

Summary of Evidence Related to COVID-19 Vaccine Effectiveness and Breakthrough Infections

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COVID-19 Literature Report Team:

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There are currently three COVID-19 vaccines authorized under an Emergency Use Authorization in the US and across the US, everyone 16 years or older is currently eligible for vaccination with at least one of the vaccines, with expansion of eligibility down to age 12 likely soon. The vaccine coverage among eligible individuals remains uneven, but high coverage among adults has been achieved in some settings. While all currently authorized vaccines have high or very high effectiveness to prevent both SARS-CoV-2 infection and COVID-19 disease, some vaccinated individual do become infected with SARS-CoV-2, resulting in what is referred to as a “breakthrough infection”. **This document is a brief summary of published evidence related to COVID-19 vaccine effectiveness and breakthrough infections. Included are manuscripts published in peer-reviewed journals or on pre-print servers through May 12, 2021.** References summarized in this report were drawn from the COVID-19 Literature Report (Lit Rep) team database. **References that appeared in the daily Lit Rep are marked with an asterisk***, and the summary is shown in the annotated bibliography below.

Executive Summary of Evidence Related to COVID-19 Vaccine Efficacy and Breakthrough Infections

- **All COVID-19 vaccines currently authorized for use under an Emergency Use Authorization in the US (Pfizer-BioNTech, Moderna, and Johnson & Johnson-Janssen) showed high vaccine efficacy (66% to 95%) to prevent COVID-19 disease in phase 3 efficacy trials.**
- **Real-world effectiveness of the currently authorized vaccines has matched the efficacy observed in the trial results.**
- **Effectiveness of the currently authorized vaccines has been similar across all age groups, but there is some indication that breakthrough infections are somewhat more common among older individuals and those who may be immunocompromised, including recipients of solid organ transplants.**
- **Vaccine effectiveness has been high among residents and staff in skilled nursing facilities, with some indication that nursing home residents who have recovered from a past SARS-CoV-2 infection tend to mount more robust immune responses following vaccination. Partial vaccination has shown >60% effectiveness among nursing home residents.**
- **Vaccinated individuals who subsequently become infected with SARS-CoV-2 are more likely to have asymptomatic or milder cases of COVID-19 and have lower viral loads compared to unvaccinated individuals who become infected. There is also direct and indirect evidence that vaccinated individuals who become infected are less likely to transmit the virus to others.**

- All vaccines currently authorized for use in the US have shown effectiveness against the B.1.1.7 variant of SARS-CoV-1 that is comparable to earlier viral strains.
- Vaccine-induced immune responses show lower levels of neutralization against the B.1.351 and P.1 variants in laboratory tests, but the effectiveness of the currently authorized vaccines do not appear to be diminished to a substantial degree against B.1.351 or P.1, particularly for prevention of severe disease.
- Similarly lower neutralization has been observed against a number of the newer variants of concern, but there is no evidence at this time that the vaccine effectiveness is reduced against any of these variants. There is not yet enough evidence to draw strong conclusions about the effectiveness of vaccines against the newest emerging variants.

Summary of Vaccine Effectiveness

Pfizer-BioNTech

The efficacy trial results used to support Emergency Use Authorization of the 2-dose mRNA Pfizer-BioNTech vaccine (BNT162b2) showed a **vaccine efficacy of 95%**, with 8 cases of COVID-19 (1 severe case) in the vaccine group and 162 cases (9 severe cases) in the placebo group (n=21,720 in vaccine group, and 21,728 in placebo group) ([Polack*](#)). Efficacy was similar across subgroups defined by age, sex, race, ethnicity, body-mass index, and presence of co-existing conditions.

There is consistent evidence from multiple countries and settings that the **Pfizer-BioNTech vaccine has maintained high effectiveness (85% to 95%) in real-world settings** ([Haas*](#), [Tang*](#), [Vasileiou*](#), [Hall*](#), [Goldberg*](#), [Bjork*](#), [Jones*](#)), with preliminary evidence that wide-scale immunization of the population has resulted in declines in the community incidence of infection and cases of severe disease and death ([Rossman*](#), [Salazar*](#)). At 21-44 days after a single vaccine dose, vaccine effectiveness was 72% in a large population-based study in the UK ([Menni*](#)).

Impact of variants of concern on the Pfizer-BioNTech vaccine effectiveness

The Pfizer-BioNTech COVID-19 vaccine has shown comparable effectiveness against the B.1.1.7 variant relative to the strains circulating at the time of the original efficacy trial ([Munitz*](#), [Abu-Raddad*](#), [Haas*](#)). There is less direct evidence of the vaccine's effectiveness against the B.1.351 and P.1 variants, but recent evidence indicates that the Pfizer-BioNTech vaccine is 75% effective against the B.1.351 variant 14 days after the second dose ([Abu-Raddad*](#), [Kustin*](#)). *In vitro* neutralization assays show lower neutralization activity against these variants, although there is general consensus that the observed decrease in neutralization is unlikely to dramatically affect the vaccine effectiveness against these variants ([Stankov*](#), [Lustig*](#), [Bates*](#), [Jangra*](#)). There is similar indirect evidence of maintained effectiveness against a number of the newer emerging variants (e.g., B.1.429, B.1.427, B.1.617, R.1).

Moderna

The efficacy trial results used to support Emergency Use Authorization of the 2-dose mRNA Moderna vaccine (mRNA-1273) showed **94% efficacy at preventing COVID-19**, including severe disease (n=15,210 placebo, 15,210 vaccine) ([Baden*](#)). Efficacy was similar across key secondary analyses, including in participants who had evidence of SARS-CoV-2 infection at baseline and analyses in participants 65 years of age or older. Serious adverse events were rare, and the incidence was similar to placebo.

The **Moderna vaccine has demonstrated high real-world effectiveness** ([Andrejko*](#)), including evidence that **partial immunization may lower the risk of hospitalization by 77% and the risk of death by 64%** ([Vahidy*](#))

Impact of variants of concern on the Moderna vaccine effectiveness

The ability of sera from individuals vaccinated with the Moderna vaccine to neutralize a number of the variants of concern, particularly B.1.351, has been shown to be lower than for early strains of SARS-CoV-2 ([Edara*](#)). However, there is currently no evidence that the effectiveness of the Moderna vaccine is substantially lower against the currently circulating variants.

Johnson & Johnson-Janssen

The efficacy trial results used to support Emergency Use Authorization of the 1-dose Johnson & Johnson-Janssen vaccine (Ad26.COV2.S) showed **66% efficacy at preventing moderate to severe–critical COVID-19 and a 77% efficacy for prevention of severe–critical COVID-19** (n=19,691 placebo, 19,630 vaccine) ([Sadoff*](#)). There is some evidence that the Johnson & Johnson-Janssen vaccine is associated with very rare but serious and sometime fatal blood clots. A review by the FDA and CDC concluded that the benefits of the vaccine outweigh the risks and have resumed authorization of the vaccine after a short pause to review the evidence of these side effects ([MacNeil*](#))

Impact of variants of concern on the Johnson & Johnson-Janssen vaccine effectiveness

The efficacy of the Johnson & Johnson-Janssen vaccine to protect against severe to critical COVID-19 was equivalent in South Africa (82% at ≥28 days after vaccination), where the B.1.351 variants accounted for 95% of infections, compared to other regions where the B.1.351 variant was not circulating (86% in the US and 88% in Brazil) ([FDA*](#), [Sadoff*](#)). The efficacy of the Johnson & Johnson-Janssen vaccine against moderate COVID-19 was somewhat lower in South Africa (64%) compared to the US (72%) and Brazil (82%).

Variants of Concern and Vaccine Effectiveness

A list of variants of concern is maintained by the [CDC](#), including a summary of evidence regarding the susceptibility of each variant to the current vaccines. Overall, **all vaccines currently authorized for use in the US have shown high effectiveness against all variants of concern** ([Lustig*](#), [Munitz*](#), [Stankov*](#), [Goel*](#)), although the effectiveness may be somewhat lower compared to earlier strains of the virus, particularly for prevention of asymptomatic or mild to moderate illness ([Sadoff*](#)). Across all of the vaccines currently authorized for use in the US, **effectiveness appears to be similar against the B.1.1.7 variant** compared to other viral lineages ([Emary*](#), [Abu-Raddad*](#)). The Pfizer-BioNTech vaccine was found to be **75% effective against the B.1.351 variant** 14 days after the second dose in a population-based study from Qatar ([Abu-Raddad*](#)). The AstraZeneca vaccine, which is not currently authorized for use in the US but is widely used around the world, has shown dramatically lower efficacy (~10%) against mild or moderate COVID-19 caused by the B.1.351 variant ([Madhi*](#)).

Across multiple studies, neutralization assays indicate somewhat lower neutralization activity against the B.1.1.7 variant compared to other viral lineages ([Xie*](#), [Wu*](#), [Weisblum](#), [Supasa*](#), [Edara*](#), [Chang*](#), [Trinite*](#)). **Authors have generally concluded that these modest reductions in neutralization activity are unlikely to result in reduced vaccine efficacy. Considerably larger reductions in neutralizing activity against the B.1.351 variant have been observed** ([Garcia-Beltran*](#), [Liu*](#), [Wu*](#), [Diamond*](#), [Fisher*](#),

[Becker*](#), [Chen*](#)) and authors have expressed concerns that this could indicate lower vaccine efficacy against B.1.351. Evidence has varied regarding the susceptibility of the P.1 variant, which was first described in Brazil, to vaccine-induced neutralization, but it appears that P.1 may be more susceptible to vaccine neutralization than the B.1.351 variant ([Dejnirattisai*](#), [Wang*](#)). **Administration of a third booster dose of the Moderna vaccine 6 months after the two-dose series induced increases in antibody neutralization titers to the wild type and variant strains B.1.351 and P.1** ([Wu](#)). However, the relationship between levels of *in vitro* neutralization and actual vaccine effectiveness remains unclear and there is no currently accepted correlate of immunity.

Breakthrough Infections

Prevention of asymptomatic infection and effectiveness of partial vaccination

In addition to preventing symptomatic infections, there is evidence that vaccination is also effective at preventing asymptomatic infection ([Tande*](#), [Angel*](#)). At least over a relatively short period of follow-up, partial vaccination with only one dose of the Pfizer-BioNTech, Moderna, and Oxford-AstraZeneca vaccines has shown a level of effectiveness that is slightly lower but approaching the level of protection seen with full vaccination ([Menni*](#), [Bouton*](#), [Yelin*](#), [Britton*](#), [Krammer*](#), [Moustsen-Helms*](#), [Bernal*](#), [Saul*](#), [Manisty*](#), [Romero-Brufau*](#)).

Disease severity and viral load in vaccinated individuals who become infected

While infections with SARS-CoV-2 occur among individuals who have been vaccinated with one of the vaccines authorized for use in the US ([Hacisuleyman*](#)), there is **consistent evidence that such infections are more likely to be asymptomatic or of lower severity compared to unvaccinated individuals** of comparable age and health status ([Hollingshurst*](#), [Moustsen-Helms*](#), [Britton*](#), [Gray*](#)). Additionally, viral loads measured in vaccinated individuals who become infected with SARS-CoV-2 tend to be lower than in unvaccinated individuals, even following a single dose of the Pfizer-BioNTech vaccine ([Jones*](#)), indicating that the risk of secondary transmission from infected vaccinated individuals may be reduced ([Harris*](#)). These findings appear to be consistent across the viral variants of concern that have been widely circulating as vaccination rollout has occurred (e.g., B.1.1.7, B.1.351, P.1), but there is not yet clear direct evidence for or against protection against more severe illness or lower viral loads for newer emerging variants.

Factors associated with breakthrough infections

In the efficacy trials conducted in advance of Emergency Use Authorization, the currently authorized vaccines showed similar efficacy across all age groups. Under real-world conditions, there is some indication that breakthrough infections are somewhat **more common among older individuals** ([Nace*](#), [Canaday*](#)) and those who may be immunocompromised ([Chavarot*](#), [Herishanu*](#), [Grupper*](#), [Simon*](#), [Yelin*](#), [Pellini*](#), [Monin*](#)), including recipients of solid organ transplants ([Boyarsky*](#), [Rozen-Zvi*](#)), although no strong associations have been observed between age and vaccine effectiveness ([Vahidy*](#)). Among those over age 65 years, mRNA vaccines were 94% effective against hospitalization for COVID-19 among fully vaccinated individuals in the US and 64% effective among partially-vaccinated individuals ([Tenforde*](#)), but antibody titers following vaccination have been observed to be lower among those older than 80 years compared to those younger than 60 ([Müller*](#)). There is some indication that antibody responses after the first vaccine dose may be lower among **pregnant and lactating women** but comparable to non-pregnant women after the second dose ([Atyeo*](#), [Rottenstreich*](#), [Prabhu*](#)). There is some indication that individuals who have **previously been infected with SARS-CoV-2 and have recovered tend to mount more rapid and robust immune responses following a first vaccine dose** compared to SARS-CoV-2-naïve individuals ([Anichini*](#), [Mishra*](#), [Ebinger*](#)), including among nursing

home residents ([Blain*](#), [Van* Praet*](#)), which may indicate more rapid protection from subsequent infection among vaccinated individuals who have recovered from a previous infection. However, there is currently no evidence to indicate whether previous infection is associated with higher vaccine efficacy at ≥ 14 days after a second vaccine dose (or after the first dose for the Johnson & Johnson-Janssen vaccine).

Skilled nursing facilities

The widespread vaccination of residents and staff in skilled nursing facilities (SNFs) has provided direct evidence of the real-world effectiveness of the currently authorized vaccines in this population, with indication that the **vaccines have remained highly effective among SNF residents and staff**. In Chicago between December 2020 and March 2021, during which an estimated 7,931 SNF residents and 6,834 staff members received two doses of COVID-19 vaccine, a total of 627 SARS-CoV-2 infections in residents (n=353) and staff (n=274) were identified across 78 SNFs ([Teran*](#)). Of these infections, 71% occurred in unvaccinated individuals, 23% in partially vaccinated, 2% in those with 2 vaccine doses but within < 14 days of the second dose, and 4% in fully vaccinated individuals. The rollout of vaccinations coincided with a sharp drop in the incidence of infections in this population. In a separate investigation in Kentucky among SNF residents and healthcare personnel (HCP), compared to those who were vaccinated, unvaccinated residents had a 3-fold higher risk of SARS-CoV-2 infection and unvaccinated HCPs had a 4.1-fold higher risk, indicating that vaccine effectiveness was similar among residents and HCPs ([Cavanaugh*](#)). This investigation was conducted at a time when the R.1 variant was widely circulating. Partial vaccination of nursing home residents with the Pfizer-BioNTech vaccine was found to be 63% effective at preventing infection with SARS-CoV-2 ([Britton*](#)).

Healthcare workers

Healthcare workers were among the first to be prioritized for vaccination and there is now clear evidence of high vaccine effectiveness among healthcare workers. In large cohort studies of healthcare workers, the currently authorized mRNA vaccines have shown to be 85% to greater than 95% effective in preventing PCR-confirmed SARS-CoV-2 infection following two doses, with 70% to 78% effectiveness among those who had received only one dose of the vaccine ([Swift*](#), [Hall*](#), [Angel*](#), [Tang*](#)). Similarly, in the UK, an increase in vaccine coverage up to 83% with a single vaccine dose was associated with significant reductions in symptomatic and asymptomatic cases of SARS-CoV-2 ([Lillie*](#)).

Other Resources

- [CDC: COVID-19 Breakthrough Case Investigations and Reporting](#)
- [SARS-CoV-2 Variant Classifications and Definitions](#)

Annotated Bibliography

Abu-Raddad et al. (May 2021). Effectiveness of the BNT162b2 Covid-19 Vaccine against the B.1.1.7 and B.1.351 Variants. The New England Journal of Medicine. <https://doi.org/10.1056/NEJMc2104974>

- The Pfizer-BioNTech vaccine was 90% effective against PCR-confirmed infection with the SARS-CoV-2 variant B.1.1.7 and 75% effective against the B.1351 variant 14 days after the second dose, according to a nationwide case-control analysis in Qatar through March 2021. Individuals with positive and negative PCR tests were matched on demographics and reason for PCR testing to account for differences in health-seeking behavior. A separate cohort analysis comparing incidence

of infection in vaccinated persons and in a national cohort who were SARS-CoV-2 antibody-negative supported the findings with an estimated vaccine effectiveness of 87% against the B.1.1.7 variant and 72% against the B.1.351 variant. Vaccine effectiveness against severe, critical, or fatal SARS-CoV-2 infection from infection with any variant was 97%. Researchers were able to assess vaccine effectiveness against infection from variants of concern because by March 2021 in Qatar, roughly half of sequenced cases were B.1.351 infections and roughly 45% were B.1.1.7 infections. Breakthrough infections have been recorded in 1,616 of 265,410 (0.6%) persons vaccinated with two doses.

Andrejko et al. (Apr 10, 2021). Early Evidence of COVID-19 Vaccine Effectiveness within the General Population of California. Pre-print downloaded Apr 12 from

<https://doi.org/10.1101/2021.04.08.21255135>

- [Pre-print, not peer-reviewed] Fully immunized individuals (either Pfizer-BioNTech or Moderna) experienced 86% protection against SARS-CoV-2 infection, and partial protection was observed following the first dose (66%) and in the first two weeks after receipt of a second dose (78%) in a case-control study conducted from February 24 to April 7, 2021. Cases were defined by a positive SARS-CoV-2 test and controls by a negative test. Among cases (n = 325), 23 (7%) and 13 (4%) received the Pfizer-BioNTech and Moderna vaccines, respectively, and 8 (2%) were fully vaccinated while among controls 49 (19%) and 49 (19%) received Pfizer-BioNTech and Moderna, respectively; 42 (16%) were fully vaccinated. Hesitancy to receive COVID-19 vaccines (when eligible) was reported among 39% and 23% of unvaccinated participants residing in rural and urban regions, respectively.

Angel et al. (May 6, 2021). Association Between Vaccination With BNT162b2 and Incidence of Symptomatic and Asymptomatic SARS-CoV-2 Infections Among Health Care Workers. JAMA.

<https://jamanetwork.com/journals/jama/fullarticle/2779853>

- The Pfizer-BioNTech vaccine was associated with a 93% lower incidence of symptomatic SARS-CoV-2 infection and 86% lower incidence of asymptomatic infection more than 7 days after the second dose in a retrospective cohort of healthcare workers (HCWs) in Israel (n=6,710). The median follow-up period was 63 days. While vaccination was associated with older age and male sex, a sensitivity analysis using propensity score matching found similar results. HCWs with prior SARS-CoV-2 infection were excluded from the study.

Anichini et al. (Apr 14, 2021). SARS-CoV-2 Antibody Response in Persons with Past Natural Infection. New England Journal of Medicine. <https://doi.org/10.1056/NEJMc2103825>

- Vaccine-elicited neutralizing antibody geometric mean titers (GMT) among healthcare workers who received the first dose of the Pfizer-BioNTech vaccine 1-2 months, 2-3 months, and more than 3 months after a prior SARS-CoV-2 infection were 437, 559, and 694 arbitrary units/mL, respectively. In contrast, healthcare workers with no prior infection had a GMT of 118 units/mL after receiving the second dose, consistent with other studies. The findings from this cohort study (n=100; 38 with prior infection) indicate a higher neutralizing antibody response when the vaccine was administered more than 3 months after infection.

Atyeo et al. (Apr 5, 2021). COVID-19 mRNA Vaccines Drive Differential Fc-Functional Profiles in Pregnant Lactating and Non-Pregnant Women. Pre-print downloaded Apr 6 from

<https://doi.org/10.1101/2021.04.04.438404>

- *[Pre-print, not peer-reviewed]* The antibody response induced by mRNA vaccines (Moderna and Pfizer-BioNTech) after the first dose was lower among pregnant (n=84) and lactating (n=31) women compared to non-pregnant age-matched controls (n=16), but after the second dose no significant differences were observed. Differences in antibody response after the first dose related to lower antibody titers and delayed kinetics in Fc-receptor-binding and antibody effector functions.

Baden et al. (Dec 30, 2020). Efficacy and Safety of the MRNA-1273 SARS-CoV-2 Vaccine. New England Journal of Medicine. <https://doi.org/10.1056/NEJMoa2035389>

- Results from a phase 3 randomized, observer-blinded, placebo-controlled trial of the Moderna SARS-CoV-2 vaccine candidate (mRNA-1273) indicated that the vaccine showed 94.1% efficacy at preventing COVID-19, including severe disease. The trial enrolled 30,420 volunteers, and symptomatic illness was confirmed in 185 participants in the placebo group and in 11 participants in the vaccine group. Efficacy was similar across key secondary analyses, including in participants who had evidence of SARS-CoV-2 infection at baseline and analyses in participants 65 years of age or older. Severe COVID-19 occurred in 30 participants, with one fatality; all 30 were in the placebo group. Serious adverse events were rare, and the incidence was similar in the two groups.

Bates et al. (Apr 9, 2021). Neutralization of SARS-CoV-2 Variants by Convalescent and Vaccinated Serum. Pre-print downloaded Apr 12 from <https://doi.org/10.1101/2021.04.04.21254881>

- *[Pre-print, not peer-reviewed]* Sera from convalescent individuals (n = 44) and individuals who received the Pfizer-BioNTech vaccine (n = 51) showed reduced neutralization activity against the SARS-CoV-2 B.1.1.7 and B.1.351 variants. Among vaccinated individuals, the geometric mean 50% receptor binding domain (RBD) antibody concentration was 1.3-fold lower for the B.1.1.7 variant and 1.4-fold lower for the B.1.351 variant. Age was negatively correlated with neutralization among vaccinated individuals, and levels of variant-specific RBD antibodies were proportional to neutralizing activity.

Becker et al. (Mar 10, 2021). Immune Response to SARS-CoV-2 Variants of Concern in Vaccinated Individuals. Pre-print downloaded Mar 11 from <https://doi.org/10.1101/2021.03.08.21252958>

- *[Pre-print, not peer-reviewed]* Sera from both individuals with prior SARS-CoV-2 infection (n=35) and individuals fully vaccinated with the Pfizer-BioNTech vaccine (n=23) showed nearly identical antibody binding responses against the B.1.1.7 Cluster 5 and CAL.20C variants compared to wild-type SARS-CoV-2. In contrast, both binding and neutralizing antibody responses among vaccinated individuals were diminished against the B.1.351 variant compared to wild-type SARS-CoV-2, although the 2nd vaccine dose appeared to confer increased neutralization capacities. In a separate analysis, the authors found that individuals with prior SARS-CoV-2 infection had higher IgA antibody titers in saliva, while vaccinated individuals had high IgG titers.

Bernal et al. (Mar 2, 2021). Early Effectiveness of COVID-19 Vaccination with BNT162b2 MRNA Vaccine and ChAdOx1 Adenovirus Vector Vaccine on Symptomatic Disease Hospitalisations and Mortality in Older Adults in England. Pre-print downloaded Mar 3 from <https://doi.org/10.1101/2021.03.01.21252652>

- *[Pre-print, not peer-reviewed]* A study of the real-world effectiveness of the Pfizer-BioNTech and Oxford-AstraZeneca vaccines in the UK indicated that vaccination with a single dose of either vaccine was associated with a significant reduction in symptomatic COVID-19 cases in older adults,

with strong protection against severe disease. Effects of the Pfizer-BioNTech vaccine among adults 80 and older were observed 10-13 days after vaccination, reaching an effectiveness of 70% from 28-34 days. From 14 days after the second dose, vaccine efficacy was 89%. For those 70 and older, vaccine effectiveness reached 61% from 28-34 days after vaccination. With the Oxford-AstraZeneca vaccine, vaccine effects were seen from 14-20 days after vaccination, efficacy was 60% from 28-34 days, and increased to 73% from day 35 onwards.

Bjork et al. (Apr 21, 2021). Effectiveness of the BNT162b2 Vaccine in Preventing COVID-19 in the Working Age Population - First Results from a Cohort Study in Southern Sweden. Pre-print downloaded Apr 22 from <https://www.medrxiv.org/content/10.1101/2021.04.20.21254636v1>

- [Pre-print, not peer-reviewed] The Pfizer-BioNTech vaccine was 86% effective in preventing infection >7 days after the second dose in a cohort study (n=806,000) in Sweden from December 2020 to February 2021. Effectiveness was only 42% >14 days after a single dose. The vaccinated population largely consisted of healthcare workers. SARS-CoV-2 incidence among unvaccinated individuals with a prior positive PCR test was considerably lower than among those without a prior positive test (28 vs. 294 cases per 100,000 person-weeks), suggesting that prior SARS-CoV-2 infection is 91% effective in preventing subsequent infection.

Blain et al. (Apr 15, 2021). Spike Antibody Levels of Nursing Home Residents With or Without Prior COVID-19 3 Weeks After a Single BNT162b2 Vaccine Dose. JAMA. <https://jamanetwork.com/journals/jama/fullarticle/2778926>

- Nursing home residents with a past history of COVID-19 were far more likely than those without a history of COVID-19 to mount an antibody response to the first dose of the Pfizer-BioNTech vaccine. Among a cohort of nursing home residents in France, all 36 residents with prior COVID-19 were seropositive for anti-spike (S) IgG antibodies after one Pfizer-BioNTech vaccine dose compared to 29 (48%) of 60 residents without prior COVID-19. The participants were tested for anti-S IgG just prior to receiving the second dose. The anti-S IgG median titer of participants with prior COVID-19 were much higher than of those without prior COVID-19 ($\geq 40,000$ vs 48 AU/mL). Prior to testing, 72% of participants with prior COVID-19 were seropositive for anti-nucleocapsid (N) IgG.

Bouton et al. (Mar 31, 2021). COVID-19 Vaccine Impact on Rates of SARS-CoV-2 Cases and Post Vaccination Strain Sequences among Healthcare Workers at an Urban Academic Medical Center a Prospective Cohort Study. Pre-print downloaded Apr 1 from <https://doi.org/10.1101/2021.03.30.21254655>

- [Pre-print, not peer-reviewed] Among a cohort of healthcare workers (HCW) from Boston Medical Center who received the first dose of either the Pfizer-BioNTech or Moderna vaccines, the SARS-CoV-2 infection rate was 27% and 82% lower 1-14 days and >14 days after receiving the first dose, respectively, compared to surrounding community infection rates. SARS-CoV-2 infections occurred in 1.4% (96 of 7109) of HCWs given at least a first dose and 0.3% (17 of 5913) of HCWs given both doses. SARS-CoV-2 infections >14 days from the first dose were more frequently asymptomatic, among older HCWs, and HCWs of Latinx ethnicity. Analysis of 48 SARS-CoV-2 genomes sequenced from first-dose infections did not indicate selection pressure towards mutations in the spike protein known to escape antibody neutralization.

Boyarsky et al. (Mar 15, 2021). Immunogenicity of a Single Dose of SARS-CoV-2 Messenger RNA Vaccine in Solid Organ Transplant Recipients. JAMA. <https://doi.org/10.1001/jama.2021.4385>

- Solid organ transplant recipients in the US were less likely to develop anti-SARS-CoV-2 antibody responses after receiving a single dose of either the Moderna or Pfizer-BioNTech vaccines. In a prospective convenience sample, only 17% (76 of 436) had detectable antibody responses at a median of 20 days after the first dose. Transplant recipients who were receiving immunosuppression therapy, older transplant recipients, and those vaccinated with the Pfizer-BioNTech vaccine (as compared to the Moderna vaccine) were less likely to develop detectable antibody responses.

Britton et al. (Mar 15, 2021). Effectiveness of the Pfizer-BioNTech COVID-19 Vaccine Among Residents of Two Skilled Nursing Facilities Experiencing COVID-19 Outbreaks — Connecticut, December 2020–February 2021. MMWR. <https://doi.org/10.15585/mmwr.mm7011e3>

- Partial vaccination with the Pfizer-BioNTech COVID-19 vaccine (from >14 days after dose 1 through 7 days after dose 2) was found to be 63% effective against SARS-CoV-2 infection among residents of two skilled nursing facilities in Connecticut that experienced outbreaks from December 2020 – February 2021. Vaccine efficacy was similar (60%) when residents with prior SARS-CoV-2 infection were excluded. The retrospective cohort study determined that 97 cases of SARS-CoV-2 infection occurred during the outbreaks, including 40 (41%) at facility A and 57 (59%) at facility B. By the end of the study, most residents (304, 66%) received 2 vaccine doses, 72 (16%) received only 1 dose, and 87 (19%) were not vaccinated.

Canaday et al. (Mar 22, 2021). Reduced BNT162b2 mRNA Vaccine Response in SARS-CoV-2-Naive Nursing Home Residents. Pre-print downloaded Mar 23 from <https://doi.org/10.1101/2021.03.19.21253920>

- *[Pre-print, not peer-reviewed]* Nursing home (NH) residents had blunted antibody responses following vaccination with BNT162b2 mRNA vaccine (Moderna) when compared to healthcare workers. SARS-CoV-2-naive NH residents mounted antibody responses with nearly 4-fold lower median neutralization titers and half the anti-spike level compared to SARS-CoV-2-naive healthcare workers. In contrast, NH residents who had recovered from infection and were subsequently vaccinated had neutralization, anti-spike, and anti-RBD titers similar to healthcare workers who had recovered from infection and were subsequently vaccinated.

Cavanaugh et al. (Apr 21, 2021). COVID-19 Outbreak Associated with a SARS-CoV-2 R.1 Lineage Variant in a Skilled Nursing Facility After Vaccination Program — Kentucky, March 2021. MMWR. <https://doi.org/10.15585/mmwr.mm7017e2>

- Unvaccinated residents and healthcare personnel (HCP) at a Kentucky skilled nursing facility had a 3 and 4.1-fold higher risk of infection compared to residents and HCP who were vaccinated with the Pfizer-BioNTech mRNA vaccine, respectively, during a SARS-CoV-2 outbreak identified on March 1, 2021. This outbreak was with a newly-introduced variant to the region called “R.1”, which is characterized by E484K and other mutations within the spike protein that have been identified in other variants of concern. 26 residents and 20 HCP tested positive, including 18 residents and four HCP who had received their second vaccine dose >14 days before the outbreak began. Vaccination was 86.5% protective against symptomatic illness among residents and 87.1% protective among HCP.

Chang et al. (Mar 15, 2021). BNT162b2 mRNA COVID-19 Vaccine Induces Antibodies of Broader Cross-Reactivity than Natural Infection but Recognition of Mutant Viruses Is up to 10-Fold Reduced. Pre-print downloaded Mar 16 from <https://doi.org/10.1101/2021.03.13.435222>

- [Pre-print, not peer-reviewed] Antibodies induced by the Pfizer-BioNTech vaccine had higher binding capacities (avidity) than antibodies induced by natural infection against the receptor binding domain (RBD) containing mutations representative of circulating SARS-CoV-2 variants of concern (N501Y, K417N, E484K, and a combination of all three). Vaccine-induced sera (n=6) reduced binding against the RBD containing the N501Y and K417 mutations (2.5-3 fold reduction) compared to wild type RBD. Of note, both the RBD with E484K mutation and RBD with all three mutations reduced binding by ~10-fold, indicating that E484K mutation (found in the B.1.351 and P.1 variant but not in the B.1.1.7 variant) substantially reduces antibody binding.

Chavarot et al. (Apr 8, 2021). Poor Anti-SARS-CoV-2 Humoral and T-Cell Responses After 2 Injections of mRNA Vaccine in Kidney Transplant Recipients Treated with Belatacept. Transplantation. <https://doi.org/10.1097/TP.0000000000003784>

- A study of kidney transplant recipients receiving belatacept (N=101), a drug to prevent organ rejection, found that humoral and T-cell immune response to the Pfizer-BioNTech vaccine was low. Only 2 patients developed spike antibodies 28 days after the first dose and 2 of 35 patients tested one month after the 2nd dose developed antibodies. A specific T-cell response was observed in only 2 of 40 patients tested 28 days after the first dose and in 7 of 23 patients tested 1 month after the 2nd dose. The authors recommend that kidney transplant recipients receiving belatacept should continue to maintain distancing and masking and household members should be vaccinated to maintain protection against COVID-19.

Chen et al. (Mar 4, 2021). Resistance of SARS-CoV-2 Variants to Neutralization by Monoclonal and Serum-Derived Polyclonal Antibodies. Nature Medicine. <https://doi.org/10.1038/s41591-021-01294-w>

- Most convalescent sera from people who had recovered from mild COVID-19 (n=29) and virtually all Pfizer-BioNTech mRNA vaccine-induced immune sera (n=24) were shown to have diminished neutralizing activity against engineered SARS-CoV-2 strains including a chimeric strain combining a strain identified in Washington state with a B.1.351 spike gene (Wash SA-B.1.351 strain), or recombinant viruses containing mutations at position 484 and 501. Several highly neutralizing monoclonal antibodies (mAbs) lost inhibitory activity against Wash SA-B.1.351 or recombinant variants with an E484K spike mutation. The authors note that targeting of highly conserved regions, enhancement of mAb potency, or adjustments to the spike sequences of vaccines may be needed to prevent loss of protection *in vivo*.

Dejnirattisai et al. Antibody Evasion by the Brazilian P.1 Strain of SARS-CoV-2. Pre-print downloaded Mar 16 from <https://doi.org/10.1101/2021.03.12.435194>

- [Pre-print, not peer-reviewed] The SARS-CoV-2 P.1 variant, which has caused large outbreaks in Brazil, is less resistant to neutralization from both convalescent serum and vaccine-induced serum than the B.1.351 variant originally identified in South Africa, despite containing similar receptor binding domain (RBD) mutations (E484K, K417N/T and N501Y). Similar to the B.1.351 variant, mutations associated with the P1 variant completely abrogated the binding of multiple neutralizing antibodies directed against the RBD, including a variety of antibodies currently in development for

therapeutic use. In contrast, the reduction in neutralization activity of convalescent plasma from recovered volunteers against the P.1 variant was only modest (~3-fold reduction versus the ancestral Victoria strain) when compared to the reduction in neutralization observed with B.1.351 variant (~13-fold reduction versus the Victoria strain). Sera from recipients of either the Pfizer-BioNTech or Oxford-AztraZeneca vaccine had similar modest reductions in neutralization activity (~3-fold) when compared to the reductions in neutralization observed with the B.1.351 variant (~8-9 fold).

Diamond et al. (Feb 2021). SARS-CoV-2 Variants Show Resistance to Neutralization by Many Monoclonal and Serum-Derived Polyclonal Antibodies. Research Square. <https://doi.org/10.21203/rs.3.rs-228079/v1>

- [Pre-print, not peer-reviewed] Most convalescent sera from people who had recovered from COVID-19 and virtually all Pfizer-BioNTech mRNA vaccine-induced immune sera were shown to have diminished neutralizing activity against engineered SARS-CoV-2 strains including a chimeric strain combining a strain identified in Washington state with a B.1.351 spike gene (Wash SA-B.1.351 strain), or recombinant viruses containing mutations at position 484 and 501. Several highly neutralizing monoclonal antibodies (mAbs) lost inhibitory activity against Wash SA-B.1.351 or recombinant variants with an E484K spike mutation. The authors note that targeting of highly conserved regions, enhancement of mAb potency, or adjustments to the spike sequences of vaccines may be needed to prevent loss of protection *in vivo*.

Ebinger et al. (Apr 1, 2021). Antibody Responses to the BNT162b2 MRNA Vaccine in Individuals Previously Infected with SARS-CoV-2. Nature Medicine. <https://doi.org/10.1038/s41591-021-01325-6>

- Among healthcare workers in California who received the Pfizer-BioNTech vaccine (n = 1,090), spike-specific IgG antibody levels and ACE2 antibody binding inhibition responses were similar between individuals who had been previously infected with SARS-CoV-2 and received a single dose (n = 35), and those who had no prior infection and received both vaccine doses (n = 228). The study measured participants' antibody levels at three time points: before or up to 3 days after dose 1; within 7–21 days after dose 1; and within 7–21 days after dose 2.

Edara et al. (Mar 2021). Infection- and Vaccine-Induced Antibody Binding and Neutralization of the B.1.351 SARS-CoV-2 Variant. Cell Host & Microbe. <https://doi.org/10.1016/j.chom.2021.03.009>

- Acutely infected COVID-19 patients and those who received the Moderna vaccine had significantly reduced IgG binding to the B.1.351 variant receptor binding domain (RBD) compared to the B.1-lineage RBD-specific IgG response. However, sera containing polyclonal antibodies to the spike protein could still effectively neutralize B.1.351. Individuals with prior infection or vaccinated individuals had a nearly 3-fold reduction in binding antibody titers to the B.1.351 variant against the RBD of the spike protein and a 3.5-fold reduction in neutralizing antibody titers compared to the B.1 variant.

Edara et al. (Mar 19, 2021). Neutralizing Antibodies Against SARS-CoV-2 Variants After Infection and Vaccination. JAMA. <https://doi.org/10.1001/jama.2021.4388>

- Neutralizing antibody activity against four SARS-CoV-2 variants, including B.1, B.1.1.7, and N501Y was maintained in sera from individuals with infection- and vaccine-induced antibodies. There was minimal reductions in serum neutralization observed across four representative SARS-CoV-2 strains. Serum was obtained from adults (n=20) hospitalized with COVID-19 5 to 19 days after symptom

onset, convalescent individuals (n=2) 32 to 94 days after symptom onset, and individuals (n=14) 14 days after the 2nd dose in the Moderna vaccine phase 1 clinical trial. Neutralizing activity was evaluated by “live virus focus reduction neutralization tests” against the A.1 lineage similar to original Wuhan strain, the B.1 lineage containing the D614G mutation that has emerged worldwide, the B.1.1.7 variant originally identified in the UK, and the N501Y engineered variant containing mutation in spike protein present across multiple emerging variants. Neutralizing activity was not significantly different across the four variants for both hospitalized COVID-19 patients and convalescent individuals. Neutralizing activity induced by vaccines was reduced for all strains compared to the original A1 strain but was similar for the B.1, B.1.1.7, and synthetic N501Y strain.

FDA. (Feb 26, 2021). *Janssen Ad26.COVS Vaccine for the Prevention of COVID-19. Vaccines and Related Biological Products Advisory Committee Meeting.* <https://www.fda.gov/media/146217/download>

- The Johnson & Johnson single-dose Ad26.COVS vaccine candidate was determined by the FDA to have met the safety and efficacy requirements for emergency use authorization. Vaccine efficacy against laboratory-confirmed moderate to severe/critical COVID-19 across all geographic areas in which the trial was conducted was 66.9% when considering cases occurring at least 14 days after the single-dose vaccination and 66.1% considering cases occurring at least 28 days after vaccination. Efficacy against severe/critical COVID-19 occurring at least 14 days and at least 28 days after vaccination was 76.7% and 85.4%, respectively. As of February 5, 2021, there were 7 COVID-19 related deaths in the placebo group and no COVID-19 related deaths in the vaccine group. A subset of participants (n=6,736) was followed for self-reported reactions to the vaccine within 7 days following vaccination, and the most common adverse reactions were mild to moderate injection site pain (48.6%), headache (38.9%), fatigue (38.2%), and myalgia (33.2%).

Fisher et al. (Mar 11, 2021). *ChAdOx1 nCoV-19 (AZD1222) protects against SARS-CoV-2 B.1.351 and B.1.1.7.* Pre-print downloaded Mar 12 from <https://doi.org/10.1101/2021.03.11.435000>

- [Pre-print, not peer-reviewed] An investigation of the Oxford-AstraZeneca (ChAdOx1 nCoV-1; AZD1222) vaccine efficacy against SARS-CoV-2 variants of concern B.1.1.7 and B.1.351 in Syrian hamsters showed a 9.5-fold reduction of virus neutralizing antibody titer in vaccinated hamster sera against B.1.351 compared to B.1.1.7. Vaccinated hamsters challenged with B.1.1.7 or B.1.351 did not lose weight compared to control animals.
- Histopathological evaluation showed extensive pulmonary pathology caused by B.1.1.7 or B.1.351 replication in the control animals, but none in the vaccinated animals. No infectious virus and minimal to no viral subgenomic RNA (sgRNA) was detected in lungs of vaccinated animals.

Garcia-Beltran et al. (Feb 18, 2021). *Circulating SARS-CoV-2 Variants Escape Neutralization by Vaccine-Induced Humoral Immunity.* Pre-print downloaded Feb 18 from <https://doi.org/10.1101/2021.02.14.21251704>

- [Pre-print, not peer reviewed] Analysis of neutralizing activity of sera from individuals vaccinated with either 1 or 2 doses of the Moderna or Pfizer vaccines (n=48) against SARS-CoV-2 pseudoviruses bearing spike proteins with the partial or full set of mutations from the B.1.351 variant show up to a 97-fold decrease in neutralization compared to wild-type. Notably, neutralization of B.1.351 was not detectable in samples from 36% (8/22) recipients of 2-dose Pfizer vaccine and 50% (2/4) recipients of 2-dose Moderna vaccine. In contrast, other variants such as the D614G variant, the B.1.1.7 variant, and variants from the P.1 lineage had relatively lower reductions in neutralization.

- Assays conducted with sera from 22 of the 2-dose Pfizer vaccine recipients show that neutralization of B.1.351 in the absence of the mutations present in the receptor binding domain (RBD) was comparable to that of D614G, suggesting that the RBD mutations of the B.1.351 variant are key to neutralization resistance.

Goel et al. (Apr 15, 2021). *Distinct Antibody and Memory B Cell Responses in SARS-CoV-2 Naïve and Recovered Individuals Following mRNA Vaccination*. *Science Immunology*.

<https://doi.org/10.1126/sciimmunol.abi6950>

- A single dose of an mRNA vaccine (Moderna or Pfizer-BioNTech) administered to SARS-CoV-2 naïve individuals produced neutralizing activity against the D614G variant in 50% of recipients and against the B.1.351 variant in 16% of recipients (n=33). Neutralizing activity improved to 100% against the D614G variant and 96% against the B.1.351 variant following a second dose. Two doses of the vaccine were also required to achieve levels of SARS-CoV-2 RBD-specific memory B cells that were comparable to what is seen in non-vaccinated individuals who have recovered from COVID-19.
- By contrast, neutralizing antibody activity and antigen-specific memory B cell levels in individuals who had recovered from a SARS-CoV-2 infection were significantly boosted after the first vaccine dose and did not significantly change after the second dose.

Goldberg et al. (Apr 24, 2021). *Protection of Previous SARS-CoV-2 Infection Is Similar to That of BNT162b2 Vaccine Protection A Three-Month Nationwide Experience from Israel*. Pre-print downloaded Apr 26 from <https://www.medrxiv.org/content/10.1101/2021.04.20.21255670v1>

- [Pre-print, not peer-reviewed] A population-based study in Israel found that the level of protection against reinfection conferred by prior infection with SARS-CoV-2 within the last 6 months was similar to that elicited by the Pfizer-BioNTech vaccine among people who had no prior infection. Vaccine effectiveness against severe disease was 66% for individuals followed from the day of the first dose until 6 days after the second dose. Overall vaccine efficacy was 94% for those followed from a week after the second dose and beyond.

Gray et al. (Mar 8, 2021). *COVID-19 Vaccine Response in Pregnant and Lactating Women a Cohort Study*. Pre-print downloaded Mar 9 from <https://doi.org/10.1101/2021.03.07.21253094>

- [Pre-print, not peer-reviewed] The Pfizer-BioNTech and Moderna vaccines elicited similar immune responses among pregnant (n=84) and lactating (n=31) women compared to non-pregnant reproductive-age women (n=16). All vaccine-induced SARS-CoV-2-specific antibody titers were higher compared to titers from a group of pregnant women (n=37) that had SARS-CoV-2 infection 4-12 weeks prior. Vaccine-induced antibodies were detected in all umbilical cord blood (n=10) and breastmilk samples (n=31), although only IgG and not IgA antibodies were increased in maternal blood and breastmilk following vaccination. No differences were noted in reactogenicity across the groups.

Grupper et al. (Apr 18, 2021). *Reduced Humoral Response to mRNA SARS-Cov-2 BNT162b2 Vaccine in Kidney Transplant Recipients without Prior Exposure to the Virus*. *American Journal of Transplantation*. <https://doi.org/10.1111/ajt.16615>

- Few kidney transplant recipients (51/136, 38.5%) who had been fully vaccinated with the Pfizer-BioNTech vaccine developed a positive response to the SARS-CoV-2 spike protein, suggesting that this population may remain at risk of infection despite vaccination. Compared to controls,

mean IgG anti-spike levels were lower (31.05 vs 200.5 AU/mL). Older age (OR = 1.7), use of high dose corticosteroids in the last 12 months (OR = 1.3), and a treatment regimen that included mycophenolate (OR = 1.5) were associated with negative serology.

Haas et al. (May 6, 2021). *Impact and Effectiveness of mRNA BNT162b2 Vaccine against SARS-CoV-2 Infections and COVID-19 Cases, Hospitalisations, and Deaths Following a Nationwide Vaccination Campaign in Israel: An Observational Study Using National Surveillance Data. The Lancet.* [https://doi.org/10.1016/S0140-6736\(21\)00947-8](https://doi.org/10.1016/S0140-6736(21)00947-8)

- Estimated real-world vaccine effectiveness 7 days or more after the second dose of the Pfizer-BioNTech vaccine was 95% against SARS-CoV-2 infection according to analysis of national surveillance data from Israel (n=4.7 million) between January to April 2021. After adjustment for age, sex, and week of infection, estimated vaccine effectiveness was 92% against asymptomatic infection and 97% against symptomatic infection. The authors calculated that vaccination led to a 97% reduction in COVID-19-related hospitalization and a 97% reduction in COVID-19-related death. 95% of tested specimens from a nationwide convenience sample (n=8,472) during the analysis period showed spike gene target failure, indicating a high prevalence of infections caused by the B.1.1.7 variant.

Hacisuleyman et al. (Apr 21, 2021). *Vaccine Breakthrough Infections with SARS-CoV-2 Variants. New England Journal of Medicine.* <https://doi.org/10.1056/NEJMoa2105000>

- 2 SARS-CoV-2 breakthrough infections (infection \geq 14 days after the second vaccine dose) were detected in a cohort of 417 employees at the Rockefeller University in New York City. Clinical symptoms of COVID-19 developed 19 days after Patient 1 (51-year-old woman) received their second dose of the Moderna vaccine, and 36 days after Patient 2 (65-year old woman) received their second dose of the Pfizer-BioNTech vaccine. Both patients were healthy and had typical clinical responses to the second dose. Viral genome sequences from both patients show that neither was infected with wild-type SARS-CoV-2. Specifically, the sequence from Patient 1 contained spike mutations including E484K, which is known to confer resistance to neutralizing antibodies. The sequences did not precisely fit any known clade.

Hall et al. (Apr 26, 2021). *COVID-19 Vaccine Coverage in Health-Care Workers in England and Effectiveness of BNT162b2 mRNA Vaccine against Infection (SIREN): A Prospective, Multicentre, Cohort Study. The Lancet.* [https://doi.org/10.1016/S0140-6736\(21\)00790-X](https://doi.org/10.1016/S0140-6736(21)00790-X)

- The Pfizer-BioNTech vaccine showed 70% effectiveness against SARS-CoV-2 infection 21 days after the first dose, and 85% effectiveness 7 days after two doses among staff working in publicly-funded hospitals in the UK. Participants were followed for two months, for a total of 1,106,905 person-days. During follow-up, 977 new infections occurred among unvaccinated individuals (14 per 10,000 person-days), compared to 71 infections 21 or more days after dose 1 in the vaccinated group (8 per 10,000 person-days) and 9 infections one week after the second dose (4 per 10,000 person-days). Among unvaccinated individuals who were infected, 543 (56%) had typical COVID-19 symptoms and 140 (14%) were asymptomatic within 14 days of testing positive, compared with infections in the vaccinated cohort, where 29 (36%) individuals had typical COVID-19 symptoms and 15 (19%) were asymptomatic.

Herishanu et al. (Apr 2021). *Efficacy of the BNT162b2 mRNA COVID-19 Vaccine in Patients with Chronic Lymphocytic Leukemia. Blood.* <https://doi.org/10.1182/blood.2021011568>

- Among patients with chronic lymphocytic leukemia (CLL, n = 169) who received two doses of the Pfizer-BioNTech vaccine, the antibody response rate was 39.5% as measured by the Elecsys Anti-SARS-CoV-2 assay at a median of 15 days after the second dose. Compared to age- and sex-matched controls, the response rate among patients with CLL was significantly reduced (aOR =0.01). The response rate was highest in patients who were in remission after treatment (79.2%), followed by 55.2% in treatment-naïve and 16% in patients undergoing treatment at the time of vaccination. In patients treated with either Bruton tyrosine kinase inhibitors or venetoclax with or without anti-CD20 antibody, response rates were low (16.0% and 13.6%, respectively).

Hollinghurst et al. (Mar 24, 2021). COVID-19 Infection Risk amongst 14104 Vaccinated Care Home Residents A National Observational Longitudinal Cohort Study in Wales United Kingdom December 2020 to March 2021. Pre-print downloaded Mar 25 from <https://doi.org/10.1101/2021.03.19.21253940>

- [Pre-print, not peer-reviewed] Only 1% of over 14,000 nursing home residents in the UK who have received the first dose of either the Pfizer-BioNTech or Oxford-AstraZeneca vaccines reported a positive SARS-CoV-2 PCR test in an observational study from December 2020 to March 2021. 90% of infections occurred within 28 days of the first dose. At 7 days post vaccination, those with prior infection had a 46% reduced hazard of a having a positive PCR. Those who received the Pfizer-BioNTech vaccine had a 3.8-fold higher hazard of having a positive test as compared to recipients of the Oxford-AstraZeneca vaccine. At 21 days post-vaccination, individuals with low or intermediate frailty (compared to high frailty) had 4.6- and 4.9-fold higher hazard of a positive PCR test, respectively.

Jangra et al. (Apr 7, 2021). SARS-CoV-2 Spike E484K Mutation Reduces Antibody Neutralisation. *The Lancet Microbe*. [https://doi.org/10.1016/S2666-5247\(21\)00068-9](https://doi.org/10.1016/S2666-5247(21)00068-9)

- An *in vitro* study of serum from persons with either prior SARS-CoV-2 infection or two doses of the Pfizer-BioNTech vaccine (N=34) found that antibody neutralization in all samples was reduced against SARS-CoV-2 virus with a single spike E484K mutation compared to the USA-WA1/2020 strain (the strain first detected in the US). The largest reductions in antibody neutralization were observed in samples with low and moderate IgG antibody levels. Samples with high IgG levels from individuals with two doses of the vaccine were still able to fully neutralize virus. The authors suggest this data may indicate that delaying the second vaccine dose may leave persons vulnerable to infection with a variant containing the E484K mutation; however, the study did not include sera from persons with only one dose as a comparison.

Jones et al. (Apr 8, 2021). Single-Dose BNT162b2 Vaccine Protects against Asymptomatic SARS-CoV-2 Infection. *ELife*. <https://doi.org/10.7554/eLife.68808>

- A study of health care workers (N~9,000) employed at Cambridge University Hospitals in Great Britain found that 1 dose of the Pfizer-BioNTech COVID-19 vaccine was associated with a 4-fold reduction in asymptomatic SARS-CoV-2 infection ≥ 12 days post-vaccination, from 0.8% to 0.2% [EDITORIAL NOTE: This is equivalent to a 75% vaccine efficacy]. Additionally, the median cycle threshold value of positive tests among those who became infected showed a non-significant increasing trend of higher viral loads among unvaccinated HCWs compared to HCWs ≥ 12 days post-vaccination, potentially indicating that vaccinated individuals who subsequently become infected

may have lower viral loads. The authors suggest that mass first-dose vaccination may reduce SARS-CoV-2 transmission.

Krammer et al. (Mar 10, 2021). Antibody Responses in Seropositive Persons after a Single Dose of SARS-CoV-2 mRNA Vaccine. New England Journal of Medicine. <https://doi.org/10.1056/NEJMc2101667>

- After a single dose of either the Pfizer-BioNTech or Moderna vaccine, US vaccinees with prior SARS-CoV-2 infection (n=43) had antibody titers 10-45 times as high as those of vaccinees without prior SARS-CoV-2 infection (n=67), according to interim results of a longitudinal study. While titers of those with prior infection did not increase after the second dose, median antibody titers were 6-fold higher than those without prior infection. No substantial difference was noted in the dynamics of antibody responses elicited by the Pfizer-BioNTech and Moderna vaccines after the first dose.
- In separate analyses within the larger longitudinal study, vaccine side effects after the first dose occurred more frequently among vaccinees with prior infection. [EDITORIAL NOTE: A pre-print related to this manuscript was summarized on February 1, 2020]

Kustin et al. (Apr 9, 2021). Evidence for Increased Breakthrough Rates of SARS-CoV-2 Variants of Concern in BNT162b2 mRNA Vaccinated Individuals. Pre-print downloaded Apr 12 from <https://doi.org/10.1101/2021.04.06.21254882>

- [Pre-print, not peer-reviewed] A case-control study of individuals with SARS-CoV-2 infection in Israel who received the Pfizer vaccine (cases) versus unvaccinated carriers (controls) found that the predominant SARS-CoV-2 variant among vaccine recipients with a positive SARS-CoV-2 PCR result differed depending on their timing in the vaccine course. Compared to controls, vaccinated individuals infected at least a week after the second dose were disproportionately infected with the B.1.351 variant (OR=8), while those infected between two weeks after the first dose and one week after the second dose were disproportionately infected by B.1.1.7 (odds ratio=2.6). The B.1.351 variant was not evaluated at this time point due to low case numbers of B.1.351. The authors suggest there may be reduced vaccine effectiveness against both variants of concern under different conditions of number of doses and dose timing. The B.1.1.7 variant was found to be the predominant strain over the study period.

Lillie et al. (Apr 24, 2021). First Dose of BNT162b2 mRNA Vaccine in a Health Care Worker Cohort Is Associated with Reduced Symptomatic and Asymptomatic SARS-CoV-2 Infection. Clinical Infectious Diseases. <https://doi.org/10.1093/cid/ciab351>

- Among healthcare workers at a hospital in the UK, increased coverage (8.3% to 82.5%) of at least one dose of the Pfizer-BioNTech vaccination was associated with significant reductions in symptomatic and asymptomatic cases of SARS-CoV-2. There was a significant negative correlation between cumulative vaccination and PCR positive cases (R = -0.91), along with a marked negative correlation between symptomatic PCR testing rates and vaccine coverage (R = -0.90). The number of staff self-isolating due to SARS-CoV-2 dropped from 325 on January 11th to 91 by February 23rd (72% decrease). The proportion of positive tests from asymptomatic screening was maintained over the study period.

Liu et al. (Feb 17, 2021). Neutralizing Activity of BNT162b2-Elicited Serum — Preliminary Report. New England Journal of Medicine. <https://doi.org/10.1056/NEJMc2102017>

- Neutralizing activity of sera from recipients of the 2-dose Pfizer vaccine (n=15, 20 serum samples) against wild-type SARS-CoV-2 (USA-WA1/2020) engineered with the full set of spike protein mutations of the B.1.351 variant was weaker than the USA-WA1/2020 strain by approximately two-thirds. Using 50% plaque reduction neutralization testing (PRNT50) on sera obtained 2-4 weeks after the second dose, geometric mean titers against USA-WA1/2020, USA-WA1/2020 with the globally dominant D614G mutation, USA-WA1/2020 with key B.1.351 mutations (K417N, E484K, and N501Y), and USA-WA1/2020 with the full set of B.1.351 mutations were 501, 485, 331, and 184, respectively.

Lustig et al. (Apr 7, 2021). Neutralizing Response against Variants after SARS-CoV-2 Infection and One Dose of BNT162b2. New England Journal of Medicine. <https://doi.org/10.1056/NEJMc2104036>

- A single dose of the Pfizer-BioNTech vaccine substantially increased neutralizing activity against SARS-CoV-2 variants B.1.1.7, B.1.351, and P.1 among healthcare workers (HCWs) previously infected with SARS-CoV-2 (n=6). Serum samples from each HCW were obtained 1-12 weeks after natural infection, immediately before vaccination, and 1-2 weeks after vaccination and were tested using a microneutralization assay containing isolates of the parent strain and SARS-CoV-2 variants. Geometric mean titers (GMTs) for neutralizing activity were low prior to vaccination against the parent strain, B.1.1.7, P.1, and B.1.351 variants (GMTs: 81, 40, 36, and 7, respectively), but increased by 114-, 203-, 81-, and 228-fold after vaccination, respectively (corresponding GMTs: 9195, 8192, 2896, and 1625).

MacNeil et al. (Apr 27, 2021). Updated Recommendations from the Advisory Committee on Immunization Practices for Use of the Janssen (Johnson & Johnson) COVID-19 Vaccine After Reports of Thrombosis with Thrombocytopenia Syndrome Among Vaccine Recipients — United States, April 2021. MMWR. <https://doi.org/10.15585/mmwr.mm7017e4>

- The Advisory Committee on Immunization Practices (ACIP) reaffirmed its interim recommendation for use of the Johnson & Johnson vaccine in all persons aged ≥ 18 years on April 23, 2021 and recommended including a warning that rare clotting events may occur in female vaccine recipients aged 18-49 years. The updated recommendations follow the recommended pause by the FDA and CDC on April 13, 2021 after reports of thrombosis with thrombocytopenia (TTS) among a small number of vaccine recipients, including central venous sinus thrombosis. As of April 21, 2021, 15 reports of TTS have been reported among approximately 8 million Johnson & Johnson vaccine doses.
- A risk-benefit analysis model that guided ACIP recommendations suggested that over 6 months, resuming vaccine use among persons aged ≥ 18 years (at 50% of administration rate before the pause) could prevent 3,926 to 9,395 COVID-19-related hospitalizations, 928 to 2,236 ICU admissions, and 586 to 1,435 deaths compared with 26 expected cases of TTS. For every 1 million doses administered to women aged 18-49 years, 297 COVID-19-related hospitalizations, 56 ICU admissions, and six deaths could be prevented, compared with 7 expected TTS cases.

Madhi et al. (Mar 16, 2021). Efficacy of the ChAdOx1 nCoV-19 Covid-19 Vaccine against the B.1.351 Variant. New England Journal of Medicine. <https://doi.org/10.1056/NEJMoa2102214>

- Two doses of the Oxford-AstraZeneca (ChAdOx1 nCoV-19) vaccine did not show protection against mild-to-moderate COVID-19 among people infected with the B.1.351 variant in a multicenter randomized trial in South Africa. Mild-to-moderate COVID-19 developed in 23 of 717 placebo recipients (3.2%) and in 19 of 750 vaccine recipients (2.5%), for an efficacy of 21.9%. Among the 42

participants who developed COVID-19, 39 (92.9%) were infected with the B.1.351 variant. Vaccine efficacy against this variant, analyzed as a secondary end point, was 10.4%. The authors note that the demographic profile of enrolled participants contributed to the lack of severe COVID-19, and therefore trial results are inconclusive regarding the vaccine's potential to protect against severe disease. [EDITORIAL NOTE: A pre-print related to this manuscript was summarized on February 12, 2020]

Manisty et al. (Feb 26, 2021). Antibody Response to First BNT162b2 Dose in Previously SARS-CoV-2-Infected Individuals. *The Lancet*. [https://doi.org/10.1016/S0140-6736\(21\)00501-8](https://doi.org/10.1016/S0140-6736(21)00501-8)

- A nested case-control study of 51 health care workers found that anti-S titers 19-29 days after the first dose of the Pfizer-BioNTech vaccine were comparable to peak titers after natural infection. Among those with a previous SARS-CoV-2 infection, vaccination increased anti-S titers more than 140-fold from peak pre-vaccine levels. Prior infection was determined by positive detection of antibodies against the SARS-CoV-2 nucleocapsid or the receptor binding domain of the SARS-CoV-2 S1 subunit of the spike protein.

Menni et al. (Apr 27, 2021). Vaccine Side-Effects and SARS-CoV-2 Infection after Vaccination in Users of the COVID Symptom Study App in the UK: A Prospective Observational Study. *The Lancet Infectious Diseases*. [https://doi.org/10.1016/S1473-3099\(21\)00224-3](https://doi.org/10.1016/S1473-3099(21)00224-3)

- SARS-CoV-2 infection rates were lower in vaccinated persons, according to reports from the COVID Symptom Study app in the UK (n=627,383). Among Pfizer-BioNTech vaccine recipients, infections were lower by 58% 12-20 days and by 72% 45-59 days after the first dose compared to frequencies in unvaccinated users, and infection rates were also lower among Oxford-AstraZeneca vaccine recipients by 39% 12-20 days and 60% 21-44 days after the first dose. Individuals with prior SARS-CoV-2 infection reported experiencing systemic side-effects 1.6 times and 2.9 times more after the first dose of the Oxford-AstraZeneca and Pfizer-BioNTech vaccines, respectively, than those without prior infection. Similarly, local side-effects were higher among individuals with prior infection. Systemic and local side-effects occurred at lower frequencies than reported in phase 3 trials.

Mishra et al. (Apr 14, 2021). Vaccination Boosts Protective Responses and Counters SARS-CoV-2-Induced Pathogenic Memory B Cells. Pre-print downloaded Apr 15 from <https://doi.org/10.1101/2021.04.11.21255153>

- [Pre-print, not peer-reviewed] SARS-CoV-2 specific B cells isolated from individuals who had recovered from SARS-CoV-2 infection appeared similar to B cells isolated previously described in individuals with chronic infections or inflammation (IgD negative, CD27 negative), according to a longitudinal study of convalescent individuals (n=22). After vaccination, the frequency of IgD/CD27 negative cells ("double negative") decreased. A more robust immune response elicited by vaccination among individuals with prior infection compared to naïve individuals was documented by comparing memory B cell responses of this cohort with those of non-infected vaccinated controls.

Monin et al. (Apr 27, 2021). Safety and Immunogenicity of One versus Two Doses of the COVID-19 Vaccine BNT162b2 for Patients with Cancer: Interim Analysis of a Prospective Observational Study. *The Lancet Oncology*. [https://doi.org/10.1016/S1470-2045\(21\)00213-8](https://doi.org/10.1016/S1470-2045(21)00213-8)

- Among patients with cancer, one dose of the Pfizer-BioNTech vaccine did not elicit a strong antibody response. In a prospective observational study, the proportion of positive anti-S IgG titers measured at 21 days after vaccination was 38% among patients with solid cancers (21/56 patients), 18% among patients with hematological cancer (8/44), and 94% (32/34) among individuals without cancer. Among participants who received a second dose 21 days later and for whom blood samples were available 2 weeks after the second dose, 95% (18/19) of patients with solid cancer, 60% (3/5) of patients with hematological cancers, and 100% of individuals without cancer were seropositive.

Moustsen-Helms et al. (Mar 9, 2021). Vaccine Effectiveness after 1st and 2nd Dose of the BNT162b2 mRNA Covid-19 Vaccine in Long-Term Care Facility Residents and Healthcare Workers - a Danish Cohort Study. Pre-print downloaded Mar 10 from <https://doi.org/10.1101/2021.03.08.21252200>

- [Pre-print, not peer-reviewed] A retrospective registry- and population-based observational cohort study in Denmark estimated that the Pfizer-BioNTech vaccine efficacy within 7 days of receipt was 52% among long term care facility residents (LTCF, n = 39,040) and 46% among health care workers (HCW, n = 331,039), which increased to 64% and 90%, respectively, beyond 7 days of immunization. No protective effect was observed for LTCF residents after the first dose. Among HCW, efficacy was 17% > 14 days after first dose (before second dose). During a median follow-up of 53 days, there were 488 and 5,663 confirmed SARS-CoV-2 cases in the unvaccinated groups, with 57 among LTCF residents and 52 among HCW within the first 7 days following the second dose, and 27 and 10 cases beyond seven days after the second dose.

Müller et al. (Apr 27, 2021). Age-Dependent Immune Response to the Biontech/Pfizer BNT162b2 COVID-19 Vaccination. *Clinical Infectious Diseases*. <https://doi.org/10.1093/cid/ciab381>

- A cohort study in Germany determined that antibody titers were significantly lower in adults over age 80 (n=83) vaccinated with the Pfizer-BioNTech vaccine compared to vaccinated individuals under age 60 (n = 93) after one and two doses of the Pfizer-BioNTech vaccine. Most participants in both groups produced IgG antibodies. The magnitude of increase of antibody levels after the second dose was higher in elderly participants, but the absolute mean titers remained lower than in the younger group. After the second vaccination, 31.3% of the older participants had no detectable neutralizing antibodies whereas only 2.2% of participants <60 had no detectable neutralizing antibodies.

Munitz et al. (Apr 17, 2021). BNT162b2 Vaccination Effectively Prevents the Rapid Rise of SARS-CoV-2 Variant B.1.1.7 in High Risk Populations in Israel. *Cell Reports Medicine*. <https://doi.org/10.1016/j.xcrm.2021.100264>

- The SARS-CoV-2 B.1.1.7 variant was 45% more transmissible than the original strain in Israel, and was identified in more than 90% of positive tests by February 4th, according to an analysis of nearly 300,000 RT-PCR samples collected between December 6, 2020 and February 10, 2021. The authors note that surveillance programs and prioritized vaccination, which initially focused on the elderly population, quickly prevented B.1.1.7-associated infections among this group. The study found a sharp decline in cases when ~50% of older adults were two weeks post-receipt of their first dose, at a time when the B.1.1.7 variant gained transmission dominance among those aged 0-59.

Nace et al. (Apr 10, 2021). Antibody Responses in Elderly Residential Care Persons Following COVID-19 mRNA Vaccination. Pre-print downloaded Apr 12 from <https://doi.org/10.1101/2021.04.07.21254925>

- [Pre-print, not peer-reviewed] While all fully vaccinated long-term care residents (n = 70) in a cross-sectional study in the Pittsburgh region between March 15 and April 1, 2021 had detectable SARS-CoV-2 antibodies, levels tended to be lower among those who were male, older, used steroid medications, or had a longer length of time since vaccination. Antibody levels tended to be higher among those who previously tested positive for SARS-CoV-2 (15.7%).

Pellini et al. (Feb 26, 2021). Obesity May Hamper SARS-CoV-2 Vaccine Immunogenicity. Pre-print downloaded Feb 26 from <https://doi.org/10.1101/2021.02.24.21251664>

- [pre-print; not peer-reviewed] Antibody titers two weeks after receiving a second dose of the Pfizer-BioNTech vaccine were lower in obese healthcare workers (BMI >30), after adjusting for age. 99.5% of the 248 participants developed a humoral immune response after vaccination, and antibody titers were higher in younger people and in women. The authors note that the importance of the magnitude of a humoral response is still under investigation.

Polack et al. (Dec 10, 2020). Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine. *New England Journal of Medicine*. <https://doi.org/10.1056/NEJMoa2034577>

- Results of the phase 3 double-blind, randomized, placebo-controlled trial for the BioNTech and Pfizer mRNA vaccine BNT162b2 (n=21,720 in vaccine group, and 21,728 in placebo group) showed a vaccine efficacy of 95% (95% CI 90.3-97.6), with 8 cases of COVID-19 (1 severe case) in the vaccine group and 162 cases (9 severe cases) in the placebo group. Efficacy was similar across subgroups defined by age, sex, race, ethnicity, body-mass index, and presence of co-existing conditions.
- Reactogenicity events were common among vaccine recipients, including arm pain, fatigue and headache. Fever (temperature $\geq 38^{\circ}\text{C}$) was reported after the second vaccine dose by 16% of participants <55 years old and 11% of participants >55. Few participants in either group had severe or serious adverse events, and the 6 deaths (2 in vaccine group, 4 in placebo group) were determined by investigators not to be related to the vaccine or placebo by investigators.
- Participants were included from 152 sites in 6 countries (130 sites in the US). The majority were aged 18-55 (58%), white (83%), and male (51%). 35% were obese and 21% had at least one coexisting condition.

Prabhu et al. (Apr 28, 2021). Antibody Response to Coronavirus Disease 2019 (COVID-19) Messenger RNA Vaccination in Pregnant Women and Transplacental Passage Into Cord Blood. *Obstetrics & Gynecology*. <https://doi.org/10.1097/AOG.0000000000004438>

- Among 122 pregnant women who delivered on or after 35 weeks gestation and received a COVID-19 mRNA vaccine by the time of delivery (n= 55 first dose, n=67 both doses), anti-SARS-CoV-2 IgG antibodies were detected in maternal blood as early as 5 days and in cord blood as early as 16 days after the first dose. An IgG response was detected in 106 women at birth, of whom 19 also produced an IgM response. In contrast, antibody responses were not detected among 16 women who were within 4 weeks of the first vaccine dose. 44% (24 of 45) of cord blood samples from single dose recipients had detectable IgG compared to 99% (65 of 67) of samples from fully vaccinated women. Maternal IgG levels were linearly associated with cord blood IgG levels and placental transfer ratios correlated with the number of weeks since receipt of the second dose. The authors state these findings suggest timing between vaccination and birth may be important to consider for vaccination strategies for pregnant women.

Romero-Brufau et al. (Feb 26, 2021). *The Public Health Impact of Delaying a Second Dose of the BNT162b2 or MRNA-1273 COVID-19 Vaccine*. Pre-print downloaded Feb 26 from <https://doi.org/10.1101/2021.02.23.21252299>

- [Pre-print, not peer-reviewed] An agent-based model estimated the impact of a strategy of delaying a second COVID-19 vaccine dose on cumulative mortality and found that a delayed second dose approach could result in reduced cumulative mortality under certain conditions, particularly in people under 65 years of age. The model was constructed using a simulated population of 100,000 agents based on a real-world US county. It predicted both a reduction in total mortality and cumulative infections at assuming and 80% and 90% first dose efficacy, resulting in absolute cumulative mortality reductions between 26 and 47 deaths per 100,000 population. The model also suggested that a delayed second dose for people under 65 years of age is optimal, assuming a first-dose efficacy of 80% and for vaccination rates at or below 0.3% population per day. The conditions in which these reductions were observed included the first dose efficacy being above 70% and vaccination rates remaining below 1% of the population per day.

Rossmann et al. (Apr 19, 2021). *COVID-19 Dynamics after a National Immunization Program in Israel*. *Nature Medicine*. <https://doi.org/10.1038/s41591-021-01337-2>

- Two months after the initiation of the SARS-CoV-2 vaccination (Pfizer-BioNTech) campaign in Israel, there were declines in the number of cases (by 77%), percentage of positive tests (by 45%), number of hospitalizations (by 68%), and number of severe hospitalizations (by 67%) compared to peak values. The authors suggest that these results are likely driven by the vaccination program since declines were greater in individuals over 60 (who were prioritized to receive the vaccine earlier), and the declines in the clinical measures occurred only after >50% of the population in a given age group had been vaccinated or recovered. In addition, the authors note that there was not a similar decline in number of cases and hospitalizations among older adults during the previous lockdown (September 18 – October 18, 2020).

Rottenstreich et al. (Apr 3, 2021). *Efficient Maternofetal Transplacental Transfer of Anti- SARS-CoV-2 Spike Antibodies after Antenatal SARS-CoV-2 BNT162b2 MRNA Vaccination*. *Clinical Infectious Diseases*. <https://doi.org/10.1093/cid/ciab266>

- In a study of women who received the Pfizer (SARS-CoV-2 BNT162b2) vaccine, all 20 women and infants had detectable anti S- and anti-RBD-specific IgG. Anti-S and anti-RBD-specific IgG antibody levels in maternal sera were positively correlated to their respective concentrations in cord blood (correlation rho= 0.72; P<0.001 and correlation rho= 0.72; P <0.001, respectively) suggesting that vaccination may provide maternal and neonatal protection.

Sadoff et al. (Apr 21, 2021). *Safety and Efficacy of Single-Dose Ad26.COVS.2 Vaccine against Covid-19*. *New England Journal of Medicine*. <https://doi.org/10.1056/NEJMoa2101544>

- Among participants in South Africa where 94.5% (86 of 91) of cases had the B.1.351 variant, vaccine efficacy of the Johnson & Johnson vaccine (Ad26.COVS.2) was 52% at onset ≥ 14 days and 64% at onset ≥ 28 days against moderate to severe-critical COVID-19. Efficacy against severe-critical COVID-19 was 73.1% at onset ≥ 14 days and 81.7% at onset ≥ 28 days.

Salazar et al. (Apr 13, 2021). *High Coverage COVID-19 mRNA Vaccination Rapidly Controls SARS-CoV-2 Transmission in Long-Term Care Facilities*. Pre-print downloaded Apr 14 from <https://doi.org/10.1101/2021.04.08.21255108>

- [Pre-print, not peer-reviewed] A study comparing documented SARS-CoV-2 infections and deaths in Spain to counterfactual model predictions from February 6 to March 28, 2021 estimated that after 70% of long-term care facility residents had been fully vaccinated with the Pfizer-BioNTech vaccine, 74% of COVID-19 deaths and 75% of all documented infections were prevented, and transmission was reduced up to 90%. The authors note that in enclosed populations such as long-term care facilities, high vaccination rates may rapidly control SARS-CoV-2 transmission.

Saul et al. (Mar 1, 2021). *Reanalysis of the Pfizer mRNA BNT162b2 SARS-CoV-2 Vaccine Data Fails to Find Any Increased Efficacy Following the Boost Implications for Vaccination Policy and Our Understanding of the Mode of Action*. Pre-print downloaded Mar 1 from <https://doi.org/10.1101/2021.02.23.21252315>

- [Pre-print, not peer-reviewed] A study exploring the timing of protection conferred by the Pfizer-BioNTech vaccine indicated that the vaccine was effective beginning 11 days following the first dose, suggesting that vaccine protection precedes the full development of neutralizing antibodies. In addition, efficacy did not increase following the second dose (compared to the period between day 11 and 28).

Simon et al. (Mar 26, 2021). *Hemodialysis Patients Show a Highly Diminished Antibody Response after COVID-19 mRNA Vaccination Compared to Healthy Controls*. Pre-print downloaded Mar 29 from <https://doi.org/10.1101/2021.03.26.21254259>

- [Pre-print, not peer-reviewed] Patients receiving hemodialysis had significantly lower anti-SARS-CoV-2 antibody titers than healthy controls 21 days after vaccination with the Pfizer-BioNTech vaccine (171 U/ml versus 2500 U/ml, respectively), according to a prospective cohort study (n = 81 patients, 80 controls). There was no correlation between antibody responses to the Hepatitis B vaccine and the SARS-CoV-2 vaccine.

Stankov et al. (Apr 16, 2021). *Humoral and Cellular Immune Responses against SARS-CoV-2 Variants and Human Coronaviruses after Single BNT162b2 Vaccination*. Pre-print downloaded Apr 19 from <https://doi.org/10.1101/2021.04.16.21255412>

- [Pre-print, not peer-reviewed] An assessment of humoral and T cell responses against a wild type SARS-CoV-2 strain, variants of concern (B.1.1.7, B.1.351, and P.1), and endemic human coronaviruses (hCoV) induced after the Pfizer-BioNTech vaccine found that IgG against the receptor-binding domain of the SARS-CoV-2 S protein was readily detectable at day 14, but inhibition of SARS-CoV-2 S-driven host cell entry was weak and particularly low for the B.1.351 variant. After one vaccine dose, frequencies of SARS-CoV-2 specific T cells were low in many vaccine recipients and influenced by immunity against endemic hCoV. The second vaccination significantly boosted T cell frequencies reactive for the wild type SARS-CoV-2 strain, as well as B.1.1.7 and B.1.351 variants.

Swift et al. (Apr 26, 2021). *Effectiveness of mRNA COVID-19 Vaccines against SARS-CoV-2 Infection in a Cohort of Healthcare Personnel*. *Clinical Infectious Diseases*. <https://doi.org/10.1093/cid/ciab361>

- The COVID-19 mRNA vaccines were up to 96% effective in preventing PCR-confirmed SARS-CoV-2 infection following two doses, according a retrospective cohort study of over 45,000 US healthcare personnel. The Pfizer-BioNTech vaccine accounted for 93% of vaccinations and the Moderna vaccine

accounted for 7%. The authors adjusted for age, gender, region, job, and week of vaccination in their analysis. Vaccine effectiveness was 78% among those receiving only one dose (n>4,000).

Supasa et al. (Feb 18, 2021). Reduced Neutralization of SARS-CoV-2 B.1.1.7 Variant by Convalescent and Vaccine Sera. Cell. <https://doi.org/10.1016/j.cell.2021.02.033>

- The B.1.1.7 variant has a 7-fold higher binding affinity to the angiotensin converting enzyme-2 (ACE2) receptor in human cells than a parent SARS-CoV-2 strain isolated from Wuhan, suggesting a mechanism for the rapid emergence of this variant. Serum from individuals vaccinated with either the Pfizer-BioNTech or the Oxford-AstraZeneca and serum recovered from infection with the Wuhan strain, had only a modest 2-3-fold reduction in neutralization titers against the B.1.1.7 variant. Sera obtained from B.1.1.7-infected individuals show no reduction in titers against the parent strain compared to the B.1.1.7 variant.

Tande et al. (Mar 10, 2021). Impact of the COVID-19 Vaccine on Asymptomatic Infection Among Patients Undergoing Pre-Procedural COVID-19 Molecular Screening. Clinical Infectious Diseases. <https://doi.org/10.1093/cid/ciab229>

- The risk of asymptomatic SARS-CoV-2 infection was significantly lower among patients who had received at least 1 dose of an mRNA COVID-19 vaccine compared to unvaccinated patients, based on a retrospective cohort study of asymptomatic adult patients (n=39,156) across multiple US states undergoing a pre-procedural SARS-CoV-2 molecular screening test. SARS-CoV-2 was detected in 3% of unvaccinated patients, compared to 1% of participants who had received at least dose prior to screening. After adjusting for age, sex, race/ethnicity and location, the risk for a positive test was significantly lower for patients who had received their first dose >10 days earlier (aRR= 0.49) and those who had received their second dose >0 days (aRR=0.27) compared to unvaccinated patients.

Tang et al. (May 6, 2021). Asymptomatic and Symptomatic SARS-CoV-2 Infections After BNT162b2 Vaccination in a Routinely Screened Workforce. JAMA. <https://jamanetwork.com/journals/jama/fullarticle/2779854>

- Vaccination with the Pfizer-BioNTech vaccine was associated with a 72% lower incidence of a positive SARS-CoV-2 PCR result during routine weekly screening for asymptomatic infection among employees of St. Jude Children's Research Hospital between December 2020 to March 2021 and a greater than 90% reduction in PCR positivity among fully vaccinated individuals. Incidence of asymptomatic infection during screening was 42% lower among vaccinated individuals compared to unvaccinated individuals within the first 11 days after the first dose, 65% lower within the first 7 days after the second dose, and 90% lower 7 days or more after the second the dose. No symptomatic infections were detected among vaccinated individuals more than 7 days after the second dose.

Tenforde et al. (Apr 28, 2021). Effectiveness of Pfizer-BioNTech and Moderna Vaccines Against COVID-19 Among Hospitalized Adults Aged ≥65 Years — United States, January–March 2021. MMWR. <https://doi.org/10.15585/mmwr.mm7018e1>

- Among adults age 65 and older (n = 417), mRNA vaccines were 94% effective against hospitalization for COVID-19 among fully vaccinated individuals, and 64% effective among partially-vaccinated individuals, according to data from US hospitals during January-March 2021. In the study, Pfizer and

Moderna vaccines were equally represented, and approximately half of participants were over the age of 75, which the authors argue provides evidence for the real-world effectiveness of these vaccines in older adults.

Teran et al. (Apr 21, 2021). *Postvaccination SARS-CoV-2 Infections Among Skilled Nursing Facility Residents and Staff Members — Chicago, Illinois, December 2020–March 2021*. *MMWR*.

<https://doi.org/10.15585/mmwr.mm7017e1>

- Twenty-two possible breakthrough SARS-CoV-2 infections (infection ≥ 14 days after the second vaccine dose) were identified among skilled nursing facility staff ($n = 10$) and residents ($n = 12$) across 15 facilities in the Chicago, IL area. Among these cases, 14 (64%) were asymptomatic, two residents were hospitalized, and one resident died due to multiple concurrent infections (Group B streptococcal bacteremia and *Pseudomonas* urinary tract infection). No facility-associated secondary transmission occurred. PCR cycle threshold values from seven patients with breakthrough infections were above 28, suggesting low viral loads.

Trinite et al. (Mar 5, 2021). *Previous SARS-CoV-2 Infection Increases B.1.1.7 Cross-Neutralization by Vaccinated Individuals*. Pre-print downloaded Mar 10 from <https://doi.org/10.1101/2021.03.05.433800>

- [Pre-print, not peer-reviewed] Sera from individuals who had been previously infected with SARS-CoV-2 and received the vaccine showed equivalent neutralizing responses against the B.1.1.7 variant and original virus strain, while sera from vaccinated individuals with no prior infection showed reduced neutralization against B.1.1.7. Neutralizing activity was assessed against pseudoviruses bearing the spike protein from the original strain or that of the D614G or B.1.1.7 variants.

Vahidy et al. (Apr 23, 2021). *Real World Effectiveness of COVID-19 mRNA Vaccines against Hospitalizations and Deaths in the United States*. Pre-print downloaded Apr 23 from

<https://doi.org/10.1101/2021.04.21.21255873>

- [Pre-print, not peer-reviewed] A large, retrospective cohort analysis of patients enrolled in a Houston, TX healthcare network ($N=91,134$) found that vaccination with 2 doses of either the Pfizer-BioNTech or Moderna vaccine reduced the risk of COVID-19 hospitalization by 96% and COVID-19 associated deaths by 99%. Additionally, the study found that persons with partial immunization, (defined as 2 weeks following the 1st dose through 7 days following the 2nd dose) had a 77% lower risk of hospitalization and a 64% lower risk of death. Effectiveness did not differ significantly across populations defined by age, race/ethnicity, area deprivation index, or comorbidities. The authors note that this is the largest cohort vaccine effectiveness study in a US population published to date.

Van Praet et al. (Apr 7, 2021). *Humoral and Cellular Immunogenicity of the BNT162b2 MRNA Covid-19 Vaccine in Nursing Home Residents*. *Clinical Infectious Diseases*. <https://doi.org/10.1093/cid/ciab300>

- Nursing home residents who had a prior SARS-CoV-2 infection were more likely than those with no history of infection to have an immunologic response within 1 week of the second dose of the Pfizer-BioNtech vaccine. Among nursing home residents in Belgium, humoral and cellular responses elicited by vaccination with the Pfizer-BioNtech vaccine were detected in 97% of those with prior SARS-CoV-2 infection ($n=64$) 1 week after the second dose (4 weeks after the first dose) but in only 37% of infection-naïve residents ($n=46$). In comparison, vaccine-elicited humoral and cellular responses were detected in 87% of 15 infection-naïve healthcare workers serving as controls.

Vasileiou et al. (Apr 26, 2021). *Interim Findings from First-Dose Mass COVID-19 Vaccination Roll-out and COVID-19 Hospital Admissions in Scotland: A National Prospective Cohort Study*. *The Lancet*. [https://doi.org/10.1016/S0140-6736\(21\)00677-2](https://doi.org/10.1016/S0140-6736(21)00677-2)

- Between December 8, 2020, and February 22, 2021, receipt of the first dose of the Pfizer-BioNTech vaccine in Scotland was associated with a vaccine effectiveness of 91% for reduced COVID-19 hospital admission at 28–34 days post-vaccination, and 88% for the Oxford-AstraZeneca vaccine. Over the study period, a total of 1,331,993 individuals who had not previously tested positive for SARS-CoV-2 were vaccinated. Vaccine efficacy against hospital admission due to COVID-19 was similar (83%) when restricting the analysis to those aged 80 years and older.

Wang et al. (Mar 2, 2021). *Increased Resistance of SARS-CoV-2 Variant P.1 to Antibody Neutralization*. Pre-print downloaded Mar 3 from <https://doi.org/10.1101/2021.03.01.433466>

- [Pre-print, not peer-reviewed] Reduced neutralization titers against the P.1 SARS-CoV-2 variant were found in both convalescent plasma (6.5-fold) and plasma from individuals who received an mRNA vaccine (2.2-2.8-fold). The P.1 variant completely resisted neutralization by multiple neutralizing monoclonal antibodies. Using a VSV-based SARS-CoV-2 pseudovirus with all 10 mutations of the P.1 variant, the authors note that the magnitude of the loss of activity from vaccinated individuals against this variant was modest relative to that observed with the B.1.351 variant.

Weisblum et al. (Oct 28, 2020). *Escape from neutralizing antibodies by SARS-CoV-2 spike protein variants*. *Elife*. <https://doi.org/10.7554/eLife.61312>

Wu et al. (Feb 17, 2021). *Serum Neutralizing Activity Elicited by mRNA-1273 Vaccine — Preliminary Report*. *New England Journal of Medicine*. <https://doi.org/10.1056/NEJMc2102179>

- Neutralizing activity of sera from recipients of the 2-dose Moderna vaccine in the phase 1 trial (n=45) were similar against a SARS-CoV-2 pseudovirus bearing the spike protein from the original Wuhan-Hu-1 isolate, the D614G variant, as well as against 20E (EU1), 20A.EU2, N439K-D614G, and mink cluster 5 variants. In contrast, neutralizing titers against the D614G variant decreased 2.7-fold against a pseudovirus with a partial set of the mutations in the B.1.351 variant (mutations K417N, E484K, and N501Y), and by 6.4-fold against the full set of B.1.351 mutations. Sera obtained from 8 participants still neutralized the B.1.351 variant at low dilutions.

Wu et al. (May 6, 2021). *Preliminary Analysis of Safety and Immunogenicity of a SARS-CoV-2 Variant Vaccine Booster*. Pre-print downloaded May 7 from <https://doi.org/10.1101/2021.05.05.21256716>

- [Pre-print, not peer-reviewed] Preliminary results from a clinical trial (N=80) of a modified Moderna mRNA COVID-19 vaccine administered as a booster 6 months after the two-dose vaccine series induced increases in antibody neutralization titers to the wild type and variant strains B.1.351 and P.1. The authors note that these results demonstrate the ability of a third vaccine dose to boost immunity to titers that may exceed peak titers following the primary two-dose vaccination series against both wild-type virus and variants.

Xie et al. (Jan 7, 2021). *Neutralization of N501Y Mutant SARS-CoV-2 by BNT162b2 Vaccine-Elicited Sera*. Pre-print downloaded Jan 8 from <https://www.biorxiv.org/content/10.1101/2021.01.07.425740v1>

- *pre-print, not peer-reviewed*] Sera from people vaccinated with the Pfizer-BioNTech mRNA vaccine (BNT162b2) (n=20) had equivalent neutralizing antibody titers to the SARS-CoV-2 strain on which the vaccine was based and a laboratory-developed SARS-CoV-2 strain carrying a N501Y substitution, which is one of the mutations associated with rapidly spreading variants in the United Kingdom and South Africa. The ratio of the 50% neutralization geometric mean titers of the sera against the Y501 virus to that against the N501 virus was 1.46, indicating no reduction in neutralization activity against the virus bearing the Y501 spike. The authors caution that the Y501 virus tested does not include all of the mutations in the spike protein that are found on the rapidly spreading strains in the UK and South Africa.

Yelin et al. (Mar 17, 2021). Associations of the BNT162b2 COVID-19 Vaccine Effectiveness with Patient Age and Comorbidities. Pre-print downloaded Mar 17 from <https://doi.org/10.1101/2021.03.16.21253686>

- [Pre-print, not peer-reviewed] Effectiveness of the Pfizer-BioNTech vaccine gradually increased starting at 12 days after the first vaccine dose and then plateaued around 35 days, according to an analysis of electronic health records from 1.79 million individuals in Israel. This period of maximum effectiveness corresponds to a period 2-weeks after the scheduled administration of the second dose and resulted in 91.2% efficacy for prevention of all infections and 99.3% for prevention of symptomatic infections. Effectiveness declined with age and for patients with type 2 diabetes and effectiveness was the same for men and women.