Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

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Supplementary Appendix

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Author contributions

HC co-designed the study, performed the statistical analyses, and co-wrote the first draft of the article. LJA conceived and co-designed the study, led the statistical analyses, and co-wrote the first draft of the article. PT and MRH conducted the multiplex, RT-qPCR variant screening and viral genome sequencing. HY, FMB, and HAK conducted viral genome sequencing. All authors contributed to data collection and acquisition, database development, discussion and interpretation of the results, and to the writing of the manuscript. All authors have read and approved the final manuscript.

Section 1. Further details on methods

Study population, data sources, and study design

Every PCR test conducted in Qatar, regardless of location or setting, is 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). 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.[1,2]

Nearly all individuals in the population were vaccinated free of charge in Qatar, rather than elsewhere. In rare situations in which an individual was vaccinated outside Qatar, that individual's vaccination details were still recorded in the health system at the port of entry upon return to Qatar, following national requirements and to benefit from privileges associated with vaccination, such as exemption from quarantine.[3]

With the high diversity of our population and having several fold more PCR-negative tests than PCR-positive tests, it was possible to find exact PCR-negative matches for the PCR-positive cases in this study, especially for the major nationality groups in Qatar.

Only the first PCR-positive test during the study, January 1, 2021 to September 5, 2021, was included for each case, and only the first PCR-negative test during the study was included for each control. All PCR tests done for pre-travel or at the port of entry were excluded from analysis, except in a sensitivity analysis. This type of testing could possibly be affected by different test-seeking behaviors in those vaccinated versus those unvaccinated, as a consequence of the travel privileges granted only to vaccinated persons, such as exemption from quarantine.[3]

All PCR-negative tests for persons included as cases were excluded from analysis. That is, no person was included as both a case and a control. These inclusion and exclusion criteria were implemented to control potential bias arising from repeated testing, such as a PCR-positive person undergoing a second PCR test a few days after infection diagnosis to test for clearance of infection, or bias arising from repeat testers among controls, that is persons with a higher level of health care-seeking behavior and presumably lower risk of infection. Modifications to these inclusion and exclusion criteria were investigated in sensitivity analyses.

Each person who had a positive PCR test result and hospital admission was subject to an infection severity assessment every three days until discharge or death, regardless of the length of stay in the hospital or time between PCR-positive test and final disease outcome. Individuals who progressed to COVID-19 disease between the time of the PCR-positive test result and the end of the study were classified based on their worst outcome, starting with death,[4] followed by critical disease,[5] and then severe disease.[5] Details of the COVID-19 severity, criticality, and fatality classification are found in Section 2.

All records of PCR testing for those vaccinated and unvaccinated during the study were examined. All persons who received mixed vaccines, or who received a vaccine other than BNT162b2 were excluded. Every case that met the inclusion criteria and that could be matched to a control was included in the analysis. Both PCR-test outcomes and vaccination status were ascertained at the time of the PCR test.

Statistical analysis

All records of PCR testing in Qatar during the study were examined, but only samples of matched cases and controls were included in the analysis. In each analysis for a specific time-

since-vaccination stratum, we included only those vaccinated in that specific time-since-vaccination stratum and those unvaccinated (our reference group). Only matched pairs of PCR-positive and PCR-negative persons, in which both members of the pair were either unvaccinated or fell within each time-since-vaccination stratum were included in the corresponding vaccine effectiveness estimate. Thus, the number of cases (and controls) varied across time-since-vaccination analyses. Effectiveness after the second dose was estimated month by month, where one month was defined as 30 days.

The analysis adjusting in conditional logistic regression for healthcare worker status specifically adjusted for being a healthcare worker at Hamad Medical Corporation, the main public healthcare provider in Qatar and the nationally designated provider for all COVID-19 healthcare needs.

Vaccine effectiveness was estimated against symptomatic infection, defined as a PCR-positive test conducted because of clinical suspicion due to presence of symptoms compatible with a respiratory tract infection, and against asymptomatic infection, defined as a PCR-positive test conducted with no reported presence of symptoms compatible with a respiratory tract infection. In the latter case, PCR testing was done strictly as part of a survey or a random testing campaign. Vaccine effectiveness was further estimated in subgroup analyses stratifying cases and controls by age, variant type, or severe forms of COVID-19 disease.

Vaccine effectiveness estimates for individual variants had wider 95% CIs, because they were derived using smaller numbers of confirmed PCR-positive cases, that is, only those confirmed as Alpha, Beta, or Delta using RT-qPCR genotyping (Section 4). Variant RT-qPCR genotyping started at a considerable scale only in the early summer of 2021, well after the large Beta wave had peaked in April, 2021, thus explaining the small sample sizes in these analyses.

Although Qatar experienced an Alpha variant wave early in 2021, this wave peaked in the first week of March, 2021, and at a much lower incidence than the peak of the Beta variant wave, which occurred in early of April, 2021.[6-10] Most incidence of Alpha occurred at a time when the number of vaccinated persons was still small; thus, Alpha infections did not contribute appreciably to the estimated effectiveness measures in this study.

Section 2. COVID-19 severity, criticality, and fatality classification

Severe Coronavirus Disease 2019 (COVID-19) disease was defined per the World health Organization (WHO) classification as a severe acute respiratory syndrome coronavirus 2 (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)".[5] Detailed WHO criteria for classifying SARS-CoV-2 infection severity can be found in the WHO technical report.[5]

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".[5] Detailed WHO criteria for classifying SARS-CoV-2 infection criticality can be found in the WHO technical report.[5]

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.[4]

Section 3. Laboratory methods

Nasopharyngeal and/or oropharyngeal swabs were collected for PCR testing and placed in Universal Transport Medium (UTM). Aliquots of UTM were: extracted on a QIAsymphony platform (QIAGEN, USA) and tested 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, USA); tested directly on the Cepheid GeneXpert system using the Xpert Xpress SARS-CoV-2 (Cepheid, USA); or loaded directly into a Roche cobas® 6800 system and assayed with a 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.

Section 4. Classification of infections by variant type

Surveillance for SARS-CoV-2 variants in Qatar is based on viral genome sequencing and multiplex, real-time reverse-transcription PCR (RT-qPCR) variant screening[11] of random positive clinical samples,[6-10] and complemented by deep sequencing of wastewater samples.[6] The ascertainment of the B.1.1.7 (Alpha[12]), B.1.351 (Beta[12]), and B.1.617.2 (Delta[12]) cases in this study was based on the results of weekly RT-qPCR genotyping of the positive clinical samples.[6,8]

Between March 22, 2021 and August 24, 2021, RT-qPCR genotyping identified 5,845 (38.7%) B.1.351-like cases, 3,523 (23.3%) B.1.1.7-like cases, 5,706 (37.7%) "other" variant cases, and 48 (0.3%) B.1.375-like and B.1.258-like cases in 15,175 randomly collected SARS-CoV-2-positive specimens.[6,8]

The accuracy of the RT-qPCR genotyping was verified against either Sanger sequencing of the receptor-binding domain (RBD) of SARS-CoV-2 surface glycoprotein (S) gene, or by viral whole-genome sequencing on a Nanopore GridION sequencing device. From 236 random samples (27 B.1.1.7-like, 186 B.1.351/P.1-like, and 23 "other" variants), the PCR genotyping results for B.1.1.7-like, B.1.351/P.1-like, and 'other' variants were in 88.8% (23 out of 27), 99.5% (185 out of 186), and 100% (23 out of 23) agreement with the SARS-CoV-2 lineages assigned by sequencing.[6,8]

Within the "other" variant category, Sanger sequencing and/or Illumina sequencing of the RBD of SARS-CoV-2 spike gene on 457 random samples confirmed that 433 (94.7%) were B.1.617.2 cases, 8 (1.8%) were B.1.617.1 cases, 3 (0.7%) were B.1 cases, 1 (0.2%) was a B.1.351/P.1 case, 1 (0.2%) was a P.1 case, and 1 (0.2%) was a B.1.617.3 case, with 10 (1.1%) samples failing

lineage assignment.[6,8] Accordingly, a Delta case was proxied as any “other” case identified through the RT-qPCR based variant screening.

All the variant RT-qPCR screening was conducted at the Sidra Medicine Laboratory following standardized protocols.

Section 5. Additional sensitivity analyses

Additional sensitivity analyses were conducted to investigate whether the generated real-world effectiveness estimates could have been biased by an unknown factor. These analyses included:

1. Sensitivity analysis in which study inclusion and exclusion criteria were modified so as to additionally exclude any case or control with a prior infection, that is any person with a PCR-positive test prior to January 1, 2021, the first day of the study (Table S7). This analysis was done to investigate whether the results could have been confounded by effect of prior infection.

2. Sensitivity analysis in which study inclusion and exclusion criteria were modified so as to include all PCR-positive and PCR-negative tests for each person, and regardless of the number of PCR-positive or PCR-negative tests each person had during the study (Table S8). This analysis was done to investigate how the results of the analyses could have been affected or biased by a broad study inclusion and exclusion criteria.

3. Sensitivity analysis in which study inclusion and exclusion criteria were modified so as to additionally include as controls persons who had a PCR-negative test during the study, in addition to the PCR-positive test during the study (Table S9). That is, persons with both PCR-positive and PCR-negative tests during the study were included both as cases and as controls, but at different time points. This analysis was done to investigate how the results of the analyses could have been affected or biased by this different study inclusion and exclusion criteria.

4. Sensitivity analysis in which study inclusion and exclusion criteria were modified so as to additionally include all PCR testing done for pre-travel or at port of entry purposes (Table

S10). This analysis was done to investigate how the results of the analyses could have been affected or biased by inclusion of this source of PCR testing in the study.

Additional sensitivity analyses were also conducted but not reported here for brevity. In these analyses we investigated the impact on the results of other different prescriptions for modifying the study inclusion and exclusion criteria, incorporating prior infection as a matching factor, a different categorization of the age variable, and interaction between age and vaccination. All analyses generated consistent results indicating the same pattern of declining effectiveness in the months following the second dose.

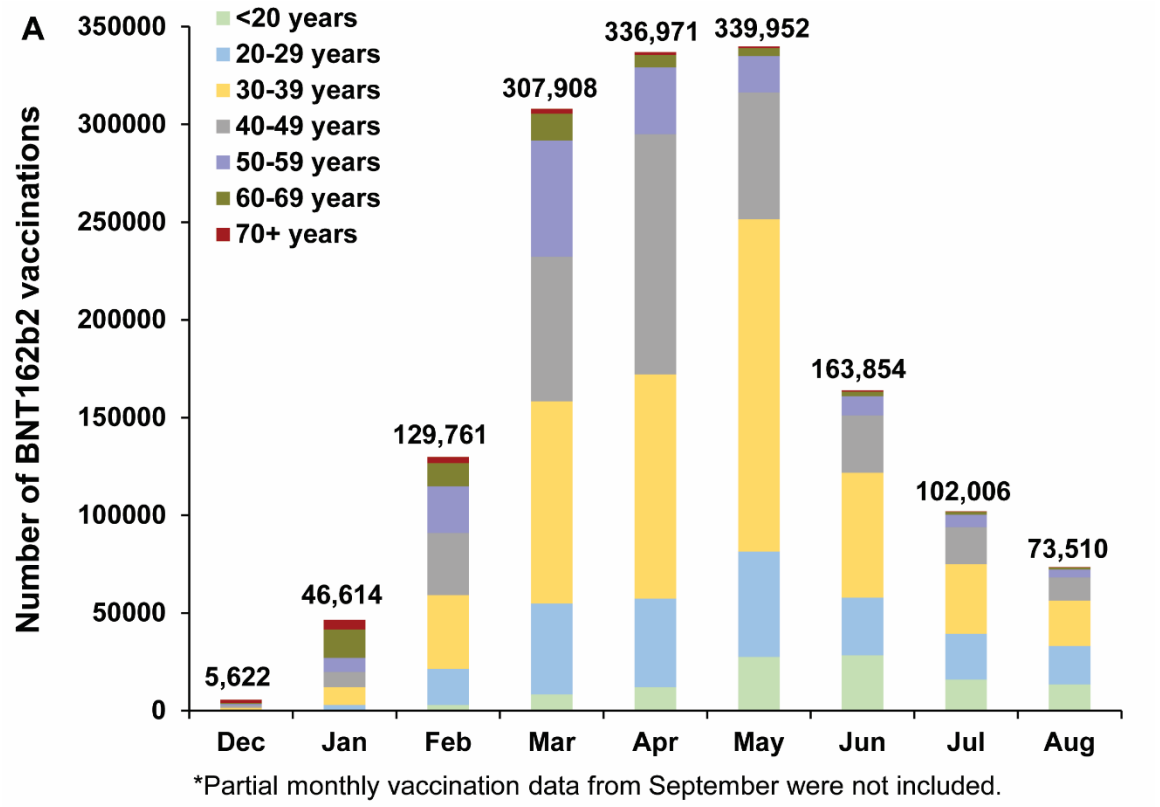
To provide further validation of study results, effectiveness was estimated using a multivariable logistic regression analysis of associations with a PCR-positive test, that is, by applying a different method from that of the main analysis of matched test-negative, case-control study design (Table S11). The derived adjusted odds ratios (AORs) were used to estimate vaccine effectiveness using the equation 1 – AOR, that is assuming odds ratio approximates risk ratio for rare outcomes. The full unmatched sample of this study was used in this analysis, that is 142,300 individuals with a first PCR-positive test and 848,240 individuals with a first PCR-negative test. The multivariable logistic regression adjusted for sex (male, female), age (0-9, 10-19, 20-29, 30-39, 40-49, 50-59, 60-69, and 70+ years), nationality (Bangladeshis, Egyptians, Filipinos, Indians, Nepalese, Pakistani, Qataris, Sri Lankans, Sudanese, and other nationalities), reason for PCR testing (clinical suspicion, contact tracing, healthcare routine testing, survey, individual request, and other), and calendar week of PCR test starting from January 1, 2021.

Table S1. STROBE checklist for case-control 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	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	4	Present key elements of study design	4-5 & Section 1
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4-5, Section 1, & Figure S2
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls	4-5, Sections 1-4, & Figure S2
		(*b*) For matched studies, give matching criteria and the number of controls per case	4 & Section 1
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4-6 & Sections 1-5
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	4-6 & Section 1
Bias	9	Describe any efforts to address potential sources of bias	4-6 & Sections 1 & 5
Study size	10	Explain how the study size was arrived at	4-5, Section 1, & Figure S2
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	4-6, Table 1, Tables S2-S3, & Table S11
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	5-6 & Sections 1 & 5
		(*b*) Describe any methods used to examine subgroups and interactions	5-6 & Sections 1 & 5
		(*c*) Explain how missing data were addressed	NA, see p. 4
		(*d*) If applicable, explain how matching of cases and controls was addressed	5 & Section 1
		(*e*) Describe any sensitivity analyses	6 & Section 5
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 S2, Table 1, Tables S2-S3, & Figure S1
		(b) Give reasons for non-participation at each stage	4, Section 1, & Figure S2
		(c) Consider use of a flow diagram	Figure S2
Descriptive data	14	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6-7, Table 1, & Tables S2-S3
		(b) Indicate number of participants with missing data for each variable of interest	NA, see p. 4
Outcome data	15	Report numbers in each exposure category, or summary measures of exposure	8-10, Tables 2-4, & Tables S4-S6
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	8-10, Tables 2-4, Figure 2, & Tables S4-S6
		(*b*) Report category boundaries when continuous variables were categorized	Table 2-4 & Tables S4-S6
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	10, Tables S4-S11
Discussion			
Key results	18	Summarise key results with reference to study objectives	10-12
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	13-14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14
Generalisability	21	Discuss the generalisability (external validity) of the study results	13
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	15

Abbreviations: NA, not applicable.

Figure S1. A) Number of BNT162b2 vaccinations by calendar month. B) Number of PCR-positive cases by calendar month that were included in the analyses of this study.



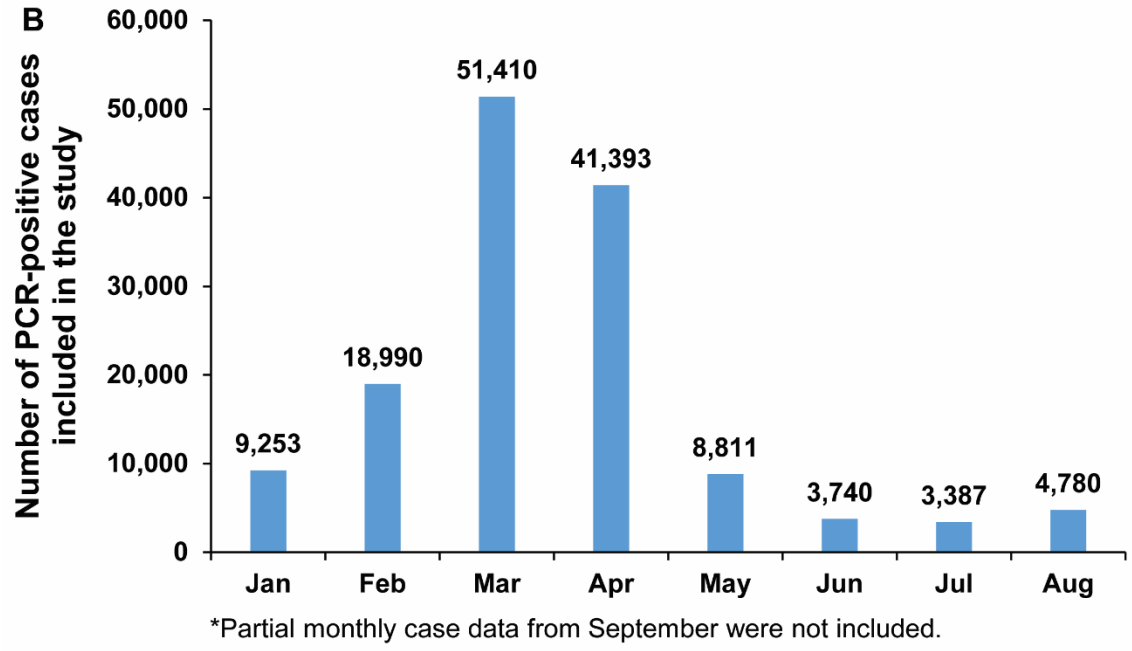
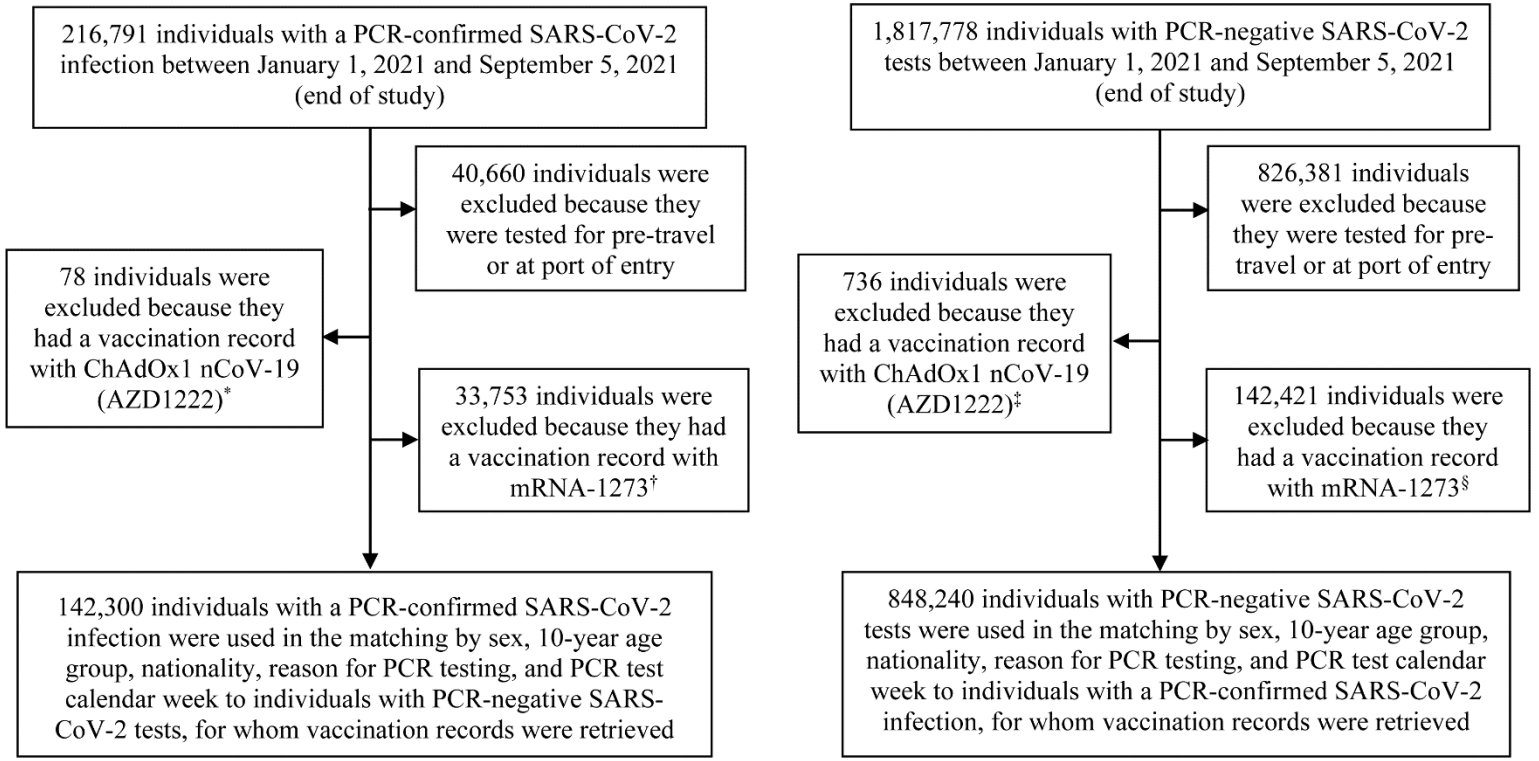


Figure S2. Flowchart describing the population selection process for investigating BNT162b2 vaccine effectiveness.



*Sample includes 1 person who had another vaccination with mRNA-1273
†Sample includes 7 persons who had another vaccination with BNT162b2
‡Sample includes 1 person who had another vaccination with BNT162b2
§Sample includes 56 persons who had another vaccination with BNT162b2

Note: In each analysis for a specific time-since-vaccination stratum, we included only those vaccinated in this specific time-since-vaccination stratum and those unvaccinated (our reference group). Only matched pairs of PCR-positive and PCR-negative persons, in which both members of the pair were either unvaccinated or fell within each time-since-vaccination stratum have been included in the corresponding vaccine effectiveness estimate. Thus, the number of cases (and controls) varied across time-since-vaccination analyses.

Table S2. Demographic characteristics of subjects and reasons for PCR testing among samples used to estimate BNT162b2 vaccine effectiveness. The table includes samples used in the 2nd-month-after-second-dose analysis, 3rd-month-after-second-dose analysis, and 4th-month-after-second-dose analysis.

Characteristics	2nd-month-after-second-dose		3rd-month-after-second-dose		4th-month-after-second-dose	
	Cases* (PCR-positive)	Controls* (PCR-negative)	Cases* (PCR-positive)	Controls* (PCR-negative)	Cases* (PCR-positive)	Controls* (PCR-negative)
	N=113,324	N=113,324	N=112,188	N=112,188	N=111,562	N=111,562
Median age (IQR) — years	31 (21-39)	31 (21-39)	31 (21-39)	31 (21-39)	31 (21-39)	31 (21-39)
Age group — no. (%)						
<20 years	26,794 (23.6)	26,794 (23.6)	26,749 (23.8)	26,749 (23.8)	26,727 (24.0)	26,727 (24.0)
20-29 years	24,477 (21.6)	24,477 (21.6)	24,339 (21.7)	24,339 (21.7)	24,355 (21.8)	24,355 (21.8)
30-39 years	35,887 (31.7)	35,887 (31.7)	35,578 (31.7)	35,578 (31.7)	35,373 (31.7)	35,373 (31.7)
40-49 years	18,638 (16.5)	18,638 (16.5)	18,351 (16.4)	18,351 (16.4)	18,196 (16.3)	18,196 (16.3)
50-59 years	5,800 (5.1)	5,800 (5.1)	5,613 (5.0)	5,613 (5.0)	5,516 (4.9)	5,516 (4.9)
60-69 years	1,347 (1.2)	1,347 (1.2)	1,179 (1.1)	1,179 (1.1)	1,077 (1.0)	1,077 (1.0)
70+ years	381 (0.3)	381 (0.3)	379 (0.3)	379 (0.3)	318 (0.3)	318 (0.3)
Sex						
Male	77,860 (68.7)	77,860 (68.7)	77,221 (68.8)	77,221 (68.8)	76,884 (68.9)	76,884 (68.9)
Female	35,464 (31.3)	35,464 (31.3)	34,967 (31.2)	34,967 (31.2)	34,678 (31.1)	34,678 (31.1)
Nationality†						
Bangladeshi	8,207 (7.2)	8,207 (7.2)	8,176 (7.3)	8,176 (7.3)	8,158 (7.3)	8,158 (7.3)
Egyptian	6,536 (5.8)	6,536 (5.8)	6,447 (5.8)	6,447 (5.8)	6,387 (5.7)	6,387 (5.7)
Filipino	10,410 (9.2)	10,410 (9.2)	10,337 (9.2)	10,337 (9.2)	10,212 (9.2)	10,212 (9.2)
Indian	29,338 (25.9)	29,338 (25.9)	29,101 (25.9)	29,101 (25.9)	28,965 (26.0)	28,965 (26.0)
Nepalese	10,345 (9.1)	10,345 (9.1)	10,320 (9.2)	10,320 (9.2)	10,318 (9.3)	10,318 (9.3)
Pakistani	5,722 (5.1)	5,722 (5.1)	5,686 (5.1)	5,686 (5.1)	5,672 (5.1)	5,672 (5.1)
Qatari	17,226 (15.2)	17,226 (15.2)	16,906 (15.1)	16,906 (15.1)	16,777 (15.0)	16,777 (15.0)
Sri Lankan	3,704 (3.3)	3,704 (3.3)	3,687 (3.3)	3,687 (3.3)	3,685 (3.3)	3,685 (3.3)
Sudanese	3,223 (2.8)	3,223 (2.8)	3,167 (2.8)	3,167 (2.8)	3,142 (2.8)	3,142 (2.8)
Other nationalities‡	18,613 (16.4)	18,613 (16.4)	18,361 (16.4)	18,361 (16.4)	18,246 (16.4)	18,246 (16.4)
Reason for PCR testing						
Clinical suspicion	40,052 (35.3)	40,052 (35.3)	39,402 (35.1)	39,402 (35.1)	39,087 (35.0)	39,087 (35.0)
Contact tracing	18,360 (16.2)	18,360 (16.2)	18,242 (16.3)	18,242 (16.3)	18,167 (16.3)	18,167 (16.3)
Healthcare routine testing	14,266 (12.6)	14,266 (12.6)	14,244 (12.7)	14,244 (12.7)	14,188 (12.7)	14,188 (12.7)
Survey	27,419 (24.2)	27,419 (24.2)	27,221 (24.3)	27,221 (24.3)	27,076 (24.3)	27,076 (24.3)
Individual request	12,773 (11.3)	12,773 (11.3)	12,653 (11.3)	12,653 (11.3)	12,628 (11.3)	12,628 (11.3)
Other	454 (0.4)	454 (0.4)	426 (0.4)	426 (0.4)	416 (0.4)	416 (0.4)

Abbreviations: IQR, interquartile range; PCR, polymerase chain reaction.

*Cases and controls were matched one-to-one by sex, 10-year age group, nationality, reason for PCR testing, and calendar week of PCR test.

†Nationalities were chosen to represent the most populous groups in Qatar.

‡These comprise 107 other nationalities in Qatar in the 2nd-month-after-second-dose analysis, 106 other nationalities in the 3rd-month-after-second-dose analysis, and 106 other nationalities in the 4th-month-after-second-dose analysis.

Table S3. Demographic characteristics of subjects and reasons for PCR testing among samples used to estimate BNT162b2 vaccine effectiveness. The table includes samples used in the 5th-month-after-second-dose analysis, 6th-month-after-second-dose analysis, and 7th-month-after-second-dose analysis.

Characteristics	5th-month-after-second-dose		6th-month-after-second-dose		7th-month-after-second-dose	
	Cases* (PCR-positive)	Controls* (PCR-negative)	Cases* (PCR-positive)	Controls* (PCR-negative)	Cases* (PCR-positive)	Controls* (PCR-negative)
	N=111,539	N=111,539	N=111,467	N=113,324	N=111,077	N=111,077
Median age (IQR) — years	31 (21-39)	31 (22-39)	31 (21-39)	31 (22-39)	31 (21-39)	31 (22-39)
Age group — no. (%)						
<20 years	26,729 (24.0)	26,729 (24.0)	26,710 (24.0)	26,710 (24.0)	26,697 (24.0)	26,697 (24.0)
20-29 years	24,342 (21.8)	24,342 (21.8)	24,303 (21.8)	24,303 (21.8)	24,213 (21.8)	24,213 (21.8)
30-39 years	35,386 (31.7)	35,386 (31.7)	35,368 (31.7)	35,368 (31.7)	35,229 (31.7)	35,229 (31.7)
40-49 years	18,215 (16.3)	18,215 (16.3)	18,223 (16.4)	18,223 (16.4)	18,104 (16.3)	18,104 (16.3)
50-59 years	5,512 (4.9)	5,512 (4.9)	5,512 (4.9)	5,512 (4.9)	5,480 (4.9)	5,480 (4.9)
60-69 years	1,061 (1.0)	1,061 (1.0)	1,057 (1.0)	1,057 (1.0)	1,056 (1.0)	1,056 (1.0)
70+ years	294 (0.3)	294 (0.3)	294 (0.3)	294 (0.3)	298 (0.3)	298 (0.3)
Sex						
Male	76,877 (68.9)	76,877 (68.9)	76,843 (68.9)	76,843 (68.9)	76,650 (69.0)	76,650 (69.0)
Female	34,662 (31.1)	34,662 (31.1)	34,624 (31.1)	34,624 (31.1)	34,427 (31.0)	34,427 (31.0)
Nationality†						
Bangladeshi	8,147 (7.3)	8,147 (7.3)	8,144 (7.3)	8,144 (7.3)	8,134 (7.3)	8,134 (7.3)
Egyptian	6,400 (5.7)	6,400 (5.7)	6,397 (5.7)	6,397 (5.7)	6,380 (5.7)	6,380 (5.7)
Filipino	10,177 (9.1)	10,177 (9.1)	10,165 (9.1)	10,165 (9.1)	10,145 (9.1)	10,145 (9.1)
Indian	28,954 (26.0)	28,954 (26.0)	28,938 (26.0)	28,938 (26.0)	28,912 (26.0)	28,912 (26.0)
Nepalese	10,315 (9.3)	10,315 (9.3)	10,308 (9.3)	10,308 (9.3)	10,307 (9.3)	10,307 (9.3)
Pakistani	5,681 (5.1)	5,681 (5.1)	5,671 (5.1)	5,671 (5.1)	5,664 (5.1)	5,664 (5.1)
Qatari	16,793 (15.1)	16,793 (15.1)	16,763 (15.0)	16,763 (15.0)	16,558 (14.9)	16,558 (14.9)
Sri Lankan	3,684 (3.3)	3,684 (3.3)	3,682 (3.3)	3,682 (3.3)	3,677 (3.3)	3,677 (3.3)
Sudanese	3,142 (2.8)	3,142 (2.8)	3,142 (2.8)	3,142 (2.8)	3,136 (2.8)	3,136 (2.8)
Other nationalities‡	18,246 (16.4)	18,246 (16.4)	18,257 (16.4)	18,257 (16.4)	18,164 (16.4)	18,164 (16.4)
Reason for PCR testing						
Clinical suspicion	39,092 (35.1)	39,092 (35.1)	39,030 (35.0)	39,030 (35.0)	38,836 (35.0)	38,836 (35.0)
Contact tracing	18,143 (16.3)	18,143 (16.3)	18,136 (16.3)	18,136 (16.3)	18,115 (16.3)	18,115 (16.3)
Healthcare routine testing	14,194 (12.7)	14,194 (12.7)	14,179 (12.7)	14,179 (12.7)	14,164 (12.8)	14,164 (12.8)
Survey	27,055 (24.3)	27,055 (24.3)	27,083 (24.3)	27,083 (24.3)	26,977 (24.3)	26,977 (24.3)
Individual request	12,646 (11.3)	12,646 (11.3)	12,628 (11.3)	12,628 (11.3)	12,578 (11.3)	12,578 (11.3)
Other	409 (0.4)	409 (0.4)	411 (0.4)	411 (0.4)	407 (0.4)	407 (0.4)

Abbreviations: IQR, interquartile range; PCR, polymerase chain reaction.

*Cases and controls were matched one-to-one by sex, 10-year age group, nationality, reason for PCR testing, and calendar week of PCR test.

†Nationalities were chosen to represent the most populous groups in Qatar.

‡These comprise 106 other nationalities in Qatar in the 5th-month-after-second-dose analysis, 106 other nationalities in the 6th-month-after-second-dose analysis, and 106 other nationalities in the 7th-month-after-second-dose analysis.

Table S4. Effectiveness of the BNT162b2 vaccine against any SARS-CoV-2 infection and against any severe, critical, or fatal COVID-19 disease, stratified by age (<60 years or ≥60 years).

Sub-studies[*]	Effectiveness against infection					Effectiveness against hospitalization and death				
	Cases[†] (PCR-positive)		Controls[†] (PCR-negative)		Effectiveness in % (95% CI)[‡]	Cases[†] (Severe, critical, or fatal disease)[§]		Controls[†] (PCR-negative)		Effectiveness in % (95% CI)[‡]
	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated		Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	
Age <60 years										
0-13 days after first dose	4,031	109,749	3,883	109,897	-4.3 (-9.3 ; 0.5)	196	3,637	236	3,597	18.6 (0.6 ; 33.3)
≥14 days after first dose and no second dose	2,172	110,137	3,386	108,923	38.7 (35.1 ; 42.1)	67	3,655	213	3,509	71.9 (62.3 ; 79.1)
1st month after the second dose	2,693	111,527	9,449	104,771	77.8 (76.7 ; 78.9)	19	3,676	459	3,236	96.9 (94.8 ; 98.2)
2nd month after the second dose	1,218	110,378	3,785	107,811	73.4 (71.4 ; 75.2)	9	3,652	200	3,461	97.0 (93.1 ; 98.6)
3rd month after the second dose	659	109,971	1,840	108,790	69.9 (66.8 ; 72.8)	4	3,639	102	3,541	97.0 (90.6 ; 99.1)
4th month after the second dose	445	109,722	777	109,390	51.6 (44.5 ; 57.7)	3	3,627	26	3,604	88.5 (61.9 ; 96.5)
5th month after the second dose	527	109,657	602	109,582	18.4 (5.7 ; 29.4)	0	3,629	21	3,608	100.0 (Omitted)[¶]
6th month after the second dose	424	109,692	474	109,642	17.4 (1.9 ; 30.5)	5	3,627	19	3,613	93.3 (49.5 ; 99.1)
7th month or greater after the second dose	101	109,622	127	109,596	24.5 (-0.9 ; 43.5)	3	3,623	7	3,619	57.1 (-65.7 ; 88.9)
Age ≥60 years										
0-13 days after first dose	197	1,349	170	1,376	-19.0 (-48.8 ; 4.8)	49	364	50	363	2.5 (-51.5 ; 37.3)
≥14 days after first dose and no second dose	186	1,335	181	1,340	-3.4 (-29.7 ; 17.6)	35	377	59	353	44.4 (13.2 ; 64.4)
1st month after the second dose	222	1,471	537	1,156	71.1 (64.8 ; 76.3)	13	406	126	293	92.6 (85.5 ; 96.3)
2nd month after the second dose	232	1,496	519	1,209	71.9 (65.4 ; 77.2)	14	410	123	301	96.5 (90.4 ; 98.7)
3rd month after the second dose	141	1,417	288	1,270	67.4 (57.4 ; 75.1)	13	387	79	321	90.4 (79.2 ; 95.6)
4th month after the second dose	47	1,348	79	1,316	53.3 (26.9 ; 70.2)	7	369	25	351	78.3 (42.8 ; 91.7)
5th month after the second dose	21	1,334	44	1,311	79.3 (50.2 ; 91.4)	0	361	12	349	100.0 (Omitted)[¶]
6th month after the second dose	36	1,315	38	1,313	15.4 (-88.8 ; 62.1)	3	361	5	359	66.7 (-220.5 ; 96.5)
7th month or greater after the second dose	34	1,320	35	1,319	6.6 (-93.4 ; 54.9)	3	360	4	359	50.0 (-451.4 ; 95.5)

Abbreviations: CI, confidence interval; PCR, polymerase chain reaction.

*In each analysis for a specific time-since-vaccination stratum, we included only those vaccinated in this specific time-since-vaccination stratum and those unvaccinated. Only matched pairs of PCR-positive and PCR-negative persons, in which both members of the pair were either unvaccinated or fell within each time-since-vaccination stratum have been included in the corresponding vaccine effectiveness estimate. Thus, the number of cases (and controls) varied across time-since-vaccination analyses.

†Cases and controls were matched one-to-one by sex, 10-year age group, nationality, reason for PCR testing, and calendar week of PCR test.

‡Vaccine effectiveness was estimated using the test-negative, case-control study design.[13,14]

§Severity,[5] criticality,[5] and fatality[4] were defined as per World Health Organization guidelines.

¶Confidence interval could not be estimated because of zero events among vaccinated.

Table S5. Effectiveness of the BNT162b2 vaccine against each of SARS-CoV-2 Alpha[12] (B.1.1.7), Beta[12] (B.1.351), and Delta[12] (B.1.617.2) variant infections.

Sub-studies[*]	Effectiveness against infection				
	Cases[†] (PCR-positive)		Controls[†] (PCR-negative)		Effectiveness in % (95% CI)[‡]
	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	
Infection with the Alpha variant[§]					
0-13 days after first dose	36	1,584	41	1,579	12.8 (-38.1 ; 45.0)
≥14 days after first dose and no second dose	27	1,581	50	1,558	47.9 (15.5 ; 67.9)
1st month after the second dose	53	1,587	184	1,456	77.1 (67.5 ; 83.8)
2nd month after the second dose	18	1,587	111	1,494	88.6 (79.2-93.7)
3rd month after the second dose	18	1,580	64	1,534	80.7 (63.2 ; 89.9)
4th month after the second dose	12	1,588	29	1,571	60.7 (21.1 ; 80.4)
5th month after the second dose	15	1,583	20	1,578	33.3 (-48.3 ; 70.0)
6th or greater month after the second dose	2	1,587	6	1,583	80.0 (-71.2 ; 97.7)
Infection with the Beta variant[§]					
0-13 days after first dose	118	2,984	99	3,003	-21.1 (-60.1 ; 8.4)
≥14 days after first dose and no second dose	72	3,000	95	2,977	25.8 (-2.0 ; 46.1)
1st month after the second dose	124	3,013	402	2,735	74.3 (67.9 ; 79.5)
2nd month after the second dose	106	3,015	230	2,891	63.9 (52.6 ; 72.5)
3rd month after the second dose	55	2,996	111	2,940	56.0 (37.3 ; 69.1)
4th month after the second dose	14	2,990	20	2,984	37.5 (-37.7 ; 71.6)
5th month after the second dose	8	2,997	14	2,991	54.5 (-30.8 ; 84.2)
6th month after the second dose	5	2,986	7	2,984	40.0 (-151.1 ; 85.7)
Infection with the Delta variant[§]					
0-13 days after first dose	27	2,132	41	2,118	37.8 (-4.6 ; 63.1)
≥14 days after first dose and no second dose	27	2,134	72	2,089	63.4 (42.6 ; 76.6)
1st month after the second dose	24	2,139	151	2,012	87.6 (79.7 ; 92.3)
2nd month after the second dose	60	2,153	200	2,013	73.3 (63.6 ; 80.4)
3rd month after the second dose	98	2,146	209	2,035	62.4 (50.2 ; 71.6)
4th month after the second dose	132	2,153	178	2,107	35.1 (14.7 ; 50.6)
5th month after the second dose	191	2,141	220	2,112	20.4 (-1.9 ; 37.8)
6th month after the second dose	145	2,144	160	2,129	17.9 (-12.9 ; 40.3)

Abbreviations: CI, confidence interval; PCR, polymerase chain reaction.

[*]In each analysis for a specific time-since-vaccination stratum, we included only those vaccinated in this specific time-since-vaccination stratum and those unvaccinated. Only matched pairs of PCR-positive and PCR-negative persons, in which both members of the pair were either unvaccinated or fell within each time-since-vaccination stratum have been included in the corresponding vaccine effectiveness estimate. Thus, the number of cases (and controls) varied across time-since-vaccination analyses.

[†]Cases and controls were matched one-to-one by sex, 10-year age group, nationality, reason for PCR testing, and calendar week of PCR test.

[‡]Vaccine effectiveness was estimated using the test-negative, case-control study design.[13,14]

[§]Ascertainment of Alpha[12] (B.1.1.7), Beta[12] (B.1.351) and Delta[12] (B.1.617.2) cases was based on RT-qPCR genotyping of positive clinical samples (Supplementary Section 3).[6,8,11]

Table S6. Effectiveness of the BNT162b2 vaccine against each of severe COVID-19 disease, critical COVID-19 disease, and fatal COVID-19 disease.

Sub-studies[*]	Cases[†] (COVID-19 disease)		Controls[†] (PCR-negative)		Effectiveness in % (95% CI)[‡]
	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	
Severe disease[§]					
0-13 days after first dose	216	3,386	230	3,372	6.8 (-13.4 ; 23.4)
≥14 days after first dose and no second dose	85	3,411	210	3,286	63.1 (51.8 ; 71.8)
1st month after the second dose	30	3,450	468	3,012	95.2 (92.7 ; 96.9)
2nd month after the second dose	16	3,441	252	3,205	97.1 (93.9 ; 98.6)
3rd month after the second dose	12	3,418	141	3,289	94.9 (89.0 ; 97.6)
4th month after the second dose	9	3,387	41	3,355	82.1 (59.9 ; 92.0)
5th month after the second dose	0	3,383	30	3,353	100.0 (Omitted)[¶]
6th month or greater after the second dose	13	3,385	31	3,367	81.8 (47.2 ; 93.7)
Critical disease[§]					
0-13 days after first dose	28	606	56	578	58.3 (29.8 ; 75.3)
≥14 days after first dose and no second dose	16	612	62	566	78.0 (59.8 ; 87.9)
1st month after the second dose	2	622	116	508	99.1 (93.8 ; 99.9)
2nd month after the second dose	6	611	69	548	95.5 (85.5 ; 98.6)
3rd month after the second dose	5	599	40	564	92.1 (74.4 ; 97.6)
4th month after the second dose	1	600	10	591	90.0 (21.9 ; 98.7)
5th month after the second dose	0	598	3	595	100.0 (Omitted)[¶]
6th month or greater after the second dose	1	596	6	591	83.3 (-38.4 ; 98.0)
Fatal disease[§]					
0-13 days after first dose	13	220	22	211	47.4 (-13.2 ; 75.5)
≥14 days after first dose and no second dose	11	229	28	212	63.0 (23.5 ; 82.1)
1st month after the second dose	5	236	67	174	95.4 (85.3 ; 98.5)
2nd month after the second dose	6	233	46	193	95.2 (80.3 ; 98.8)
3rd month after the second dose	1	228	23	206	95.7 (67.8 ; 99.4)
4th month after the second dose	2	219	2	219	0.0 (-609.9 ; 85.9)
5th month after the second dose	0	221	1	220	100.0 (Omitted)[¶]
6th month or greater after the second dose	0	215	0	215	Omitted[**]

Abbreviations: CI, confidence interval; PCR, polymerase chain reaction.

[*]In each analysis for a specific time-since-vaccination stratum, we included only those vaccinated in this specific time-since-vaccination stratum and those unvaccinated. Only matched pairs of PCR-positive and PCR-negative persons, in which both members of the pair were either unvaccinated or fell within each time-since-vaccination stratum have been included in the corresponding vaccine effectiveness estimate. Thus, the number of cases (and controls) varied across time-since-vaccination analyses.

[†]Cases and controls were matched one-to-one by sex, 10-year age group, nationality, reason for PCR testing, and calendar week of PCR test.

[‡]Vaccine effectiveness was estimated using the test-negative, case-control study design.[13,14]

[§]Severity,[5] criticality,[5] and fatality[4] were defined as per World Health Organization guidelines.

[¶]Confidence interval could not be estimated because of zero events among vaccinated.

[**]There were no vaccinated persons among cases and controls; thus effectiveness could not be estimated.

Table S7. Sensitivity analysis in which study inclusion and exclusion criteria were modified so as to additionally exclude any case or control with a prior infection, that is any person with a PCR-positive test prior to January 1, 2021, the first day of the study. Effectiveness of the BNT162b2 vaccine against any SARS-CoV-2 infection and against any severe, critical, or fatal COVID-19 disease.

Sub-studies[*]	Effectiveness against infection					Effectiveness against hospitalization and death				
	Cases[†] (PCR-positive)		Controls[†] (PCR-negative)		Effectiveness in % (95% CI)[‡]	Cases[†] (Severe, critical, or fatal disease)[§]		Controls[†] (PCR-negative)		Effectiveness in % (95% CI)[‡]
	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated		Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	
0-13 days after first dose	4,050	108,783	3,848	108,985	-5.8 (-10.9 ; -1.0)	247	3,960	272	3,935	10.3 (-7.7 ; 25.3)
≥14 days after first dose and no second dose	2,292	109,091	3,492	107,891	37.0 (33.4 ; 40.3)	102	3,996	307	3,791	70.7 (62.7 ; 77.0)
1st month after the second dose	2,829	110,641	9,618	103,852	77.0 (75.9 ; 78.1)	30	4,040	628	3,442	96.1 (94.2 ; 97.4)
2nd month after the second dose	1,420	109,449	4,240	106,629	73.9 (72.1 ; 75.7)	22	4,022	335	3,709	95.7 (92.7 ; 97.5)
3rd month after the second dose	793	109,041	1,988	107,846	67.5 (64.3 ; 70.4)	17	3,985	183	3,819	94.9 (90.0 ; 97.4)
4th month after the second dose	479	108,690	791	108,378	47.6 (40.3 ; 54.0)	11	3,951	57	3,905	86.8 (71.0 ; 94.0)
5th month after the second dose	533	108,627	665	108,495	28.3 (17.5 ; 37.7)	0	3,955	28	3,927	100.0 (Omitted)[¶]
6th month after the second dose	449	108,622	500	108,571	17.2 (2.0 ; 30.1)	8	3,949	26	3,931	94.7 (60.7 ; 99.3)
7th month or greater after the second dose	131	108,561	149	108,543	18.2 (-9.7 ; 39.0)	6	3,952	12	3,946	60.0 (-27.5 ; 87.5)

Abbreviations: CI, confidence interval; PCR, polymerase chain reaction.

[*]In each analysis for a specific time-since-vaccination stratum, we included only those vaccinated in this specific time-since-vaccination stratum and those unvaccinated. Only matched pairs of PCR-positive and PCR-negative persons, in which both members of the pair were either unvaccinated or fell within each time-since-vaccination stratum have been included in the corresponding vaccine effectiveness estimate. Thus, the number of cases (and controls) varied across time-since-vaccination analyses.

[†]Cases and controls were matched one-to-one by sex, 10-year age group, nationality, reason for PCR testing, and calendar week of PCR test.

[‡]Vaccine effectiveness was estimated using the test-negative, case-control study design.[13,14]

[§]Severity,[5] criticality,[5] and fatality[4] were defined as per World Health Organization guidelines.

[¶]Confidence interval could not be estimated because of zero events among vaccinated.

Table S8. Sensitivity analysis in which study inclusion and exclusion criteria were modified so as to include all PCR-positive and PCR-negative tests for each person, and regardless of the number of PCR-positive or PCR-negative tests each person had during the study, January 1, 2021 to September 5, 2021. Effectiveness of the BNT162b2 vaccine against any SARS-CoV-2 infection and against any severe, critical, or fatal COVID-19 disease. This analysis appears to have been affected by a positive bias due to perhaps inclusion of repeat testing, such as more "repeat testers" among controls, that is persons with a higher level of health care-seeking behavior and presumably lower risk of infection. This can be seen in the results for vaccine effectiveness at 0-13 days after the first dose. Based on evidence from the clinical trials and biological plausibility, it is not expected to observe a positive effectiveness against specifically *infection* in the first two weeks after the first dose, but the analysis indicated a small statistically significant positive effectiveness.

Sub-studies[*]	Effectiveness against infection					Effectiveness against hospitalization and death				
	Cases[†] (PCR-positive)		Controls[†] (PCR-negative)		Effectiveness in % (95% CI)[‡]	Cases[†] (Severe, critical, or fatal disease)[§]		Controls[†] (PCR-negative)		Effectiveness in % (95% CI)[‡]
	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated		Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	
0-13 days after first dose	4,842	138,197	5,428	137,611	11.9 (8.2 ; 15.4)	290	5,082	323	5,049	11.4 (-4.8 ; 25.1)
≥14 days after first dose and no second dose	3,877	138,574	5,682	136,769	34.8 (31.9 ; 37.6)	183	5,082	412	4,853	60.7 (52.5 ; 67.5)
1st month after the second dose	3,558	139,618	13,205	129,971	79.0 (78.1 ; 79.9)	41	5,133	760	4,414	96.1 (94.4 ; 97.3)
2nd month after the second dose	1,864	138,751	6,613	134,002	77.8 (76.5 ; 79.1)	32	5,124	447	4,709	95.6 (93.1 ; 97.2)
3rd month after the second dose	1,106	138,393	3,547	135,952	76.3 (74.3 ; 78.1)	29	5,106	267	4,868	94.4 (90.5 ; 96.8)
4th month after the second dose	657	138,056	1,398	137,315	61.6 (57.3 ; 65.6)	13	5,079	83	5,009	86.4 (74.5 ; 92.8)
5th month after the second dose	700	138,016	1,073	137,643	48.8 (42.1 ; 54.6)	6	5,063	52	5,017	93.9 (80.4 ; 98.1)
6th month after the second dose	576	137,980	784	137,772	41.6 (32.5 ; 49.4)	8	5,047	39	5,016	91.2 (71.3 ; 97.3)
7th month or greater after the second dose	201	137,991	314	137,878	49.6 (36.9 ; 59.7)	8	5,051	19	5,042	60.0 (-3.1 ; 84.5)

Abbreviations: CI, confidence interval; PCR, polymerase chain reaction.

[*]In each analysis for a specific time-since-vaccination stratum, we included only those vaccinated in this specific time-since-vaccination stratum and those unvaccinated. Only matched pairs of PCR-positive and PCR-negative persons, in which both members of the pair were either unvaccinated or fell within each time-since-vaccination stratum have been included in the corresponding vaccine effectiveness estimate. Thus, the number of cases (and controls) varied across time-since-vaccination analyses.

[†]Cases and controls were matched one-to-one by sex, 10-year age group, nationality, reason for PCR testing, and calendar week of PCR test.

[‡]Vaccine effectiveness was estimated using the test-negative, case-control study design.[13,14]

[§]Severity,[5] criticality,[5] and fatality[4] were defined as per World Health Organization guidelines.

Table S9. Sensitivity analysis in which study inclusion and exclusion criteria were modified so as to additionally include as controls persons who had a PCR-negative test during the study, in addition to their PCR-positive test during the study. That is, persons with both PCR-positive and PCR-negative tests during the study, January 1, 2021 to September 5, 2021, were included both as cases and as controls, but at different time points. Effectiveness of the BNT162b2 vaccine against any SARS-CoV-2 infection and against any severe, critical, or fatal COVID-19 disease.

Sub-studies[*]	Effectiveness against infection					Effectiveness against hospitalization and death				
	Cases[†] (PCR-positive)		Controls[†] (PCR-negative)		Effectiveness in % (95% CI)[‡]	Cases[†] (Severe, critical, or fatal disease)[§]		Controls[†] (PCR-negative)		Effectiveness in % (95% CI)[‡]
	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated		Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	
0-13 days after first dose	4,480	115,794	3,893	116,381	-17.2 (-22.6 ; -11.9)	262	4,041	230	4,073	-15.8 (-39.8 ; 4.0)
≥14 days after first dose and no second dose	2,530	116,239	3,813	114,956	36.5 (33.0 ; 39.7)	106	4,067	282	3,891	65.9 (56.8 ; 73.1)
1st month after the second dose	3,021	117,009	9,418	110,612	74.1 (72.8 ; 75.2)	33	4,092	508	3,617	95.0 (92.5 ; 96.7)
2nd month after the second dose	1,532	116,309	3,946	113,895	68.0 (65.8 ; 70.1)	25	4,095	267	3,853	94.9 (91.1 ; 97.1)
3rd month after the second dose	841	116,025	1,919	114,947	62.8 (59.2 ; 66.0)	17	4,083	165	3,935	93.1 (87.3 ; 96.2)
4th month after the second dose	508	115,832	770	115,570	41.2 (33.2 ; 48.3)	10	4,039	39	4,010	80.6 (56.3 ; 91.3)
5th month after the second dose	570	115,771	633	115,708	14.5 (1.8 ; 25.5)	1	4,044	26	4,019	96.2 (71.7-99.5)
6th month after the second dose	477	115,781	509	115,749	11.0 (-5.2 ; 24.8)	7	4,038	21	4,024	87.5 (45.6 ; 97.1)
7th month or greater after the second dose	141	115,749	150	115,740	8.5 (-20.5 ; 30.5)	6	4,039	9	4,036	42.9 (-95.2 ; 83.3)

Abbreviations: CI, confidence interval; PCR, polymerase chain reaction.

[*]In each analysis for a specific time-since-vaccination stratum, we included only those vaccinated in this specific time-since-vaccination stratum and those unvaccinated. Only matched pairs of PCR-positive and PCR-negative persons where both members of the pair were either unvaccinated or fell within each time-since-vaccination stratum have been included in the corresponding vaccine effectiveness estimate. Thus, the number of cases (and controls) varied across time-since-vaccination analyses.

[†]Cases and controls were matched one-to-one by sex, 10-year age group, nationality, reason for PCR testing, and calendar week of PCR test.

[‡]Vaccine effectiveness was estimated using the test-negative, case-control study design.[13,14]

[§]Severity,[5] criticality,[5] and fatality[4] were defined as per World Health Organization guidelines.

Table S10. Sensitivity analysis in which study inclusion and exclusion criteria were modified so as to additionally include all PCR testing done for pre-travel or at port of entry purposes. Effectiveness of the BNT162b2 vaccine against any SARS-CoV-2 infection and against any severe, critical, or fatal COVID-19 disease. Inclusion of this testing appears to introduce a negative bias, possibly because this testing could have been affected by different test-seeking behaviors of those vaccinated versus those unvaccinated, as a consequence of the travel privileges granted only to vaccinated persons, such as exemption from quarantine. This bias specifically affected the time-since-vaccination estimates of ≥5 months after the second dose, as incidence in these time-since-vaccination categories coincided with the summer travel season.

Sub-studies[*]	Effectiveness against infection					Effectiveness against hospitalization and death				
	Cases[†] (PCR-positive)		Controls[†] (PCR-negative)		Effectiveness in % (95% CI)[‡]	Cases[†] (Severe, critical, or fatal disease)[§]		Controls[†] (PCR-negative)		Effectiveness in % (95% CI)[‡]
	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated		Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	
0-13 days after first dose	4,199	141,811	4,007	142,003	-5.4 (-10.4 ; -0.7)	250	4,023	292	3,981	15.8 (-0.6 ; 29.6)
≥14 days after first dose and no second dose	2,387	142,207	3,668	140,926	37.7 (34.2 ; 41.0)	101	4,054	309	3,846	71.2 (63.3 ; 77.4)
1st month after the second dose	3,302	143,905	11,041	136,166	77.4 (76.4 ; 78.5)	33	4,120	616	3,537	96.5 (94.6 ; 97.7)
2nd month after the second dose	1,738	142,649	4,764	139,623	71.0 (69.1 ; 72.8)	22	4,085	316	3,791	96.1 (93.0 ; 97.8)
3rd month after the second dose	1,105	142,097	2,310	140,892	59.4 (56.0 ; 62.6)	18	4,052	173	3,897	93.4 (87.8 ; 96.4)
4th month after the second dose	808	141,700	961	141,547	19.8 (10.8 ; 27.8)	7	4,022	56	3,973	92.5 (79.1 ; 97.3)
5th month after the second dose	933	141,678	826	141,785	-19.3 (-33.6 ; -6.6)	2	3,997	28	3,971	96.3 (72.7-99.5)
6th month after the second dose	737	141,642	585	141,794	-45.9 (-67.8 ; -26.9)	7	4,001	14	3,994	77.8 (-2.8 ; 95.2)
7th month or greater after the second dose	220	141,617	153	141,684	-75.2 (-127.4 ; -35.1)	6	3,996	9	3,993	42.9 (-95.2 ; 83.3)

Abbreviations: CI, confidence interval; PCR, polymerase chain reaction.

[*]In each analysis for a specific time-since-vaccination stratum, we included only those vaccinated in this specific time-since-vaccination stratum and those unvaccinated. Only matched pairs of PCR-positive and PCR-negative persons, in which both members of the pair were either unvaccinated or fell within each time-since-vaccination stratum have been included in the corresponding vaccine effectiveness estimate. Thus, the number of cases (and controls) varied across time-since-vaccination analyses.

[†]Cases and controls were matched one-to-one by sex, 10-year age group, nationality, reason for PCR testing, and calendar week of PCR test.

[‡]Vaccine effectiveness was estimated using the test-negative, case-control study design.[13,14]

[§]Severity,[5] criticality,[5] and fatality[4] were defined as per World Health Organization guidelines.

Table S11. Effectiveness of the BNT162b2 vaccine against any SARS-CoV-2 infection, symptomatic SARS-CoV-2 infection, or asymptomatic SARS-CoV-2 infection, with effectiveness estimated using a multivariable logistic regression analysis of associations with a PCR-positive test, January 1, 2021 to September 5, 2021, adjusting for sex, age, nationality, reason for PCR testing, and calendar week of PCR test[*].

	Original sample size	SARS-CoV-2 positive	Multivariable regression analysis	Vaccine effectiveness
	N (%)	N (%)	AOR (95% CI)	% (95% CI)
Any SARS-CoV-2 infection				
Unvaccinated	806,169 (81.4)	126,242 (15.7)	1.00	
0-13 days after first dose	23,382 (2.4)	5,088 (21.8)	1.05 (1.02-1.09)	-5.3 (-9.0 ; -1.7)
≥14 days after first dose and no second dose	16,578 (1.7)	2,897 (17.5)	0.67 (0.65-0.70)	32.5 (29.5 ; 35.4)
1st month after the second dose	58,187 (5.9)	3,296 (5.7)	0.22 (0.21-0.23)	78.0 (77.1 ; 78.8)
2nd month after the second dose	31,702 (3.2)	1,758 (5.5)	0.29 (0.27-0.30)	71.4 (69.9 ; 72.8)
3rd month after the second dose	21,717 (2.2)	1,007 (4.6)	0.36 (0.33-0.38)	64.3 (61.9 ; 66.7)
4th month after the second dose	12,471 (1.3)	593 (4.8)	0.59 (0.54-0.64)	41.3 (36.0 ; 46.1)
5th month after the second dose	9,414 (1.0)	680 (7.2)	1.11 (1.03-1.21)	-11.4 (-21.1 ; -2.5)
6th month after the second dose	8,897 (0.9)	558 (6.3)	1.21 (1.10-1.33)	-20.6 (-32.5 ; -9.8)
7th month or greater after the second dose	2,023 (0.2)	181 (8.9)	1.43 (1.22-1.68)	-43.4 (-68.3 ; -22.1)
Symptomatic SARS-CoV-2 infection[†]				
Unvaccinated	158,926 (80.3)	48,943 (30.8)	1.00	
0-13 days after first dose	6,352 (3.2)	2,630 (41.4)	1.04 (0.99-1.10)	-4.3 (-10.2 ; 1.2)
≥14 days after first dose and no second dose	5,523 (2.8)	1,486 (26.9)	0.53 (0.50-0.57)	46.8 (43.2 ; 50.1)
1st month after the second dose	8,719 (4.4)	1,100 (12.6)	0.18 (0.17-0.20)	81.6 (80.3 ; 82.8)
2nd month after the second dose	6,011 (3.0)	840 (14.0)	0.29 (0.26-0.31)	71.4 (69.1 ; 73.6)
3rd month after the second dose	4,862 (2.5)	488 (10.0)	0.34 (0.31-0.38)	66.1 (62.5 ; 69.3)
4th month after the second dose	3,167 (1.6)	307 (9.7)	0.57 (0.50-0.64)	43.5 (36.0 ; 50.1)
5th month after the second dose	2,386 (1.2)	381 (16)	1.27 (1.13-1.43)	-26.9 (-42.6 ; -13.0)
6th month after the second dose	1,466 (0.7)	277 (18.9)	1.66 (1.44-1.90)	-65.5 (-90.3 ; -44.0)
7th month or greater after the second dose	571 (0.3)	94 (16.5)	1.38 (1.10-1.73)	-37.7 (-73.1 ; -9.6)
Asymptomatic SARS-CoV-2 infection[‡]				
Unvaccinated	325341 (81.8)	28094 (8.6)	1.00	
0-13 days after first dose	9003 (2.3)	1021 (11.3)	1.12 (1.04-1.20)	-11.8 (-19.8 ; -4.3)
≥14 days after first dose and no second dose	5505 (1.4)	546 (9.9)	0.90 (0.82-0.99)	9.9 (1.1 ; 17.8)
1st month after the second dose	21643 (5.4)	818 (3.8)	0.28 (0.26-0.30)	71.7 (69.5 ; 73.7)
2nd month after the second dose	12517 (3.1)	418 (3.3)	0.38 (0.35-0.42)	61.7 (57.5; 65.5)
3rd month after the second dose	9270 (2.3)	266 (2.9)	0.59 (0.52-0.67)	41.4 (33.3 ; 48.5)
4th month after the second dose	4737 (1.2)	130 (2.7)	0.89 (0.75-1.07)	10.6 (-7.1 ; 25.4)
5th month after the second dose	3575 (0.9)	120 (3.4)	1.12 (0.92-1.36)	-12.2 (-36.2 ; 7.5)
6th month after the second dose	5242 (1.3)	140 (2.7)	0.80 (0.65-0.98)	20.0 (2.1 ; 34.7)
7th month or greater after the second dose	731 (0.2)	41 (5.6)	1.83 (1.32-2.55)	-83.2 (-155.1 ; -31.6)

Abbreviations: AOR: adjusted odds ratio; CI, confidence interval.

[*]In this table vaccine effectiveness was estimated using the equation 1 – AOR, that is assuming odds ratio approximates risk ratio for rare outcomes. The AORs were derived using a multivariable logistic regression analysis of the associations with a PCR-positive test, that is by applying a different method from that of the main analysis of matched test-negative, case-control study design. The full unmatched sample of this study was used in this analysis, that is 142,300 individuals with a first PCR-positive test and 848,240 individuals with a first PCR-negative test. The multivariable logistic regression adjusted for sex (male, female), age (0-9, 10-19, 20-29, 30-39, 40-49, 50-59, 60-69, and 70+ years), nationality (Bangladeshis, Egyptians, Filipinos, Indians, Nepalese, Pakistani, Qataris, Sri Lankans, Sudanese, and other nationalities), reason for PCR testing (clinical suspicion, contact tracing, healthcare routine testing, survey, individual request, and other), and calendar week of PCR test starting from January 1, 2021.

[†]A symptomatic infection was defined as a PCR-positive test conducted because of clinical suspicion due to presence of symptoms compatible with a respiratory tract infection.

[‡]An asymptomatic infection was defined as a PCR-positive test conducted with no reported presence of symptoms compatible with a respiratory tract infection. That is, the PCR testing was done as part of a survey or a random testing campaign.

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