Rapid Review: What is the effectiveness, immunogenicity and safety of COVID-19 vaccines in persons who have had a prior, confirmed COVID-19 infection?

Prepared by: The National Collaborating Centre for Methods and Tools

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Please Note: An update of this review may be available. Access the most current version of this review by visiting the National Collaborating Centre for Methods and Tools COVID-19 Rapid Evidence Service at the above link.

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Executive Summary

Background

To date in Canada, four vaccines have been approved to prevent coronavirus disease 2019 (COVID-19): AstraZeneca/COVISHIELD, Janssen (Johnson & Johnson), Moderna and Pfizer-BioNTech. While their efficacy and effectiveness in preventing COVID-19 infections in the general population has been shown to be strong, the effectiveness specifically in those with prior confirmed COVID-19 infection is not known, as they were excluded from clinical trials. Given the immune system's previous exposure to the virus, it is not known whether the two-dose schedule is appropriate for those with prior infection, what differences may exist in immunogenicity response between those with and without prior infection (infection naïve), and whether there may be differences in adverse events in response to vaccination in those with prior infection.

This rapid review was produced to support public health decision makers' response to the COVID-19 pandemic. This review seeks to identify, appraise, and summarize emerging research evidence to support evidence-informed decision making.

This rapid review includes evidence available up to June 21, 2021, to answer the question: **What is the effectiveness, immunogenicity and safety of COVID-19 vaccines in persons who have had a prior, confirmed COVID-19 infection?**

Key Points

- Only two studies were identified that compared the efficacy or effectiveness of vaccines in those with previous COVID-19 infection compared to those without previous infection. Given the small number of events and short follow-up time the answer to this question is currently unknown. The certainty of evidence is very low (GRADE).
- Only one study compared rates of infection in those with previous COVID-19 infection who were vaccinated compared to those who were not vaccinated. No infections were found in either group, therefore the effectiveness of vaccination in those with prior infection cannot be determined. The certainty of evidence is very low (GRADE).
- Across the 37 studies reporting on the humoral immune response to vaccination those with a prior COVID-19 infection had a stronger response than those without a prior infection after both one and two doses; in many cases the response after the first dose in those with prior infection appears similar to infection naïve after two doses. The certainty of the evidence is moderate (GRADE).
- The humoral immune response in individuals with prior COVID-19 infection was compared in those who had received vaccines to those who were not vaccinated in two studies. Vaccination may result in a humoral immune response, but the evidence is very uncertain given the limited data. The certainty of the evidence is very low (GRADE).
- Across three studies that compared cellular immune response following vaccination in those with prior COVID-19 infection compared to naïve individuals the evidence is very inconsistent. The certainty of the evidence is very low (GRADE).
- Only one study compared cellular immune response following vaccination of previously infected individuals compared to those who are unvaccinated. Vaccinated individuals showed an 8.6-fold increase in Memory B cells. Given the limited data the certainty of evidence is very low (GRADE).

- Those with prior infection may be at increased risk of local or systemic adverse effects after vaccination than infection naïve individuals, and one study found a small increased risk of emergency department visits/hospitalizations. The certainty of the evidence on safety is very low (GRADE).

Overview of Evidence and Knowledge Gaps

- There is very limited data on efficacy and effectiveness of vaccination to prevent infection specific to those with prior infection, and no information on the effectiveness of the vaccine to prevent re-infection in those with prior infections following one vs. two doses of the vaccine.
- Across immunogenicity studies, findings are consistent that those with a prior infection have a stronger response after the first vaccine dose than those without prior infection; the data is more inconsistent with respect to differences between these two groups after two doses.
- Several studies compared humoral response to one dose of a vaccine in those who had a prior COVID-19 infection to two doses of a vaccine in naïve individuals; findings were consistent in that responses were similar between groups at these time points. It is important to note that the time period for follow-up was short and it is not known whether this will translate into similar long-term protection against infection.
- Heterogeneity in findings across studies is likely influenced by variations in time since infection, time between the first and second dose, the timing of data collection following vaccination and loss to follow-up which varies across studies.
- Immunogenicity studies explored differences by age, or between groups representing older vs. younger populations (e.g., long-term care residents vs. staff). Findings suggest that humoral response to vaccination in those previously infected is lower in older age groups.
- Within the studies that compared immunogenicity response by severity of previous infection, it was generally found that symptomatic infections resulted in a larger response than asymptomatic; in some instances results from asymptomatic infections were not different from naïve participants.
- Effectiveness and immunogenicity following infections from new variants of concern (VoC) were not explored; several studies did explore immune responses to VoC in vitro and found that consistent with responses to wild type (also called Wuhan strain) infections immune responses are greater in those with a previous infection than infection naïve individuals.
- Most adverse events reported within studies were mild in nature, however methods of collecting these data were not well described.

Methods

Research Question

What is the effectiveness, immunogenicity and safety of COVID-19 vaccines in persons who have had a prior, confirmed COVID-19 infection?

Search

On June 21, 2021, the Public Health Agency of Canada's database of COVID-19 literature scan was searched The search strategy for this database includes the following databases using key terms COVID-19, SARS-CoV-2, SARS-Coronavirus-2, nCov, "novel CoV", (novel AND coronavirus) for published and pre-print studies from January 28, 2021 through June 21, 2021. Systematic and rapid reviews are not included in this database.

- PubMed
- Scopus
- BioRxiv preprint server
- MedRxiv preprint server
- SSRN
- Research Square

We screened the database at the title and abstract level for studies related to immunogenicity, adverse events and vaccine effectiveness/efficacy.

Additionally, on June 21, we manually searched select repositories known to include syntheses on public health topics in COVID-19 for additional evidence that met this review's inclusion criteria.

- McMaster Health Forum
- Cochrane Rapid Reviews Question Bank
- Cochrane Reviews
- NCCMT COVID-19 Rapid Evidence Reviews
- Institute national d'excellence en santé et en services sociaux (INESSS)
- Uncover (USHER Network for COVID-19 Evidence Reviews)
- Alberta Health Services
- Newfoundland & Labrador Centre for Applied Health Research
- Public Health Ontario
- Public Health England

A copy of the full search strategy is available in Appendix 1.

Study Selection Criteria

English-language, peer-reviewed sources and sources published ahead-of-print before peer review were included. Surveillance sources were excluded.

Studies which did not report a statistical comparison between exposed and comparator groups were excluded.

Given the large number of studies and rapid timeframe for this review, studies with outcomes related to immunogenicity with sample sizes less than 20 per group were also excluded. A list of these studies is available in Appendix 2.

	Inclusion Criteria	Exclusion Criteria
Population	Persons (any age) who had a prior, confirmed COVID-19 infection or are seropositive at the baseline of the study	
Exposure	COVID-19 vaccines which Canada has currently authorized for use (AstraZeneca, Janssen/J&J, Moderna, Pfizer/BioNTech)	Vaccines not approved in Canada
Comparisons	a) COVID-19 vaccination in persons without a previous confirmed SARS-CoV-2 infection or, persons with seronegative status at baseline b) Unvaccinated persons with a previous confirmed COVID-19 infection	
Outcomes	Effectiveness: • Confirmed COVID-19 infection (PCR or serologic), asymptomatic or symptomatic • Hospitalizations due to COVID-19 • ICU admissions due to COVID-19 • Deaths due to COVID-19 Immunogenicity: • Humoral immune responses (e.g., binding antibodies, neutralizing antibodies); • Cellular immune responses (e.g., B cells, CD4+ and CD8+ T-cells, and associated cytokine responses) Safety: • Local reactions due to vaccine • Systemic reactions due to vaccine • Serious adverse events due to vaccine	
Study designs	Interventional trials or observational studies.	Case reports Case series

Data Extraction and Synthesis

Data relevant to the research question, such as study design, setting, location, population characteristics, interventions or exposure and outcomes were extracted when reported. We synthesized the results narratively due to the variation in methodology and outcomes for the included studies.

Appraisal of Evidence Quality

We evaluated the quality of included evidence using critical appraisal tools as indicated by the study design below. Quality assessment was completed by one reviewer and verified by a second reviewer. Conflicts were resolved through discussion.

Study Design	**Critical Appraisal Tool**
Cohort	Joanna Briggs Institute (JBI) Checklist for Cohort Studies
Cross-sectional	Joanna Briggs Institute (JBI) Checklist for Analytical Cross Sectional Studies

Completed quality assessments for each included study are available on request.

The Grading of Recommendations, Assessment, Development and Evaluations (GRADE) (Schünemann *et al.*, 2013) approach was used to assess the certainty in the findings based on eight key domains.

In the GRADE approach to quality of evidence, **observational studies,** as included in this review, provide **low quality** evidence, and this assessment can be further reduced based on other domains:

- High risk of bias
- Inconsistency in effects
- Indirectness of interventions/outcomes
- Imprecision in effect estimate
- Publication bias

and can be upgraded based on:

- Large effect
- Dose-response relationship
- Accounting for confounding.

The overall certainty in the evidence for each outcome was determined taking into account the characteristics of the available evidence (observational studies, some not peer-reviewed, unaccounted-for potential confounding factors, different tests and testing protocols, lack of valid comparison groups). A judgement of 'overall certainty is very low' means that the findings are very likely to change as more evidence accumulates.

Findings

Summary of the Certainty of Evidence

A total of 47 single studies are included in this review. Observational studies included cohort and cross-sectional designs. The certainty of the evidence included is as follows:

Outcome	Studies included		Overall certainty of evidence (GRADE)	Key findings
	Study design	n		
Risk of infection amongst vaccinated individuals, comparing those previously vs. not previously infected	Observational	2	⊕◯◯◯ Very low[1]	The evidence is very uncertain about the risk of infection following vaccination in individuals with previous COVID-19 infection compared to those without previous infection.
Risk of infection amongst those with previous infection, comparing those who received vaccination vs. unvaccinated	Observational	1	⊕◯◯◯ Very low[1]	The evidence is very uncertain about the risk of infection in individuals with previous COVID-19 infection who receive vaccination compared to those who remain unvaccinated.
Humoral immune responses (e.g., binding antibodies, neutralizing antibodies) amongst vaccinated individuals, comparing those previously vs. not previously infected	Observational	37	⊕⊕⊕◯ Moderate[2]	Those with prior infection likely have a stronger humoral immune response to vaccination than those with no prior infection.
Humoral immune responses (e.g., binding antibodies, neutralizing antibodies) amongst those with previous infection, comparing those who received vaccination vs. unvaccinated	Observational	2	⊕◯◯◯ Very low[1]	Vaccination may result in a greater humoral immune response in those with previous infection compared to those who are not vaccinated, but the evidence is very uncertain.
Cellular immune responses (e.g., B cells, CD4+ and CD8+ T-cells, and associated cytokine responses) amongst vaccinated individuals, comparing those previously vs. not previously infected	Observational	3	⊕◯◯◯ Very low[1]	The evidence is very uncertain about the cellular immune response in individuals with previous COVID-19 infection who receive vaccination compared to those who remain unvaccinated.
Cellular immune responses (e.g., B cells, CD4+ and CD8+ T-cells, and associated cytokine responses) amongst those with previous infection, comparing those who received vaccination vs. unvaccinated	Observational	1	⊕◯◯◯ Very low[1]	Vaccination may result in a greater cellular immune response in those with previous infection compared to those who are not vaccinated, but the evidence is very uncertain.
Safety (including local, systemic, and serious vaccine reactions) amongst vaccinated individuals comparing those previously infected vs. not previously infected.	Observational	9	⊕◯◯◯ Very low[1]	Those with prior infection may be at increased risk of local and systemic reactions following vaccination than naïve individuals, but the evidence is very uncertain.
[1]In the GRADE approach to quality of evidence, **observational studies,** as included in this review, provide **low quality** evidence, and this assessment was further downgraded due to imprecision, risk of bias				

[2]In the GRADE approach to quality of evidence, **observational studies,** as included in this review, provide **low quality** evidence, and this assessment was upgraded due to large effect.

Warning

Given the need to make emerging COVID-19 evidence quickly available, many emerging studies have not been peer reviewed. As such, we advise caution when using and interpreting the evidence included in this rapid review. We have provided a summary of overall certainty of the evidence to support the process of decision making. Where possible, make decisions using the highest quality evidence available.

Abbreviations

Ab: antibody
AU: arbitrary unit
CI: confidence interval
HCW: health care worker
IgG: immunoglobulin G
LTC: long-term care
nAb: neutralizing antibody
NR: not reported
PCR: polymerase chain reaction
RBD: receptor-binding domain

Table 1: Clinical Effectiveness

Reference	Date Released	Study Design	Population	Case definition	Comparator	Vaccine	Effectiveness measure	Effect size	Notes	Quality Rating:
Risk of infection amongst those who are vaccinated, comparing those who had a previous infection vs. no infection (n = 2)										
Shrestha, N. K., Burke, P. C., Nowacki, A. S., Terpeluk, P., Nowacki, A. S. & Gordon, S. M. (2021). Necessity of COVID-19 vaccination in previously infected individuals: A retrospective cohort study. *Preprint.*	Jun 19, 2021	Cohort	Vaccinated health system employees, USA	Confirmed by RT-PCR n=1220 Mean age 39± SD 13 Time since infection NR	COVID-19 infection naïve confirmed by nucleic acid amplification n=51,018 Mean age 42± SD 13	Pfizer/BioNTech (37%) Moderna (63%) 14 days after 1st dose	Cumulative incidence of infection	Prior infection: 0/1220 (0%) Naïve: 15/51,018 (0.03%)	Previously infected were younger (39±13 vs. 42±13, p<0.001), had patient-facing jobs (62% vs. 51%, p<0.001)	Moderate ***PREPRINT***
							Hazard ratio (Prior infection vs. naïve)	HR: 0.313 (95% CI: 0,∞)		
Chauhan, N., Chahar, A.S., Singh, P., Bhavesh, N.S., Tandon, R., & Chaturvedi, R. (2021). SARS-CoV-2 Vaccine-Induced Antibody Response and Reinfection in Persons with Past Natural Infection. *Preprint.*	May 18, 2021	Cohort	HCWs, India Mean age 42	Confirmed by RT-PCR, antigen test or seropositivity n=40 Time since infection NR	No history of COVID-19 n=65	AstraZeneca 28 days after 2nd dose	Infection	Prior infection: 1/40 (2.5%) Naïve: 14/65 (22%), p=0.0082	None	Moderate ***PREPRINT***

Risk of infection amongst those with previous infection, comparing those who received vaccination vs. unvaccinated (n = 1)										
Shrestha, N. K., Burke, P. C., Nowacki, A. S., Terpeluk, P., Nowacki, A. S. & Gordon, S. M. (2021). Necessity of COVID-19 vaccination in previously infected individuals: A retrospective cohort study. *Preprint.*	Jun 19, 2021	Cohort	Health system employees, USA	Confirmed by RT-PCR, receiving vaccination n=1220 Mean age 39± SD 13 Time since infection NR	Confirmed by RT-PCR, not receiving vaccination n=1359 Mean age 42± SD 13	Pfizer/BioNTech (37%), Moderna (63%) 14 days after 1st dose	Cumulative incidence of infection	Vaccinated: 0/1220 Unvaccinated: 0/1359, p>0.9999	None	Moderate ***PREPRINT***

Table 2: Immunogenicity

Reference	Date Released	Study Design	Population	Case definition	Comparator	Dose and follow-up	Immunogenicity measure	Unit	Effect size	Notes	Quality Rating:
Humoral immune responses (e.g., binding antibodies, neutralizing antibodies) amongst vaccinated individuals, comparing those previously vs. not previously infected (n = 37)											
Borkakoty, B., Das Sarmah, M., Bhattacharjee, K., Bali, N., & Gogoi, G. (2021). Antibody response after a single dose of ChAdOx1-nCOV (Covishield™ ®) vaccine in subjects with prior SARS-CoV2 infection: Is a single dose sufficient? *Preprint.*	Jun 15, 2021	Cohort	Vaccinated adults, India Mean age 33.7	Confirmed seropositive n=46	Confirmed seronegative n=75	AstraZeneca 25-35 days after 1st dose, 25-35 days after 2nd dose	IgG antibodies	Optical density at 450 nm (mean ± SD)	After 1st dose: Previously infected: 4.59 ± 1.04 Naïve: 2.98 ± 1.53, p<0.0001. After 2nd dose: Previously infected: 4.31 ± 0.89 Naïve: 3.08 ± 1.22, p<0.0001. Previously infected 1st dose higher than naïve 2nd dose: 4.59±1.04 vs. 3.08±1.22, p<0.0001)	None	Moderate ***PREPRINT***
Pannus, P., Neven, K. Y., De Craeye, S., Heydrickx, L., Kerckhove, S. V., Georges, D., … Marchant, A. (2021). Poor antibody response to BioNTech/Pfizer COVID-19 vaccination in SARS-CoV-2 naïve	Jun 9, 2021	Cohort	Vaccinated LTC residents and staff, Belgium	Confirmed by RT-PCR or seropositivity n = 41 Time since infection 269-315 days	Confirmed seronegative n = 39	Pfizer/BioNTech 0, 21, 28, and 49 days after 2nd dose	Spike-binding IgG RBD	AU/ml	21, 49 days after 2nd dose: Higher in previously infected vs. naïve staff, values NR, p<0.001 Higher in previously infected vs. naïve residents, values NR, p<0.001	Lower response in LTC residents vs. staff In both previously infected and naïve staff and residents, neutralization significantly higher for wild	Moderate ***PREPRINT***

residents of nursing homes. *Preprint.*							Spike-binding IgG S1	AU/ml	21, 49 days after 2nd dose: Higher in previously infected vs. naïve staff, values NR, p<0.001 Higher in infected vs. naïve residents, values NR, p<0.001	type Hu-1 vs. B.1.351 variant	
							Spike binding IgG S2	AU/ml	21 days after 2nd dose: No significant difference in previously infected vs. naïve staff, values NR 49 days after 2nd dose: Higher in previously infected vs. naïve staff, values NR, p<0.001 21, 49 days after 2nd dose: Higher in previously infected vs. naïve residents, values NR, p<0.001		

							RBD Ab avidity	K_{off} in 1/s	49 days after 2nd dose: Higher in previously infected vs. naïve staff, values NR, p<0.001 Higher in previously infected vs. naïve residents, values NR, p<0.001		
							Neutralizing Ab against SARS-CoV-2 wild type Hu-1	Lower limit of quantification	49 days after 2nd dose: Higher in previously infected vs. naïve staff, values NR, p<0.001 Higher in infected vs. naïve residents, values NR, p<0.001		

Singh, A. K., Phatak, S. R., Singh, R., Bhattacharjee, K., Singh, N. K., Gupta, A., & Sharma, A. (2021). Antibody response after second-dose of ChAdOx1-nCOV (Covishield™®) and BBV-152 (Covaxin™®) among health care workers in India: Final results of cross-sectional coronavirus vaccine-induced antibody titre (COVAT) study. *Preprint.*	Jun 4, 2021	Cross-sectional	Vaccinated HCW, India	Confirmed by unspecified test n=55 Time since infection > 6 weeks before 1st dose	No history of COVID-19 n=370	AstraZeneca 21-36 days after 2nd dose	Anti-spike antibody	Proportion (%) >15 AU/ml	Previously infected: 100% Naïve: 97.8%, p=0.271	None	High ***PREPRINT***
							Anti-spike antibody titer	AU/mL Median (IQR)	Previously infected: 400 (278-400) Naïve: 115 (75.75-199.25), p<0.001		
Forgacs, D., Jang, H., Abreu, R.B., Hanley, H.B., Gattiker, J.L., Jefferson, A.M., & Ross, T.M. (2021). Functional characterization of SARS-CoV-2 vaccine elicited antibodies in immunologically naïve and pre-immune humans. *Preprint*.	May 31, 2021	Cohort	Vaccinated adults, USA Mean age 45	Confirmed by PCR and/or seropositivity n=20	Confirmed seronegative n=32	Pfizer/BioNTech (79%), Moderna (21%) 14 days after 2nd dose	Anti-RBD IgG	Proportion > 1.139 ug/mL	Previously infected higher than naïve, values NR, p<0.0001.	None	Moderate ***PREPRINT***

Ontañón, J., Blas, J., de Cabo, C., Santos, C., Ruiz-Escribano, E., García, A., … Solera, J. (2021). Influence of past infection with SARS-CoV-2 on the response to the BioTech/Pfizer BNT162b2 mRNA vaccine in health care workers: kinetics and durability of the humoral response. *Preprint.*	May 26, 2021	Cohort	Vaccinated HCW, Spain	Confirmed by seropositivity n=33 Median age 53 (range 25-67) Time since infection median 303 days (range 131-338 days)	Confirmed seronegative n=30 Median age 41 (range 25-63)	Pfizer/BioNTech 7, 14 and 21 days after 1st dose 7, 14 and 21 days after 2nd dose	Anti-spike RBD IgG	Proportion (%) > 50 AU/mL	7 days after 1st dose: Previously infected: 88% Naïve: 16.7%, p<0.01	Participants taking immunosuppressant medications were excluded.	Moderate ***PREPRINT***
								Geometric mean, AU	14 days after 1st dose Previously infected: 40,701 (95% CI=4,161, 47,241) Naïve: 774 (95% CI=416, 1132) p<0.01 All time points after 2nd dose: Higher in previously infected vs. naïve, values NR, p<0.01 2 months after 2nd dose: Previously infected: 25003 Naïve: 6595, p<0.001		

van Gils, M. J., van Willigen, H. D., Wynberg, E., Han, A. X., van der Straten, K., Verveen, A., ... RECoVERED Study Group. (2021). Single-dose SARS-CoV-2 vaccine in a prospective cohort of COVID-19 patients. *Preprint.*	May 25, 2021	Cohort	Vaccinated participants in existing observational cohort, Netherlands	Confirmed by laboratory (test not specified) n =155 Time since infection: median 9 months (IQR 5-12 months)	Confirmed seronegative n = 49	Pfizer/BioNTech Previously infected: 1 week after 1st dose Naïve: 4 weeks after 2nd dose	Anti-S IgG	Median fold increase	Significantly higher in previously infected, values NR	Antibodies correlated with COVID-19 severity and time since infection	Moderate ***PREPRINT***
							Anti-RBD IgG	Median fold increase	Significantly higher in previously infected, values NR		
							Neutralizing antibodies	ID_{50} >100	Significantly higher in previously infected, values NR		
Sasikala, M., Shashidhar, J., Deepika, G., Ravikanth, V., Krishna, V. V., Sadhana, Y., ... Reddy, D. N. (2021). Immunological memory and neutralizing activity to a single dose of COVID-19 vaccine in previously infected individuals. *International Journal of Infectious Diseases*, *108*, 183–186.	May 19, 2021	Cohort	Vaccinated HCW, India	Confirmed by RT-PCR n=131 Age range 19-53 (females), 20-58 (males) Time since infection 5.0 months	Confirmed seronegative n=149 Age range 18-60 (females), 18-58 (males)	AstraZeneca 28 days after 1st dose	Neutralizing antibodies	AU/mL	After dose 1: Previously infected: 1124.73 ± 869.13 Naïve: 94.23 ± 140.06, p=0.0001	None	Moderate

Chauhan, N., Chahar, A.S., Singh, P., Bhavesh, N.S., Tandon, R., & Chaturvedi, R. (2021). SARS-CoV-2 vaccine-induced antibody response and reinfection in persons with past natural infection. *Preprint*.	May 18, 2021	Cohort	Vaccinated HCW, India Mean age 42	Confirmed by RT-PCR, antigen test or seropositivity n = 40	No history of COVID-19 n = 65	AstraZeneca 28 days after 2nd dose	Anti-spike IgG	AU/ml Mean	Prior infection: 2881 (95% CI= 2286, 3475 Naïve: 540 (95% CI=318, 763), p<0.0001	None	Moderate ***PREPRINT***
Vicenti, I., Gatti, F., Scaggiante, R., Boccuto, A., Zago, D., Basso, M., ... Parisi, S. G. (2021). Single-dose BNT162b2 mRNA COVID-19 vaccine significantly boosts neutralizing antibody response in health care workers recovering from asymptomatic or mild natural SARS-CoV-2 infection. *International journal of Infectious Diseases*, *108*, 176–178.	May 18, 2021	Cohort	Vaccinated HCW, Italy	Confirmed by seropositivity n=45 Median age 45 Time since infection median 313.0 days (IQR 285.5-322.5)	No history of COVID-19 n=16 Median age 49	Pfizer/BioNTech 21 days after 1st dose	Neutralizing antibodies	Titers (ID_{50}) Median (IQR)	Prior infection: 1544 (732-2232) Naïve: 26 (10-88), p<0.0001	None	Low

Vaquero, S. T., de Campos-Mata, L., Ramada, J. M., Díaz, P., Navarro-Berriuso, J., Ribas-Llaurado, C., ... Magri, G. (2021). SARS-CoV-2 naïve and recovered individuals show qualitatively different antibody responses following mRNA vaccination. *Preprint.*	May 14, 2021	Cohort	Vaccinated adults, Spain	Confirmed by seropositivity n=20 Mean age 41	Confirmed seronegative n=28 Mean age 37	Pfizer/BioNTech (4.2%), Moderna (95.8%) 2-3 weeks after 1st dose, 1 month after 2nd dose	Anti-RBD IgG1	AUC	After 1st dose: Previously infected had higher levels than naïve, values NR, p<0.01 After 2nd dose: No difference between previously infected and naïve	None	Low ***PREPRINT***
							Anti-RBD IgG2	AUC	After 1st dose: Previously infected had higher levels than naïve, values NR, p<0.01 After 2nd dose: Previously infected had higher levels than naïve, values NR, p<0.05		
							Anti-RBD IgG3	AUC	After 1st dose: No difference between prior infection and naïve After 2nd dose: Previously infected had higher levels than naïve, values NR, p<0.05		

							Anti-RBD IgG4	AUC	After 1st dose: Previously infected had higher levels than naïve, values NR, p<0.05 After 2nd dose: No difference between prior infection and naïve		
Cavalcanti, E., Isgrò, M.A., Rea, D., Di Capua, L., Trillò, G., Russo, L., ... Bianchi, A.A.M. (2021). Vaccination strategy and anti - SARS-CoV-2 S titers in healthcare workers of the INT – IRCCS "Fondazione Pascale" Cancer Center (Naples, Italy). *Infectious Agents and Cancer 16*(1), 32.	May 12, 2021	Cohort	Vaccinated HCW, Italy Mean age 48.1± 9.7	Confirmed by seropositivity n=35 Time since infection NR	Confirmed seronegative n=158	Pfizer/BioNTech 20 days after 1st dose and 20 days after 2nd dose	Anti-S-RBD	BAU/mL Median (IQR)	After 1st dose: Prior infection: >25000 Naïve: 18.9 (4.3-58.2), p<0.001 After 2nd dose, Naïve: 2111.0 (713.8->2500), lower than prior infection after 1st dose, p<0.001	None	Moderate

Favresse, J., Bayart, J.L., Mullier, F., Dogné, J.M., Closset, M., & Douxfils, J. (2021). Early antibody response in healthcare professionals after two doses of SARS-CoV-2 mRNA vaccine (BNT162b2). *Clinical Microbiology and Infection*. Epub ahead of print.	May 8, 2021	Cohort	Vaccinated HCW, Belgium Mean age 42.6	Confirmed by PCR or seropositivity n=73 Time since infection mean 99 days (range 34-337)	Confirmed seronegative n=158	Pfizer/BioNTech 14, 28 days after 2nd dose (both seropositive and seronegative) 2, 4, 7, 10, 21 days after 1st dose (seropositive)	Anti-S titers	U/mL	Seropositive higher titers than seronegative at all time points, values NR, (p<0.001) Seropositive 7 days after 1st dose comparable to seronegative 14 days after 2nd dose, 6347 vs. 1312, p<0.05	None	Moderate
Salvagno, G. L., Henry, B. M., di Piazza, G., Pighi, L., De Nitto, S., Bragantini, D., … Lippi, G. (2021). Anti-SARS-CoV-2 receptor-binding domain total antibodies response in seropositive and seronegative healthcare workers undergoing COVID-19 mRNA BNT162b2 vaccination. *Diagnostics*, *11*(5), 832.	May 4, 2021	Cohort	Vaccinated sanitary, administrative staff, hospital, Italy	Confirmed by seropositivity n=206	Confirmed seronegative n=71	Pfizer/BioNTech 21 days after 1st dose 50 days after 2nd dose	Anti-RBD antibodies	U/mL Median (IQR)	After 1st dose: Prior infection: 11,782 (4848-25,000) Naïve: 42 (15-98), p<0.001 After dose 2: Prior infection: 15,142 (6824-25,000) Naïve: 1364 (761–2174), p<0.001	None	High

Tut, G., Lancaster, T., Krutikov, M., Sylla, P., Bone, D., Kaur, N., … Moss, P. (2021). Profile of humoral and cellular immune responses to single BNT162b2 or ChAdOx1 vaccine in residents and staff within residential care homes (VIVALDI study). *Preprint.*	May 4, 2021	Cohort	Vaccinated LTC residents and HCW, UK	Confirmed by seropositivity n=30 Time since infection NR	Confirmed seronegative n=94	Pfizer/BioNTech (79%) or Oxford AstraZeneca (21%) 40, 80 days after 1st dose	ACE2-spike binding inhibition	%	Previously infected had higher response vs. naïve for wild type Hu-1, B1.1.1.7, B.1.351 and P.1 variants, values NR, p<0.001	Not reported	High ***PREPRINT***
Reynolds, C. J., Pade, C., Gibbons, J. M., Butler, D. K., Otter, A. D., Menacho, K., … Boyton, R. (2021). Prior SARS-CoV-2 infection rescues B and T cell responses to variants after first vaccine dose. *Science*. Epub ahead of print.	Apr 30, 2021	Cohort	Vaccinated HCW, UK	Confirmed by seropositivity (n=24) Time since infection approximately 39 weeks	Confirmed seronegative (n=20)	Pfizer/BioNTech, 16-18 weeks after 1st dose	nAb for B.1.1.7 variant	Number seropositive	After 1st dose: Previously infected: 24/24 Naïve: 2/20, p-value NR	None	Moderate
							nAb for B.1.351 variant	Number seropositive	After 1st dose: Previously infected: 23/24 Naïve: 3/20, p-value NR		

Zipeto, D., Carbonare, L. D., Valenti, M. T., Bisoffi, Z., Piubelli, C., Pizzato, M., ... Tiberti, N. (2021). Antibody response to BTN162b2 mRNA vaccination in naïve versus SARS-CoV-2 infected subjects with and without waning immunity. *Preprint.*	Apr 30, 2021	Cohort	Vaccinated HCW, Italy	Confirmed by seropositivity n=51 Infection during first wave (n=25) or second wave (n=26)	Confirmed seronegative n=50	Pfizer/BioNTech Measured prior to 1st dose, prior to 2nd dose, 21 days after 2nd dose	IgG-S	AU/ml Fold increase	After 1st dose: Prior infection: 20,131 Naïve: 1673, p<0.0001 (12-fold difference) After 2nd dose: Prior infection: 37,607 Naïve: 19,551, p<0.4583 (1.9-fold difference) No significant difference in titers of previously infected after 1st dose (20,131) vs. naïve after 2nd dose (19,551), p<0.9999	None	High ***PREPRINT***
Blain, H., Tuaillon, E., Gamon, L., Pisoni, A., Miot, S., Picot, M. C., & Bousquet, J. (2021). Spike antibody levels of nursing home residents with or without prior COVID-19 3 Weeks after a single BNT162b2 vaccine dose. *JAMA*.	Apr 15, 2021	Cohort	Vaccinated LTC residents, France	Confirmed by PCR and seropositivity n=36	Confirmed seronegative n=60	Pfizer/BioNTech 3 weeks after 1st dose	IgG S-protein	Proportion (%) >50 AU/mL threshold	After 1st dose: Previously infected: 100% Naïve: 49.2%, p<0.001	None	Moderate
							S-protein IgG antibody	AU/mL Median and IQR	After 1st dose: Previously infected: ≥40,000 (22,801-≥40,000) Naïve: 48.0 (14.0-278.0), p<0.001		

Anichini, G., Terrosi, C., Gandolfo, C., Savellini, G. Gori, F., Simonetta, M., … Cusi, M. G. (2021). SARS-CoV-2 antibody response in persons with past natural infection. *New England Journal of Medicine*.	Apr 14, 2021	Cohort	Vaccinated HCW, Italy	Documented COVID-19 infection (test not reported). n=38 Mean age 35 Time since infection mean 111 days	No history of COVID-19 n=62 Mean age 44.7	Pfizer/BioNTech Previously infected: 10 days after 1st dose Naïve: 10 days after 2nd dose	Anti-spike IgG	Mean AU/ml	After 1st dose: Previously infected: 20,120 (95% CI=16,400, 23,800); Naïve: 22,639 (95% CI=19,400, 25,900), no significant difference	No difference in effect by age or sex. Longer time from infection associated with higher neutralizing antibodies (p-value not provided)	Low
							Neutralizing antibodies	Geometric mean titer	After 1st dose: Previously infected 569 (95% CI=467, 670) Naïve: 118 (95% CI=85, 152), p<0.001		
Jeewandara, C., Kamaladasa, A., Pushpakumara, P.D., Jayathilaka, D., Sepali, I., Danasekara, S., Guruge, Dinuka, … Malavige, G.N. (2021). Antibody and T-cell responses to a single dose of the AZD1222/Covishield vaccine in previously SARS-CoV-2 infected and naïve health care workers in Sri Lanka. *Preprint*.	Apr 13, 2021	Cohort	Vaccinated HCW, Sri Lanka Median age 41 (range 21-81)	Confirmed by seropositivity n=26	Confirmed seronegative n=69	AstraZeneca, 28-32 days after 1st dose	Anti-spike RBD Wild type Hu-1	Number over threshold titer 1:20	After 1st dose: Previously infected: 25/26 Naïve: 54/69 p>0.0001	None	Moderate ***PREPRINT***
							Anti-spike RBD B.1.1.7 variant	Number over threshold titer 1:20	After 1st dose: Previously infected: 25/26 Naïve: 45/69 p>0.0001		
							Anti-spike RBD B.1.351 variant	Number over threshold titer 1:20	After 1st dose: Previously infected: 20/26 Naïve: 11/69 p>0.0001		

Angyal, A., Longet, S., Moore, S., Payne, R.P., Harding, A., Tipton, T., … Pitch Consortium. (2021). T-Cell and Antibody Responses to First BNT162b2 Vaccine Dose in Previously SARS-CoV-2-Infected and Infection-Naïve UK Healthcare Workers: A Multicentre, Prospective, Observational Cohort Study. *Preprint*.	Apr 13, 2021	Cohort	Vaccinated HCW, UK	Confirmed by PCR and/or seropositivity n = 113 Mean age 46 Time since infection median 8.9 months (IQR 7.9-9.5)	Confirmed by PCR and/or seronegative n = 103 Mean age 37	Pfizer/BioNTech 28 +/- 7 days after 1st and 2nd dose	IgG to spike	Fold-increase	After 1st dose: 6.8-fold higher in previously infected vs. naïve, p < 0.0001 After 2nd dose: 2.9-fold higher in previously infected vs. naïve, p=0.03	Following both doses, plasma in previously infected showed higher *in vitro* neutralization of B.1.351 IgG vs. naïve (data NR)	Moderate ***PREPRINT***
							RBD IgG	Fold-increase	After 1st and 2nd dose: Similar levels as anti-spike IgG levels, values NR		
Ujjainia, R., Tyagi, A., Sardana, V., Naushin, S., Bhatheja, N., Kumar, K., … Sengupta, S. (2021). Effect monitoring and insights from vaccination program of healthcare workforce from a tertiary level hospital in India against SARS-CoV-2. *Preprint.*	Apr 12, 2021	Cohort	Vaccinated HCW, India	Confirmed by PCR (n = 33) or seropositivity (n = 129) Time since infection NR	COVID-19 infection naïve confirmed by seronegative n = 178	AstraZeneca, 7, 28 days after 1st dose Subgroup: 17±3 days after 2nd dose (n=50 previously infected, n=87 naïve)	Log-antibody titers	U/mL	7, 14, 28 days after 1st dose: Previously infected higher than naïve, values NR, p<0.0001	None	Moderate ***PREPRINT***
									After 2nd dose: no further increase in previously infected		
							Neutralizing antibodies	%	After 1st dose: Previously infected: 98%, naïve: 45%, p<0.0001		
									After 2nd dose: Previously infected: 100% Naïve: 82%, no significant difference		

Krammer F., Srivastava, K., Alshammary, H., Amoako, A.A., Awawda, M.H., Beach, K.F., … Simon, V. (2021). Antibody Responses in Seropositive Persons after a Single Dose of SARS-CoV-2 mRNA Vaccine. *New England Journal of Medicine*.	Apr 8, 2021	Cohort	HCWs in existing observational cohort, USA	Confirmed seronegative n=43 Mean age 41.4	Confirmed seronegative n=67 Mean age 41.3	Pfizer/BioNTech (80%), Moderna (20%) 0-4, 5-8, 9-12, 13-16, 17-20, 21-27 days after 1st dose Unspecified time after 2nd dose.	Anti-spike IgG	AUC	0-4 days after 1st dose: Seropositive: 133 Seronegative: 1 5-8 days after 1st dose: Seropositive: 14,208 Seronegative: 1 9-12 days after 1st dose: Seropositive: 20,783 Seronegative: 439 13-16 days after 1st dose: Seropositive: 25,927 Seronegative: 1016 17-20 days after 1st dose: Seropositive: 11,755 Seronegative: 21-27 days after 1st dose: Seropositive: 19,953 Seronegative: 1293 After 1st dose: Seropositive: 22,509 Seronegative: 3316	None	Low

Konstantinidis, T., Zisaki, S., Mitroulis, I., Konstantinidou, E., Kontekaki, E.G., Romanidoui, G., … Panopoulou, M. (2021). Levels of produced antibodies after vaccination with mRNA vaccine; effect of previous infection with SARS-CoV-2. *Preprint*.	Apr 7, 2021	Cohort	Vaccinated HCW, Greece	Confirmed by PCR. n=23 Mean age 47.1 Time since infection mean 2-3.5 months	Confirmed seronegative n=487 Mean age 48.4	Pfizer/BioNTech 1-month after 2nd dose	Anti-spike IgG	AU/mL Mean ± SD	Previously infected: 25,599.5 ± 10,646.8 Naïve: 19,221.3 ± 1803.66, p<0.049	None	Moderate ***PREPRINT***
Kanji, J.N., Bailey, A., Fenton, J., Ling, S.H., Rivera, R., Plitt, S., … Charlton, C.L. (2021). Detection of SARS-CoV-2 antibodies formed in response to the BNT162b2 and mRNA-1237 mRNA vaccine by commercial antibody tests. *Preprint*.	Apr 6, 2021	Cohort	Vaccinated LTC residents, Canada Median age 84	Confirmed by unspecified test (n=16)	No history of COVID-19 (n=28)	Moderna, 21-28 days post dose 1.	Anti-RBD IgG	AU/mL Median (IQR)	Prior infection: 40,000 (37,257.3-40,000 Naïve: 280.9 (88.1-909.5), p<0.001	None	Moderate ***PREPRINT***
							Trimeric S-IgG	AU/mL Median (IQR)	Prior infection: 800 (651-800) Naïve: 258.2 (13.8-113), p<0.001		
							Neutralizing antibody	ng/mL Median (IQR)	Prior infection: 33,874.2 (2179.4-48,052.8) Naïve: 185.4 (0-386.2), p<0.001		

Ebinger, J.E., Fert-Bober, J., Printsev, I., Wu, M., Sun, N., Prostko, J.C., ... Sobhani, K. (2021). Antibody responses to the BNT162b2 mRNA vaccine in individuals previously infected with SARS-CoV-2. *Nature Medicine 27*, 981-984.	Apr 01, 2021	Cohort	Vaccinated HCW, USA	Confirmed by PCR or seropositivity n=78	Confirmed seronegative n=903	Pfizer/BioNTech, Moderna, AstraZeneca (% for each NR) 7-21 days after 1st dose, 7-21 days after 2nd dose	Log IgG (S-RBD)	Value NR Median (IQR)	After 1st dose: Previously infected: 10 (9.2-10.4) Naïve: 7.0 (6.3-7.6), p<0.001 After 2nd dose: Previously infected: 10.6 (10.3-10.7) Naïve: 9.9 (9.4-10.3), p<0.001	All comparisons made to shifted time points (comparing prior infection after 1st dose to naïve after 2nd dose) found no significant differences	Moderate
							Log IgM(S)	Value NR Median (IQR)	After 1st dose: Previously infected: 0.1 (-0.4, 1.0) Naïve: 0.1 (-0.8, 0.8), p=0.43 After 2nd dose: Previously infected: -0.1 (-0.6-1.4) Naïve: 0.7 (-0.1-1.3), p=0.59		
							ACE2 binding	% Threshold NR Median (IQR)	After 1st dose: Previously infected: 99.6 (97.4-100.0) Naïve: 42.5 (26.1-58.0), p<0.001 After 2nd dose: Previously infected: 100.0 (99.0-100.0) Naïve: 98.6 (96.9-99.2), p<0.001		

							IgG(S-RBD)	Proportion (%) >4160 AU/ml)	After 1st dose: Previously infected: 77.1% Naïve: 7.6%, p<0.001 After 2nd dose: Previously infected: 100% Naïve: 97.4%, p=1.00		
							ACE binding	Proportion ≥50%	After 1st dose: Previously infected: 94.3% Naïve: 37.3%, p<0.001 After 2nd dose: Previously infected: 100% Naïve: 97.8%, p=1.00		
Kontopoulou, K., Ainatzoglou, A., Nakas, C., Ifantidou, A., Goudi, G., Antoniadou, E., … Papazisis, G. (2021). Second dose of the BNT162b2 mRNA vaccine in Greece: The value of timely administration. *Preprint*.	Apr 1, 2021	Cohort	Vaccinated HCW, Greece	Confirmed by PCR n=59 Time since infection 1-4.5 months	No history of COVID-19 n=342	Pfizer/BioNTech 14 days after 2nd dose	Neutralizing IgG	AU/ml Geometric mean	Previously infected: 21,041.75 (95% CI=16,406.04, 26,987.35) Naïve: 28,020.87 (95% CI=23,959.37, 32,770.87), p=0.0543	Response of previously infected to 1st dose was more intense than response of naïve to 2nd dose (p<0.001)	Moderate ***PREPRINT***

Callegaro, A., Borleri, D., Farina, C., Napolitano, G., Valenti, D., Rizzi, M., & Maggiolo, F. (2021). Antibody response to SARS-CoV-2 vaccination is extremely vivacious in subjects with previous SARS-CoV-2 infection. *Journal of Medical Virology, 93*(7), 4612-4615.	Mar 31, 2021	Cohort	Vaccinated HCW, Italy n=184	Confirmed by PCR or seropositivity (n=21), diagnosis (method not specified) (n=53) Time since infection NR	No history of COVID-19 n=110	Pfizer/BioNTech 7-10 days after 2nd dose	Antibody response spike-RBD	Log U/ml Median (IQR)	Prior infection: 43,073 (31,605-61,903) Naïve: 1974.5 (895-3455) p<0.001	Titers higher for those infected 8-11 months prior vs. 2-3 months prior, values NR, (p<0.017) Titers higher in symptomatic vs. asymptomatic, values NR	Moderate
Kelsen, S.G., Braverman, A.S., Patel, P., Aksoy, M.O., Hayman, J., Rajput, C., ... Gentile, N. (2021). Heightened COVID-19 vaccine response following SARS-CoV-2 infection. *Preprint*.	Mar 30, 2021	Cohort	Vaccinated HCW, USA	Confirmed by PCR or seropositivity n = 24 Mean age 46 Time since infection mean 200 days (range 25-277 days)	Confirmed seronegative (n=25) Mean age 45	Pfizer/BioNTech, 14, 28, 35, 42 and 56 days after 1st dose 2nd dose on day 21	Anti-spike RBD antibody	µg/mL Mean ± SE	14 days after 1st dose: Previously infected: 39.0 ± 6.9 Naïve: 2.5 ± 0.6, p<0.001 Subsequent time points: No significant difference in previously infected or naïve, values NR	None	Moderate ***PREPRINT***

							Neutralization assay	mean IC_{50}	14 days after 1st dose: Previously infected: $3.6x10^{-4}$ Naïve: $1x10^{-2}$, p<0.001 Subsequent time points: Not significantly different in previously infected or infection naïve, values NR		
Eyre, D.W., Lumley, S.F., Wei, J., Cox, S., James, T., Justice, A., Jesuthasan, … Jeffery, K. (2021). Quantitative SARS-CoV-2 anti-spike responses to Pfizer-BioNTech and Oxford-AstraZeneca vaccines by	Mar 26, 2021	Cohort	Vaccinated HCW, UK	Confirmed by PCR (symptomatic) or PCR and/or seropositivity (asymptomatic) n=501	No history of COVID-19 n=3109	Pfizer/BioNTech (75.3%), AstraZeneca (24.7%) 14 days after 1st dose, 14 days after 2nd dose	IgG	Proportion % ≥1.4 threshold	1st dose overall: Previously infected vs. naïve: Adjusted odds ratio (aOR) 6.99 (95% CI=0.95, 51.3) p<0.06	No difference by sex or ethnicity. Older HCWs less likely to be seropositive. Values after 1st dose in prior infection similar to	Moderate ***PREPRINT***

previous infection status. *Preprint*.							IgG	AU/mL Median (IQR)	After 1st dose Pfizer/BioNTech: Previously infected: 14,604 (7644-22,291) Naïve: 1028 (564-1985), p<0.001 After 1st dose AstraZeneca: Previously infected: 10,095 (5354-17,096) Naïve: 435 (203-962) p<0.001	second dose in naïve	
Korodi, M., Rákosi, K., Jenei, Z., Hudák, G., Horváth, I., Kákes, M., … Fejer, S.N. (2021). Longitudinal determination of mRNA-vaccination induced strongly binding SARS-CoV-2 IgG antibodies in a cohort of healthcare workers with and without prior exposure to the novel coronavirus. *Preprint*.	Mar 25, 2021	Cohort	HCW, Romania	Confirmed by PCR or seropositivity n=44 Mean age 43.55 (SD 10.73)	Confirmed seronegative n=78 Mean age 44.29 (SD 12.96)	Pfizer/BioNTech, immediately prior to 1st dose, 2 weeks after 1st dose, 2 weeks after 2nd dose	Anti-spike protein IgG	AU/mL	After 1st and 2nd doses, those with prior infection had higher responses than naïve participants at all time points (values NR), p value <0.001	None	High ***PREPRINT***

Bradley, T., Grundberg, E., Selvarangan, R., LeMaster, C., Fraley, E., Banerjee, D., … Schuster, J. (2021). Antibody Responses after a Single Dose of SARS-CoV-2 mRNA Vaccine. *New England Journal of Medicine*.	Mar 23, 2021	Cohort	HCW United States	Confirmed by PCR n=36 Time since infection NR	Confirmed by negative PCR n=152	Pfizer/BioNTech 21 days after 1st dose	Anti-spike S1, S2, RBD	Mean fold increase	Previously infected had significantly higher titers to the S1, S2 and RBD compared to infection naïve; values NR, p<0.0001	None	Moderate
							Neutralizing antibodies proxy	%	Previously infected: 96.3 Naïve: 59, p-value NR		
Velasco, M., Galán, M. I., Casas, M. L., Pérez-Fernández, E., Martínez-Ponce, D., González-Piñeiro, B., … Working Group Alcorcón COVID-19. (2021). Impact of previous COVID-19 on immune response after a single dose of BNT162b2 SARS-CoV-2 vaccine. *Preprint.*	Mar 14, 2021	Cross-sectional	Vaccinated HCW, country NR Mean age 45.8	Confirmed by PCR or seropositivity n = 284 Time since infection NR	Confirmed seronegative n = 284	Pfizer/BioNTech 21 days after 1st dose , 3 days after 2nd dose	Median IgG-S titers	Fold-increase	After 1st dose: 20-fold higher in previously infected vs. naïve, p<0.001	More severe disease associated with increased IgG-S titers after first dose Differences maintained after adjusting for age, gender and comorbidities	Moderate ***PREPRINT***
									After 2nd dose: 1.27-fold increase since 1st dose in previously infected vs. 12.6-fold increase since 1st dose in naïve, p>0.01		
									In previously infected, response after 1st dose higher than response after 2nd dose in naïve, p<0.01		

Demonbreun, A.R., Sancilio, A., Velez, M.E., Ryan, D.T., Saber, R., Vaught, L.A., … McDade, T.W. (2021). Comparison of IgG and neutralizing antibody responses after one or two doses of COVID-19 mRNA vaccine in previously infected and uninfected persons. *Preprint*.	Mar 8, 2021	Cohort	Vaccinated, community-dwelling adults, USA n=290 Median age: 38	Self-reported positive by RT-PCR Identified seropositive at baseline n=42 Time since infection NR	Seronegative at baseline n = 143	Pfizer/BioNTech (77%), Moderna (23%) 10 days after 1st dose (n=140), 6 days after 2nd dose (n = 170)	Anti-spike RBD IgG	Median µg/ml	After 1st dose: Confirmed COVID-19: 47.71 Seropositive: 3.37 Seronegative: 216, p<0.05 for all After 2nd dose: Confirmed COVID-19: 43.60 Seropositive: 27.34, p<0.05 Seronegative: 23.5 (no significant difference from seropositive)	Seropositive likely representative of asymptomatic cases vs. confirmed COVID-19. Assay calibration questionable.	Moderate ***PREPRINT***
							Antibody-mediated neutralization of spike-ACE2 RBD	% neutralization Median	After 1st dose: Confirmed COVID-19: 99.9 Seropositive: 62.8, p<0.01 Seronegative: 39.5 (no significant difference from seropositive) After 2nd dose: Confirmed COVID-19: 99.9 Seropositive: 98.3, p<0.001 Seronegative: 98.5 (no significant difference from seropositive)		

Capetti, A.F, Stangalini, C.A, Borgonovo, F., Mileto, D., Oreni, L., Dedivitiis, G., … Rizzardini, G. (2021). Impressive boosting of anti-S1/S2 IgG production in COVID-19-experienced patients after the first shot of the BNT162b2 mRNA COVID-19 Vaccine. *Clinical Infectious Diseases*. Epub ahead of print.	Mar 6, 2021	Cohort	Vaccinated LTC HCW and residents, Italy	Confirmed by PCR, antigen test, or seropositivity n=39 (HCW) n=30 (residents) Time since infection NR	Confirmed seronegative n=22 (HCW) n=30 (residents)	Pfizer–BioNTech Median 9 days (IQR 7-11) after 1st dose	anti S1/S2 IgG	AU/mL Median (IQR)	After 1st dose: Prior infection: 53.0 (30.7, 93.6) to 1800.0 (353.0, 3590.0) Naïve: 3.8 (3.8, 3.8) to 3.70 (3.7, 4.9) Between-group difference, p<0.001)	No difference in response by COVID-19 severity	Moderate
Saadat, S., Rikhtegaran Tehrani, Z., Logue, J., Newman, M., Frieman, M. B., Harris, A. D., & Sajadi, M. M. (2021). Binding and neutralization antibody titers after a single vaccine dose in health care workers previously infected with SARS-CoV-2. *JAMA, 325*(14), 1467–1469.	Mar 1, 2021	Cohort	Vaccinated HCW, USA n=59	Confirmed by seropositivity n=16 (asymptomatic) n=26 (symptomatic) Mean age 38 (asymptomatic) Mean age 40 (symptomatic) Time since infection NR	Confirmed seronegative n = 17 Mean age 38	Pfizer/BioNTech (49.2%), Moderna (50.8%) 7, 14 days after 1st dose	Anti-spike IgG	Median reciprocal half-maximal binding titers	7 days after 1st dose: Asymptomatic: 29,364 Symptomatic: 32,301 Naïve: <50, p<0.001	Higher response in symptomatic vs. asymptomatic	High
									14 days after 1st dose: Asymptomatic: 34,033 Symptomatic: 35,460 Naïve: 924, p<0 .001 for all		
								Median reciprocal ID_{99} virus neutralization titers	14 days after 1st dose: Asymptomatic: 40,960 Symptomatic: 40,960 Naïve: 80 p<0.0001 for all		

Manisty, C., Otter, A. D., Treibel, T. A., McKnight, Á., Altmann, D. M., Brooks, T., … Moon, J. C. (2021). Antibody response to first BNT162b2 dose in previously SARS-CoV-2-infected individuals. *The Lancet*, *397*(10279), 1057–1058.	Feb 25, 2021	Cohort	Vaccinated HCW, England	Confirmed by seropositivity n=24	Confirmed seronegative n=27	Pfizer/BioNTech, 19-29 days after 1st dose	Anti-spike	U/mL	Prior infection: 140-fold greater than in naïve, values NR, p<0.0001	None	Low
Kontopoulou, K., Ainatzoglou, A., Ifantidou, A., Nakas, C., Goudi, G., Antoniadou, E., … Papazisis, G. (2021). Immunogenicity after the First Dose of the BNT162b2 mRNA COVID-19 Vaccine: Real-World Evidence from Greek Healthcare Workers. *Preprint*.	Feb 19, 2021	Cohort	HCW, Greece	Confirmed by PCR n=63 Time since infection 1-4.5 months	No history of COVID-19 n=362	Pfizer/BioNTech 14 days after 1st dose	IgG antibodies RBD-S1	Geometric mean concentration AU/ml	Prior infection: 19,993.61 (95% CI=15,560.60, 25,689.52) Naïve: 278.24 (95% CI=242.66, 319.05, p<0.001	No difference by age in those 20-50, but response begins to drop with age >60	Moderate ***PREPRINT***
Humoral immune responses (e.g., binding antibodies, neutralizing antibodies) amongst those with previous infection, comparing those who received vaccination vs. unvaccinated (n = 2)											
Wang, Z., Muecksch, F., Schaefer-Babajew, D., Finkin, S., Viant, C., Gaebler, C., … Nussenzweig, M. C.	Jun 14, 2021	Cohort	Convalescent participants, USA	Confirmed seropositive, vaccinated n=26	Confirmed seronegative, unvaccinated n=37	Pfizer/BioNTech, Moderna (% NR)	RBD B cell memory	# RBD binding B cells	12 months after infection: Higher in vaccinated vs. unvaccinated, values NR	Vaccinated had higher NT_{50} in response to B.1.351, B.1.1.7, B.1.526, P.1	Moderate

(2021). Naturally enhanced neutralizing breadth against SARS-CoV-2 one year after infection. *Nature.* Epub ahead of print.			Median age 47 1.3, 6.2, 12 months after infection				Anti-RBD IgG	AUC	12 months after infection: Higher in vaccinated vs. unvaccinated, values NR, p<0.0001	compared to unvaccinated (all p<0.001)	
							Anti-N IgG	AUC	12 months after infection: No significant difference between vaccinated and unvaccinated at 12-months, values NR, p>0.99		
							IgA	# IG class RBD binding B cells	12 months after infection: Higher in vaccinated vs. unvaccinated, values NR, p=0.04		
							IgM	# IG class RBD binding B cells	12 months after infection: Higher in vaccinated vs. unvaccinated, values NR, p<0.13		
							IgG	# IG class RBD binding B cells	12 months after infection: Higher in vaccinated vs. unvaccinated, values NR, p=0.04		
							NT_{50}	Fold increase	At 12 months post-infection: Vaccinated: 3684 Unvaccinated: 75 (50-fold increase), p<0.01		

Canaday, D.H, Carias, L., Oyebanji, O.A, Keresztesy, D., Wilk, D., Payne, M., … King, C.L (2021). Reduced BNT162b2 mRNA vaccine response in SARS-CoV-2-naïve nursing home residents. *Clinical Infectious Diseases*. Epub ahead of print.	May 16, 2021	Cohort	HCW, USA Time since infection 29-94 days	Confirmed by PCR, antigen test and/or seropositivity n=34 Mean age 49	Confirmed by PCR, antigen test and/or seropositivity, unvaccinated. n=22 Mean age 46	Pfizer/BioNTech 14±3 days after 2nd dose	Anti-spike	AU	Vaccination increased AU, values NR, p< 0.001	None	Low
							Anti-RBD	AU	Vaccination increased AU, values NR, p< 0.001		
							Neutralizing titer	pNT50	Vaccination increased AU, values NR, p< 0.001		
Cellular immune responses (e.g., B cells, CD4+ and CD8+ T-cells, and associated cytokine responses) amongst vaccinated individuals, comparing those previously vs. not previously infected (n = 3)											
Reynolds, C. J., Pade, C., Gibbons, J. M., Butler, D. K., Otter, A. D., Menacho, K., … Boyton, R. (2021). Prior SARS-CoV-2 infection rescues B and T cell responses to variants after first vaccine dose. *Science*. Epub ahead of print.	Apr 30, 2021	Cohort	Vaccinated HCW, UK	Confirmed by seropositivity n=25 Time since infection ~39 weeks	Confirmed seronegative n=26	Pfizer/BioNTech 16-18 weeks after 1st dose	T-cell response to spike protein	Proportion (%) above threshold	Prior infection: 96% Naïve: 70%, p=0.0557	None	Moderate

Angyal, A., Longet, S., Moore, S., Payne, R.P., Harding, A., Tipton, T., … Pitch Consortium. (2021). T-Cell and Antibody Responses to First BNT162b2 Vaccine Dose in Previously SARS-CoV-2-Infected and Infection-Naïve UK Healthcare Workers: A Multicentre, Prospective, Observational Cohort Study. *Preprint*.	Apr 13, 2021	Cohort	Vaccinated HCW, UK	Confirmed by PCR and/or seropositivity n=113 Mean age 46 Time since infection median 8.9 months (IQR 7.9-9.5)	Confirmed by PCR and/or seronegative n=103 Mean age 37	Pfizer/BioNTech 28±7 days after 1st and 2nd dose	Spike-specific T-cell response	SFU/10^6	After 1st dose: Previously infected: 340 Naïve: 58, p<0.0001 After 2nd dose, Response in naïve was comparable to previously infected after 1st dose (158 vs. 165, p=0.65)	None	Moderate ***PREPRINT***
Camara, C., Lozano-Ojalvo, D., Lopez-Granados, E., Paz-Artal, E., … Ochando, J. (2021). Differential effects of the second SARS-CoV-2 mRNA vaccine dose on T cell immunity in naïve and COVID-19 recovered individuals. *Preprint*.	Mar 22, 2021	Cohort	Vaccinated adults, USA	Confirmed by PCR and/or antigen test n = 23 Mean age 44.3 Time since infection: Range 1-9 months • 6-9 months (39%) • 3-6 months (26%) • 1-3 months (35%)	Confirmed seronegative n = 23 Mean age 39.9	Pfizer/BioNTech 20 days after 1st dose, 20-days after 2nd dose	IFN-gamma secretion	pg/mL Mean	After 2nd dose: Previously infected: 136.0 Naïve: 87.5, no significant difference	None	Low ***PREPRINT***

Cellular immune responses (e.g., B cells, CD4+ and CD8+ T-cells, and associated cytokine responses) amongst those with previous infection, comparing those who received vaccination vs. unvaccinated (n = 1)											
Wang, Z., Muecksch, F., Schaefer-Babajew, D., Finkin, S., Viant, C., Gaebler, C., ... Nussenzweig, M. C. (2021). Naturally enhanced neutralizing breadth against SARS-CoV-2 one year after infection. *Nature.* Epub ahead of print.	Jun 14, 2021	Cohort	Convalescent participants, USA Median age 47 1.3, 6.2, 12 months after infection	Confirmed seropositive, vaccinated n=26	Confirmed seropositive, unvaccinated n=37	Pfizer/BioNTech, Moderna (% NR) 1st dose	Memory B cells	Fold-increase	Vaccinated individuals had an 8.6-fold increase over unvaccinated at 12 months, p<0.001	Symptom persistence was not associated with vaccination status (values not reported), p<0.0001	Moderate

Table 3: Safety

Reference	Date Released	Study Design	Population	Case definition	Comparator	Dose	Local Adverse Events	Systemic Adverse Events	Serious Adverse Events	Notes	Quality Rating:
Safety in vaccinated individuals, comparing those previously infected vs. naïve (n = 9)											
d'Armini, M.A., Tavelli, A., Perrone, P. M., Za, A., Razzini, K., Tomasoni, D., ... Colosio, C. (2021). Association between previous infection with SARS CoV-2 and the risk of self-reported symptoms after mRNA BNT162b2 vaccination: Data from 3,078 health care workers. *EClinicalMedicine 36,* 100914.	May 31, 2021	Cohort	Vaccinated HCW, Italy	Confirmed by PCR or antigen test n=270 Median age 45 (IQR 30-54)	No history of COVID-19 n=1710 Median age 48 (IQR 35-56)	Pfizer/ BioNTech	Local symptoms: Previously infected: 69.2% Naïve: 55.2%, p<0.001	Any systemic symptoms After 1st dose: Prior infection: 52.0% Naïve: 29.4%, p<0.001 After 2nd dose: No significant difference	None reported	None	Moderate
Sasikala, M., Shashidhar, J., Deepika, G., Ravikanth, V., Krishna, V. V., Sadhana, Y., ... Reddy, D. N. (2021). Immunological memory and neutralizing activity to a single dose of COVID-19 vaccine in previously infected individuals. *International Journal of Infectious Diseases*, *108*, 183–186.	May 19, 2021	Cohort	Vaccinated HCW, India	Confirmed by PCR n=131 Age range: 19-53 (female), 20-58 (male) Time since infection mean 5.0 months	Confirmed seronegative n=149 Age range: 18-60 (female), 18-58 (male)	AstraZeneca	Local side effects: No significant difference	Fever: Previously infected: 29% Naïve: 18.79%, p=0.04 Body pains: Previously infected: 29% Naïve: 16.77%, p=0.01 Fatigue: Previously infected: 68.70% Naïve: 40.26%, p=0.0001 No difference for headache, back pain	None reported	None	Moderate

Menni, C., Klaser, K., May, A., Polidori, L., Capdevila, J., Louca, P., … Spector, T. D. (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.* Epub ahead of print.	Apr 27, 2021	Cohort	General population, vaccinated, UK Mean age: 50.6 (SD 19.2)	Confirmed by PCR or lateral flow assay n=30,851	No history of COVID-19 n=617,028	Pfizer/ BioNTech (46.7%) AstraZeneca (53.5%)	NR	Previously infected vs. naïve (overall systemic symptoms) After 1st dose Pfizer/BioNTech: OR 3.97 (95% CI 3.83, 4.12) After 2nd dose Pfizer/BioNTech: OR 2.37 (95% CI 2.17, 2.60) After 1st dose AstraZeneca: OR 2.31 (95% CI 2.23, 2.38)	None reported	Study conducted through smart phone app	Moderate
Raw, R. K., Kelly, C., Rees, J., Wroe, C., & Chadwick, D. R. (2021). Previous COVID-19 infection but not Long-COVID is associated with increased adverse events following BNT162b2/Pfizer vaccination. *Preprint.*	Apr 22, 2021	Cross-sectional	Vaccinated HCW, UK	Confirmed by PCR or seropositivity n=265 Mean age 48.9 Time since infection median 8.9 months	No history of COVID-19 n=709 Mean age 47.0	Pfizer/ BioNTech (Dose NR)	No significant difference, values NR	Fever OR 2.87 (95% CI 1.10, 7.51) Fatigue OR 1.78 (95% CI 1.12, 2.84) Myalgia OR 2.34 (95% CI 1.44, 3.88) Lymphadenopathy OR 5.18 (95% CI 1.19, 22.63) No difference in gastrointestinal symptoms	None reported	30 participants reported Long-COVID, median duration 9.3 months	Low ***PREPRINT***

Krammer, F., Srivastava, K., the PARIS team, & Simon, V. (2021). Robust spike antibody responses and increased reactogenicity in seropositive individuals after a single dose of SARS-CoV-2 mRNA vaccine. *Preprint.*	Apr 8, 2021	Cohort	HCWs in existing observational cohort, USA	Confirmed by seronegative n=43 Mean age 41.4	Confirmed seronegative n=67 Mean age 41.3	Pfizer/BioNTech (80%), Moderna (20%)	No significant difference, values NR	Fatigue, headache, chills, muscle pain, fever, joint paint more frequent in seropositive than seronegative, values NR	None reported	None	Low ***PREPRINT***
Ebinger, J. E., Fert-Bober, J., Printsev, I., Wu, M., Sun, N., Prostko, J. C., … Sobhani, K. (2021). Antibody responses to the BNT162b2 mRNA vaccine in individuals previously infected with SARS-CoV-2. *Nature Medicine 27*. 981-984.	Apr 01, 2021	Cohort	Vaccinated HCW, USA	Confirmed by PCR or seropositivity n=78	Confirmed seronegative n=903	Pfizer/BioNTech, Moderna, AstraZeneca (% NR)	Previously infected had post vaccine symptoms more frequently than naïve, values NR, p=0.03	NR	NR	None	Moderate
Callegaro, A., Borleri, D., Farina, C., Napolitano, G., Valenti, D., Rizzi, M., & Maggiolo, F. (2021). Antibody response to SARS-CoV-2 vaccination is extremely vivacious in subjects with previous SARS-CoV-2 infection. *Journal of Medical Virology 93*(7). 4612-4615.	Mar 31, 2021	Cohort	Vaccinated HCW, Italy	Confirmed by PCR or seropositivity (n=21), diagnosis (method not specified) (n=53) Time since infection NR	No history of COVID-19 n=110	Pfizer/BioNTech	Mean number of adverse events reported: After 1st dose: Previously infected: 1.23 (95% CI=0.89, 1.50) Naïve: 0.77 (95% CI=0.55, 1.00), p=0.002 After 2nd dose: Previously infected: 2.35 (95% CI=1.87, 2.82) Naïve: 1.63 (95% CI=1.29, 1.98), p=0.015			None	Moderate

Efrati, S., Catalogna, M., Hamed, R. A., Hadanny, A., Bar-Chaim, A., Benveniste-Levkovitz, P., & Levtzion-korach, O. (2021). Safety and Humoral Responses to SARS-CoV-2 mRNA Vaccination of Previously Infected and Naïve Populations. *Preprint*.	Mar 25, 2021	Cohort	Vaccinated, General population, Israel	Confirmed by seropositivity n=78 Median age 46 (IQR 31-60) Time since infection median 116.5 days (IQR 96-155 days)	No history of COVID-19 n=177 Median age 46 (IQR 36-59)	Pfizer/ BioNTech	No significant difference	1st dose, Chills Previously infected: 20.3% Naïve: 4.5%, p<0.0001 No difference between groups after 1st or 2nd dose for fever, fatigue, headache, nausea, vomiting, diarrhea, muscle aches, join ache or allergic reaction	Emergency department visit or hospitalization 1st dose: Prior infection: 6.8% Naïve: 0.6%, p=0.011 2nd dose: Prior infection: 6.8% Naïve: 0%, p=0.002	None	Moderate ***PREPRINT***
Mathioudakis, A. G., Ghrew, M., Ustianowski, A., Ahmad, S., Borrow, R., Papavasileiou, L. P., … Bakerly, N. D. (2021). Self-reported real-world safety and reactogenicity of COVID-19 vaccines: A vaccine recipient Survey. *Life*, *11*(3), 249.	Mar 17, 2021	Cross-sectional	Vaccinated HCW, United Kingdom (78.6%), Greece (16.6%) Median age 45 (IQR 35-50)	Confirmed by PCR or seropositivity n=532	No history of COVID-19 n=1470	Pfizer/BioNTech (1673), AstraZeneca (282), Other (24) or Unknown (5) 1st dose	Localized reaction RR=1.11 (1.06-1.16) No difference in skin rash, tingling, swelling	Fever, RR=2.45, 95% CI=2.01, 3.00 Flu-like illness, RR=1.92, 95% CI=1.61, 2.29 Shortness of breath, RR=2.06, 95%CI= 1.22, 3.49 Fatigue or tiredness, RR=1.39, 95% CI=1.24, 1.56 Other, RR=1.45, 95% CI=1.12, 1.87	No difference in anaphylaxis	None	Low

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