	NR	Ab+ ("not susceptible")	Ab- ("susceptible")
Staff and residents who had a valid pseudo-identifier (enabling linkage of Ab results to PCR results); lived or worked in an LTCF owned by FSHCG; and had at least one PCR test and 1 Ab test during analysis period.	Staff >65 years and residents <65 years were excluded.	Ab+	Ab-

Adults 20-74 yrs living in the canton of Geneva and their households	Children 5-12 yrs	Ab+	Two negative serology propensity matched (age, gender, immunodeficiency, BMI, smoking status, education level) to each case of positive serology
All symptomatic and asymptomatic staff working at four teaching hospitals in Oxfordshire, UK	NR	Ab+	Ab-

Adult residents of Trento Italy with serological screening (IgG assay)	NR	Ab+	Ab-
All Austrian residents	Austrian residents who died from COVID-19 between first and second waves	All individuals in Austria who had a PCR+ test minus all reported COVID-19 deaths from Feb 22-April 30, 2020	Austrian residents minus those who with PCR+ during the first wave
All 17 to 24 year old students at Clemson University tested between 8/19/20 and 11/25/20	Students testing positive between 10/6/20 and 12/28/20	Tested positive (serology or PCR) during the Fall 2020 semester	Did not test positive (serology or PCR) during the Fall 2020 semester
Patients of one health system in Ohio and one in Florida tested for COVID-19 via PCR from March 12, 2020 to February 24, 2021	Health system employees; patients with baseline negative status who tested positive within 90 days of their initial test.	PCR+ prior to August 30, 2020	PCR- prior to August 30, 2020
All ages, people in Italy with PCR testing during first infection surge, recruited from screening and contact-tracing programs	NR	PCR+	PCR-

Age: Mean (SD) years or Median (IQR)	**Race stratified, N (%)**	**Male Sex/Gender, N (%)**
Median (Range): 46 (NR) Age group, N (%) Total population 18-30: 290 (14.1) 31-40: 403 (19.5) 41-50: 536 (26.0)	Total population White European: 1,964 (95.5) Other White: 16 (0.8) South Asian: 36 (1.7) Chinese: 10 (0.5) Black: 8 (0.4)	378 (18.3)
Median (IQR) Positive Men: 38 (31-47) Women: 35 (28-45) Negative Men: 39 (30-50) Women: 35 (28-47)	NR	Positive: 34,091 (79.2) Negative: 74,019 (49.4)
Range: 18-71 yrs	NR	NR
Median (IQR): Positive: 39 (30-51) Negative: 39 (30-50)	NR	Positive: 91 (23.2) Negative: 197 (21.5)
3,107,000 (49)* Note: % was calculated from the summary numbers provided in Table 1	NR	NR

Median (IQR): Total: 45.7 (35.4-53.5) Positive: 45.6 (34.6-53.8) Negative: 45.7 (35.8-53.9)	Total White: 22,404 (87.3) Mixed: 1,773 (6.9) Asian: 525 (2.0) Black: 412 (1.6) Chinese: 346 (1.3) Other: 151 (0.6) NR: 50 (0.2) Positive White: 6,969 (84.2) Mixed: 724 (8.7) Asian: 236 (2.9) Black: 134 (1.6) Chinese: 147 (1.8) Other: 51 (0.6) NR: 17 (0.2) Negative White: 15,435 (88.8) Mixed: 1,049 (6.0) Asian: 289 (1.7) Black: 278 (1.6) Chinese: 199 (1.1) Other: 100 (0.6) NR: 33 (0.2)	Total Male: 4,010 (15.6) Other: 34 (0.1) Positive Male: 1,425 (17.2) Other: 13 (0.2) Negative Male: 2,585 (14.9) Other: 21 (0.1)
Positive: 39.5 (30-49) Negative: 40 (30-50)	Positive BAME: 107 (11.2%) Negatve BAME: 796 (8.4%)	Positive: 169 (17.4) Negative: 1,882 (19.4)
Number per age group Positive and re-test positive in second surge 0-19: 4 20-34: 15 35-50: 20 50-64: 16 65-79: 8 80+: 9 Negative and re-test positive in second surge 0-19: 1,881 20-34: 4,789 35-50: 4,358 50-64: 3,925 65-79: 1,255 80+: 611	NR	Second surge re-test positive participants only Positive: 26 Negative: 6,335

Positive: 44.3 (18.1) Negative: 47.7 (17.6)	NR	Positive: 171,240 (45.8) Negative: 1,219,912 (43.2)
Median (IQR) Care home A: 84 (76-89) Care home L: 85 (78-89) Staff ages NR for both care homes	NR	n/N (%) Care home A: 13/46 (26.3) Care home L: 21/57 (36.8*) Staff gender NR for both care homes
Median [IQR] (Range) Residents Total: 86 [79-91] (65-103) Positive: 86 [79-91] (65-103) Negative: 86 [80-92] (65-102) Staff Total: 47 [34-56] (18-65) Positive: 48 [36-57] (20-65) Negative: 46 [33-56] (18-65)	NR	Residents Total: 208 (30.5) Positive: 71 (31.4) Negative: 137 (30) Staff Total: 174 (12.2) Positive: 52 (12.8) Negative: 122 (12)

Positive: 46.6 (16.6) Negative: 47.3 (16.3)	NR	Positive: 242 (48.5) Negatie: 486 (48.8)
Median (IQR) Positive: 38 (29-49), range 17-69 Negative, no infection during follow-up: 38 (29-49), range 16-86 Negative, then seroconverted during follow-up: 41 (28-49), range 21-67	Positive (n=1,177) White: 703 (59.7) Asian: 287 (24.4) Black: 81 (6.9) Chinese: 9 (0.8) Other: 97 (8.2) Negative (n=11,276) White: 8,313 (73.7) Asian: 1,719 (15.2) Black: 425 (3.8) Chinese: 121 (1.1) Other: 698 (6.2) Negative, then seroconverted during follow-up (n=88) White: 58 (66) Asian: 20 (23) Black: 4 (5) Chinese: 0 (0) Other: 6 (7)	Positive Male: 339 (28.8); Other: 3 (0.3); Negative Male: 2,900 (25.7); Other: 16 (0.1); Negative, then seroconverted during follow-up Male: 20 (23); Other: 0 (0)

Median (IQR) Total: 50 (32-63) Baseline positive: 46 (8-94) Baseline negative: 48 (8-98) Re-test positive: 64 (51-88) Re-test negative: 47 (9-98)	NR	NR
Reinfection group at the time of first infection, median age (25th-75th percentile; min-max): 39.8 (25.9 to 54.5; 15.4-93.8)	NR	Only given for reinfection group: 15 (37.5)
20.3 (1.5)	NR	7,793 (48.4)
Data reported for patients with tests performed before August 30 Positive: 52.3 (21.8) Negative: 54.8 (21.4)	NR	Data reported for patients with tests performed before August 30: Positive: 4,240 (47.9) Negative: 63,278 (44.7)
Median (IQR): 59 (40-78)	Positive at baseline White: 1,449 (91.8) Asian: 41 (2.6) Black: 22 (1.4) Latinx: 59 (3.7) Other: 8 (0.5) Negative at baseline and follow-up White: 11,390 (87.8) Asian: 578 (4.5) Black: 466 (3.6) Latinx: 506 (3.9) Other: 28 (0.2) Negative at baseline then converted to positive during follow-up White: 494 (93.6) Asian: 15 (2.8) Black: 7 (1.3) Latinx: 12 (2.3)	Positive at baseline: 808 (51.2) Negative at baseline and follow-up: 6,008 (46.3) Negative at baseline then converted to positive during follow-up: 213 (40.3)

Occupation and/or Employment Status, N (%)	Comorbidities, N (%)	Assay Type
Role, Total population Doctor: 237 (11.5) Nurse: 601 (29.2) Alied health professional (AHP): 239 (11.6) Pharmacy staff: 69 (3.4) Healthcare assistant: 172 (8.4) Student: 25 (1.2)	NR	CLIA
NR	NR	ECLIA
Employees of SpaceX: 4,411 (100)	NR	ELISA
Hospital healthcare employees: 1,309 (100)	NR	ELISA; LFA; CMIA
NR	NR	Unvaccinated & previously diagnosed with SARS-CoV-2 between June 1 and September 30

Total Nursing: 10.891 (42.2) Administrator/executive: 3,903 (15.2) Doctor: 2,783 (10.8) Specialist staff: 1,548 (6.0) Health-care scientist: 894 (3.5) Midwife: 649 (2.5) Pharmacist: 390 (1.5) Estates, porters, or security: 256 (1) Other hospital staff: 4,347 (16.9) Positive Nursing: 3,751 (45.3) Admininstrator/executive: 1,090 (13.2) Doctor: 999 (121) Specialist staff: 489 (5.9) Health-care scientist: 225 (2.7) Midwife: 189 (2.3) Pharmacist: 112 (1.4) Estates, porters, or security: 95 (1.1) Other hospital staff: 1,328 (16.0) Negative Nursing: 7,140 (41.1) Administrator/executive: 2,813 (16.2) Doctor: 1,784 (10.3) Specialist staff: 1,059 (6.1) Health-care scientist: 669 (3.8) Midwife: 460 (2.6) Pharmacist: 278 (1.6)	Total Chronic respiratory conditions: 3,248 (12.7) Chronic non-respiratory conditions: 2,746 (10.7) Immunosuppression: 542 (2.1) Positive Chronic respiratory conditions: 1,019 (12.3) Chronic non-respiratory conditions: 909 (11.0) Immunosuppression: 155 (1.9) Negative Chronic respiratory conditions: 2,229 (12.8) Chronic non-respiratory conditions: 1,837 (10.6) Immunosuppression: 387 (2.2)	Type NR; Serology done using "locally validated assays"
NR	NR	NR
Nurses, doctors, social workers, healthcare assistants: 15,604 (3)	NR	ELISA

NR	Positive Hypertension: 52,700 (24.7) Ischemic heart disease: 10,423 (4.9) Coronary heart disease: 8,333 (3.9) Vitamin D deficiency: 30,930 (14.5) Obesity: 42,890 (19.5) Negative Hypertension: 430,516 (24.2) Ischemic heart disease: 96,920 (5.4) Coronary heart disease: 80,730 (4.5) Vitamin D deficiency: 219,142 (12.3)	NR
NR	NR Note: Nursing home A provides dementia care and residential care; Nursing home L provides nursing and residential care	Indirect ELISA RBD; Commercial anti-N assay
NR	NR	CMIA

NR	Positive Diabetes: 12 (2.4) Hypertension" 48 (9.6) CPD: 19 (3.8) Cancer: 10 (2.0) Immunodeficiency: 9 (1.8) Negative Diabetes: 27 (2.7) Hypertension: 96 (9.0) CPD: 48 (4.8) Cancer: 27 (2.7) Immunodeficiency: 18 (1.8)	ELISA (all positive results were confirmed by rIFA)
Positive Nurse or health care assistant: 555 (47.2) Physician: 184 (15.6) Administration: 95 (8.1) Student: 36 (3.1) Lab staff: 36 (3.1) Physical/Occupational/Speech therapist: 37 (3.1) Porter or domestic worker: 58 (4.9) Security, estates, catering: 23 (2.0) Other: 153 (13.0) Negative Nurse or health care assistant: 3,930 (34.9) Physician: 1,671 (14.8) Administration: 1,452 (12.9) Student: 578 (5.1) Lab staff: 413 (3.7) Physical/Occupational/Speech therapist: 342 (3.0) Porter or domestic worker: 319 (2.8) Security, estates, catering: 245 (2.2) Other: 2,326 (20.6) Negative, then seroconverted during follow-up Nurse or health care assistant: 43 (49) Physician: 4 (5) Administration: 10 (11) Student: 6 (7) Lab staff: 3 (3) Physical/Occupational/Speech therapist: 7 (8) Porter or domestic worker: 0 (0)	NR	ELISA; CMIA

NR	NR	CLIA
NR	NR	NR
Total Students: 16,101 (100) Residential status On campus: 5,442 (33.8); Off campus: 10,659* (66.2)*	NR	NR
NR	NR	NR
NR	NR	NR

Assay Brand	Definition of reinfection	Follow-up test type	Frequency of follow-up testing
Siemens SARS-CoV-2 Total Ab Assay (Anti-S, Total Ab)	Any new RT-PCR confirmed infection up to 2/12/2020 in positive cohort (previously Ab+ HCWs)	PCR	NR
Roche Elecsys Anti-SARS-CoV-2 assay	Individuals in the positive cohort who had at least one PCR+ swab ≥14 days after the primary Ab+ test. Conducted genomic sequencing on a subset of suspected reinfections and used the proportion of confirmed reinfections to determine "likely" reinfections.	PCR (viral genome sequencing of a subset)	Positive: 1.9 tests per-person; 0.5 tests per-person after first Ab+ test Negative:1.7 tests per-person; 0.9 tests per-person after first Ab+ test
In-house IgG RBD ELISA (82.4% sensitivity and 99.6 specificity)	Defined as a new PCR+ test >30 days after primary seropositve result for an individual in the positive cohort	PCR	NR. Note: Symptomatic and asymptomatic PCR testing were widely available for employees, with data available from April 2020 - January 2021.
EDI Novel COVID-19 IgG ELISA; Biosyenx (COVID-19 BSS IgG/IgM) LFA; Abbott Architect SARS-CoV-2 IgG Quant assay	Time of exposition began two month after primary infection (date of first symptoms or RT-PCR+ or primary positive serology) for positive cohort	Immunoassay (Patient-reported symptoms also used in lieu of PCR)	Conducted at months: 1; 3-6; 7-9; 11-13
Unvaccinated & not previously infected with SARS-CoV-2	Cases occurring ≥3 months after the first diagnosis	PCR	NR From December 20, 2020 to March 20, 2021, 4,606247 PCR tests were performed (8,040 per million person-days)

NR	Possible reinfection defined as a positive cohort participant with two PCR+ samples ≥90 days apart, or a positive cohort participant with a new PCR+ test at least 4 weeks after the primary Ab+ result	PCR	All participants attended regular PCR and Ab testing (every 2-4 weeks) and completed questionnaires every 2 weeks on symptoms and exposures. Tests per 1000 days of follow-up Positive: 64 Negative: 70
NR	Individuals in the positive cohort (PCR+) during the first surge of the epidemic (before July 2020) and had PCR+ confirmed primary infection during the second surge (Jul 7, 2020 - Novemeber 20, 2020)	PCR	Provided upon presentation of symptoms and differed in positive and negative cohorts. Only 128/1,038 in positive cohort had second test.
NR	Individuals in the positive cohort (PCR+) during the first surge of the epidemic (before June 2020) with a PCR+ confirmed infection during the second surge (Sept 1, 2020 - Dec 31, 2020)	PCR	Number of tests during second surge (%) Positive 0 tests: 3,525 (32) 1 test: 2,426 (22) 2-3 tests: 2,719 (25) 4+ tests: 2,398 (22) Negative 0 tests: 124,165 (24) 1 test: 117,711 (23); 2-3 tests: 154,359 (30) 4+ tests: 118,036 (23)

NR Ab testing was performed by commercial labs and included a limited set of high-throughput Ab tests with validation against a known standard providing 90-100% agreement with Ab+ and Ab- specimens (95%CI 99%-100%); The majority of Ab tests were for IgG (>91%)	Positive diagnostic test post-primary test in individuals in the positive cohort, measured in 30-day intervals (0-30, 31-60, 61-90, >90 days); this outcome was not strictly defined as "reinfection"	NAAT	Mean number of NAATs over follow-up period Positive: 3.3 Negative: 2.3
In-house RBD (IgG, Anti-S); Abbott (IgG, Anti-N)	Individuals testing PCR+ in the positive cohort (i.e. those having evidence of previous seropositivity by any assay, or a previous PCR+ result more than 90 days earlier in an individual without serological analysis (assumed	PCR	Mass testing occurred at days 0 and 7; clearence testing was conducted day 28; then homes returned to "routine testing" (monthly for residents, weekly for staff)
Abbott ARCHITECT I system (IgG, anti-N)	All PCR+ tests post-baseline were considered to indicate infection in the negative cohort or reinfection in the positive cohort. Note: all participants had 2 or more PCR- tests between baseline Ab test and PCR+ test (and most participants had at least 90 days between baseline	PCR	Residents tested monthly, staff tested weeklly (but individuals with a positive test not re-tested for 90 days)

Euroimmun (Lubeck, Germany)	Participants in the positive cohort who tested positive during follow-up were clinically investigated by two independent adjudicators who have experience in clinical management of SARS-CoV-2, and evaluated suspected cases via EHR or phone interview with participants. Conflicts were resolved by a third person. Even if no viral RNA sequencing was available for comparison, each case of potential reinfection was identified and individually verified by adjudicators. Cases were classified as "likely" or "unlikely" by adjudicators	PCR	NR (data from centralized registry of PCR+)
University of Oxford (Anti-S ELISA); Abbott Architect i2000 IgG (Anti-N CMIA)	PCR+ tests occurring in the positive cohort ≥90 days after primary PCR+ test	PCR	Tests per 10,000 days at risk Positive: 8.0 Negative: 8.7 Asymptomatic health care workers invited for PCR every 2 weeks and serology tests every 2 months

Abbott SARS-CoV-2 IgG	NR explicitly, but authors began recording new infections approximately 1 month after primary serological result (IgG survey May 5-15 2020; new infection tracking occurred June 1, 2020 - Jan 31, 2021)	PCR	"Regular surveillance activities" conducted to control the pandemic was used to identify new positive cases (but the study notes that participants were not enrolled for regular PCR testing following the IgG survey)
NR	Patients in the positive cohort with PCR+ test during both the first and second wave of infections were determined as "tentative reinfections" (tentative due to the possibility that there may have been a false-positive result in the first and/or second wave)	PCR	NR
NR	Positive primary test (Fall 2020) and positive re-test during follow-up (Spring 2021) with a negative test provided between both positive tests. Individuals who did not provide a negative test between the initial infection and reinfection were excluded	PCR	Residential students (living in university residence halls) were subject to 2 weeks of surveillance-based informative testing followed by repeated weekly testing; non-residential students were subject to random surveillance testing only
NR	PCR+ confirmed infection in positive cohort ≥90 days after primary positive test (ignoring repeat positive tests within 90 days)	PCR	Median tests per patient was 1 (IQR 1-2)
NR	Defined as a new PCR+ test in positive cohort >90 days after primary positve result with 2 consecutive negative tests between episodes	PCR	Median (IQR) number of tests Positive at baseline: 3 (3-5) Negative at baseline and follow-up: 3 (3-4) Negative then converted to positive during follow-up: 4 (4-5)

Waiting interval, in months	Primary infection status in positive cohort - symptomatic only vs any infection event	Total N included in analysis	n total positive cohort included in analysis
0	Any (56/300 or 18.7% asymptommatic)	2,063	300
0.5	Any (% asymptomatic NR)	192,967	43,044
1	Any (% asymptomatic NR)	4411	309
2	Any (6/393 or 1.5% asymptomatic)	1,309	393
NA	NA (% asymptomatic NR)	NA	NA

3	Any (% asymptomatic NR)	25,661	8,278
7	Symptomatic only	11175	1038
3	Any (% asymptomatic NR)	525,339	11,068

3	Symptomatic only	3,255,379	378,606
3	Any (% asymptomatic NR)	161	88
0	Any (% asymptomatic NR)	2,111	634

0	Any (44/498 or 8.8% asymptomatic)	1,494	498
3	Any (401/1265 or 31.6% asymptomatic)	12,541	1,246

1	Any (% asymptomatic NR)	6,074	1,402
4	Symptomatic only	8,900,480	15,424
5	Any (% asymptomatic NR)	16,101	2,021
3	Symptomatic only	150,325	8,845
3	Any (474/1579 or 30% asymptomatic)	15075	1579

n total negative cohort included in analysis	n suspected reinfections	n positive cohort with no reinfection	n infections in negative cohort
1,763	1 (0/1 or 0% asymptomatic)	299	38
149,923	129 (5/129 or 3.8% asympomatic*) **only 8 reinfections had documented symptom severity*	42,915	3,185
4,102	14 (% asymptomatic NR)	295	NR
916	1 (1/1 or 100% asymptomatic)	392	69
NA	NA (% asymptomatic NR)	NA	NA

17,383	155 (76/155 or 49% asymptomatic)	8,123	1,704
10137	0 (% asymptomatic NR)	1038	290
514,271	72 (% asymptomatic NR)	10,996	16,819

2,876,773	1,136 (% asymptomatic NR)	377,470	86,303
73	0 (% asymptomatic NR)	44	15
1,477	4 (0/4 or 0% asymptomatic for resident only reinfections)	222	93

996	5 (1/5 or 20% asymptomatic)	493	154
11052	3 (2/3 or 66.7% asymptomatic)	1,174	223

4,672	4 (2/4 or 50% asymptomatic)	1,398	217
8,885,640	40 (% asymptomatic NR)	15,384	253,581
14,080	44 (% asymptomatic NR)	1,977	1703.68
141,480	62 (31/62 or 50% asymptomatic)	8783	5449
13496	5 (0/5 or 0% asymptomatic)	1574	528

n negative cohort with no infection	Main finding for risk of reinfection or protective effect of natural immunity
1,725	Hazards ratio:0.15 (95%CI: 0.06-0.35) p=0.026
146,738	Efficacy of natural infection: 95.2% (95% CI: 94.1%-96.0%)
NR	Adjusted odds ratio: 0.09 (95% CI: 0.005 - 0.48)
847	Relative reduction of incidence of 96.7% p<0.0001)
NA	NA

15,679	Adjusted incident rate ratio: 0.159 (95% CI: 0.13-0.19)
9847	0 reinfections/128 retested
497,452	Efficacy of natural immunity: 80.5% (95%CI: 75.4%-84.5%)

2,790,470	Reinfections occurred in 0.3% of positive cohort and infections occurred in 3% of negative cohort.
25	Efficacy of natural infection: 96.2% (95% CI: 72%-99.5%)
363	Residents adjusted Hazards Ratio: 0·15 (95% CI 0·05–0·44) p=0·0006

842	Efficacy of natural immunity: 94% (95%CI: 86%-98%) p<0.001
11141	Adjusted incidence rate raio: 0.11; 95% CI: 0.03-0.44) p=0.002

4,455	Adjusted odds ratio: 0.054 (95% CI: 0.009 - 0.169)
8,632,059	Odds ratio: 0.09 (95% CI 0.07 - 0.13)
12,376	Efficacy of natural immunity: 84% (95% CI: 78-88%)
136031	Any reinfection: 81.8% (95% CI: 76.6% - 85.8%) Symptomtic reinfection: 84.5% (95% CI: 77.9 - 89.1%)
12968	Hazard Ratio:0.06 (95%CI 0.05-0.08) p<0.001

Authors

Mark Helfand, M.D., M.P.H.[1]

Celia Fiordalisi, M.S.[1]

Jack Wiedrick, M.S.[2]

Katrina L. Ramsey, M.P.H.[2]

Charlotte Armstrong, B.A.[1]

Emily Gean, Ph.D.[1]

Kara Winchell, M.A.[1]

Irina Arkhipova-Jenkins, M.D.[1]

1. Scientific Resource Center to the AHRQ EPC Program
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Disclaimers

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The information in this report is intended to help health care decision makers—patients and clinicians, health system leaders, and policymakers, among others—make well-informed decisions and thereby improve the quality of health care services. This report is not intended to be a substitute for the application of clinical judgment. Anyone who makes decisions concerning the provision of clinical care should consider this report in the same way as any medical reference and in conjunction with all other pertinent information, i.e., in the context of available resources and circumstances presented by individual patients.

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Afterword

Recognized for excellence in conducting comprehensive systematic reviews, the Agency for Healthcare Research and Quality (AHRQ) Evidence-based Practice Center (EPC) program is developing a range of rapid evidence products to assist end-users in making specific decisions in a limited timeframe.

The AHRQ EPC Program recognizes that people are struggling with urgent questions on how to address the COVID-19 pandemic. To shorten timelines, reviewers make strategic choices about which review processes to abridge. The adaptations made for expediency may limit the certainty and generalizability of the findings from the review, particularly in areas with a large literature base. Transparent reporting of the methods used and the resulting limitations of the evidence synthesis are extremely important.

Given the rapidly evolving field, the AHRQ EPC Program will update this review to keep the medical community and public up to date as more studies are published through 2021. If you have comments or have unpublished data to share related to this report, they may be sent by mail to the Task Order Officer named below at: Agency for Healthcare Research and Quality, 5600 Fishers Lane, Rockville, MD 20857, or by email to epc@ahrq.hhs.gov and will be considered in the next version of the report.

David Meyers, M.D.
Acting Director
Agency for Healthcare Research and Quality

Arlene Bierman, M.D., M.S.
Director
Center for Evidence and Practice Improvement
Agency for Healthcare Research and Quality

Craig A. Umscheid M.D., M.S.
Director
Evidence-based Practice Center Program
Center for Evidence and Practice Improvement
Agency for Healthcare Research and Quality

Elise Berliner, Ph.D.
Task Order Officer
Evidence-based Practice Center Program
Center for Evidence and Practice Improvement
Agency for Healthcare Research and Quality

Christine Chang, M.D., M.P.H.
Task Order Officer
Evidence-based Practice Center Program
Center for Evidence and Practice Improvement
Agency for Healthcare Research and Quality

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Comment

NIH recommends that whatever messaging accompanies the release of this report emphasizes the time frame and scope of the data analyzed, and the limitations of this report with regards to studying reinfection by the delta variant.

NIH Comment: It would be helpful to the reader to see both the pooled estimates from metanalysis as well as ranges from individual studies for risk of reinfection (or reduction of risk) as well as efficacy of protection from prior infection.

NIH Comment: Some studies reported 96, 97% reduced risk. Why is the range mentioned at 80-90% and not up to 97%?

Cell 3X: “up to 2/12/2020” Should this be 2021?

Cell 2AB: the column name states “symptomatic only vs any infection event” but the data are for asymptomatic vs any infection event.

Cells 7V and 7W: text seems out of place. Should this be NR if the type of test is not reported?

Cell 7F, reference, does provide estimates from the model which are not included in the results. What is the reason for this?

Consider adding a date to place in perspective with the literature review.

Please spell out “strength of evidence (SOE)”. First time of use.

Consider adding a date to place in context.

I suggest adding the hyperlink here.

Please add “cohort”.

Sometimes refers to cohort and sometimes refers to group. Please be consistent.

I recommend changing “estimate of efficacy” to “protection estimate”. Here and in the rest of the document.

Protection estimates.

This rationale needs reconsideration as no therapeutic or medical countermeasure is being administered. There is no randomized clinical trial being conducted to estimate “efficacy”. This term should be applied only when referring to a vaccine or a therapeutic that has undergone a RCT. Please revise. This is only assessing natural immunity and no pharmaceutical intervention is applied.

I recommend deleting this text.

If PCR only then there is no assessment of natural immunity. Unless positive PCR results were followed upon and were documented as two sequential negative PCRs. Please clarify history of follow up.

Comment from Harrel Chesson.

Not everyone who acquires infection will develop antibodies, and antibodies wane over time. So, there are some people who have acquired infection in the past who did not develop antibodies or might no longer have detectable antibodies at the time of the study.
rADS Comment. Therefore, I recommend adding another limitation to the study or another footnote on the comment above. “Prior infection from SARS-CoV-2 reduced the risk of another infection by 80-90% among people with detectable antibodies as baseline.”

This language is better in describing the outcomes than efficacy.
Please see comment above.

This should be qualified according to the variants evaluated in the studies or in circulation at the time of the studies and in the countries where the studies were conducted. Further evaluation of new variants. i.e., Delta variant should be considered in the future. This variant is more transmissible, has viral loads that are 1000 times higher than the previous variants and there is now evidence that vaccinated individuals can carry this variant. Therefore, it is also likely that unvaccinated, naturally immune persons can also carry this variant and have no symptoms. This remains to be assessed.

I recommend adding a footnote with a clarification regarding variants in circulation during the timeframe of the studies included. i.e., for reference 27. 12 March 2020 to 30 August 2020
Consider using Protection Estimate instead of Efficacy in the title of the second to last column.
Please provide a date. As of xx/yyyy…
As of July 30, 2021 there are only 4 variants of concern in circulation in the United States.
SARS-CoV-2 Variant Classifications and Definitions (cdc.gov)
Please consider qualifying that this is for reinfections with the P1 (Gamma variant).
I recommend adding a footnote indicating that this is based on the variants in circulation around the world during the timeframe of the studies included. New estimates will need to be calculated as new studies are published with the more recent variants.
I recommend adding the key questions (2 and 3) listed in page one at the start of the methods and then list the deferred key questions (1 and 4).
Please add a comma after i.e., here and through out the text.

Not clear why the n=200 were excluded, You could add some text similar to the box below to arrive the final n=18.

Since this metanalysis is for protection due to natural immunity, efficacy is not the right term. It should be reserved for vaccine efficacy studies. Perhaps using: "Protection conferred by natural immunity" or "Protection against reinfection" or "Protection estimate", since there is no treatment or medical countermeasure involved.

Consider using Protection Estimate instead of Efficacy in the title of the second to last column.

rADS. Comment. There is a P value listed at the bottom of the table as p=0.00. Please list as p <0.001

Please capitalize to read ELISA.

"Covid-19" Sometime capitalized and others not. Please be consistent.

Hyphen missing in this cell.

"ConvP" Convalescent patients? Please spell out.

Plural not singular "are"

Same as above.

Lower case, with

Delete space.

Response

Thank you, we will take this into account when we craft messaging with AHRQ's Office of Communications.

We now provide both of them as requested.

The text has been updated to reflect the upper limit of 97%.

The date in this cell was originally formatted in the European style; the correct date is December 2, 2020 (or 12/2/2020). This error been corrected in Table B-1.

Column AB captures whether the study included asymptomatic infections which is equivalent to "any infection" and includes a breakdown of the N/% of asymptomatic patients in that study, as opposed to "symptomatic only." The column header has been updated to more clearly reflect this distinction.

A copy-paste error caused this confusion. All previously misplaced cells have been corrected.

This study used modeling, rather than patient-level data, to estimate protection, and was therefore not included in our data table. A footnote has been added to Table B-1 to clarify this point. Additionally, Cell 7F has been updated to present the study's modeled estimate of protection.

This change has been incorporated. It now says "In March, 2021, we published a living rapid review…"

This change has been incorporated.

This change has been incorporated. It now says "Between March 2021 and August, 2021, several epidemiological studies have been published…."

This change has been incorporated. Added hyperlink to www.covid19reviews.org

This change has been incorporated.

This change has been incorporated.

This change has been incorporated here and throughout the paper.

This change has been incorporated.

This change has been incorporated. It now reads "These outcome metrics termed “protection,” are analogous to the efficacy endpoints used in studies of vaccine efficacy…"

This change has been incorporated. We have deleted of “ of efficacy”

Some studies had no assessment of natural immunity because while this update is part of a larger, living review about immunity, the update focuses on reinfection rates after COVID-19 infection. That is a related topic but isn't directly on immunity. As studies

elaborate the precise relationship between immunity and protection against reinfection, we will update this review so that the link between markers of immunity (both humeral and cellular) to reinfection risk is explicit. We think the studies we reviewed are likely to do this in future publications, but at this time, understandably, they had published their reinfection results before delineating the direct relationship to immunity. While not perfect, studies that followed up people who had a positive PCR were useful for estimating reinfection rates. In lieu of a negative PCRs, some studies used a "waiting period" during which most or all patients would be expected to have a negative PCR if tested. We found that studies that used this substitute for confirmation by negative PCRs had estimates similar to those studies that used negative PCRs to confirm resolution of viral shedding.

On the related issue of antibodies, we have added the limitation " Also important, the studies did not delineate whether the risk of reinfection depends on the development or persistence of detectable antibodies. Results may be different in people who did not develop or have lost an antibody response." We did not use the wording the reviewer suggested ("among people with detectable antibodies at baseline") because in some studies baseline antibodies were not documented, so some patients who did not have detectable antibodies may have been included in the cohort. At stated above, in the next

Thank you for your feedback.

This change has been incorporated. "Efficacy" changed to "protection." Here and throughout.

We agree it is very likely that unvaccinated naturally immune persons can carrry this variant and have no symptoms and that the effect on reinfection risk of prior infection with another variant, or primary infection with delta, are uncertain. Rather than a footnote, we have added several statements about the lack of data on reinfection in the setting of the Delta (and Lambda) variants.

This change has been incorporated into Figure 1.

This change has been incorporated. We have added "As of August 10, 2021…"

This change has been incorporated.

This change has been incorporated.

This change has been incorporated into the section text. We have added "These findings are based on the variants in circulation around the world during the timeframe of these studies."

Appendix A has been updated to direct the reader to the PROSPERO protocol, which presents the most up-to-date key questions.

This change has been incorporated throughout the report.

Additional clarifying text has been added to the figure.

This change has been incorporated.

This change has been incorporated.

This change has been incorporated.
This change has been incorporated throughout the report.
This change has been incorporated.
ConvP abbreviation was for "convalescent plasma" group - this cell has been updated to clarify.
This change has been incorporated.
This change has been incorporated.
This change has been incorporated.
This change has been incorporated.

From: Porras, Jessica (OS/IOS) <Jessica.Porras@hhs.gov>
Sent: Thu, 4 Nov 2021 11:06:48 -0500
To: Undisclosed recipients:
Subject: HHS Cabinet Affairs Report- Week ending November 5
Attachments: HHS_Agency Weekly Report_11_4_21.docx

Hi Colleagues,

This week's HHS Cabinet Affairs report is attached. As ever, reach out if you have questions.
Thanks,
Jessica

Jessica Porras
Policy Advisor, Immediate Office of the Secretary
Department of Health and Human Services
E: jessica.porras@hhs.gov
C: (b) (6)

WEEKLY REPORT

November 4, 2021

MEMORANDUM FOR THE CABINET SECRETARY

FROM: SEAN MCCLUSKIE, CHIEF OF STAFF, HHS, (202) 740-3247

SUBJECT: HHS Weekly Report | Week ending November 5, 2021

AMERICAN RESCUE PLAN (ARP) / BIPARTISAN INFRASTRUCTURE FRAMEWORK (BIF) / BUILD BACK BETTER AGENDA (BBB) / ECONOMY

- **Significant activity for consideration to raise to the attention of POTUS:**
  - **ARP Workforce Funding**: During the week of November 1st (tentative), the White House will announce the largest number of awards in history for its health workforce loan repayment and scholarship programs, the National Health Service Corps (NHSC) and Nurse Corps, which require participants to commit to working in underserved communities. The overall number of participants in these programs will top 22,700, with nearly 20,000 NHSC members, more than 2,500 Nurse Corps nurses, and approximately 250 awardees under a new program, the Substance Use Disorder Treatment and Recovery Loan Repayment Program. The Health Resources and Services Administration (HRSA) will also be announcing the release of the application cycles for the Fiscal Year 2022 NHSC Program, partially funded by ARP, including: $282.5 million for the NHSC Loan Repayment Program; $107 million for the NHSC Substance Use Disorder Workforce Loan Repayment Program; and $55 million for the NHSC Rural Community Loan Repayment Program.

- **Past Week Accomplishments and Setbacks/Obstacles:**
  - **Center for Medicaid & Children's Health Insurance Program (CHIP) Services (CMCS) Informational Bulletin: Basic**

Health Program (BHP); Revised Federal Funding for New York and Minnesota: On November 5th, CMS will publish the "Basic Health Program (BHP); Revised Federal Funding Methodologies for Program Years 2020 and 2021 and Operational Questions & Answers." This CMCS Informational Bulletin (CIB) specifies updated values for factors needed to calculate the federal BHP payment rates for 2020 and 2021 as a result of ARP. The two states (Minnesota and New York) that operate BHPs will receive an increase in their federal BHP payments for 2020-2022 as a result of the changes to the BHP payment methodologies required by ARP. Through BHPs, states can provide coverage to individuals who are citizens or lawfully present non-citizens; who do not qualify for Medicaid, CHIP, or other minimum essential coverage; and who have incomes between 133% and 200% of the federal poverty level.

- **Healthcare Infection Prevention and Control Funding Award:** On October 27th,the Centers for Disease Control and Prevention (CDC) awarded $885 million as part of a $2.1 billion investment in ARP funding to expand efforts that protect Americans from COVID-19 infections and other emerging infectious diseases across healthcare settings.
- **Administration for Community Living (ACL) Technical Assistance (TA) to Senate HELP and Finance and House Education & Labor Committees**: On October 30, ACL and the Assistant Secretary for Legislation (ASL) provided TA to staff from the Senate HELP and House Education & Labor committees regarding provisions in the reconciliation bill to implement Older Americans Act (OAA) home and community based supportive services, nutrition, caregiver, and other services and related infrastructure for older adults and the workforce that supports them. On November 1st and 2nd, ACL and ASL provided TA to Senate Finance committee related to Elder Justice Act programs and ombudsman programs in the Medicaid home and community-based services provisions.
- **Administration for Children and Families (ACF) Office of Child Care (OCC) Participates in ARP TA Office Hours Opportunity**: On November 4th, ACF OCC TA Centers facilitated Office Hours opportunities to discuss TA questions, needs, and resources with grantees. The session included an

overview of available TA resources and stabilization grant topics.

- **Office of Population Affairs Telehealth Notice of Funding Opportunity (NOFO):** The Office of Population Affairs (OPA) within the Office of the Assistant Secretary for Health (OASH) anticipates releasing a $35M funding competition to support telehealth enhancement and expansion in the Title X program to mitigate access barriers to quality family planning services for clients, especially for vulnerable and hard-to-reach populations. The NOFO, which is targeted for release the second week of November, is supported by COVID ARP funding, and will offer successful applicants of the Title X family planning service grants national competition the ability to request one-time awards to support telehealth in their systems. The NOFO is currently in the HHS clearance process and should move to OMB for clearance by November 1st.

- **Requests for White House Collaboration:**
  - N/A

- **Next Week – Upcoming Events / Tasks / Developments:**
  - **OPA Title X Dire Need NOFO:** On or around November 5th, OPA anticipates releasing a NOFO to address dire needs for family planning services. The $9.25M competition, which was announced as part of HHS's response to Texas SB8, will support increased demand for emergency contraception and other Title X family planning services for clients both within and outside of Texas. The 15-month award, which is supported by COVID ARP funding, is the complement to HHS's action to provide approximately $750,000 in supplemental funding to Every Body Texas, the primary Title X family planning grantee, for its increased need for emergency contraceptive and family planning services in the state.
  - **ACF Office of Early Childhood Development (ECD) Live Webinar on Early Childhood Policy Updates from the Biden-Harris Administration:** On November 9th, ACF ECD will describe efforts to build a strong and stable early childhood workforce and address current workforce shortages. They will also highlight how HHS will help the early childhood education

workforce access health benefits during the CMS Week of Action starting November 14th.

COVID-19

- **Significant activity for consideration to raise to the attention of POTUS:**
  - N/A

- **Past Week Accomplishments and Setbacks/Obstacles:**
  - **Availability of Vaccines:** On October 29th, FDA authorized the emergency use of the Pfizer-BioNTech COVID-19 Vaccine for the prevention of COVID-19 to include children 5 through 11 years of age, following a thorough review by the Agency and independent advice from FDA's Vaccines and Related Biological Products Advisory Committee at a meeting on October 26.
  - **Health Care Staff Vaccinations Against COVID-19 for Medicare- and Medicaid-certified Health Providers [CLOSE HOLD]:** On November 4th, CMS will release an emergency regulation requiring staff vaccinations for 15 specific health care provider and supplier types participating in Medicare and Medicaid programs to address the urgent need to protect patients against COVID-19. These requirements will apply to approximately 50,000 providers and cover more than 17 million health care workers. Impacted health care providers will have 30 days from the publication of the regulation to establish a policy to ensure their staff have received a one-dose COVID-19 vaccine or the first dose of a two-dose COVID-19 vaccine prior to providing any care, treatment, or other services. Sixty days after the publication of the regulation, staff for all health care provider and supplier types included in the regulation must be fully vaccinated.
  - **Advisory Committee on Immunization Practices (ACIP) Meeting:** On November 2nd and 3rd, CDC conducted a meeting of the ACIP that was open to the public and webcast live. The agenda included discussions on Pfizer COVID-19 vaccine use in children aged 5-11 years and a recommendation vote was scheduled to be conducted on November 2nd. Recommendation votes were scheduled to be conducted for

hepatitis, orthopoxviruses and Ebola vaccines, and the immunization schedule on November 3rd.

- **Pediatric COVID-19 Vaccine Update:** On November 3rd, CMS provided an update for stakeholders on pediatric COVID-19 vaccinations following the FDA authorization of the Pfizer-BioNTech COVID-19 Vaccine for the prevention of COVID-19 in children 5 through 11 years of age and a recommendation from the CDC. CMS reminded eligible consumers that coverage is available without cost-sharing under Medicare, Medicaid, the Children's Health Insurance Program (CHIP), and in the commercial market for this critical protection from the virus. CMS also issued fact sheet updates regarding COVID-19 vaccinations.
- **COVID-19 Vaccines for Ages 5 to 11**: In anticipation of the November 2nd announcement approving the Pfizer vaccine for ages 5-11, the Indian Health Service (IHS) Vaccine Task Force assessed pediatric vaccine needs across Indian Country and continued to coordinate rollout, including efforts to prepare for distribution and administration logistics and disseminate clinical education.
- **COVID-19 Health Equity Task Force, Final Meeting October 28, 2021:** The COVID-19 Health Equity Task Force hosted its final meeting on Thursday October 28th. The meeting included a walkthrough of the final report, reflections and remarks from members, opportunity for public comment, and a vote on deliverables. Dr. Marcella Nunez- Smith provided opening and closing remarks, with the ASH, Admiral Rachel Levine, providing remarks during the meeting.
- **Availability of Diagnostics:** Between October 26th and 29th, FDA issued Emergency Use Authorizations (EUAs) to enable the emergency use of 1 diagnostic for COVID-19 (the 11th over-the-counter (OTC) COVID-19 test) and reissued 6 EUAs for diagnostics for COVID-19.
- **New CDC Study Shows Vaccination Offers Higher Protection than Previous COVID-19 Infection:** On October 29th, CDC issued a media statement on new science reinforcing that vaccination is the best protection against COVID-19. In a new *Morbidity and Mortality Weekly Report* examining more than 7,000 people across 9 states who were hospitalized with COVID-like illness, CDC found that those who

were unvaccinated and had a recent infection were 5 times more likely to have COVID-19 than those who were recently fully vaccinated and did not have a prior infection.

- **Accepted Vaccines:** More than 765 million doses of COVID-19 vaccines have been accepted by the Assistant Secretary for Preparedness and Response (ASPR).
- **AstraZeneca International Donations:** Following the October 22nd FDA determination that two additional lots of AstraZeneca's COVID-19 vaccine are acceptable for export, ASPR and AstraZeneca are in discussions and planning for international donations.
- **International Vaccine Donations:** ASPR continues working with the Countermeasures Acceleration Group (CAG) to provide on the ground support for international donations of vaccines. To date, vaccine transfers have been made to 95 countries and ASPR has directly supported vaccine transfers of over 87 million doses.
- **Delay of Regeneron Delivery:** Delayed release of Regeneron's co-formulated REGEN-COV has extended the delivery schedule by two weeks. The CAG distribution team is mitigating this delay to meet allocation demands. Supply continues to be limited for a few more weeks.
- **IHS/CDC Vaccination Program** memorandum of agreement (**MOA) Extension**: On October 28th, the MOA between the IHS and CDC regarding the CDC Coronavirus Disease 2019 (COVID-19) Federal Agency Vaccination Program was extended until November 17th, which reflects a one year extension from the initial agreement.
- **Vaccines and Testing in Indian Country**: IHS, tribal, and urban Indian program sites receiving the vaccine through the IHS have reported administering 1,722,756 doses of the COVID-19 vaccine as of October 31st. The IHS, tribal, and urban Indian program sites reporting to IHS performed a total of 3,227,274 COVID-19 tests as of October 30th, with 271,784 of those tests being positive.
- **CDC Safe Resumption of Global International Travel Order:** During the week of November 1st, CDC will publish a notice in the *Federal Register* announcing an Amended Order (including accompanying attestation form and technical instructions) signed by the CDC director on October 30th to implement the

new Biden administration travel policy to safely resume global travel to the United States. On November 8th, non-U.S. citizens who are not immigrants to the United States will be required to be fully vaccinated and provide proof of their vaccination status to fly to the United States, with only limited exceptions.

- **CDC Global Contact Tracing Order:** During the week of November 1st, CDC will publish a notice in the *Federal Register* announcing an Order (including accompanying technical instructions) signed by the CDC director on October 25th to require all airlines and operators of flights arriving into the United States from a foreign point of last departure to collect passenger and maintain crewmember contact information.
- **CDC Amendment of the Global Testing Order:** During the week of November 1st, CDC will publish a notice in the *Federal Register* announcing an Amended Order (including accompanying attestation form) signed by the CDC director on October 25th requiring negative pre-departure COVID-19 test results or documentation of recovery from COVID-19 for all airline or other aircraft passengers arriving into the United States from any foreign country. This Amended Order supersedes the previous Order signed on January 25, 2021.
- **Phase Two of Mask Innovation Challenge:** ASPR will launch phase two of the Mask Innovation Challenge on November 3rd. Phase two of the challenge focuses on laboratory testing and prototype development of more effective, comfortable face masks for personal use that resolve common concerns about wearing masks. Prototypes will be tested by the National Institute for Occupational Safety and Health (NIOSH), the National Institute of Standards and Technology (NIST) and partner labs.
- **COVID-19 Surge Support:** ASPR continues to support COVID-19 Surge with National Disaster Medical System (NDMS) and Health and Medical Task Force (HMTF) teams responding to COVID-19 in the AK, MT, NY, WI, and the District of Columbia: The week of November 8th, ASPR will mobilize teams in UT, WI and potentially in MN, CO, and NM. Media, relevant Congressional delegations, and key stakeholders will be apprised of the teams' activities.

- **Deployment of Strategic National Stockpile Materiel:** ASPR delivered the following assets to support surge requirements over the course of the last several weeks.
    - WI: Personal Protective Equipment (PPE) push package and fit test cache
    - MT: Forty-five ventilators along with resupply Kits
    - AK: Five dialysis machines and one service contract
    - Federal Emergency Management Agency (FEMA) (Washington, DC): A controlled substance cache for replenishment of the national medical transport and support ambulance contract
- **Rural Vaccine Distribution:** As of November 1st, 177 Rural Health Clinics (RHCs) in 28 states are participating in the Health Resources and Services Administration (HRSA) RHC COVID-19 Vaccine Distribution Program and have placed orders for a total of 163,480 doses of COVID-19 vaccines.
- **Vaccine Administration:** As of October 22nd, a total of 6,823,344 COVID-19 vaccine doses have been administered through the Health Center COVID-19 Vaccine Program; 76 percent to racial and/or ethnic minority patients. In total, 15,425,031 COVID-19 vaccine doses have been administered by health centers; 67 percent to racial and/or ethnic minority patients. Specifically, 7.8 million patients initiated a vaccination series; 7.5 million patients completed a vaccination; and 177,178 patients received an additional booster vaccine. The total number of vaccine doses administered increased from 15,175,856 to 15,425,031 (a 1.6 percent increase) in the last two weeks.
- **Vaccine Administration to Adolescents:** Through October 22nd, health centers have administered 593,612 COVID-19 vaccine doses to children aged 12 to 17 years old provided through the Health Center COVID-19 Vaccine Program.
- **Vaccine Distribution:** For delivery during the week of November 1st, the Health Center COVID-19 Vaccine Program approved orders for a total of 202,100 doses of COVID-19 vaccines. This includes 120,900 pediatric COVID-19 vaccine doses that health centers were able to order for the first time this week. The Program now has 872 participating health centers that have placed at least one order during any week. To

date, health centers have ordered 9,805,550 doses for 2,415 sites.

- **Monoclonal Antibodies:** Between August 14th and October 22nd, 113 health centers have administered 11,323 doses of monoclonal antibody therapy directly to patients.
- **Pediatric COVID-19 Vaccine Checklist:** In the October 22nd Primary Health Care Digest newsletter, HRSA's Bureau of Primary Health Care shared the HRSA/CDC Action Checklist of Pediatric COVID-19 Vaccination and additional CDC resources with the health center community.
- **COVID-19 Compensation Claims:** As of November 1st, 4,682 claims alleging injuries/deaths from COVID-19 countermeasures have been filed with the Countermeasures Injury Compensation Program, including 2,229 claims alleging injuries from COVID-19 vaccines; an increase of 133 in total claims over the prior week. About 90 percent of claims are awaiting medical records for review. To date, 91 claims are in medical review, 3 claims have been denied compensation, 1 claim has been determined medically eligible for compensation; however, the program is still working with the claimant to obtain the necessary information to determine the compensation amount.
- **Provider Relief Fund**: On October 21st, HRSA's Provider Relief Fund issued four Phase 3 reconsideration payments totaling approximately $48,800.
- **COVID-19 Uninsured Program:** As of October 27th, HRSA's COVID-19 Uninsured Program has paid over 103.3 million claims, totaling over $12.2 billion, to health care providers for testing, treatment, and vaccine administration for uninsured individuals. Approximately $875 million has been paid for over 22.8 million vaccine claims, $4.1 billion for about 9.3 million treatment claims, and $7.2 billion for over 71.2 million testing claims.
- **COVID-19 Coverage Assistance Fund**: As of October 29th, 16,920 providers have enrolled in HRSA's COVID-19 Coverage Assistance Fund and 12,717 providers have been approved to submit claims. A total of 55,771 claims, totaling over $1.4 million, have been paid to reimburse health care providers for costs associated with administering vaccines to underinsured individuals.

- **Decision-Support Tool for Individuals Deciding When to Test for COVID-19:** On November 3rd, the National Institutes of Health's (NIH) National Institute of Biomedical Imaging and Bioengineering (NIBIB) announced the When to Test Calculator for Individuals, a free online tool that uses a mathematical model to determine an individual's relative risk of having or getting COVID-19 and spreading the infection to others. This project and the associated When to Test Calculator for Organizations were funded through the NIH Rapid Acceleration of Diagnostics (RADx) Initiative.
- **Stakeholder Engagement on Health Equity: Vaccinating Children with Disabilities:** On November 5th, Acting ACL Administrator Alison Barkoff and team members from ACL, CDC, and Department of Education met with disability stakeholders regarding forthcoming vaccines for children with disabilities, given lessons learned from successes and barriers from the rollout to adolescents with disabilities.
- ***Morbidity and Mortality Weekly Report* (*MMWR*):** CDC released a series of COVID-19 related *MMWRs* (see Appendix)

- **Requests for White House Collaboration:**
  - N/A

- **Next Week – Upcoming Events / Tasks / Developments:**
  - **COVID-19 Vaccines for the Pediatric Population:** On November 12th, the Health Resources and Services Administration (HRSA) Region 2 (New Jersey, New York, Virginia, Puerto Rico) is organizing and hosting a webinar in Spanish for HRSA supported Health Centers healthcare professionals in Puerto Rico on COVID-19 vaccines for the pediatric population and what health center clinicians should know about the upcoming recommendations for COVID-19 vaccinations in ages 5 to 11.
  - **Medicaid and CHIP Public Health Emergency Unwinding Punchlist:** On November 8th, CMS will publish a tool to help states identify and adopt strategies for maintaining continuity of coverage among eligible individuals during the COVID-19 unwinding period. This "punch list" of strategies includes operational and policy recommendations in several areas,

which states are encouraged to adopt to prevent inappropriate terminations when the public health emergency ends.

- **Health Equity Funding for COVID-19 Vaccines:** During the week of November 8th, (tentative), as part of a White House Health Equity Announcement, HRSA will announce over $143 million to support community-based organizations that will provide information and education on COVID-19 vaccines to the medically vulnerable or underserved and racial and ethnic minority groups with low vaccination rates. This funding includes a new $66.5 million funding opportunity announcement and $77 million to support an additional nine Community-Based Workforce for COVID-19 Vaccine Outreach award recipients.
- **Medicaid and CHIP COVID-19 Data Snapshot:** On November 12th, CMS will release an updated Medicaid and CHIP data snapshot, providing insight into the impact of COVID-19 on beneficiaries and service utilization through May 2021. The snapshot includes updates to data released previously on COVID-19 testing, treatment, and acute care; service utilization for Medicaid and CHIP beneficiaries age 18 and under; services delivered via telehealth; and services for mental health and substance-use disorders. It also includes a new section on reproductive health services for female beneficiaries of reproductive age. The results demonstrate that, although telehealth services surged during the public health emergency and remain above prior years' rates, there has been a decline in use for many primary, preventive, behavioral, and reproductive health services
- **Medicaid Telehealth Toolkit Update:** On November 9th, CMS will release an update to the State Medicaid and CHIP Telehealth Toolkit: Policy Considerations for States Expanding Use of Telehealth, COVID-19 Version. This update will include revisions to a supplement clarifying the availability of audio-only telehealth in Medicaid regardless of the public health emergency. CMS has heard from stakeholders that there is confusion about payment for Medicaid services using audio-only technology; these revisions specify Medicaid's approach.

CLIMATE

- **Significant activity for consideration to raise to the attention of POTUS:**
  - N/A

- **Past Week Accomplishments and Setbacks/Obstacles:**
  - **Extreme Heat Interagency Working Group (IWG):** The Extreme Heat IWG was formally launched on October 27th. This IWG co-chair principles Secretary Becerra, Administrator Regan (EPA) and Administrator Spinrad (NOAA) joined the kick-off to provide remarks of support and marching to the steering committee. The outcomes of the discussion included the identification of deliverables and subsequently, the IWG will convene in the coming weeks to address next steps for achieving the deliverables.
  - **President's Task Force on Environmental Health Risks and Safety Risks (PTFCEH) Subcommittee on Climate, Environment, and Disasters:** The Principals of the PTFCEH met on October 28th to reinvigorate and charge the working group. As part of that meeting, a new Subcommittee on Climate, Environment and Disasters will be officially added to the PTFCEH.)
  - **ACF Office of Community Services (OCS) Participates in U.S. Department of Energy's (DOE) Weatherization Assistance Program Interagency Collaboration on Client Eligibility:** On November 4th, DOE hosted an interagency group meeting with the U.S. Department of Housing and Urban Development and ACF OCS's Low Income Home Energy Assistance Program (LIHEAP). They reviewed grantee contact offices across the country for program coordination and technical assistance design.

- **Requests for White House Collaboration:**
  - N/A

- **Next Week – Upcoming Events / Tasks / Developments:**
  - **HHS Participation in Conference of Parties (COP26) in Glasgow, Scotland:** On November 8th, the Assistant Secretary for Health will travel to Glasgow, Scotland to

participate in the United Nations Climate Change Convention COP 26. The HHS delegation includes Assistant Secretary for Health Admiral Levine, Office for Global Affairs (OGA) staff Stephanie Psaki, Maya Levine and Noila Sorensen, and the Office of Climate Change and Health Equity (OCCHE) interim Director John Balbus.

- **HHS will participate in the COP26 Health Program:** On November 8, HHS/OCCHE will host an official side event at the US Center that will feature comments from Assistant Secretary for Health Admiral Rachel Levine, CDC National Center for Environmental Health (NCEH) Director Pat Breysse, and NOAA Administrator Rick Spinrad, before a panel discussion moderated by John Balbus featuring Admiral Levine, Trust for America's Health CEO Dr. Nadine Gracia, and Health Care Without Harm's Gary Cohen. HHS will also participate in other official and unofficial events at the COP. Several bilateral side meetings are being set up for the HHS delegation to meet with counterparts from the UK, Canada, and civil society.

EQUITY FOR UNDERSERVED COMMUNITIES

- **Significant activity for consideration to raise to the attention of POTUS:**
  - N/A

- **Past Week Accomplishments and Setbacks/Obstacles:**
  - **ACF ECD Discusses Build Back Better Agenda at Tribal Consultation:** On November 4th, Katie Hamm, Deputy Assistant Secretary for ECD, presented at a Tribal Consultation to discuss proposed Tribal Early Childhood Initiatives in BBB.
  - **G20 Finance and Health Ministerial (October 29) and G20 Leaders' Summit (October 30/31):** Both of these events laid groundwork to improve the sustainable financing of future global pandemic preparedness - 1) through the creation of a G20 Finance-Health Task Force to better connect health and finance officials for pandemic preparedness, and 2) through continued G20 consideration of a new financing mechanism for pandemic preparedness. HHS worked closely with Treasury and in support of NSC to help secure relevant text for these initiatives in the outcome documents for these events. Secretary Becerra participated in the G20 Finance and Health

Ministerial alongside Secretary Yellen. One setback was that we were unable to get specific mention of a Financial Intermediary Fund, our preference for a new financing mechanism, in either document; but we will continue to push for consideration of it as G20 discussions continue.

- **Medicaid and CHIP Afghan Evacuee Coverage Fact Sheet:** On November 1st, CMS posted an updated fact sheet to Medicaid.gov that provides information based on recent legislative changes on health coverage options for Afghan evacuees arriving in the United States. Most evacuees will be eligible for health insurance through Medicaid, CHIP, the Marketplace, Refugee Medical Assistance, or other coverage provided by the Office of Refugee Resettlement. The fact sheet will provide additional information on eligibility for each coverage program based on immigration status and state of residence.
- **Health Equity and Maternal Health**: On November 2nd, HRSA Region 7 (Iowa, Missouri, Nebraska, Kansas) hosted the first session in a learning series on Advancing Equity in Maternal & Infant Health in collaboration with Region 7 Office of Assistant Secretary of Health for maternal health organizations, health care providers, health centers, rural health clinics, hospitals, community and faith-based organizations in Region 7. This three-part series defines health equity, highlights disparities in maternal and infant health outcomes among disproportionally affected populations in Region 7 and identifies systemic issues that are contributing to these health disparities.
- **National Institutes for Health (NIH) Study Suggests Health Care Costs for Rare Diseases Are Similar to Cancer and Heart Failure:** A new retrospective study of millions of medical and insurance records by the National Center for Advancing Translational Sciences (NCATS) researchers and their collaborators indicates health care costs for individuals with a rare disease are three to five times greater than the costs for those without a rare disease, suggesting nationwide medical costs are similar to those for cancer and heart failure. The study provides new evidence of the potential impact of rare diseases on public health, suggesting that the number of individuals with rare diseases and their medical costs have been underestimated.

- **A Powerful Tool for Studying the Risk of Heart Disease:** (Update) Planned for November 10th, the National Human Genome Research Institute (NHGRI) will announce a large-scale study of people from diverse ancestries in which researchers narrowed down the number of genomic variants that are strongly associated with blood lipid levels and generated a polygenic risk score to predict elevated low-density lipoprotein cholesterol levels, a major risk factor for heart disease.
- **Federal Hypertension Control Leadership Council:** The Office on Women's Health (OWH) presented OWH's Hypertension Challenge Phase 1 results at the Federal Hypertension Control Leadership Council.
- **Health Equity Quarterly Newsletter:** On November 1st, CMS's Office of Minority Health distributed the third edition of Health Equity Quarterly, a newsletter highlighting recent CMS activities and recent reports.
- **Biomedical Advanced Development and Research Authority (BARDA) Industry Day:** Dr. Marcella Nunez-Smith, Senior Adviser to the White House COVID-19 response team and Chair of the Presidential COVID-19 Health Equity task force will be the keynote speaker for the upcoming BARDA Industry Day. She is expected to emphasize the importance of increasing representation in our workforce and among our leadership as well as equitable access to participation in clinical trials.

- **Requests for White House Collaboration:**
  - N/A

- **Next Week – Upcoming Events / Tasks / Developments:**
  - N/A

SIGNIFICANT EXECUTIVE ORDER (EO) & AGENCY ACTIVITY

- **Significant activity for consideration to raise to the attention of POTUS:**
  - **ACF Office of Community Services (OCS) Low-Income Home Energy Assistance Program (LIHEAP) Funding Release:** ACF's OCS announced the release of approximately $3.37 billion of Federal Fiscal Year (FY) 2022 regular block

grant funding to LIHEAP grantees. Funds were certified October 29th, and a press release went out on November 1st. All 50 states, the District of Columbia, territories, and 122 tribes received their Notice of Award. This funding is provided under the Extending Government Funding and Delivering Emergency Assistance Act, which the President signed into law on September 30, 2021 (Public Law 117-43). This release will reflect 90 percent of the total or annualized amount of funds available under the Continuing Resolution (CR) to grantees at the beginning of the program year.

- **IHS Behavioral Health Funding Opportunities**: On November 4th, the IHS anticipates announcing six notice of funding opportunities totaling $46 million to address suicide, domestic violence, substance abuse, and an integrative approach to the delivery of behavioral health services for American Indians and Alaska Natives.
- **CDC Updates Blood Lead Reference Value for Children:** On October 28th, CDC issued a press release announcing its recently updated blood lead reference value (BLRV) from 5 µg/dL to 3.5 µg/dL in response to the Lead Exposure Prevention and Advisory Committee recommendation made on May 14, 2021. The BLRV is intended to identify children with higher levels of lead in their blood compared to most children, based on the 97.5th percentile of the blood lead level distribution in U.S. children ages 1–5 years.

- **Past Week Accomplishments and Setbacks/Obstacles:**
  - **Marketplace Open Enrollment Campaign Announcement:** On November 1st, CMS announced the start of Marketplace open enrollment, which runs from November 1st, 2021-January 15th, 2022. Consumers can visit HealthCare.gov to enroll in health care plans for calendar year 2022 and take advantage of historically low premiums. To ensure more people have access to the health care they need, CMS is increasing consumer assistance on the ground to support the largest open enrollment outreach campaign to-date.
  - **Sidecar Health Qualified Health Plan Application Denial:** On November 3rd, CMS sent a third and final denial letter to Sidecar Health. This completes the appeal submitted by the

company regarding the denial of an application for its health plans to be considered as qualified health plans in 2023.

- **Calendar Year 2022 Medicare Outpatient Prospective Payment System and Ambulatory Surgical Center Payment System Final Rule:** On November 2nd, CMS posted the Calendar Year 2022 Medicare Outpatient Prospective Payment System and Ambulatory Surgical Center Payment System Final Rule in the Federal Register. The rule will finalize proposed payment policies for outpatient treatment and ambulatory surgical centers in Medicare.
- **Calendar Year 2022 Medicare Physician Fee Schedule Final Rule:** On November 2nd, CMS posted the Calendar Year 2022 Medicare Physician Fee Schedule Final Rule in the Federal Register. The rule will finalize proposed payment policies for physicians and other health professionals under Medicare.
- **Calendar Year 2022 Home Health Prospective Payment System Final Rule:** On November 2nd, CMS posted the Calendar Year 2022 Home Health Prospective Payment System Final Rule in the Federal Register. The rule finalizes proposed payment policies for Medicare home health care for older adults and people with disabilities.
- **The American Association for Blood Banks (AABB) States U.S Blood Supply is Classified as Red**: AABB reports that the status of the U.S. blood supply remains classified as RED (less than 1-day supply) for the seventh week in a row. This status indicates that the majority of blood center inventories are critically low on blood and need donations as soon as possible. The OASH is working on the National Blood and Plasma Donation Campaign, mandated in the CARES Act to understand donor motives, create materials and advertisements for use to encourage blood and plasma donors, particularly among underrepresented donors.
- **Interoperability and the Connected Health Care System Blog:** On/about November 5th, CMS will publish a blog about its commitment to advancing interoperability in health care. The blog will highlight how the agency believes increasing access to health data is a critical step on the path to better informed decision making, improved patient outcomes, and reduced administrative burden.

- **Data Visualization on Recent Trends in Hospitalization Use**: On November 4th, the Agency for Healthcare Research and Quality (AHRQ) updated the data for public data visualization tools and tables that provide details on US hospital use through 2021. The updated data allows users to see the impact of the pandemic on hospital utilization for a wide variety of hospital services and conditions, including COVID-19. For instance, the data shows a large reduction in the number of surgeries in all states, which coincides with the emergence of COVID-19-related hospitalizations in April 2020. In some states, the number of surgeries has not returned to pre-pandemic levels.
- **Report of Technical Expert Panel on the Feasibility of a Quality Measure for Malnutrition**: In response to a request from the House and Senate Appropriations Subcommittees on Labor-HHS, AHRQ convened a Technical Expert Panel (TEP) to examine the feasibility of a quality measure related to malnutrition. The TEP concluded that a hospital-level accountability metric related to readmission outcomes for malnutrition is premature at this point in time. The TEP also highlighted a new hospital-level process measure that has recently been endorsed by the National Quality Forum. The TEP's findings have been incorporated into a report, "AHRQ Technical Expert Panel: Quality Measurement of Malnutrition in Hospitalized Patients." That report will be submitted to Rep. Roybal-Allard (D-CA) who serves on the House Appropriations Subcommittee on Labor-HHS.
- **"Users of Retail Medications for Opioid Use Disorders Faced High Out-of-Pocket Prescription Spending in 2011-2017":** On October 26th, a paper published in the *Journal of Substance Abuse and Treatment* and authored, in part, by staff from AHRQ, provides national estimates of financial costs faced by the population receiving retail medications for Opioid Use Disorder (MOUD). Patients with retail MOUD prescriptions spent 3.4 times more out-of-pocket for prescriptions on average than the rest of the U.S. population, with 18.8% of this population paying entirely out-of-pocket for their MOUD prescriptions. Insurance coverage is associated with reduced annual out-of-pocket MOUD expenditures between $316 and $328 per year.

- **Behavioral Health Support for Operation Allies Welcome:** At the request of the Unified Coordination Group, ASPR is designing and implementing a system for operational coordination, command and control of behavioral health and protection services across all the Afghan safe harbor sites. This week, the team implemented the first consistent behavioral health coordination and reporting system for safe harbor sites.
- **Ebola Testing Reagent Availability for ASPR Partners:** ASPR continues to support its partners with reagent availability for the Ebola diagnostic test. The Department of Defense owns the relevant reagents and access is currently limited to procurement by federal government entities. While ASPR supports the analyses of clinical samples from partners (Merck and Janssen), reagent access has become an issue for partners that are not funded by the United States Government.
- **Summary of ASPR Funded Countermeasures Used in Ebola Virus Outbreak:** Ebanga, Inmazeb and ERVEBO are products in the ASPR countermeasure portfolio that have been used to treat people infected with Ebola in the current outbreak.
    - As of October 26th, there are 6 confirmed cases and 3 probable cases (all probable cases are deceased).
    - Four of the six confirmed cases died and two are in recovery, with one likely to be released from the Ebola treatment unit.
    - Two recovering patients received monoclonal antibody therapeutics. One received Ridgeback's Ebanga while the other received Regeneron's Inmazeb. An additional two patients received therapeutics but did not survive.
    - As of October 26th, 249 people, including contacts and frontline workers, have been vaccinated with ERVEBO.
- **2021 Small Group Market Premium Benchmarks for the IRS**: The Affordable Care Act of 2010 (ACA) established the Small Employer Health Insurance Tax Credit (henceforth, credit) to help small employers provide health insurance to employees. Moreover, Section 1421 of ACA required the Secretary of HHS (HHS) to compute every year, for the Internal Revenue Service (IRS), the average small group market premiums that form the basis of the credit. ASPE submitted projected 2021 average health insurance premium provided by small employers for each state-rating-area in the country to the

IRS on November 1st. The IRS publishes in the fall of each year the benchmarks in the Instructions for Form 8941, Credit for Small Employer Health Insurance Premiums.
    - **Paperwork Reduction Act Waiver**: On behalf of the HHS Secretary, ASPE reviews requests to waive the Paperwork Reduction Act during public health emergencies. During the COVID-19 public health emergency, the Secretary has approved 33 Paperwork Reduction Act (PRA) waivers. To date, 22 remain in effect. On November 1st, the Secretary approved the 33rd PRA waiver to allow the HHS Assistant Secretary for Public Affairs to collect information to inform the COVID-19 Public Education Campaign. This is ASPA's 5th PRA waiver pertaining to the Campaign.
    - **2021 Samuel J. Heyman Service to America Medal for Science and Environment:** On October 28th, Dr. Reem Ghandour from HRSA's Maternal and Child Health Bureau received this award for her work on the National Survey for Children's Health, the largest national- and state-level survey on the health and health care needs of children ages 0-17, their families, and their communities.

- **Requests for White House Collaboration:**
    - N/A

- **Next Week – Upcoming Events / Tasks / Developments:**
    - **Marketplace Open Enrollment Weekly Snapshot [TENTATIVE]:** On November 12th, CMS will share its first snapshot of updates from Marketplace open enrollment. CMS will issue the snapshot on a regular schedule as part of open enrollment.
    - **Prescription Drug and Health Care Spending Interim Final Rule with Comment Period (No Surprises Act Requirements, Part III):** On November 10th, CMS will issue a third interim final rule with comment period related to Title II (Transparency) of Division BB of the Consolidated Appropriations Act, 2021, which established new protections for consumers related to surprise billing in health care. The rule will require health plans and issuers to submit key data, which the Departments of Health & Human Services, Labor, and the Treasury will use to report and better understand prescription

drug pricing trends and their impact on consumers' premiums and out-of-pocket costs. In addition to reporting information on average monthly premiums and drug spending for enrollees versus their employers and/or health insurance issuers, plans and issuers will be required to report total health care spending by the type of care patients receive. The reporting requirements apply beginning with the data for the 2020 calendar year. The Departments anticipate releasing their first public report in 2023, and biennially thereafter.

- **Iowa Medicaid State Plan Amendment Disapproval [CLOSE HOLD]:** On/about November 9th, CMS will issue a disapproval to Iowa for its Medicaid state plan amendment.
- **Primary Care First Model Seriously Ill Population Component Cancellation:** On November 9th, CMS will announce that it will not be moving forward with the Seriously Ill Population component of the Primary Care First Model. CMS has determined that the proposed outreach method is unlikely to result in sufficient beneficiary uptake, which is necessary for model evaluation. Primary Care First is a set of voluntary alternative five-year payment options that reward value and quality by offering an innovative payment structure to support the delivery of advanced primary care.
- ***All of Us* Research Program Leadership Updates:** On November 3rd, NIH's *All of Us* Research Program announced the selection of Dr. Geoffrey Ginsburg as the Chief Medical and Scientific Officer. Dr. Ginsburg is currently at Duke University School of Medicine Center for Applied Genomics & Precision Medicine. In mid-December, founding Director Eric Dishman will step down from his role as Chief Innovation Officer.

APPENDIX

- **Week ahead messaging:**

HHS Priorities Included/Excluded from Build Back Better

- HHS is carefully preparing for anything in the bill that comes under the broad HHS umbrella.
- There is a lot of work ahead of the Department—the opportunity to negotiate drug prices to lower costs for Medicare beneficiaries, help

millions of Americans get coverage through the ACA, and support American families with childcare, strengthen our public health activities, just to name a few.
- These are all things the Department is preparing to do.

Afghan Minors at Licensed Shelter Program in the Chicago Area

Background: Senator Durbin called for HHS OIG to investigate ORR actions concerning a recent story about allegations of Afghan kids not receiving needed services at one of ORR's licensed shelter programs in the Chicago area.

- The care and well-being of children in our custody continues to be a top priority for HHS.
- ORR takes any allegations regarding the safety and wellbeing of kids in our care very seriously, and we have had a team of staff at ORR headquarters working closely with all providers who are caring for unaccompanied Afghan minors.
- We appreciate the support and engagement of our congressional partners on our shared commitment to ensuring the wellbeing of children in our care.
- For each of these providers, ORR has been very clear about the requirement related to interpreters and translators available to support services and case management at these sites.
- ORR staff regularly visit all shelters to ensure that providers are meeting the required standards of service, and staff has been onsite at the Heartland programs recently.
- In accordance with grant requirements, Heartland is in the process of adding in-person translators to the staff, with 10 on site today, and 36 to be on site by this Friday.
- ORR requires facilities to have translators on site, provide weekly individual counseling sessions and twice weekly group counseling sessions for the children, as well as individual sessions whenever requested - and we take appropriate corrective action for any facilities not meeting required services.
- We will continue to work closely with all providers serving unaccompanied Afghan minors to ensure that their needs are being met, including mental and behavioral health services, in partnership with community organizations and Congress.

- To date, we have reunited more than 1000 UAMs with an appropriate sponsor. There are 269 UAMs in ORR care right now, which is roughly one third of one percent of the share of Afghan arrivals.

COVID-19 Vaccine for Kids 5-11 Vaccination

All kids 5 and older are now eligible to get vaccinated.

- This is a safe and effective vaccine. It has undergone rigorous review, and now has been authorized by FDA and recommended by CDC for kids ages 5-11, after thorough testing for safety in thousands of children.

The COVID-19 vaccine is the best way to keep your child safe.

- The best way to protect your child against COVID-19, including the Delta variant, is to get them vaccinated.
- Kids are being infected with COVID-19, and some are getting seriously ill or sadly even dying. Even if your child doesn't get severely ill, they could face long-term health consequences or pass the virus to others.
- If your child gets COVID-19, the negative health effects can be serious and last months; but the most common side effect of the vaccine is a sore arm.
- We know that many parents are trying to decide what is right for their child and their family. If you have questions about your child and the COVID-19 vaccine, talk to a pediatrician, school nurse, or another trusted health care provider.

Vaccines help protect your child, your family, and your community.

- 15 million adolescents have already been vaccinated.
- The vaccines offer lasting protection to prevent your child from getting infected or, worse, having severe outcomes. The vaccine is more than 90% effective.
- Getting vaccinated will help keep schools open, sports going, and help our kids maintain a more normal lifestyle, thanks to the comfort and protection provided by the vaccines.

HHS Takes Further Action to Reduce Prescription Drug and Medical Costs (No Surprises Third Interim Final Rule)

- The Biden-Harris Administration continues its charge to reduce high, unexpected health care costs.
- The Departments of Health and Human Services, Labor, Treasury (collectively, the Departments) and the Office of Personnel Management—will implement a reporting requirement for prescription drug costs and a list of medical expenses that are commonly culprits of surprise bills.
- These reporting requirements will ultimately help gather information to publish and better understand prescription drug pricing trends and their impact on premiums and consumers' out-of-pocket costs.
- The "Prescription Drug and Health Care Spending" interim final rule is the latest in a series of actions that make good on President Biden's commitment to protect millions of consumers long plagued by surprise medical bills.
- HHS will continue to take aggressive steps to better identify and combat barriers to the affordable, comprehensive and person-centered care that all Americans deserve.

  - **Travel:**
    - October 22, 2021 Secretary Becerra traveled to New York, New York
    - October 27, 2021 Secretary Becerra traveled to Baltimore, Maryland
    - October 29, 2021 Secretary Becerra traveled to San Francisco, California
    - November 1, 2021 Secretary Becerra traveled to Sacramento, California
    - November 8-9, 2021 Secretary Becerra will travel to Chicago, Illinois
    - November 10, 2021 Secretary Becerra will travel to Rochester, Minneapolis, and St. Paul, Minnesota
    - November 18, 2021 Secretary Becerra will likely travel to either MD or VA
    - November 19, 2021 Secretary Becerra will likely travel to Wilmington, Delaware
    - Week of November 22, 2021 no tentative travel planned
    - Week of November 29, 2021 no tentative travel planned

- Anticipated November 8, 2021: The Assistant Secretary for Health will travel to Glasgow, Scotland to participate in the Conference of Parties (COP26) Event.
- IHS: (Tentative) On November 18th, Acting IHS Director Ms. Elizabeth Fowler will participate in COVID-19 vaccine promotion events in Oakland, California, focused on vaccines for ages 5-11 years old.

- **Speeches:**
  - ACL: On November 10, Acting ACL Administrator Alison Barkoff will join CMS Deputy Administrator Daniel Tsai in delivering keynote remarks at the 2021 Annual Conference hosted by the National Association of State Directors of Developmental Disabilities Services (NASDDDS). She will highlight Administration priorities and ACL activities related to people with developmental disabilities.
  - ACL: On November 17, Acting ACL Administrator Alison Barkoff will deliver prerecorded remarks at the Community Care Corps Symposium hosted by USAging. Her remarks will focus on the critical services and supports for older adults, people with disabilities and caregivers available through innovative volunteer caregiver models.
  - ACL: On November 17, Acting ACL Administrator Alison Barkoff will deliver prerecorded remarks at the Annual Gala hosted by the Autistic Self Advocacy Network. She will thank disability stakeholders for their efforts throughout the COVID-19 pandemic and highlight Administration and ACL priorities related to people with disabilities, including COVID-19 response efforts.
  - ACL: On November 17, Acting ACL Administrator Alison Barkoff will deliver remarks at the American Academy of Nursing Policy Conference hosted by American Academy of Nursing. She will highlight Administration priorities related to caregiving and discuss ACL's policy and program activities to support family caregivers.
  - CDC: Dr. Rochelle Walensky, CDC Director, spoke at the following events:
    - October 27th: Council on Foreign Relations fireside chat (COVID-19)

        - November 1st: Keynote speech at the Annual Medical Education Innovations and Scholarship Conference at New York University's Grossman School of Medicine (COVID-19 and the future of health care and medical education at large)
- CDC: Dr. Rochelle Walensky, CDC Director, will speak at the following events:
    - November 4th: Keynote speech at the 2021 National Center for AIDS Research (CFAR) Scientific Symposium (CDC's role in Ending the HIV Epidemic)
    - November 9th: Panel discussion at the Bill and Melinda Gates Foundation Grand Challenges Annual Meeting (pandemic preparedness and response)
- CMS: On November 2nd, CMS Principal Deputy Administrator/Chief Operating Officer Jon Blum addressed attendees at the American Diabetes Association's Cost of Care Summit.
- CMS: On November 2nd, Robert Wood participated in a technology transformation roundtable.
- CMS: On November 3rd, CMS Administrator Chiquita Brooks-LaSure will address attendees at the National Conference of State Legislatures.
- CMS: On November 3rd, CMS Principal Deputy Administrator/Chief Operating Officer Jon Blum will address attendees at the Senior Care Pharmacy Coalition Annual Membership Meeting.
- CMS: On November 3rd, Dr. LaShawn McIver will address attendees at the Digital Health Equity Summit.
- CMS: On November 4th, CMS Administrator Chiquita Brooks-LaSure will address attendees at the 45th Annual Moving Forward Together Conference.
- CMS: On November 4th, CMS Administrator Chiquita Brooks-LaSure will participate in a fireside chat hosted by *The Hill*, entitled "Diabetes Technology: Disparities, Access, & Equity."
- CMS: On November 4th, Liz Fowler will address attendees at the Harvard Business School Health Care Alumni Association 22nd Annual Conference.
- CMS: On November 5th, Dr. LaShawn McIver will address attendees at the United States Professional Association for Transgender Health 2021 Scientific Symposium.

- CMS: On November 9th, Dr. Natalia Chalmers will participate as a panelist for an oral health webinar hosted by the National Institute for Health Care Management.
- CMS: On November 9th, Sharon Graham will participate in a virtual event on Medicare open enrollment hosted by Representative Dwight Evans (PA).
- CMS: On November 9th, Liz Fowler will participate in a keynote, point-counterpoint address hosted by Moss Adams Healthcare. The event is intended for health policy experts and will focus on value-based care and national trends.
- CMS: On November 9th, Robert Wood will participate in the Converge@Xcelerate Symposium hosted by the Institute for Critical Infrastructure Technology.
- CMS: On November 10th, Dr. LaShawn McIver will address attendees at the National Association of State Directors of Developmental Disabilities Services Annual Conference.
- CMS: On November 12th, Dr. Meena Seshamani will participate as a panelist for the University of Pennsylvania Leonard David Institute Seminar.
- FDA: On November 2, 2021, Acting Commissioner Woodcock provided remarks and participated in Q&A at the Robert Wood Johnson Foundation Health Policy Fellows Meeting.
- FDA: On November 8, Acting Commissioner Woodcock will provide a keynote at the GRx+Biosims event.
- FDA: On November 9, Acting Commissioner Woodcock will participate in a discussion with Scott Gottlieb, MD at the Friends of Cancer Research Virtual Annual Meeting.
- FDA: On November 15, Acting Commissioner Woodcock will provide a keynote and participate in Q&A at the Harvard University MEDLIFE event.
- FDA: On November 15, Acting Commissioner Woodcock will participate on a panel at The Children's Inn at NIH. The panel topic is "Collaboration Insights: What We've Learned and How It Will Change The Way We Work."
- FDA: On November 17, Acting Commissioner Woodcock will provide remarks at the Lausanne VIII: Building Global Momentum for Interventions in Alzheimer's Disease event.
- FDA: On November 18, Acting Commissioner Woodcock will provide introductory remarks at the Closer to Zero Action Plan:

Impacts of Toxic Element Exposure and Nutrition at Different Crucial Development Stages for Babies and Young Children.

- FDA: On November 19, Acting Commissioner Woodcock will participate in a fireside chat with Dean Lloyd Minor as part of Stanford University's series of events on lessons learned from the pandemic.
- HRSA: On November 2nd, Jim Macrae, Associate Administrator of HRSA's Bureau of Primary Health Care, spoke at the Association of Clinicians for the Underserved Annual Conference on Health Center Program priorities and updates.
- HRSA: On November 3rd, Jim Macrae, Associate Administrator of HRSA's Bureau of Primary Health Care, spoke at the Centers for Disease Control and Prevention/HRSA Advisory Committee on HIV, Viral Hepatitis and Sexually Transmitted Disease Prevention & Treatment on the Health Center Program and Ending the HIV Epidemic in the United States.
- On November 4th, Dr. Michael Warren, Associate Administrator for the Maternal and Child Health Bureau (MCHB) spoke at the 2021 Healthy Start Virtual Grantees' Meeting. He provided an update on MCHB's strategic direction and information regarding MCHB's Infant Health Equity 2030 initiative. Healthy Start provides grants to support community-based strategies to reduce disparities in infant mortality and improve perinatal outcomes for women and children in high-risk communities throughout the nation.
- On November 8th, Dr. Michael Warren, Associate Administrator for the Maternal and Child Health Bureau, spoke at the Region 5 Infant Mortality Initiative on Accelerating Upstream Together to Eliminate Racial Disparities in Infant Health by 2030. Region 5 (Illinois, Indiana, Michigan, Minnesota, Ohio, and Wisconsin) accounts for 21 percent of all U.S. Black infant deaths and four of the top 10 counties with the Black infant deaths are in Region V. Region 5 also accounts for 12 percent of all U.S. American Indian/Alaskan Native infant deaths.
- IEA: On November 2nd, IEA Director Marvin Figueroa spoke to the National Hispanic Medical Association on HHS priorities at their COVID-19 #Vaccinate4All Campaign training meeting for Latino health care leadership.

- IEA: On November 2nd, IEA Director Marvin Figueroa spoke to the National Organization of Black Elected Legislative Women on HHS priorities.
- IHS: On October 28th, Acting IHS Director Ms. Elizabeth Fowler participated in a Tribal Leader discussion on Tribal economies during the White House Council on Native American Affairs and HHS Nation to Nation Dialogue on the Ongoing COVID-19 Response.
- IHS: On October 29th, Acting IHS Director Ms. Elizabeth Fowler provided remarks during the National Council of Urban Indian Health Board Meeting.
- IHS: On November 2nd, Acting IHS Director Ms. Elizabeth Fowler provided remarks during the National Indian Health Board 3rd Quarter Board Meeting.
- IHS: On November 3rd, Acting IHS Director Ms. Elizabeth Fowler will provide remarks during the IHS Contract Support Cost Workgroup meeting.
- IHS: On November 8th, Acting IHS Director Ms. Elizabeth Fowler will participate in COVID-19 vaccine promotion events focused on vaccines for ages 5-11 years old. Events will include Tribes in the Anadarko, Oklahoma, area and a Bureau of Indian Education site.
- IHS: On November 9th, Acting IHS Director Ms. Elizabeth Fowler will provide remarks during the virtual FY 2022 Oklahoma City Area Tribal Consultation and FY 2024 Budget Formulation Session.
- IHS: On November 9th, Acting IHS Director Ms. Elizabeth Fowler will provide remarks and participate in open discussion on mandatory funding for the IHS with OMB and Tribal Leaders during the IHS Tribal Self-Governance Advisory Committee meeting.
- IHS: On November 18th, Acting IHS Director Ms. Elizabeth Fowler will provide remarks during the IHS monthly call with Tribal leaders and Urban Indian Organization leaders.
- IHS: On November 19th, Acting IHS Director Ms. Elizabeth Fowler will provide remarks during the virtual IHS National Director’s Awards Ceremony.
- IHS: On November 30th, Acting IHS Director Ms. Elizabeth Fowler will provide remarks during virtual Tribal Consultation on

designating the State of Arizona as a Purchased/Referred Care Delivery Area.

- IHS: On December 8th, Acting IHS Director Ms. Elizabeth Fowler will provide remarks during virtual Tribal Consultation on designating the State of Arizona as a Purchased/Referred Care Delivery Area.
- OASH: November 1st, the Assistant Secretary for Health will speak at the Callen-Lorde Community Health Awards Gala via a pre-recorded video.
- OASH: On November 4th, the Assistant Secretary for Health will speak at Pharmacy Executive Leadership Alliance via a pre-recorded video.
- OASH: On November 4th, the Assistant Secretary for Health will participate in the Brazda Breakfast Reporter Series.
- OASH: On November 5th, the Assistant Secretary for Health will provide Keynote remarks via a pre-recorded video in the Western States Opioid Stimulant Summit.
- OASH: Anticipated on November 12th, the Assistant Secretary for Health will provide pre-recorded remarks for the Representation Matters Event.
- OASH: Anticipated on November 16th, the Assistant Secretary for Health will provide a pre-record video for Transgender Awareness Week.
- OASH: Anticipated on November 15th & 17th, the Assistant Secretary for Health will provide remarks on Day 1 and/or Day 2 of the 72nd Presidential Advisory Council on HIV/AIDS (PACHA) Meeting.
- OASH: Anticipated on November 17th, the Assistant Secretary for Health will provide remarks at the National Council November Wellbeing Wednesday Webinar.
- OASH: Anticipated on December 2nd, the Assistant Secretary for Health will provide keynote remarks for the United States Conference on HIV/AIDS (USCHA) Annual Meeting.
- OASH: Anticipated on December 2nd, the Assistant Secretary for Health will participate in Reuters NEXT Fireside Chat.
- OASH: Anticipated on December 2nd, the Assistant Secretary for Health will provide opening remarks at the International LGBTQ Leaders Conference.
- OCR: On November 8th, Timothy Noonan, the Office for Civil Rights' Deputy Director for Health Information Privacy, will be

presenting to the Health Care Compliance Association, on Cybersecurity in Health Care.

- OCR: On October 28th, Carla Carter, the Office for Civil Rights' Associate Deputy Director for Civil Rights, presented to the 2021 National Environmental Justice and Training Program, 13th Annual National Conference on Health Disparities.
- OCR: On November 2, 2021, WHIAANHPI's Executive Director Krystal Ka'ai joined the Deputy Assistant to the President and Senior AA and NHPI Liaison in speaking to the National Asian Pacific American Caucus of State Legislators (NAPACSL) during the annual National Conference of State Legislatures Summit.
- ONC: Dr. Micky Tripathi, National Coordinator for Health IT, delivered remarks at the following event:
  - November 4th: California Exposure Notification Virtual Symposium to discuss technology related to future pandemics. The event was open to the public.
- ONC: Dr. Micky Tripathi, National Coordinator for Health IT, will speak at the following events:
  - November 9th: Healthcare Revolution and Transformation Summit to discuss public health after COVID-19. The event is open to the public.
  - November 9th: CommonWell Fall Summit to discuss healthy equity. The event is open to the public.
  - November 16th: Scottsdale Institute 2021 Fall Symposium to discuss federal agency coordination. The event is closed to the public.
  - November 16th: Veeva Clinical Research Sites Forum to discuss ONC's priorities and public health data modernization. The event is open to the public.
  - November 17th: South Florida HIMSS Annual Conference to discuss health equity and health data portability. The event is open to the public.
  - November 18th: Government CIO Media & Research EHR Summit to discuss EHR modernization and patient empowerment of data. The event is open to the public.
  - November 18th: Federal Electronic Health Record Modernization (FEHRM) Program Office Industry Interoperability Roundtable to discuss EHR modernization efforts. The event is closed to the public.

- NIH
  - NIH Director Dr. Francis Collins' recent and upcoming speeches:
    - November 3rd: Livestreamed conversation with Pfizer Scientific Director Dr. Mikael Dolsten at the American Federation for Aging Research's 40th Anniversary Scientific Symposium and Award Ceremony. The discussion will center on how the Accelerating Medicines Partnership between Pfizer and NIH helped provide a roadmap for the Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) public-private partnership.
    - November 4th: Pre-recorded presentation on SARS-CoV-2 lessons for science and health policy at the Pontifical Academy of Sciences meeting on COVID-19: New insights into the causes, actions and consequences of the pandemic, and implications for science and health policy.
    - November 8th, 9th: Opening keynote and participant on a panel titled "A New Model for Global Health & Development Innovation" at the Grand Challenges Annual Meeting, which fosters international innovation partnerships to address the greatest challenges in health and development.
  - On November 9th, National Institute on Minority Health and Health Disparities (NIMHD) Director Dr. Eliseo Pérez-Stable, NIH Chief Officer for Scientific Workforce Diversity (COSWD) Dr. Marie Bernard, and National Heart, Lung, and Blood Institute (NHLBI) Medical Officer Dr. Patrice Desvigne-Nickens will participate in the National Coalition of 100 Black Women, Inc. Anne Arundel County Chapter's webinar titled "Combating Vaccine Hesitancy in the African-American and Hispanic Communities: What We Know About the COVID-19 Vaccines, Vaccinating Children, Community Acceptance, Booster Shots, and Safe Practices for Holiday Gatherings."
- SAMHSA: On November 9th, Acting Deputy Assistant Secretary Tom Coderre will present on the new HHS Overdose Prevention Strategy during his keynote at the 2021 Symposium on Substance Use Research hosted by the RDAR Center, the

COBRE on Opioids and Overdose, WVCTSI, the WV-INBRE, and the CADRE.
    - SAMHSA: On December 2nd, Assistant Secretary Delphin-Rittmon will be interviewed by Dr. Karen Kangas from the Hartford HealthCare for their Recovery Leadership Academy. The topics for the interview include the opioid crisis and mental health.

- **Media:**
    - October 25, 2021 Secretary Becerra participated in interviews with MSNBC and CNN on COVID-19 testing
    - October 26, 2021 Secretary Becerra participated in interviews ahead of the Overdose Prevention Strategy rollout
    - October 27, 2021 Secretary Becerra participated in a press conference on the Administration's Overdose Prevention Strategy
    - October 28, 2021 Secretary Becerra participated in a press call on postpartum care in New Jersey
    - October 29, 2021 Secretary Becerra participated in interviews on open enrollment
    - November 1, 2021 Secretary Becerra participated in a press conference on open enrollment in California
    - November 1, 2021 Secretary Becerra participated in interviews at events in Sacramento
    - November 3, 2021 Secretary Becerra participated in interviews on open enrollment
    - November 4, 2021 Secretary Becerra will participate in an interview with the New York Times on HHS priorities and accomplishments
    - November 8-9, 2021 Secretary Becerra will likely participate in interviews in IL and MN
    - FDA: On November 3, Acting Commissioner Woodcock participated in an on-camera Zoom interview with TIME magazine for kids, with one of their "kid reporters" to discuss the Pfizer/BioNTech COVID-19 vaccine authorization.
    - NIH
        - NIH Director Dr. Francis Collins' recent media engagements:

        - October 26th: ABC News' *Good Morning America*
        - October 27th: Fox News' Neil Cavuto
        - November 1st: Walter Isaacson for *Amanpour & Company*, a late-night public affairs series on PBS
        - November 2nd: NPR's *Planet Money* podcast
      - On November 1st, the *All of Us* Research Program launched the Social Determinants of Health survey, which is designed to collect information from participants on various factors that may affect health and wellbeing. An announcement with detailed information about the survey was released on November 4th.
      - On November 3rd, leaders from multiple NIH Institutes and Centers participated in a press briefing at the annual meeting of the Society for Neuroscience. The discussion centered around research addressing the effect of COVID-19 on the opioid epidemic, individuals with substance use disorders, and the pediatric population.
    - OASH: ADM Levine was interviewed by the New York Times, Washington Post, Bloomberg, Forbes, USA Today, NPR, The Blade, and LGBTQ Nation about her appointment as the first openly transgender four-star officer and first female four-star admiral of the U.S. Public Health Service Commissioned Corps.
    - OASH: On October 28th, the Assistant Secretary for Health will be featured on the Johns Hopkins University Podcast with Joshua M. Sharfstein, MD, Vice Dean for Public Health Practice and Community Engagement, JHU Bloomberg School of Public Health.

- **Principal level meetings or calls with Governors, Mayors, or other elected officials of note:**
    - October 27, 2021 Secretary Becerra met with Secretary Alejandro Mayorkas
    - October 29, 2021 Secretary Becerra participated in an event with San Francisco Mayor London Breed
    - October 29, 2021 Secretary Becerra participated in the G20 Health and Finance Ministers Meeting
    - November 3, 2021 Secretary Becerra will meet with CFPB Director Rohit Chopra

- November 4, 2021 Secretary Becerra will meet with Ambassador Kathryn Tai
- November 12, 2021 Secretary Becerra will meet with the UK Health Minister
- Week of November 15, 2021 Secretary Becerra will likely have dinner with the Latino cabinet members
- ACF OCS Low Income Household Water Assistance Program (LIHWAP) Presentation: Leveraging Multiple Federal Funding Sources for COVID-19 Response and Recovery: On November 1st, ACF OCS presented at the Bloomberg Philanthropies/ United States Conference of Mayors (USCM) e311 Workshop. They presented on what funds to use and when to use them, and on resources for water affordability and infrastructure projects. The panel included Environmental Protection Agency and the Department of Treasury.
- November 3rd: Dr. Rochelle Walensky, CDC Director, will participate in the White House governor's call.
- CMS: On October 31st, Administrator Brooks-LaSure, Principal Deputy Administrator Blum, and Deputy Administrator and Director Seshamani participated in a meeting with Senator Bernie Sanders (I-VT) regarding drug pricing.
- CMS: On November 5th, Administrator will participate in a call with Sen. Cassidy (R-LA) regarding surprise medical billing.
- IEA: On Thursday, October 28th and Friday, October 29th IEA Tribal Affairs and the White House Council on Native American Affairs held a two-day virtual Nation-to-Nation dialogue to hear input, recommendations, and perspectives on how federal resources and assistance can best support Tribes' response to Public Health Emergencies and improve health systems across Indian Country.
- OASH: The week of November 1, 2021, **t**he Assistant Secretary for Legislation (ASL) will call designated Congressional leaders to inform them that the National Fitness Foundation Board member appointments process is under way, pending Office of Disease Prevention and Health Promotion (ODPHP), Office of the Assistant Secretary for Health, outreach to potential nominees.
- OASH: The Office of Disease Prevention and Health Promotion (ODPHP) within the Office of the Assistant Secretary for Health

(OASH) is working with the Assistant Secretary for Legislation (ASL) to schedule a briefing to the Appropriations Committees. GAO Report released on September 16th and a response and briefing are supposed to be within 60 days of release.

- **Noteworthy public engagement:**
  - October 26, 2021 Secretary Becerra met with the Alliance of Community Health Plans Board of Directors
  - October 27, 2021 Secretary Becerra hosted a roundtable with stakeholder groups to discuss their priorities and HHS efforts
  - October 27, 2021 Secretary Becerra participated in the Nation-Nation Conversation on COVID-19
  - October 28, 2021 Secretary Becerra participated in the AARP Global Conference
  - November 2, 2021 Secretary Becerra met with the American Health Care Association and the California Association of Health Facilities
  - November 3, 2021 Secretary Becerra hosted a roundtable with stakeholder groups to discuss their priorities and HHS efforts
  - November 3, 2021 Secretary Becerra participated in First Focus' Children's Budget Summit
  - Week of November 15, 2021 Secretary Becerra will host two roundtables with stakeholder groups to discuss their priorities and HHS efforts
  - November 15, 2021 Secretary Becerra will participate in the White House's Tribal Nations Summit
  - November 18, 2021 Secretary Becerra will participate in a Children's Education Week COVID-19 event
  - OASH: The Office of Climate Change and Health Equity (OCCHE) team joined a meeting of the collaborative's working group on policy, financing and measurement on October 26th, and Assistant Secretary for Health, Admiral Levine, provided updates to the collaborative's steering committee on our plans for the COP26 meeting on November 1st.
  - OCR: On October 27th, the White House Initiative on Asian Americans, Native Hawaiians, and Pacific Islanders (WHIAANHPI) and the White House Office of Public

Engagement held a national AA and NHPI Stakeholder Briefing featuring updates from the WH Presidential Personnel Office, HHS, and the Department of Education, in addition to updates on the Child Tax Credit.

- OCR: On October 28th, WHIAANHPI and the White House Office of Public Engagement hosted a virtual Filipino American History Month event to recognize the contributions of Filipino Americans. The event featured a conversation between Air Force Under Secretary Gina Ortiz Jones and Deputy Assistant to the Secretary Erika Moritsugu, speeches from California Attorney General Rob Bonta, San Antonio Mayor Ron Nirenberg, as well as a panel with Filipino American Biden-Harris appointees and a panel with representatives from various Filipino American community organizations.
- OCR: On October 29th, WHIAANHPI and the White House marked National Women's Small Business Month by convening a closed-door, virtual listening session for AA and NHPI small business advocates and women small business owners to hear about their concerns and recommendations to ensure that AA and NHPI small businesses are included in the federal government's ongoing economic recovery efforts.
- OCR: On November 3rd, WHIAANHPI will partner with the COVID-19 Health Equity Task Force and the WH Office of Public Engagement to host an AA and NHPI stakeholder briefing as part of the Task Force's release of its Final Report and proposed implementation plan.
- ACF: On November 8th, as part of developing action plans in alignment with the President's EO on Equity, ACF ANA will hold a listening session with American Indian, Alaska Native, Native Hawaiian and Pacific Indigenous grant recipients to get input on improving training and technical Assistance for Indigenous communities, access to ACF grants and services for Indigenous populations, and ACF's cultural competency in working with and providing resources to Indigenous communities.
- ACF: On November 10th, Family Equality and HRC will host a discussion on how to center the experiences of LGBTQ+ youth and families in ACF's programs and services.
- ACF Children's Bureau (CB) Participates in Child Welfare Discussion: On November 1st, Associate Commissioner of CB, Aysha Schomburg, participated in Day 3 of *Accountability*

Dialogues, three 90-minute conversations designed to set the stage for transformative policy development on behalf of families who experience domestic violence and who have been involved in the child welfare system. These conversations were hosted by Futures Without Violence, Latinos United for Peace and Equity, Ujima: National Center on Violence Again Women in the Black Community, and Women Transforming Families.

- ACF Office of Trafficking in Persons (OTIP) Participates in Multi-Session Anti-Racism and Racial Equity Training: On November 2nd, 3rd, and 4th, Ra'Shya Ghee, a subject matter expert within the anti-trafficking field, and OTIP delivered a 10-week anti-racism and racial equity training for grantees and OTIP staff. The training equipped participants with the shared framework, language, historical context, and strategies necessary to embed a racial equity lens at the core of their organizational operations and culture.
- ACF Office of Refugee Resettlement (ORR) Participates on Panel: On November 3rd, ACF ORR Director Cindy Huang participated in a panel discussion on Operational and Legal Challenges at the U.S. Southern Border with the United Nations High Commissioner for Refugees.
- ACF Office of Head Start (OHS) Virtual Listening Session with Michigan Head Start Associations: On November 3rd, Dr. Bernadine Futrell, Director, ACF OHS, hosted a virtual listening session with Michigan Head Start Associations. ACF OHS gathered input and feedback from associations on challenges within their programs.
- ACF OHS Virtual Listening Session - Fall Series: On November 3rd, Dr. Bernadine Futrell, Director, OHS, hosted the second listening session in the virtual fall series with state associations in regions I, III, IV, VI, VII, IX, and XI. These sessions are being hosted to discuss best practices and challenges with full enrollment, workforce wages and benefits, recruiting and retaining staff, and Universal PreK.
- ACF Panel on Families First Prevention Services Act (FFPSA): On November 3rd, a national discussion on adapting to changes from the pandemic into a new era of FFPSA was conducted with Region 7 Regional Administrator (RA) Christie

Appelhanz, Embrace Families (Florida), Children's Alliance (Kentucky), and Heartland for Children (Florida).

- ACF OHS Health Webinar: On November 4th, OHS hosted the webinar "Strategies to Promote Staff Physical Health and Infection Control: As Early Care and Education Programs," with a focus on protecting staff from COVID-19, and more common staff health concerns that may be overlooked, such as injuries, stress, and infections. This webinar covered the recommended components of an initial staff health examination and a periodic re-examination, and screening or tests for communicable diseases. The webinar explored strategies to reduce stress and prevent injuries among ECE staff.
- ACF OHS Chatathon Series: On November 4th, ACF OHS hosted the Chatathon Live Series: "Emergency Rental Assistance and Housing Vouchers" (SPANISH). A panel of experts came together for the fourth live chat to learn more about how ARP makes rental assistance and housing vouchers available for people with overdue rent or who are at risk of homelessness. ACF OHS staff was on hand to respond to as many questions as possible.
- ACF Federal Policy Opportunities to Advance Equity and Well-Being for Youth and Young Adults: On November 4th, Acting Assistant Secretary JooYeun Chang, Acting Assistant Attorney General of the Office of Justice Programs Amy Solomon, and Senior Advisor of the Department of Labor Brent Parton spoke on Policy Opportunities for Supporting the Well-Being of Youth and Young Adults at an event hosted by Youth Transition Funders Group.
- OHS Head Start Virtual Site Visit: On November 5th, Dr. Bernadine Futrell, Director, ACF OHS, virtually visited a Head Start center in Region VIII. She greeted the teaching staff, read to students, and hosted a listening session with program staff.
- ACF ECD Participates in Event Promoting Equity and Celebrating Resilience in Tribal Early Childhood Programs: On November 8th, the first of a two-part webinar series will be conducted on promoting equity in tribal early childhood programs and celebrating the resilience and creativity of tribal communities as they serve young American Indian and Alaska Native (AI/AN) children and families. The second part of the series will be held on November 16th.

- ACF ANA to Participate in Intimate Partner Violence Assistance Program (IPVAP) External Stakeholder Meeting for a Special Fall Summit: On November 9th, ANA Acting Commissioner Michelle Sauve will discuss Missing or Murdered Indigenous People (MMIP) Vulnerable populations. The meeting will include the IPVAP Internal Stakeholder Council, IPVAP External Stakeholder Council, and Leadership Council Executive members and specials guests.
- ACF OTIP to Participate in Pennsylvania (PA) Rural Human Trafficking Summit: On November 9th, OTIP will moderate a panel discussion titled, “Trafficking Prevention and Risk Factors: Approaches to Prevention and How Systems Can Respond” at the upcoming PA Rural Human Trafficking Summit. The panel will consist of three survivor leaders.
- On November 8th and 16th, the ACF Office of Early Childhood Development (ECD) will present a two-part webinar series focused on promoting equity in tribal early childhood programs and celebrating the resilience and creativity of tribal communities as they serve young American Indian and Alaska Native (AI/AN) children and families. These webinars are part of a larger series of webinars on topics related to implementation and coordination of early childhood programs in AI/AN communities.
- ACF OHS Head Start Virtual Site Visit: On November 12th, Dr. Bernadine Futrell, Director, ACF OHS, will virtually visit a center in Region XI. She will greet the teaching staff, read to the students, and host a brief listening session with program staff.
- ACF OHS Virtual Listening Session - Fall Series: On November 12th, Dr. Bernadine Futrell, Director, ACF OHS, will host the third listening session in the virtual fall series with grantees from all twelve regions. These listening sessions are being hosted to discuss best practices and challenges with full enrollment, workforce wages and benefits, recruiting and retaining staff, and Universal PreK.
- ASPR: November 4 is BARDA Industry Day 2021
- FDA: On November 1, Acting Commissioner Woodcock and Center for Biologics Evaluation & Research (CBER) director Peter Marks M.D., Ph.D., participated in a stakeholder call with multisector COVID partners/health care professionals, patient advocacy groups, trade associations, consumer organizations,

national immunization organizations, and state and local public health organizations, to discuss a request to amend Pfizer-BioNTech's EUA for administration of their COVID-19 mRNA vaccine to children 5 through 11 years of age.

- FDA: On November 2, Dr. Peter Marks, Director of the Center for Biologics Evaluation and Research, participated in a call with leadership and members of the Association of State and Territorial Health Officials (ASTHO) to discuss COVID-19 vaccine issues, including those related to boosters and the authorization of the emergency use of the Pfizer-BioNTech COVID-19 Vaccine for the prevention of COVID-19 to include children 5 through 11 years of age.
- On November 2nd and November 3rd, the Bureau of Health Workforce convened its Advisory Committee on Training in Primary Care Medicine and Dentistry. Discussion and presentations included Title VII support for Indian Health Service and other tribal entity training sites, feedback on the HRSA Data Warehouse, HRSA efforts focused on children with special health care needs, and dental therapy. The Committee also discussed their upcoming Report which includes topics on workforce diversity, implicit bias, and intellectual and development disabilities
- IEA: On Wednesday, November 3rd, IEA facilitated a roundtable on sickle cell disease with Secretary Becerra. The stakeholder invites included MTS Sickle Cell Foundation, Sickle Cell Disease Association of America, Sickle Cell Consortium, Children's Hospital of Chicago, VCU Health, Bost Medical Center, and one sickle cell patient.
- IEA: On Wednesday, November 3rd, IEA facilitated 11 stakeholder briefings with the COVID-19 health Equity Task Force as part of the release of the final report and proposed implementation of the plan. Members of the task force and experts from across HHS and the White House presented.
- IEA: On Monday, 11/1, through Friday, 11/12, IEA will facilitate approximately 11 stakeholder listening sessions with OCR regarding the implementation of regulations for Section 1557 of the Affordable Care Act (Section 1557).
- IEA: On Monday, 11/8, IEA will host a stakeholder briefing on Title X.

- IEA: On 11/10, 11/17, 12/1, and 12/15, the IEA Center for Faith-based and Neighborhood Partnerships will host a webinar series in partnership with the DHS Center, “Welcome to the Neighborhood! Faith and Community Partnerships Serving our new Afghan Neighbors.” This series of webinars will be providing information, education, and training to help faith and community partners support new Afghan neighbors settling into communities. (Dates are tentative.)
- NIH: On October 27th, the NIH Tribal Advisory Committee met with NIH officials to exchange views, share information, and seek advice concerning intergovernmental responsibilities related to the implementation and administration of NIH research programs affecting American Indian and Alaska Native communities.
- OASH: On October 29th, the Assistant Secretary for Health met with the American Academy of Pediatrics (AAP), CDC, ASPR, and the Department of Ed. to continue the discussion and provide a weekly update on the severity of the delta in the pediatric population.
- OASH: On November 1st, the Assistant Secretary for Health participated in the National Academy of Medicine’s Action Collaborative Steering Committee November Call. The Steering Committee represents a public-private partnership of leaders from across the health system committed to addressing the sector’s environmental impact while strengthening its sustainability and resilience.
- OASH: On November 1st, the Assistant Secretary for Health met with the National Alliance for State and Territorial AIDS Directors (NASTAD) regarding eliminating viral hepatitis and improving the lives of people living with the virus.
- OASH: On November 3rd, the Assistant Secretary for Health will have an introductory meeting with the Testing and Diagnostics Working Group (TDWG) Leadership.
- OASH: On November 3rd, the Assistant Secretary for Health will have an introductory meeting with Public Responsibility in Medicine and Research (PRIM&R).
- OASH: On November 4th, the Assistant Secretary for Health will meet with the Federal AIDS Policy Partnership (FAPP) Convening Group.

- OASH: On November 5th, the Assistant Secretary for Health will meet with the American Academy of Pediatrics (AAP), CDC, ASPR, and the Department of Ed. to continue the discussion and provide a weekly update on the severity of the delta in the pediatric population.
- OASH: On November 5th, the Assistant Secretary for Health will meet with World Professional Association for Transgender Health (WPATH) in follow up to a previous discussion with Dr. Walter Bouman.
- OASH: On November 12th, the Assistant Secretary for Health will meet with Big Cities Health Coalition.
- OASH: On November 12th, the Assistant Secretary for Health will meet with the American Academy of Pediatrics (AAP), CDC, ASPR, and the Department of Ed. to continue the discussion and provide a weekly update on the severity of the delta in the pediatric population.
- OASH: On November 15th, the Assistant Secretary for Health will meet with Dr. Katharine Dalke, Penn State, Dr. Louise Pyle, Children's Hospital of Philadelphia, and Dr. Frances Grimstad, Children's Harvard, to discuss the clinical care for intersex individuals.
- OASH: On November 17th, the Assistant Secretary for Health will meet with the Minority AIDS Initiative (MAI).
- OASH: On November 19th, the Assistant Secretary for Health will meet with the American Academy of Pediatrics (AAP), CDC, ASPR, and the Department of Ed. to continue the discussion and provide a weekly update on the severity of the delta in the pediatric population.
- OASH: On November 22nd, the Assistant Secretary for Health will meet with Big Cities Health Coalition as part of their quarterly meeting series.
- OASH: On November 26th, the Assistant Secretary for Health will meet with the American Academy of Pediatrics (AAP), CDC, ASPR, and the Department of Ed. to continue the discussion and provide a weekly update on the severity of the delta in the pediatric population.
- October 2, Loyce Pace, Director, OGA and Mara Burr, Director, Multilateral Team, OGA spoke with the U.S. Chamber of Commerce's Global Initiative on Health and the Economy, to discuss partnership opportunities with the board, including USG

commitments as part of the COVID Summit, ACT-A, and COVAX.
    - ONC: On November 10th, ONC will convene its Federal Advisory Committee, the Health IT Advisory Committee (HITAC), for its monthly meeting. The agenda will include topics ranging from an update on Department of Defense and Veterans Affairs Interoperability Modernization Strategy, ONC benchmarks and measurement, and the HITAC's CY2022 work plan.

- **Principal level meetings or calls with Members of Congress:**
    - October 28, 2021 Secretary Becerra met with Representative Barbara Lee
    - October 28, 2021 Secretary Becerra met with Representative Tony Cardenas
    - October 28, 2021 Secretary Becerra participated in an event on preventative care with Senator Amy Klobuchar
    - October 29, 2021 Secretary Becerra participated in an event in Sacramento, California with Representative Barbara Lee
    - November 1, 2021 Secretary Becerra met with Senator Jack Reed
    - November 2, 2021 Secretary Becerra met with the Congressional Asian Pacific American Caucus
    - November 8, 2021 Secretary Becerra will participate in events with Representative Laura Underwood in Chicago, Illinois
    - November 9, 2021 Secretary Becerra will participate in events with Representative Brad Schneider in Chicago, Illinois
    - November 10, 2021 Secretary Becerra will participate in events with Senator Amy Klobuchar and Representative Angie Craig in Minnesota
    - November 17, 2021 Secretary Becerra will meet with the House Rules Committee
    - November 19, 2021 Secretary Becerra will likely participate in events with Representative Lisa Blunt Rochester in Wilmington, Delaware
    - Week of November 15, 2021 Secretary Becerra will make calls to members of the Congressional Hispanic Caucus

- November 16, 2021 Secretary Becerra will likely meet with Representative Ted Deutch
- Week of November 22, 2021 Secretary Becerra will make calls to members of the Congressional Hispanic Caucus
- Week of November 29, 2021 Secretary Becerra will make calls to members of the Congressional Hispanic Caucus
- ASL: October 29th: Secretary had a call with Congresswoman Jackie Walorski (R-IN) about Foster Care Issues.
- ASL: November 1st: Secretary Becerra had a call with Senator Reed about LIHEAP in Rhode Island.
- ASL: November 2nd: Secretary Becerra will attend the Congressional Asian and Pacific American Caucus (CAPAC) Weekly Member Meeting to discuss the White House Initiative on Asian Americans, Native Hawaiians and Pacific Islanders (WHIAANHPI); COVID-19 Health data sets and disparities between communities; language access in health care settings; immigrant access to health care; and AANHPI focused health care research.
- ASL: November 8th and 9th: Secretary Becerra will travel to Illinois to discuss Build Back Better, Maternal Health, ACA Open Enrollment & Pediatric COVID-19 Vaccines with the following Representatives Schneider (IL-10), Underwood (IL-13)
- ASL: November 10th: Secretary Becerra will travel to Rochester & Twin Cities, MN to discuss Build Back Better, Drug Pricing, ACA Open Enrollment & Pediatric COVID-19 Vaccines with Representatives Angie Craig (MN-02) and Sen. Amy Klobuchar(D-MN).
- ASPR: On October 28, ASPR provided a briefing to Senate Health, Education, Labor and Pensions (HELP) and House Energy and Commerce staff on the transfer of HHS Protect and Tiberius to CDC. Representatives from the Centers for Disease Control and Prevention (CDC) and the Office of the Chief Information Officer participated in this briefing.
- ASPR: On October 29, ASPR provided a briefing to Senate HELP oversight staff on the Industrial Base Expansion (IBx) program; highlighting program establishment, current status, and future of the program (goals and objectives).

- ASPR: On October 29, Assistant Secretary, Dawn O'Connell, met with the Government Accountability Office (GAO) health care team following their request to update Assistant Secretary O'Connell on the status of reviews in process and provide a general overview of their approach.
- ASPR: On November 1, ASPR provided a briefing to Senate HELP on the transfer of the Testing and Diagnostic Working Group to ASPR and CDC. Representatives from CDC also participated.
- ASPR: On November 4, Senate HELP Committee Hearing – COVID-19 Task Force Update; the ASPR will serve as a witness.
- ASPR: On November 5, ASPR will brief the Appropriations Committee staff (House/Senate Majority/Minority) on obligations and planned spending related to the COVID-19 supplementals.
- November 3rd: Dr. Rochelle Walensky, CDC Director, will participate in a call with Sen. Richard Burr (R-NC) on COVID-19.
- November 4th: Dr. Rochelle Walensky, CDC Director, will participate in an in-person hearing for the Senate Committee on Health, Education, Labor and Pensions on the COVID-19 response.
- FDA: On November 4, Acting Commissioner Woodcock testified in a hearing before Senate HELP on *Next Steps: The Road Ahead for the COVID-19 Response*.
- NIH
    - On October 27th, NIH Director Dr. Francis Collins, *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) Director Dr. Diana Bianchi, National Institute of Nursing Research (NINR) Director Dr. Shannon Zenk, and National Institute on Minority Health and Health Disparities (NIMHD) Director Dr. Eliseo Pérez-Stable briefed the Congressional Nursing Caucus on the impact of nursing research.
    - On October 29th, NHLBI Clinical Research and Strategic Initiatives Deputy Director Dr. Amy Patterson briefed Senator Tim Kaine's (D-VA) staff on the Researching COVID to Enhance Recovery (RECOVER) initiative to study Long COVID.

        - On October 29th, NIBIB Director Dr. Bruce Tromberg briefed the House Energy and Commerce Committee majority staff on the COVID-19 Independent Test Assessment Program, an accelerated pathway to help bring to market over-the-counter diagnostic tests for COVID-19 that are not yet authorized by the FDA.
        - On October 29th, NCATS Office of Policy, Communications, and Education Director Dr. Penny Burgoon briefed Rep. Anna Eshoo's (D-CA) staff on the contract award to Palantir Technologies, Inc. to support the National COVID Cohort Collaborative (N3C) and the N3C Data Enclave.
        - On November 4th, National Institute of Allergy and Infectious Diseases (NIAID) Director Dr. Anthony Fauci testified at a hearing of the Senate HELP Committee titled "Next Steps: The Road Ahead for the COVID-19 Response."

- **Noteworthy inquiries from Congressional committees or Members of Congress; scheduled testimony by Secretary or Deputy Secretary:**
    - CDC: Sen. Rand Paul (R-KY) wrote to the CDC director regarding her scheduled appearance to testify before the U.S. Senate Committee on Health, Education, Labor, and Pensions on Thursday, November 4th, asking if she would agree to testify under oath or affirmation.
    - ASL: On November 4th (10am), Senate HELP Committee Hearing on the COVID Task Force. HHS witnesses include Dr. Fauci, CDC Director Walensky, ASPR Dawn O'Connell, and Acting FDA Director Dr. Janet Woodcock)
    - ASL: On November 1st, ACF briefing with Rep. Soto's Staff on Health Professions Opportunity Grants (HPOG)
    - ASL: On November 1st, ASPR/CDC briefing with Senate HELP and E&C on COVID-19 Testing Diagnostic Working Group (TDWG)
    - ASL: On November 2nd, CMS briefing call for staff of the Authorizing Committees and House and Senate leadership to provide a high-level overview of provisions in the CY 2022 Home Health PPS final rule.

- ASL: On November 2nd CMS briefing Call for staff of the Authorizing Committees and House and Senate leadership to provide a high-level overview of provisions in the CY 2022 Physician Fee Schedule final rule.
- ASL: On November 2nd, CMS briefing with HELP Minority Staff on No Surprises IFR #2
- ASL: On November 2nd, FDA briefing for Energy and Commerce Bipartisan Health LAs re: OTC hearing aid proposed rule and PSAP guidance.
- ASL: On November 2nd, FDA briefing with Rep. Boyle Briefing on Animal Alternatives (CDER, OCS)
- ASL: On November 2nd, ASPR briefing with HELP Minority on IBx Program
- ASL: On November 2nd, FDA briefing with Senator Cornyn's staff on the Affordable Prescriptions for Patients Act (S. 1435) and impact on Rx-to-OTC switches
- CMS: On October 29th, CMS Office of Legislation provided follow-up information requested by House Energy and Commerce Committee Minority Staff regarding the status of states receiving enhanced matching funds made available under Section 9817 of ARP for home and community-based services (HCBS). The staff had additional questions about the process for awarding states federal Medicaid funds and the role of supplemental grant awards.
- FDA: On October 25, FDA received a letter from Rep. Scott Peters urging FDA's Office of Women's Health (OWH) to quickly update the Birth Control Guide.
- FDA: On November 2, Center for Tobacco Products (CTP) Director Zeller briefed E&C Majority on Synthetic Nicotine
- FDA: On November 3, Center for Biologics Evaluation and Response (CBER) Director Marks joined CDC to brief staff of committees of jurisdiction and Congressional leadership on Pfizer COVID Vaccine for Ages 5 – 11.
- On October 25th, the staff of Sen. Ron Wyden (D-OR), Chair, Senate Finance Committee, Rep. Frank Pallone (D-NJ), Chair, House Committee on Energy & Commerce (E&C) requested technical assistance on a bill regarding a Children's Health Insurance Program rebate program. HRSA responded to the Office of the Assistant Secretary of Legislation.

- On October 26th, HRSA and ASL briefed the staff of Sen. Joe Manchin (D-WV), Sen. Debbie Stabenow (D-MI), Sen. Jeanne Shaheen (D-NH), and Sen. Jon Tester (D-MT) regarding the Provider Relief Fund American Rescue Plan rural distribution.
- On October 27th, Rep. Debbie Wasserman Schultz's (D-FL) office requested technical assistance for a cancer survivorship bill. HRSA is working to respond to this request.
- On October 28th, Rep. Susie Lee's (D-NV) office requested technical assistance regarding H.R. 5141, the "Maximizing Outcomes through Better Investments in Lifesaving Equipment for (MOBILE) Health Care Act." HRSA is working to respond to this request.

- **Noteworthy rulemaking in the Federal Register:**
  - Week of November 1st: CDC will publish a notice in the *Federal Register* announcing an Amended Order (including accompanying attestation form and technical instructions) signed by the CDC director on October 30th to implement the new Biden administration travel policy to safely resume global travel to the United States. On November 8th, non-U.S. citizens who are not immigrants to the United States will be required to be fully vaccinated and provide proof of their vaccination status to fly to the United States, with only limited exceptions.
  - Week of November 1st: CDC will publish a notice in the *Federal Register* announcing an Order (including accompanying technical instructions) signed by the CDC director on October 25th to require all airlines and operators of flights arriving into the United States from a foreign point of last departure to collect passenger and maintain crewmember contact information.
  - Week of November 1st: CDC will publish a notice in the *Federal Register* announcing an Amended Order (including accompanying attestation form) signed by the CDC director on October 25th requiring negative pre-departure COVID-19 test results or documentation of recovery from COVID-19 for all airline or other aircraft passengers arriving into the United States from any foreign country. This Amended Order supersedes the previous Order signed on January 25, 2021.

- CMS: Displayed October 29, 2021: CY 2022 Changes to the End-Stage Renal Disease (ESRD) Prospective Payment System and Quality Incentive Program Final
- CMS: November 2, 2021 *[Target pending OFR confirmation]:* CY 2022 Home Health Prospective Payment System Rate Update Quality Reporting Requirements Final Rule
- CMS: Week of November 1, 2021 *[Target pending timely resolution of HHS & OMB comments]:* Interoperability and Patient Access; Enforcement Discretion Notice
- CMS: November 2, 2021 *[Target pending OFR confirmation]:* Revisions to Payment Policies under the Medicare Physician Fee Schedule, Quality Payment Program and Other Revisions to Part B for CY 2022 Final Rule
- CMS: November 2, 2021 *[Target pending OFR confirmation]:* Opioid Treatment Programs: CY 2022 Methadone Payment Exception Interim Final Rule
- CMS: November 2, 2021 *[Target pending OFR confirmation]*: CY 2022 Hospital Outpatient PPS Policy Changes and Payment Rates and Ambulatory Surgical Center Payment System Policy Changes and Payment Rates Final Rule
- CMS: November 4, 2021 *[Confirmed]:* Omnibus COVID-19 Health Care Staff Vaccination Interim Final Rule
- CMS: November 10, 2021 *[Target pending timely resolution of HHS & OMB comments]:* Prescription Drug and Health Care Spending Interim Final Rule
- CMS: November 12, 2021 *[Target pending timely resolution of HHS & OMB comments]:* MCIT Repeal Final Rule
- CMS: November TBD *[Target pending timely resolution of HHS & OMB comments]:* Establishing Minimum Standards in Medicaid State DUR and Supporting VBP for Drugs Covered in Medicaid, Revising Medicaid Drug Rebate and TPL Requirements; Delay of Effective Date for Specific Provisions Final Rule
- FDA: On November 3, FDA issued a draft guidance, Content of Premarket Submissions for Device Software Functions, that describes the information that the Agency considers important during its evaluation of the safety and effectiveness for device software with one or more device functions, including both software in a medical device and software as a medical device. It is anticipated this draft guidance, which fulfills FDA's

commitment in MDUFA IV, once finalized, will provide clarity, simplicity and harmonization with current best practices, and recognized voluntary consensus standards once finalized.
    - OASH: In November/December, the Office of Disease Prevention and Health Promotion (ODPHP) will conduct a 4-6 week public comment period to seek public input on the three proposed new Healthy People 2030 objectives and will accept proposals on additional new objectives. Departmental clearance of any new objectives is expected to occur in January/February 2022.

- **Funding Announcements:**
    - **Community Services Block Grant (CSBG)**: On October 29th ACF OCS announced the release of approximately $181,508,890 of Federal Fiscal Year (FY) 2022 regular block grant funding to CSBG grantees. All 50 states, the District of Columbia, 3 territories, and over 65 tribal grantees received funding. This funding was provided under the CR, which the President signed into law on September 30, 2021 (Public Law 117-43). This release reflects one quarter of the annualized amount of funds available under the CR to grantees at the beginning of the program year.
    - **Title X Family Planning Services NOFO:** On October 27, HHS will announce the availability of up to $256 million in grant funding to support high-quality family planning services delivered through the Title X family planning program. The national services competition, which will provide up to five-year awards, supplements the recent effort by HHS to restore and strengthen the Title X program through updated rulemaking, effective November 8, and is a critical opportunity to restore highly qualified providers not only in the service areas without Title X care but also in other states and communities across the country that saw losses in access.
    - Press releases announcing FY2021 awards in OASH clearance. Anticipated dissemination the week of 11/1/2021.
        - MP-CPI-21-005: National Lupus Outreach and Clinical Trial Education Program: Five awards issued.
        - MP-CPI-21-008: Minority Leaders Development Program: Three awards issued.

- **Grant Notices (NOFA/NOFOs):**
  - On October 29th, HRSA released the Rural Health Network Development Planning Program funding opportunity. This includes a total of $2 million to support 20 award recipients. Funding will support the development of an integrated health networks to deliver services in HRSA-designated rural area, particularly for populations that have historically been underserved and have poorer health outcomes.
  - PA-FPH-22-001: Family Planning Services Grants
    - Anticipated Application deadline: January 5, 2022
    - Estimated Total: $258,000,000
    - Anticipated Number of Awards: 90
    - Period of Performance: up to 5 years
    - Anticipated Start Date: April 1, 2022
    - Program: Existing
    - https://www.grants.gov/web/grants/view-opportunity.html?oppId=334698
  - PA-FPH-22-002: Family Planning Telehealth Infrastructure Enhancement and Expansion Grants
    - Anticipated Application deadline: January 15, 2022
    - Estimated Total: $35,000,000
    - Anticipated Number of Awards: 60
    - Period of Performance: 1 year
    - Anticipated Start Date: April 15, 2022
    - Program: Existing
    - https://www.grants.gov/web/grants/view-opportunity.html?oppId=334704
  - PA-FPH-22-003: Funding to Address Dire Need for Family Planning Purposes
    - Anticipated Application deadline: TBD no less than 31 days after posting the NOFO
    - Estimated Total: $9,250,000
    - Anticipated Number of Awards: 10
    - Period of Performance: up to 15 months
    - Anticipated Start Date: January 1, 2022
    - Program: Existing
    - https://www.grants.gov/web/grants/view-opportunity.html?oppId=335742
  - IHS: Substance Abuse and Suicide Prevention (SASP): On October 29th, the IHS requested Federal Register (FR)

publication of the Suicide Prevention, Intervention, and Postvention NOFO for approximately $14 million. The focus of this program is to reduce the prevalence of suicide among American Indian and Alaska Native populations. The NOFO is expected to be public on the FR website on November 4th.

- IHS: SASP: On October 29th, the IHS requested FR publication of the Substance Abuse Prevention, Treatment, and Postvention NOFO for approximately $14 million. The focus of this program is to reduce the prevalence of substance abuse and decrease the overall use of addicting and illicit substances among American Indian and Alaska Native populations. The NOFO is expected to be public on the FR website on November 4th.
- IHS: Domestic Violence Prevention (DVP): On October 29th, the IHS requested FR publication of the DVP NOFO for approximately $7.89 million. The purpose of this program is to support the development and/or expansion of DVP programs by incorporating prevention efforts addressing social, spiritual, physical, and emotional well-being of victims through the integration of culturally appropriate practices and trauma-informed services for Tribes, Tribal organizations, and Urban Indian organizations serving American Indian and Alaska Native populations. The NOFO is expected to be public on the FR website on November 4th.
- IHS: DVP: On October 29th, the IHS requested FR publication of the Forensic Healthcare NOFO for approximately $2.5 million. The purpose of this program is to provide access to treatment for American Indian and Alaska Native victims of domestic and sexual violence by supporting the development and/or expansion of forensic health care services that are culturally appropriate and trauma-informed. The NOFO is expected to be public on the FR website on November 4th.
- IHS: Behavioral Health Integration Initiative (BH2I): On October 29th, the IHS requested FR publication of the BH2I NOFO for approximately $6 million. The purpose of this program is to improve the physical and mental health status of people with behavioral health issues by developing an integrated and coordinated system of care, by increasing capacity among Tribal and urban Indian organization health facilities to implement an integrative approach in the delivery of behavioral

health services. The NOFO is expected to be public on the FR website on November 4th.

- IHS: Zero Suicide Initiative (ZSI): On October 29th, the IHS requested FR publication of the ZSI NOFO for approximately $2 million. This purpose of this program is to improve the system of care for those at risk for suicide by implementing a comprehensive, culturally informed, multi-setting approach to suicide prevention in Indian health systems. The NOFO is expected to be public on the FR website on November 4th.
- IHS: Tribal Self-Governance Planning Cooperative Agreement (TSGP): By November 15th, the IHS anticipates publishing the TSGP NOFO for approximately $600,000. The purpose of this program is to provide resources to Tribes interested in entering the Tribal Self-Governance program and to existing Self-Governance Tribes interested in assuming new or expanded Programs, Services, Functions, and Activities. Title V of the Indian Self-Determination and Education Assistance Act requires a Tribe or Tribal organization to complete a planning phase to the satisfaction of the Tribe.
- IHS: Tribal Self-Governance Negotiation Cooperative Agreement (TSGN): By November 15th, the IHS anticipates publishing the TSGN NOFO for approximately $240,000. The purpose of this program is to provide Tribes with resources to help defray the costs associated with preparing for and engaging in Tribal Self-Governance program negotiations. Because each Tribal situation is unique, a Tribe's successful transition into the Tribal Self-Governance Program, or expansion of their current program, requires focused discussions between the Federal and Tribal negotiation teams about the Tribe's specific health care concerns and plans.
- IHS: Urban Indian Health Programs 4-in-1 grant program (UIHP2): By November 30th, the IHS anticipates publishing the UIHP2 NOFO for approximately $8.5 million. The purpose is to ensure the highest possible health status for Urban Indians. Funding will be used to support the following four health program objectives: health promotion and disease prevention services; immunization services; alcohol and substance abuse related services; and mental health services.

- **CDC released a series of COVID-19 related *Morbidity and Mortality Weekly Reports*:**
    - October 29th Early Releases
        - Laboratory-Confirmed COVID-19 Among Adults Hospitalized with COVID-19–Like Illness with Infection-Induced or mRNA Vaccine-Induced SARS-CoV-2 Immunity — Nine States, January–September 2021
        - The Advisory Committee on Immunization Practices' Interim Recommendations for Additional Primary and Booster Doses of COVID-19 Vaccines — United States, 2021
    - October 29th
        - Routine Vaccination Coverage — Worldwide, 2020
    - November 2nd Early Release
        - Effectiveness of 2-Dose Vaccination with mRNA COVID-19 Vaccines Against COVID-19–Associated Hospitalizations Among Immunocompromised Adults — Nine States, January–September 2021

- **CDC will release a series of COVID-19 related *Morbidity and Mortality Weekly Reports* (Please note that the titles, content, and timing might change):**
    - November 5th: No COVID-19 related *MMWR*'s are currently scheduled
    - November 12th (summaries currently not available and will be provided at a later date):
        - Administration of Influenza Vaccination During the COVID-19 Pandemic — 11 U.S. Jurisdictions, September–December 2020
        - Community Based Testing Sites for COVID-19 — United States, March 2020–September 2021

- **CDC will release a series of National Center for Health Statistics (NCHS) Reports:**
    - COVID-19 provisional death data from the National Vital Statistics System is released on a daily and weekly (usually on Wednesday) basis on CDC's website.
    - **COVID-19-related data is available on CDC's website**.
    - November 3rd: Provisional Numbers and Rates of Suicide by Month and Demographic Characteristics: United States: 2020

        - This report presents provisional numbers of deaths due to suicide by demographic characteristics (sex and race and Hispanic origin) and by month for 2020 and compares them with final numbers for 2019. Both age-adjusted and age-specific suicide rates are presented by sex and race and Hispanic origin and compared with final 2019 rates.
    - November 9th (summary currently not available and will be provided at a later date):
        - Mortality Profile of the Non-Hispanic American Indian or Alaska Native Population, 2019
    - November 10th (summary currently not available and will be provided at a later date):
        - Sepsis-Related Mortality Among Adults Aged 65 and Over: United States, 2019

From: Brooks, John T. (CDC/DDID/NCHHSTP/DHP) <zud4@cdc.gov>
Sent: Fri, 27 Aug 2021 16:14:27 -0500
To: Fauci, Anthony (NIH/NIAID) [E];Murthy, Vivek (HHS/OASH);Collins, Francis (NIH/OD) [E];Walensky, Rochelle (CDC/OD);Eric Lander
Cc: Beckman, Adam (HHS/OASH)
Subject: RE: Post infection protection vs vaccine immunity
Attachments: Bar-On 2021 - rapid and robust increase in VE following 3rd dose BNT162b2 Israel - medRxiv.pdf

I also received this paper today from Israeli colleagues (attached) in which they present evidence that their booster program has restored the loss in vaccine effectiveness that had been observed among persons fully vaccinated with the 2-dose Pfizer vaccine series in whom VE against infection was decreasing.

They used two basic approaches to analyze these retrospective data: a series of Poisson regressions and a case-control matching method. All analyses point in the same direction and the results seem impressive.

I am a having trouble wrapping my head around how they detected such a potent effect of an intervention started in late July and delivered to about 3 M Israelis in just a few weeks. It just seemed mighty fast, but perhaps in this case the anamnestic response primed by prior vaccination kicked in hard and fast.

As I digest this one (with the sage input of smarter colleagues here whose career work is VE), I wanted to ensure all were aware the paper is out there.

-john

John T. Brooks, MD
Chief Medical Officer, CDC COVID-19 Response
Email: zud4@cdc.gov
Apologies for errors in my messages that may be due to my need to dictate.

From: Fauci, Anthony (NIH/NIAID) [E] [redacted (b) (6)]>
Sent: Friday, August 27, 2021 2:37 PM
To: Murthy, Vivek (HHS/OASH) <Vivek.Murthy@hhs.gov>; Collins, Francis (NIH/OD) [E] <[redacted (b) (6)]; Walensky, Rochelle (CDC/OD) <aux7@cdc.gov>; Eric Lander

<eric.s.lander@ostp.eop.gov>; Brooks, John T. (CDC/DDID/NCHHSTP/DHP) <zud4@cdc.gov>
Cc: Beckman, Adam (HHS/OASH) <Adam.Beckman@hhs.gov>
Subject: RE: Post infection protection vs vaccine immunity

The data as reported in the news article look rather impressive despite the caveat that it is a retrospective study and the testing was voluntary. I have not seen the details of the actual data, but I would imagine that it is more complicated than we think. It very well may be that people who have had an asymptomatic or minimally symptomatic infection (upper airway only) will not have a greater post-infection protection against subsequent infection then those who get fully vaccinated. However, it is conceivable and possibly likely that those who have had a serious systemic infection develop a high level of immunity that even surpasses that of full vaccination. I would like to see if they broke the data on the infected people down into those two groups.

Anthony S. Fauci, MD
Director
National Institute of Allergy and Infectious Diseases
Building 31, Room 7A-03
31 Center Drive, MSC 2520
National Institutes of Health
Bethesda, MD 20892-2520
Phone: (b) (6)
FAX: (301) 496-4409
E-mail: (b) (6)

From: Murthy, Vivek (HHS/OASH) <Vivek.Murthy@hhs.gov>
Sent: Friday, August 27, 2021 1:57 PM
To: Collins, Francis (NIH/OD) [E] <(b) (6)>; Fauci, Anthony (NIH/NIAID) [E] <(b) (6)>; Walensky, Rochelle (CDC/OD) <aux7@cdc.gov>; Eric Lander <(b) (6)>; Brooks, John T. (CDC/DDID/NCHHSTP/DHP) <zud4@CDC.GOV>
Cc: Beckman, Adam (HHS/OASH) <Adam.Beckman@hhs.gov>
Subject: Post infection protection vs vaccine immunity

Do you have thoughts on this recent study from Israel? And how this fits with the recent MMWR findings (Kentucky study showing higher risk of reinfection in the unvaccinated compared to risk of infection in the vaccinated)?

https://www.sciencemag.org/news/2021/08/having-sars-cov-2-once-confers-much-greater-immunity-vaccine-no-infection-parties

Having SARS-CoV-2 once confers much greater immunity than a vaccine—but no infection parties, please | Science | AAAS

Having SARS-CoV-2 once confers much greater immunity than a vaccine—but no infection parties, please. By Meredith Wadman Aug. 26, 2021 , 8:02 PM. The natural immune protection that develops ...

www.sciencemag.org

BNT162b2 vaccine booster dose protection: A nationwide study from Israel

Yinon M. Bar-On[†1], Yair Goldberg[†2*], Micha Mandel[†3], Omri Bodenheimer[4], Laurence Freedman[5], Nir Kalkstein[6], Barak Mizrahi[6], Sharon Alroy-Preis[4], Nachman Ash[4], Ron Milo[&1], Amit Huppert[&5,7]

27/8/2021

[1] Weizmann Institute of Science, Israel

[2] Technion - Israel Institute of Technology, Israel

[3] The Hebrew University of Jerusalem, Israel

[4] Israel Ministry of Health, Israel

[5] The Gertner Institute for Epidemiology & Health Policy Research, Sheba Medical Center, Israel

[6] KI Research Institute, Kfar Malal, Israel

[7] Tel Aviv University, Israel

[†]Contributed equally.

[&]Contributed equally.

*corresponding author

email: yairgo@technion.ac.il

Abstract

Background: On July 30, 2021, a third (booster) dose of the Pfizer BNT162b2 vaccine was approved in Israel for individuals 60 years or older who had been fully vaccinated (i.e., received two doses) at least five months previously. Here, we estimate the reduction in relative risk for confirmed infection and severe COVID-19 provided by the booster dose.

Methods: 1,144,690 individuals aged 60y and older who were eligible for a booster dose were followed between July 30 and August 22, 2021. We defined dynamic cohorts where individuals initially belong to the 'non-booster' cohort, leave it when receiving the booster dose and join the 'booster' cohort 12 days later. Rates of infection and severe COVID-19 outcomes per person-days at risk were compared between the cohorts using Poisson regression, adjusting for possible confounding factors.

Results: Twelve days or more after the booster dose we found an 11.4-fold (95% CI: [10.0, 12.9]) decrease in the relative risk of confirmed infection, and a >10-fold decrease in the relative risk of severe illness. Under a conservative sensitivity analysis, we find ≈5-fold protection against confirmed infection.

Conclusions: In conjunction with safety reports, this study demonstrates the effectiveness of a third vaccine dose in both reducing transmission and severe disease and indicates the great potential of curtailing the Delta variant resurgence by administering booster shots.

Introduction

The rapid development of effective vaccines against SARS-CoV-2 and their deployment to the general population has been proven to be a highly successful strategy for reducing transmission and disease burden. In Israel, a swift vaccination campaign led to more than half of the population being fully vaccinated by the end of March 2021 [1]. Consequently, COVID-19 incidence dropped from ≈900 cases per million per day in mid-January 2021 to less than 2 cases per million per day by June 2021 [1]. Nevertheless, the emergence of new variants of concern (VOC), and specifically the Delta variant, has led to a recent infection resurgence in Israel both in infection and severe disease [2]. There are several possible causes for the high levels of transmission of the Delta variant, including increased infectiousness of the Delta variant [3], waning vaccine-elicited immunity [2,4], and heightened immune evasion by the variant [5], the latter two of which directly contribute to a decrease in vaccine efficacy. Analysis of the Israeli data on the Delta outbreak indicated strong waning immunity. In an effort to address the challenge presented by the Delta variant and reduce the load on the healthcare system, Israeli authorities approved the administration of a booster dose, first to high-risk populations, on July 12, 2021, and then to the entire 60+ population, on July 30, 2021.

Initial studies have suggested that a BNT162b2 booster dose, i.e., an additional dose given to individuals who have previously received two BNT162b2 vaccine doses, increases antibody neutralization levels ~10-fold, on average, compared to levels achieved after the second dose [6]. It is thought that an increased neutralization titer could lead to increased protection against infection and severe illness [7]. However, in terms of real-world efficacy, the size of such an effect remains unclear. Here, we use initial data from the Israeli Ministry of Health (MOH) database on the incidence of confirmed infection and severe illness among two cohorts of individuals above 60 years of age: those who received only two vaccine doses, and those who received an additional booster dose. We use the data to quantify the protective effect that the booster dose provides against confirmed infection and severe illness.

The protection gained by the booster shot is not expected to reach its maximal capacity immediately on vaccination, but to build up over the week following vaccination [8,9]. At the same time, during the first days after vaccination, significant behavioral changes in the booster-vaccinated population are expected (Figure S1 in the Supplementary Appendix). One such expected change is added avoidance of exposure to excess risk until the booster dose becomes effective. Another expected change is a reduced rate of testing for COVID-19 around the time of receiving the booster, as demonstrated in Figure S2 (Supplementary Appendix). Moreover, we analyzed confirmed COVID-19 infections based on the date of the positive PCR test, and testing occurs only several days following exposure. For all these reasons, it is preferable to assess the effect of the booster only after a sufficient period has passed since its administration.

Methods

Our analysis is based on medical data from the MOH database extracted on August 24, 2021. There were 1,186,780 Israeli residents aged 60 and older who had been fully vaccinated at least five months (became fully vaccinated before March 1, 2021), and were still alive on July 30, 2021. We removed from these data individuals who: had missing gender; were abroad in August 2021; had been infected with COVID-19 before July 30, 2021; received a booster dose before July 30, 2021; or became fully vaccinated before January 16. A total of 1,144,690 individuals met the inclusion criteria for the analysis (see Figure 1). The data included vaccination dates (first, second and third doses), RT-qPCR tests (dates and results), COVID-19 hospitalization date (if relevant), demographic variables such as age, gender, and demographic group (General Jewish, Arab, ultra-Orthodox Jewish) [10], and clinical status (mild, severe). Severe disease was defined as: resting respiratory rate >30 breaths per minute, or oxygen saturation on room air <94%, or ratio of PaO2 to FiO2 <300 [11].

We considered 12 days as the time it took the booster dose to affect the observed number of confirmed infections. Our study period started at the beginning of the booster vaccination campaign on July 30, 2021. The end date was chosen as August 22, 2021, to minimize the effects of missing outcome data due to delays in the reporting of test results. Choosing 12 days following booster vaccination as the cutoff is scientifically justified from an immunological perspective, as studies have shown that following the booster dose, neutralization levels increase only after several days [6]. Using confirmed infections (i.e., PCR positivity) as an outcome, there is a delay between infection and testing. For symptomatic cases, infections occur on average 5-6 days prior to testing, similar to the incubation period of COVID-19 [12,13].

To estimate the level of protection provided by the booster dose, we analyzed data on the incidence of confirmed infections and severe illness of two distinct cohorts: people who received two vaccine doses and the booster dose ('booster' cohort), and people who received only two vaccine doses ('no-booster' cohort). These cohorts were dynamic; individuals initially belonged to the 'non-booster' cohort, left it when receiving the booster dose, and joined the 'booster' cohort 12 days later (Figure S3 in the Supplementary Appendix) provided they did not have a confirmed infection in the interim period. We considered data on two outcomes of interest, confirmed infection and severe COVID-19, and counted the number of events of each type during the study period.

For each cohort, we calculated the incidence rate of both confirmed infection and severe COVID-19 per person-days at risk. For each person in the 'booster' cohort, days at risk started when entering the cohort (12 days after receiving the third dose), and ended either with the occurrence of an outcome or at the end of the study period. For the 'no-booster' cohort, days at risk started at the beginning of the study period (August 10, 2021), and ended either with the

occurrence of an outcome, the end of the study period, or when receiving a booster dose. Since cohort membership was dynamic, many individuals contributed person-days at risk to both cohorts.

We fitted a Poisson regression (using the glm function in the R Statistical Software)[14] to estimate the incidence rate of a specific outcome, controlling for several important covariates: age (60-69, 70-79, 80+), gender, demographic group (General Jewish, Arab, ultra-Orthodox Jewish) [10], and date of second vaccine dose (in half-month intervals). Since the overall incidence rate of both confirmed infection and severe COVID-19 increased exponentially during the study period, days at the beginning of the study period had lower exposure risk than days at the end. To account for growing exposure risk, we included calendar date as an additional covariate. Accounting for these covariates, we used the study cohort ('booster' or 'no-booster') as a factor in the regression and estimated its impact on the incidence rate. The effect of the booster dose is estimated as one divided by the exponent of the regression coefficient associated with the treatment cohort, which is akin to a relative risk. For reporting uncertainty around our estimate, we used the exponent of the 95% confidence limits for the regression coefficient.

As a sensitivity analysis, we compared infection rates before and after the booster dose became effective. Specifically, we repeated the Poisson regression analysis described above but compared infection rates on days 4-6 to 12+ after the booster dose. Our hypothesis was that the booster dose was not yet effective during the former period [8]. This analysis compares different periods following booster vaccination based only on those who received the booster dose, and may reduce selection bias. On the other hand, people might perform less PCR testing and behave more cautiously with regard to virus exposure just after getting the booster vaccination (Figure S2), so we conjecture that the protection effect is underestimated in this analysis, providing a lower bound to the real effect.

To further examine the protection as a function of time from the booster dose, we fitted a Poisson regression comparing the 'booster' and 'no-booster' cohorts as above, while including each day, from day 1 up to day 24 after the booster vaccination, as a separate factor in the model. The period before receiving the booster dose ('no-booster' cohort) was used as the reference category. The analysis is similar to the Poisson modeling described above, with one divided by the exponents of the regression coefficients representing the protection on different days post the booster vaccination. The follow-up time for this analysis started on July 30, 2021, and ended on August 22, 2021.

As further sensitivity analyses, we applied two methods based on case-control matching. The first method was similar to that used by Dagan et. al[15]. Each person who received the booster was matched, using the same covariates as used in the Poisson regression model, to a person

who had not yet received it on that date. We compared the probabilities of COVID-19 infection 12 days or more after the matching time of those receiving the booster dose and those who did not. In the second method, we matched person-days rather than individuals, ensuring that person-days in the two cohorts are comparable in terms of covariates and exposure risk. On each day we identified the group of individuals for whom 12 days or more had passed since receiving the booster dose and who had not been infected in the interim ('booster' cohort). We randomly matched a day of a 'no-booster' individual from those who had received only two vaccine doses by that same date, had not been previously infected, and had the same characteristics (age, gender, second vaccination period, and demographic group). We then calculated the risk ratio of infection and severe COVID-19 between the two groups. A detailed description of both approaches is given in Supplementary Methods 1 in the Supplementary Appendix.

Results

The baseline characteristics of both cohorts are shown in Table 1. As our primary analysis adjusts for person-days at risk, and since individuals contribute days to both cohorts, we compare characteristics according to person-days at risk. There are about 4.0 million person-days in the 'no-booster' cohort with 3,473 confirmed infections and 330 cases of severe COVID-19, and about 3.4 million person-days in the 'booster' cohort with 313 confirmed infections and 32 cases of severe COVID-19. The 'booster' cohort tends to have more men (50% vs 43%), more general Jewish people (93% vs 82%), more older people (60% vs 47% aged 70+ years), and people who were vaccinated earlier (79% vs 40% vaccinated in January). These significant differences are adjusted for when estimating protection.

The full Poisson regression analysis for confirmed infection is given in Table S1 of the Supplementary Appendix, and the results for the booster dose protection are summarized in Table 2. The booster dose provides significant protection – an estimate of 11.4-fold (95% CI: [10, 12.9]) decrease in the relative risk of a confirmed infection. In the Supplementary Appendix, we provide the results of alternative analyses using matching techniques. The first analysis, following Dagan et. al.[15], resulted in a higher estimate of the decrease in relative risk of 13.4 (95% CI: [8.2-21.4]) and the second, relying on matching by days, gave a slightly smaller estimate for the decrease in the relative risk of 9.6 (95% CI: [8.1, 11.4]).

The sensitivity analysis that compared the risk of infections during 12+ days after booster to 4-6 days after booster, gave a decrease in relative risk of 4.7 (95% CI: [4, 5.4]), about half of that in the main analysis.

The protection conferred by the booster dose against severe disease also appeared high. For people with a more-than-12-days lag between the booster vaccination and severe illness, we

found that the booster dose decreases the relative risk of severe disease by 15.5-fold (95% CI: [10.5, 22.8]). We validated our results using the matching-by-day analysis that gave 9.5-fold protection against severe illness (95% CI [5-19.6]).

Figure 2 presents the results of the Poisson regression analysis with the number of days after booster vaccination as additional covariates, demonstrating the protection as a function of time from the booster vaccination. After about 12 days, protection starts stabilizing at about 10-12 fold reduction in risk in line with the results presented above. As shown in Figure 2, there is an apparent protection for the booster-vaccinated group in the first days following vaccination. This apparent protection (i.e., days 1-4) is likely the result of the aforementioned behavioral changes that follow vaccination. As the time since vaccination progresses, the magnitude of this apparent protection decreases, indicating that the effect of behavioral change decreases. Levels of protection appear to start increasing again from day 7 post vaccination. As shown in Figure S4 these results are robust across different study periods.

Discussion

Our analysis shows that the booster dose of the BNT162b2 vaccine is highly effective in reducing the risk of both confirmed infection and severe illness. For example, if the combined effect of waning immunity and the Delta variant decrease the efficacy of a vaccine given >6 months ago against infection to ≈50%, as recent reports have suggested [16,17], and if the booster dose reduces the relative risk by 10-fold, it means that the probability of a booster-vaccinated individual to being susceptible to infection would decrease to ≈5% (=50%/10) relative to unvaccinated individuals. This brings vaccine efficacy for booster-vaccinated individuals to ≈95%, similar to the original "fresh" vaccine efficacy reported against the Alpha strain [11,15].

On average, severe illness develops ≈5 days after the first positive-sample date (Figure S5 in the Supplementary Appendix). Thus, the follow-up period in our data is short and confidence intervals for protection against severe disease are wide. Moreover, some individuals from the booster cohort for severe illness were likely infected prior to or immediately after receiving the booster, and this could lead to an underestimate in the inferred protection against severe illness.

While our analysis attempts to address possible biases in the source data, such as the effects of confounders and behavioral changes following vaccination, there are some sources of bias that we may not correct adequately. These include differences between those receiving and not receiving the booster in care-seeking behaviors and cautiousness, and in comorbidities. Some of these possible biases are transient and fade with time since the booster vaccination, as schematically shown in Figure S1 in the Supplementary Appendix, implying that the real

effectiveness of vaccination can be estimated when comparing infection rates before receiving the booster dose and after enough time has elapsed (e.g. after 12 days, Figure S1 in the Supplementary Appendix). While independent research is required in order to fully understand this behavioral model, several indications suggest that our 12 days cutoff is reasonable. First, as shown in Figure S2 in the Supplementary Appendix, people tend to perform fewer PCR tests a few days before and after the vaccination day, which is a clear source for detection bias. Over time, the number of tests that vaccinated individuals perform increases, which reduces this bias. Consistent with such behavioral change is the pattern in Figure 2, which shows a large reduction in infection risk on the first day after vaccination that monotonically decreases during the first few days, before starting to increase as the booster dose becomes effective.

Yet, confounding biases may still explain part of the observed effectiveness, and these may not disappear over time. We can put a crude lower bound on the booster efficacy by looking at time points at which the booster efficacy is not expected to be significant and behavioral differences are smaller, e.g. days 4-6 after the booster dose, and attributing the whole observed effectiveness to confounding bias. Our sensitivity analysis compared the cohort of booster-vaccinated individuals 12+ days after receiving the booster dose to the same group at days 4-6, when the booster effect is expected to be only minimally translated into a reduction in confirmed infections (Figure 2). This analysis yielded an estimate of 4.7-fold (95% CI [4.0, 5.4]) protection against confirmed infection. Even under this conservative interpretation, the demonstrated protection highlights the important role that a booster dose could play in mitigating the effects of waning immunity and immune evasion, and in mitigating the spread of VOC such as the Delta variant.

There are significant behavioral differences between the main demographic groups in Israel. Table 1 shows that the 'booster' cohort is highly biased toward the general Jewish population; 93% vs 82% in the 'no-booster' cohort. This may be a source of a selection bias that is not fully accounted for in the main analysis. We, therefore, repeated the analysis for the subset of people from the general Jewish sector. The results of the Poisson analysis were very similar to those shown in Table 2, with protection against confirmed infection of 10.9 (95% CI [9.6, 12.4]). This validates the ≈10-fold protection against infection findings of the main analysis.

Understanding the protection gained by a booster dose is critical for policy making. On July 30, 2021, Israel was the first country in the world to make available a third dose of Pfizer BNT162b2 vaccine against COVID-19 to all people aged 60 or over who had been vaccinated at least five months previously. The results of such a policy are of importance for countries that seek strategies to mitigate the pandemic. Our findings give clear indications of the effectiveness of a booster dose even against the currently dominant Delta variant.

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Ethics statement

The study was approved by the Institutional Review Board of the Sheba Medical Center. Helsinki approval number: SMC-8228-21.

Competing interests statement

All authors declare no competing interests.

Funding

None.

Data sharing

Table 1: Demographic and clinical characteristics of the study population for the two study cohorts. Since the cohorts are dynamic and individuals can contribute to both cohorts, the table presents the number of person-days at risk instead of the number of individuals.

	2nd dose only ("no-booster" cohort)	12+ days from 3rd dose ("booster" cohort)
Person-days at risk	4,018,929	3,351,598
Confirmed Infections	3,473	313
Severe COVID-19	330	32
Gender = male (%)	1,712,000 (43%)	1,681,085 (50%)
Sector (% of person-days at risk)		
General Jewish	3,318,512 (82%)	3,127,545 (93%)
Arab	514,357 (13%)	114,671 (3%)
Orthodox Jews	186,060 (5%)	109,382 (3%)
Age category (% of person-days at risk)		
60-69	2,138,861 (53%)	1,353,160 (40%)
70-79	1,173,437 (29%)	1,341,000 (40%)
80+	706,631 (18%)	657,438 (20%)
2nd vaccination period (% of person-days at risk)		
Jan, 16-31	1,613,977 (40%)	2,664,230 (79%)
Feb, 1-15	1,849,978 (46%)	634,870 (19%)

Feb, 16-28	554,974 (14%)	52,498 (2%)

Table 2. Summary of the results of the Poisson regression analysis for different cohorts: people who received only two vaccine doses and people for whom 12 days or more have passed since their booster dose. For each group, we provide the total number of person-days at risk for each cohort, the number of confirmed infections and severe COVID-19 in each cohort, and the estimated protection of the booster against confirmed infection and severe illness, given as a fold change in relative risk.

Cohort	Person-days at risk	Confirmed infections	Severe COVID-19	Estimated booster protection (95% CI)	
				Against confirmed infection	Against severe illness
2 doses only ("no-booster" cohort)	4,018,929	3,473	330	1	1
12+ days from 3rd dose ("booster" cohort)	3,351,598	313	32	11.4 [10, 12.9]	15.5 [10.5, 22.8]

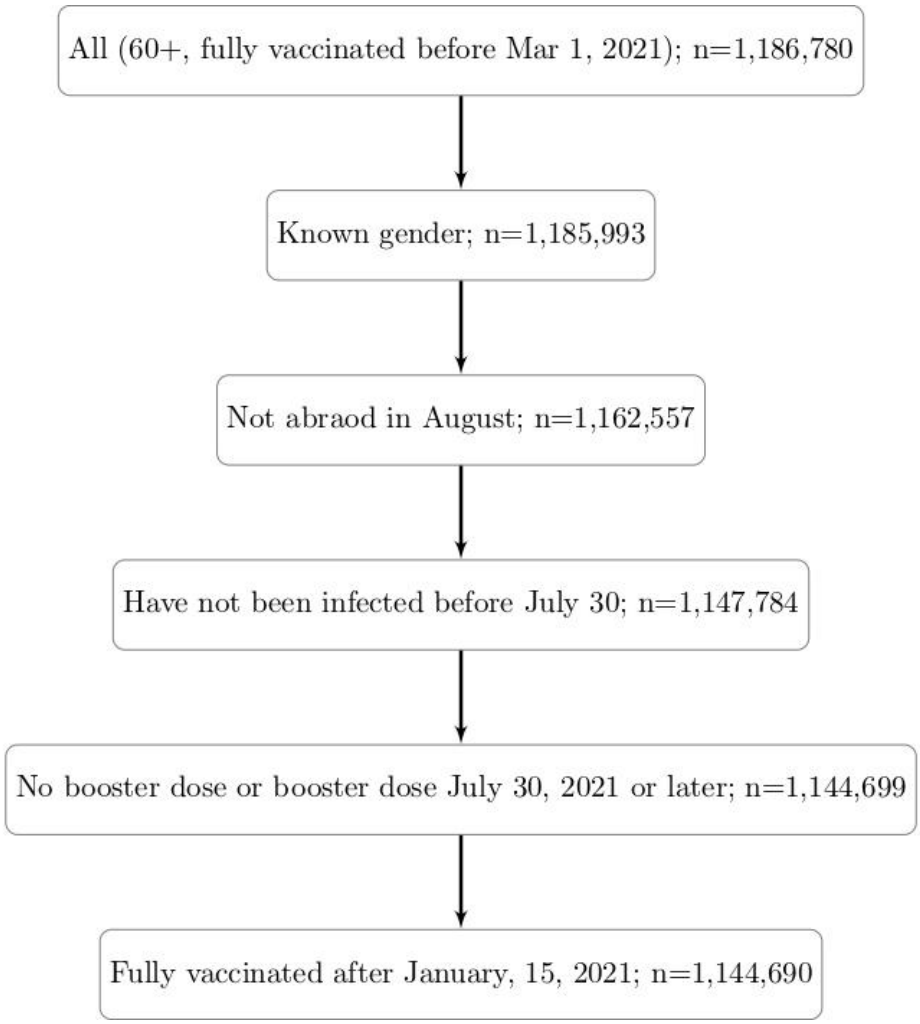

Figure 1. Study population. The population includes people who were fully vaccinated prior to March 1, 2021, were not abroad during August 2021, and had no documented SARS-CoV-2 PCR-positive result before July 30, 2021.

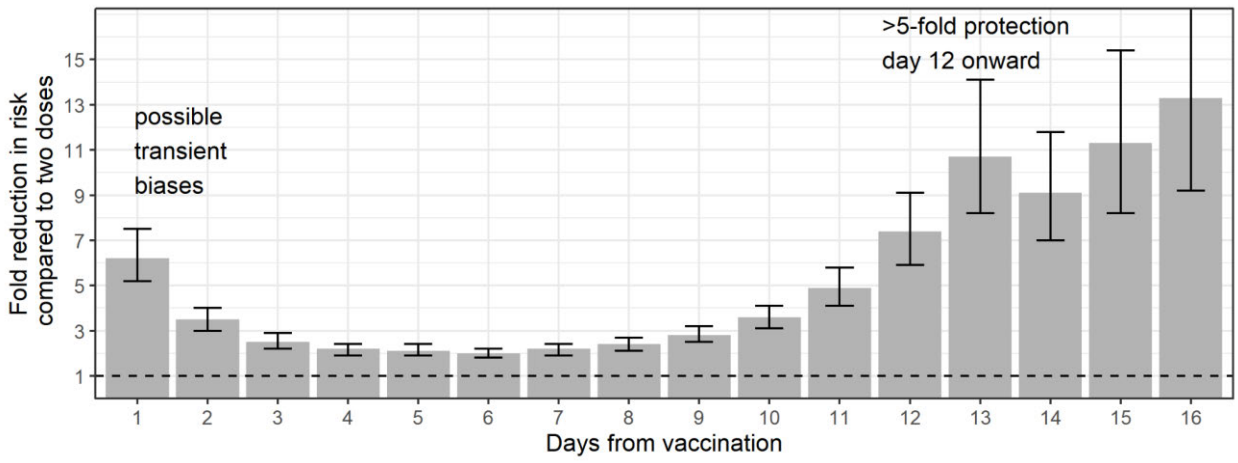

Figure 2. Booster protection against confirmed infection as a function of the number of days following the booster dose. Because of wide confidence intervals, only days 1-16 are shown. Protection is given as a fold reduction in risk relative to people who received only two vaccine doses. Data is based on about 1 million individuals aged 60 or older, who received the 3rd dose boost. The dashed line represents no added protection by the booster dose.

Supplementary Appendix

BNT162b2 vaccine booster dose protection: A nationwide study from Israel

Yinon M. Bar-On[†1], Yair Goldberg[†2*], Micha Mandel[†3], Omri Bodenheimer[4], Laurence Freedman[5], Nir Kalkstein[6], Barak Mizrahi[6], Sharon Alroy-Preis[4], Nachman Ash[4], Ron Milo[&1], Amit Huppert[&5,7]

[1] Weizmann Institute of Science, Israel

[2] Technion - Israel Institute of Technology, Israel

[3] The Hebrew University of Jerusalem, Israel

[4] Israel Ministry of Health, Israel

[5] The Gertner Institute for Epidemiology & Health Policy Research, Sheba Medical Center, Israel

[6] KI Research Institute, Kfar Malal, Israel

[7] Tel Aviv University, Israel

[†]Contributed equally.

[&]Contributed equally.

*corresponding author

email: yairgo@technion.ac.il

Supplementary Methods 1 - matching approaches

In order to validate our findings, we conducted two independent secondary analyses which rely on matching fully vaccinated individuals who received a booster dose with similar individuals who received only two vaccine doses.

The first matching approach was similar to that conducted by Dagan et.al.[15]. Briefly, each individual in the 'booster' cohort was matched to an individual who was in the 'no-booster' cohort on the booster-vaccination day based on the following characteristics: age group - (60-69,70-79 and 80+), gender, second vaccine dose week and demographic group (General Jewish, Arab, ultra-Orthodox). Follow-up for both individuals ended at the time of infection. Both individuals in a pair were censored at the end of the study or at the time the 'no-booster' individual got a booster dose. We calculated the probability of being free of infection in the two cohorts as a function of time using the Kaplan-Meier estimator, and compared the survival probabilities of the two cohorts at the end of the study. For each cohort, we calculated the probability of an event occurring between day 12 following the boost and the end of the study, among individuals still at risk on day 12. We used the ratio between the probabilities of the two cohorts as an estimate for the risk ratio for our population over the study time. We generated 95% confidence intervals around this estimate using the percentile bootstrap method with 100 repetitions.

A second approach matched days rather than individuals, ensuring that days in the two cohorts are comparable. Matching was performed as follows: on each day in the study period, we identified the group of individuals for whom 12 days or more passed since their booster dose (or 10 days for the severe illness analysis), and who were not previously infected ('booster' cohort). We randomly matched a 'no-booster' individual from those who received only two vaccine doses (by that same day), was not previously infected, and had the same characteristics (age group in five year window, gender, second vaccine dose week and demographic group: General Jewish, Arab, ultra-Orthodox). In order to be able to match all individuals in the 'booster' cohort, we conducted matching with replacement, so the same 'no-booster' individual could be assigned to multiple 'booster' individuals.

After matching was performed, we calculated the number of events (confirmed infection or severe COVID-19) occuring on the same calendar day in each of the two groups. An individual is considered severely ill at the date of first positive sample if the individual deteriorated to the corresponding condition within the study period. The ratio between the incidence of the outcomes in the 'booster' and 'no-booster' cohorts was used to estimate the marginal protection provided by the booster dose. We used non-parametric bootstrapping, with 200 bootstrap samples, followed by random matching, and reported the median ratio as the protection estimate and the 95% confidence intervals around it. Overall, out of 603,953

individuals for whom 12 days or more passed since their booster dose, 603,953 matched pairs were found.

For the first type of matching, our analysis yielded an estimate of 13.4-fold (95% CI [8.2-21.4]) for protection against confirmed infection. Due to the very small number of severe cases following the booster a reliable estimate of the protection versus severe illness using this approach was not possible.

For the second type of matching, our analysis yielded an estimate of 9.6-fold protection against confirmed infection (95% CI [8.1-11.4]) and 9.5-fold protection against severe illness (95% CI [5-19.6]). The overall agreement between the main and secondary analyses gives further reassurance that our results are robust to the employed statistical methodology.

Supplementary Figures

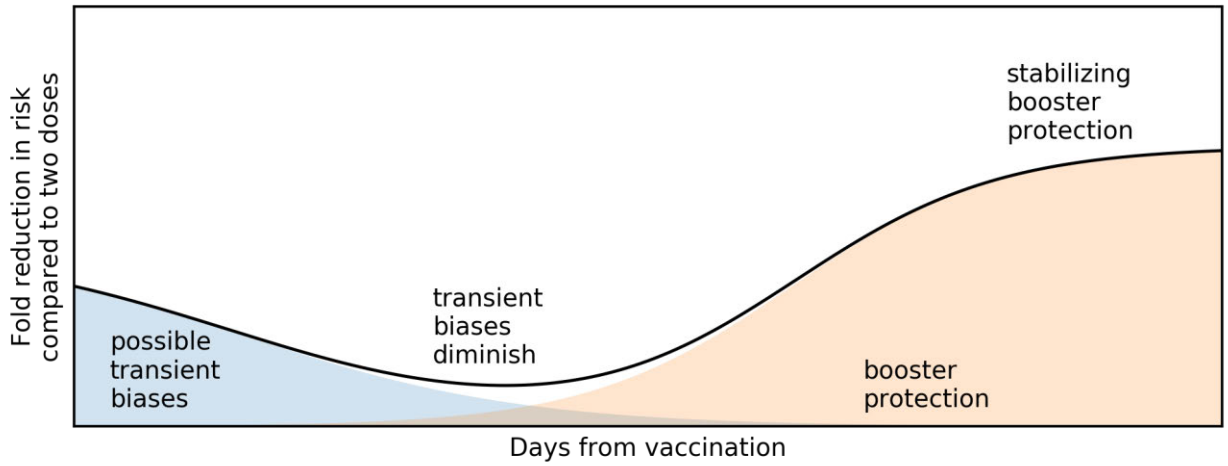

Figure S1. A conceptual schematic demonstrating the possible underlying dynamics of the results in Figure 2.

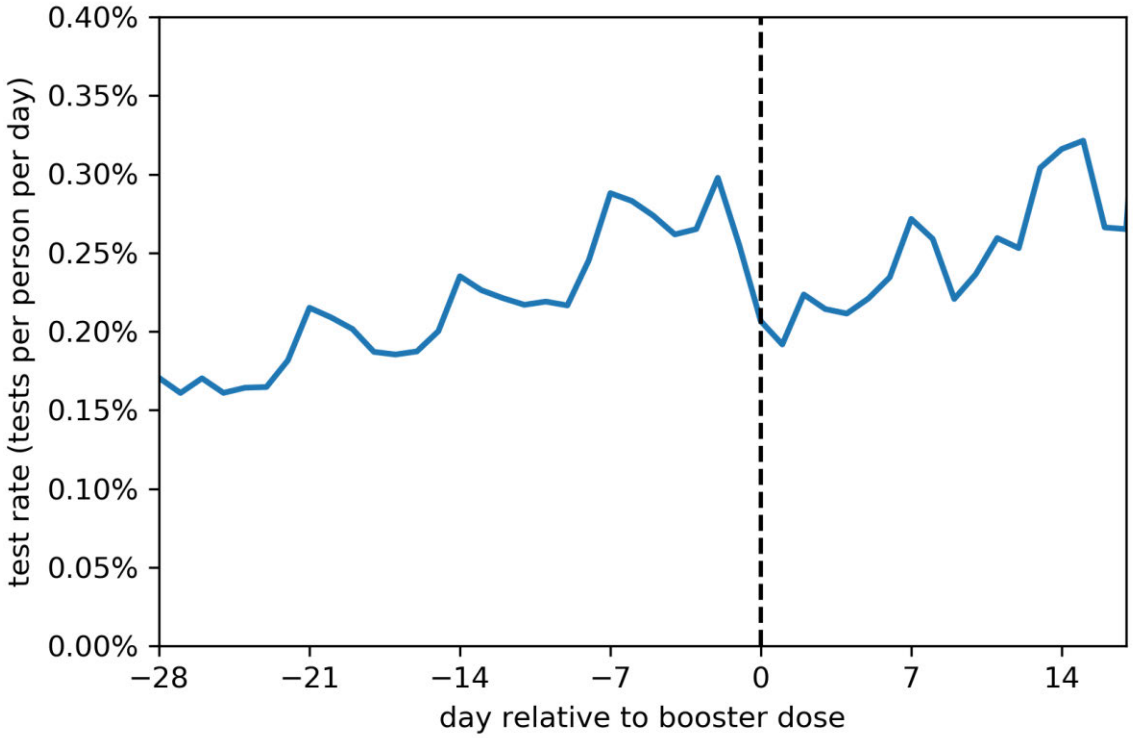

Figure S2. The daily rate of tests per person as a function of the time relative to the administration of the booster dose. A decrease in the rate of testing is observable just after the administration of the booster, likely reflecting transient behavioural changes in care-seeking behaviour or risk-avoidance.

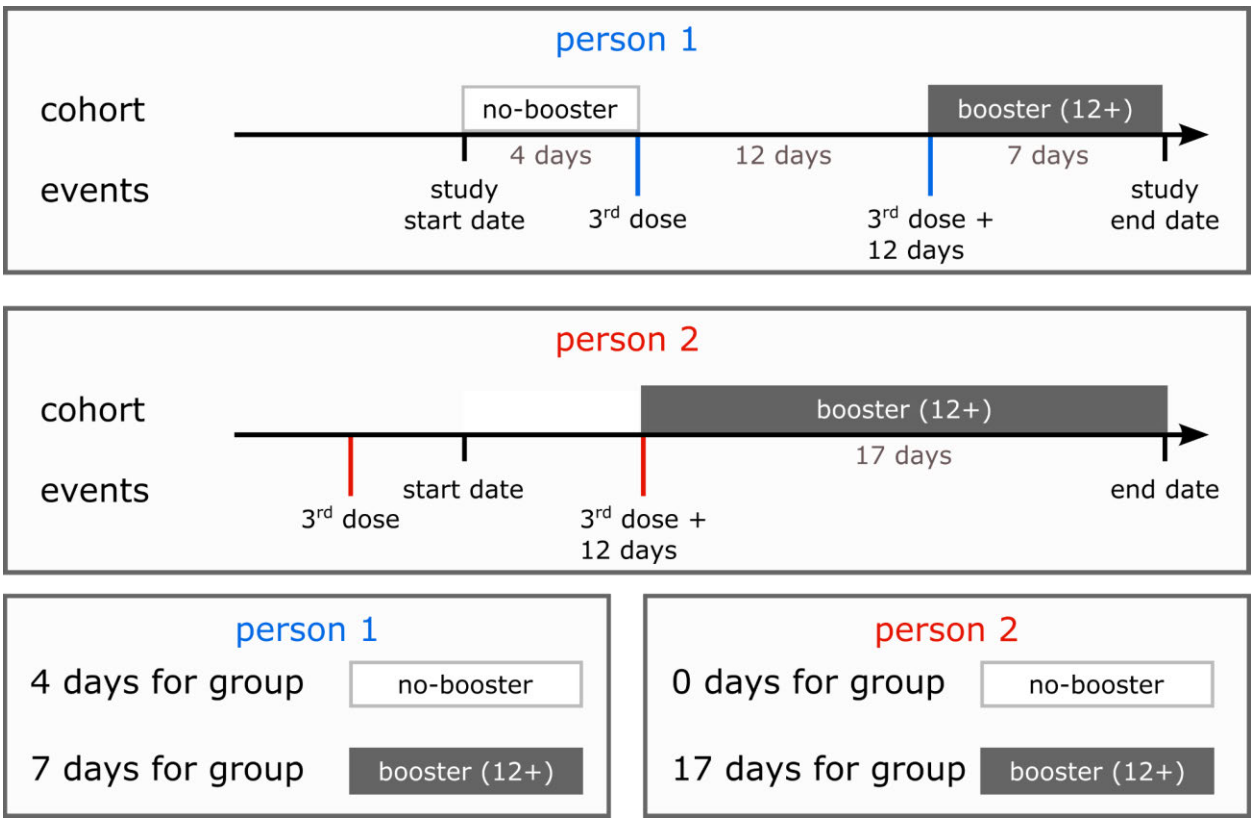

Figure S3. A schematic illustration of the allocation for the dynamic cohorts. We show two example timelines for two different individuals, and detail the cohort they contribute to at each point in time as well as the total days-at-risk for each person in each cohort.

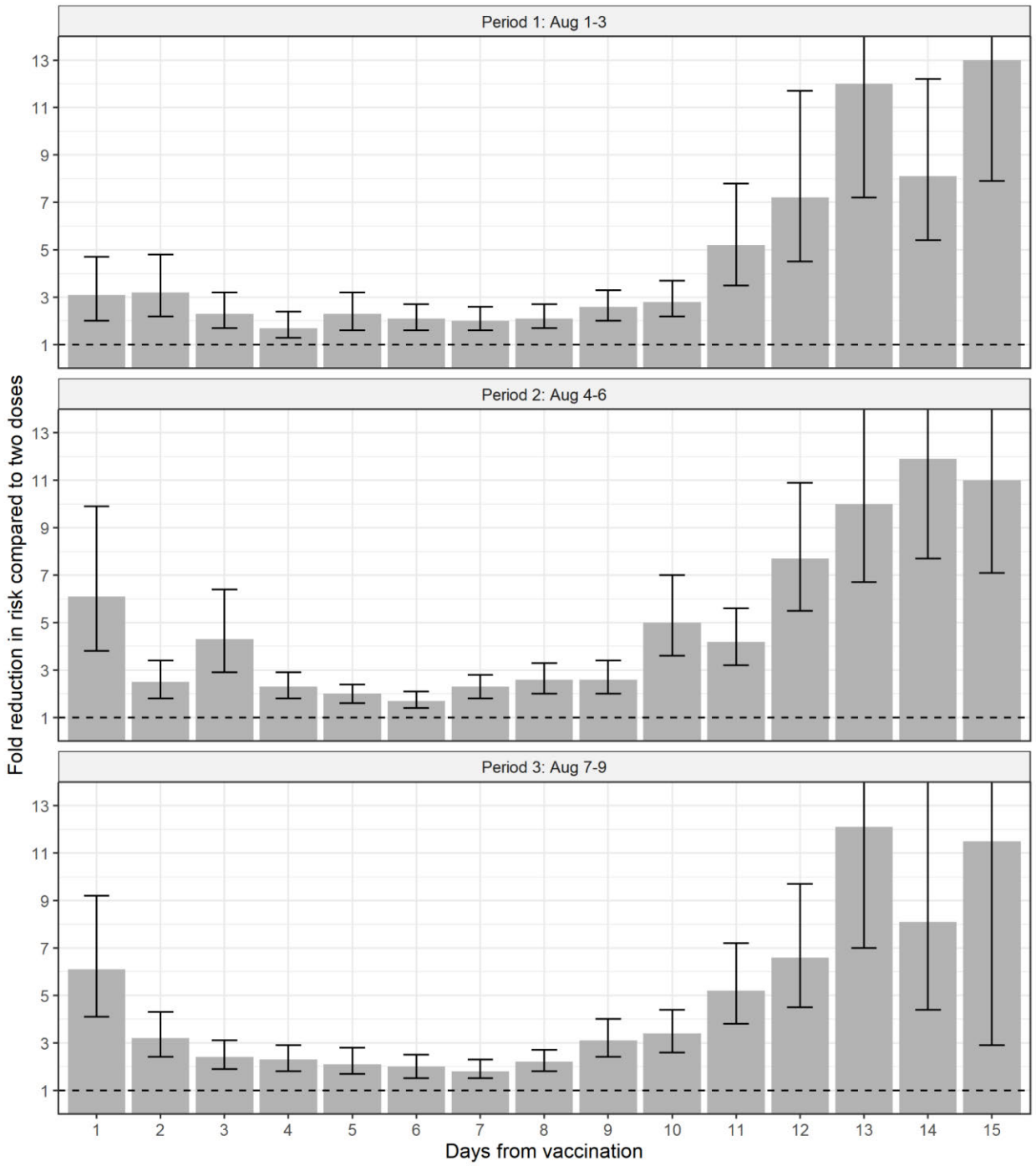

Figure S5. Sensitivity analysis across periods of booster vaccination for the booster protection against confirmed infection as a function of the number of days following the booster dose. Protection is given as a fold change in risk relative to people who received only two vaccine doses.

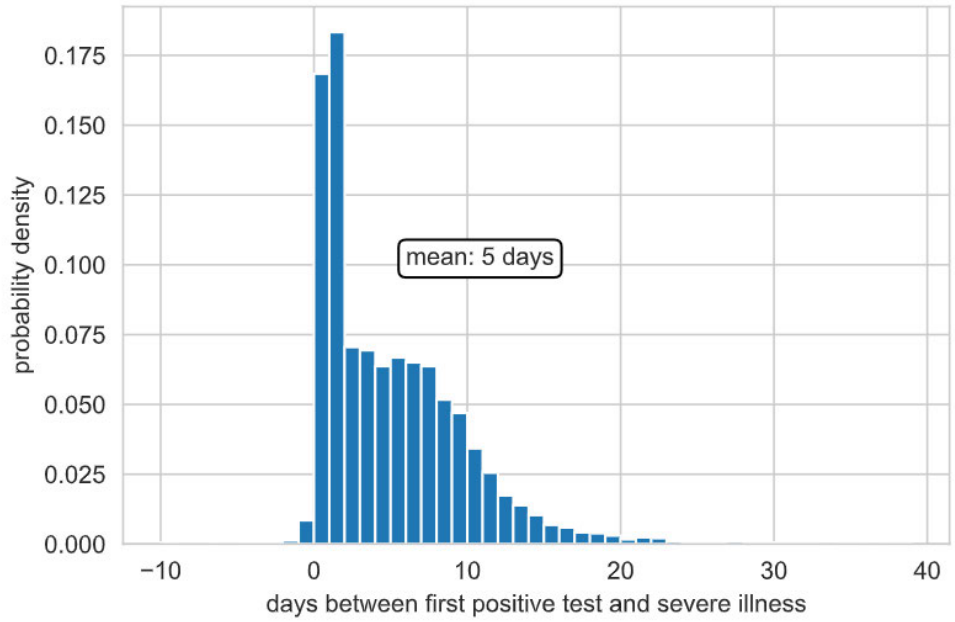

Figure S4. The distribution of time between first positive test and severe illness for confirmed cases between November 1st, 2020 and March 1st, 2021.

Table S1: Poisson regression results for confirmed SARS-CoV-2 infection.

term	estimate	std.error	statistic	p.value
(Intercept)	-6.96	0.06	-124.31	<0.001
age_category70-79	-0.11	0.04	-2.87	0.004
age_category80+	-0.12	0.05	-2.69	0.007
Gender = male	0.16	0.03	4.77	<0.001
date2021-08-11	-0.02	0.07	-0.22	0.830
date2021-08-12	0.17	0.07	2.48	0.013
date2021-08-13	-0.10	0.08	-1.31	0.191
date2021-08-14	-0.39	0.09	-4.57	<0.001
date2021-08-15	-0.14	0.08	-1.72	0.085
date2021-08-16	0.49	0.07	7.02	<0.001
date2021-08-17	0.19	0.08	2.43	0.015
date2021-08-18	0.33	0.08	4.36	<0.001
date2021-08-19	0.34	0.08	4.31	<0.001
date2021-08-20	0.24	0.08	2.96	0.003
date2021-08-21	-0.15	0.09	-1.69	0.092
date2021-08-22	-0.06	0.09	-0.63	0.531
vac_periodFeb 1-15	-0.19	0.04	-5.40	<0.001
vac_periodFeb 16-28	-0.37	0.06	-6.37	<0.001
Sector: Arab	-0.83	0.07	-11.41	<0.001
Sector: ultra Orthodox	0.30	0.07	4.51	<0.001
Cohort ‘booster’	-2.43	0.06	-38.18	<0.001

Table S2: Poisson regression results for severe COVID-19 disease.

term	estimate	std.error	statistic	p.value
(Intercept)	-10.94	0.23	-47.78	<0.001
age_category70-79	0.86	0.14	5.99	<0.001
age_category80+	1.79	0.13	13.26	<0.001
Gender = male	0.96	0.11	8.67	<0.001
date2021-08-11	0.24	0.26	0.94	0.349
date2021-08-12	0.42	0.25	1.66	0.097
date2021-08-13	0.32	0.27	1.22	0.224
date2021-08-14	0.11	0.28	0.40	0.69
date2021-08-15	0.74	0.25	2.97	0.003
date2021-08-16	0.44	0.27	1.62	0.106
date2021-08-17	0.77	0.26	3.00	0.003
date2021-08-18	0.48	0.28	1.69	0.091
date2021-08-19	0.56	0.28	1.97	0.049
date2021-08-20	0.66	0.28	2.37	0.018
date2021-08-21	0.69	0.28	2.51	0.012
date2021-08-22	0.95	0.26	3.62	<0.001
vac_periodFeb 1-15	-0.31	0.11	-2.78	0.006
vac_periodFeb 16-28	-0.84	0.22	-3.77	<0.001
Sector: Arab	-0.21	0.19	-1.10	0.273
Sector: ultra Orthodox	-0.07	0.26	-0.27	0.790
Cohort ‘booster’	-2.74	0.20	-13.77	<0.001

From: Fauci, Anthony (NIH/NIAID) [E]
Sent: Sat, 28 Aug 2021 12:58:21 -0500
To: Follmann, Dean (NIH/NIAID) [E];Lane, Cliff (NIH/NIAID) [E]
Cc: Collins, Francis (NIH/OD) [E]
Subject: FW: Post infection protection vs vaccine immunity
Attachments: Bar-On 2021 - rapid and robust increase in VE following 3rd dose BNT162b2 Israel - medRxiv.pdf

Dean:

Please see John Brooks's concern about the data in the Israeli paper. Is there any validity to his concern? The data are really rather impressive and it would be important to determine the strength of their validity. Please take a look at this paper and help us determine if it is in fact a strong study. I hate to impose upon you about this , but this is really an important issue . Many thanks.

Best regards,

Tony

Anthony S. Fauci, MD
Director
National Institute of Allergy and Infectious Diseases
Building 31, Room 7A-03
31 Center Drive, MSC 2520
National Institutes of Health
Bethesda, MD 20892-2520
Phone: (b) (6)
FAX: (301) 496-4409
E-mail: (b) (6)

From: Brooks, John T. (CDC/DDID/NCHHSTP/DHP) <zud4@cdc.gov>
Sent: Friday, August 27, 2021 5:14 PM
To: Fauci, Anthony (NIH/NIAID) [E] (b) (6); Murthy, Vivek (HHS/OASH) <Vivek.Murthy@hhs.gov>; Collins, Francis (NIH/OD) [E] (b) (6); Walensky, Rochelle (CDC/OD) <aux7@cdc.gov>; Eric Lander (b) (6)>
Cc: Beckman, Adam (HHS/OASH) <Adam.Beckman@hhs.gov>
Subject: RE: Post infection protection vs vaccine immunity

I also received this paper today from Israeli colleagues (attached) in which they present evidence that their booster program has restored the loss in vaccine effectiveness that had been observed among persons fully vaccinated with the 2-dose Pfizer vaccine series in whom VE against infection was decreasing.

They used two basic approaches to analyze these retrospective data: a series of Poisson regressions and a case-control matching method. All analyses point in the same direction and the results seem impressive.

I am a having trouble wrapping my head around how they detected such a potent effect of an intervention started in late July and delivered to about 3 M Israelis in just a few weeks. It just seemed mighty fast, but perhaps in this case the anamnestic response primed by prior vaccination kicked in hard and fast.

As I digest this one (with the sage input of smarter colleagues here whose career work is VE), I wanted to ensure all were aware the paper is out there.

-john

John T. Brooks, MD
Chief Medical Officer, CDC COVID-19 Response
Email: zud4@cdc.gov
Apologies for errors in my messages that may be due to my need to dictate.

From: Fauci, Anthony (NIH/NIAID) [E] (b) (6)>
Sent: Friday, August 27, 2021 2:37 PM
To: Murthy, Vivek (HHS/OASH) <Vivek.Murthy@hhs.gov>; Collins, Francis (NIH/OD) [E] (b) (6); Walensky, Rochelle (CDC/OD) <aux7@cdc.gov>; Eric Lander (b) (6)>; Brooks, John T. (CDC/DDID/NCHHSTP/DHP) <zud4@cdc.gov>
Cc: Beckman, Adam (HHS/OASH) <Adam.Beckman@hhs.gov>
Subject: RE: Post infection protection vs vaccine immunity

The data as reported in the news article look rather impressive despite the caveat that it is a retrospective study and the testing was voluntary. I have not seen the details of the actual data, but I would imagine that it is more complicated than we think. It very well may be that people who have had an asymptomatic or minimally symptomatic infection (upper airway only) will not have a greater post-infection protection against subsequent infection then those who get fully vaccinated. However, it is conceivable and possibly likely that those who have had a serious systemic infection develop a high level of immunity that even surpasses

that of full vaccination. I would like to see if they broke the data on the infected people down into those two groups.

Anthony S. Fauci, MD
Director
National Institute of Allergy and Infectious Diseases
Building 31, Room 7A-03
31 Center Drive, MSC 2520
National Institutes of Health
Bethesda, MD 20892-2520
Phone: (b) (6)
FAX: (301) 496-4409
E-mail: (b) (6)

From: Murthy, Vivek (HHS/OASH) <Vivek.Murthy@hhs.gov>
Sent: Friday, August 27, 2021 1:57 PM
To: Collins, Francis (NIH/OD) [E] (b) (6)>; Fauci, Anthony (NIH/NIAID) [E] (b) (6); Walensky, Rochelle (CDC/OD) <aux7@cdc.gov>; Eric Lander (b) (6)>; Brooks, John T. (CDC/DDID/NCHHSTP/DHP) <zud4@CDC.GOV>
Cc: Beckman, Adam (HHS/OASH) <Adam.Beckman@hhs.gov>
Subject: Post infection protection vs vaccine immunity

Do you have thoughts on this recent study from Israel? And how this fits with the recent MMWR findings (Kentucky study showing higher risk of reinfection in the unvaccinated compared to risk of infection in the vaccinated)?

https://www.sciencemag.org/news/2021/08/having-sars-cov-2-once-confers-much-greater-immunity-vaccine-no-infection-parties

Having SARS-CoV-2 once confers much greater immunity than a vaccine—but no infection parties, please | Science | AAAS

Having SARS-CoV-2 once confers much greater immunity than a vaccine—but no infection parties, please. By Meredith

Wadman Aug. 26, 2021 , 8:02 PM. The natural immune protection that develops ...

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BNT162b2 vaccine booster dose protection: A nationwide study from Israel

Yinon M. Bar-On[†1], Yair Goldberg[†2*], Micha Mandel[†3], Omri Bodenheimer[4], Laurence Freedman[5], Nir Kalkstein[6], Barak Mizrahi[6], Sharon Alroy-Preis[4], Nachman Ash[4], Ron Milo[&1], Amit Huppert[&5,7]

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[1] Weizmann Institute of Science, Israel

[2] Technion - Israel Institute of Technology, Israel

[3] The Hebrew University of Jerusalem, Israel

[4] Israel Ministry of Health, Israel

[5] The Gertner Institute for Epidemiology & Health Policy Research, Sheba Medical Center, Israel

[6] KI Research Institute, Kfar Malal, Israel

[7] Tel Aviv University, Israel

[†]Contributed equally.

[&]Contributed equally.

*corresponding author

email: yairgo@technion.ac.il

Abstract

Background: On July 30, 2021, a third (booster) dose of the Pfizer BNT162b2 vaccine was approved in Israel for individuals 60 years or older who had been fully vaccinated (i.e., received two doses) at least five months previously. Here, we estimate the reduction in relative risk for confirmed infection and severe COVID-19 provided by the booster dose.

Methods: 1,144,690 individuals aged 60y and older who were eligible for a booster dose were followed between July 30 and August 22, 2021. We defined dynamic cohorts where individuals initially belong to the 'non-booster' cohort, leave it when receiving the booster dose and join the 'booster' cohort 12 days later. Rates of infection and severe COVID-19 outcomes per person-days at risk were compared between the cohorts using Poisson regression, adjusting for possible confounding factors.

Results: Twelve days or more after the booster dose we found an 11.4-fold (95% CI: [10.0, 12.9]) decrease in the relative risk of confirmed infection, and a >10-fold decrease in the relative risk of severe illness. Under a conservative sensitivity analysis, we find ≈5-fold protection against confirmed infection.

Conclusions: In conjunction with safety reports, this study demonstrates the effectiveness of a third vaccine dose in both reducing transmission and severe disease and indicates the great potential of curtailing the Delta variant resurgence by administering booster shots.

Introduction

The rapid development of effective vaccines against SARS-CoV-2 and their deployment to the general population has been proven to be a highly successful strategy for reducing transmission and disease burden. In Israel, a swift vaccination campaign led to more than half of the population being fully vaccinated by the end of March 2021 [1]. Consequently, COVID-19 incidence dropped from ≈900 cases per million per day in mid-January 2021 to less than 2 cases per million per day by June 2021 [1]. Nevertheless, the emergence of new variants of concern (VOC), and specifically the Delta variant, has led to a recent infection resurgence in Israel both in infection and severe disease [2]. There are several possible causes for the high levels of transmission of the Delta variant, including increased infectiousness of the Delta variant [3], waning vaccine-elicited immunity [2,4], and heightened immune evasion by the variant [5], the latter two of which directly contribute to a decrease in vaccine efficacy. Analysis of the Israeli data on the Delta outbreak indicated strong waning immunity. In an effort to address the challenge presented by the Delta variant and reduce the load on the healthcare system, Israeli authorities approved the administration of a booster dose, first to high-risk populations, on July 12, 2021, and then to the entire 60+ population, on July 30, 2021.

Initial studies have suggested that a BNT162b2 booster dose, i.e., an additional dose given to individuals who have previously received two BNT162b2 vaccine doses, increases antibody neutralization levels ~10-fold, on average, compared to levels achieved after the second dose [6]. It is thought that an increased neutralization titer could lead to increased protection against infection and severe illness [7]. However, in terms of real-world efficacy, the size of such an effect remains unclear. Here, we use initial data from the Israeli Ministry of Health (MOH) database on the incidence of confirmed infection and severe illness among two cohorts of individuals above 60 years of age: those who received only two vaccine doses, and those who received an additional booster dose. We use the data to quantify the protective effect that the booster dose provides against confirmed infection and severe illness.

The protection gained by the booster shot is not expected to reach its maximal capacity immediately on vaccination, but to build up over the week following vaccination [8,9]. At the same time, during the first days after vaccination, significant behavioral changes in the booster-vaccinated population are expected (Figure S1 in the Supplementary Appendix). One such expected change is added avoidance of exposure to excess risk until the booster dose becomes effective. Another expected change is a reduced rate of testing for COVID-19 around the time of receiving the booster, as demonstrated in Figure S2 (Supplementary Appendix). Moreover, we analyzed confirmed COVID-19 infections based on the date of the positive PCR test, and testing occurs only several days following exposure. For all these reasons, it is preferable to assess the effect of the booster only after a sufficient period has passed since its administration.

Methods

Our analysis is based on medical data from the MOH database extracted on August 24, 2021. There were 1,186,780 Israeli residents aged 60 and older who had been fully vaccinated at least five months (became fully vaccinated before March 1, 2021), and were still alive on July 30, 2021. We removed from these data individuals who: had missing gender; were abroad in August 2021; had been infected with COVID-19 before July 30, 2021; received a booster dose before July 30, 2021; or became fully vaccinated before January 16. A total of 1,144,690 individuals met the inclusion criteria for the analysis (see Figure 1). The data included vaccination dates (first, second and third doses), RT-qPCR tests (dates and results), COVID-19 hospitalization date (if relevant), demographic variables such as age, gender, and demographic group (General Jewish, Arab, ultra-Orthodox Jewish) [10], and clinical status (mild, severe). Severe disease was defined as: resting respiratory rate >30 breaths per minute, or oxygen saturation on room air <94%, or ratio of PaO2 to FiO2 <300 [11].

We considered 12 days as the time it took the booster dose to affect the observed number of confirmed infections. Our study period started at the beginning of the booster vaccination campaign on July 30, 2021. The end date was chosen as August 22, 2021, to minimize the effects of missing outcome data due to delays in the reporting of test results. Choosing 12 days following booster vaccination as the cutoff is scientifically justified from an immunological perspective, as studies have shown that following the booster dose, neutralization levels increase only after several days [6]. Using confirmed infections (i.e., PCR positivity) as an outcome, there is a delay between infection and testing. For symptomatic cases, infections occur on average 5-6 days prior to testing, similar to the incubation period of COVID-19 [12,13].

To estimate the level of protection provided by the booster dose, we analyzed data on the incidence of confirmed infections and severe illness of two distinct cohorts: people who received two vaccine doses and the booster dose ('booster' cohort), and people who received only two vaccine doses ('no-booster' cohort). These cohorts were dynamic; individuals initially belonged to the 'non-booster' cohort, left it when receiving the booster dose, and joined the 'booster' cohort 12 days later (Figure S3 in the Supplementary Appendix) provided they did not have a confirmed infection in the interim period. We considered data on two outcomes of interest, confirmed infection and severe COVID-19, and counted the number of events of each type during the study period.

For each cohort, we calculated the incidence rate of both confirmed infection and severe COVID-19 per person-days at risk. For each person in the 'booster' cohort, days at risk started when entering the cohort (12 days after receiving the third dose), and ended either with the occurrence of an outcome or at the end of the study period. For the 'no-booster' cohort, days at risk started at the beginning of the study period (August 10, 2021), and ended either with the

occurrence of an outcome, the end of the study period, or when receiving a booster dose. Since cohort membership was dynamic, many individuals contributed person-days at risk to both cohorts.

We fitted a Poisson regression (using the glm function in the R Statistical Software)[14] to estimate the incidence rate of a specific outcome, controlling for several important covariates: age (60-69, 70-79, 80+), gender, demographic group (General Jewish, Arab, ultra-Orthodox Jewish) [10], and date of second vaccine dose (in half-month intervals). Since the overall incidence rate of both confirmed infection and severe COVID-19 increased exponentially during the study period, days at the beginning of the study period had lower exposure risk than days at the end. To account for growing exposure risk, we included calendar date as an additional covariate. Accounting for these covariates, we used the study cohort ('booster' or 'no-booster') as a factor in the regression and estimated its impact on the incidence rate. The effect of the booster dose is estimated as one divided by the exponent of the regression coefficient associated with the treatment cohort, which is akin to a relative risk. For reporting uncertainty around our estimate, we used the exponent of the 95% confidence limits for the regression coefficient.

As a sensitivity analysis, we compared infection rates before and after the booster dose became effective. Specifically, we repeated the Poisson regression analysis described above but compared infection rates on days 4-6 to 12+ after the booster dose. Our hypothesis was that the booster dose was not yet effective during the former period [8]. This analysis compares different periods following booster vaccination based only on those who received the booster dose, and may reduce selection bias. On the other hand, people might perform less PCR testing and behave more cautiously with regard to virus exposure just after getting the booster vaccination (Figure S2), so we conjecture that the protection effect is underestimated in this analysis, providing a lower bound to the real effect.

To further examine the protection as a function of time from the booster dose, we fitted a Poisson regression comparing the 'booster' and 'no-booster' cohorts as above, while including each day, from day 1 up to day 24 after the booster vaccination, as a separate factor in the model. The period before receiving the booster dose ('no-booster' cohort) was used as the reference category. The analysis is similar to the Poisson modeling described above, with one divided by the exponents of the regression coefficients representing the protection on different days post the booster vaccination. The follow-up time for this analysis started on July 30, 2021, and ended on August 22, 2021.

As further sensitivity analyses, we applied two methods based on case-control matching. The first method was similar to that used by Dagan et. al[15]. Each person who received the booster was matched, using the same covariates as used in the Poisson regression model, to a person

who had not yet received it on that date. We compared the probabilities of COVID-19 infection 12 days or more after the matching time of those receiving the booster dose and those who did not. In the second method, we matched person-days rather than individuals, ensuring that person-days in the two cohorts are comparable in terms of covariates and exposure risk. On each day we identified the group of individuals for whom 12 days or more had passed since receiving the booster dose and who had not been infected in the interim ('booster' cohort). We randomly matched a day of a 'no-booster' individual from those who had received only two vaccine doses by that same date, had not been previously infected, and had the same characteristics (age, gender, second vaccination period, and demographic group). We then calculated the risk ratio of infection and severe COVID-19 between the two groups. A detailed description of both approaches is given in Supplementary Methods 1 in the Supplementary Appendix.

Results

The baseline characteristics of both cohorts are shown in Table 1. As our primary analysis adjusts for person-days at risk, and since individuals contribute days to both cohorts, we compare characteristics according to person-days at risk. There are about 4.0 million person-days in the 'no-booster' cohort with 3,473 confirmed infections and 330 cases of severe COVID-19, and about 3.4 million person-days in the 'booster' cohort with 313 confirmed infections and 32 cases of severe COVID-19. The 'booster' cohort tends to have more men (50% vs 43%), more general Jewish people (93% vs 82%), more older people (60% vs 47% aged 70+ years), and people who were vaccinated earlier (79% vs 40% vaccinated in January). These significant differences are adjusted for when estimating protection.

The full Poisson regression analysis for confirmed infection is given in Table S1 of the Supplementary Appendix, and the results for the booster dose protection are summarized in Table 2. The booster dose provides significant protection – an estimate of 11.4-fold (95% CI: [10, 12.9]) decrease in the relative risk of a confirmed infection. In the Supplementary Appendix, we provide the results of alternative analyses using matching techniques. The first analysis, following Dagan et. al.[15], resulted in a higher estimate of the decrease in relative risk of 13.4 (95% CI: [8.2-21.4]) and the second, relying on matching by days, gave a slightly smaller estimate for the decrease in the relative risk of 9.6 (95% CI: [8.1, 11.4]).

The sensitivity analysis that compared the risk of infections during 12+ days after booster to 4-6 days after booster, gave a decrease in relative risk of 4.7 (95% CI: [4, 5.4]), about half of that in the main analysis.

The protection conferred by the booster dose against severe disease also appeared high. For people with a more-than-12-days lag between the booster vaccination and severe illness, we

found that the booster dose decreases the relative risk of severe disease by 15.5-fold (95% CI: [10.5, 22.8]). We validated our results using the matching-by-day analysis that gave 9.5-fold protection against severe illness (95% CI [5-19.6]).

Figure 2 presents the results of the Poisson regression analysis with the number of days after booster vaccination as additional covariates, demonstrating the protection as a function of time from the booster vaccination. After about 12 days, protection starts stabilizing at about 10-12 fold reduction in risk in line with the results presented above. As shown in Figure 2, there is an apparent protection for the booster-vaccinated group in the first days following vaccination. This apparent protection (i.e., days 1-4) is likely the result of the aforementioned behavioral changes that follow vaccination. As the time since vaccination progresses, the magnitude of this apparent protection decreases, indicating that the effect of behavioral change decreases. Levels of protection appear to start increasing again from day 7 post vaccination. As shown in Figure S4 these results are robust across different study periods.

Discussion

Our analysis shows that the booster dose of the BNT162b2 vaccine is highly effective in reducing the risk of both confirmed infection and severe illness. For example, if the combined effect of waning immunity and the Delta variant decrease the efficacy of a vaccine given >6 months ago against infection to ≈50%, as recent reports have suggested [16,17], and if the booster dose reduces the relative risk by 10-fold, it means that the probability of a booster-vaccinated individual to being susceptible to infection would decrease to ≈5% (=50%/10) relative to unvaccinated individuals. This brings vaccine efficacy for booster-vaccinated individuals to ≈95%, similar to the original "fresh" vaccine efficacy reported against the Alpha strain [11,15].

On average, severe illness develops ≈5 days after the first positive-sample date (Figure S5 in the Supplementary Appendix). Thus, the follow-up period in our data is short and confidence intervals for protection against severe disease are wide. Moreover, some individuals from the booster cohort for severe illness were likely infected prior to or immediately after receiving the booster, and this could lead to an underestimate in the inferred protection against severe illness.

While our analysis attempts to address possible biases in the source data, such as the effects of confounders and behavioral changes following vaccination, there are some sources of bias that we may not correct adequately. These include differences between those receiving and not receiving the booster in care-seeking behaviors and cautiousness, and in comorbidities. Some of these possible biases are transient and fade with time since the booster vaccination, as schematically shown in Figure S1 in the Supplementary Appendix, implying that the real

effectiveness of vaccination can be estimated when comparing infection rates before receiving the booster dose and after enough time has elapsed (e.g. after 12 days, Figure S1 in the Supplementary Appendix). While independent research is required in order to fully understand this behavioral model, several indications suggest that our 12 days cutoff is reasonable. First, as shown in Figure S2 in the Supplementary Appendix, people tend to perform fewer PCR tests a few days before and after the vaccination day, which is a clear source for detection bias. Over time, the number of tests that vaccinated individuals perform increases, which reduces this bias. Consistent with such behavioral change is the pattern in Figure 2, which shows a large reduction in infection risk on the first day after vaccination that monotonically decreases during the first few days, before starting to increase as the booster dose becomes effective.

Yet, confounding biases may still explain part of the observed effectiveness, and these may not disappear over time. We can put a crude lower bound on the booster efficacy by looking at time points at which the booster efficacy is not expected to be significant and behavioral differences are smaller, e.g. days 4-6 after the booster dose, and attributing the whole observed effectiveness to confounding bias. Our sensitivity analysis compared the cohort of booster-vaccinated individuals 12+ days after receiving the booster dose to the same group at days 4-6, when the booster effect is expected to be only minimally translated into a reduction in confirmed infections (Figure 2). This analysis yielded an estimate of 4.7-fold (95% CI [4.0, 5.4]) protection against confirmed infection. Even under this conservative interpretation, the demonstrated protection highlights the important role that a booster dose could play in mitigating the effects of waning immunity and immune evasion, and in mitigating the spread of VOC such as the Delta variant.

There are significant behavioral differences between the main demographic groups in Israel. Table 1 shows that the 'booster' cohort is highly biased toward the general Jewish population; 93% vs 82% in the 'no-booster' cohort. This may be a source of a selection bias that is not fully accounted for in the main analysis. We, therefore, repeated the analysis for the subset of people from the general Jewish sector. The results of the Poisson analysis were very similar to those shown in Table 2, with protection against confirmed infection of 10.9 (95% CI [9.6, 12.4]). This validates the ≈10-fold protection against infection findings of the main analysis.

Understanding the protection gained by a booster dose is critical for policy making. On July 30, 2021, Israel was the first country in the world to make available a third dose of Pfizer BNT162b2 vaccine against COVID-19 to all people aged 60 or over who had been vaccinated at least five months previously. The results of such a policy are of importance for countries that seek strategies to mitigate the pandemic. Our findings give clear indications of the effectiveness of a booster dose even against the currently dominant Delta variant.

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Ethics statement

The study was approved by the Institutional Review Board of the Sheba Medical Center. Helsinki approval number: SMC-8228-21.

Competing interests statement

All authors declare no competing interests.

Funding

None.

Data sharing

Table 1: Demographic and clinical characteristics of the study population for the two study cohorts. Since the cohorts are dynamic and individuals can contribute to both cohorts, the table presents the number of person-days at risk instead of the number of individuals.

	2nd dose only ("no-booster" cohort)	12+ days from 3rd dose ("booster" cohort)
Person-days at risk	4,018,929	3,351,598
Confirmed Infections	3,473	313
Severe COVID-19	330	32
Gender = male (%)	1,712,000 (43%)	1,681,085 (50%)
Sector (% of person-days at risk)		
General Jewish	3,318,512 (82%)	3,127,545 (93%)
Arab	514,357 (13%)	114,671 (3%)
Orthodox Jews	186,060 (5%)	109,382 (3%)
Age category (% of person-days at risk)		
60-69	2,138,861 (53%)	1,353,160 (40%)
70-79	1,173,437 (29%)	1,341,000 (40%)
80+	706,631 (18%)	657,438 (20%)
2nd vaccination period (% of person-days at risk)		
Jan, 16-31	1,613,977 (40%)	2,664,230 (79%)
Feb, 1-15	1,849,978 (46%)	634,870 (19%)

Feb, 16-28	554,974 (14%)	52,498 (2%)

Table 2. Summary of the results of the Poisson regression analysis for different cohorts: people who received only two vaccine doses and people for whom 12 days or more have passed since their booster dose. For each group, we provide the total number of person-days at risk for each cohort, the number of confirmed infections and severe COVID-19 in each cohort, and the estimated protection of the booster against confirmed infection and severe illness, given as a fold change in relative risk.

Cohort	Person-days at risk	Confirmed infections	Severe COVID-19	Estimated booster protection (95% CI)	
				Against confirmed infection	Against severe illness
2 doses only ("no-booster" cohort)	4,018,929	3,473	330	1	1
12+ days from 3rd dose ("booster" cohort)	3,351,598	313	32	11.4 [10, 12.9]	15.5 [10.5, 22.8]

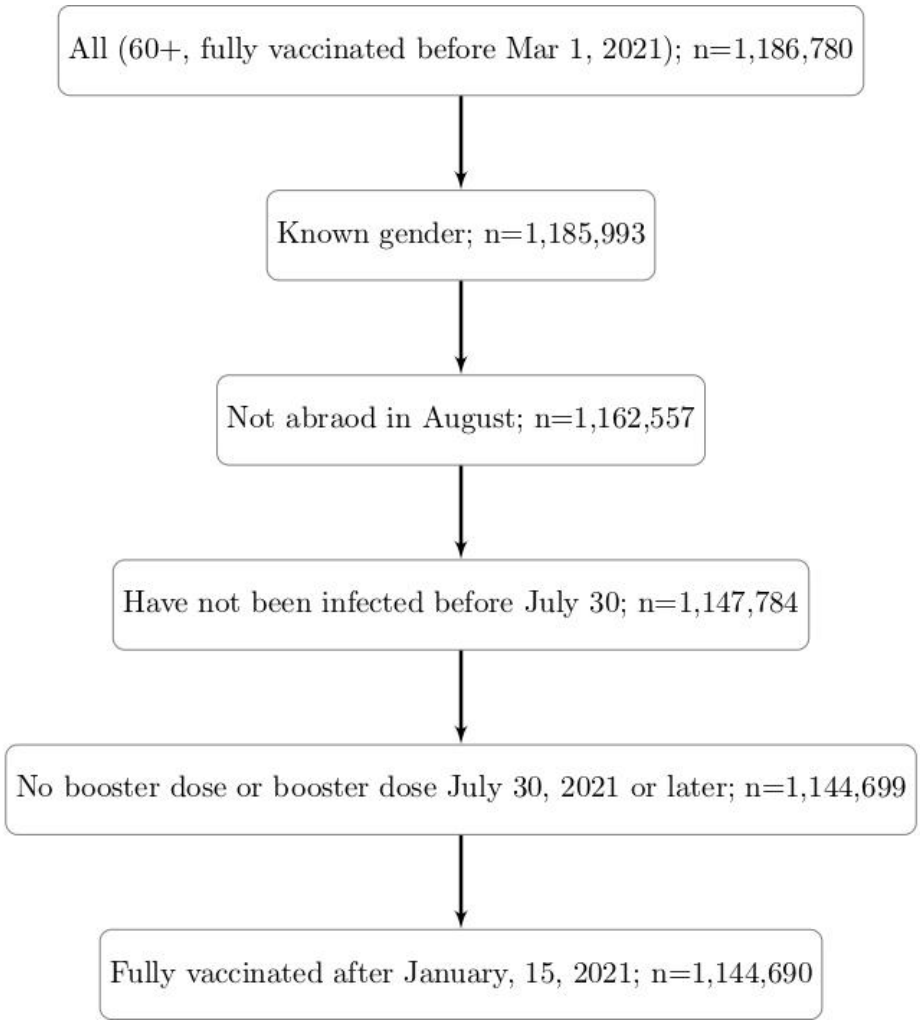

Figure 1. Study population. The population includes people who were fully vaccinated prior to March 1, 2021, were not abroad during August 2021, and had no documented SARS-CoV-2 PCR-positive result before July 30, 2021.

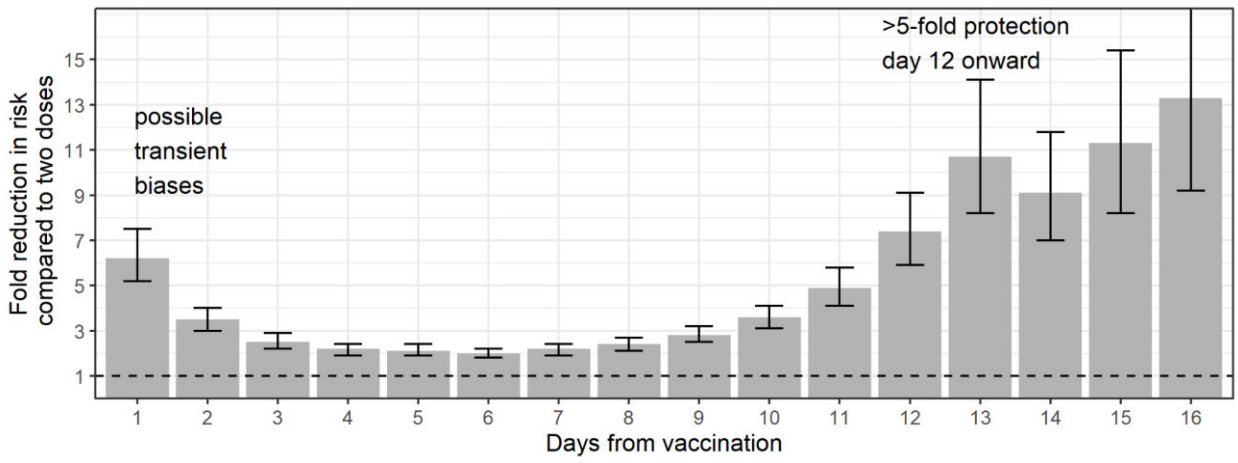

Figure 2. Booster protection against confirmed infection as a function of the number of days following the booster dose. Because of wide confidence intervals, only days 1-16 are shown. Protection is given as a fold reduction in risk relative to people who received only two vaccine doses. Data is based on about 1 million individuals aged 60 or older, who received the 3rd dose boost. The dashed line represents no added protection by the booster dose.

Supplementary Appendix

BNT162b2 vaccine booster dose protection: A nationwide study from Israel

Yinon M. Bar-On[†1], Yair Goldberg[†2*], Micha Mandel[†3], Omri Bodenheimer[4], Laurence Freedman[5], Nir Kalkstein[6], Barak Mizrahi[6], Sharon Alroy-Preis[4], Nachman Ash[4], Ron Milo[&1], Amit Huppert[&5,7]

[1] Weizmann Institute of Science, Israel

[2] Technion - Israel Institute of Technology, Israel

[3] The Hebrew University of Jerusalem, Israel

[4] Israel Ministry of Health, Israel

[5] The Gertner Institute for Epidemiology & Health Policy Research, Sheba Medical Center, Israel

[6] KI Research Institute, Kfar Malal, Israel

[7] Tel Aviv University, Israel

[†]Contributed equally.

[&]Contributed equally.

*corresponding author

email: yairgo@technion.ac.il

Supplementary Methods 1 - matching approaches

In order to validate our findings, we conducted two independent secondary analyses which rely on matching fully vaccinated individuals who received a booster dose with similar individuals who received only two vaccine doses.

The first matching approach was similar to that conducted by Dagan et.al.[15]. Briefly, each individual in the 'booster' cohort was matched to an individual who was in the 'no-booster' cohort on the booster-vaccination day based on the following characteristics: age group - (60-69,70-79 and 80+), gender, second vaccine dose week and demographic group (General Jewish, Arab, ultra-Orthodox). Follow-up for both individuals ended at the time of infection. Both individuals in a pair were censored at the end of the study or at the time the 'no-booster' individual got a booster dose. We calculated the probability of being free of infection in the two cohorts as a function of time using the Kaplan-Meier estimator, and compared the survival probabilities of the two cohorts at the end of the study. For each cohort, we calculated the probability of an event occurring between day 12 following the boost and the end of the study, among individuals still at risk on day 12. We used the ratio between the probabilities of the two cohorts as an estimate for the risk ratio for our population over the study time. We generated 95% confidence intervals around this estimate using the percentile bootstrap method with 100 repetitions.

A second approach matched days rather than individuals, ensuring that days in the two cohorts are comparable. Matching was performed as follows: on each day in the study period, we identified the group of individuals for whom 12 days or more passed since their booster dose (or 10 days for the severe illness analysis), and who were not previously infected ('booster' cohort). We randomly matched a 'no-booster' individual from those who received only two vaccine doses (by that same day), was not previously infected, and had the same characteristics (age group in five year window, gender, second vaccine dose week and demographic group: General Jewish, Arab, ultra-Orthodox). In order to be able to match all individuals in the 'booster' cohort, we conducted matching with replacement, so the same 'no-booster' individual could be assigned to multiple 'booster' individuals.

After matching was performed, we calculated the number of events (confirmed infection or severe COVID-19) occuring on the same calendar day in each of the two groups. An individual is considered severely ill at the date of first positive sample if the individual deteriorated to the corresponding condition within the study period. The ratio between the incidence of the outcomes in the 'booster' and 'no-booster' cohorts was used to estimate the marginal protection provided by the booster dose. We used non-parametric bootstrapping, with 200 bootstrap samples, followed by random matching, and reported the median ratio as the protection estimate and the 95% confidence intervals around it. Overall, out of 603,953

individuals for whom 12 days or more passed since their booster dose, 603,953 matched pairs were found.

For the first type of matching, our analysis yielded an estimate of 13.4-fold (95% CI [8.2-21.4]) for protection against confirmed infection. Due to the very small number of severe cases following the booster a reliable estimate of the protection versus severe illness using this approach was not possible.

For the second type of matching, our analysis yielded an estimate of 9.6-fold protection against confirmed infection (95% CI [8.1-11.4]) and 9.5-fold protection against severe illness (95% CI [5-19.6]). The overall agreement between the main and secondary analyses gives further reassurance that our results are robust to the employed statistical methodology.

Supplementary Figures

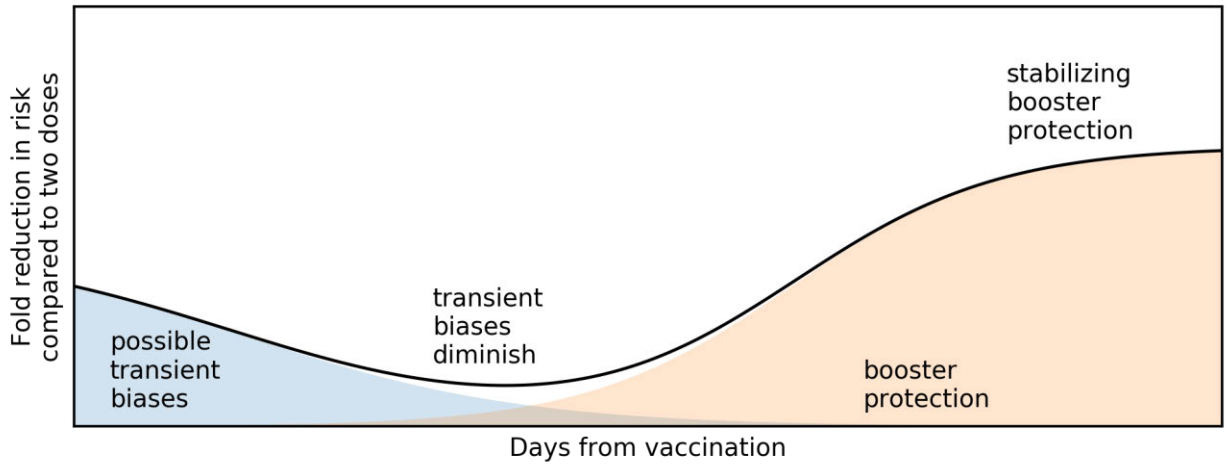

Figure S1. A conceptual schematic demonstrating the possible underlying dynamics of the results in Figure 2.

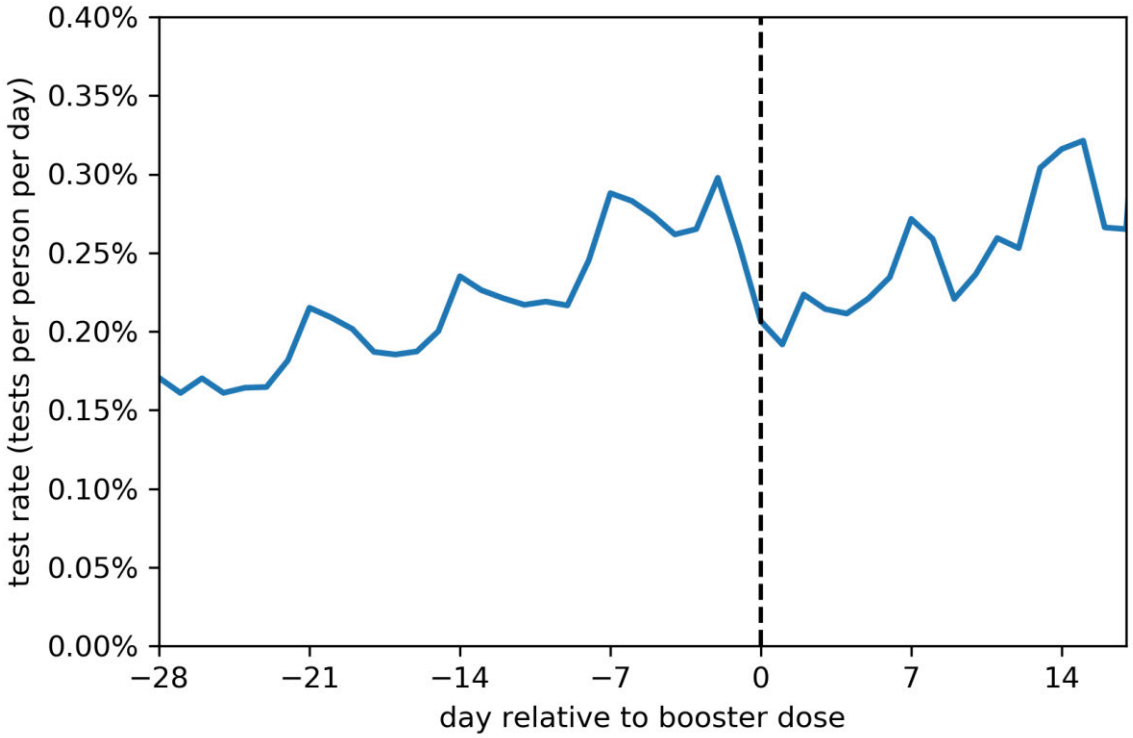

Figure S2. The daily rate of tests per person as a function of the time relative to the administration of the booster dose. A decrease in the rate of testing is observable just after the administration of the booster, likely reflecting transient behavioural changes in care-seeking behaviour or risk-avoidance.

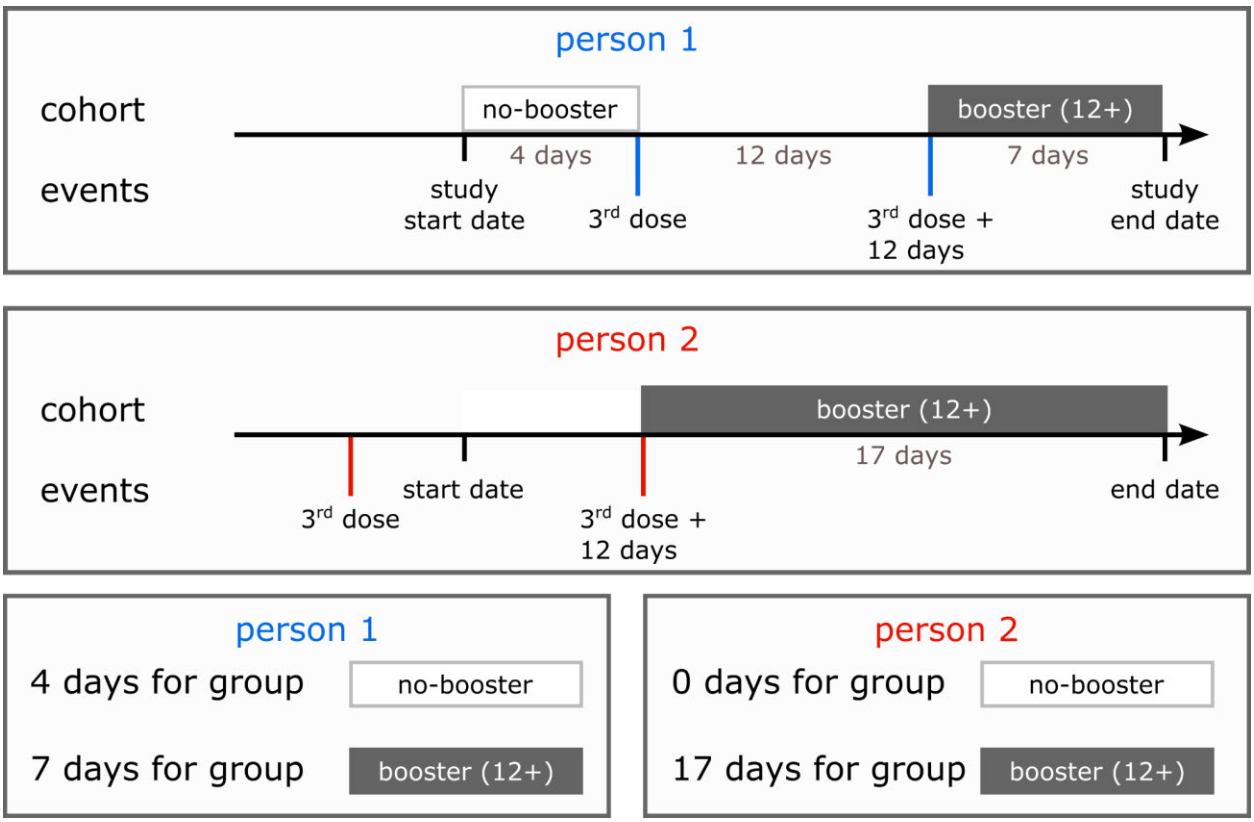

Figure S3. A schematic illustration of the allocation for the dynamic cohorts. We show two example timelines for two different individuals, and detail the cohort they contribute to at each point in time as well as the total days-at-risk for each person in each cohort.

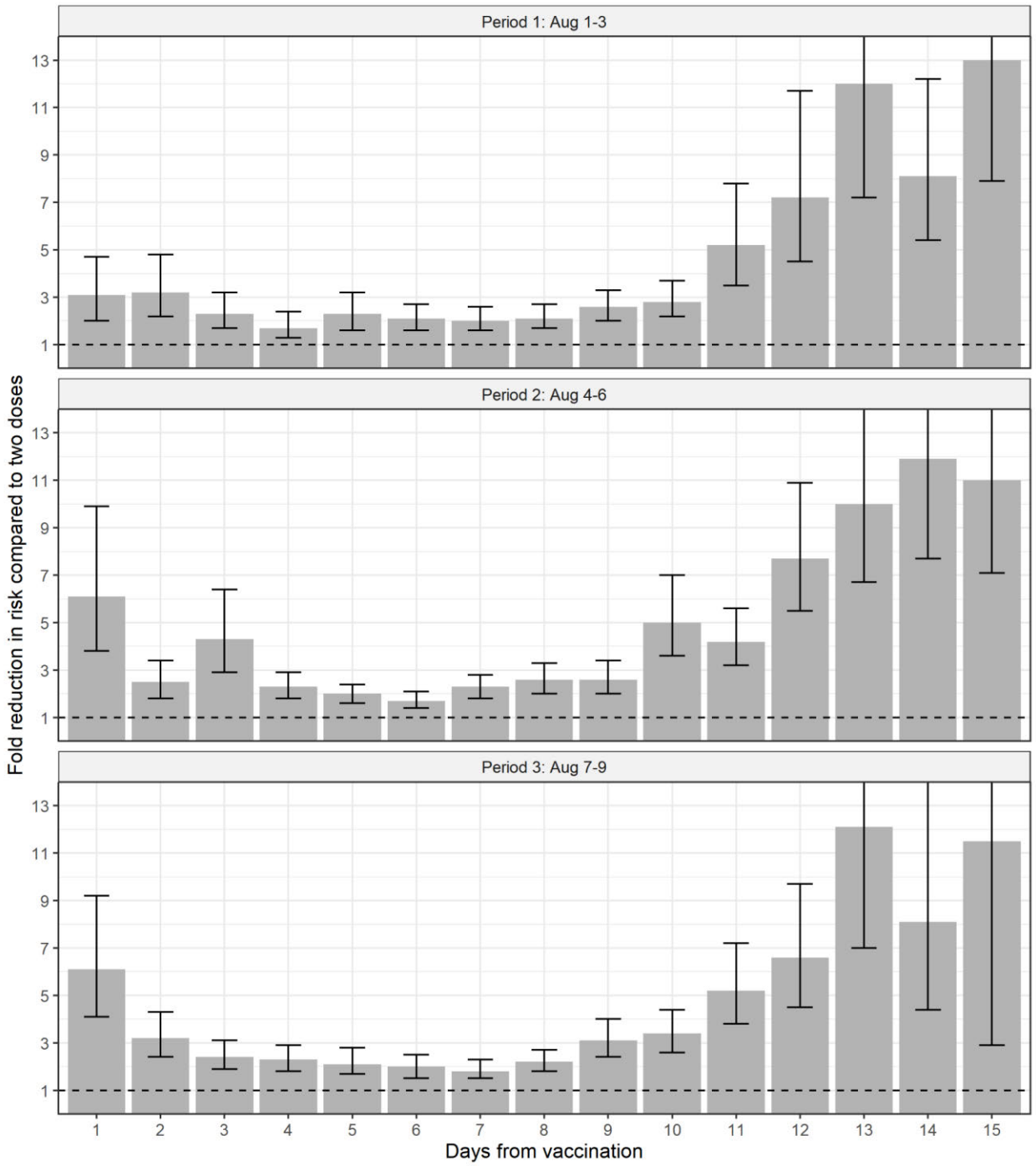

Figure S5. Sensitivity analysis across periods of booster vaccination for the booster protection against confirmed infection as a function of the number of days following the booster dose. Protection is given as a fold change in risk relative to people who received only two vaccine doses.

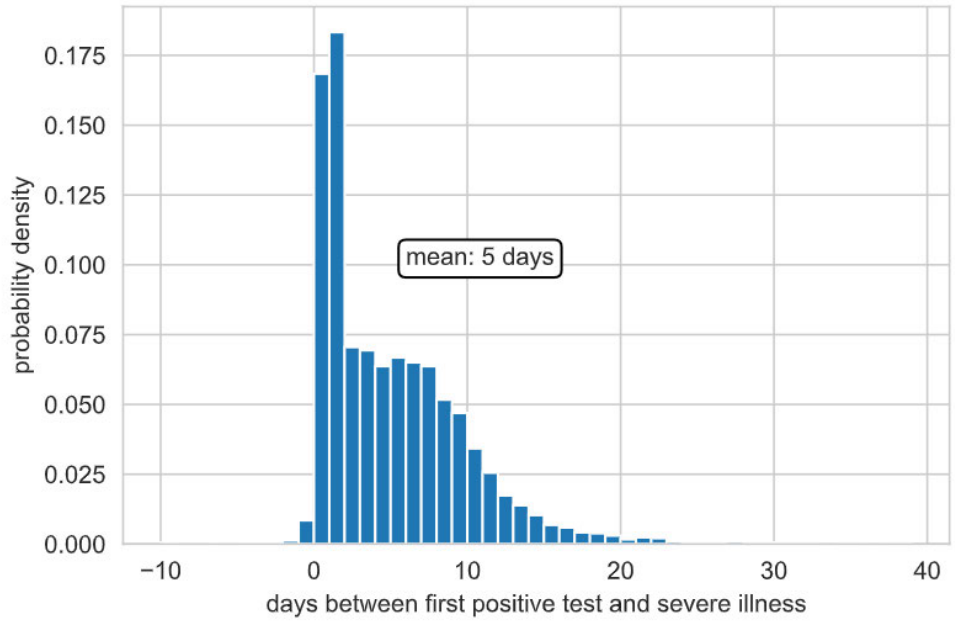

Figure S4. The distribution of time between first positive test and severe illness for confirmed cases between November 1st, 2020 and March 1st, 2021.

Table S1: Poisson regression results for confirmed SARS-CoV-2 infection.

term	estimate	std.error	statistic	p.value
(Intercept)	-6.96	0.06	-124.31	<0.001
age_category70-79	-0.11	0.04	-2.87	0.004
age_category80+	-0.12	0.05	-2.69	0.007
Gender = male	0.16	0.03	4.77	<0.001
date2021-08-11	-0.02	0.07	-0.22	0.830
date2021-08-12	0.17	0.07	2.48	0.013
date2021-08-13	-0.10	0.08	-1.31	0.191
date2021-08-14	-0.39	0.09	-4.57	<0.001
date2021-08-15	-0.14	0.08	-1.72	0.085
date2021-08-16	0.49	0.07	7.02	<0.001
date2021-08-17	0.19	0.08	2.43	0.015
date2021-08-18	0.33	0.08	4.36	<0.001
date2021-08-19	0.34	0.08	4.31	<0.001
date2021-08-20	0.24	0.08	2.96	0.003
date2021-08-21	-0.15	0.09	-1.69	0.092
date2021-08-22	-0.06	0.09	-0.63	0.531
vac_periodFeb 1-15	-0.19	0.04	-5.40	<0.001
vac_periodFeb 16-28	-0.37	0.06	-6.37	<0.001
Sector: Arab	-0.83	0.07	-11.41	<0.001
Sector: ultra Orthodox	0.30	0.07	4.51	<0.001
Cohort ‘booster’	-2.43	0.06	-38.18	<0.001

Table S2: Poisson regression results for severe COVID-19 disease.

term	estimate	std.error	statistic	p.value
(Intercept)	-10.94	0.23	-47.78	<0.001
age_category70-79	0.86	0.14	5.99	<0.001
age_category80+	1.79	0.13	13.26	<0.001
Gender = male	0.96	0.11	8.67	<0.001
date2021-08-11	0.24	0.26	0.94	0.349
date2021-08-12	0.42	0.25	1.66	0.097
date2021-08-13	0.32	0.27	1.22	0.224
date2021-08-14	0.11	0.28	0.40	0.69
date2021-08-15	0.74	0.25	2.97	0.003
date2021-08-16	0.44	0.27	1.62	0.106
date2021-08-17	0.77	0.26	3.00	0.003
date2021-08-18	0.48	0.28	1.69	0.091
date2021-08-19	0.56	0.28	1.97	0.049
date2021-08-20	0.66	0.28	2.37	0.018
date2021-08-21	0.69	0.28	2.51	0.012
date2021-08-22	0.95	0.26	3.62	<0.001
vac_periodFeb 1-15	-0.31	0.11	-2.78	0.006
vac_periodFeb 16-28	-0.84	0.22	-3.77	<0.001
Sector: Arab	-0.21	0.19	-1.10	0.273
Sector: ultra Orthodox	-0.07	0.26	-0.27	0.790
Cohort ‘booster’	-2.74	0.20	-13.77	<0.001

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Sent: Sat, 28 Aug 2021 12:59:53 -0500
To: Brooks, John T. (CDC/DDID/NCHHSTP/DHP);Murthy, Vivek (HHS/OASH);Collins, Francis (NIH/OD) [E];Walensky, Rochelle (CDC/OD);Eric Lander
Cc: Beckman, Adam (HHS/OASH)
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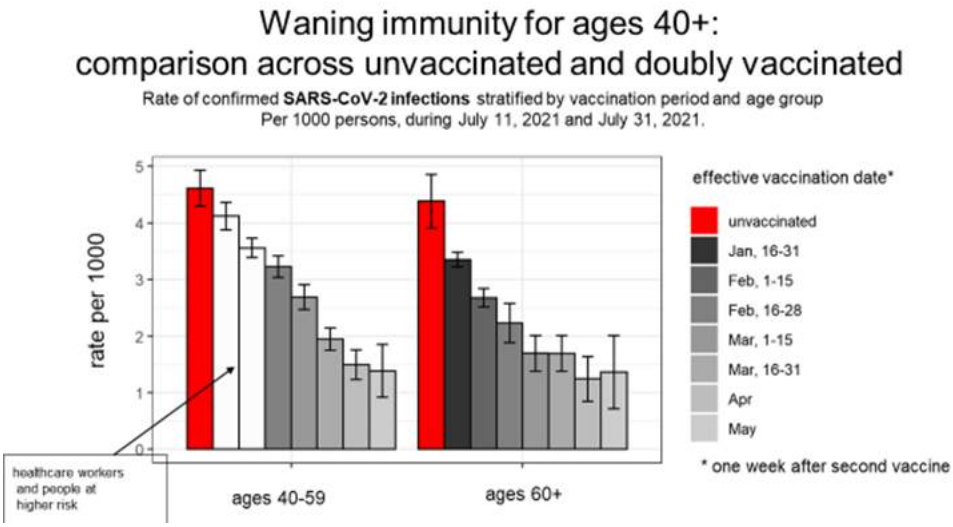

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Dean:

Please see John Brooks's concern about the data in the Israeli paper. Is there any validity to his concern? The data are really rather impressive and it would be important to determine the strength of their validity. Please take a look at this paper and help us determine if it is in fact a strong study. I hate to impose upon you about this , but this is really an important issue . Many thanks.

Best regards,

Tony

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Terrific,

Our vaccine effectiveness experts in consultation with Marc Lipsitch at Harvard opined that overall it holds water. A valid finding in their opinion.

Cheers,

-john

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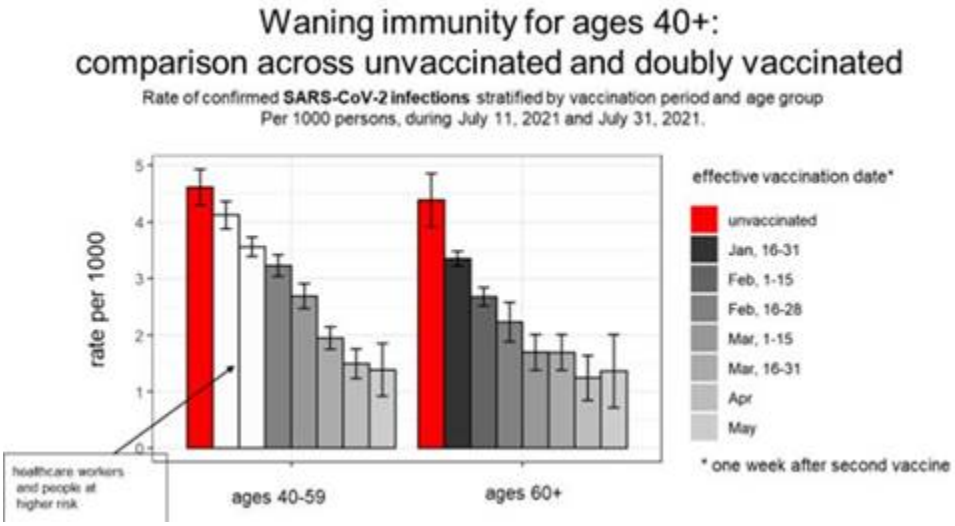

I think the presentation we'll see Monday will

From: Fauci, Anthony (NIH/NIAID) [E] (b) (6)>
Sent: Saturday, August 28, 2021 1:58 PM
To: Follmann, Dean (NIH/NIAID) [E] (b) (6)>; Lane, Cliff (NIH/NIAID) [E] (b) (6)>
Cc: Collins, Francis (NIH/OD) [E] (b) (6)
Subject: FW: Post infection protection vs vaccine immunity

Dean:

Please see John Brooks's concern about the data in the Israeli paper. Is there any validity to his concern? The data are really rather impressive and it would be important to determine the strength of their validity. Please take a look at this paper and help us determine if it is in fact a strong study. I hate to impose upon you about this , but this is really an important issue . Many thanks.

Best regards,

Tony

Anthony S. Fauci, MD
Director
National Institute of Allergy and Infectious Diseases
Building 31, Room 7A-03
31 Center Drive, MSC 2520
National Institutes of Health
Bethesda, MD 20892-2520
Phone: (b) (6)
FAX: (301) 496-4409
E-mail: (b) (6)

From: Brooks, John T. (CDC/DDID/NCHHSTP/DHP) <zud4@cdc.gov>
Sent: Friday, August 27, 2021 5:14 PM
To: Fauci, Anthony (NIH/NIAID) [E] (b) (6); Murthy, Vivek (HHS/OASH) <Vivek.Murthy@hhs.gov>; Collins, Francis (NIH/OD) [E] (b) (6)>; Walensky, Rochelle (CDC/OD) <aux7@cdc.gov>; Eric Lander (b) (6)
Cc: Beckman, Adam (HHS/OASH) <Adam.Beckman@hhs.gov>
Subject: RE: Post infection protection vs vaccine immunity

I also received this paper today from Israeli colleagues (attached) in which they present evidence that their booster program has restored the loss in vaccine effectiveness that had been observed among persons fully vaccinated with the 2-dose Pfizer vaccine series in whom VE against infection was decreasing.

They used two basic approaches to analyze these retrospective data: a series of Poisson regressions and a case-control matching method. All analyses point in the same direction and the results seem impressive.

I am a having trouble wrapping my head around how they detected such a potent effect of an intervention started in late July and delivered to about 3 M Israelis in just a few weeks. It just seemed mighty fast, but perhaps in this case the anamnestic response primed by prior vaccination kicked in hard and fast.

As I digest this one (with the sage input of smarter colleagues here whose career work is VE), I wanted to ensure all were aware the paper is out there.

-john

John T. Brooks, MD
Chief Medical Officer, CDC COVID-19 Response
Email: zud4@cdc.gov
Apologies for errors in my messages that may be due to my need to dictate.

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Sent: Friday, August 27, 2021 2:37 PM
To: Murthy, Vivek (HHS/OASH) <Vivek.Murthy@hhs.gov>; Collins, Francis (NIH/OD) [E] (b) (6); Walensky, Rochelle (CDC/OD) <aux7@cdc.gov>; Eric Lander (b) (6) Brooks, John T. (CDC/DDID/NCHHSTP/DHP) <zud4@cdc.gov>
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The data as reported in the news article look rather impressive despite the caveat that it is a retrospective study and the testing was voluntary. I have not seen the details of the actual data, but I would imagine that it is more complicated than we think. It very well may be that people who have had an asymptomatic or minimally symptomatic infection (upper airway only) will not have a greater post-infection protection against subsequent infection then those who get fully vaccinated. However, it is conceivable and possibly likely that those who have had a serious systemic infection develop a high level of immunity that even surpasses that of full vaccination. I would like to see if they broke the data on the infected people down into those two groups.

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https://www.sciencemag.org/news/2021/08/having-sars-cov-2-once-confers-much-greater-immunity-vaccine-no-infection-parties

Having SARS-CoV-2 once confers much greater immunity than a vaccine—but no infection parties, please | Science | AAAS

Having SARS-CoV-2 once confers much greater immunity than a vaccine—but no infection parties, please. By Meredith Wadman Aug. 26, 2021 , 8:02 PM. The natural immune protection that develops

...

www.sciencemag.org

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Sent: Mon, 30 Aug 2021 15:17:38 -0500
To: Mascola, John (NIH/VRC) [E]
Cc: Fauci, Anthony (NIH/NIAID) [E];Lane, Cliff (NIH/NIAID) [E];Tabak, Lawrence (NIH/OD) [E]
Subject: FW: Post infection protection vs vaccine immunity

Hey John,

I'd be really curious to know your response to this intriguing summary from John Brooks.

I'm still wondering how much of the difference in immune protection between natural infection and vaccine is due to delta.

Tx, Francis

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Cc: Beckman, Adam (HHS/OASH) <Adam.Beckman@hhs.gov>
Subject: RE: Post infection protection vs vaccine immunity

Hi all,

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But it's a scan of what's coming out that I hope may help guide how everyone is thinking about things. Not anything definitive but data I think this group would merit knowing about.

First, I too think (and so do my colleagues) that the Gazit et al. paper suggesting natural infection is more immunizing that vaccine is well-done: something is going on here. Likewise, so too is the Bar-On et al. paper demonstrating rather rapid restoration of protection by vaccination given as a third dose of BNT162b2 (Pfizer) to people who completed the two-dose series of the same vaccine > 5 months prior.

So what do we know first about the trajectory of the immune response to *infection vs. immunization*. I think a paper by Israel et al. (who is incidentally from Israel and Israeli…) is illustrative. They compared anti-SARS-CoV-2 IgG values in ~2,500 BNT162b2 vaccinees (following from data of second vaccination) and ~4,300 persons recovered from infection (convalescents from data of confirmed PCR positive specimen). Robust numbers and solid analysis, in my opinion. Note that the convalescent were younger by about 15 years on average than vaccinated (42 ± 16 years vs. 56 ± 16 years, in case you are concerned about immunosenescence); their analysis strived t account for this difference.

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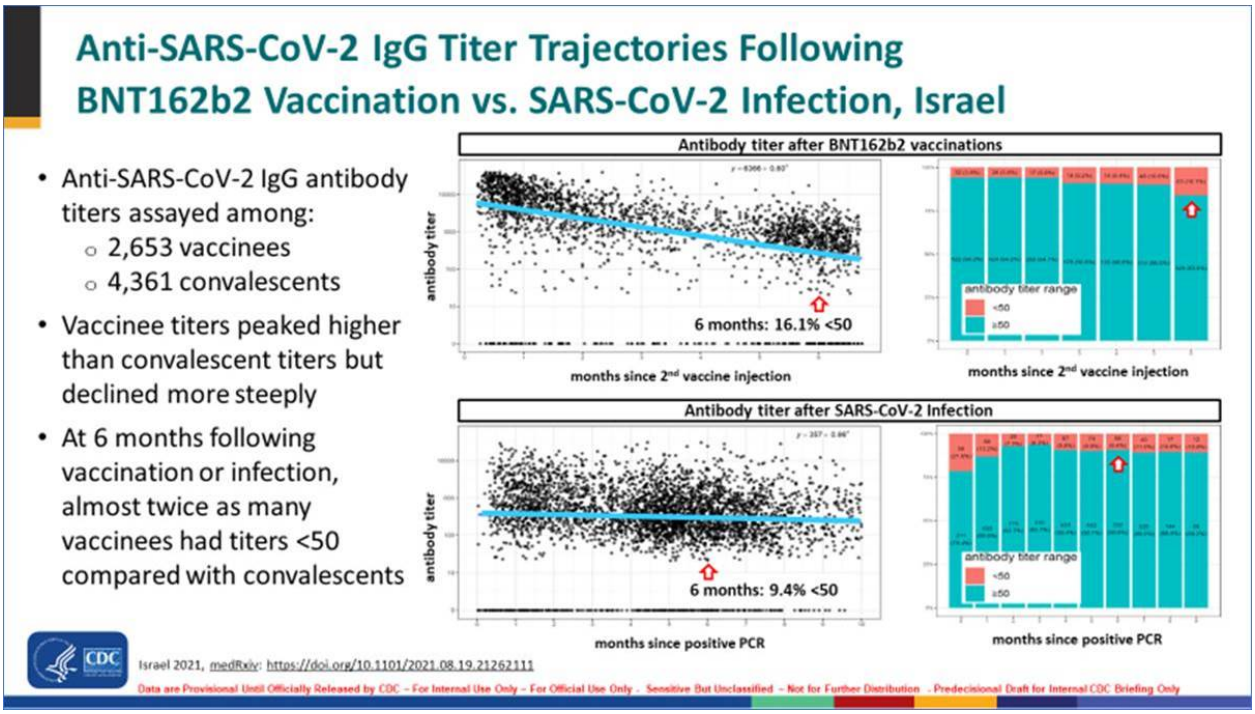

The take-away here to me is that although vaccine-induced antibody titers (BNT162b2) peak higher, they decline more swiftly than infection-induced titers and begin falling below infection-induced antibody titers after 6 months. The authors note that "In vaccinated subjects, antibody titers decreased by up to 40% each subsequent month while in convalescents they decreased by less than 5% per month." Unfortunately, convalescent titers were not stratified by COVID-19 illness severity; however, the authors note (using standard multivariable logistic regression) that among convalescents higher antibody titers were associated with

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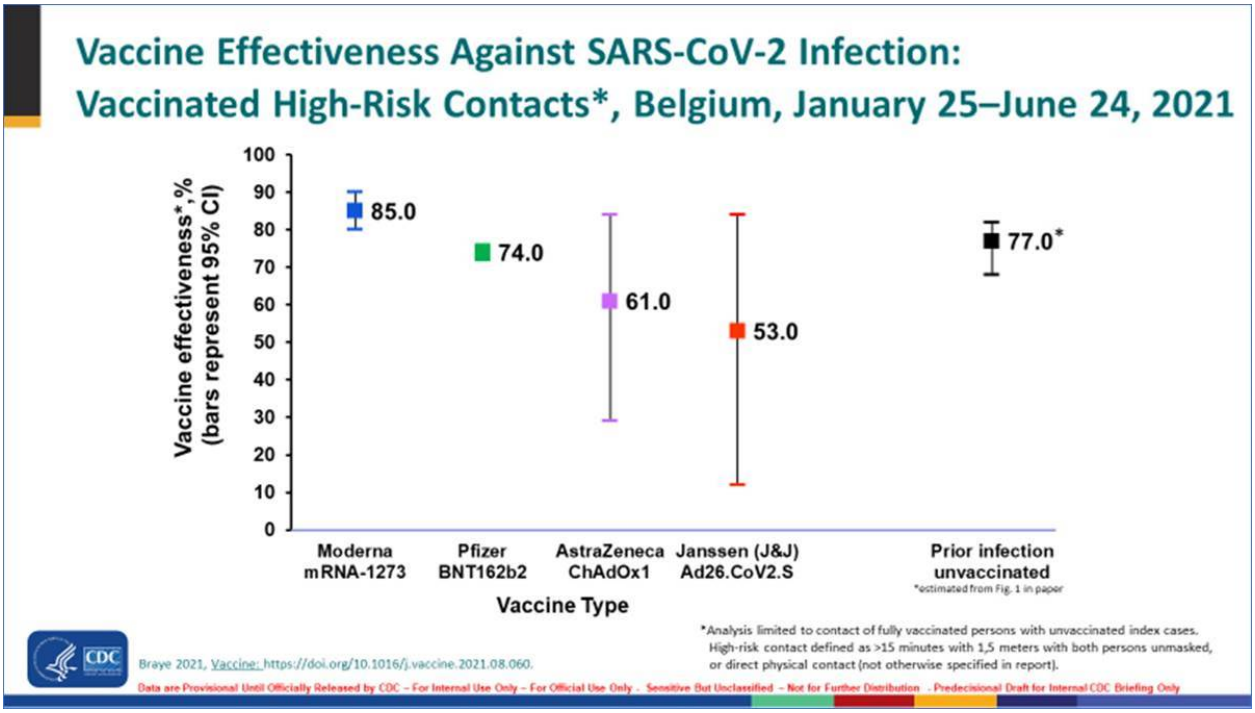
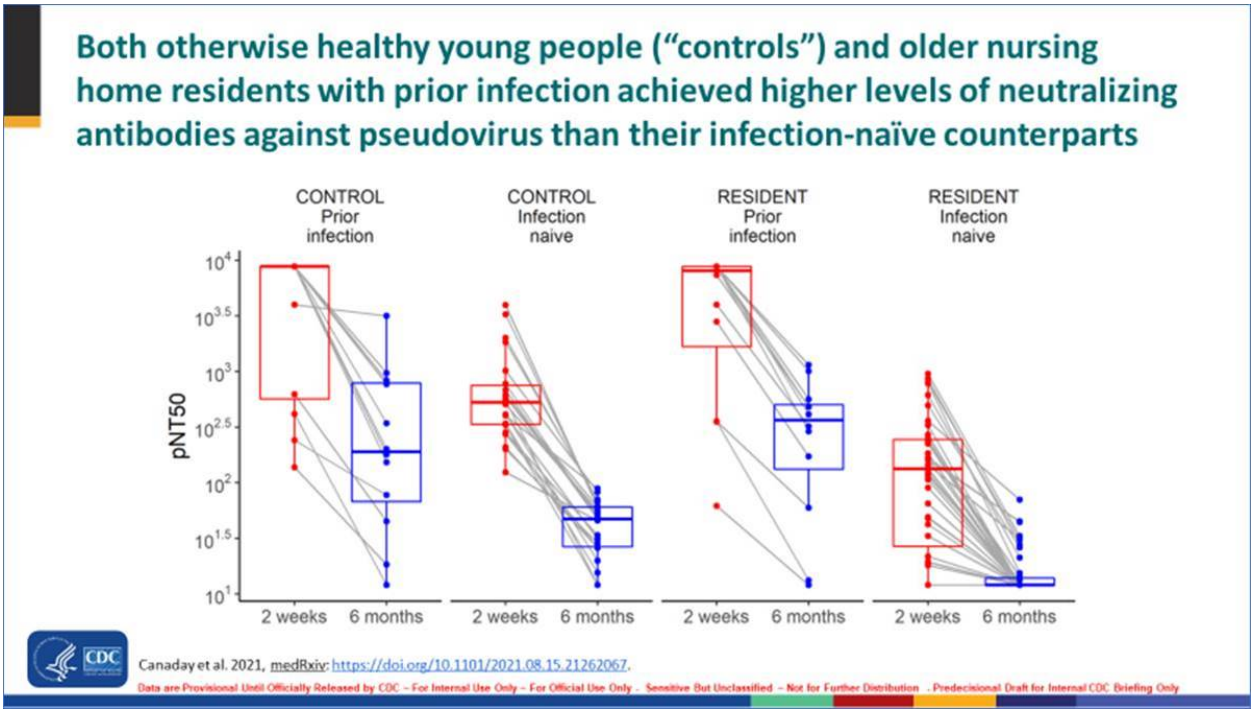
Another study, this one from Belgium authored by Braye et al., assessed vaccine effectives against infection among high-risk *fully vaccinated contacts* of *unvaccinated index patients* as well as among persons recovered from COVID-19 (*convalescent) for >90 days* who were contact of unvaccinated index patients. Again, robust numbers of high-risk contacts (HRCs) in the mRNA vaccine arms (~7,900) and the convalescent arm (~700), and a solid analytic approach. Note that their data are unclear on the precise numbers of contact events that involved unvaccinated index cases but the majority of index cases (97%) were unvaccinated. The data do not take into account time since vaccination/illness and are a conglomeration of contact tracing data from January-June 2021. There data show that the VE for prior infection (in black, I had the infer the data to make this figure since the paper doesn't provide the actual values) was about the same at the VE for mRNA vaccination (in blue and green). The adenovirus-vectored vaccine data are also interesting but fewer numbers (introduced near the middle of the study period in Belgium); this is where analysis limited to time since vaccination/infection would be helpful.

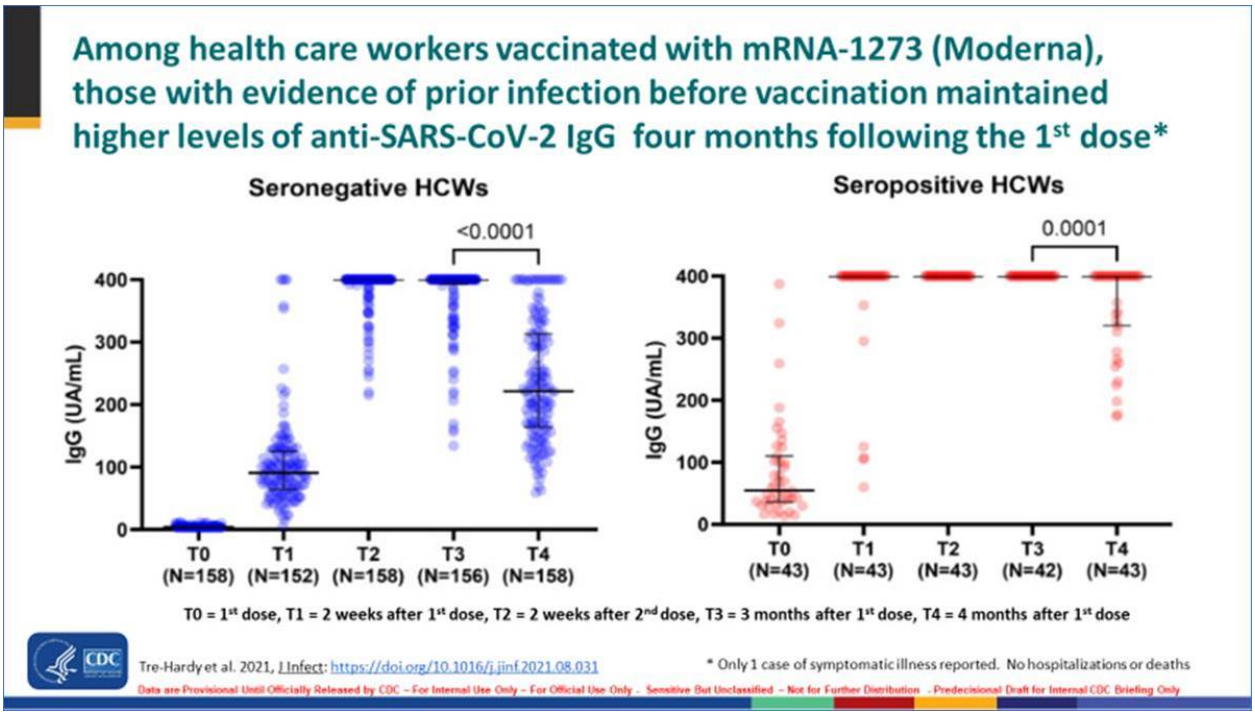


OK, so it seems now from at least three very different analyses of different data that at least mRNA vaccine effectiveness is about as good as infection-induced immunity but that vaccine-induced immunity wanes over time (especially that induced by BNT162b2) whereas infection-induced may be more durable up to at least the 4-6 month mark (like the Gazit et al. paper). *Note that we may not have seen this before because most investigators are looking at vaccinated people and not including and comparing data from persons recovered from infection.*

The good news here is that boosters look like a solution, not just based on Bar-On et al. paper but also the following data.

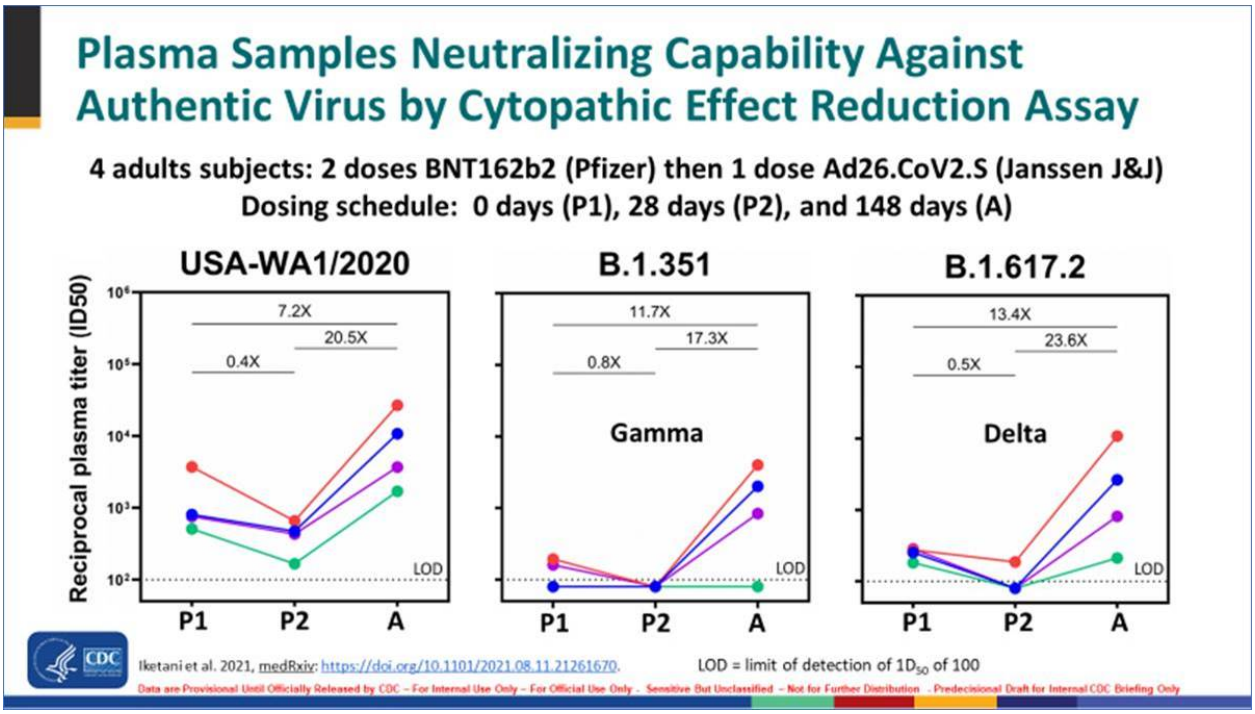
At least two studies have now shown that vaccination after infection produces a larger and more durable antibody response (Canady et al. and Tre-Hardy et al., slides below). So three-stimulus "booster-like" scenario.





And when you look at Iketani et al., giving a true booster dose of vaccine (2 doses Pfizer BNT162b2 followed by 1 dose Janssen J&J), that "boost" substantially increased neutralizing antibody levels (measured as serum neutralizing capacity against real SARS-CoV-2 virus) to both "ancestral" variants and two key variants of

concern, Gamma (B.1.351) and Beta (B.1.617.2). *Note: these data are derived from FOUR SUBJECTS only.*



So….I'm not sure *exactly* what is going on here *and like so much with this virus it's not at all what I would have expected*, but with the data we have before us I see this:

- Both vaccine and infection are immunizing.
- We only have epidemiologic data on both forms of immunity out to about 6 months
- Vaccine effectiveness from 2-dose mRNA vaccine may wane earlier than infection-induced immunity, which may persist longer and in this way may also provide better protection, at least up to about 6 months or so.
- However, we want to avoid infection-induced immunity; comes at too great a cost and vaccination is safe.
- We have epidemiologic data that three episodes of immune stimulation (infection followed by mRNA vaccination) as well as a booster vaccine dose (2 dose mRNA vaccination followed by single dose adenovirus-vectored vaccine) increase markers of immunity (serum neutralizing capacity and antibody response) and per Bar-On et al. also appears to reverse decline in vaccine effectiveness, at least in the short term.

- May this will be a three-dose vaccine after all…

Therefore, we should offer booster doses.

To folks calling out that "convalescents" do not need vaccination I would respond:

1. We only have epidemiologic data on both forms of immunity out to about 6 months, and we don't know how much longer and how well infection-induced immunity may protect (i.e., how durable that immunity is).
2. We have epidemiologic data (Kentucky MMWR) that vaccination after recovery substantially reduces risk of reinfection by (risk of reinfection if *unvaccinated* was odds ratio 2.34, 95% CI 1.58-3.47). The Gazit et al. observed a similar phenomenon but it was non-significant (risk of reinfection *if vaccinated* odd ratio 0.68, 95% CI 0.38-1.12, p-0.188). BTW inverse of 0.68 is 1.47, and inverse of 2.34 is 0.43 😉

If you see any errors here, or in the slide images, please let me know. I welcome corrections!

Cheers,

-john

John T. Brooks, MD
Chief Medical Officer, CDC COVID-19 Response
Email: zud4@cdc.gov
Apologies for errors in my messages that may be due to my need to dictate.

From: Collins, Francis (NIH/OD) [E] (b) (6)>
Sent: Monday, August 30, 2021 10:33 AM
To: Fauci, Anthony (NIH/NIAID) [E] (b) (6); Murthy, Vivek (HHS/OASH) <Vivek.Murthy@hhs.gov>; Walensky, Rochelle (CDC/OD) <aux7@cdc.gov>; Eric Lander (b) (6)>; Brooks, John T. (CDC/DDID/NCHHSTP/DHP) <zud4@cdc.gov>
Cc: Beckman, Adam (HHS/OASH) <Adam.Beckman@hhs.gov>
Subject: RE: Post infection protection vs vaccine immunity

Hi Vivek et al.,

Thanks for pointing out this somewhat puzzling publication. The Israeli preprint https://www.medrxiv.org/content/10.1101/2021.08.24.21262415v1.full.pdf does seem to describe a well-designed (albeit retrospective) study. Their cases of prior natural infection were just all comers with positive PCR tests, they didn't break this down by severity. But the magnitude of the difference between protection from natural infection and vaccination is significantly large (13x) that it's hard to imagine that the first group were all people with really serious prior systemic infection. On the other hand, one has to wonder whether vaccinated individuals were more likely to seek diagnosis in the presence of mild or absent symptoms, identifying them as breakthrough cases – whereas those with prior infection may have been less likely to seek testing.

The CDC Kentucky MMWR study https://www.cdc.gov/mmwr/volumes/70/wr/mm7032e1.htm didn't ask quite the same question – that study was aimed at determining whether vaccination after natural infection adds additional protection. The answer is clearly yes (2.34x), and the Israeli study showed that too.

Does CDC have a ready meta-analysis of all of the studies that have compared the immunity from natural infection to vaccination? Most of us have been saying up until now that vaccines are actually better for providing immunity – what does the overall synthesis of the data now say?

Francis

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Sent: Friday, August 27, 2021 2:37 PM
To: Murthy, Vivek (HHS/OASH) <Vivek.Murthy@hhs.gov>; Collins, Francis (NIH/OD) [E] (b) (6); Walensky, Rochelle (CDC/OD) <aux7@cdc.gov>; Eric Lander (b) (6)>; Brooks, John T. (CDC/DDID/NCHHSTP/DHP) <zud4@CDC.GOV>
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Subject: RE: Post infection protection vs vaccine immunity

Francis,

This is a really solid summary. Adding Alan Embry here as we are trying to follow this together. We would agree with John's analysis.

Also, We had a call with Israeli MOH officials today to hear more about their data – and the sense from their team is that vaccine efficacy clearly wanes with time, including against severe disease. They can't fully disentangle Delta from waning over time, but they think the time factor is dominant, and that Delta may further exacerbate. Though interesting, there was some disagreement on their own team – so I think its fair to say we don't know yet.
Other data we are seeing support waning levels of protection – but again, hard to disentangle time vs Delta.

Either way – its seems that the case for boosting is getting stronger. The Israeli MOH is going to recommend boosting all age groups. They are currently boosting older and more vulnerable.

John

From: Collins, Francis (NIH/OD) [E] (b) (6)
Sent: Monday, August 30, 2021 4:18 PM
To: Mascola, John (NIH/VRC) [E] (b) (6) v>
Cc: Fauci, Anthony (NIH/NIAID) [E] (b) (6); Lane, Cliff (NIH/NIAID) [E] (b) (6) Tabak, Lawrence (NIH/OD) [E] (b) (6)>
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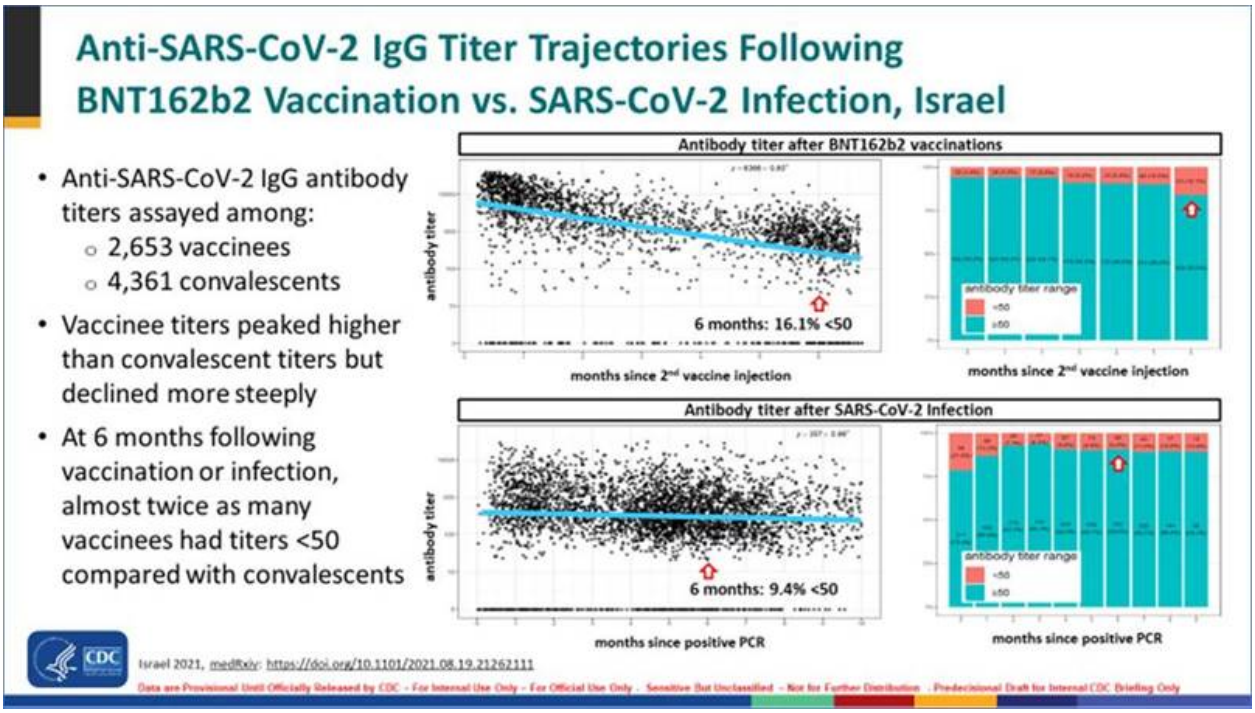

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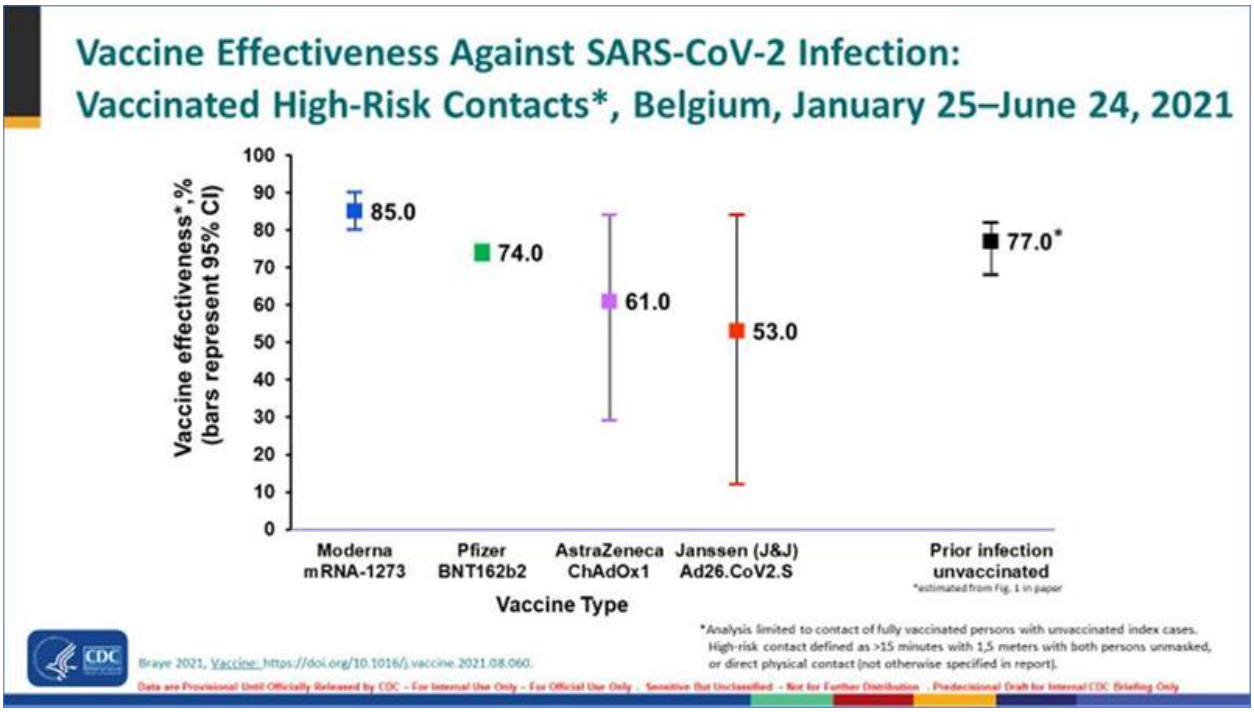

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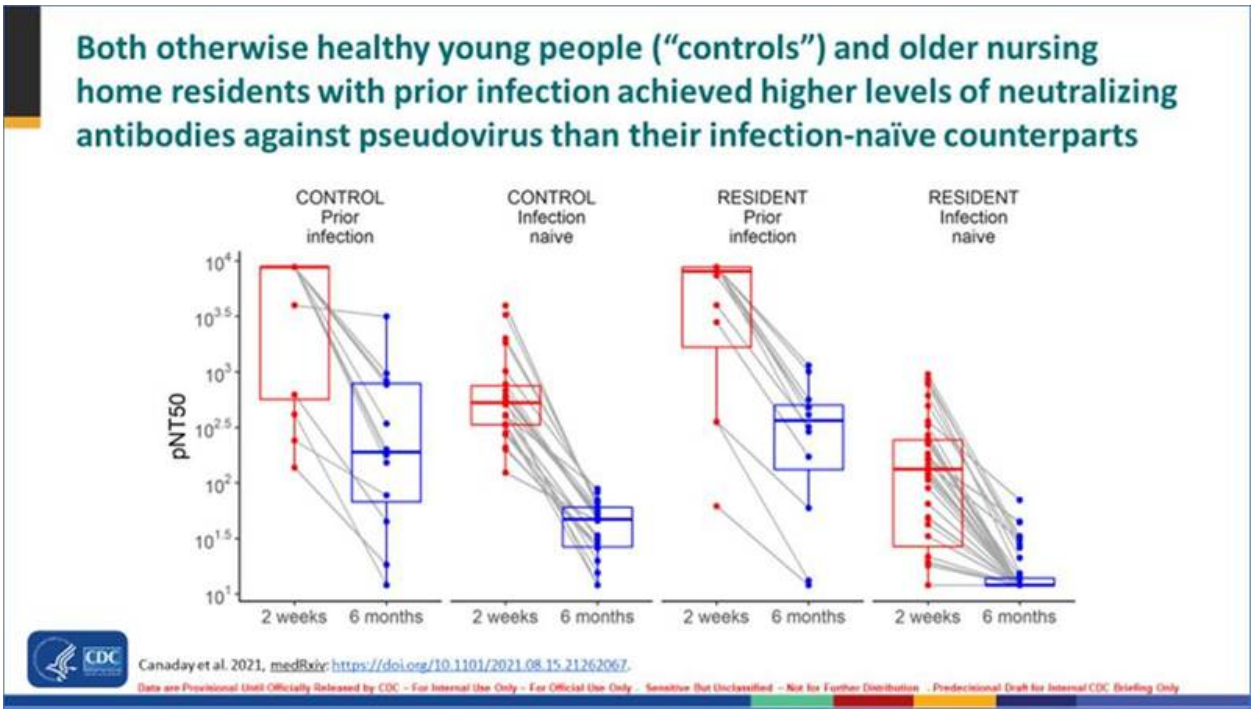

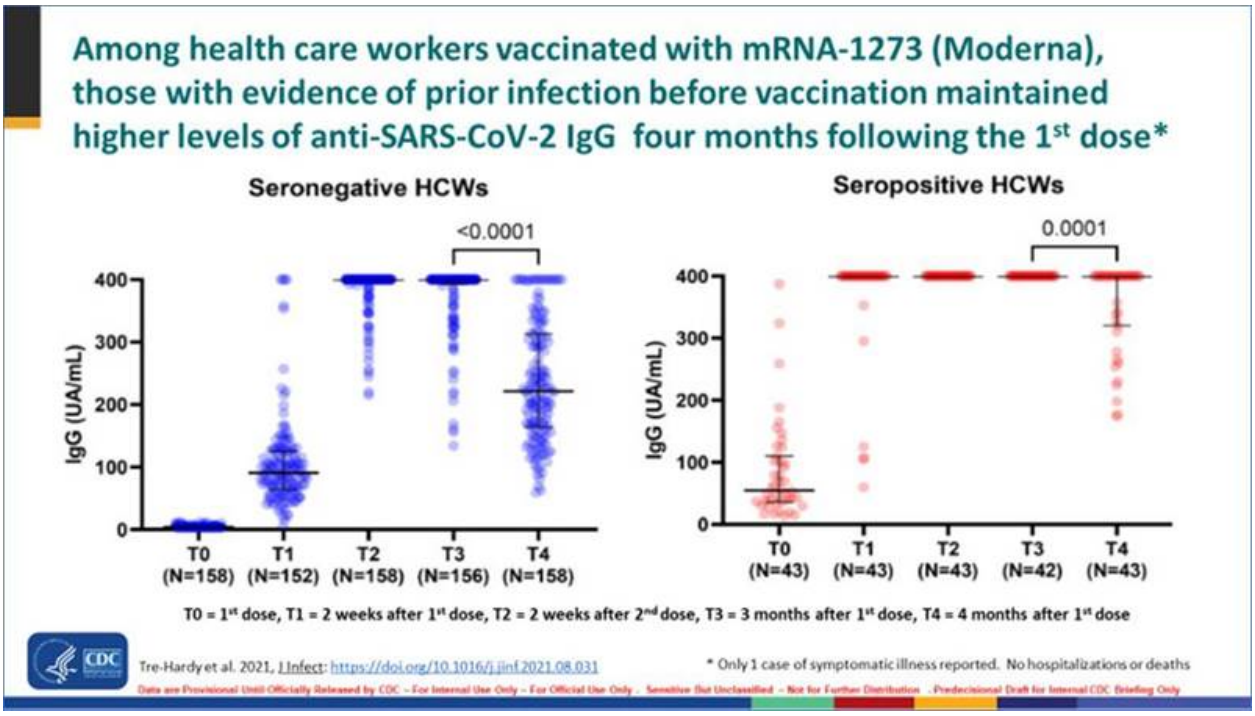

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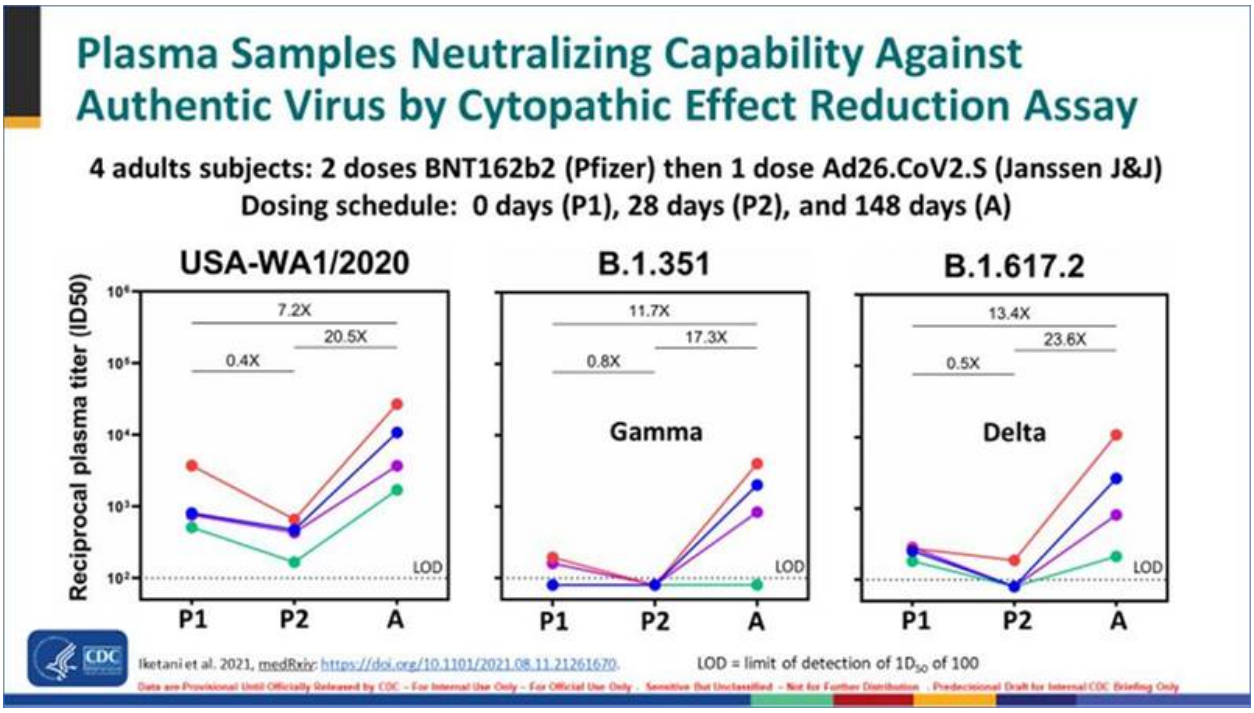

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Cc: Beckman, Adam (HHS/OASH)
Subject: RE: Post infection protection vs vaccine immunity

John:

Many thanks for providing this thorough analysis of the immunity landscape. I appreciate very much the effort that you put into synthesizing all of this important information.

Best regards,

Tony

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Hi all,

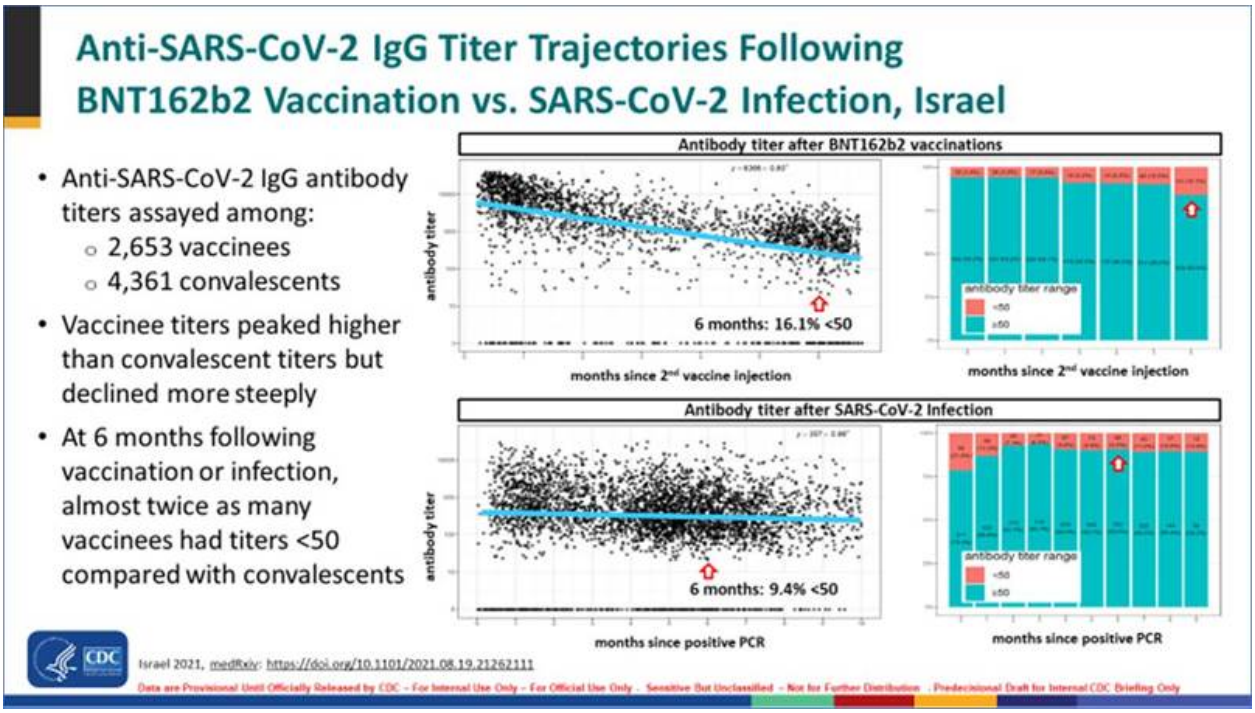
Over the weekend I tried to pull together what we know from some select papers among the cavalcade of publications coming out in the realm of infection-induced vs. vaccine-induced immunity. This is not a meta-analysis, and I'm not sure we have enough data of the same type yet to embark on a meta-analysis.

But it's a scan of what's coming out that I hope may help guide how everyone is thinking about things. Not anything definitive but data I think this group would merit knowing about.

First, I too think (and so do my colleagues) that the Gazit et al. paper suggesting natural infection is more immunizing that vaccine is well-done: something is going on here. Likewise, so too is the Bar-On et al. paper demonstrating rather rapid restoration of protection by vaccination given as a third dose of BNT162b2 (Pfizer) to people who completed the two-dose series of the same vaccine > 5 months prior.

So what do we know first about the trajectory of the immune response to *infection vs. immunization*. I think a paper by Israel et al. (who is incidentally from Israel and Israeli…) is illustrative. They compared anti-SARS-CoV-2 IgG values in ~2,500 BNT162b2 vaccinees (following from data of second vaccination) and ~4,300 persons recovered from infection (convalescents from data of confirmed PCR positive specimen). Robust numbers and solid analysis, in my opinion. Note that the convalescent were younger by about 15 years on average than vaccinated (42 $\pm$ 16 years vs. 56 $\pm$ 16 years, in case you are concerned about immunosenescence); their analysis strived t account for this difference.

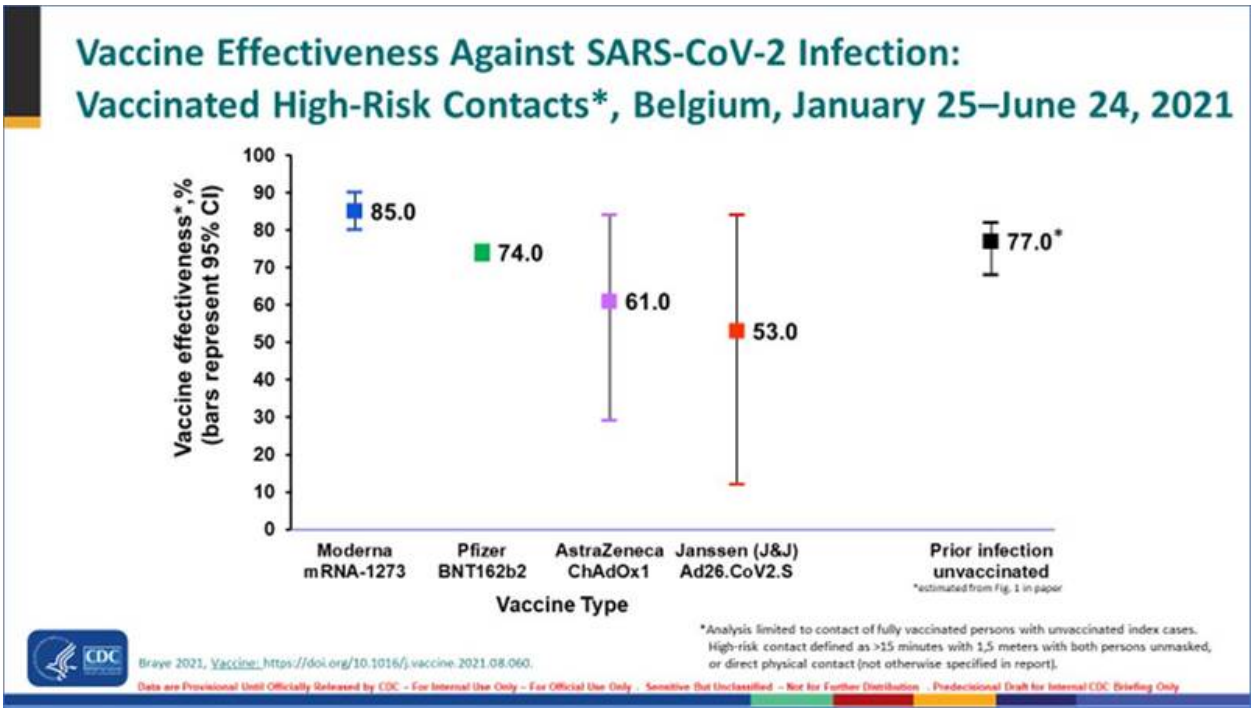
The figures from the paper are shown below.



The take-away here to me is that although vaccine-induced antibody titers (BNT162b2) peak higher, they decline more swiftly than infection-induced titers and begin falling below infection-induced antibody titers after 6 months. The authors note that "In vaccinated subjects, antibody titers decreased by up to 40% each subsequent month while in convalescents they decreased by less than 5% per month." Unfortunately, convalescent titers were not stratified by COVID-19 illness severity; however, the authors note (using standard multivariable logistic regression) that among convalescents higher antibody titers were associated with symptomatic illness, hospitalization, and having at least one risk factors for severe illness (e.g., older age, diabetes, obesity, chronic renal disease, hypertension). Still, I would really like to see data from people who had very mild illness or who were asymptomatically infected.

Another study, this one from Belgium authored by Braye et al., assessed vaccine effectives against infection among high-risk *fully vaccinated contacts* of *unvaccinated index patients* as well as among persons recovered from COVID-19 (*convalescent) for >90 days* who were contact of unvaccinated index patients. Again, robust numbers of high-risk contacts (HRCs) in the mRNA vaccine arms (~7,900) and the convalescent arm (~700), and a solid analytic approach. Note that their data are unclear on the precise numbers of contact events that involved unvaccinated index cases but the majority of index cases (97%) were

unvaccinated. The data do not take into account time since vaccination/illness and are a conglomeration of contact tracing data from January-June 2021. There data show that the VE for prior infection (in black, I had the infer the data to make this figure since the paper doesn't provide the actual values) was about the same at the VE for mRNA vaccination (in blue and green). The adenovirus-vectored vaccine data are also interesting but fewer numbers (introduced near the middle of the study period in Belgium); this is where analysis limited to time since vaccination/infection would be helpful.



OK, so it seems now from at least three very different analyses of different data that at least mRNA vaccine effectiveness is about as good as infection-induced immunity but that vaccine-induced immunity wanes over time (especially that induced by BNT162b2) whereas infection-induced may be more durable up to at least the 4-6 month mark (like the Gazit et al. paper). *Note that we may not have seen this before because most investigators are looking at vaccinated people and not including and comparing data from persons recovered from infection.*

The good news here is that boosters look like a solution, not just based on Bar-On et al. paper but also the following data.

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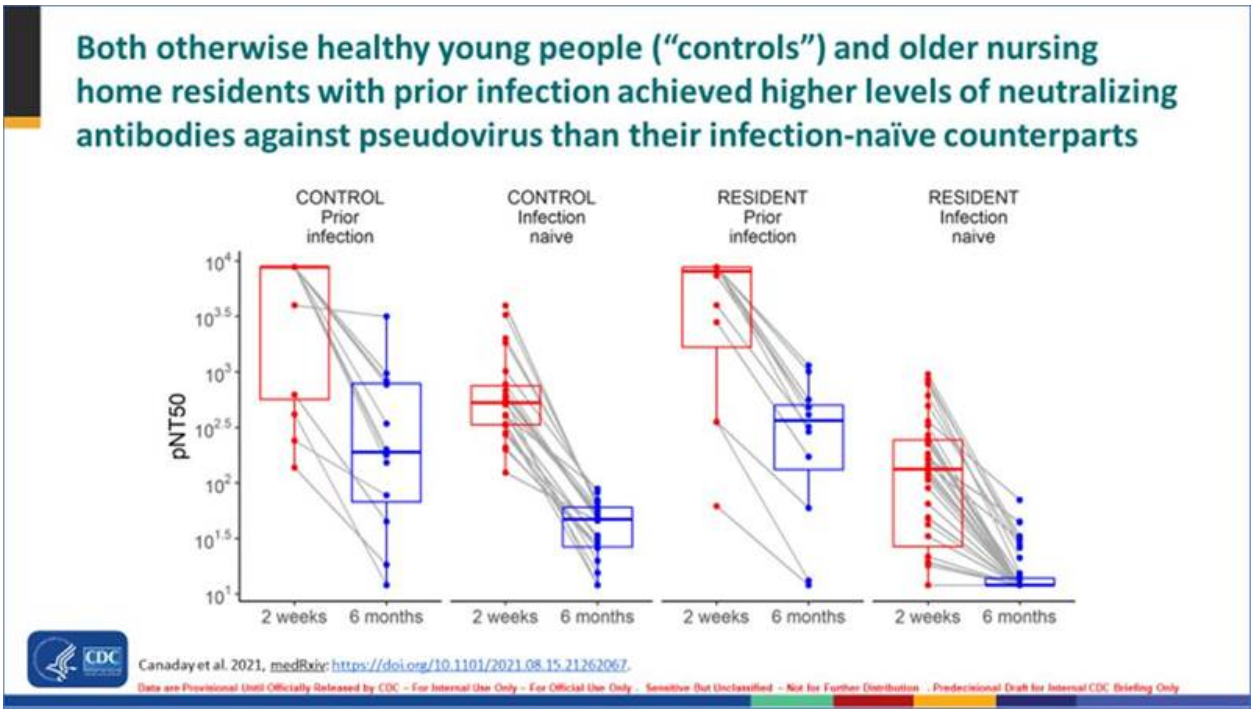

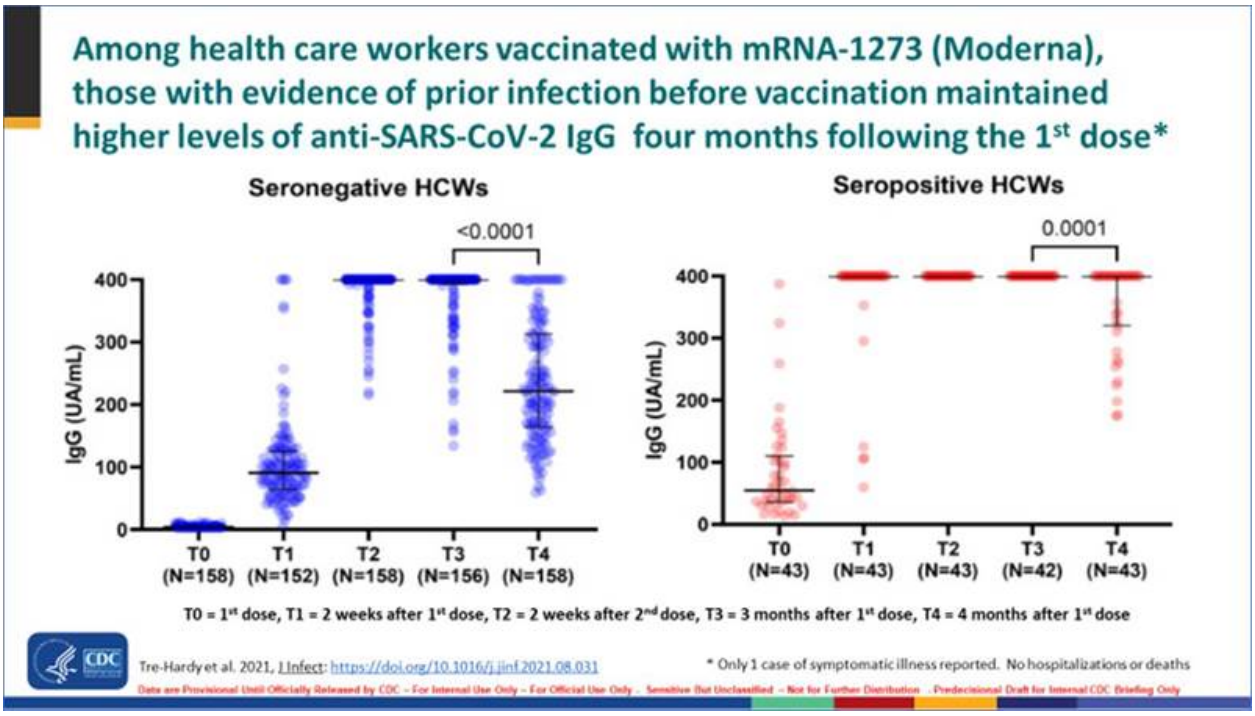

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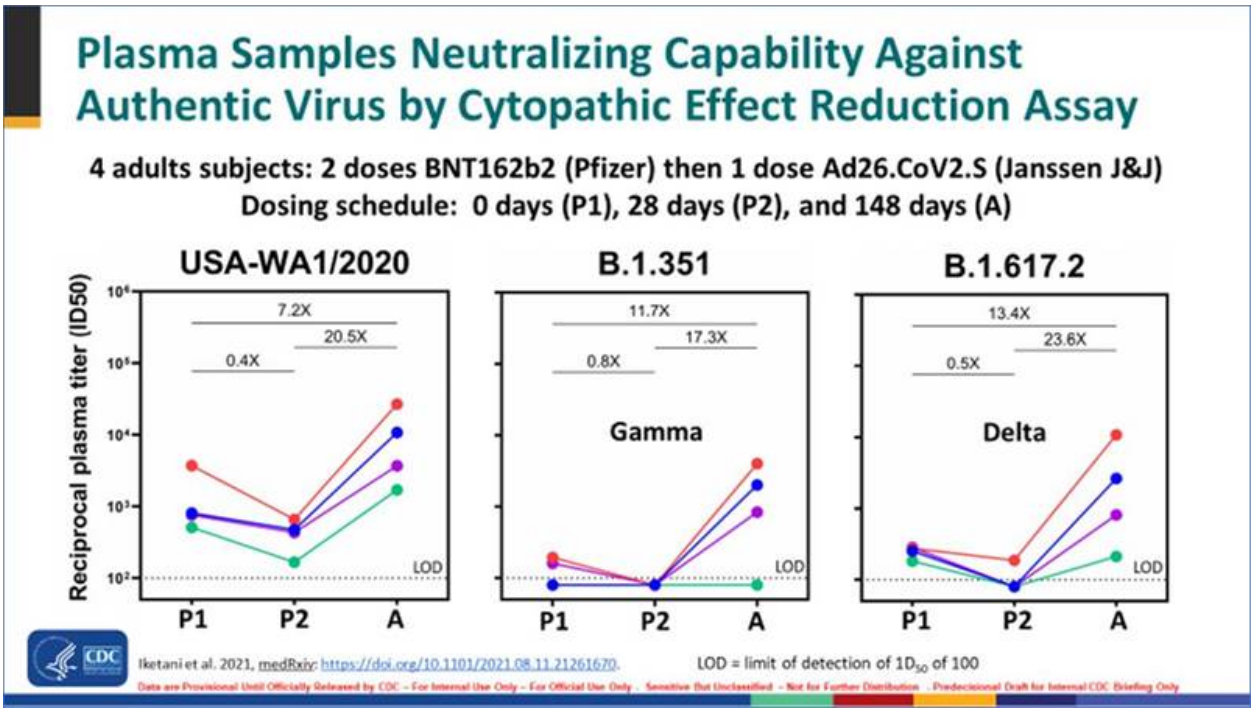

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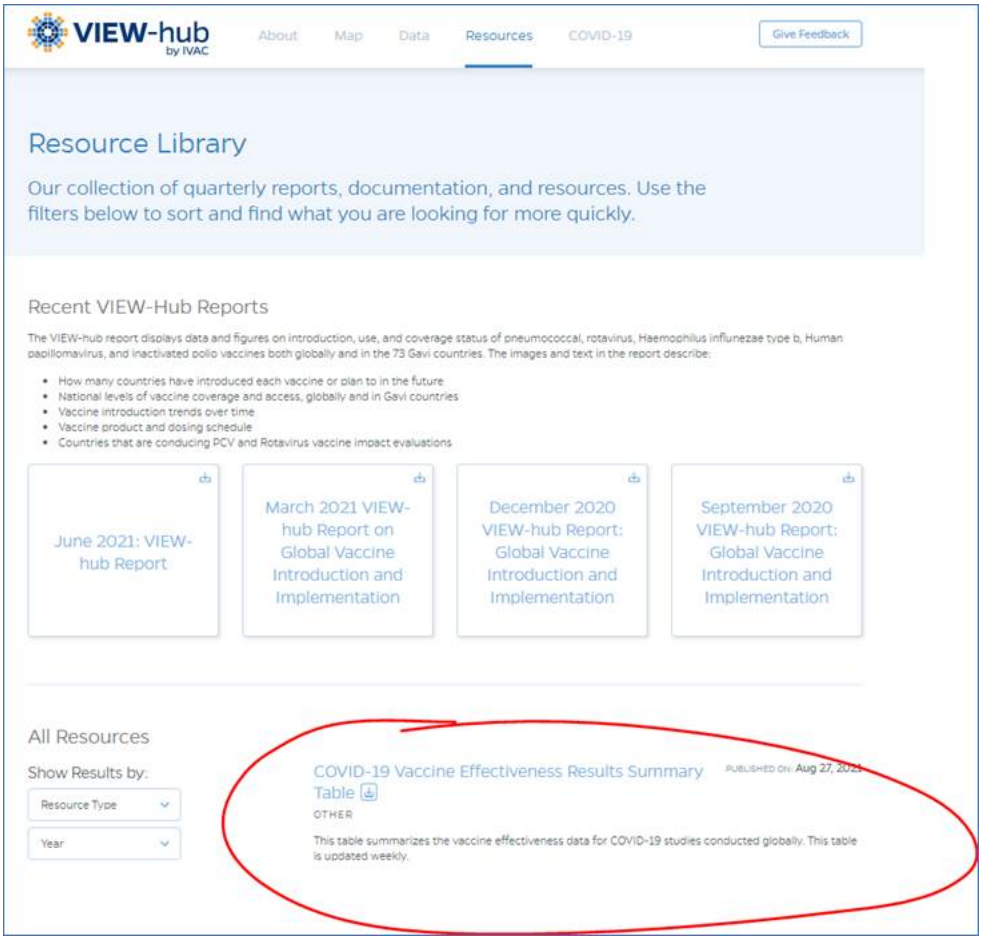
Francis,

First, thanks for that new reference!

To your question, there is a terrific resource you can check to get an overview of what's been reported in terms of real-world vaccine effectiveness studies. Go here: [Resource Library | ViewHub (view-hub.org)](), then scroll down and click the report you want (usually the one at the top is most current. Be aware these data come from all sort of sources, time frames, populations, etc.



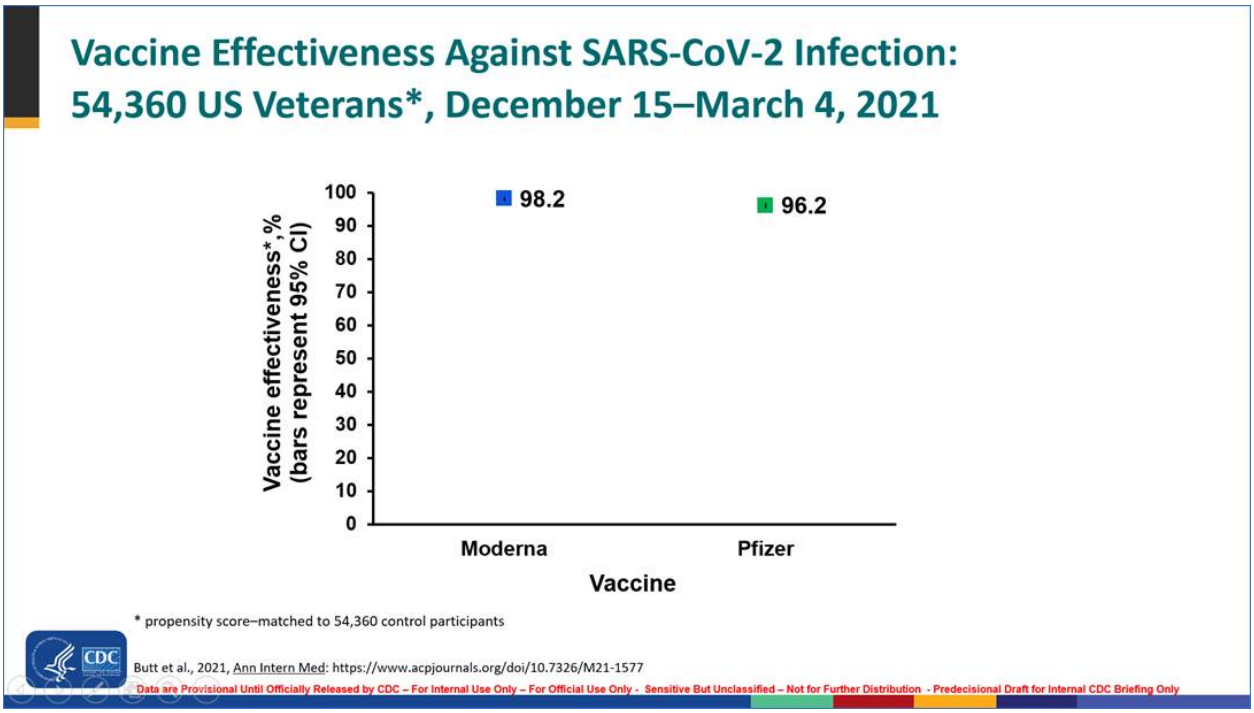
Below the "Table" is nice document labeled Forest Plots. You can use that document to find the comparison you'd like then cut and paste what you're looking for and eyeball a comparison.

Still, it's not all apples-to-apples (a bit of a mixed fruit basket).

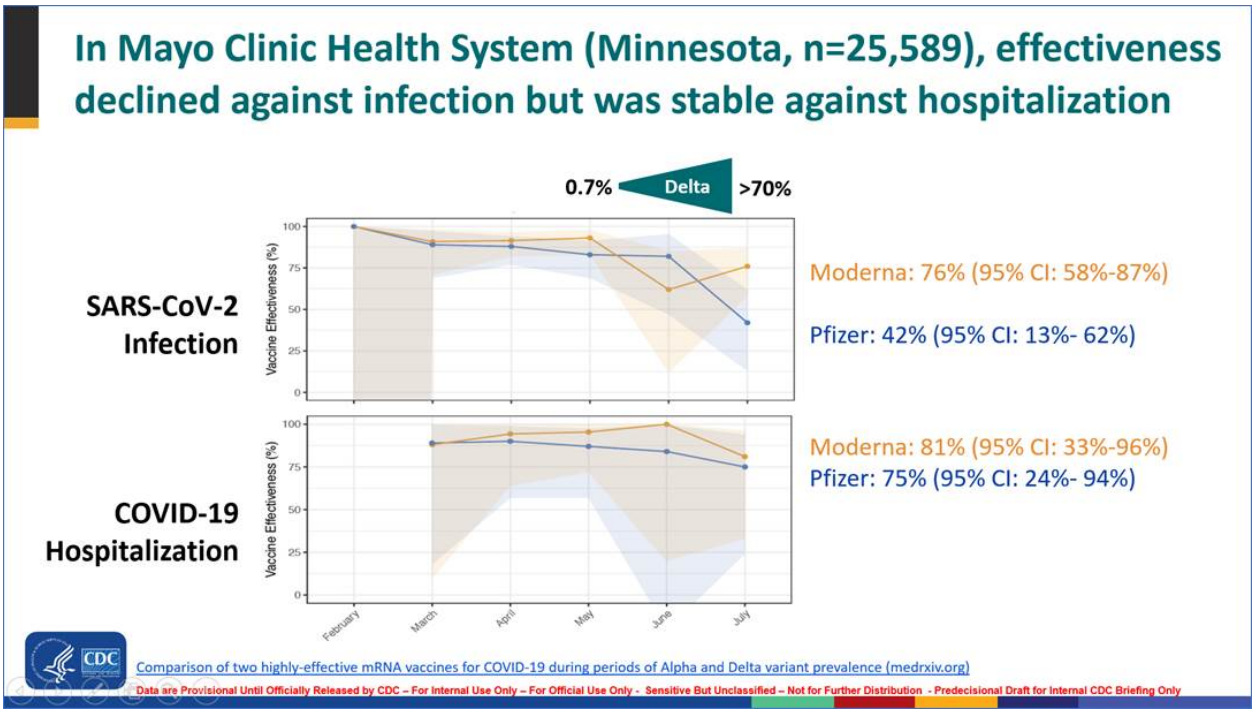
So, among the papers of which I am aware that looked at **real-world vaccine effectiveness comparing fully vaccinated adults in the same community some of whom rec'd Moderna and others Pfizer**, I have not seen a clear trend one way or the other in my admittedly non-exhaustive survey trying to keep up as they're published. Some examples below (note time frames)

4 Studies from General Community

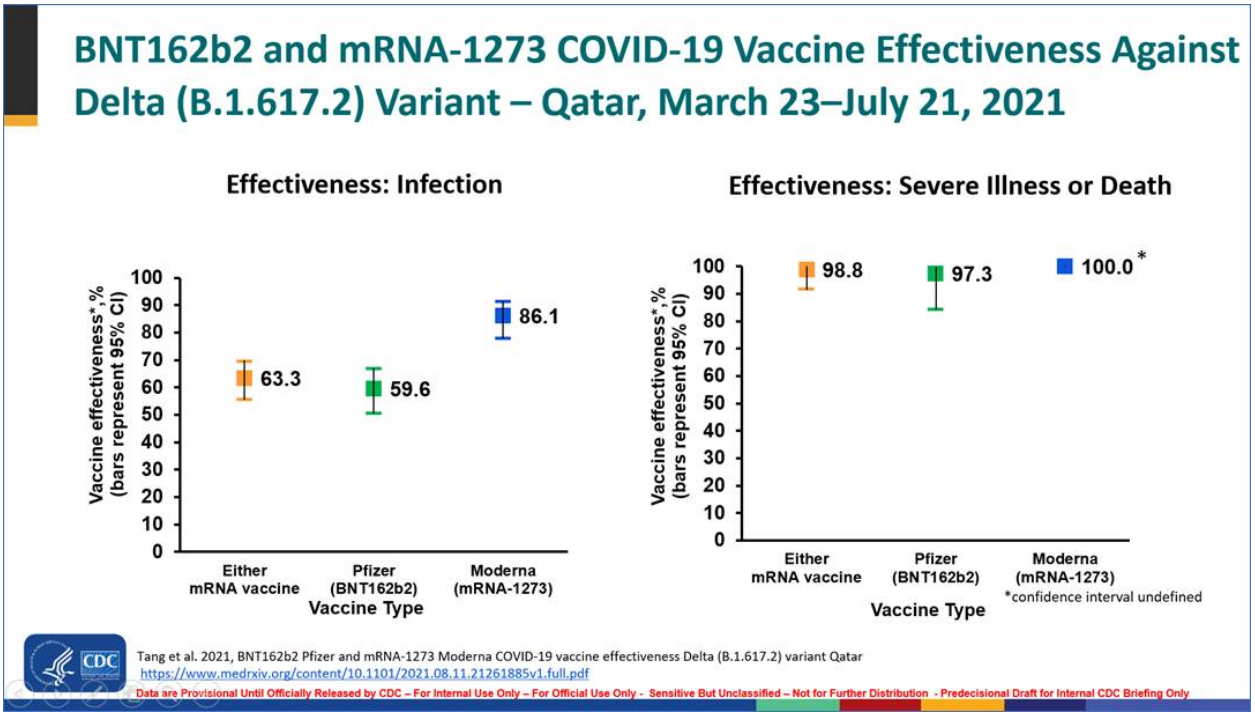
Butt et al. SARS-Cov-2 Vaccine Effectiveness In a High-Risk National Population In A Real-World Setting – Annals of Internal Medicine
https://www.acpjournals.org/doi/pdf/10.7326/M21-1577



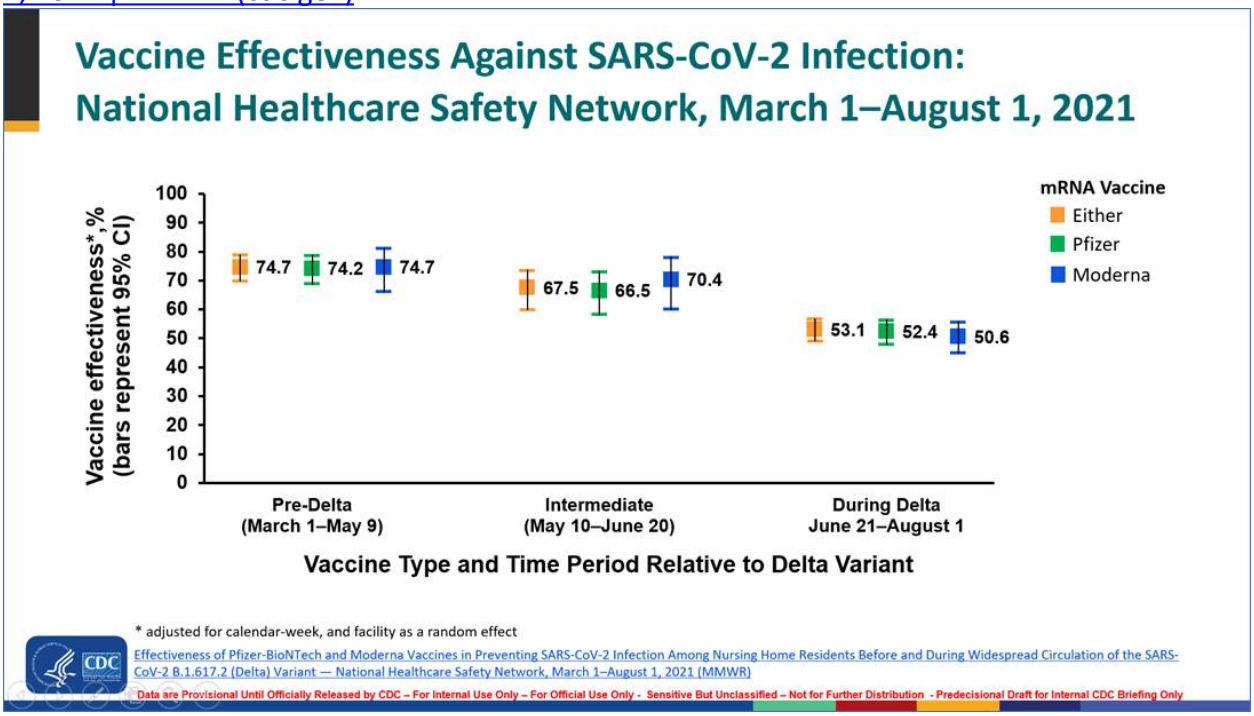
Puranik et al. Comparison of two highly-effective mRNA vaccines for COVID-19 during periods of Alpha and Delta variant prevalence (medrxiv.org)



Tang et al. [BNT162b2 and mRNA-1273 COVID-19 vaccine effectiveness against the Delta (B.1.617.2) variant in Qatar (medrxiv.org)]

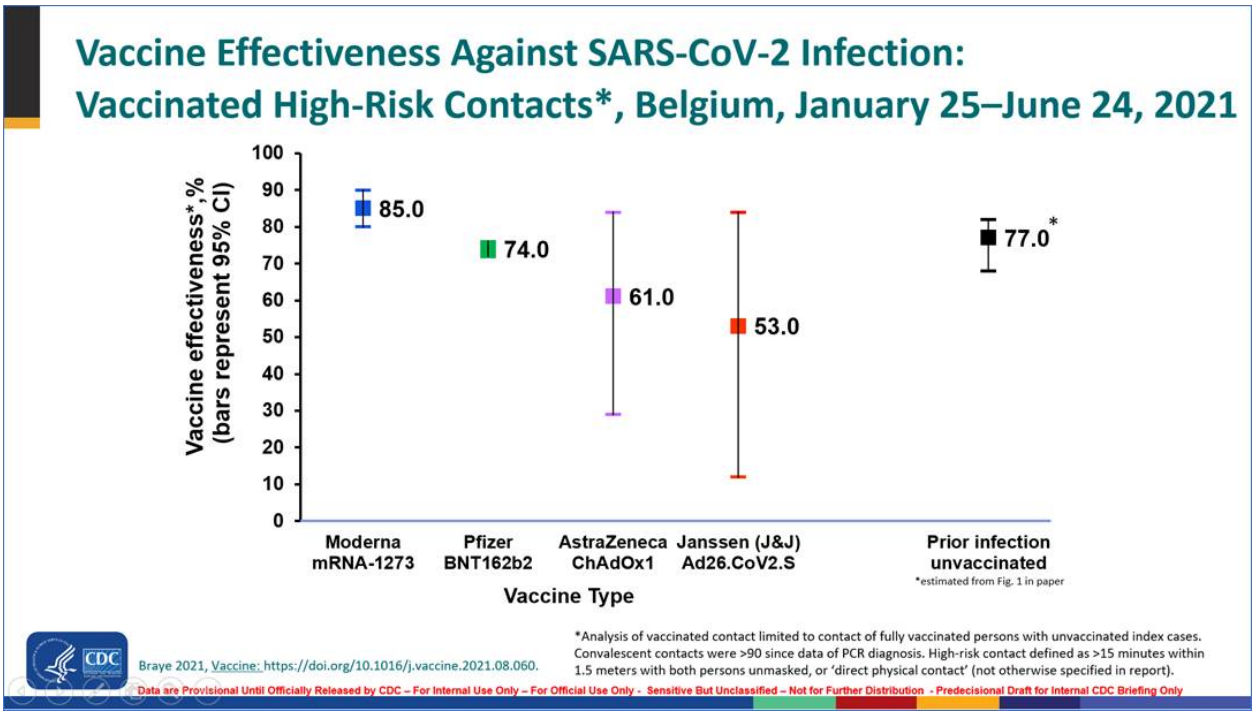


Nanduri et al. [Effectiveness of Pfizer-BioNTech and Moderna Vaccines in Preventing SARS-CoV-2 Infection Among Nursing Home Residents Before and During Widespread Circulation of the SARS-CoV-2 B.1.617.2 (Delta) Variant — National Healthcare Safety Network, March 1–August 1, 2021 | MMWR (cdc.gov)]

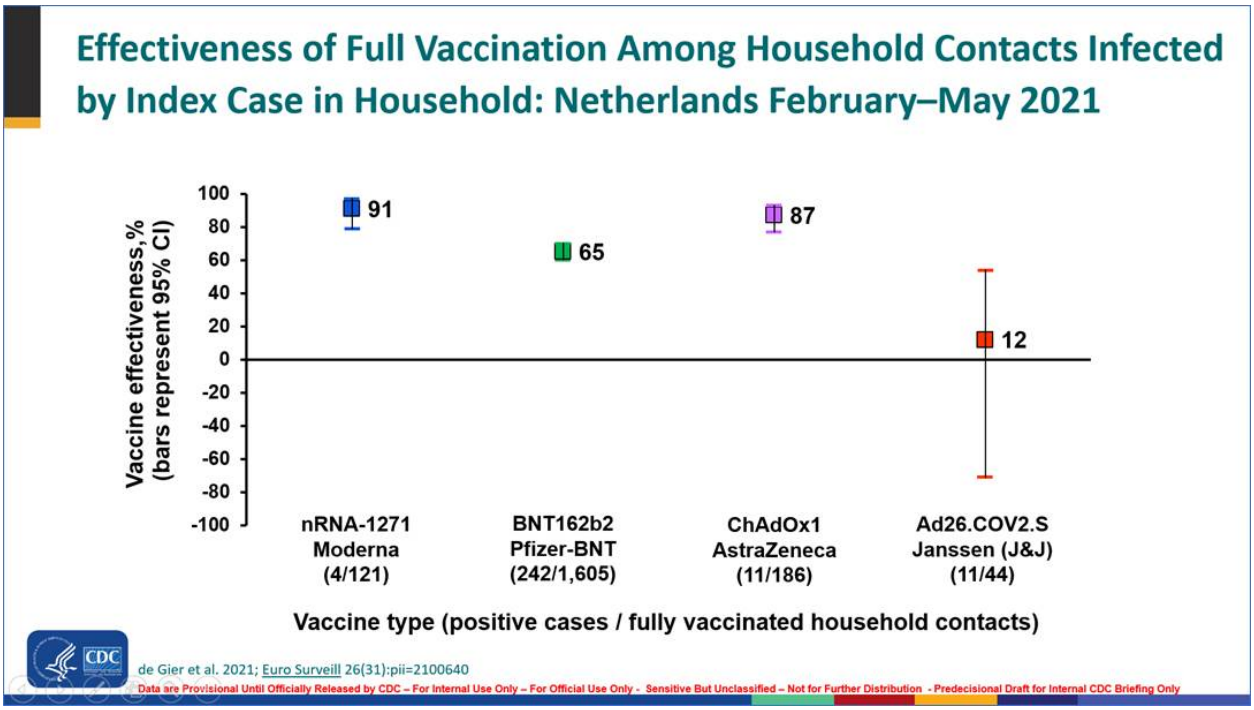


2 Studies from of Contacts Evaluated through Community Contact Tracing Efforts

Braye et al. [Vaccine effectiveness against infection and onwards transmission of COVID-19: Analysis of Belgian contact tracing data, January-June 2021 - ScienceDirect]



de Grier et al. [Eurosurveillance | Vaccine effectiveness against SARS-CoV-2 transmission and infections among household and other close contacts of confirmed cases, the Netherlands, February to May 2021]



Cheers,

-john

John T. Brooks, MD
Chief Medical Officer, CDC COVID-19 Response
Email: zud4@cdc.gov
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From: Collins, Francis (NIH/OD) [E] (b) (6)
Sent: Monday, August 30, 2021 5:48 PM
To: Murthy, Vivek (HHS/OASH) <Vivek.Murthy@hhs.gov>; Brooks, John T. (CDC/DDID/NCHHSTP/DHP) <zud4@cdc.gov>; Fauci, Anthony (NIH/NIAID) [E] (b) (6) Walensky, Rochelle (CDC/OD) <aux7@cdc.gov>; Eric Lander (b) (6)
Cc: Beckman, Adam (HHS/OASH) <Adam.Beckman@hhs.gov>
Subject: RE: Post infection protection vs vaccine immunity

HI all,

Let me add my thanks to John for this survey and summary. Nicely done!

Of course the Israel data is solely Pfizer-BioNTech. A real world paper just out today in JAMA documents significantly higher antibody titers from Moderna:

https://jamanetwork.com/journals/jama/fullarticle/2783797?guestAccessKey=6ead80fe-bf08-4d53-8c5c-607249932480&utm_source=silverchair&utm_medium=email&utm_campaign=article_alert-jama&utm_content=olf&utm_term=083021

One wonders whether the comparison of natural infection vs. vaccination, and the timetable for waning of protection, would be different in Moderna recipients. Do any of the CDC cohorts have the potential to answer that question?

Francis

From: Murthy, Vivek (HHS/OASH) <Vivek.Murthy@hhs.gov>
Sent: Monday, August 30, 2021 5:21 PM
To: Brooks, John T. (CDC/DDID/NCHHSTP/DHP) <zud4@CDC.GOV>; Collins, Francis (NIH/OD) [E]

<collinsf@od.nih.gov>; Fauci, Anthony (NIH/NIAID) [E] (b) (6)>; Walensky, Rochelle (CDC/OD) <aux7@cdc.gov>; Eric Lander <(b) (6)
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Hi John, what a thoughtful review of some of the other studies out there - thank you for this. The durability of infection-based immunity is the big question it seems. I also wonder if the strength and durability of such protection differs based on whether one's infection was with alpha vs delta - have you seen anything that would speak to this?
thanks
vivek

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Sent: Monday, August 30, 2021 2:57 PM
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Cc: Beckman, Adam (HHS/OASH) <Adam.Beckman@hhs.gov>
Subject: RE: Post infection protection vs vaccine immunity

Hi all,

Over the weekend I tried to pull together what we know from some select papers among the cavalcade of publications coming out in the realm of infection-induced vs. vaccine-induced immunity. This is not a meta-analysis, and I'm not sure we have enough data of the same type yet to embark on a meta-analysis.

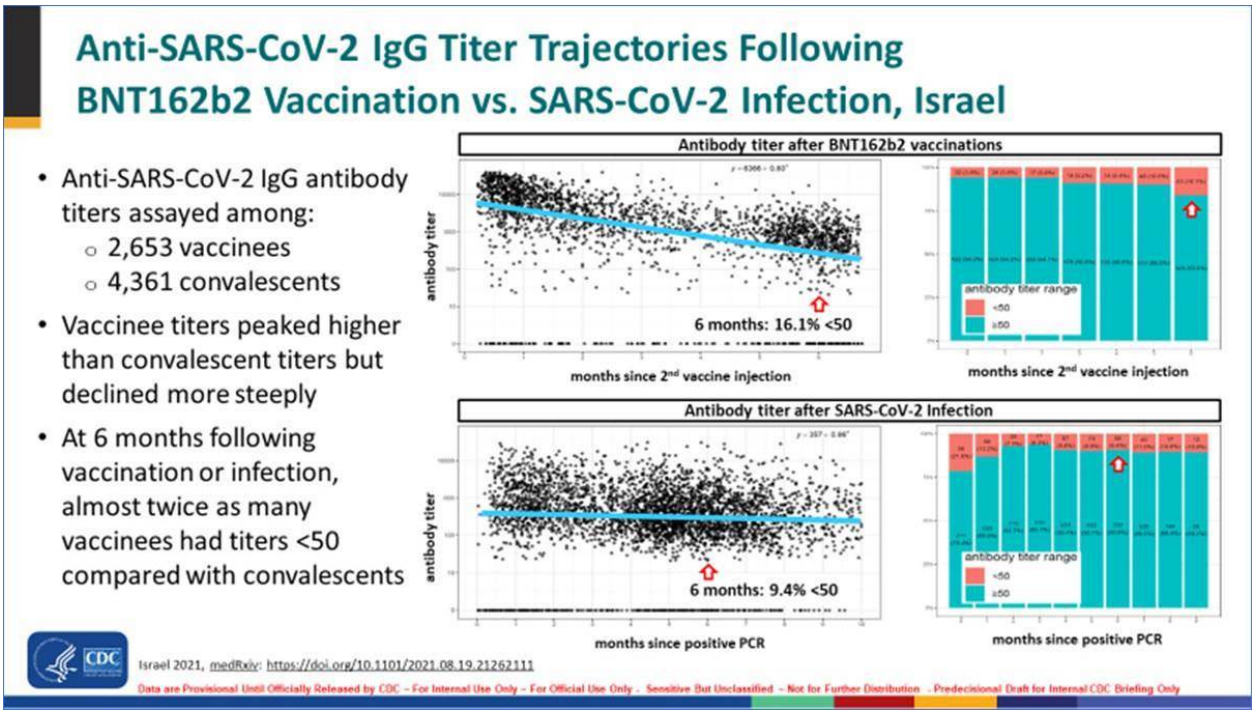
But it's a scan of what's coming out that I hope may help guide how everyone is thinking about things. Not anything definitive but data I think this group would merit knowing about.

First, I too think (and so do my colleagues) that the Gazit et al. paper suggesting natural infection is more immunizing that vaccine is well-done: something is going on here. Likewise, so too is the Bar-On et al. paper demonstrating rather rapid restoration of protection by vaccination given as a third dose of BNT162b2 (Pfizer) to people who completed the two-dose series of the same vaccine > 5 months prior.

So what do we know first about the trajectory of the immune response to *infection vs. immunization*. I think a paper by Israel et al. (who is incidentally from Israel and Israeli…) is illustrative. They compared anti-SARS-CoV-2 IgG values in ~2,500 BNT162b2 vaccinees (following from data of second vaccination) and

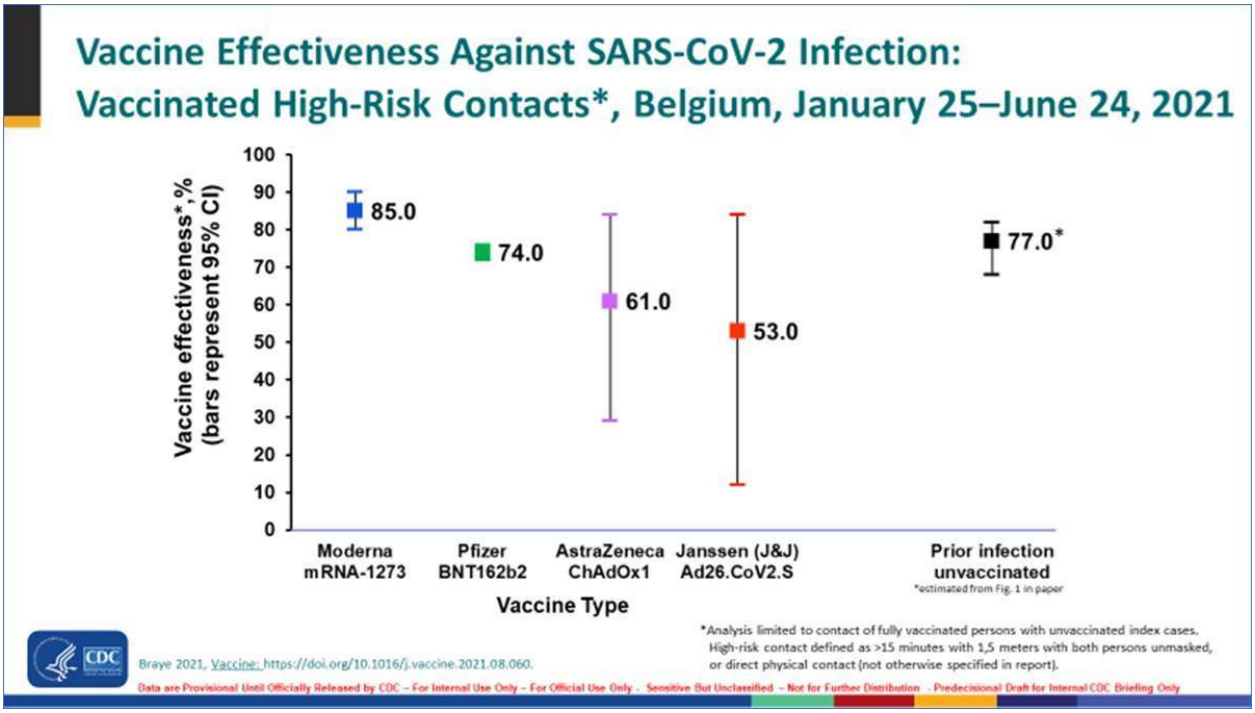
~4,300 persons recovered from infection (convalescents from data of confirmed PCR positive specimen). Robust numbers and solid analysis, in my opinion. Note that the convalescent were younger by about 15 years on average than vaccinated (42 ± 16 years vs. 56 ± 16 years, in case you are concerned about immunosenescence); their analysis strived t account for this difference.

The figures from the paper are shown below.



The take-away here to me is that although vaccine-induced antibody titers (BNT162b2) peak higher, they decline more swiftly than infection-induced titers and begin falling below infection-induced antibody titers after 6 months. The authors note that "In vaccinated subjects, antibody titers decreased by up to 40% each subsequent month while in convalescents they decreased by less than 5% per month." Unfortunately, convalescent titers were not stratified by COVID-19 illness severity; however, the authors note (using standard multivariable logistic regression) that among convalescents higher antibody titers were associated with symptomatic illness, hospitalization, and having at least one risk factors for severe illness (e.g., older age, diabetes, obesity, chronic renal disease, hypertension). Still, I would really like to see data from people who had very mild illness or who were asymptomatically infected.

Another study, this one from Belgium authored by Braye et al., assessed vaccine effectives against infection among high-risk *fully vaccinated contacts* of *unvaccinated index patients* as well as among persons recovered from COVID-19 (*convalescent) for >90 days* who were contact of unvaccinated index patients. Again, robust numbers of high-risk contacts (HRCs) in the mRNA vaccine arms (~7,900) and the convalescent arm (~700), and a solid analytic approach. Note that their data are unclear on the precise numbers of contact events that involved unvaccinated index cases but the majority of index cases (97%) were unvaccinated. The data do not take into account time since vaccination/illness and are a conglomeration of contact tracing data from January-June 2021. There data show that the VE for prior infection (in black, I had the infer the data to make this figure since the paper doesn't provide the actual values) was about the same at the VE for mRNA vaccination (in blue and green). The adenovirus-vectored vaccine data are also interesting but fewer numbers (introduced near the middle of the study period in Belgium); this is where analysis limited to time since vaccination/infection would be helpful.

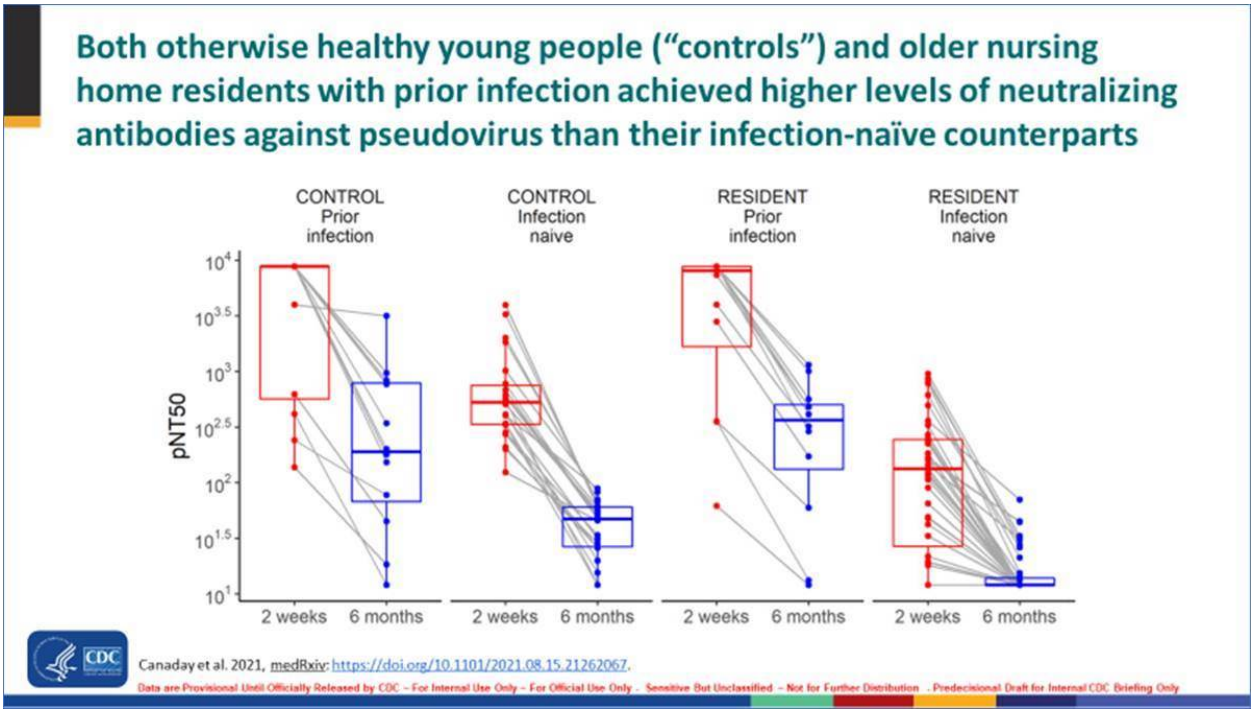


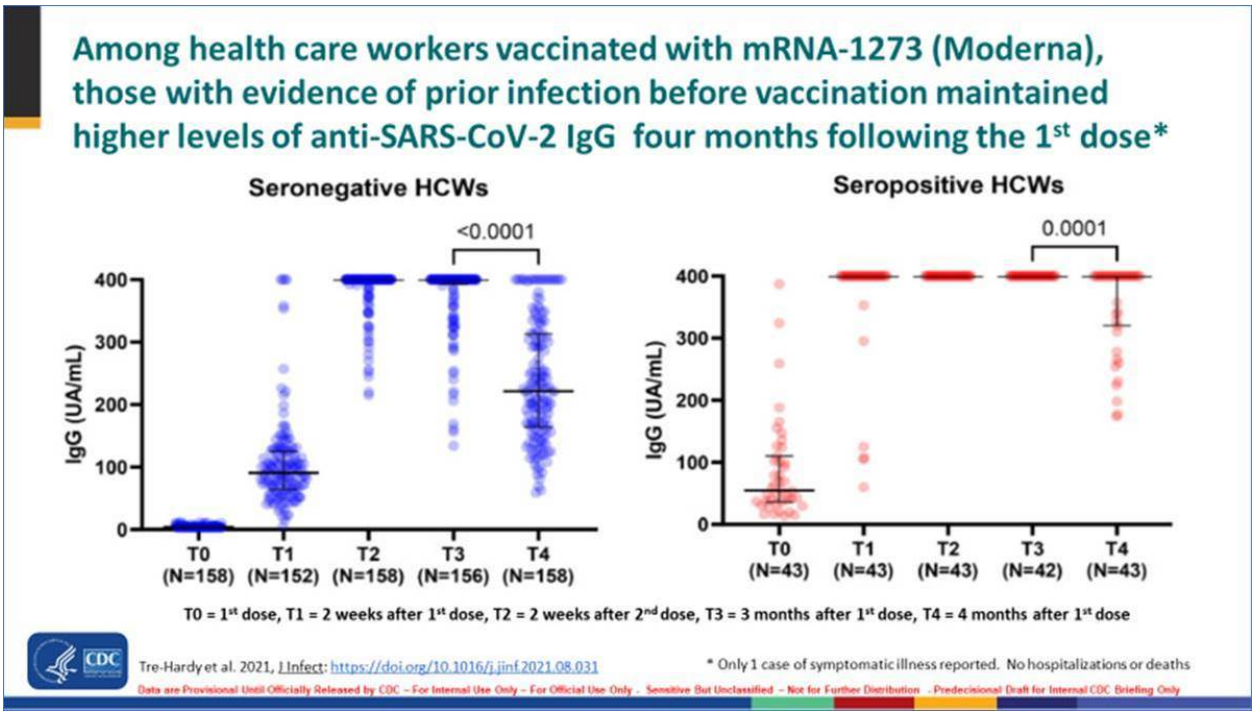
OK, so it seems now from at least three very different analyses of different data that at least mRNA vaccine effectiveness is about as good as infection-induced immunity but that vaccine-induced immunity wanes over time (especially

that induced by BNT162b2) whereas infection-induced may be more durable up to at least the 4-6 month mark (like the Gazit et al. paper). *Note that we may not have seen this before because most investigators are looking at vaccinated people and not including and comparing data from persons recovered from infection.*

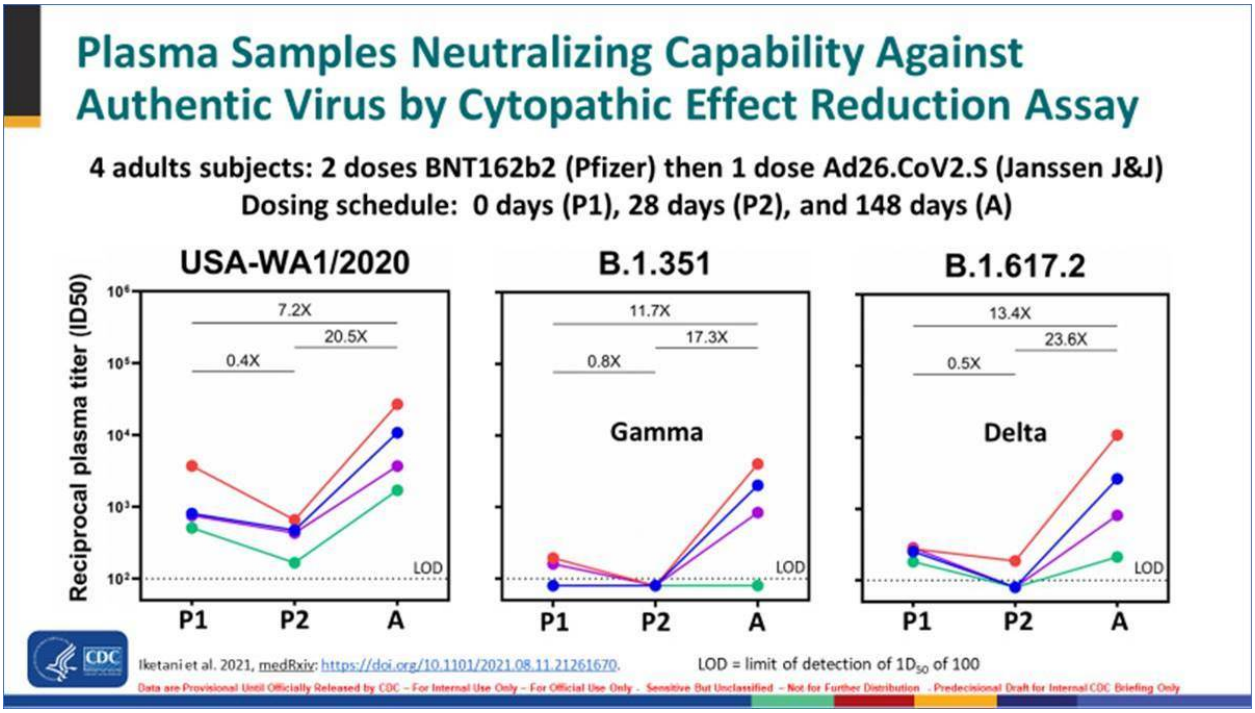
The good news here is that boosters look like a solution, not just based on Bar-On et al. paper but also the following data.

At least two studies have now shown that vaccination after infection produces a larger and more durable antibody response (Canady et al. and Tre-Hardy et al., slides below). So three-stimulus "booster-like" scenario.





And when you look at Iketani et al., giving a true booster dose of vaccine (2 doses Pfizer BNT162b2 followed by 1 dose Janssen J&J), that "boost" substantially increased neutralizing antibody levels (measured as serum neutralizing capacity against real SARS-CoV-2 virus) to both "ancestral" variants and two key variants of concern, Gamma (B.1.351) and Beta (B.1.617.2). *Note: these data are derived from FOUR SUBJECTS only.*



So….I'm not sure *exactly* what is going on here *and like so much with this virus it's not at all what I would have expected*, but with the data we have before us I see this:

- Both vaccine and infection are immunizing.
- We only have epidemiologic data on both forms of immunity out to about 6 months
- Vaccine effectiveness from 2-dose mRNA vaccine may wane earlier than infection-induced immunity, which may persist longer and in this way may also provide better protection, at least up to about 6 months or so.
- However, we want to avoid infection-induced immunity; comes at too great a cost and vaccination is safe.
- We have epidemiologic data that three episodes of immune stimulation (infection followed by mRNA vaccination) as well as a booster vaccine dose (2 dose mRNA vaccination followed by single dose adenovirus-vectored vaccine) increase markers of immunity (serum neutralizing capacity and antibody response) and per Bar-On et al. also appears to reverse decline in vaccine effectiveness, at least in the short term.
- May this will be a three-dose vaccine after all…

Therefore, we should offer booster doses.

To folks calling out that "convalescents" do not need vaccination I would respond:

1. We only have epidemiologic data on both forms of immunity out to about 6 months, and we don't know how much longer and how well infection-induced immunity may protect (i.e., how durable that immunity is).
2. We have epidemiologic data (Kentucky MMWR) that vaccination after recovery substantially reduces risk of reinfection by (risk of reinfection if *unvaccinated* was odds ratio 2.34, 95% CI 1.58-3.47). The Gazit et al. observed a similar phenomenon but it was non-significant (risk of reinfection *if vaccinated* odd ratio 0.68, 95% CI 0.38-1.12, p-0.188). BTW inverse of 0.68 is 1.47, and inverse of 2.34 is 0.43 😉

If you see any errors here, or in the slide images, please let me know. I welcome corrections!

Cheers,

-john

John T. Brooks, MD
Chief Medical Officer, CDC COVID-19 Response
Email: zud4@cdc.gov
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From: Collins, Francis (NIH/OD) [E] (b) (6)
Sent: Monday, August 30, 2021 10:33 AM
To: Fauci, Anthony (NIH/NIAID) [E] (b) (6); Murthy, Vivek (HHS/OASH) <Vivek.Murthy@hhs.gov>; Walensky, Rochelle (CDC/OD) <aux7@cdc.gov>; Eric Lander (b) (6); Brooks, John T. (CDC/DDID/NCHHSTP/DHP) <zud4@cdc.gov>
Cc: Beckman, Adam (HHS/OASH) <Adam.Beckman@hhs.gov>
Subject: RE: Post infection protection vs vaccine immunity

Hi Vivek et al.,

Thanks for pointing out this somewhat puzzling publication. The Israeli preprint https://www.medrxiv.org/content/10.1101/2021.08.24.21262415v1.full.pdf does seem to describe a well-designed (albeit retrospective) study. Their cases of prior natural infection were

just all comers with positive PCR tests, they didn't break this down by severity. But the magnitude of the difference between protection from natural infection and vaccination is significantly large (13x) that it's hard to imagine that the first group were all people with really serious prior systemic infection. On the other hand, one has to wonder whether vaccinated individuals were more likely to seek diagnosis in the presence of mild or absent symptoms, identifying them as breakthrough cases – whereas those with prior infection may have been less likely to seek testing.

The CDC Kentucky MMWR study https://www.cdc.gov/mmwr/volumes/70/wr/mm7032e1.htm didn't ask quite the same question – that study was aimed at determining whether vaccination after natural infection adds additional protection. The answer is clearly yes (2.34x), and the Israeli study showed that too.

Does CDC have a ready meta-analysis of all of the studies that have compared the immunity from natural infection to vaccination? Most of us have been saying up until now that vaccines are actually better for providing immunity – what does the overall synthesis of the data now say?

Francis

From: Fauci, Anthony (NIH/NIAID) [E] (b) (6)
Sent: Friday, August 27, 2021 2:37 PM
To: Murthy, Vivek (HHS/OASH) <Vivek.Murthy@hhs.gov>; Collins, Francis (NIH/OD) [E] (b) (6); Walensky, Rochelle (CDC/OD) <aux7@cdc.gov>; Eric Lander (b) (6)>; Brooks, John T. (CDC/DDID/NCHHSTP/DHP) <zud4@CDC.GOV>
Cc: Beckman, Adam (HHS/OASH) <Adam.Beckman@hhs.gov>
Subject: RE: Post infection protection vs vaccine immunity

The data as reported in the news article look rather impressive despite the caveat that it is a retrospective study and the testing was voluntary. I have not seen the details of the actual data, but I would imagine that it is more complicated than we think. It very well may be that people who have had an asymptomatic or minimally symptomatic infection (upper airway only) will not have a greater post-infection protection against subsequent infection then those who get fully vaccinated. However, it is conceivable and possibly likely that those who have had a serious systemic infection develop a high level of immunity that even surpasses that of full vaccination. I would like to see if they broke the data on the infected people down into those two groups.

Anthony S. Fauci, MD
Director
National Institute of Allergy and Infectious Diseases

Building 31, Room 7A-03
31 Center Drive, MSC 2520
National Institutes of Health
Bethesda, MD 20892-2520
Phone: (b) (6)
FAX: (301) 496-4409
E-mail: (b) (6)

From: Murthy, Vivek (HHS/OASH) <Vivek.Murthy@hhs.gov>
Sent: Friday, August 27, 2021 1:57 PM
To: Collins, Francis (NIH/OD) [E] <(b) (6); Fauci, Anthony (NIH/NIAID) [E] (b) (6)>; Walensky, Rochelle (CDC/OD) <aux7@cdc.gov>; Eric Lander (b) (6)>; Brooks, John T. (CDC/DDID/NCHHSTP/DHP) <zud4@CDC.GOV>
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Subject: Post infection protection vs vaccine immunity

Do you have thoughts on this recent study from Israel? And how this fits with the recent MMWR findings (Kentucky study showing higher risk of reinfection in the unvaccinated compared to risk of infection in the vaccinated)?

https://www.sciencemag.org/news/2021/08/having-sars-cov-2-once-confers-much-greater-immunity-vaccine-no-infection-parties

Having SARS-CoV-2 once confers much greater immunity than a vaccine—but no infection parties, please | Science | AAAS

Having SARS-CoV-2 once confers much greater immunity than a vaccine—but no infection parties, please. By Meredith Wadman Aug. 26, 2021 , 8:02 PM. The natural immune protection that develops …

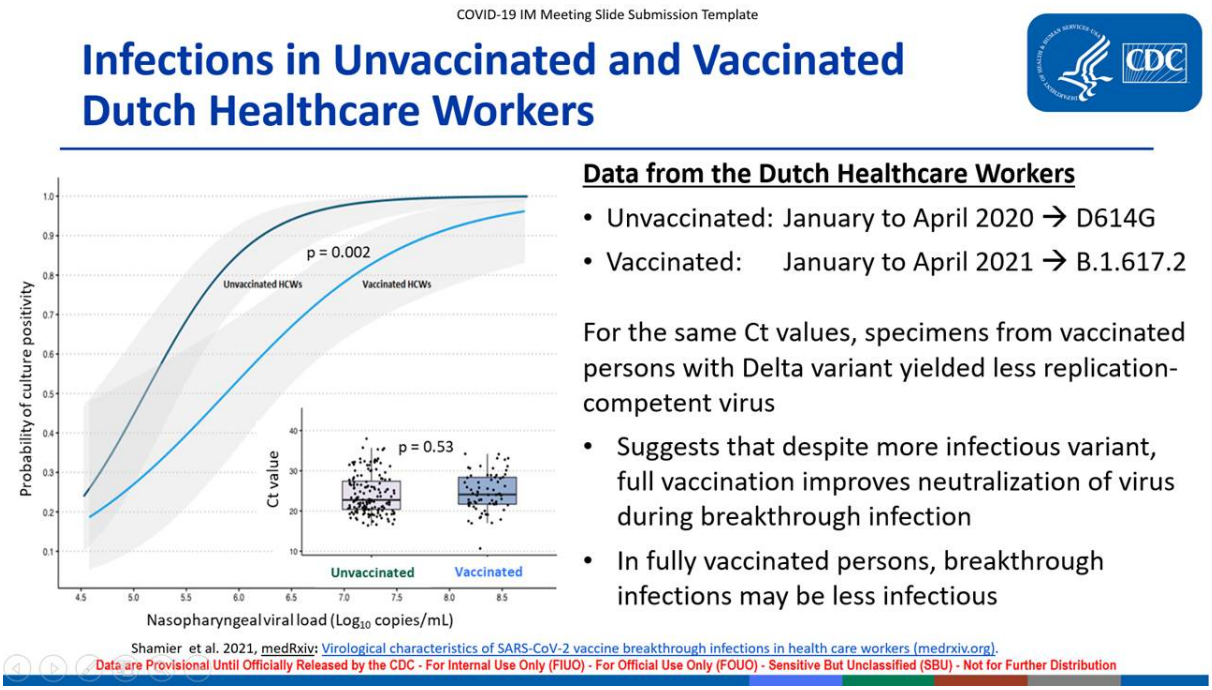
www.sciencemag.org

From: Brooks, John T. (CDC/DDID/NCHHSTP/DHP) <zud4@cdc.gov>
Sent: Mon, 30 Aug 2021 17:24:49 -0500
To: Murthy, Vivek (HHS/OASH);Collins, Francis (NIH/OD) [E];Fauci, Anthony (NIH/NIAID) [E];Walensky, Rochelle (CDC/OD);Eric Lander
Cc: Beckman, Adam (HHS/OASH)
Subject: RE: Post infection protection vs vaccine immunity

Hi Vivek,

Nothing that would speak to differences in the duration of infection-induced immunity according to the infecting variant that I'm aware of (but I could cerctainly have missed it). Many of the studies cited below included pre- and peri-Delta data.

However, this paper by Shamier et al. may be informative insofar as it suggests that despite the fact that Delta breakthrough infections in vaccinated people achieve Ct values as low as those of non-Delta infections in unvaccinated persons, when you look at the presence of culturable virus, vaccinated persons are significantly less likely to have virus cultured from an NP swab than unvaccinated with no-Delta *at the same Ct value.* Why? Perhaps because in vaccinated and unvaccinated with same amount of virus replication in the tissue sample by NP swab, vaccinated people are neutralizing that virus better leaving behind RNA wreckage from dead virus that is picked up by PCR.



The paper has *plenty o' limitations* but it's really intriguing, biologically plausible, and perhaps reassuring.

It also makes the good point that Ct value does not equal infectiousness or burden of live virus.

Reminiscent of the problem with Zika in semen: virions produced in the immune-protected testes (still not sure whence the tropism for those cells, maybe someone knows) eventually started getting neutralized by the native immune response as they left the safe harbor of the testes and got zapped along their way through epididymis, vas deferens, seminal vesicle, and lastly the prostate (reminds me of a drive-thru car wash). So some guys had RNA-positive semen for MONTHS but no live virus had really been in that semen after 30 days. Same reason we don't do test of cure with PCR for GC and chlamydia – at least not within a week or so of treatment; the detectable genetic flotsam and jettison treatment leaves behind obviate you're ability to tell if infection is really gone or really still there.

-john

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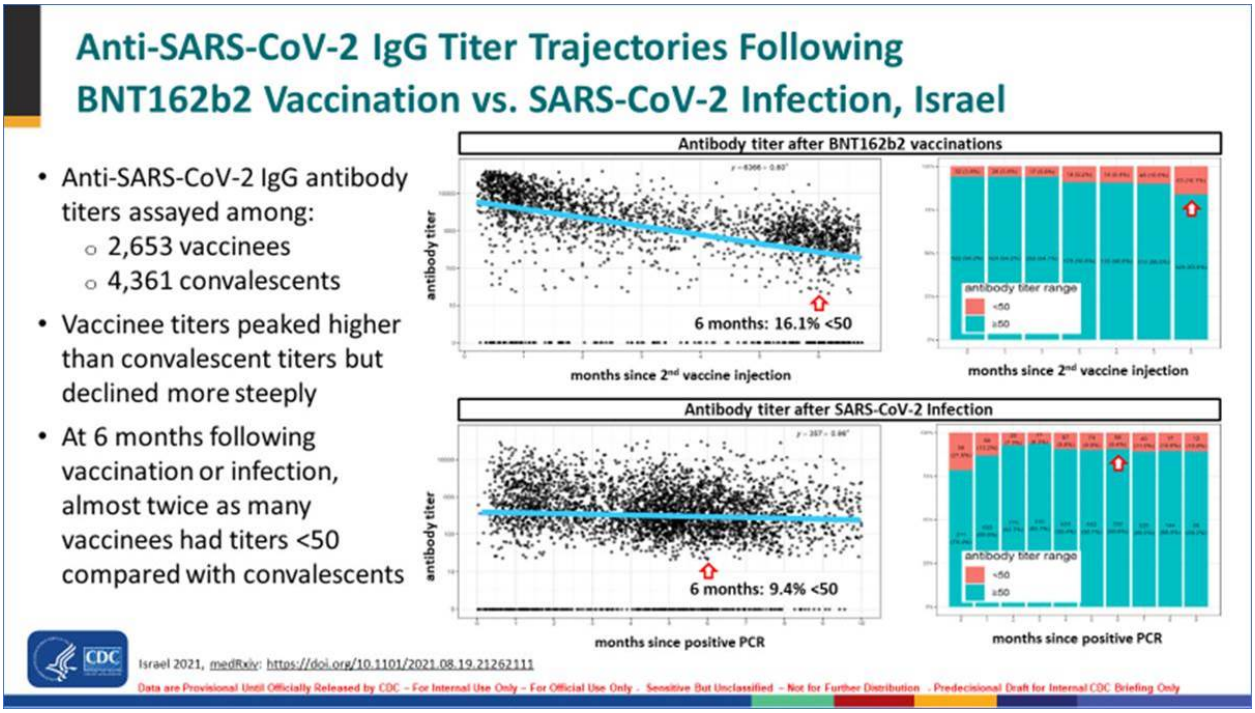

The take-away here to me is that although vaccine-induced antibody titers (BNT162b2) peak higher, they decline more swiftly than infection-induced titers and begin falling below infection-induced antibody titers after 6 months. The authors note that ”In vaccinated subjects, antibody titers decreased by up to 40%

each subsequent month while in convalescents they decreased by less than 5% per month." Unfortunately, convalescent titers were not stratified by COVID-19 illness severity; however, the authors note (using standard multivariable logistic regression) that among convalescents higher antibody titers were associated with symptomatic illness, hospitalization, and having at least one risk factors for severe illness (e.g., older age, diabetes, obesity, chronic renal disease, hypertension). Still, I would really like to see data from people who had very mild illness or who were asymptomatically infected.

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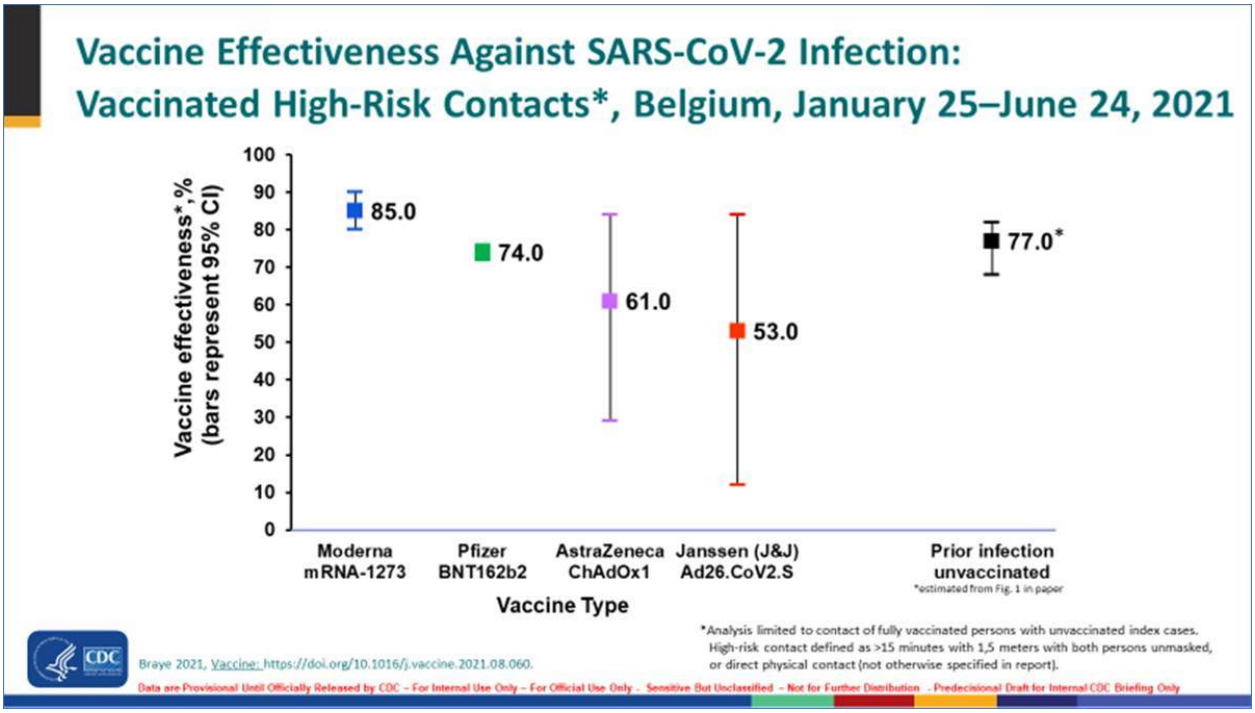

OK, so it seems now from at least three very different analyses of different data that at least mRNA vaccine effectiveness is about as good as infection-induced immunity but that vaccine-induced immunity wanes over time (especially that induced by BNT162b2) whereas infection-induced may be more durable up to at least the 4-6 month mark (like the Gazit et al. paper). *Note that we may not have seen this before because most investigators are looking at vaccinated people and not including and comparing data from persons recovered from infection.*

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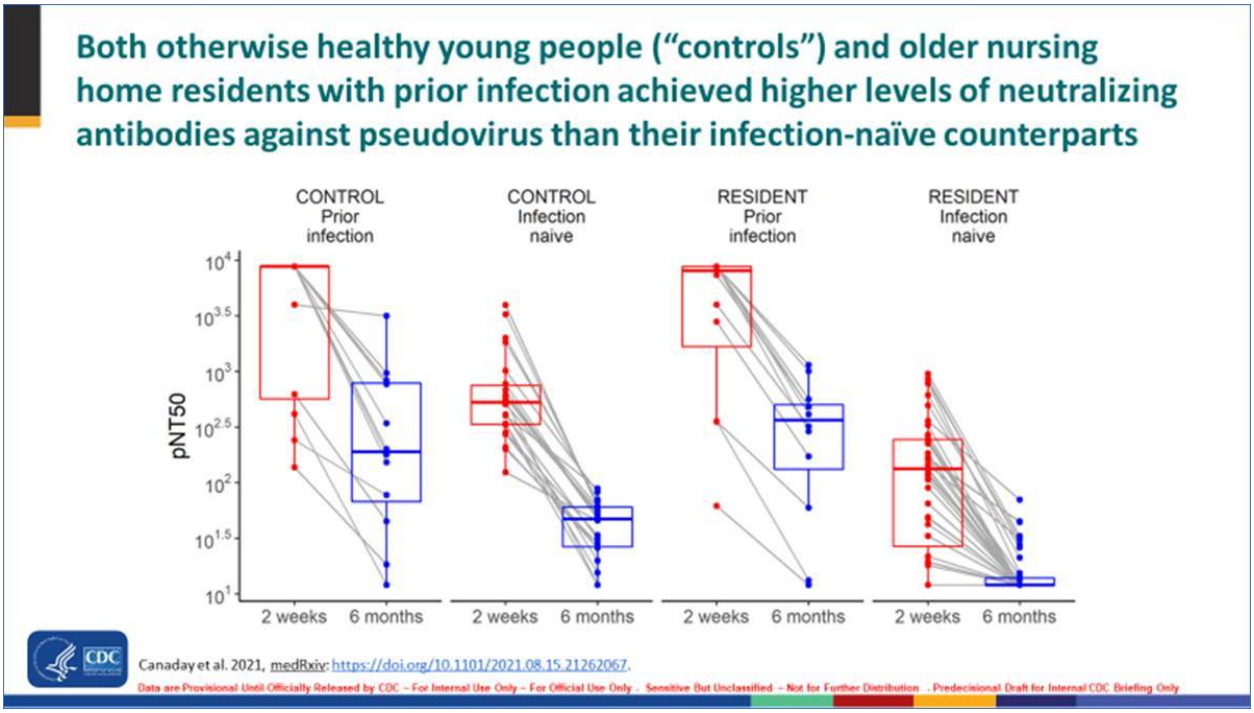
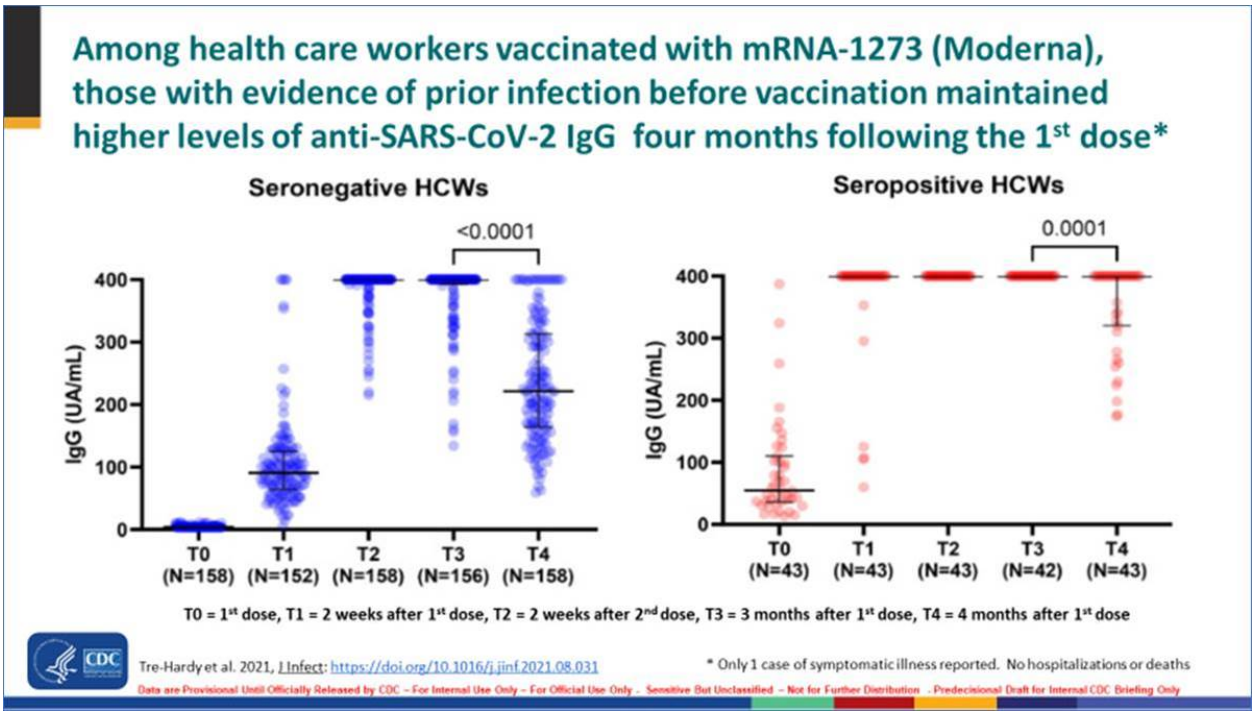
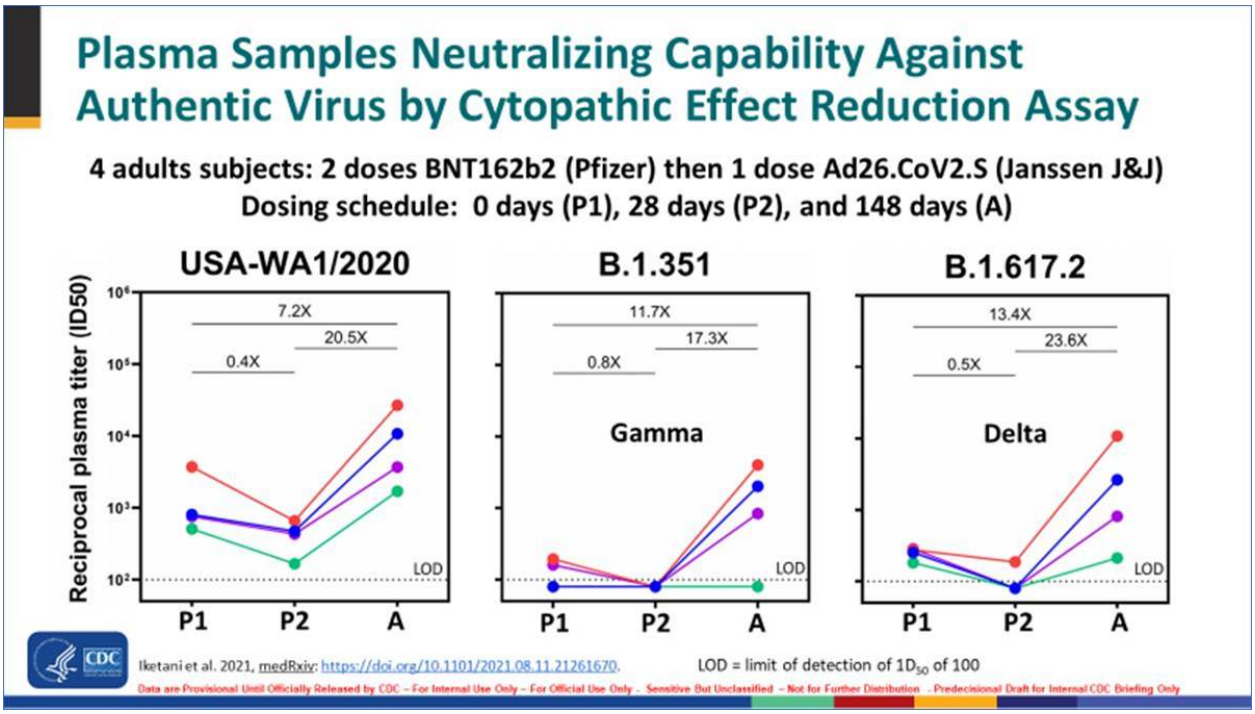




And when you look at Iketani et al., giving a true booster dose of vaccine (2 doses Pfizer BNT162b2 followed by 1 dose Janssen J&J), that "boost" substantially increased neutralizing antibody levels (measured as serum neutralizing capacity against real SARS-CoV-2 virus) to both "ancestral" variants and two key variants of

concern, Gamma (B.1.351) and Beta (B.1.617.2). *Note: these data are derived from FOUR SUBJECTS only.*



So….I'm not sure *exactly* what is going on here *and like so much with this virus it's not at all what I would have expected*, but with the data we have before us I see this:

- Both vaccine and infection are immunizing.
- We only have epidemiologic data on both forms of immunity out to about 6 months
- Vaccine effectiveness from 2-dose mRNA vaccine may wane earlier than infection-induced immunity, which may persist longer and in this way may also provide better protection, at least up to about 6 months or so.
- However, we want to avoid infection-induced immunity; comes at too great a cost and vaccination is safe.
- We have epidemiologic data that three episodes of immune stimulation (infection followed by mRNA vaccination) as well as a booster vaccine dose (2 dose mRNA vaccination followed by single dose adenovirus-vectored vaccine) increase markers of immunity (serum neutralizing capacity and antibody response) and per Bar-On et al. also appears to reverse decline in vaccine effectiveness, at least in the short term.

- May this will be a three-dose vaccine after all…

Therefore, we should offer booster doses.

To folks calling out that "convalescents" do not need vaccination I would respond:

1. We only have epidemiologic data on both forms of immunity out to about 6 months, and we don't know how much longer and how well infection-induced immunity may protect (i.e., how durable that immunity is).
2. We have epidemiologic data (Kentucky MMWR) that vaccination after recovery substantially reduces risk of reinfection by (risk of reinfection if *unvaccinated* was odds ratio 2.34, 95% CI 1.58-3.47). The Gazit et al. observed a similar phenomenon but it was non-significant (risk of reinfection *if vaccinated* odd ratio 0.68, 95% CI 0.38-1.12, p-0.188). BTW inverse of 0.68 is 1.47, and inverse of 2.34 is 0.43 😉

If you see any errors here, or in the slide images, please let me know. I welcome corrections!

Cheers,

-john

John T. Brooks, MD
Chief Medical Officer, CDC COVID-19 Response
Email: zud4@cdc.gov
Apologies for errors in my messages that may be due to my need to dictate.

From: Collins, Francis (NIH/OD) [E] <(b) (6)>
Sent: Monday, August 30, 2021 10:33 AM
To: Fauci, Anthony (NIH/NIAID) [E] (b) (6)>; Murthy, Vivek (HHS/OASH) <Vivek.Murthy@hhs.gov>; Walensky, Rochelle (CDC/OD) <aux7@cdc.gov>; Eric Lander (b) (6)>; Brooks, John T. (CDC/DDID/NCHHSTP/DHP) <zud4@cdc.gov>
Cc: Beckman, Adam (HHS/OASH) <Adam.Beckman@hhs.gov>
Subject: RE: Post infection protection vs vaccine immunity

Hi Vivek et al.,

Thanks for pointing out this somewhat puzzling publication. The Israeli preprint https://www.medrxiv.org/content/10.1101/2021.08.24.21262415v1.full.pdf does seem to describe a well-designed (albeit retrospective) study. Their cases of prior natural infection were just all comers with positive PCR tests, they didn't break this down by severity. But the magnitude of the difference between protection from natural infection and vaccination is significantly large (13x) that it's hard to imagine that the first group were all people with really serious prior systemic infection. On the other hand, one has to wonder whether vaccinated individuals were more likely to seek diagnosis in the presence of mild or absent symptoms, identifying them as breakthrough cases – whereas those with prior infection may have been less likely to seek testing.

The CDC Kentucky MMWR study https://www.cdc.gov/mmwr/volumes/70/wr/mm7032e1.htm didn't ask quite the same question – that study was aimed at determining whether vaccination after natural infection adds additional protection. The answer is clearly yes (2.34x), and the Israeli study showed that too.

Does CDC have a ready meta-analysis of all of the studies that have compared the immunity from natural infection to vaccination? Most of us have been saying up until now that vaccines are actually better for providing immunity – what does the overall synthesis of the data now say?

Francis

From: Fauci, Anthony (NIH/NIAID) [E] <(b) (6)
Sent: Friday, August 27, 2021 2:37 PM
To: Murthy, Vivek (HHS/OASH) <Vivek.Murthy@hhs.gov>; Collins, Francis (NIH/OD) [E] (b) (6)>; Walensky, Rochelle (CDC/OD) <aux7@cdc.gov>; Eric Lander (b) (6); Brooks, John T. (CDC/DDID/NCHHSTP/DHP) <zud4@CDC.GOV>
Cc: Beckman, Adam (HHS/OASH) <Adam.Beckman@hhs.gov>
Subject: RE: Post infection protection vs vaccine immunity

The data as reported in the news article look rather impressive despite the caveat that it is a retrospective study and the testing was voluntary. I have not seen the details of the actual data, but I would imagine that it is more complicated than we think. It very well may be that people who have had an asymptomatic or minimally symptomatic infection (upper airway only) will not have a greater post-infection protection against subsequent infection then those who get fully vaccinated. However, it is conceivable and possibly likely that those who have had a serious systemic infection develop a high level of immunity that even surpasses

that of full vaccination. I would like to see if they broke the data on the infected people down into those two groups.

Anthony S. Fauci, MD
Director
National Institute of Allergy and Infectious Diseases
Building 31, Room 7A-03
31 Center Drive, MSC 2520
National Institutes of Health
Bethesda, MD 20892-2520
Phone: (b) (6)
FAX: (301) 496-4409
E-mail: (b) (6)

From: Murthy, Vivek (HHS/OASH) <Vivek.Murthy@hhs.gov>
Sent: Friday, August 27, 2021 1:57 PM
To: Collins, Francis (NIH/OD) [E] <(b) (6); Fauci, Anthony (NIH/NIAID) [E] (b) (6); Walensky, Rochelle (CDC/OD) <aux7@cdc.gov>; Eric Lander (b) (6)>; Brooks, John T. (CDC/DDID/NCHHSTP/DHP) <zud4@CDC.GOV>
Cc: Beckman, Adam (HHS/OASH) <Adam.Beckman@hhs.gov>
Subject: Post infection protection vs vaccine immunity

Do you have thoughts on this recent study from Israel? And how this fits with the recent MMWR findings (Kentucky study showing higher risk of reinfection in the unvaccinated compared to risk of infection in the vaccinated)?

https://www.sciencemag.org/news/2021/08/having-sars-cov-2-once-confers-much-greater-immunity-vaccine-no-infection-parties

Having SARS-CoV-2 once confers much greater immunity than a vaccine—but no infection parties, please | Science | AAAS

Having SARS-CoV-2 once confers much greater immunity than a vaccine—but no infection parties, please. By Meredith

Wadman Aug. 26, 2021 , 8:02 PM. The natural immune protection that develops ...

www.sciencemag.org

From: Collins, Francis (NIH/OD) [E]
Sent: Tue, 31 Aug 2021 18:05:32 -0500
To: Fauci, Anthony (NIH/NIAID) [E]
Cc: Lane, Cliff (NIH/NIAID) [E];Mascola, John (NIH/VRC) [E]
Subject: RE: Post infection protection vs vaccine immunity

Thanks! That's a slide set I hadn't seen – very impressive.

FC

From: Fauci, Anthony (NIH/NIAID) [E] <(b) (6)
Sent: Tuesday, August 31, 2021 6:59 PM
To: Collins, Francis (NIH/OD) [E] (b) (6)>
Cc: Lane, Cliff (NIH/NIAID) [E] (b) (6); Mascola, John (NIH/VRC) [E] (b) (6)
Subject: RE: Post infection protection vs vaccine immunity

Francis:
It is in the attached slide-set that the Israelis sent to me. It is shown on slides #7 and #18.
Best,
Tony

From: Collins, Francis (NIH/OD) [E] (b) (6)
Sent: Tuesday, August 31, 2021 6:27 PM
To: Fauci, Anthony (NIH/NIAID) [E] (b) (6)
Cc: Lane, Cliff (NIH/NIAID) [E] (b) (6) Mascola, John (NIH/VRC) [E] (b) (6)>
Subject: FW: Post infection protection vs vaccine immunity

Hi Tony,

I went back to this paper after our discussion just now to look for the conclusion about reduction of R0 after boosters. And I don't see it – does that come from a different source?

Francis

From: Fauci, Anthony (NIH/NIAID) [E] (b) (6)>
Sent: Saturday, August 28, 2021 1:58 PM
To: Follmann, Dean (NIH/NIAID) [E] <(b) (6)>; Lane, Cliff (NIH/NIAID) [E] (b) (6)

Cc: Collins, Francis (NIH/OD) [E] (b) (6)>
Subject: FW: Post infection protection vs vaccine immunity

Dean:

Please see John Brooks's concern about the data in the Israeli paper. Is there any validity to his concern? The data are really rather impressive and it would be important to determine the strength of their validity. Please take a look at this paper and help us determine if it is in fact a strong study. I hate to impose upon you about this , but this is really an important issue . Many thanks.

Best regards,

Tony

Anthony S. Fauci, MD
Director
National Institute of Allergy and Infectious Diseases
Building 31, Room 7A-03
31 Center Drive, MSC 2520
National Institutes of Health
Bethesda, MD 20892-2520
Phone: (b) (6)
FAX: (301) 496-4409
E-mail: (b) (6)

From: Brooks, John T. (CDC/DDID/NCHHSTP/DHP) <zud4@cdc.gov>
Sent: Friday, August 27, 2021 5:14 PM
To: Fauci, Anthony (NIH/NIAID) [E] (b) (6); Murthy, Vivek (HHS/OASH) <Vivek.Murthy@hhs.gov>; Collins, Francis (NIH/OD) [E] <(b) (6)>; Walensky, Rochelle (CDC/OD) <aux7@cdc.gov>; Eric Lander (b) (6)>
Cc: Beckman, Adam (HHS/OASH) <Adam.Beckman@hhs.gov>
Subject: RE: Post infection protection vs vaccine immunity

I also received this paper today from Israeli colleagues (attached) in which they present evidence that their booster program has restored the loss in vaccine effectiveness that had been observed among persons fully vaccinated with the 2-dose Pfizer vaccine series in whom VE against infection was decreasing.

They used two basic approaches to analyze these retrospective data: a series of Poisson regressions and a case-control matching method. All analyses point in the same direction and the results seem impressive.

I am a having trouble wrapping my head around how they detected such a potent effect of an intervention started in late July and delivered to about 3 M Israelis in just a few weeks. It just seemed mighty fast, but perhaps in this case the anamnestic response primed by prior vaccination kicked in hard and fast.

As I digest this one (with the sage input of smarter colleagues here whose career work is VE), I wanted to ensure all were aware the paper is out there.

-john

John T. Brooks, MD
Chief Medical Officer, CDC COVID-19 Response
Email: zud4@cdc.gov
Apologies for errors in my messages that may be due to my need to dictate.

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To: Murthy, Vivek (HHS/OASH) <Vivek.Murthy@hhs.gov>; Collins, Francis (NIH/OD) [E] (b) (6) Walensky, Rochelle (CDC/OD) <aux7@cdc.gov>; Eric Lander (b) (6) Brooks, John T. (CDC/DDID/NCHHSTP/DHP) <zud4@cdc.gov>
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Phone: (b) (6)
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Sent: Friday, August 27, 2021 1:57 PM
To: Collins, Francis (NIH/OD) [E] <(b) (6)>; Fauci, Anthony (NIH/NIAID) [E] <(b) (6); Walensky, Rochelle (CDC/OD) <aux7@cdc.gov>; Eric Lander (b) (6); Brooks, John T. (CDC/DDID/NCHHSTP/DHP) <zud4@CDC.GOV>
Cc: Beckman, Adam (HHS/OASH) <Adam.Beckman@hhs.gov>
Subject: Post infection protection vs vaccine immunity

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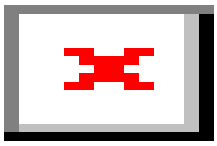
https://www.sciencemag.org/news/2021/08/having-sars-cov-2-once-confers-much-greater-immunity-vaccine-no-infection-parties



[Having SARS-CoV-2 once confers much greater immunity than a vaccine—but no infection parties, please | Science | AAAS]

Having SARS-CoV-2 once confers much greater immunity than a vaccine—but no infection parties, please. By Meredith Wadman Aug. 26, 2021 , 8:02 PM. The natural immune protection that develops …

www.sciencemag.org

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
Freedom of Information Office
Building 1, Room 344
1 Center Drive, MSC 0188
Bethesda, Maryland 20892-0188
phone: (301) 496-5633
fax: (301) 402-4541

Via Email: GLawkowski@Dhillonlaw.com

December 10, 2024

Gary Lawkowski
Dhillon Law Group, Inc.
2121 Eisenhower Avenue
Suite 402
Alexandria, VA 22314

Re: NIH FOIA Case No.: 57539; Protect the Public's Trust v. NIH, Case No. 22-cv-0866

Dear Mr. Lawkowski:

This is a partial response to the Freedom of Information Act (FOIA) request that is the subject of the complaint filed in *Protect the Public's Trust v. NIH, Case No. 22-cv-0866*, now pending in the U.S. District Court for the District of Columbia. Your FOIA request, dated December 20, 2021, was received by the National Institutes of Health Office of the Director on the same day.

You requested records relating to both the Center for Disease Control (CDC) and NIH's publicized statements by senior leadership on a scientific study purported to demonstrate vaccination offers higher protection than previous infection with COVID-19. Specifically, you requested:

> 1. Meeting Requests: All records for meeting requests, meeting memos, briefing documents, schedules, communications, and any other records related to preparation, dissemination, and press scheduling related to the press release on August 6, 2021 titled, "New CDC Study: Vaccination Offers Higher Protection than Previous COVID-19 Infection,"[1] and any and all of the same documents regarding NIH Director Francis Collins' subsequent statements made to the media on the study titled "Reduced Risk of Reinfection with SARS-CoV-2 After COVID-19 Vaccination — Kentucky, May–June 2021"[2] ("Kentucky study") highlighted in the release. This also includes meetings discussing, planning, briefing, or scheduling any media appearances or media communications regarding the topic of this study by any employee within the Department of Health and Human Services (HHS), CDC, and NIH, including each division's respective communications and ethics departments.
>
> 2. Internal and External Communications: Any and all internal communications, documents, or other records related to the CDC press release on August 6, 2021, titled, "New CDC Study: Vaccination Offers Higher Protection than Previous COVID-19 Infection," the Kentucky study, and related to any subsequent statements and press appearances made by NIH Director Francis Collins. This includes all communications, documents, briefing materials, and other records to, from or between any party within HHS, the CDC, and NIH.

External communication includes any and all communications, documents, and other records to, from, or between a party within the CDC, NIH, Office of the Secretary, Office of the Assistant Secretary for Public Affairs, Office of the Assistant Secretary for Health and the White House. This includes any documents from the Department's communication staff, and any and all communications between government employees and external media organizations and any other external parties and entities on this subject. The search should include all such communications dating back to June 1 until the date the search begins.

3. Communications pertaining to an article appearing in the Louisville Courier Journal on August 9, 2021, by Deborah Yetter titled "CDC study of Kentuckians disputes Rand Paul, Thomas Massie claims about Covid-19 immunity."[3] The search should include all HHS communications and external affairs offices that may have communicated with or had outreach with Ms. Yetter, her editors, the Louisville Courier Journal, Kevin Kavanagh, or other employees of the organization Health Watch USA prior to prior to publication of the article. For individuals within those offices, search terms should include "Rand Paul" "Thomas Massie" "natural immunity" "Israeli Health Ministry" or related terms.

During this court proceeding you amended your request to the following:

1. From June 1, 2021 through October 27, 2021, records of calendar invitations (along with associated invitations and attachments) and records of meetings concerning press release on August 6, 2021 titled, "New CDC Study: Vaccination Offers Higher Protection than Previous COVID-19 Infection," and NIH Director Francis Collins' subsequent statements made to the media on the study titled "Reduced Risk of Reinfection with SARS-CoV-2 After COVID-19 Vaccination — Kentucky, May–June 2021" highlighted in the release.

2. From June 1, 2021 through October 27, 2021, records of communications between Director Collins and his Chief of Staff, the NIH Communications director, the NIH press secretary, the NIH deputy press secretary, the Office of the Secretary, the Office of the Assistant Secretary for Public Affairs, Office of the Assistant Secretary for Health, and the White House (Executive Office of the President); and communications between Director Collins, his Chief of Staff, the NIH Communications director, the NIH press secretary, the NIH deputy press secretary, the Office of the Secretary, the Office of the Assistant Secretary for Public Affairs, Office of the Assistant Secretary for Health and the press, including Fox News, CNN, the Washington Post, Politico, and Axios, concerning the CDC press release on August 6, 2021, titled, "New CDC Study: Vaccination Offers Higher Protection than Previous COVID-19 Infection," and/or the Kentucky study.

3. From June 1, 2021 to October 27, 2021, Communications between Director Collins, his Chief of Staff, the NIH Communications director, the NIH press secretary, the NIH deputy press secretary, the Office of the Secretary, the Office of the Assistant Secretary for Public Affairs, Office of the Assistant Secretary for Health and the Louisville Courier Journal and/or Deborah Yetter.

Attached to this letter are 337 pages that have been returned to us from consultation. This completes our production of records responsive to this case.

I have determined to withhold portions of the enclosed pages under FOIA exemption (b)(6). The information being withheld is protected from release pursuant to Exemptions 6 of the FOIA, 5 U.S.C. § 552 (b)(6); and section 5.31(f) of the HHS FOIA Regulations, 45 CFR Part 5. Exemption 6 permits the withholding of privacy information, the release of which would constitute a clearly unwarranted invasion of personal privacy.

Please direct any questions regarding this response to Stephanie Johnson of the Department of Justice, who can be reached at stephanie.johnson5@usdoj.gov.

Sincerely,

KAREN E. LAMPE -S

Digitally signed by KAREN E. LAMPE -S
Date: 2024.12.10 12:53:38 -06'00'

for Gorka Garcia-Malene
Freedom of Information Act Officer, NIH