Impact of Previous Infection or Vaccination on Clinical Symptoms and Viral Load of Acute SARS-CoV-2 Infection

Zeyu Zhu

A thesis

submitted in partial fulfillment of the

requirements for the degree of

Master of Science

University of Washington

2025

Committee:

Paul K. Drain

Steve Mooney

Program Authorized to Offer Degree:

Epidemiology

University of Washington

Abstract

Impact of Previous Infection or Vaccination on Clinical Symptoms and Viral Load of Acute SARS-CoV-2 Infection

Zeyu Zhu

Chair of the Supervisory Committee:

Paul K. Drain

Department of Epidemiology

Background: SARS-CoV-2 vaccination or previous infection can induce protective immunity. This study aims to evaluate the impact on clinical symptoms and viral load during a subsequent infection.

Methods: Adults with symptoms of SARS-CoV-2 infection were prospectively enrolled into a cohort study between December 2021 and May 2023 (Omicron variant). Nasal swabs were collected for quantitative reverse transcription polymerase chain reaction (RT-qPCR) testing. Descriptive statistics, t-tests, linear regression, logistic regression, and ANOVA were used to investigate the associations between symptoms and vaccination or infection histories.

Results: Among 1,140 participants tested, 352 (30.9%) participants tested positive by RT-qPCR for SARS-CoV-2 infection. Among positives, mean (SD) age was 42.3 (15.2) years, 182 (51.7%) of them were female, and mean (SD) number of symptoms was 6.8 (2.4). 89.5% were vaccinated and 16.2% reported having had a prior infection. Prior infection was associated with higher relative risk of shortness of breath, smell loss, nasal congestion, and vomiting during the current reinfection. 2 doses of vaccine was associated with lower risk of nausea and diarrhea, and 3 doses of vaccine was associated with lower risk of chills, fever and vomiting. A higher cycle threshold (CT) value on a positive test was associated with fewer reported symptoms (15.6 increase in CT value per 1 fewer reported symptoms), even after adjustment for time since last vaccination. CT value was approximately 0.1 units lower for each month duration since last vaccination. No statistically significant difference in CT value was observed across different vaccination or infection histories.

Conclusions: Vaccine dosage and recency were associated with fewer symptoms among people testing positive for SARS-CoV-2. Vaccine dosage was further associated with fewer presentation of certain symptoms, while prior infection was associated with more presentation of certain symptoms. Prior infection or vaccination mildly impact viral load (as measured by test CT value) only when certain symptoms present. SARS-CoV-2 vaccination and infection may prime the immune system and thus modify symptoms of COVID-19.

Introduction

According to the World Health Organization (WHO), SARS-CoV-2 has infected over 750 million people and caused 7 million COVID-19 deaths worldwide since December 2019[1]; these numbers may be vastly underestimated[2]. Over the course of its five-year evolution, COVID-19 has passed its acute pandemic phase and become a common pathogen of acute respiratory disease[3].This is in part due to a shifting immune landscape. In the United States, most people have had some exposure—infection, vaccination, or both—to SARS-CoV-2. As of September 2022, 96.4% of Americans had tested positive for COVID-19 serum antibodies.[4] Since the onset of the COVID-19 pandemic, SARS-CoV-2 has also evolved through several major variants, including pre-Delta, Delta, and Omicron. These variants have trended toward decreasing virulence and increasing transmissibility over successive waves.[3,5,6]

The shifting epidemiology of SARS-CoV-2 infections has coincided with prevention-focused strategies including vaccination, early diagnosis and the avoidance of severe cases via early medical intervention.[7] At the end of 2024, 80.7% of Americans had received at least one dose of a COVID-19 vaccine, but only 22.8% had received a booster dose.[8] Recent vaccination or infection against SARS-CoV-2 does not completely block transmission due to the capacity for immune escape of SARS-CoV-2 and waning immunity within 1 year.[9–13] As a result, breakthrough infections among vaccinated people continue to occur, with one study suggesting cumulative incidence as high as 38% among 6,088 vaccinated participants.[14] Vaccination induces a faster immune response that effectively reduces incidence of severe disease, hospitalization, and death.[14–19] Wu et al. further reported that the cumulative effect of vaccination to increase antibody levels is significant only for the first and second dose of vaccine.[20] However, few studies have reported the detailed protective effect of either vaccination or prior infection on outpatient symptoms and whether such an effect might be used to motivate booster uptake in the population.

This study aims to estimate the impact of vaccination and previous infection on symptom presentation and viral load (as measured by testing CT value) at time of outpatient diagnostic testing, and analyze possible mechanisms of these changes including the cumulative effect of vaccination, different features of immunity generated by vaccination and prior infection and waning immunity which were indicated by the quantity of virus detected.[21–25] Under the context of low booster reception rate and declining public trust,[1] our findings aim to offer public health administrators strong evidence to support booster advocacy and reaffirm the effectiveness of SARS-CoV-2 vaccination.

Methods

Study design and population

Individuals presenting for SARS-CoV-2 testing with at least one COVID-19 symptom between February 17, 2021 through May 11, 2023 were recruited as part of a larger diagnostic accuracy study that began enrolling in June 2020.[26] December 13, 2021 was selected as the earliest date for participants to be included in this analysis because it was a date at which surveillance data suggested regional SARS-CoV-2 prevalence was nearly entirely Omicron (per Washington State's Department of Health data on the circulation of predominant variants).[27] The methods of the main study have been described previously.[2] Briefly, adult participants with onset of symptoms consistent with

COVID-19 in the 5 days prior to enrollment, were recruited from 7 testing locations in King County, Washington. At each site, participants self-collected an anterior nasal swab, which was placed in a labeled tube containing viral transport media and frozen at -80°C for transport to a laboratory for RT-PCR (Smart Detect SARS-CoV-2 rRT-PCR Kit, InBios International, Inc., Seattle, WA; EUA200180). Demographic information including sex, gender, race, ethnicity, age and related information including received COVID-19 vaccine doses, vaccination date, and symptoms were self-reported by the participants at time of testing.

Statistical Analysis

CT values of RT-qPCR among positive cases were compared across participants grouped by vaccination or infection histories. The CT value was defined as the number of amplification cycles required for the fluorescence signal of the PCR product to exceed the background fluorescence level. All tests were performed on the same RT-qPCR assay. Vaccination status was categorized as binary (any vs. none), as well as by categorical dose (0,1,2,3,4,5, or 6). Previous infection was coded as binary (ever vs. never). A person was considered COVID-19 positive if they had a positive RT-qPCR result.

Descriptive analyses for demographic data were conducted, and a series of statistical analyses were applied to evaluate the relationships and differences in our data. One-sample t-tests were used to calculate the mean and 95% confidence intervals (CI) for age and CT values. Poisson regression was used to calculate the relative risk between prior infection or vaccination and individual symptom occurrence. Independent two-sample t-tests were employed to assess the statistical differences in number of symptoms between groups categorized by vaccination history or infection history. Logistic regression was conducted to calculate the odds ratio for each symptom by each number of vaccine doses received. Multivariable linear regression was applied to assess the association between number of symptoms and CT value adjusting for time since last vaccination. Univariate linear regression was employed to assess the association between number of symptoms and CT value. We also divided participants into 2 groups by vaccine doses and employed two-sample t-test to examine the association between number of symptoms and CT value. Two-sample t-test was also applied to examine the impact of vaccination or prior infection on the role between CT value and each individual symptom. To confirm the potential waning of vaccine-induced immunity over time, univariable linear regression was also employed to assess the association between CT value and days since last vaccination. To further find the critical time point of waning immunity, we dichotomized participants by 6 to 12 months since their last vaccine dose and tested the statistical difference of CT value by independent two-sample t-test. Univariable linear regression was employed to assess the association between number of symptoms and age. All analyses were completed with R, version 4.4.0 (R Project for Statistical Computing). Significance was determined at a two-sided p-value of <0.05.

Ethical approval

The study received ethical approval from the University of Washington (Protocol STUDY00009981), and participants provided verbal informed consent.

Results

A total of 1,957 participants from 7 clinical sites were recruited for the clinical study, of which 28 were excluded due to study protocol exclusion criteria, 204 were excluded due to incomplete specimen collection or data results, and 585 were excluded because their enrollment preceded the Omicron period (Figure 1). Among1140 participants with a valid PCR result, mean (standard deviation) age was 42.3 (15.2) years and half (51.7%) were female. Most participants were vaccinated [315 (89.5%)] and 48 (13.6%) participants reported prior infection. Of 1140 participants with valid PCR testing results, we restricted the analysis to 352 PCR-positive tests. Mean cycle threshold value among the positives was 27.3 (95% CI, 26.8-27.8), and mean number of symptoms was 6.8. Detailed demographic data is described in Table 1.

Vaccination and prior infection were associated with different symptom patterns (Table 2). Participants with a prior infection were more likely to report shortness of breath (RR = 1.61, $p = 0.03$), smell loss (RR = 2.59, $p = 0.02$), nasal congestion (RR = 1.16, $p < 0.01$) and vomiting (RR = 3.77, $p < 0.01$) as symptoms with their current infection. By contrast, vaccination was associated with lower risk of several non-respiratory symptoms: fever (RR = 0.62, $p < 0.01$), chills (RR = 0.69, $p < 0.01$), nausea (RR = 0.38, $p < 0.01$), vomiting (RR = 0.37, $p = 0.04$) and diarrhea (RR = 0.31, $p < 0.01$). Despite the difference in prevalence of individual symptoms, there was no significant difference in the number of symptoms between vaccinated and unvaccinated participants (6.7 vs. 7.7, $p = 0.05$) or previously infected and never infected participants (7.2 vs. 6.7, $p = 0.34$).

The cumulative effect of COVID-19 vaccination was significant in this study. Participants who received more than 2 doses of vaccine experienced 0.9 fewer number of symptoms on average when compared with participants who received 1 or 2 doses of vaccine (6.2 vs. 7.1, $p < 0.01$). For individual symptoms, we found significantly lower odds of diarrhea and nausea for participants who received 2 doses of vaccine and fever, chills, and vomit for participants who received 3 doses of vaccine when comparing with unvaccinated participants (Figure 2).

Considering the theoretical intermediate role of decreasing viral load between vaccine doses and milder symptoms, we further analyzed whether vaccine dose and symptoms were associated with CT value. We found a small effect of viral quantity on symptoms. After adjusting for time since last vaccination, patients with higher CT values (lower viral quantities) tended to present with fewer symptoms than those with lower CT values ($p=0.04$), but the magnitude of change per 1-unit increase in CT value was small: 0.06 fewer symptoms (i.e., a 15.6-unit increase in CT value was associated with 1 fewer reported symptom. However, for viral load and vaccine doses, we found no evidence of association between them using a linear regression model (0.24-unit decrease in CT value per 1 extra dose of vaccine, $p = 0.30$). We also failed to find a significant association by t-test when we divided participants into 2 groups according to their vaccine doses, regardless of the cutoff dose (Table S.1).

Although vaccination or prior infection does not directly affect viral load, they play a role on the association between symptoms with viral quantity. Average CT values among individuals grouped by vaccination and prior infection status were similar (Table 3). However, while the difference in average CT between people with and without individual symptoms was generally equivalent among participants with prior infection, fever and cough were both associated with lower CT values among

people without prior infection. Among vaccinated participants, cough was associated with a lower average CT value. Among unvaccinated participants, nasal congestion was associated with a higher average CT value (Figure 3).

In terms of the waning immunity against SARS-CoV-2, our data shows that the CT value decreases by 0.12 per month since vaccination ($p = 0.02$) (Figure 4). CT value was also associated with symptoms during infection and days since last vaccination. The mean CT value of tests from participants with fewer than 8 months since vaccination was significantly higher than those of participants with more (27.9 vs. 26.5, $p = 0.02$).

Discussion

This study systematically examined the impact of SARS-CoV-2 vaccination and previous infection on clinical symptoms and laboratory findings in positive cases and supports the role of vaccination and booster vaccine in reducing symptoms, which is one of the core goals of current preventive strategies. With a wide variety of vaccination and prior infection histories, our population shows the symptom and CT result patterns of a typical outpatient setting during the Omicron period. We identified symptom patterns differed by vaccination and prior infection, highlighting the potential need for SARS-CoV-2 testing in patients with milder symptoms than in previous years, as more people are vaccinated. By analyzing the association between symptoms and viral load , vaccine history and prior infection, our study highlights the individual-level impact of immunity and viral dynamic change associated with vaccination and reinfection.

In our study, vaccination is associated with fewer non-respiratory clinical symptoms. This concurs with previous studies, in which serum immunity against SARS-CoV-2 is effectively generated while mucosal immune reaction is weak, and most mucosal antibodies are migrated from serum.[22,28,29] Consistent with prior studies showing minimal changes in mucosal antibodies after repeated vaccination, our findings revealed no notable differences in the odds of respiratory symptoms across 1 to 5 vaccine doses.[29] Different from expectation, we found that previous infection was associated with more presentation of shortness of breath, smell loss, nasal congestion and vomit. This is align with previous findings that the mucosal IgG induced by vaccination is significantly lower than that induced by prior infection,[22] and further indicating the different mechanism and location of immune response induced by vaccination and previous infection.

Our findings on the cumulative effect of vaccination also align with a previous study that serum antibody level does not increase after the 2nd or 3rd dose of vaccine.[17,20,21,30] It is possible that more than 3 doses of vaccine can also induce fewer presentations of other symptoms, but this was not statistically significant in our study, possibly due to the small number of SARS-CoV-2 positive cases who had received 4 or 5 doses of vaccine at the time of our study. The confirmation of the cumulative effect suggests that 3 doses of vaccine was required to prevent some non-respiratory symptoms. Together with the evidence that prior infection are associated with more symptoms, our study further highlights the necessity of multiple doses of SARS-CoV-2 vaccine.

Our study also confirmed the necessity of booster, supporting the recommendation of US Centers for Disease Control and Prevention (CDC). According to our cohort, the viral load of patients

significantly increased 8 months after their last vaccination, indicating a weakened immunity against SARS-CoV-2. This is consistent with previous research, in which found the immunity weakens between 6 to 8 months.[13,18,31]

The different changes in CT values between vaccinated and unvaccinated individuals, as well as between those previously infected and never infected, suggests a potentially distinct symptom generation mechanism. Although no significant association was found between CT values and previous infection history or vaccination, it is worth noting that despite a lack of statistical significance in 10 of 15 symptoms (vomiting, throat pain, taste loss, smell loss, shortness of breath, nasal congestion, nausea, headache, fever, difficulty breathing, and chills), previously infected participants with the symptom have higher mean CT values, whereas never infected participants had lower mean CT values than the mean CT value of participants without the corresponding symptom. In terms of vaccination, 5 symptoms (throat pain, shortness of breath, difficulty breathing, fatigue, and diarrhea) had higher mean CT values in vaccinated participants and lower mean CT value in unvaccinated participants than the mean CT value in participants without the corresponding symptom. These reversed patterns might indicate that among vaccinated or previously infected participants, immune-associated inflammation plays a greater role than viral replication-driven inflammation in the development of certain symptoms.

Strengths and Limitations

A major strength of our study is the large sample size of positive Omicron tests, with corresponding individual-level clinical data, including symptoms, vaccine history and infection history. However, a major limitation to the interpretation of our results is that they are limited to the population of ambulatory people who presented for testing (i.e., had symptoms and motivation to present for SARS-CoV-2 testing). Although this study took place at a time when home-based testing was in limited availability, this study population may be more representative of people in need of clinically documented tests (e.g., to receive subsequent clinical care or access services that require test documentation). This study only recruited participants within 5 days of their symptom onset, and previous studies showed that some patients were diagnosed positive outside of this time period, which can lead to false-negative result of RT-qPCR test.[32] Additionally, we relied on geographic surveillance testing, rather than individual genotyping, to identify Omicron infections and thus some misclassification is possible. It is also possible that different sub-strains of Omicron could have different clinical presentations, thus confounding our results.

Conclusion

Receiving ≥3 COVID-19 vaccine doses was significantly associated with fewer symptoms. Vaccinated individuals reported less fever, chills, nausea, vomiting, and diarrhea. In contrast, prior infection was associated with a higher risk of shortness of breath, loss of smell, nasal congestion, and vomiting. Our findings also reinforce the evidence of waning immunity that becomes significant 8 months after last vaccination, highlighting the importance of a timely booster doses for optimal protection.

Neither vaccination nor prior infection significantly affected viral load, as measured by CT values. However, we noticed that the association between viral load and certain symptoms associations can

be differed by immune history. This suggests that SARS-CoV-2 vaccination and infection may prime immune responses without directly altering viral burden, possibly influencing symptom expression via other immunologic mechanisms.

Conflict of Interest Disclosures: Dr. Drain reported receiving grants from InBios International during the conduct of the study; research funding, paid to his institution, from the National Institutes of Health (NIH), the US Centers for Disease Control and Prevention, the Bill and Melinda Gates Foundation, and Abbott; and consulting fees from Gilead Sciences, ThermoFisher, Cepheid, InBios International, Abbott, PATH, LumiraDx, and Alveo Technologies.

References

1. Prasad V. An Evidence-Based Approach to Covid-19 Vaccination. *The New England Journal of Medicine*. Published online 2025. doi:10.1056/NEJMsb2506929
2. Drain PK, Bemer M, Morton JF, et al. Accuracy of 2 Rapid Antigen Tests During 3 Phases of SARS-CoV-2 Variants. *JAMA Netw Open*. 2022;5(8):e2228143. doi:10.1001/jamanetworkopen.2022.28143
3. Contreras S, Iftekhar EN, Priesemann V. From emergency response to long-term management: the many faces of the endemic state of COVID-19. *The Lancet Regional Health - Europe*. 2023;30:100664. doi:10.1016/j.lanepe.2023.100664
4. Jones JM, Manrique IM, Stone MS, et al. Estimates of SARS-CoV-2 Seroprevalence and Incidence of Primary SARS-CoV-2 Infections Among Blood Donors, by COVID-19 Vaccination Status — United States, April 2021–September 2022. *MMWR Morb Mortal Wkly Rep*. 2023;72(22):601-605. doi:10.15585/mmwr.mm7222a3
5. Karimizadeh Z, Dowran R, Mokhtari-azad T, Shafiei-Jandaghi NZ. The reproduction rate of severe acute respiratory syndrome coronavirus 2 different variants recently circulated in human: a narrative review. *Eur J Med Res*. 2023;28(1):94. doi:10.1186/s40001-023-01047-0
6. Ito K, Piantham C, Nishiura H. Estimating relative generation times and reproduction numbers of Omicron BA.1 and BA.2 with respect to Delta variant in Denmark. *MBE*. 2022;19(9):9005-9017. doi:10.3934/mbe.2022418
7. Centers for Disease Control and Prevention, COVID-19 - Prevention. Accessed by April 22, 2024. https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/prevention.html
8. COVID-19 Vaccination Coverage and Intent for Vaccination, Children 6 months through 17 years, United States. https://www.cdc.gov/covidvaxview/weekly-dashboard/child-coverage-vaccination.html
9. Hall V, Foulkes S, Insalata F, et al. Protection against SARS-CoV-2 after Covid-19 Vaccination and Previous Infection. *N Engl J Med*. 2022;386(13):1207-1220. doi:10.1056/NEJMoa2118691
10. Altarawneh HN, Chemaitelly H, Ayoub HH, et al. Effects of previous infection, vaccination, and hybrid immunity against symptomatic Alpha, Beta, and Delta SARS-CoV-2 infections: an observational study. *eBioMedicine*. 2023;95:104734. doi:10.1016/j.ebiom.2023.104734
11. Bergwerk M, Gonen T, Lustig Y, et al. Covid-19 Breakthrough Infections in Vaccinated Health Care Workers. *N Engl J Med*. 2021;385(16):1474-1484. doi:10.1056/NEJMoa2109072
12. Aga AM, Mulugeta D, Gebreegziabxier A, et al. Correlation of COVID-19 vaccination and RT-PCR ct value among cases in Addis Ababa, Ethiopia: implication for future preparedness. *BMC Infect Dis*. 2024;24(1):1127. doi:10.1186/s12879-024-10061-4
13. Havervall S, Ng H, Jernbom Falk A, et al. Robust humoral and cellular immune responses and low risk for reinfection at least 8 months following asymptomatic to mild COVID-19. *J Intern Med*. 2022;291(1):72-80. doi:10.1111/joim.13387
14. Janke C, Rubio-Acero R, Weigert M, et al. Understanding the Omicron Variant Impact in Healthcare Workers: Insights from the Prospective COVID-19 Post-Immunization Serological Cohort in Munich (KoCo-Impf) on Risk Factors for Breakthrough and Reinfections. *Viruses*. 2024;16(10):1556. doi:10.3390/v16101556
15. Core Prevention Strategies. https://www.cdc.gov/covid/prevention/index.html
16. Krüger LJ, Gaeddert M, Köppel L, et al. Evaluation of the accuracy, ease of use and limit of detection of novel, rapid, antigen-detecting point-of-care diagnostics for *SARS-CoV-2*. Published

online October 4, 2020. doi:10.1101/2020.10.01.20203836
17. Goux H, Green J, Wilson A, et al. Performance of rapid antigen tests to detect SARS-CoV-2 variant diversity and correlation with viral culture positivity: implication for diagnostic development and future public health strategies. Paraskevis D, ed. *mBio*. 2024;15(12):e02737-24. doi:10.1128/mbio.02737-24
18. Khoury DS, Cromer D, Reynaldi A, et al. Neutralizing antibody levels are highly predictive of immune protection from symptomatic SARS-CoV-2 infection. *Nat Med*. 2021;27(7):1205-1211. doi:10.1038/s41591-021-01377-8
19. Wang Y, So HC, Tsang NNY, et al. Clinical profile analysis of SARS-CoV-2 community infections during periods with omicron BA.2, BA.4/5, and XBB dominance in Hong Kong: a prospective cohort study. *The Lancet Infectious Diseases*. 2025;25(3):276-289. doi:10.1016/S1473-3099(24)00574-7
20. Wu J, Jiang M, Li J, et al. Heterogeneity of SARS-CoV-2 immune responses after the nationwide Omicron wave in China. Rajao DS, ed. *Microbiol Spectr*. 2024;12(11):e01117-24. doi:10.1128/spectrum.01117-24
21. Goel RR, Apostolidis SA, Painter MM, et al. Distinct antibody and memory B cell responses in SARS-CoV-2 naïve and recovered individuals after mRNA vaccination. *Sci Immunol*. 2021;6(58):eabi6950. doi:10.1126/sciimmunol.abi6950
22. Alkharaan H, Al-Qarni H, Aldosari MA, et al. Salivary Antibody Responses to Two COVID-19 Vaccines following Different Vaccination Regimens. *Vaccines*. 2023;11(4):744. doi:10.3390/vaccines11040744
23. Huang N, Pérez P, Kato T, et al. SARS-CoV-2 infection of the oral cavity and saliva. *Nat Med*. 2021;27(5):892-903. doi:10.1038/s41591-021-01296-8
24. HCA Lung Biological Network, Sungnak W, Huang N, et al. SARS-CoV-2 entry factors are highly expressed in nasal epithelial cells together with innate immune genes. *Nat Med*. 2020;26(5):681-687. doi:10.1038/s41591-020-0868-6
25. Peeling RW, Heymann DL, Teo YY, Garcia PJ. Diagnostics for COVID-19: moving from pandemic response to control. *The Lancet*. 2022;399(10326):757-768. doi:10.1016/S0140-6736(21)02346-1
26. Symptoms of COVID-19. https://www.cdc.gov/covid/signs-symptoms/index.html
27. SARS-CoV-2 Sequencing and Variants in Washington State. https://doh.wa.gov/sites/default/files/2022-02/420-316-SequencingAndVariantsReport.pdf
28. Declercq J, Gerlo S, Van Nevel S, et al. Repeated COVID-19 mRNA-based vaccination contributes to SARS-CoV-2 neutralizing antibody responses in the mucosa. *Sci Transl Med*. 2024;16(770):eadn2364. doi:10.1126/scitranslmed.adn2364
29. Sundar S, Ramadoss R, Shanmugham R, et al. Salivary Antibody Response of COVID-19 in Vaccinated and Unvaccinated Young Adult Populations. *Vaccines*. 2022;10(11):1819. doi:10.3390/vaccines10111819
30. Painter MM, Mathew D, Goel RR, et al. Rapid induction of antigen-specific CD4+ T cells is associated with coordinated humoral and cellular immunity to SARS-CoV-2 mRNA vaccination. *Immunity*. 2021;54(9):2133-2142.e3. doi:10.1016/j.immuni.2021.08.001
31. Hall V, Foulkes S, Insalata F, et al. Protection against SARS-CoV-2 after Covid-19 Vaccination and Previous Infection. *N Engl J Med*. 2022;386(13):1207-1220. doi:10.1056/NEJMoa2118691
32. Wölfel R, Corman VM, Guggemos W, et al. Virological assessment of hospitalized patients

with COVID-2019. *Nature*. 2020;581(7809):465-469. doi:10.1038/s41586-020-2196-x

Table 1. Characteristics of participants enrolled in this study

Characteristics	RT-qPCR Positive (N = 352)	Tested Cohort (N = 1140)
Sex at birth		
Male	170 (48.3%)	490 (43.0%)
Female	182 (51.7%)	650 (57.0%)
Gender		
Man	169 (48.0%)	476 (41.8%)
Woman	180 (51.1%)	643 (56.4%)
Transgender man	0	1 (0.1%)
Transgender woman	0	1 (0.1%)
Nonbinary or gender queer	3 (0.9%)	15 (1.3%)
An identity not listed or unknown	0	4 (0.1%)
Race		
American Indian or Alaskan Native	6 (1.7%)	13 (1.1%)
Native Hawaiian or Pacific Islander	16 (4.5%)	31 (2.7%)
Hispanic or Latinx	45 (12.8%)	139 (12.2%)
Asian	59 (16.8%)	210 (18.4%)
White	208 (59.1%)	681 (59.7%)
Black or African American	27 (7.7%)	92 (8.1%)
Not listed or not answered	10 (2.9%)	40 (3.5%)
Age, mean (SD), yr	42.3 (15.2)	41.8 (15.0)
Prior infection	48 (13.6%)	230 (20.2%)
Prior vaccination	315 (89.5%)	1052 (92.3%)
COVID-19 vaccine doses		
0	37 (10.5%)	88 (7.7%)
1	9 (2.6%)	30 (2.6%)
2	133 (37.8%)	373 (32.7%)
3	131 (37.2%)	475 (41.7%)
4	33 (9.4%)	130 (11.4%)
5	9 (2.6%)	43 (3.8%)
Contact with person positive for SARS-CoV-2 infection within prior 2 weeks		
Yes	145 (41.2%)	438 (38.4%)
No	173 (49.1%)	610 (53.5%)
Unknown	34 (9.7%)	92 (8.1%)
Time since symptom onset, median (IQR), days	2 (1-3)	2 (1-3)
Ct values by RT-qPCR among participants positive for SARS-CoV-2, mean (95%CI)	27.3 (26.8–27.8).	/
Number of symptoms in SARS-CoV-2 positive participants, mean (SD)	6.8 (2.4)	/

Table 2. Relative risk of individual symptoms among people with positive COVID tests, by previous infection status or vaccination.

Symptom	Relative risk (p-value)	
	Previously infected vs. Never infected (ref)	**Vaccinated vs. Unvaccinated (ref)**
Fever	0.76 (0.21	0.62 (<0.01)
Cough	1.04 (0.34)	1.03 (0.65)
Throat pain	1.05 (0.52)	1.06 (0.54)
Chills	0.89 (0.43)	0.69 (<0.01)
Shortness of Breath	1.61 (0.03)	1.07 (0.82)
Difficulty Breathing	1.48 (0.17)	0.97 (0.94)
Taste Loss	1.37 (0.51)	0.79 (0.65)
Smell Loss	2.59 (0.02)	1.06 (0.92)
Nose Congestion	1.16 (<0.01)	1.12 (0.24)
Nausea	0.93 (0.80)	0.38 (<0.01)
Vomit	3.77 (<0.01)	0.38 (0.04)
Diarrhea	1.23 (0.54)	0.31 (<0.01)
Headache	0.93 (0.49)	0.90 (0.23)
Muscle ache	0.83 (0.13)	0.97 (0.81)
Fatigue	1.07 (0.38)	0.98 (0.79)

Table 3. The mean CT value of PCR-positive participants with and without prior infection and vaccination histories.

	Overall		**Vaccinated**		**Unvaccinated**	
	Positive/ All	*Cycle threshold (Mean, 95%CI)*	*Positive/ All*	*Cycle threshold (Mean, 95%CI)*	*Positive /All*	*Cycle threshold (Mean, 95%CI)*
Overall	352/1140	27.30 (26.81, 27.80)	315/1052	27.31 (26.78, 27.84)	37/88	27.25 (25.85, 28.66)
Prior infection	48/230	28.52 (27.16, 29.87)	41/213	28.06 (26.70, 29.43)	7/17	31.19 (27.03, 35.35)
No prior infection	249/717	27.15 (26.58, 27.72)	219/655	27.26 (26.64, 27.88)	30/62	26.34 (25.03, 27.64)

Figure 1. Participant flow diagram for inclusion in the final analytical sample

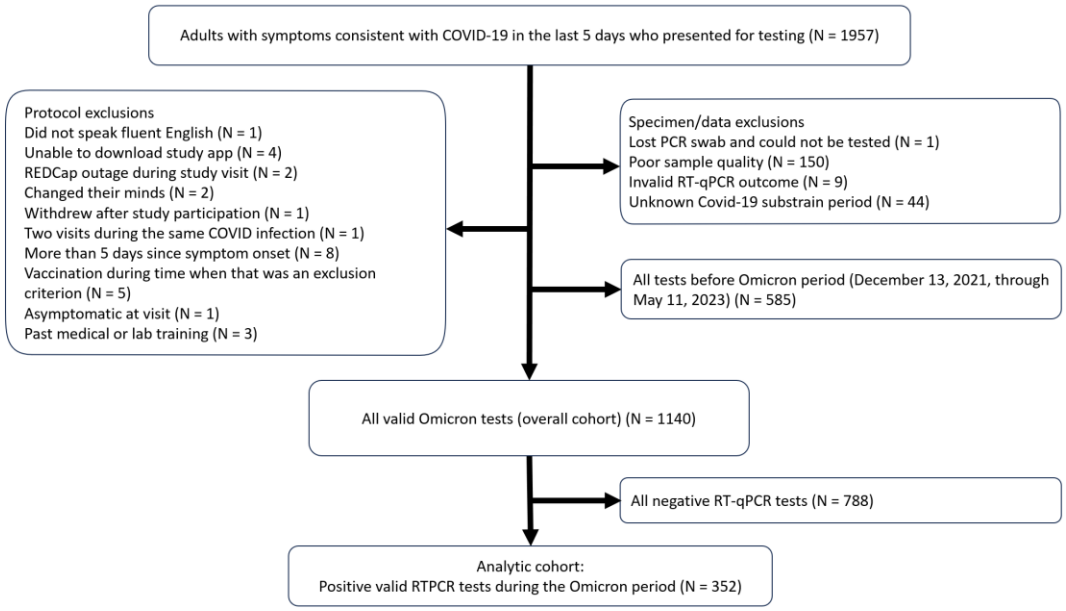


Figure 2. Odds ratios and 95% CI for symptom occurrence following each COVID-19 vaccine dose

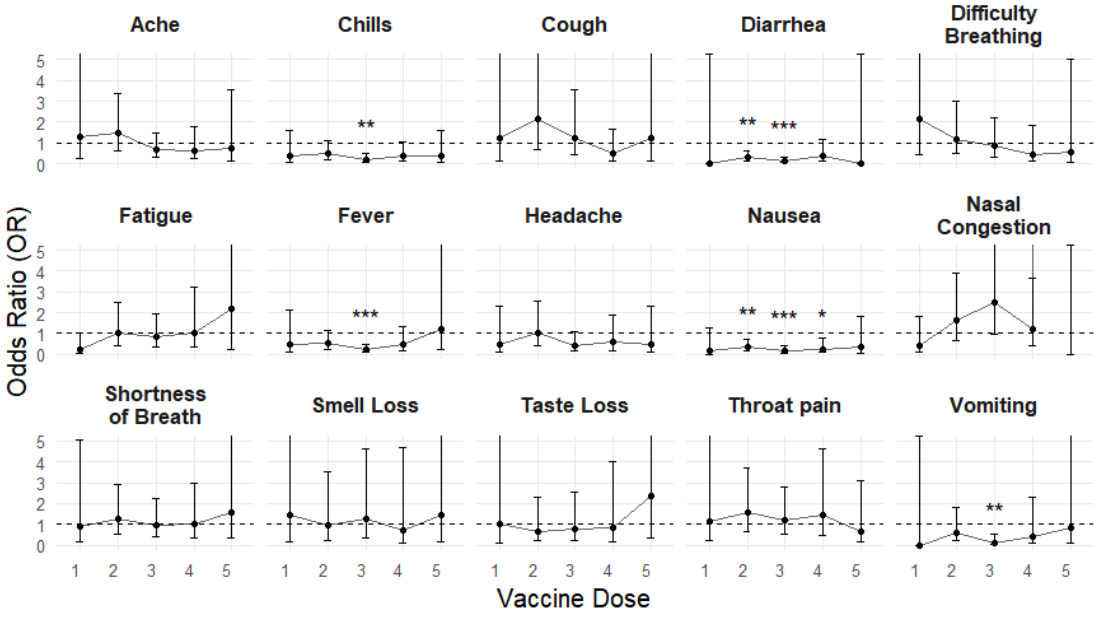


Figure 3. The difference between mean CT values of SARS-CoV-2 infected participants with and without certain symptoms. Participants are stratified by their infection histories or vaccination histories. The zero line represents the average CT value among participants without the symptom.

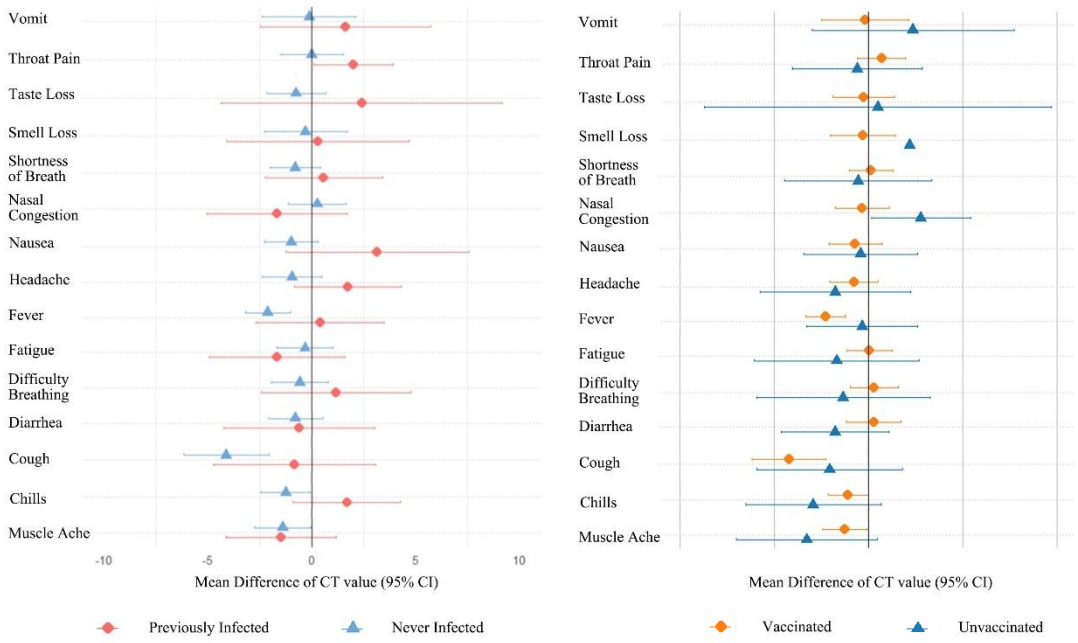
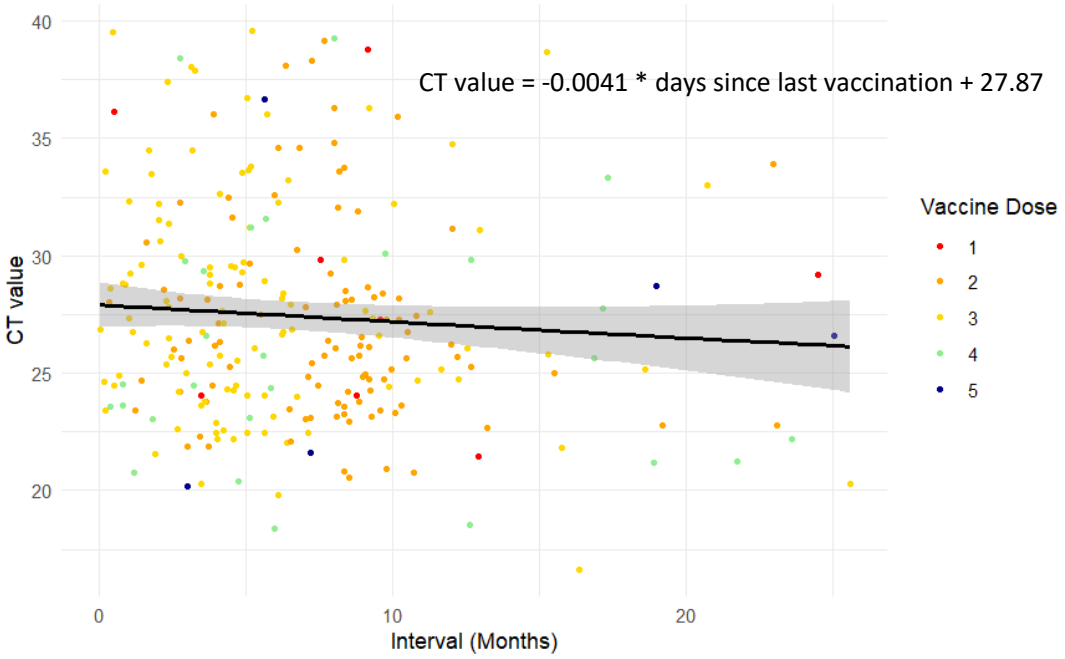


Figure 4. Association between time since last vaccination and SARS-CoV-2 RT-qPCR CT value



Supplemental Data

Table S.1. CT Values by Vaccine Dose Among RT-qPCR Positive COVID-19 Cases

Vaccine dose	Mean CT value (95% CI) of RT-qPCR tested positive participants
0 dose of vaccine	27.25 (25.82, 28.69)
1 to 5 doses of vaccine	27.31 (26.78, 27.84)
0 to 1 doses of vaccine	27.37 (25.98, 28.77)
2 to 5 doses of vaccine	27.29 (26.76, 27.83)
0 to 2 doses of vaccine	27.31 (26.66, 27.97)
3 to 5 doses of vaccine	27.29 (26.53, 28.05)
0 to 3 doses of vaccine	27.52 (27.00, 28.03)
4 to 5 doses of vaccine	25.72 (23.99, 27.45)
0 to 4 doses of vaccine	27.41 (26.91, 27.90)
5 doses of vaccine	23.37 (18.59, 28.14)