Journal of Travel Medicine

International Society of Travel Medicine
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Journal of Travel Medicine, 2021, 1–5
https://doi.org/10.1093/jtm/taab190
Advance Access Publication Date: 9 December 2021
Original Article

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Comparison of antibody immune responses between BNT162b2 and mRNA-1273 SARS-CoV-2 vaccines in naïve and previously infected individuals

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Submitted 6 October 2021; Revised 27 November 2021; Editorial Decision 29 November 2021; Accepted 7 December 2021

Abstract

Background: Two mRNA vaccines, Pfizer-BNT162b2 and Moderna-mRNA-1273, obtained the Emergency Use Listing by WHO for preventing COVID-19. However, little is known about the difference in antibody responses induced by these two mRNA vaccines in naïve and previously infected (PI) individuals.

Method: We investigated the levels of anti-S-RBD (total, IgG and IgA) levels in naïve and PI individuals, 1–13 (median = 6) weeks following the second dose of either vaccine. Results in the naïve-vaccinated group, the mRNA-1273 vaccine induced significantly higher levels of anti-S-RBD total antibodies (3.5-fold; $P < 0.001$), IgG (2-fold, $P < 0.01$) and IgA (2.1-fold, $P < 0.001$) as compared with the BNT162b2 vaccine. In addition, both vaccines produced significantly higher anti-S-RBD total antibody levels in the PI-group compared with naïve-vaccinated group. The PI group elicited a higher level of anti-S-RBD IgG than the naïve-BNT162b2 ($P = 0.05$), but not more than the naïve-mRNA-1273 ($P = 0.9$) group. Interestingly, the PI vaccinated group elicited a comparable level of IgA ratio to the naïve-mRNA-1273 group but significantly higher than the naïve-BNT162b2 group (1.6-fold, $P < 0.001$).

Conclusion: Our results showed that the PI-vaccinated group produces a higher level of antibodies than the naïve vaccinated group, particularly for those vaccinated with BNT162b2.

Key words: Pfizer-BNT162b2, Moderna-mRNA-1273, S-RBD IgA, S-RBD IgG, immune response

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Introduction

Since the beginning of the COVID-19 pandemic, over 226 million people have been infected with the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), including more than 5 million reported deaths.[1] To combat the widespread of SARS-CoV-2, major vaccination campaigns have been launched worldwide, providing 7.6 billion vaccine doses to date (23 November 2021).[2] Pfizer-BNT162b2 and Moderna-mRNA-1273 COVID-19 vaccines obtained Emergency Use Listing by WHO in December 2020 and April 2021, respectively.

Recent clinical studies and controlled trials demonstrated high safety and efficacy of the BNT162b2 (Pfizer-BioNTech) and the mRNA-1273 (Moderna) vaccines, exceeding 94% protection against the original strain.[3,4] Recently, we completed a nationwide study assessing protection from SARS-CoV-2 breakthrough infection after mRNA vaccination among persons with or without prior SARS-CoV-2 infection.[5] The study showed that prior SARS-CoV-2 infection was associated with a statistically significantly lower risk for breakthrough infection among individuals receiving the BNT162b2 and mRNA-1273 vaccines, and more so for the BNT162b2 vaccine.[5] We also demonstrated that the mRNA-1273 and BNT162b2 vaccines provide similar protection patterns.[6] Although the mRNA-1273 vaccine appears to be more effective against SARS-CoV-2 variants, including the B.1.351 Beta variant.[7–9] Different parameters of antibody immune response, such as IgA and total anti-S-RBD antibodies to both mRNA COVID-19 vaccines, have not been extensively studied especially in people with previous SARS-CoV-2 infection emphasizing the need to evaluate the vaccines' durability and comparative effectiveness.

The primary objective of this study is to compare the antibody immune response between the naïve and previously infected (PI) individuals after administering two doses of mRNA vaccines and to compare the antibody response between the two types of the mRNA vaccines (mRNA-1273 and BNT162b2 SARS-CoV-2). Both vaccines have been approved for emergency use in Qatar by the Department of Pharmacy and Pharmaceutical Control in the Ministry of Public Health.

Material and Methods

Sample collection and ethical approval

Participants who received two BNT162b2 or mRNA-1273 vaccine doses were eligible for inclusion. A total of 289 samples were collected between April and October 2021 from staff and students at Qatar University, the largest national university in Qatar. Peripheral blood was collected 1–13 weeks following the administration of the second dose of vaccine (BNT162b2 median = 6, mRNA-1273 median = 5, PI median = 6). Participants were either naïve or PI with SARS-CoV-2. The study was reviewed and approved by the Institutional Review Board at Qatar University (QU-IRB 1537-FBA/21). Plasma was separated from whole venous blood and stored at −80°C until performing the immunoassay testing. Demographic information and information on previous infection with SARS-CoV-2 was collected through a self-administered questionnaire.

Serology testing

Serological testing was done using the automated analyzer CL-900i® from Mindray Bio-Medical Electronics[10–12] using two chemiluminescence immunoassays to detect the vaccine-induced antibodies: (i) the anti-SARS-CoV-2 S-receptor binding domain (S-RBD) IgG (catalog No. SARS-CoV-2 S-RBD IgG122, Mindray, China) with a cut off index of ≥10–1000 BAU/ml and (ii) the anti-S-RBD SARS-CoV-2 total antibodies (IgG, IgA and IgM) (Catalog No. SARS-CoV-2 Total Antibodies 122, Mindray, China) with positive cut off index of ≥10–2000 AU/ml. All samples with readings higher than the reference range were diluted with phosphate-buffered saline and retested. In addition, the Euroimmun anti-SARS-CoV-2 IgA ELISA (Catalog No. EI 2606-9601 A, Germany) was used to measure the anti-S1 IgA antibody levels.[13] The IgA ratio was calculated by dividing the extinction of the sample by the calibrator. Ratios ≥1.1 were considered positive, > 0.8 negative and ≥0.8 to > 1 borderline. Some samples were not tested for IgA (40/289) because of limited plasma volume. All tests were carried out according to the manufacturers' instructions.

In addition to the reported information on previous history of infection, we used nucleoprotein-specific IgG (anti-N IgG) to denote prior SARS-CoV-2 exposure as the PI but not the naïve vaccinated volunteers would have IgG to the N protein. All samples were tested for the presence of anti-N SARS-CoV-2 IgG using the Architect automated chemiluminescent assay (Abbott Laboratories, USA) according to the manufacturer's instructions.[12] Accordingly, the PI is defined as anti-N positivity and/or reported history of positive polymerase chain reaction results collected from the participants' questionnaires.

Statistical analysis

Data were analyzed using GraphPad Prism 9.2.0. (San Diego, CA, USA). Results in the graphs are plotted as mean values with standard deviation. One-way ANOVA tests were performed to compare the groups, and *P*-values ≤0.05 were considered statistically significant. In all graphs, significance was (*) $P \leq 0.05$, (**) $P \leq 0.01$ or (***) $P \leq 0.001$.

Results

Participant characteristic

Participants' demographics are described in Table 1. A total of 289 naïve-vaccinated and PI-vaccinated volunteers participated in this study. The cohort was divided into three groups: BNT162b2 naïve-vaccinated ($n = 218$), mRNA-1273 naïve-vaccinated ($n = 45$) and PI vaccinated participants ($n = 26$; 23 with BNT162b2 vaccine and 3 with mRNA-1273 and). Further details about participants are provided in Table S1 (Supplementary data are available at *JTM* online).

Antibody immune response assessment following vaccination

Anti-S-RBD total antibodies response. All naïve-BNT162b2, naïve-mRNA-1273 and PI-vaccinated groups had positive

Table 1. Demographic characteristics of the study sample ($n = 289$)

	Characteristic	BNT162b2 (%)		mRNA-1273 (%)	
		Naïve	PI	Naïve	PI
Gender					
	Male	114 (52.29)	14 (60.86)	23 (51.11)	1 (33.33)
	Female	104 (47.70)	9 (39.13)	22 (48.88)	2 (66.66)
	Total	218	23	45	3
Age (years)					
	>30	71 (43.29)	8 (34.78)	26 (57.77)	1 (33.33)
	30–50	104 (50.24)	14 (60.86)	16 (35.55)	2 (66.66)
	>50	32 (15.45)	1 (4.34)	2 (4.44)	–
	Unknown	–	–	1 (2.22)	–
	Total	218	23	45	3

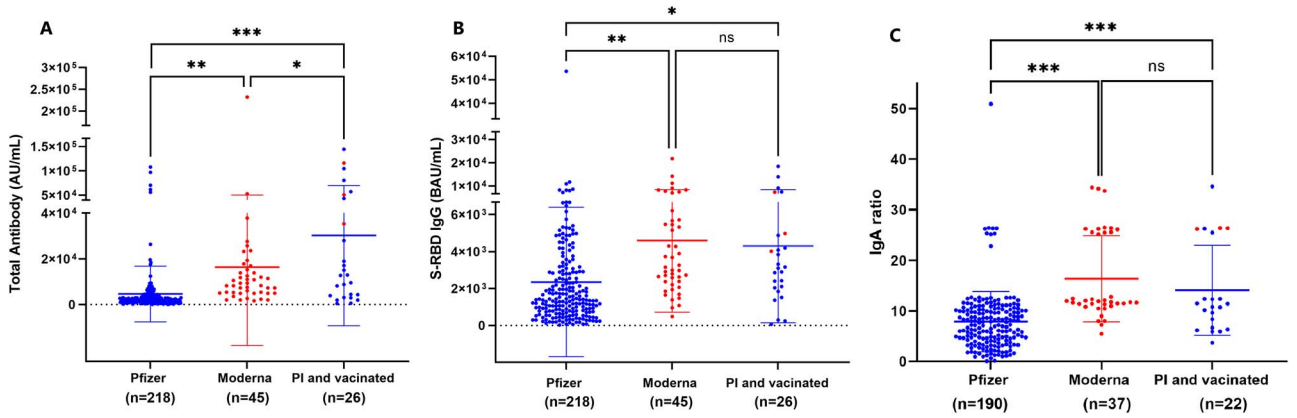

Figure 1. Antibody levels in mRNA vaccinated participants after 1–13 (median = 6) weeks of receiving two doses, and participants with prior infection with two doses of vaccine. The tests were performed using the automated analyzer Mindray CI-900i (a), anti-S-RBD Total antibodies level (AU/ml) (b) and anti-S-RBD IgG antibody levels (BAU/ml) (c) anti-S IgA antibody levels using Euroimmun ELISA. ns $P > 0.05$, $^{*}P \leq 0.05$, $^{**}P \leq 0.01$, $^{***}P \leq 0.001$.

total antibodies response (Figure 1a), with mean levels of 4.6×10^3 (95%CI: 3.0–6.2 $\times 10^3$), 1.6×10^4 (95%CI: 6.1 $\times 10^3$–2.7 $\times 10^4$) and 3.0×10^4 AU/ml (95%CI: 1.4–4.6 $\times 10^4$), respectively. The PI-vaccinated group harbored significantly higher levels of total anti-S-RBD antibodies compared with the naïve-BNT162b2 (6.5-fold, $P < 0.001$) and naïve-mRNA-1273 (1.9-fold, $P < 0.05$) vaccinated groups. Furthermore, the naïve-mRNA-1273-vaccinated group had significantly higher total antibody levels than the naïve-BNT162b2 (3.5-fold, $P < 0.01$).

Anti-S-RBD IgG response. Anti-S-RBD IgG response was detected in all naïve-BNT162b2, naïve-mRNA-1273 and PI-vaccinated groups (Figure 1b), with mean IgG levels of 2.3×10^3 (95%CI: 1.8–2.8 $\times 10^3$), 4.6×10^3 (95%CI: 3.4–5.7 $\times 10^3$) and 4.3×10^3 BAU/ml (95%CI: 2.6–5.9 $\times 10^3$), respectively. The PI group had a higher level of anti-S-RBD IgG than the naïve-BNT162b2 ($P = 0.05$) but not more than the naïve-mRNA-1273 ($P = 0.9$) vaccinated group. Interestingly, the naïve-mRNA-1273 group elicited significantly higher IgG levels than the naïve-BNT162b2 vaccinated group (2-fold, $P = 0.002$).

Anti-S-RBD IgA response. IgA antibodies were detected in all of the PI and the naïve mRNA-1273 vaccinated groups (Figure 1c). However, in the naïve-BNT162b2 group, 96.8% (184/190) were positive for anti-S-RBD IgA, 1.6% (3/190) were negative and 1.6% (3/190) were borderline. The mean IgA ratios of the PI vaccinated group [14.1 (95%CI: 10.1–18.1)] were significantly ($P < 0.001$) higher than the naïve-BNT162b2 vaccinated group [7.9 (95%CI: 7.1–8.7)]. Furthermore, the naïve-mRNA-1273 group had significantly higher IgA ratios [16.4 (95%CI: 13.5–19.2)] than the naïve-BNT162b2 vaccinated group ($P < 0.001$). Our results collectively indicate that the mRNA-1273 vaccine induces a significantly higher sera IgA antibody response in the naïve and the PI vaccinated individuals than the BNT162b2 vaccine.

Correlation of age and antibody responses

Samples from the naïve-BNT162b2-vaccinated participants were categorized in different age groups <30, 30–50 and >50 years old; the mean total antibodies level for each group were 3.7×10^3, 4.7×10^3 and 6.7×10^3 AU/ml, respectively. The mean anti-S-RBD IgG level for each group was 2.8×10^3, 2.2×10^3 and 1.5×10^3 BAU/ml, respectively. The mean anti-S-RBD IgA ratio for each group was 9.5, 7.2 and 6.4, respectively. The differences in all antibody responses between the three age groups were not statistically significant (Figure 2).

Discussion

The mRNA vaccines, BNT162b2 and mRNA-1273, offer great promise for curbing the spread of SARS-CoV-2 infection. They

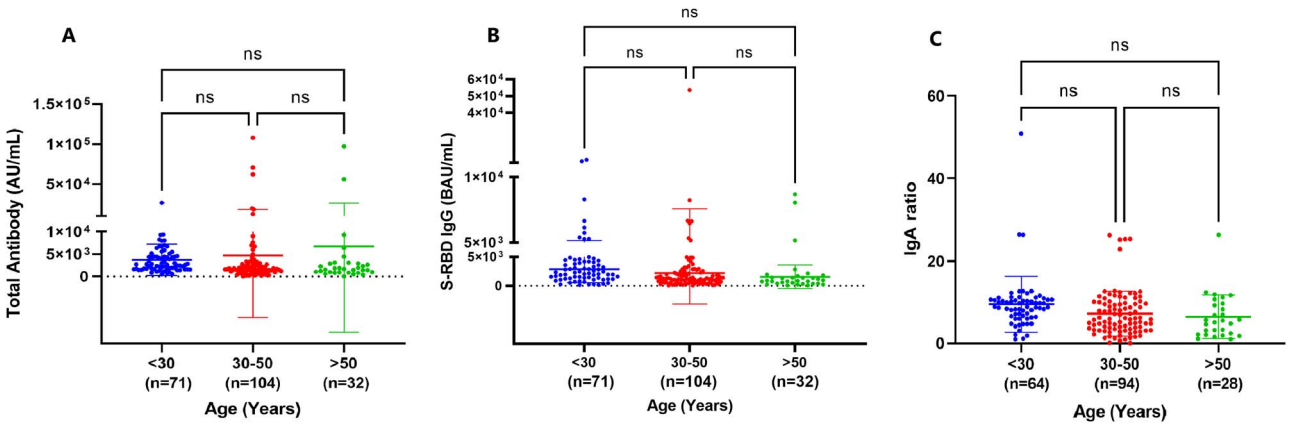

Figure 2. Antibody levels in BNT162b2 vaccinated participants according to age groups. (a) Total antibodies level (Au/ml), (b) Anti-S-RBD IgG antibody levels (BAU/ml) and (c) anti-S IgA antibody levels. ns $P > 0.05$.

showed an efficacy rate of more than 94%[3,4] against the original SARS-CoV-2 virus and were reported to be safe. A relationship between neutralization level after SARS-CoV-2 vaccination and protection against COVID-19 was previously demonstrated.[14] The level of the antibody response after vaccination correlates with neutralizing antibody titers, which might be clinically significant.[15] Natural infection mediates viral neutralization through the production of IgA antibodies, yet little is known about the vaccine-induced IgA immune response.[16] A recent study demonstrated that IgA dominates the early neutralizing antibody response to SARS-CoV-2,[17] which could be clinically significant for protection.

The novelty of our study stems from comparing antibody responses in naïve and PI-vaccinated individuals. We tested three different parameters of antibody responses, including the sera IgA response, which was not previously measured.[18] In the current study, robust antibody responses were clearly observed in both mRNA vaccinated groups. All participants elicited anti-S-RBD total antibodies and anti-S-RBD IgG, and almost all produced anti-S-RBD sera-IgA responses (Figure 1), with differences in antibody responses observed between BNT162b2 and mRNA-1273 vaccinated groups.[18] We specifically tested the total and the IgG responses not to the whole spike S protein but only to the S-RBD. It has been documented that anti-SRBD antibodies specifically correlate with the antibody neutralizing activity as both targeted the S-RBD.[11,19]

As expected, we showed that PI participants who received two doses of mRNA vaccines produced significantly higher total antibodies titers than the naïve vaccinated group (Figure 1a), which is in agreement with a previous study.[18] In addition, PI-vaccinated group produced higher antibody levels compared with the naïve BNT162b2-vaccinated group. However, no significant difference in the levels of S-RBD IgG and anti-S IgA was observed between PI-vaccinated and naïve mRNA-1273-vaccinated individuals (Figure 1b). These results emphasize that the elicited antibodies in response to mRNA vaccines include IgA, which explains the differences in the total antibodies level (Figure 1a). In addition, our PI cohort included samples with different times of infection, which might explain the variation in antibody titers and response to the vaccine. The reason why mRNA-1273 produced higher IgA levels needs further investigation. Wheeler *et al.*[20] reported no differences in antibody responses (anti-S1, anti-RBD and anti-S2) between mRNA-1273 and BNT162b after receiving the first or the second dose. Here, we showed that the mRNA-1273 vaccine induces significantly higher antibody response levels for anti-S-RBD IgG, anti-S IgA and total antibodies compared with BNT162b2 with at least 2-fold in all antibody tested parameters (Figure 1). These results are in agreement with Steensels *et al.*[18] where they demonstrated that the mRNA-1273 vaccine produces a significantly higher total antibodies level to the whole S-spike protein. In addition, the level of the antibodies elicited by the BNT162b2 starts to decrease from the second month after vaccination.[21] The differences in the level of antibody response are potentially due to each vaccine's formulation, dose content and the interval between the doses. For instance, it is reported that mRNA-1273 has higher mRNA content than BNT162b2 (100 vs. 30 μg, respectively).[4,7,22] Furthermore, the mRNA-1273 vaccine has two doses 28 days apart, while BNT162b2 doses are given 21 days apart. Therefore, this might have affected the build-up of immunity after vaccination.[23]

On the other hand, it was expected to see a distinct antibody response in different age groups. Although we showed that the youngest age group (<30 year) produces higher levels than the other two age groups (30–50 and >50), however, this difference was not significant ($P > 0.5$) (Figure 2). Some studies reported that the initial response to different SARS-CoV-2 antigens is age-dependent. For instance, Jalkanen *et al.* reported that after receiving the first dose of BNT162b2, the levels of antibodies were significantly lower in elderly (>50) compared with the younger age groups. However, the difference in antibody responses disappears after receiving the second dose.[24,25] In fact, Wheeler *et al.*[20] reported the minimal effect of age and gender on antibody responses after vaccination. The study has some limitations: other immune parameters (SRBD-IgM and the neutralizing antibodies), the durability and the kinetics of antibodies after vaccination need further investigation to provide a complete immune response profile. Furthermore, most of the PI group received the BNT162b2, and only a few received the mRNA-1273 vaccine.

In conclusion, our ongoing study showed that the antibody response induced by mRNA-1273 was approximately 3-fold higher than BNT162b2. In addition, higher total antibodies

titer was reported in PI and vaccinated compared with naïve-vaccinated participants. While both mRNA SARS-CoV-2 vaccines seem to have high efficacy and strongly protect against infection, mRNA-1273 remains the most effective over time. However, it is premature to conclude on the implications of these findings on vaccine public health policy. Further evidence is needed in the form of population-based cohorts where the incidence of breakthrough infection is assessed and can reveal the implications of these differences in the immune response.

Acknowledgement

We thank Ms Amira Elsharafi, Ms Fatima AlHamaydeh, Ms Tala Jamaleddin and Ms Huda Abdul Hameed for their help in collecting the blood samples. We would also like to thank Ms Sahar Aboalmaaly, Ms Afra Al Farsi, Ms Reeham Al-Buainain, Ms Samar Ataelmannan and Ms Jiji Paul, the laboratory technologists at the Medical Commission Laboratory Section, Ministry of Public Health, Qatar, for their help in performing the Architect® immunoassay.

Funding

This work was made possible by grant number UREP28-173-3-057 from the Qatar National Research Fund (a member of Qatar Foundation). The statements made herein are solely the responsibility of the authors.

Conflict of interest

We would like to declare that all kits used in this paper were provided by Mindray as in-kind support for GKN lab.

References

1. JHCR Center. *Covid-19 map*, 2021.
2. Bloomberg. *Covid-19 tracker*, 2021.
3. Baden LR, El Sahly HM, Essink B *et al.* Efficacy and safety of the mrna-1273 sars-cov-2 vaccine. *N Engl J Med* 2020; **384**:403–16.
4. Polack FP, Thomas SJ, Kitchin N *et al.* Safety and efficacy of the bnt162b2 mrna covid-19 vaccine. *N Engl J Med* 2020; **383**:2603–2615.
5. Abu-Raddad LJ, Chemaitelly H, Ayoub HH *et al.* Association of prior sars-cov-2 infection with risk of breakthrough infection following mrna vaccination in Qatar. *JAMA* 2021; **326**:1930–9.
6. Abu-Raddad LJ, Chemaitelly H, Ayoub HH *et al.* Protection offered by mrna-1273 versus bnt162b2 vaccines against sars-cov-2 infection and severe covid-19 in Qatar. *medRxiv* 2021; 2021.11.12.21266250.
7. Chemaitelly H, Yassine HM, Benslimane FM *et al.* Mrna-1273 covid-19 vaccine effectiveness against the b. 1.1. 7 and b. 1.351 variants and severe covid-19 disease in Qatar. *Nat Med* 2021; 1614–1621.
8. Abu-Raddad LJ, Chemaitelly H, Butt AA. National Study Group for C-V. Effectiveness of the bnt162b2 covid-19 vaccine against the b.1.1.7 and b.1.351 variants. *N Engl J Med* 2021; **385**:187–9.
9. Abu-Raddad LJ, Chemaitelly H, Yassine HM *et al.* Pfizer-biontech mrna bnt162b2 covid-19 vaccine protection against variants of concern after one versus two doses. *J Travel Med* 2021; **28**.
10. Nasrallah GK, Dargham SR, Shurrab F *et al.* Analytic comparison between three high-throughput commercial sars-cov-2 antibody assays reveals minor discrepancies in a high-incidence population. *Sci Rep* 2021; **11**:1–10.
11. Younes S, Al-Jighefee H, Shurrab F *et al.* Diagnostic efficiency of three fully automated serology assays and their correlation with a novel surrogate virus neutralization test in symptomatic and asymptomatic sars-cov-2 individuals. *Microorganisms* 2021; **9**: 245.
12. Ismail A, Shurrab FM, Al-Jighefee HT *et al.* Can commercial automated immunoassays be utilized to predict neutralizing antibodies after sars-cov-2 infection. *A comparative study between three different assays* 2021.
13. Gededzha MP, Mampeule N, Jugwanth S *et al.* Performance of the euroimmun anti-sars-cov-2 elisa assay for detection of Iga and igg antibodies in South Africa. *PLoS One* 2021; **16**:e0252317.
14. Khoury D, Cromer D, Reylandi A. Neutralizing antibody levels are highly predictive of immune protection from symptomatic sars-cov-2 infectionpublished online ahead of print may 17. *Nat Med* 2021; **10**:1205–1211.
15. Rubio-Acero R, Castelletti N, Fingerle V *et al.* In search of the sars-cov-2 protection correlate: head-to-head comparison of two quantitative s1 assays in pre-characterized oligo−/asymptomatic patients. *Infect Dis Ther* 2021; **10**:1505–1518. https://doi.org/10.1007/s40121-021-00475-x
16. Wisnewski AV, Campillo Luna J, Redlich CA. Human igg and Iga responses to covid-19 mrna vaccines. *PLoS One* 2021; **16**: e0249499.
17. Sterlin D, Mathian A, Miyara M *et al.* Iga dominates the early neutralizing antibody response to sars-cov-2. *Sci Transl Med* 2021; **13**.
18. Steensels D, Pierlet N, Penders J *et al.* Comparison of sars-cov-2 antibody response following vaccination with bnt162b2 and mrna-1273. *JAMA* 2021; **326**:1533–1535.
19. Dolscheid-Pommerich R, Bartok E, Renn M *et al.* Correlation between a quantitative anti-sars-cov-2 igg elisa and neutralization activity. *J Med Virol* 2021; **94**:388–392.
20. Wheeler SE, Shurin GV, Yost M *et al.* Differential antibody response to mrna covid-19 vaccines in healthy subjects. *Microbiology Spectrum* 2021; **9**:e00341–21.
21. Ponticelli D, Antonazzo IC, Caci G *et al.* Dynamics of antibody response to bnt162b2 mrna covid-19 vaccine after 6 months. *J Travel Med* 2021.
22. Baden LR, El Sahly HM, Essink B *et al.* Efficacy and safety of the mrna-1273 sars-cov-2 vaccine. *N Eng J Med* 2021; **384**: 403–16.
23. Puranik A, Lenehan PJ, Silvert E *et al.* Comparison of two highly-effective mrna vaccines for covid-19 during periods of alpha and delta variant prevalence. *medRxiv* 2021.
24. Jalkanen P, Kolehmainen P, Häkkinen HK *et al.* Covid-19 mrna vaccine induced antibody responses against three sars-cov-2 variants. *Nat Commun* 2021; **12**:3991.
25. Abe KT, Hu Q, Mozafarihashjin M *et al.* Neutralizing antibody responses to sars-cov-2 variants in vaccinated Ontario long-term care home residents and workers. *medRxiv* 2021.