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SPOR Evidence Alliance

Strategy for Patient-Oriented Research SPOR Putting Patients First

COVID-END COVID-19 Evidence Network to support Decision-making ... in Canada

Rapid Review Update 1: What is the ongoing effectiveness, immunogenicity, and safety of COVID-19 vaccines in persons who have had a prior, confirmed COVID-19 infection?

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Prepared for: National Advisory Committee on Immunization (NACI)

Date: October 15, 2021

Suggested Citation:

National Collaborating Centre for Methods and Tools. (2021, October 15). *Rapid Review Update 1: What is the effectiveness, immunogenicity, and safety of COVID-19 vaccines in persons who have had a prior, confirmed COVID-19 infection?* https://www.nccmt.ca/covid-19/covid-19-rapid-evidence-service/36

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.

This work was funded in collaboration with the SPOR Evidence Alliance (SPOR EA) and COVID-19 Evidence Network to support Decision-making (COVID-END), which are supported by the Canadian Institutes of Health Research (CIHR) through the Canadian 2019 Novel Coronavirus (COVID-19) Rapid Research Funding opportunity.

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, questions remain as to the comparable effectiveness in those with prior confirmed COVID-19 infection. Given the immune system's previous exposure to the virus, it is not known whether the same vaccination schedule recommended for the general populations 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. As questions emerge about waning immunity over time, and booster shots are planned, it is also not known whether those with previous infection should receive boosters on the same schedule.

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 October 6, 2021, to answer the question: **What is the ongoing effectiveness, immunogenicity, and safety of COVID-19 vaccines in persons who have had a prior, confirmed COVID-19 infection?**

What Has Changed in This Version?

- 15 new studies were identified and included in this updated review
- To address emerging questions about waning immunity and the need for booster shots in specific populations, additional exclusion criteria were applied. To be eligible for inclusion, studies must report data on outcomes of interest collected at least three months, 12 weeks, or 90 days post-completion of vaccination regime.
    - This resulted in 46 studies that were previously included being excluded from the current update, and 1 study remaining
- Given the limited data, the previous criteria which required a minimum sample size of 20 to be included has been removed. This did not result in any previously excluded studies being included in this review.

Key Points

- Only three studies were identified that compared the efficacy or effectiveness of vaccines in those with previous COVID-19 infection compared to those without previous infection. Vaccination in individuals with previous COVID-19 infection may be slightly more effective compared to those without previous infection, although the number of breakthrough infections was low in both groups. The certainty of evidence is low (GRADE).
- Only two studies compared rates of infection in those with previous COVID-19 infection who were vaccinated compared to those who were not vaccinated. Given the small

number of events in both groups, the effectiveness of vaccination in those with prior infection cannot be determined. The certainty of evidence is very low (GRADE).
- Across the 13 studies reporting on the humoral immune response to vaccination those with a prior COVID-19 infection likely have a stronger response than those without a prior infection after two doses, with the magnitude of the difference decreasing over time. The certainty of the evidence is moderate (GRADE).
- No studies compared humoral immune response in individuals with prior COVID-19 infection who had received vaccines to those who were not vaccinated with follow-up greater than three months.
- No studies reported on cellular immune responses with follow-up greater than three months.
- No studies compared local or systemic adverse effects with follow-up greater than three months.

Overview of Evidence and Knowledge Gaps

- There is very limited long-term (> 3 months) data on efficacy and effectiveness of vaccination to prevent infection specific to those with prior infection. The findings across studies were consistent: in all but one comparison, vaccinated individuals with prior infection had a small but statistically significant different decrease in the number of breakthrough infections compared to vaccinated individuals without prior infection. The largest difference was seen in residents (mean age 84.6) of a long-term care facility experiencing an outbreak of the delta variant of concern (1.3% vs. 53.7%). This suggests that any additional protection from prior infection may be more important in older adults.
- Within studies reporting on vaccine effectiveness, only the number of cases were reported without additional information on severity of infection, hospitalization, or death.
- Across all studies, vaccinated individuals with and without prior infection have vastly reduced rates of infection compared to unvaccinated individuals.
- Across immunogenicity studies, findings are consistent that those with a prior infection have a stronger response with follow-up periods closer to receipt of vaccination. The magnitude of the difference between groups appears to decrease over time, and in several studies was no longer statistically significant at the longest follow-up periods (5-7 months).
- Despite noted differences in immunogenicity, it is not clear whether the differences seen are meaningful in terms of protection offered against infection, severe infection, hospitalization, or death. One study found that IgG levels following vaccination did not predict protection in infection naïve older adults; it is not known whether this finding applies to other age groups or those with prior infection.
- Heterogeneity in findings across studies is likely influenced by variations in time since infection in previously infected individuals, interval between the first and second dose, the timing of data collection following vaccination and loss to follow-up which varies across studies. There is insufficient evidence available to draw conclusions as to whether interval between infection and vaccination, or vaccine product received, or interval between vaccine doses impacts effectiveness or immune response.

- No included studies reported on vaccine effectiveness or immunogenicity in populations where vaccines were mixed between first and second doses.
- 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, findings were mixed, and no conclusions can be drawn based on severity of infection.
- Several studies collected data on either effectiveness and immunogenicity during periods where new variants of concern (VoC) were prevalent however effectiveness findings were generally not separated by VoC in those with and without prior infection.

Implications for Policy Making

- While the evidence included in this review suggests that vaccinated individuals with prior infection may have greater protection against COVID-19 and a stronger immune response than vaccinated individuals without prior infection, given the small number of infections in each group, short follow-up time and uncertainty with respect to how absolute values of humoral or cellular immune response markers correlate to or predict future infection, this data should be interpreted with caution with respect to recommendations about needs for additional booster doses in this population.

Methods

Research Question

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

Search

On October 6, 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 October 6, 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.

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.

	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 with at least a 3-month follow-up period.	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 considering 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

In this update, 15 new single studies were identified. 46 **previously included** studies were excluded based on new eligibility criteria, for a total of 16 publications addressing the research question.

A full list of studies that were previously included that are now excluded is available in Appendix 2.

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	3	⊕◯◯◯ Low[1]	Vaccination in individuals with previous COVID-19 infection may be slightly more effective compared to those without previous infection.
Risk of infection amongst those with previous infection, comparing those who received vaccination vs. unvaccinated	Observational	2	⊕◯◯◯ Very low[2]	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	13	⊕⊕⊕◯ Moderate[2]	Those with prior infection likely have a stronger humoral immune response to vaccination than those with no prior infection.

[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
[2]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 and risk of bias
[3]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
Anti-S: anti-S antibodies
%B/B0: %bound/maximum bound
CI: confidence interval
dR: relative dissociation rate
GMC: geometric mean count
HCW: health care worker
IC_{50}: half maximal inhibitory concentration
IgG: immunoglobulin G
IQR: interquartile range
LTC: long-term care
mAb: monoclonal antibody
nAb: neutralizing antibody
NR: not reported
RFU: relative fluorescence unit
RT-PCR: real time polymerase chain reaction
RBD: receptor-binding domain
SD: standard deviation
SNAb: serum neutralizing antibody
Tab: total anti-capsid antibody
VoC: variant(s) of concern

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=3)										
New evidence reported on October 15, 2021										
Blain, H., Tuaillon, E., Pisono, A., Soriteau, L., Million, E., Leglise, M., Bussereau, I., Miot, S., Rolland, Y., Picot, M., Christine, Jean, J. (2021). Prior Covid-19 and high RBD-IgG levels correlate with protection against VOC-δ SARS-CoV-2 infection in vaccinated nursing home residents. *Preprint.*	Sep 21, 2021	Cohort	Vaccinated nursing home residents during outbreak of delta-variant France Mean age 84.6 ±9.5	RT-PCR Confirmed seropositive n=44	RT-PCR Confirmed seronegative n=96	Pfizer-BioNTech 3-5 months prior to outbreak	Cumulative incidence	Previously infected: 1/44 (1.3%) Infection naïve: 55/96 (57.3%) p<0.0001	Delta-variant outbreak	Moderate ***PREPRINT***
Abu-Raddad, L.J., Chemaitelly, H., Ayoub, H.H., Yassine, H.M., Benslimane, F.M., Al Khatib, H.A. … Bertollini, R. (2021). Protection afforded by the BNT162b2 and mRNA-1273 COVID-19 vaccines	Jul 26, 2021	Cohort	Vaccinated adults Qatar Median age 39 (range 32-48)	Confirmed RT-PCR, seropositive n=24,052	Confirmed RT-PCR seronegative n=24,052	Pfizer/BioNTech or Moderna 14-146 days after 2nd dose Pfizer 14-60 days after 2nd dose Moderna	Cumulative incidence	Pfizer/BioNTech Previously infected: 0.16% (95% CI=0.11, 0.23) Naïve: 1.45% (95% CI=1.20, 1.76) p<0.05	Alpha and beta variants dominant in region during study follow-up period.	High ***PREPRINT***

in fully vaccinated cohorts with and without prior infection. *Preprint*.								Moderna: Previously infected: 0.06% (95% CI=0.03, 0.12) Naïve: 0.08% (95% CI=0.04, 0.15) *p-value NR*		
							Incident rate ratio	Pfizer-BioNTech: 0.15 (95% CI=0.11, 0.20)		
								Moderna: 0.85 (95% CI=0.34, 2.05)		
Previously reported evidence										
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: median 143 days (76,179)	COVID-19 infection naïve confirmed by nucleic acid amplification n=28 855 Mean age 42± SD 13	Pfizer/BioNTech (37%) Moderna (63%) Up to 108 days after the 2nd dose	Cumulative incidence of infection	Prior infection: 0/1220 (0%) Naïve: 15/28 855 (0.05%) *p-value NR*	Previously infected were younger (39±13 vs. 42±13, p<0.001), had patient-facing jobs (62% vs. 51%, p<0.001).	Moderate ***PREPRINT***

Risk of infection amongst those with previous infection, comparing those who received vaccination vs. unvaccinated (n = 2)										
New evidence reported on October 15, 2021										
Bruxvoort, K., Sy, L.S., Qian, L., Ackerson, B.K., Luo, Y., Lee, G.S., … Tseng, H.F. (2021). Real-World Effectiveness of the mRNA-1273 Vaccine Against COVID-19: Interim Results from a Prospective Observational Cohort Study. *Preprint*.	Sep 2, 2021	Cohort	Confirmed seropositive adults San Diego, USA Median age 65 (range 45-73)	Vaccinated (prior symptomatic infection) n=27	Unvaccinated (prior symptomatic infection) n=3	Moderna 14 days post index date to 3 months	Cumulative incidence	Vaccinated: 3.99 (95% CI=2.73,5.81) Unvaccinated: 5.48 (95% CI=3.85, 7.79)	This study was funded by Moderna Variants included delta (47.1%), alpha (21.4%), gamma (11.4%), epsilon (4.2%), Iota (4.3%) amongst vaccinated.	Moderate ***PREPRINT***
							Adjusted hazard ratio	0.66 (95% CI=0.38, 1.15)		
							Adjusted vaccine efficacy	33.6% (95% CI=0.0, 65.8)		
				Vaccinated (prior asymptomatic infection) n=44	Unvaccinated (prior asymptomatic infection) n=40	Moderna 14 days post index date to 3 months	Cumulative incidence	Vaccinated: 6.50 (95% CI=4.84, 8.763) Unvaccinated: 7.07 (95% CI: 5.19, 9.64)		
							Adjusted hazard ratio	0.92 (95% CI=0.58, 1.45)		
							Adjusted vaccine efficacy	8.2% (95% CI=0.0,47.3)		
Previously reported evidence										
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 with confirmed RT-PCR infection, USA Time since infection: median 143 days (76,179)	Vaccinated n=1220 Mean age 39± SD 13	Unvaccinated N = 1359 Mean age 42± SD 13	Pfizer/BioNTech (37%), Moderna (63%)	Cumulative incidence of infection	Vaccinated: 0/1220 Unvaccinated: 0/1359 p>0.9999	-	Moderate ***PREPRINT***
							Adjusted hazard ratio	0.313 (95% CI=0, Infinity)		

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 = 13)											
New evidence reported on October 15, 2021											
Blain, H., Tuaillon, E., Pisono, A., Soriteau, L., Million, E., Leglise, M., Bussereau, I., Miot, S., Rolland, Y., Picot, M., Christine, Jean, J. (2021). Prior Covid-19 and high RBD-IgG levels correlate with protection against VOC-δ SARS-CoV-2 infection in vaccinated nursing home residents. *Preprint.*	Sep 21, 2021	Cohort	Vaccinated nursing home residents France Mean age 84.6 $\pm$9.5	RT-PCR Confirmed seropositive n=32	RT-PCR Confirmed seronegative n=25	Pfizer-BioNTech 6-weeks post 2nd dose	IgG (anti-RBD)	AU/mL Median (IQR)	Previously infected: 31,553 (19 667, 40 000) Naïve: 1050 (334, 3504) *p-value NR*	Naïve individual post-vaccination RBD IgG levels did not predict subsequent protection from Delta VoC infection.	Moderate ***PREPRINT***
						During outbreak, 3-5 months post 2nd dose (RT-PCR negative only)			Previously infected: 22,880 (12 296, 22 888) Naïve: 260 (79, 696) p<0.0001		
Kontopoulou, K., Nakas, C., Ntenti, C., Katsioulis, C., Goulas, A., & Papazisis, G. (2021). Antibody titers 3-months post-vaccination with the Pfizer/BioNTech vaccine in Greece. *Preprint.*	Sep 3, 2021	Cohort	Vaccinated HCW, Greece Vaccinated HCW, Greece	Confirmed seropositive n=38	Confirmed seronegative n=243	Pfizer-BioNTech 3 months post 2nd does (data not provided)	IgG-S (anti-RBD)	GMC (AU/mL)	Previously infected: 7460.91 (95% CI=5872.7, 9477.32) Naïve: 2534.43 (95% CI=2246.59, 2859.14) p<0.001	>99% of the study sample exceeded seropositivity threshold of 50 AU/mL. The authors conclude that although a decline in titers occurs at 6-months, these levels were still deemed.	High ***PREPRINT***
								GMC fold change relative to 2nd dose	Previously infected: 0.29 (95% CI=0.24, 0.33) Naïve: 0.17 (95% CI=0.16, 0.19) p<0.001		

Kontopoulou, K., Nakas, C., Ainatzoglou, A., Goudi, G., Katsioulis, C., & Papazisis, G. (2021). Evolution of Antibody Titers Up to 6 Months Post-Immunization with the BNT162b2 Pfizer/BioNTech Vaccine in Greece. *Preprint*. **Note, unique publications but from same study cohort as above*	Sep 15, 2021			N = 33	n = 213	6 months after 2nd dose	IgG	GMC (AU/mL)	Previously infected: 2848 (95% CI=2120.77, 3826.68) Naïve: 825.98 (95% CI=745.96, 914.60) p<0.001	satisfactory to prevent infection.	High ***PREPRINT***
								GMC fold change relative to 2nd dose	Previously infected: 0.10 (95% CI=0.08, 0.13) Naïve: 0.06 (95% CI=0.05, 0.06) p<0.05		
								GMC fold change relative to 3-months	Previously infected: 0.39 (95% CI=0.34, 0.45) Naïve: 0.33 (95% CI=0.31, 0.35) p<0.05		
Chen, Y., Tong, P., Whiteman, N.B., Moghaddam, A.S., Zuiani, A., Habibi, S., … Wesemann, D.R. (2021). Differential antibody dynamics to SARS-CoV-2 infection and vaccination. *Preprint*.	Sep 10, 2021	Cohort	Vaccinated adults, USA	Confirmed seropositive n=28 Median age 46.4 (range 23-77)	Confirmed seronegative n=18 Median age 39.8 (range 22-77)	Pfizer/BioNTech or Moderna 195 days after 2nd dose	IgG (anti-S and RBD)	mAb μg/mL	Previously infected had higher anti-S and anti-RBD than naïve up until 7 months (values NR). p<0.0001	-	High ***PREPRINT***

Racine-Brostek, S.E., Yee, J., Sukhu, A., Qiu, Y., Rand, S., Barone, P., ... Zhao, Z. (2021). More rapid, robust, and sustainable antibody responses to mRNA COVID-19 vaccine in convalescent COVID-19 individuals. *JCI Insight*. Epub ahead of print.	Sep 9, 2021	Cohort	Vaccinated HCW	Confirmed seropositive n=19 Mean age 42.5 ±11.6 Median days after onset of symptoms to 1st dose: 262 (range: 101.5, 275.0)	Confirmed seronegative n=49 Mean age 46.3 ±13.3	Pfizer-BioNTech 6-8 weeks post 2nd dose	TAb	RFU Median (IQR)	Previously infected higher than naïve (values NR) p<0.001	Naïve had a 50% decrease by 6 months.	Moderate
						~5 months post 1st dose			Previously infected: 8997 (7179, 9916) Naïve: 2706 (1667, 4511), Between-group difference 3.3-fold p<0.001		
						6-8 weeks post 2nd dose	SNAb	%B/B0 Median (IQR)	Previously infected: 0.8% (0.47, 1.22) Naïve: 17.35% (10.81, 28.76) p<0.001		
						~5 months post 2nd dose			Previously infected: 1.6% (1.359, 4.42) Naïve: 17.35% (10.81, 28.76) p<0.01		
						6-8 weeks post 2nd dose	Avidity	dR Median (IQR)	Previously infected: 3.89 (3.46, 4.89) Naïve: 7.0 (6.34, 3.38) p<0.001		
						~5 months post 2nd dose			Previously infected: 4.43 (3.39, 5.64) Naïve: 5.36 (4.5, 5.98) p=0.115		

						~5 months post 2nd dose	S-antibodies	U/mL	Previously infected: >2500 at all time points up to 6 months Naïve: 720 (565, 1269) p<0.001		
Erice, A., Varillas-Delgado, D., & Caballero, C. (2021). Decline of antibody titres 3 months after two doses of BNT162b2 in non-immunocompromised adults. *Clinical Microbiology and Infection*. Epub ahead of print.	Sep 8, 2021	Cohort	Vaccinated HCW, Spain Mean age=46±11	Confirmed by RT-PCR or seropositivity n=36	Confirmed seronegative n=194	Pfizer/BioNTech 1.5 months after 2nd dose	IgG (anti-RBD)	AU/mL Median (IQR)	Previously infected: 19,016 (7974,27 885) Naïve: 8,747 (5,631, 15,409) p<0.001	Median antibodies decreased by 58% in all participants (51% in previously infected). Titers higher in men, not statistically significant.	High
						3 months after 2nd dose			Previously infected: 9,364 (3975, 22 233) Naïve: 3,724 (2003, 7137) p<0.001		
Kertes, J., Gez, S.B., Saciuk, Y., Supino-Rosin, L., Stein, N.S. … Zohar, A.E. (2021). Effectiveness of the mRNA BNT162b2 vaccine six months after vaccination: findings from a large Israeli HMO. *Preprint*.	Sep 7, 2021	Cohort	Vaccinated individuals, Israel	Confirmed seropositive n = 365	Confirmed seronegative	Pfizer/BioNTech 7 days after 2nd dose 6 months after 2nd dose	IgG	% <300 AU/mL	Prior infection: 40.3% Naïve: 65.2% p<0.001	-	Moderate ***PREPRINT***

Bayart, J.L., Douxfils, J., Gillot, C., David, C., Mullier, F., Elsen, M., ... Favresse, J. (2021). Waning of IgG, total and neutralizing antibodies 6 months post-vaccination with BNT162b2 in healthcare workers. *Preprint*.	Sep 3, 2021	Cohort	Vaccinated HCW, Mean age 44	Confirmed seropositive n=73	Confirmed seronegative n=157	Pfizer-BioNTech Time after 2nd dose: 69 days	Mean total antibodies	U/mL Ratio (+/-)	Previously infected: 8,919 (95% CI=7201, 10637) Naïve: 1,262 (95% CI=1104, 1420) p<0.0001 Ratio: 7.1	-	Moderate ***PREPRINT***
						159 days			Previously infected: 4,270 (95% CI=3324, 5215) Naïve: 998 (95% CI=848, 1148) p<0.0001 Ratio: 4.3		
						69 days	IgG	AU/mL	Previously infected: 14,509 (95% CI=12 477, 16 541) Naïve: 6050 (95% CI=5371, 6729) p<0.001 Ratio 2.4		
						159 days			Previously infected: 6,333 (95% CI=5 072, 7 593) Naïve: 1,949 (95% CI=1 565, 2 332), p<0.342 Ratio: 3.2		

						69 days	NAbs	IC_{50} Median (IQR)	Previously infected: 163.1 (95% CI=83.5,243) Naïve: 127.6 (95% CI=84.3, 170.9) p=0.390 Ratio: 1.3		
						159 days			Previously infected: 30.5 (95% CI=18.2, 42.7) Naïve: 26.1 (95% CI=20.1, 32.1) p=0.4653 Ratio: 1.2		
Kosiorek, P., Kazberuk, D., Hrynieqicz, A., Milewski, R., Stróż, S., & Stasiak-Barmuta, A. (2021). Systemic COVID-19 vaccination also enhances the humoral immune response after SARS CoV-2 infection. An approach to criteria for COVID-19 re-immunization is needed. Do we need a third dose? *Preprint*.	Sep 2, 2021	Case-control	Vaccinated HCW, Poland Age range: 18-89 (45% >50)	Confirmed seropositive n=312	Confirmed seronegative n=472	Pfizer-BioNTech 90 days post 2nd dose	IgM IgG IgG (anti-S RBD)	AU/mL	IgM, IgG and S-RBD levels were significantly higher in those vaccinated and previously infected (values NR). p<0.0001	-	High ***PREPRINT***

Vicenti, I., Basso, M., Gatti, F., Scaggiante, R., Boccuto, A., Zago, D., ... Zazzi, M. (2021). Faster decay of neutralizing antibodies in never infected than previously infected healthcare workers three months after the second BNT162b2 mRNA COVID-19 vaccine dose. *International Journal of Infectious Diseases*. Epub ahead of print.	Sep 1, 2021	Cohort	Vaccinated HCW Veneto, Italy Median age 42 (range 33-47)	Confirmed seropositive, symptomatic n=9 Confirmed seropositive, asymptomatic n=14 Median time since infection 292 days (range 267-300)	Confirmed seronegative n=13	Pfizer/BioNTech or Moderna 20±3 days after 2nd dose	NtAbs	ID_{50} Median (range)	Previously infected, symptomatic: 1707.5 (1371.5, 3769.2) Previously infected, asymptomatic: 1450.3 (797.1, 2310) p=0.2076 Naïve: 176 (94.7, 299.7) vs. symptomatic p=0.0003 Naïve: 176 (94.7, 299.7) vs. asymptomatic p=0.0001	No difference between symptomatic and asymptomatic previously infected, but naïve participants had lower NtAbs than both.	High
						90±2 days after 2nd dose			Previously infected, symptomatic: 647 (308.4, 1439.7) Previously infected, asymptomatic: 520.5 (342,669.9) p=0.438 Naïve: 20 (17.5, 37) vs. symptomatic p<0.0001 Naïve: 20 (17.5, 37) vs. asymptomatic p=0.0001		

Tré-Hardy, M., Cupaiolo, R., Wilmet, A., Antoine-Moussiaux, T., Vecchia, A.D., ... Blairon, L. (2021). Six-month interim analysis of ongoing immunogenicity surveillance of the mRNA-1273 vaccine in healthcare workers: A third dose is expected. *Journal of Infection*. Epub ahead of print.	Aug 22, 2021	Cohort	Vaccinated HCW, Belgium Median age 50.1 (range: 46.9-52.4)	Confirmed seropositive n=43	Confirmed seronegative n=158	Moderna 2 months after 2nd dose 5 months after 2nd dose	IgG	AU/mL Median (IQR)	Previously infected: 400 (400, 400) Naïve: 400 (400, 400) Previously infected: 400 (365.5, 400) Naïve: 221.0 (202.3, 241.2) Decline from 2 to 5 months was greater in naïve vs. previously infected. p<0.0001	Among those previously infected, at 6 months 5/43 needed an additional booster to reach the 400 AU/mL threshold. All were >40 years (values not provided).	Moderate
Kannian, P., Mahanathi, P., Cohort Ashwini, V., & Kum Cohort arasamy, N. (2021). Booster and anergic effects of the Covishield vaccine among healthcare workers in South India. *Preprint*.	Aug 7, 2021	Cohort	Vaccinated HCW, South India	Confirmed seropositive Mild Covid n=13	No symptoms of COVID-19 n=88	AstraZeneca 14 days post 2nd dose 28 days post 2nd dose 3 months post 2nd dose	Anti-SARS-CoV2 spike antibodies	U/mL Median (IQR)	Previously infected: 13,584 (2692, 64 920) Naïve: 1206 (47,16 084) p<0.00001 Previously infected: 12,039 (3032, 37 476) Naïve: 870 (29, 12 824) p<0.00001 Previously infected: 6545 (1376, 22 004) Naïve: 306 (16, 2660) p=0.03	-	High ***PREPRINT***

Jeulin, H., Craus, D., Labat, C., & Benetos, A. (2021). Comparative analysis of post-vaccination anti-spike IgG antibodies in old Nursing Home Residents and in middle-aged Healthcare workers. *Preprint*.	Aug 4, 2021	Cohort	Vaccinated nursing home residents and HCW, France	Confirmed seropositive Residents n=109 median age 89 (range: 79-93) HCW n=21 median age 46 (range: 42-56)	Confirmed seronegative Residents, n=234 median age 88 (range: 83-92) HCW, n=187 median age 45 (Range: 38-54)	Not specified HCW: 123-141 days post 2nd dose Residents: 51-84 days post 2nd dose	IgG(S)	AIU Median (IQR)	*Residents:* Previously infected: 800 (800, 800) Naïve: 76 (20,287) p<0.01 *HCW:* Previously infected: 781 (481, 800) Naïve: 304 (182, 762) p<0.0001	Age was associated with IgG(S) decline only in naïve participants	Moderate ***PREPRINT***

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