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Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Chemaitelly H, Ayoub HH, Tang P, et al. Long-term COVID-19 booster effectiveness by infection history and clinical vulnerability and immune imprinting: a retrospective population-based cohort study. *Lancet Infect Dis* 2023; published online March 10. https://doi.org/10.1016/S1473-3099(23)00058-0.

Supplementary Appendix

Table of Contents

Section S1: Further details on methods

Data sources and testing

Qatar's national and universal public healthcare system uses the Cerner-system advanced digital health platform to track all electronic health record encounters of each individual in the country, including all citizens and residents registered in the national and universal public healthcare system. Registration in the public healthcare system is mandatory for citizens and residents.

The databases analyzed in this study are data-extract downloads from the Cerner-system that have been implemented on a regular (twice weekly) schedule since the onset of pandemic by the Business Intelligence Unit at Hamad Medical Corporation. Hamad Medical Corporation is the national public healthcare provider in Qatar. At every download all tests, coronavirus disease 2019 (COVID-19) vaccinations, hospitalizations related to COVID-19, and all death records regardless of cause are provided to the authors through .csv files. These databases have been analyzed throughout the pandemic not only for study-related purposes, but also to provide policymakers with summary data and analytics to inform the national response.

Every health encounter in the Cerner-system is linked to a unique individual through the HMC Number that links all records for this individual at the national level. Databases were merged and analyzed using the HMC Number to link all records whether for testing, vaccinations, hospitalizations, and deaths. All deaths in Qatar are tracked by the public healthcare system. All COVID-19-related healthcare was provided only in the public healthcare system. No private entity was permitted to provide COVID-19-related healthcare. COVID-19 vaccination was also provided only through the public healthcare system. These health records were tracked throughout the COVID-19 pandemic using the Cerner system. This system has been

implemented in 2013, before the onset of the pandemic. Therefore, we had all health records related to this study for the full national cohort of citizens and residents throughout the pandemic. This allowed us to follow each person over time.

Demographic details for every HMC Number (individual) such as sex, age, and nationality are collected upon issuing of the universal health card, based on the Qatar Identity Card, which is a mandatory requirement by the Ministry of Interior to every citizen and resident in the country.

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) testing in Qatar is done at a mass scale where close to 5% of the population are tested every week.[1,2] All SARS-CoV-2 testing in any facility in this country is tracked nationally in one database, the national testing database. This database covers all testing in all locations and facilities throughout the country, whether public or private. Every polymerase chain reaction (PCR) test and an increasing proportion of the facility-based rapid antigen tests conducted in Qatar, regardless of location or setting, are classified on the basis of symptoms and the reason for testing (clinical symptoms, contact tracing, surveys or random testing campaigns, individual requests, routine healthcare testing, pre-travel, at port of entry, or other). Based on the distribution of the reason for testing up to October 31, 2022, most of the tests that have been conducted in Qatar were conducted for routine reasons, such as being travel-related. About 75% of those diagnosed are also diagnosed not because of appearance of symptoms, but because of routine testing.[1,2] All testing results in the national testing database during follow-up in the present study were factored in the analyses of this study.

The first large omicron wave that peaked in January of 2022 was massive (Figure S3) and strained the testing capacity in the country.[1,3] Accordingly, rapid antigen testing was introduced to relieve the pressure on PCR testing. Implementation of this change in testing occurred quickly

precluding incorporation of reason for testing in large proportion of the rapid antigen tests for several months. While the reason for testing is available for all PCR tests, it is not available for all rapid antigen tests. Availability of reason for testing for the rapid antigen tests also varied with time.

Rapid antigen test kits are available for purchase in pharmacies in Qatar, but outcome of home-based testing is not reported nor documented in the national databases. Since SARS-CoV-2-test outcomes are linked to specific public health measures, restrictions, and privileges, testing policy and guidelines stress facility-based testing as the core testing mechanism in the population. While facility-based testing is provided free of charge or at low subsidized costs, depending on the reason for testing, home-based rapid antigen testing is de-emphasized and not supported as part of national policy. There is no reason to believe that home-based testing could have differentially affected the followed matched cohorts to affect our results.

The infection detection rate is defined as the cumulative number of documented infections, that is diagnosed and laboratory-confirmed infections, over the cumulative number of documented and undocumented infections. Serological surveys and other analyses suggest that a substantial proportion of infections in Qatar and elsewhere are undocumented.[4-10] With absence of recent serological surveys in Qatar, it is difficult to estimate the current or recent infection detection rate, but mathematical modeling analyses and their recent updates suggest that at present no less than 50% of infections are never documented.[7,11]

Qatar has unusually young, diverse demographics, in that only 9% of its residents are ≥50 years of age, and 89% are expatriates from over 150 countries.[12,13] Further descriptions of the study population and these national databases were reported previously.[1,2,13-15]

Matching of cohorts

Each person in the three-dose cohort was first exactly matched one-to-one by sex, 10-year age group, nationality, number of coexisting conditions, vaccine type, and calendar week of the second vaccine dose to a SARS-CoV-2 test for a person in the two-dose cohort that occurred during the same calendar week of the third-dose vaccination of the person in the three-dose cohort. Whenever two or more SARS-CoV-2 tests for a given individual in the two-dose cohort matched, only one of these tests was retained; the others were dropped and replaced by SARS-CoV-2 tests for controls that have not yet been matched. Accordingly, an individual in the three-dose cohort was matched to only one unique individual in the two-dose cohort.

Matching was performed iteratively such that persons in the two-dose cohort were alive, had no record before the start date of follow-up for a third dose or for a SARS-CoV-2-positive test within 90 days, and had the same prior infection status as their match at the start of the follow-up. Controls that did not fulfil these criteria were dropped and replaced by other eligible controls. The matching algorithm was implemented using *ccmatch* command in Stata supplemented with conditions to retain only controls that fulfil the eligibility criteria and was iterated using loops with as many replications as needed until exhaustion (i.e., no more matched pairs could be identified).

Persons in the matched two-dose cohort contributed follow-up time before receiving the third dose (and matched to three-dose-vaccinated persons), and subsequently contributed follow-up time in the three-dose cohort, if they received a third dose (and matched to two-dose-vaccinated persons). Introducing this cross-over in the study design provides a basis for separating vaccination effects from other effects and may reduce potential differences arising from unmeasured risk behaviors related to vaccination status.

Since this study was designed to emulate a target trial,[15,16] the matching algorithm was developed and exact matching was used to ensure that both cohorts are similar in terms of all factors known, or have any potential to affect, risk of infection, other than the booster effect. Informed by prior epidemiologic studies on this population, including established associations with infection,[4,5,7,10,13] as well possibility that prior infection status may affect booster effectiveness, matching was done to control for any differences in risk of infection between cohorts, for the same purpose as that of randomization in a randomized controlled trial. Just as randomized controlled trials select a sample of the national population that fits eligibility criteria, this study selected a sample of the national population conditional on an exact balance of observed confounders between study arms. Yet, despite the strict matching, the study matched sample is 10-fold larger than a typical COVID-19 vaccine randomized controlled trial.

The use of exact matching, matching timing of the second dose for both cohorts, matching third dose to a test, differences in age distribution between those who received three doses and those who received only two doses, and differences in nationality distribution between those who received three doses and those who received only two doses contributed to loss of persons during the matching. With 182 nationalities in this national sample, finding an exact nationality match is more difficult for nationalities with small numbers. This is not the case for nationalities with large numbers, such as Indians and Qataris, and thus they are more represented in the matched sample.

Since both study cohorts were matched by calendar week of the second dose, the time of the second dose provides a natural anchor to measure prior testing in these cohorts. The testing rate from second dose up to one day before study recruitment was 2.5 tests per person-year (534,129

tests in 213,485.8 person-years) in the three-dose cohort and 3.1 tests per person-year (655,634 tests in 213,289.8 person-years) in the two-dose cohort.

Comorbidity classification

Comorbidities were ascertained and classified based on the ICD-10 codes for chronic conditions as recorded in the electronic health record encounters of each individual in the Cerner-system national database that includes all citizens and residents registered in the national and universal public healthcare system. The public healthcare system provides healthcare to the entire resident population of Qatar free of charge or at heavily subsidized costs, including prescription drugs. With the mass expansion of this sector in recent years, facilities have been built to cater to specific needs of subpopulations. For example, tens of facilities have been built, including clinics and hospitals, in localities with high density of craft and manual workers.[10]

All encounters for each individual were analyzed to determine the comorbidity classification for that individual, as part of a recent national analysis to assess healthcare needs and resource allocation. The Cerner-system national database includes encounters starting from 2013, after this system was launched in Qatar. As long as each individual had at least one encounter with a specific comorbidity diagnosis since 2013, this person was classified with this comorbidity.

Individuals who have comorbidities but never sought care in the public healthcare system, or seek care exclusively in private healthcare facilities, were classified as individuals with no comorbidity due to absence of recorded encounters for them. This misclassification bias is not likely to affect the study results. The results for those more clinically vulnerable will not be affected, as this misclassification bias would have only resulted in a smaller cohort of these persons. This cohort was large enough for precise estimation of outcomes. As for those less

clinically vulnerable, the misclassification bias could imply that some of them may have been more clinically vulnerable. However, this proportion is likely to be very small compared to the proportion of those with one or no comorbidity in the young population of Qatar. The effect on study outcomes is thus likely to be negligible.

Section S2: Laboratory methods and variant ascertainment

Real-time reverse-transcription polymerase chain reaction testing

Nasopharyngeal and/or oropharyngeal swabs were collected for polymerase chain reaction (PCR) testing and placed in Universal Transport Medium (UTM). Aliquots of UTM were: 1) extracted on KingFisher Flex (Thermo Fisher Scientific, USA), MGISP-960 (MGI, China), or ExiPrep 96 Lite (Bioneer, South Korea) followed by testing with real-time reverse-transcription PCR (RT-qPCR) using TaqPath COVID-19 Combo Kits (Thermo Fisher Scientific, USA) on an ABI 7500 FAST (Thermo Fisher Scientific, USA); 2) tested directly on the Cepheid GeneXpert system using the Xpert Xpress SARS-CoV-2 (Cepheid, USA); or 3) loaded directly into a Roche cobas 6800 system and assayed with the cobas SARS-CoV-2 Test (Roche, Switzerland). The first assay targets the viral S, N, and ORF1ab gene regions. The second targets the viral N and E-gene regions, and the third targets the ORF1ab and E-gene regions.

All PCR testing was conducted at the Hamad Medical Corporation Central Laboratory or Sidra Medicine Laboratory, following standardized protocols.

Rapid antigen testing

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) antigen tests were performed on nasopharyngeal swabs using one of the following lateral flow antigen tests: Panbio COVID-19 Ag Rapid Test Device (Abbott, USA); SARS-CoV-2 Rapid Antigen Test (Roche, Switzerland); Standard Q COVID-19 Antigen Test (SD Biosensor, Korea); or CareStart COVID-19 Antigen Test (Access Bio, USA). All antigen tests were performed point-of-care according to each manufacturer's instructions at public or private hospitals and clinics throughout Qatar with prior authorization and training by the Ministry of Public Health (MOPH). Antigen test results

were electronically reported to the MOPH in real time using the Antigen Test Management System which is integrated with the national Coronavirus Disease 2019 (COVID-19) database.

Classification of infections by variant type

Surveillance for the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variants in Qatar is based on viral genome sequencing and multiplex real-time reverse-transcription polymerase chain reaction (RT-qPCR) variant screening[17] of random positive clinical samples,[2,18-22] complemented by deep sequencing of wastewater samples.[20,23,24] Further details on the viral genome sequencing and multiplex RT-qPCR variant screening throughout the SARS-CoV-2 waves in Qatar can be found in previous publications.[1-3,15,18-22,25-29]

Section S3: COVID-19 severity, criticality, and fatality classification

Classification of Coronavirus Disease 2019 (COVID-19) case severity (acute-care hospitalizations),[30] criticality (intensive-care-unit hospitalizations),[30] and fatality[31] followed World Health Organization (WHO) guidelines. Assessments were made by trained medical personnel independent of study investigators and using individual chart reviews, as part of a national protocol applied to every hospitalized COVID-19 patient. Each hospitalized COVID-19 patient underwent an infection severity assessment every three days until discharge or death. We classified individuals who progressed to severe, critical, or fatal COVID-19 between the time of the documented infection and the end of the study based on their worst outcome, starting with death,[31] followed by critical disease,[30] and then severe disease.[30]

Severe COVID-19 disease was defined per WHO classification as a SARS-CoV-2 infected person with "oxygen saturation of <90% on room air, and/or respiratory rate of >30 breaths/minute in adults and children >5 years old (or ≥60 breaths/minute in children <2 months old or ≥50 breaths/minute in children 2-11 months old or ≥40 breaths/minute in children 1–5 years old), and/or signs of severe respiratory distress (accessory muscle use and inability to complete full sentences, and, in children, very severe chest wall indrawing, grunting, central cyanosis, or presence of any other general danger signs)".[30] Detailed WHO criteria for classifying Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection severity can be found in the WHO technical report.[30]

Critical COVID-19 disease was defined per WHO classification as a SARS-CoV-2 infected person with "acute respiratory distress syndrome, sepsis, septic shock, or other conditions that would normally require the provision of life sustaining therapies such as mechanical ventilation

(invasive or non-invasive) or vasopressor therapy".[30] Detailed WHO criteria for classifying SARS-CoV-2 infection criticality can be found in the WHO technical report.[30]

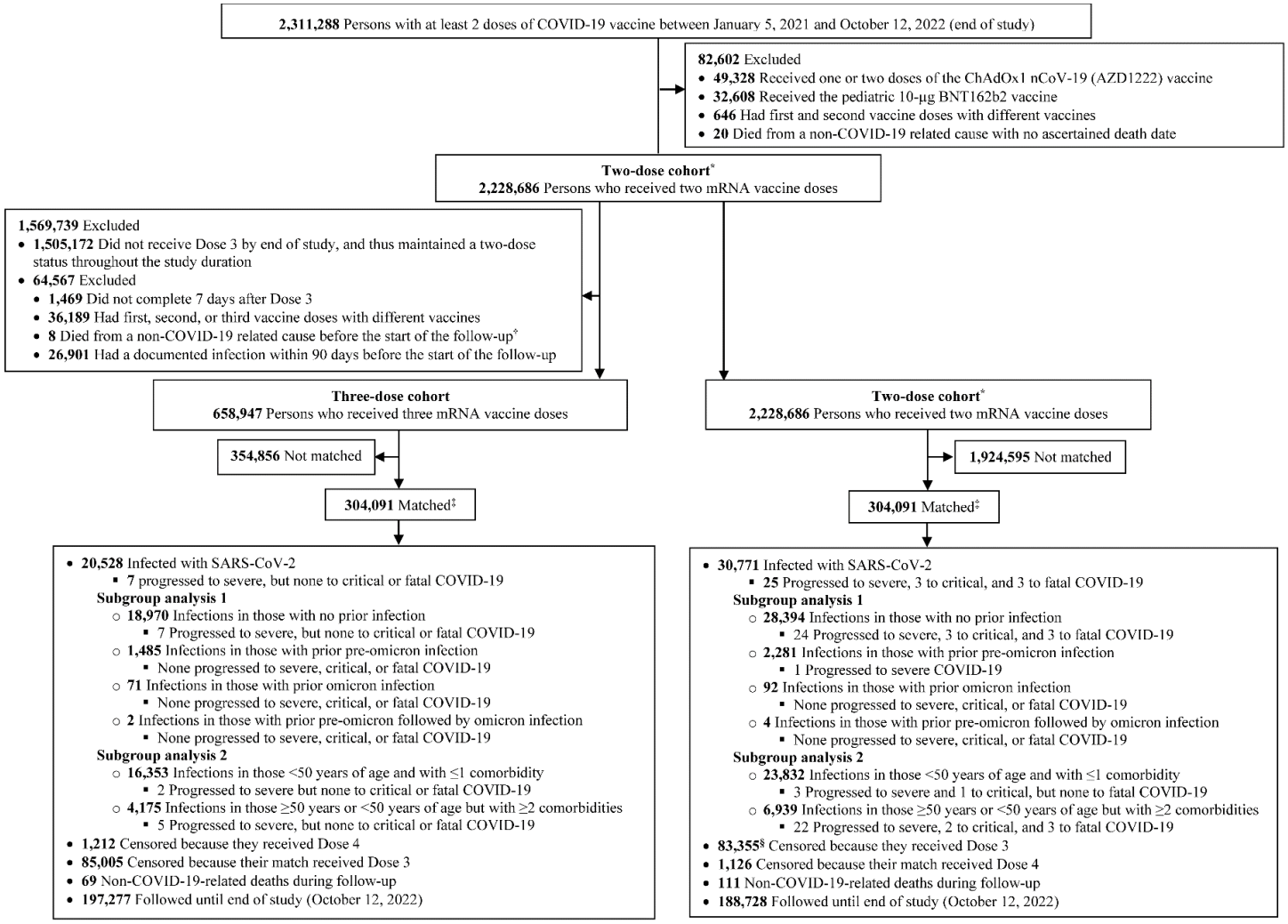
COVID-19 death was defined per WHO classification as "a death resulting from a clinically compatible illness, in a probable or confirmed COVID-19 case, unless there is a clear alternative cause of death that cannot be related to COVID-19 disease (e.g. trauma). There should be no period of complete recovery from COVID-19 between illness and death. A death due to COVID-19 may not be attributed to another disease (e.g. cancer) and should be counted independently of preexisting conditions that are suspected of triggering a severe course of COVID-19". Detailed WHO criteria for classifying COVID-19 death can be found in the WHO technical report.[31]

Table S1: STROBE checklist for cohort studies.

	Item No	Recommendation	Main Text page
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	Abstract
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	Abstract
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Introduction
Objectives	3	State specific objectives, including any prespecified hypotheses	Introduction
Methods			
Study design	4	Present key elements of study design early in the paper	Methods ('Study design and cohorts' & 'Cohort matching and follow-up') & Section S1 in Appendix
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Methods ('Study design and cohorts' & 'Cohort matching and follow-up'), & Figure S1 & Sections S1-S3 in Appendix
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	Methods ('Study design and cohorts' & 'Cohort matching and follow-up'), & Figure S1 & Section S1 in Appendix
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Methods ('Study design and cohorts' & 'Cohort matching and follow-up'), Table 1, & Figure S1 & Sections S1-S3 in Appendix.
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Methods ('Study population and data sources' & 'Statistical analysis', paragraph 1), Table 1, & Sections S1-S3 in Appendix
Bias	9	Describe any efforts to address potential sources of bias	Methods ('Cohort matching and follow-up' & 'Statistical analysis') & Section S1 in Appendix
Study size	10	Explain how the study size was arrived at	Figure S1 in Appendix
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Methods ('Cohort matching and follow-up') & Table 1
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	Methods ('Statistical analysis')
		(*b*) Describe any methods used to examine subgroups and interactions	Methods ('Statistical analysis')
		(*c*) Explain how missing data were addressed	Not applicable, see Methods ('Study population and data sources')
		(*d*) If applicable, explain how loss to follow-up was addressed	Not applicable, see Methods ('Study population and data sources')
		(*e*) Describe any sensitivity analyses	Methods ('Statistical analysis', paragraph 2)
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Figure S1 in Appendix
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Results (paragraphs 1-3), & Table 1
		(b) Indicate number of participants with missing data for each variable of interest	Not applicable, see Methods ('Study population and data sources')
		(c) Summarise follow-up time (eg, average and total amount)	Results (paragraph 4), Figure 1, & Table S2 in Appendix
Outcome data	15	Report numbers of outcome events or summary measures over time	Results (paragraph 5), Figure 1, & Figure S1 & Table S2 in Appendix

Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Results (paragraphs 6-10), Table 2, Figure 2, & Table S2 & Figure S4 in Appendix.
		(b) Report category boundaries when continuous variables were categorized	Table 1
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Not applicable
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Results (paragraphs 11-12), Figures 3-4, & Figures S5-S6 in Appendix
Discussion			
Key results	18	Summarise key results with reference to study objectives	Discussion, paragraphs 1-7
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Discussion, paragraphs 8-16
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Discussion, paragraph 17
Generalisability	21	Discuss the generalisability (external validity) of the study results	Discussion, paragraphs 8-16
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Acknowledgements

***Figure S1*: Cohort selection for investigating the effectiveness of mRNA booster (third dose) vaccination relative to that of primary-series (two-dose) vaccination.**



COVID-19 denotes coronavirus disease 2019, and SARS-CoV-2 severe acute respiratory syndrome coronavirus 2.
*This cohort includes everyone with at least 2 mRNA vaccine doses, therefore it also includes those who eventually received a third dose some time after the second dose.
†Each matched pair was followed from >7 days after the third vaccine dose for the individual in the three-dose cohort.
‡Cohorts were matched exactly one-to-one by sex, 10-year age group, nationality, number of coexisting conditions, vaccine type, prior infection status, and calendar week of the second vaccine dose. Persons who received their third vaccine dose in a specific calendar week in the three-dose cohort were additionally matched to persons who had a record for a SARS-CoV-2 test in that same calendar week in the two-dose cohort, to ensure that matched pairs had presence in Qatar over the same time period.
§These persons became part of the three-dose cohort (n=658,947) after receiving dose 3.

Figure S2: **Uptake of A) second and B) third vaccine doses month-by-month in Qatar.**

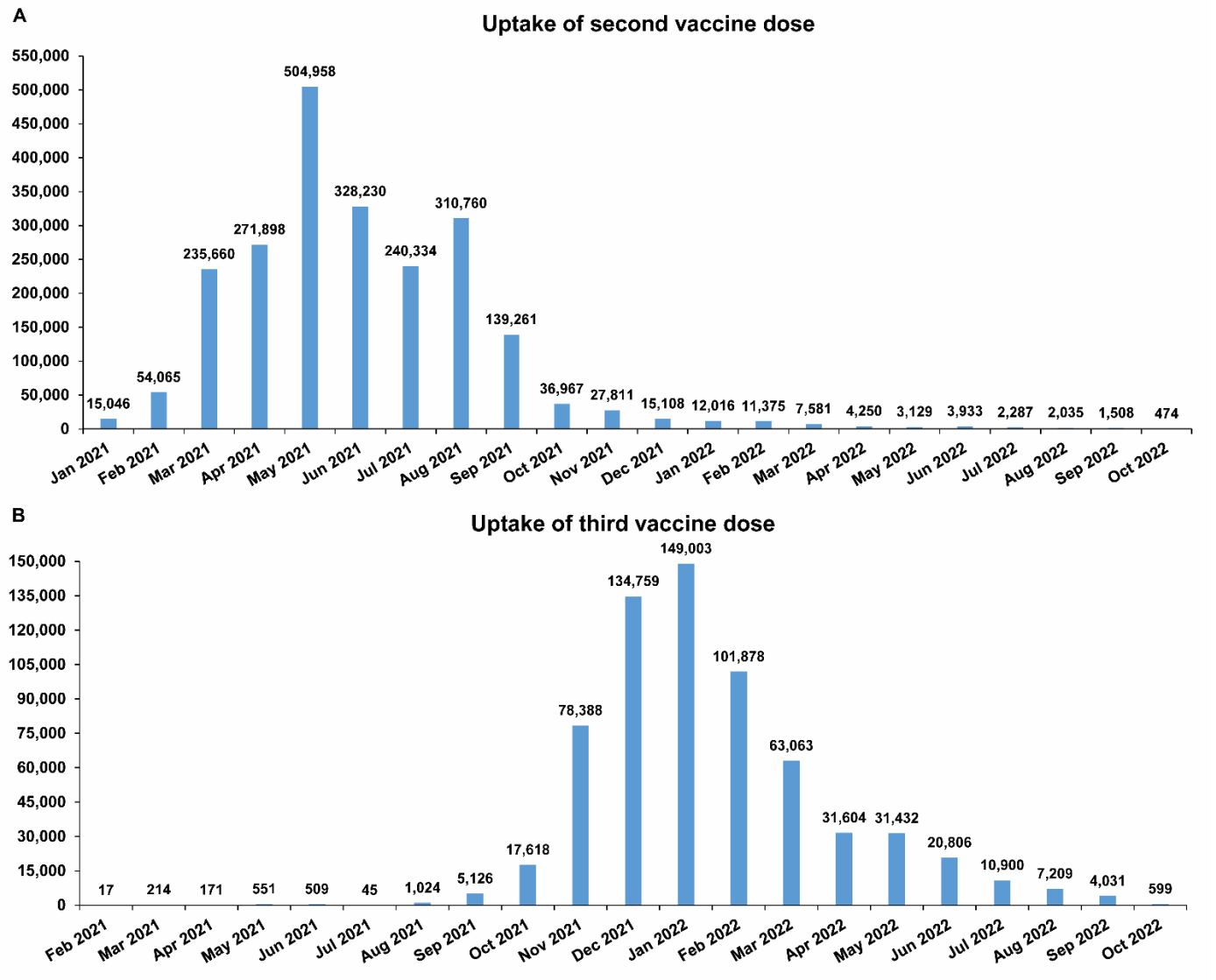


***Figure S3*: Incident infections by variant/subvariant during the different waves of the SARS-CoV-2 pandemic in Qatar.**

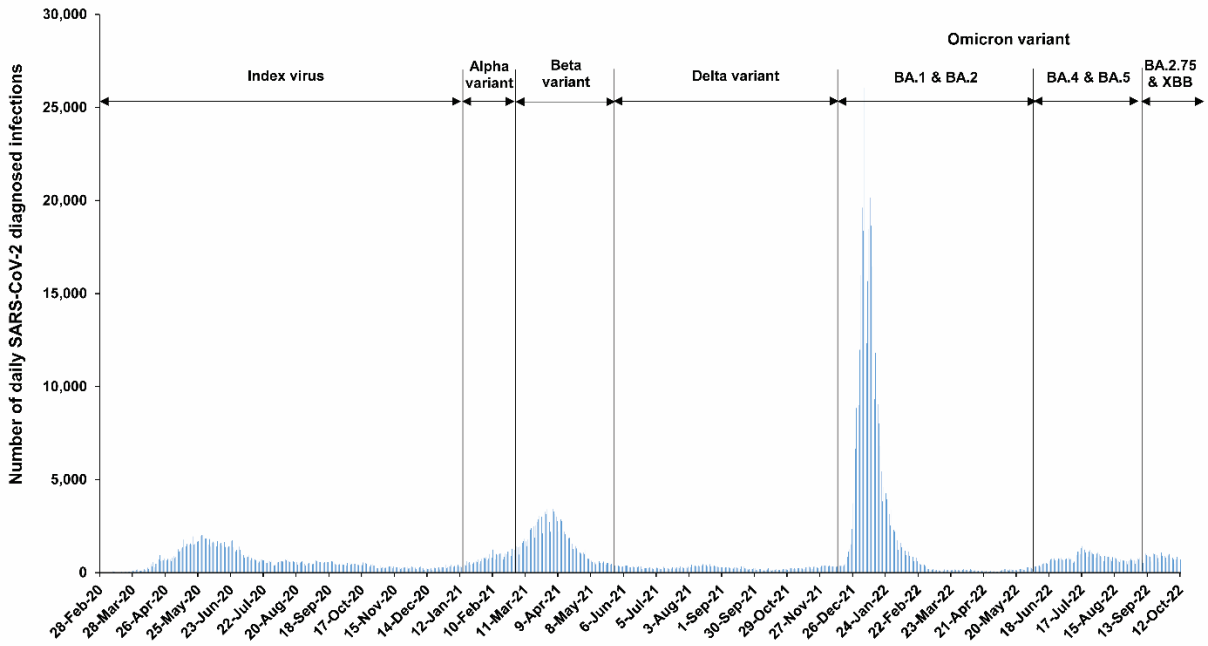


Table S2: Hazard ratios for incidence of SARS-CoV-2 infection and severe, critical, or fatal COVID-19 in the three-dose cohort versus the two-dose cohort.

Epidemiological measure	Three-dose cohort*	Two-dose cohort*
Main analysis		
Sample size	304,091	304,091
Number of incident infections	20,528	30,771
Total follow-up time (person-weeks)	7,427,502	7,024,855
Incidence rate of infection (per 10,000 person-weeks; 95% CI)	27.6 (27.3 to 28.0)	43.8 (43.3 to 44.3)
Adjusted hazard ratio for SARS-CoV-2 infection (95% CI)†	0.74 (0.71 to 0.76)	
Effectiveness of booster against infection in % (95% CI)†	26.2 (23.6 to 28.6)	
Adjusted hazard ratio for severe, critical, or fatal COVID-19 (95% CI)†	0.25 (0.10 to 0.60)	
Effectiveness of booster against severe, critical, or fatal COVID-19 in % (95% CI)†	75.1 (40.2 to 89.6)	
Estimates by prior infection status		
No prior infection		
Adjusted hazard ratio for SARS-CoV-2 infection (95% CI)†	0.74 (0.71 to 0.76)	
Effectiveness of booster against infection in % (95% CI)†	26.3 (23.6 to 28.8)	
Adjusted hazard ratio for severe, critical, or fatal COVID-19 (95% CI)†	0.26 (0.11 to 0.62)	
Effectiveness of booster against severe, critical, or fatal COVID-19 in % (95% CI)†	74.4 (38.3 to 89.4)	
Prior pre-omicron infection		
Adjusted hazard ratio for SARS-CoV-2 infection (95% CI)†	0.75 (0.68 to 0.83)	
Effectiveness of booster against infection in % (95% CI)†	24.9 (17.4 to 31.6)	
Adjusted hazard ratio for severe, critical, or fatal COVID-19 (95% CI)†	--‡	
Effectiveness of booster against severe, critical, or fatal COVID-19 in % (95% CI)†	--‡	
Prior omicron infection		
Adjusted hazard ratio for SARS-CoV-2 infection (95% CI)†	0.78 (0.56 to 1.10)	
Effectiveness of booster against infection in % (95% CI)†	21.9 (-8.7 to 44.3)	
Adjusted hazard ratio for severe, critical, or fatal COVID-19 (95% CI)†	--‡	
Effectiveness of booster against severe, critical, or fatal COVID-19 in % (95% CI)†	--‡	
Prior pre-omicron & omicron infections		
Adjusted hazard ratio for SARS-CoV-2 infection (95% CI)†	0.37 (0.07 to 2.10)	
Effectiveness of booster against infection in % (95% CI)†	62.8 (-52.3 to 93.4)	
Adjusted hazard ratio for severe, critical, or fatal COVID-19 (95% CI)†	--‡	
Effectiveness of booster against severe, critical, or fatal COVID-19 in % (95% CI)†	--‡	
Estimates by clinical vulnerability to severe COVID-19		
Persons less clinically vulnerable to severe COVID-19		
Adjusted hazard ratio for SARS-CoV-2 infection (95% CI)†	0.77 (0.74 to 0.79)	
Effectiveness of booster against infection in % (95% CI)†	23.4 (21.1 to 25.7)	
Adjusted hazard ratio for severe, critical, or fatal COVID-19 (95% CI)†	0.42 (0.08 to 2.25)	
Effectiveness of booster against severe, critical, or fatal COVID-19 in % (95% CI)†	57.9 (-55.6 to 92.1)	
Persons more clinically vulnerable to severe COVID-19		
Adjusted hazard ratio for SARS-CoV-2 infection (95% CI)†	0.66 (0.59 to 0.73)	
Effectiveness of booster against infection in % (95% CI)†	34.2 (27.0 to 40.6)	
Adjusted hazard ratio for severe, critical, or fatal COVID-19 (95% CI)†	0.23 (0.08 to 0.66)	
Effectiveness of booster against severe, critical, or fatal COVID-19 in % (95% CI)†	76.6 (34.5 to 91.7)	
Estimates by vaccine type		
Vaccinated with BNT162b2		
Adjusted hazard ratio for SARS-CoV-2 infection (95% CI)†	0.70 (0.67 to 0.73)	
Effectiveness of booster against infection in % (95% CI)†	30.4 (27.5 to 33.3)	
Adjusted hazard ratio for severe, critical, or fatal COVID-19 (95% CI)†	0.26 (0.11 to 0.63)	
Effectiveness of booster against severe, critical, or fatal COVID-19 in % (95% CI)†	74.0 (37.2 to 89.2)	
Vaccinated with mRNA-1273		
Adjusted hazard ratio for SARS-CoV-2 infection (95% CI)†	0.91 (0.87 to 0.95)	
Effectiveness of booster against infection in % (95% CI)†	9.1 (5.0 to 13.0)	
Adjusted hazard ratio for severe, critical, or fatal COVID-19 (95% CI)†	--‡	
Effectiveness of booster against severe, critical, or fatal COVID-19 in % (95% CI)†	--‡	

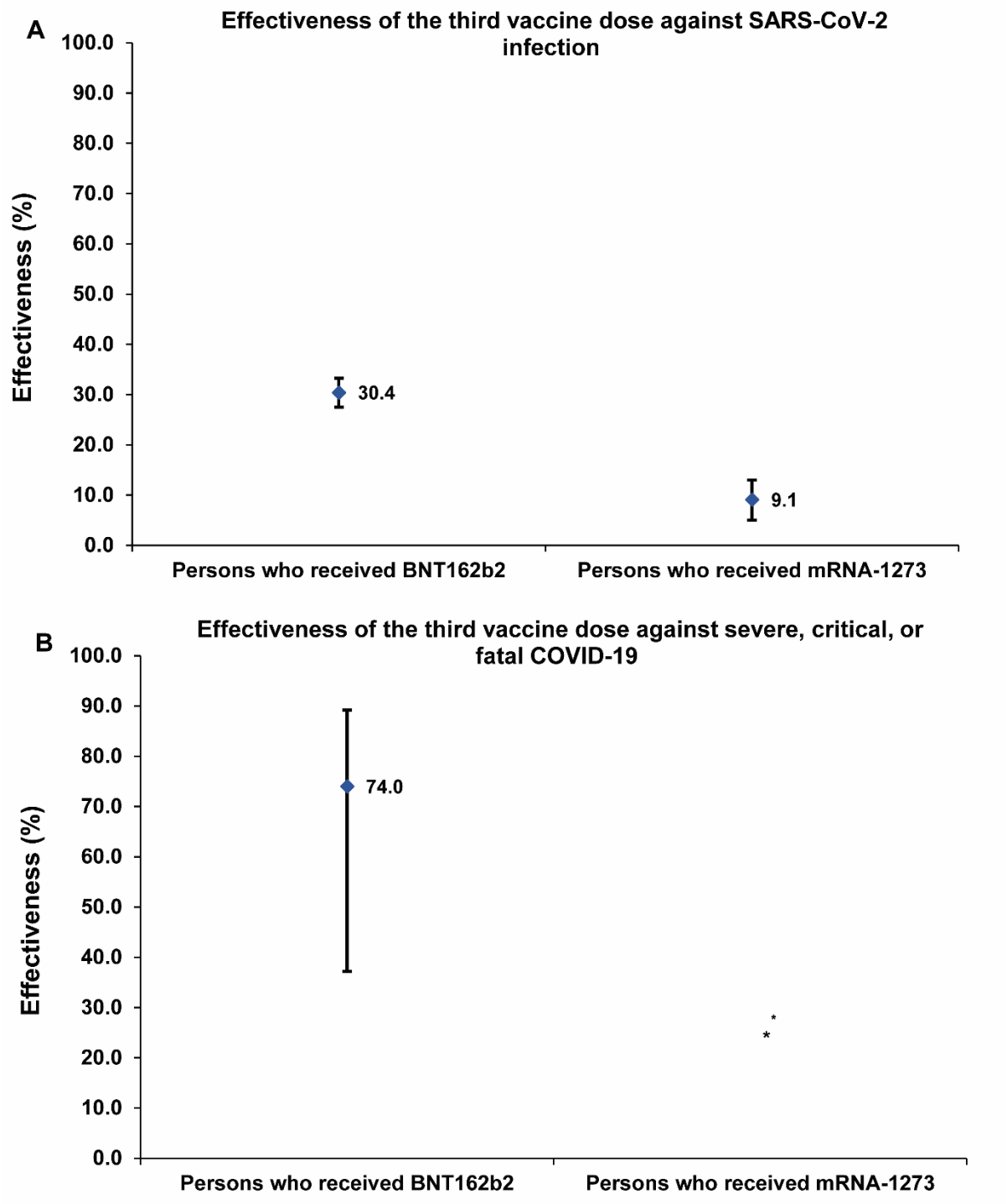
CI denotes confidence interval, COVID-19, coronavirus disease 2019, and SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

*Cohorts were matched exactly one-to-one by sex, 10-year age group, nationality, number of coexisting conditions, vaccine type, prior infection status, and calendar week of the second vaccine dose. Persons who received their third vaccine dose in a specific calendar week in the three-dose cohort were additionally matched to persons who had a record for a SARS-CoV-2 test in that same calendar week in the two-dose cohort, to ensure that matched pairs had presence in Qatar over the same time period.

†Adjusted for sex, 10-year age group, 10 nationality groups, number of coexisting conditions, prior infection status, calendar week of second vaccine dose, and calendar week of third vaccine dose/SARS-CoV-2 test.

‡Could not be estimated or estimates were unstable because there were too few or no infections that progressed to severe, critical, or fatal COVID-19.

***Figure S4*: Booster effectiveness relative to primary series by mRNA vaccine type A) against SARS-CoV-2 infection and B) against severe, critical, or fatal COVID-19.**



*Vaccine effectiveness could not be estimated because there were too few infections that progressed to severe, critical, or fatal COVID-19.

***Figure S5*: Sensitivity analysis. Booster effectiveness relative to primary series against SARS-CoV-2 infection by month since the start of the follow-up additionally adjusted for differences in testing rates across cohorts.**

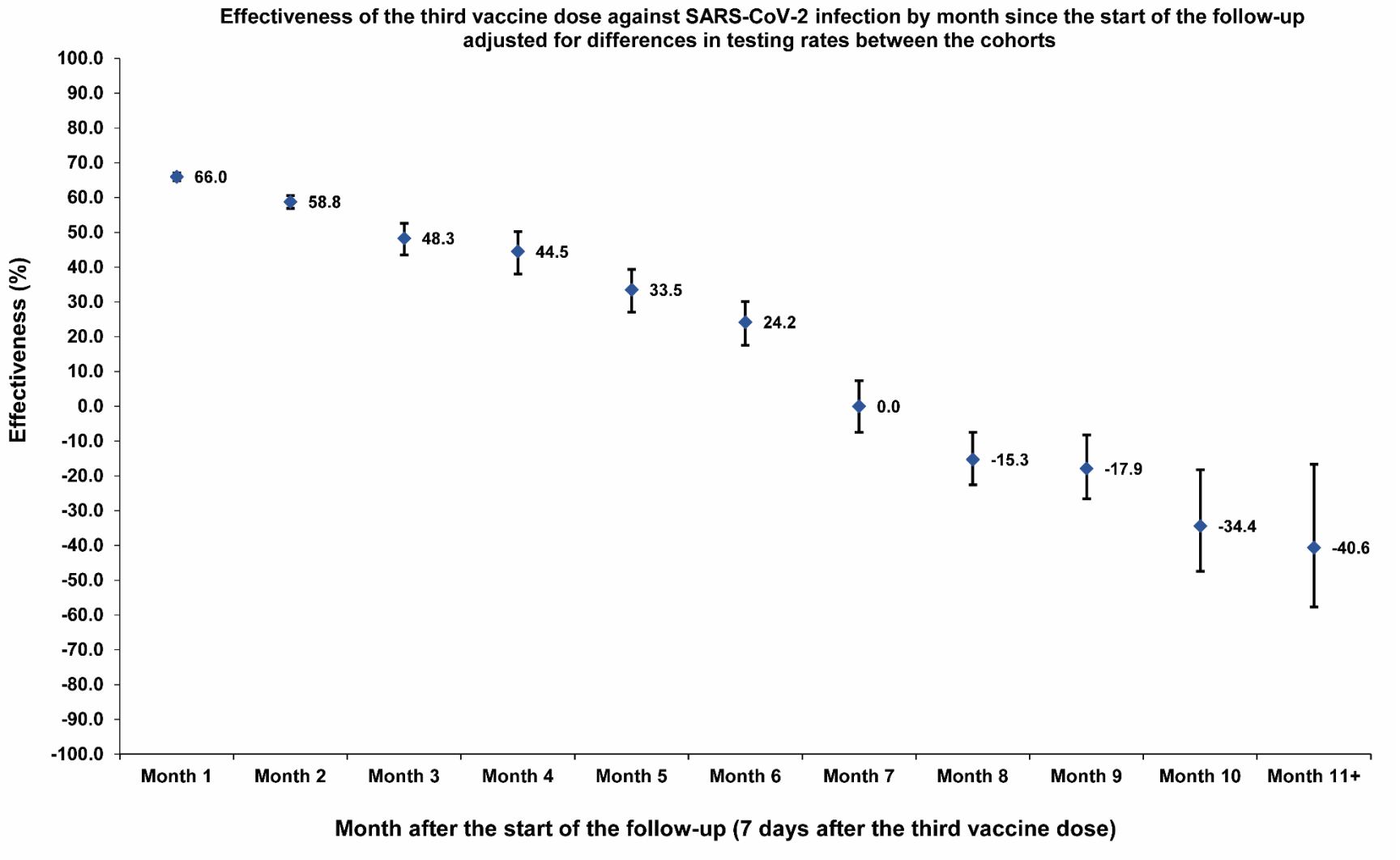
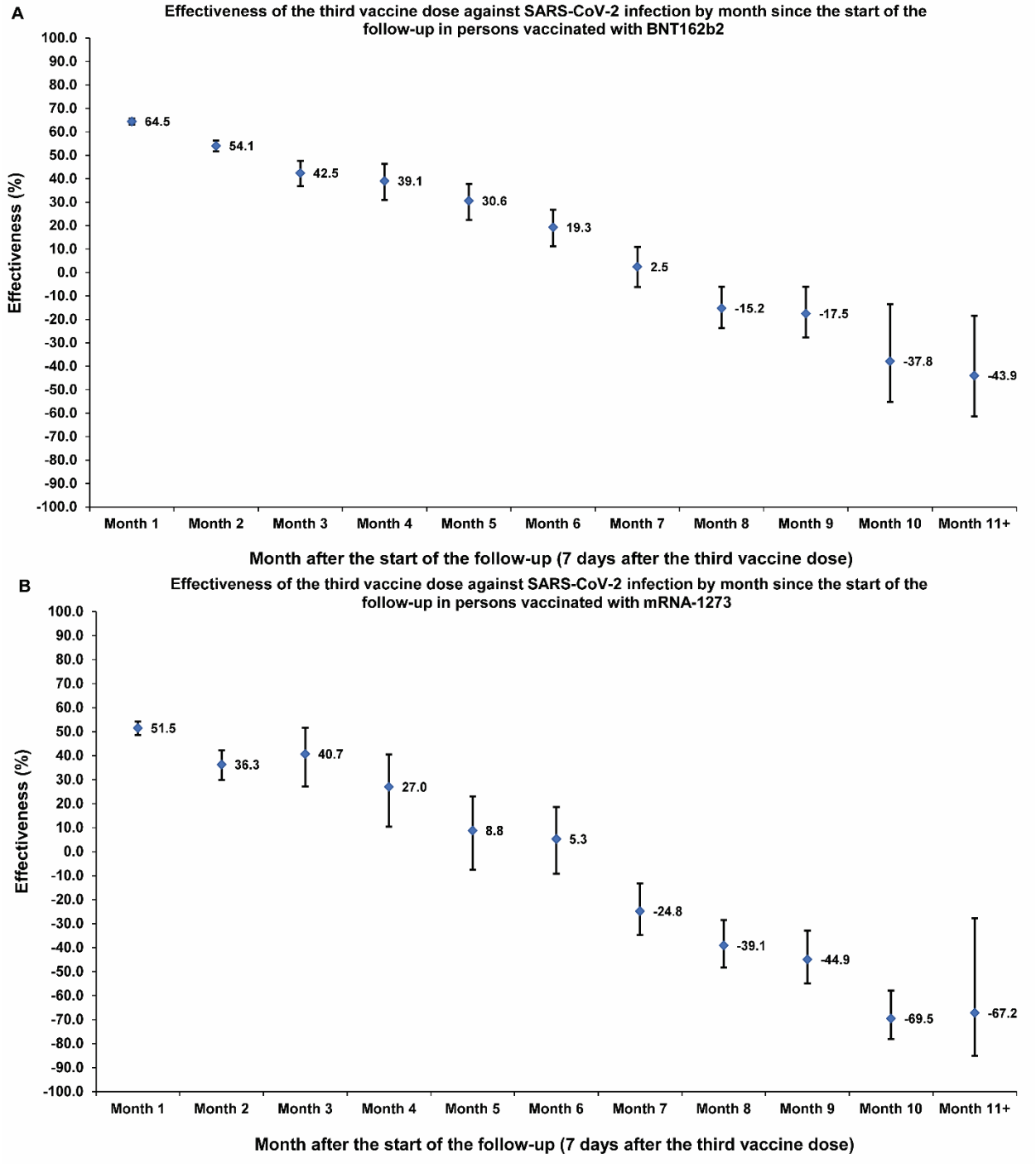


***Figure S6*: Booster effectiveness relative to primary series against SARS-CoV-2 infection by month since the start of the follow-up for each of (A) BNT162b2 and (B) mRNA-1273 vaccines.**



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