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BNT162b2 and mRNA-1273 COVID-19 vaccine effectiveness against the SARS-CoV-2 Delta variant in Qatar

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With the global expansion of the highly transmissible SARS-CoV-2 Delta (B.1.617.2) variant, we conducted a matched test-negative case–control study to assess the real-world effectiveness of COVID-19 messenger RNA vaccines against infection with Delta in Qatar's population. BNT162b2 effectiveness against any, symptomatic or asymptomatic, Delta infection was 45.3% (95% CI, 22.0–61.6%) ≥14 d after the first vaccine dose, but only 51.9% (95% CI, 47.0–56.4%) ≥14 d after the second dose, with 50% of fully vaccinated individuals receiving their second dose before 11 May 2021. Corresponding mRNA-1273 effectiveness ≥14 d after the first or second dose was 73.7% (95% CI, 58.1–83.5%) and 73.1% (95% CI, 67.5–77.8%), respectively. Notably, effectiveness against Delta-induced severe, critical or fatal disease was 93.4% (95% CI, 85.4–97.0%) for BNT162b2 and 96.1% (95% CI, 71.6–99.5%) for mRNA-1273 ≥ 14 d after the second dose. Our findings show robust effectiveness for both BNT162b2 and mRNA-1273 in preventing Delta hospitalization and death in Qatar's population, despite lower effectiveness in preventing infection, particularly for the BNT162b2 vaccine.

Appreciable community transmission of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) Delta (B.1.617.2) variant was first noted in Qatar by end of March 2021 (refs. [1–3]). Although Delta incidence has increased along with a recent surge in cases and hovered at about 200 cases per day in the summer of 2021, it remains low compared to earlier variant incidences with no signal for an epidemic wave materializing as of 19 September 2021. Between 23 March 2021 and 7 September 2021, 43% of diagnosed infections were Delta infections (Methods)[1,3]. Delta dominance was, however, preceded by two large consecutive SARS-CoV-2 Alpha (B.1.1.7) and Beta (B.1.351) waves earlier in 2021 (refs. [1–5]). The rapid scale-up of Coronavirus Disease 2019 (COVID-19) vaccination in Qatar may have impeded efficient Delta transmission. As of 19 September 2021, it is estimated that over 80% of Qatar's resident population has received two doses of either the BNT162b2 (ref. [6]) (Pfizer-BioNTech) vaccine or the mRNA-1273 (ref. [7]) (Moderna) vaccine[8]. This study assessed BNT162b2 and mRNA-1273 vaccines' real-world effectiveness against the Delta variant in Qatar from 23 March 2021 to 7 September 2021 and compared these estimates to those in other countries.

Results

Study population. From 21 December 2020 to 7 September 2021, 950,232 people had at least one BNT162b2 vaccine dose (median date of first dose was 21 April 2021) and 916,290 were fully vaccinated (median date of second dose was 11 May 2021). Administration of the second dose was within a median of 21 d after the first dose (interquartile range (IQR) 21–22 d), with full-vaccination of 97.4% of individuals within 30 d of first dose.

Over this timeframe, 564,468 individuals had at least one mRNA-1273 vaccine dose (median date of first dose was 19 May 2021) and 509,322 were fully vaccinated (median date of second dose was 24 May 2021); distributions for both doses were skewed with means of 16 May 2021 and 11 June 2021, respectively. Administration of the second dose was within a median of 28 d after the first dose (IQR 28–31 d), with full-vaccination of 74.7% of individuals within 30 d of the first dose.

With greater and regular vaccine availability, coverage for BNT162b2 has been steadily increasing since December 2020. In contrast, coverage for mRNA-1273 depended on dispatch of large shipments and did not reach considerable levels before March 2021.

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Table 1 | Demographic characteristics of cases (PCR-positive for SARS-CoV-2 Delta variant) and controls (PCR-negative) in the ≥14-d-after-first-dose analysis of vaccine effectiveness of sample A (BNT162b2), B (mRNA-1273) and C (BNT162b2 or mRNA-1273)

Study type	A Effectiveness of BNT162b2 vaccine		B Effectiveness of mRNA-1273 vaccine		C Effectiveness of BNT162b2 or mRNA-1273 vaccines	
Characteristics	Cases[a] (PCR-positive for Delta variant)	Controls[a] (PCR-negative)	Cases[a] (PCR-positive for Delta variant)	Controls[a] (PCR-negative)	Cases[a] (PCR-positive for Delta variant)	Controls[a] (PCR-negative)
	n = 2,783	*n* = 11,201	*n* = 2,781	*n* = 11,287	*n* = 2,934	*n* = 11,974
Median age (IQR) years	27 (11–35)	26 (10–34)	27 (12–35)	27 (10–35)	27 (12–36)	27 (11–35)
Age group no. (%)						
0–19 years	935 (33.6)	3,844 (34.3)	913 (32.8)	3,771 (33.4)	940 (32.0)	3,879 (32.4)
20–29 years	683 (24.5)	2,888 (25.8)	685 (24.6)	2,877 (25.5)	726 (24.7)	3,073 (25.7)
30–39 years	755 (27.1)	3,046 (27.2)	757 (27.2)	3,099 (27.5)	811 (27.6)	3,356 (28.0)
40–49 years	323 (11.6)	1,161 (10.4)	342 (12.3)	1,277 (11.3)	361 (12.3)	1,370 (11.4)
50–59 years	66 (2.4)	213 (1.9)	65 (2.3)	219 (1.9)	72 (2.5)	239 (2.0)
60–69 years	11 (0.4)	26 (0.2)	12 (0.4)	29 (0.3)	14 (0.5)	34 (0.3)
70+ years	10 (0.4)	23 (0.2)	7 (0.3)	15 (0.1)	10 (0.3)	23 (0.2)
Sex						
Male	1,810 (65.0)	7,832 (69.9)	1,820 (65.4)	7,941 (70.4)	1,899 (64.7)	8,273 (69.1)
Female	973 (35.0)	3,369 (30.1)	961 (34.6)	3,346 (29.6)	1,035 (35.3)	3,701 (30.9)
Nationality[b]						
Bangladeshi	207 (7.4)	954 (8.5)	224 (8.1)	1,022 (9.1)	242 (8.3)	1,107 (9.3)
Egyptian	76 (2.7)	316 (2.8)	79 (2.8)	315 (2.8)	84 (2.9)	343 (2.9)
Filipino	240 (8.6)	720 (6.4)	245 (8.8)	821 (7.3)	263 (9.0)	917 (7.7)
Indian	495 (17.8)	2,342 (20.9)	504 (18.1)	2,399 (21.3)	527 (18.0)	2,517 (21.0)
Nepalese	206 (7.4)	997 (8.9)	208 (7.5)	1,017 (9.0)	212 (7.2)	1,032 (8.6)
Pakistani	244 (8.8)	1,069 (9.5)	249 (9.0)	1,086 (9.6)	256 (8.7)	1,121 (9.4)
Qatari	749 (26.9)	3,090 (27.6)	709 (25.5)	2,904 (25.7)	752 (25.6)	3,117 (26.0)
Sri Lankan	44 (1.6)	168 (1.5)	45 (1.6)	181 (1.6)	50 (1.7)	193 (1.6)
Sudanese	44 (1.6)	143 (1.3)	43 (1.6)	137 (1.2)	46 (1.6)	148 (1.2)
Other nationalities[c]	478 (17.2)	1,402 (12.5)	475 (17.1)	1,405 (12.5)	502 (17.1)	1,479 (12.4)
Reason for PCR testing						
Clinical suspicion	1,277 (45.9)	5,061 (45.2)	1,278 (46.0)	5,150 (45.6)	1,370 (46.7)	5,588 (46.7)
Contact tracing	468 (16.8)	1,667 (14.9)	464 (16.7)	1,655 (14.7)	489 (16.7)	1,763 (14.7)
Survey	468 (16.8)	1,984 (17.7)	474 (17.0)	2,019 (17.9)	491 (6.7)	2,075 (17.3)
Individual request	449 (16.1)	2,083 (18.6)	449 (16.2)	2,080 (18.4)	456 (15.5)	2,115 (17.7)
Healthcare routine testing	97 (3.5)	372 (3.3)	96 (3.5)	356 (3.2)	103 (3.5)	396 (3.3)
Other	24 (0.9)	34 (0.3)	20 (0.7)	27 (0.2)	25 (0.9)	37 (0.3)

[a]Cases and controls were matched one-to-five by sex, 5-year age group, nationality, reason for PCR testing and calendar week of PCR test. [b]Nationalities were chosen to represent the most populous groups in Qatar. [c]These comprise 37 other nationalities in Qatar in sample A, 35 other nationalities in sample B and 37 other nationalities in sample C.

We defined a Delta 'case' as a PCR-positive swab with the Delta variant, irrespective of the reason for the PCR test or symptom presence or absence (Methods). Infections with other variants were excluded, except for Beta in an additional analysis. All records of vaccination for both BNT162b2 and mRNA-1273 were included. Extended Data Figs. 1–3 show flowcharts depicting the selection of study populations to estimate effectiveness of BNT162b2 (Extended Data Fig. 1), mRNA-1273 vaccine (Extended Data Fig. 2) and either of these vaccines (Extended Data Fig. 3) against the Delta variant. Tables 1 and 2 describe the samples used in estimation of effectiveness ≥14 d after the first dose and ≥14 d after the second dose, respectively. The median age of participants ranged from 26–30 years; only 9% of Qatar's residents are ≥50 years of age and 89% are residents from more than 150 countries[9,10].

Delta vaccine-breakthrough infections. Delta cases were ascertained using real-time PCR with reverse transcription (RT–qPCR) genotyping of randomly collected clinical samples (Methods)[1,3]. There were 88 and 1,126 Delta breakthrough infections between 23 March 2021 and 7 September 2021 among vaccinated individuals with one or two BNT162b2 doses, respectively and 60 and 187 Delta breakthrough infections among vaccinated individuals with one or two mRNA-1273 doses, respectively.

Additionally, by 7 September 2021, there were 4 and 15 severe Delta COVID-19 cases (acute care hospitalizations[11]; Methods)

Table 2 | Demographic characteristics of cases (PCR-positive for SARS-CoV-2 Delta variant) and controls (PCR-negative) in the ≥14-d-after-second-dose analysis of vaccine effectiveness of sample A (BNT162b2), B (mRNA-1273) and C (BNT162b2 or mRNA-1273)

Study type	A Effectiveness of BNT162b2 vaccine		B Effectiveness of mRNA-1273 vaccine		C Effectiveness of BNT162b2 or mRNA-1273 vaccines	
Characteristics	Cases[a] (PCR-positive for Delta variant)	Controls[a] (PCR-negative)	Cases[a] (PCR-positive for Delta variant)	Controls[a] (PCR-negative)	Cases[a] (PCR-positive for Delta variant)	Controls[a] (PCR-negative)
	n = 3,846	*n* = 15,977	*n* = 2,947	*n* = 12,151	*n* = 4,150	*n* = 17,490
Median age (IQR) years	30 (18–38)	29 (17–37)	28 (12–36)	28 (11–35)	30 (20–39)	30 (19–38)
Age group no. (%)						
0–19 years	1,025 (26.7)	4,383 (27.4)	919 (31.2)	3,799 (31.3)	1,034 (24.9)	4,430 (25.3)
20–29 years	891 (23.2)	3,900 (24.4)	720 (24.4)	3,071 (25.3)	966 (23.3)	4,253 (24.3)
30–39 years	1,076 (28.0)	4,564 (28.6)	825 (28.0)	3,470 (28. 6)	1,191 (28.7)	5,174 (29.6)
40–49 years	581 (15.1)	2,224 (13.9)	385 (13.1)	1,503 (12.4)	659 (15.9)	2,623 (15.0)
50–59 years	184 (4.8)	649 (4.1)	76 (2.6)	254 (2.1)	203 (4.9)	730 (4.2)
60–69 years	59 (1.5)	170 (1.1)	14 (0.5)	37 (0.3)	67 (1.6)	191 (1.1)
70+ years	30 (0.8)	87 (0.5)	8 (0.3)	17 (0.1)	30 (0.7)	89 (0.5)
Sex						
Male	2,316 (60.2)	10,057 (63.0)	1,879 (63.8)	8,223 (67.7)	2,464 (59.4)	10,808 (61.8)
Female	1,530 (39.8)	5,920 (37.1)	1,068 (36.2)	3,928 (32.3)	1,686 (40.6)	6,682 (38.2)
Nationality[b]						
Bangladeshi	228 (5.9)	1,054 (6.6)	230 (7.8)	1,061 (8.7)	266 (6.4)	1,237 (7.1)
Egyptian	129 (3.4)	543 (3.4)	91 (3.1)	374 (3.1)	150 (3.6)	637 (3.6)
Filipino	308 (8.0)	1,291 (8.1)	280 (9.5)	1,119 (9.2)	359 (8.7)	1,614 (9.2)
Indian	588 (15.3)	2,825 (17.7)	523 (17.8)	2,499 (20.6)	639 (15.4)	3,081 (17.6)
Nepalese	212 (5.5)	1,018 (6.4)	210 (7.1)	1,024 (8.4)	220 (5.3)	1,060 (6.1)
Pakistani	263 (6.8)	1,181 (7.4)	257 (8.7)	1,134 (9.3)	281 (6.8)	1,286 (7.4)
Qatari	1,307 (34.0)	5,594 (35.0)	745 (25.3)	3,060 (25.2)	1,336 (32.2)	5,771 (33.0)
Sri Lankan	55 (1.4)	195 (1.2)	47 (1.6)	193 (1.6)	63 (1.5)	237 (1.4)
Sudanese	56 (1.5)	202 (1.3)	48 (1.6)	157 (1.3)	63 (1.5)	228 (1.3)
Other nationalities[c]	700 (18.2)	2,074 (13.0)	516 (17.5)	1,530 (12.6)	773 (18.6)	2,339 (13.4)
Reason for PCR testing						
Clinical suspicion	1,932 (50.2)	7,933 (49.7)	1,356 (46.0)	5,573 (45.9)	2,092 (50.4)	8,788 (50.3)
Contact tracing	552 (14.4)	2,011 (12.6)	479 (16.3)	1,716 (14.1)	584 (14.1)	2,181 (12.5)
Survey	700 (18.2)	3,091 (19.4)	528 (17.9)	2,323 (19.1)	780 (18.8)	3,455 (19.8)
Individual request	495 (12.9)	2,328 (14.6)	457 (15.5)	2,136 (17.6)	510 (12.3)	2,403 (13.7)
Healthcare routine testing	133 (3.5)	551 (3.5)	102 (3.5)	371 (3.1)	145 (3.5)	589 (3.4)
Other	34 (0.9)	63 (0.4)	25 (0.9)	32 (0.3)	39 (0.9)	74 (0.4)

[a]Cases and controls were matched one-to-five by sex, 5-year age group, nationality, reason for PCR testing and calendar week of PCR test. [b]Nationalities were chosen to represent the most populous groups in Qatar. [c]These comprise 41 other nationalities in Qatar in sample A, 35 other nationalities in sample B and 41 other nationalities in sample C.

among vaccinated individuals with one or two BNT162b2 doses, respectively and 3 and 1 severe disease cases among vaccinated individuals with one or two mRNA-1273 doses, respectively.

Furthermore, there were one and two critical Delta COVID-19 cases (intensive care unit (ICU) hospitalization[11]; Methods) among vaccinated individuals with one or two BNT162b2 doses, respectively. The critical disease case reported after only one BNT162b2 vaccine dose also led to COVID-19 death (COVID-19 deaths[12]; Methods). There were no critical or fatal COVID-19 cases among those vaccinated with mRNA-1273.

Effectiveness ≥14 d after the first vaccine dose. Effectiveness against Delta infection ≥14 d after only one dose was estimated at 45.3% (95% confidence interval (CI), 22.0–61.6%) for BNT162b2, 73.7% (95% CI, 58.1–83.5%) for mRNA-1273 and 58.0% (95% CI, 44.4–68.2%) for either of these vaccines (Table 3).

Effectiveness against any Delta-induced severe[11], critical[11] or fatal[12] COVID-19 disease (Methods), 14 or more days after only one dose, ranged between 80–87% for BNT162b2, mRNA-1273 and either of these vaccines, but 95% confidence intervals were wide given the relatively small number of Delta disease cases (Table 3).

Effectiveness ≥14 d after the second vaccine dose. Effectiveness against Delta infection 14 or more days after the second dose was 51.9% (95% CI, 47.0–56.4%) for BNT162b2, 73.1% (95% CI,

Table 3 | Effectiveness of the BNT162b2 and mRNA-1273 vaccines against the Delta variant ≥14 d after the first dose and ≥14 d after the second dose

Sub-studies[a]	≥14 d after first dose and no second dose					≥14 d after second dose				
	Cases[b] (PCR-positive)		Controls[b] (PCR-negative)		Effectiveness in % (95% CI)[c]	Cases[b] (PCR-positive)		Controls[b] (PCR-negative)		Effectiveness in % (95% CI)[c]
	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated		Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	
Effectiveness against infection										
BNT162b2	39	2,744	254	10,947	45.3 (22.0; 61.6)	998	2,848	5,592	10,385	51.9 (47.0; 56.4)
mRNA-1273	21	2,760	259	11,028	73.7 (58.1; 83.5)	150	2,797	1,568	10,583	73.1 (67.5; 77.8)
BNT162b2 or mRNA-1273	61	2,873	508	11,466	58.0 (44.4; 68.2)	1,174	2,976	6,862	10,628	55.5 (51.2; 59.4)
Effectiveness against severity, criticality and fatality[d]										
BNT162b2	1	96	16	317	79.7 (−59.5; 97.4)	13	104	231	222	93.4 (85.4; 97.0)
mRNA-1273	1	100	23	334	86.7 (−1.4; 98.3)	1	103	71	305	96.1 (71.6; 99.5)
BNT162b2 or mRNA-1273	2	104	34	343	80.8 (18.3; 95.5)	14	113	256	252	93.6 (85.9; 97.1)

[a]In each time-since-vaccination stratum, for first and second doses, we analyzed only those vaccinated in this specific time-since-vaccination stratum and those unvaccinated (our reference group). Accordingly, the sample size for cases (and controls) varied in the different time-since-vaccination analyses. [b]Cases and controls were matched one-to-five by sex, 5-year age group, nationality, reason for PCR testing and calendar week of PCR test. [c]Vaccine effectiveness was estimated using the test-negative, case-control study design[43,44]. [d]Effectiveness against severe, critical or fatal COVID-19. Severity[11], criticality[11] and fatality[12] were defined as per World Health Organization (WHO) guidelines.

Table 4 | Sensitivity analyses for effectiveness of the BNT162b2 and mRNA-1273 vaccines against the Delta variant ≥14 d after the first dose and ≥14 d after the second dose, adjusting for previous infection and health worker status in conditional logistic regression analysis

Sub-studies[a]	≥14 d after first dose and no second dose					≥14 d after second dose				
	Cases[b] (PCR-positive)		Controls[b] (PCR-negative)		Effectiveness in % (95% CI)[c]	Cases[b] (PCR-positive)		Controls[b] (PCR-negative)		Effectiveness in % (95% CI)[c]
	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated		Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	
Effectiveness against infection										
BNT162b2	39	2,744	254	10,947	42.8 (18.2; 60.1)	998	2,848	5,592	10,385	50.6 (45.4; 55.3)
mRNA-1273	21	2,760	259	11,028	73.2 (57.3; 83.2)	150	2,797	1,568	10,583	72.0 (66.1; 76.9)
BNT162b2 or mRNA-1273	61	2,873	508	11,466	56.9 (42.8; 67.5)	1,174	2,976	6,862	10,628	54.1 (49.7; 58.2)
Effectiveness against severity, criticality and fatality[d]										
BNT162b2	1	96	16	317	84.5 (−25.2; 98.1)	13	104	231	222	94.1 (85.9; 97.6)
mRNA-1273	1	100	23	334	87.5 (4.8; 98.4)	1	103	71	305	96.1 (71.4; 99.5)
BNT162b2 or mRNA-1273	2	104	34	343	82.0 (23.4; 95.8)	14	113	256	252	93.4 (85.0; 97.1)

[a]In each time-since-vaccination stratum, for first and second doses, we analyzed only those vaccinated in this specific time-since-vaccination stratum and those unvaccinated (our reference group). Accordingly, the sample size for cases (and controls) varied in the different time-since-vaccination analyses. [b]Cases and controls were matched one-to-five by sex, 5-year age group, nationality, reason for PCR testing and calendar week of PCR test. [c]Vaccine effectiveness was estimated using the test-negative, case-control study design[43,44]. [d]Effectiveness against severe, critical or fatal COVID-19. Severity[11], criticality[11] and fatality[12] were defined as per WHO guidelines.

Table 5 | Effectiveness of the BNT162b2 and mRNA-1273 vaccines against symptomatic and asymptomatic infection with the Delta variant ≥14 d after the first dose and ≥14 d after the second dose

Sub-studies[a]	≥14 d after first dose and no second dose					≥14 d after second dose				
	Cases[b] (PCR-positive)		Controls[b] (PCR-negative)		Effectiveness in % (95% CI)[c]	Cases[b] (PCR-positive)		Controls[b] (PCR-negative)		Effectiveness in % (95% CI)[c]
	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated		Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	
Effectiveness against symptomatic infection[d]										
BNT162b2	23	1,254	181	4,880	56.2 (30.6; 72.4)	633	1,299	3,237	4,696	44.4 (37.0; 50.9)
mRNA-1273	10	1,268	161	4,989	82.5 (65.2; 91.2)	75	1,281	821	4,752	73.9 (65.9; 79.9)
BNT162b2 or mRNA-1273	33	1,337	342	5,246	67.3 (52.4; 77.6)	717	1,375	3,891	4,897	49.2 (42.8; 54.9)
Effectiveness against asymptomatic infection[e]										
BNT162b2	4	464	27	1,957	46.7 (−56.2; 81.8)	216	484	1,210	1,881	46.0 (32.3; 56.9)
mRNA-1273	4	470	38	1,981	61.8 (−9.6; 86.7)	53	475	368	1,955	53.6 (33.4; 67.6)
BNT162b2 or mRNA-1273	8	483	53	2,022	47.0 (−13.8; 75.3)	279	501	1,533	1,922	45.9 (33.3; 56.1)

[a]In each time-since-vaccination stratum, for first and second doses, we analyzed only those vaccinated in this specific time-since-vaccination stratum and those unvaccinated (our reference group). Accordingly, the sample size for cases (and controls) varied in the different time-since-vaccination analyses. [b]Cases and controls were matched one-to-five by sex, 5-year age group, nationality, reason for PCR testing and calendar week of PCR test. [c]Vaccine effectiveness was estimated using the test-negative, case-control study design[43,44]. [d]A symptomatic infection is defined as a PCR-positive test conducted because of clinical suspicion due to presence of symptoms compatible with a respiratory tract infection. [e]An asymptomatic infection is defined as a PCR-positive test conducted with no reported presence of symptoms compatible with a respiratory tract infection (PCR testing was conducted as part of a survey or a random testing campaign).

Table 6 | Effectiveness of the BNT162b2 and mRNA-1273 vaccines against the Beta variant ≥14 d after the first dose and ≥14 d after the second dose

Sub-studies[a]	≥14 d after first dose and no second dose					≥14 d after second dose				
	Cases[b] (PCR-positive)		Controls[b] (PCR-negative)		Effectiveness in % (95% CI)[c]	Cases[b] (PCR-positive)		Controls[b] (PCR-negative)		Effectiveness in % (95% CI)[c]
	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated		Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	
Effectiveness against infection										
BNT162b2	97	3,386	520	15,288	18.9 (−1.8; 35.4)	290	3,438	3,170	13,983	74.3 (70.3; 77.7)
mRNA-1273	64	3,278	707	14,336	66.3 (55.8; 74.2)	19	3,268	345	14,421	80.8 (69.0; 88.2)
BNT162b2 or mRNA-1273	166	4,235	1,243	18,956	44.9 (34.7; 53.5)	313	4,279	3,725	17,537	76.4 (72.9; 79.4)
Effectiveness against severity, criticality and fatality[d]										
BNT162b2	2	147	33	609	74.8 (−7.6; 94.1)	7	152	178	520	92.7 (81.5; 97.1)
mRNA-1273	3	143	42	581	72.5 (7.7; 91.8)	0	143	17	589	100.0 (Omitted)[e]
BNT162b2 or mRNA-1273	7	192	83	781	67.7 (28.6; 85.4)	7	196	201	697	93.4 (83.5; 97.4)

[a]In each time-since-vaccination stratum, for first and second doses, we analyzed only those vaccinated in this specific time-since-vaccination stratum and those unvaccinated (our reference group). Accordingly, the sample size for cases (and controls) varied in the different time-since-vaccination analyses. [b]Cases and controls were matched one-to-five by sex, 5-year age group, nationality, reason for PCR testing and calendar week of PCR test. [c]Vaccine effectiveness was estimated using the test-negative, case-control study design[43,44]. [d]Effectiveness against severe, critical or fatal COVID-19. Severity[11], criticality[11] and fatality[12] were defined as per WHO guidelines. [e]CI could not be estimated because of zero events among vaccinated.

67.5–77.8%) for mRNA-1273 and 55.5% (95% CI, 51.2–59.4%) for either of these vaccines (Table 3).

Effectiveness against any Delta-induced severe[11], critical[11] or fatal[12] COVID-19 disease 14 or more days after the second dose was 93.4% (95% CI, 85.4–97.0%) for BNT162b2, 96.1% (95% CI, 71.6–99.5%) for mRNA-1273 and 93.6% (95% CI, 85.9–97.1%) for either of these vaccines (Table 3).

Additional analyses. Sensitivity analyses adjusting for previous infection and health worker status in conditional logistic regression analysis confirmed the main findings (Table 4).

Vaccine effectiveness against Delta infection for those ≥50 years of age was lower than that for those <50 for both vaccines (Supplementary Table 1). However, this result should be seen in the context that those ≥50 years of age received their second dose earlier than those <50. The median date of second vaccine dose for those ≥50 years of age was 9 April 2021, but was 19 May 2021 for those <50 years.

Effectiveness against symptomatic Delta infection 14 or more days after the second dose was estimated at 44.4% (95% CI, 37.0–50.9%) for BNT162b2, 73.9% (95% CI, 65.9–79.9%) for mRNA-1273 and 49.2% (95% CI, 42.8–54.9%) for either of these vaccines (Table 5). Symptomatic infection was defined as a PCR-positive swab collected based on clinical suspicion (symptoms indicative of a respiratory tract infection).

Effectiveness against asymptomatic Delta infection 14 or more days after the second dose was estimated at 46.0% (95% CI, 32.3–56.9%) for BNT162b2, 53.6% (95% CI, 33.4–67.6%) for mRNA-1273 and 45.9% (95% CI, 33.3–56.1%) for either of these vaccines (Table 5). Asymptomatic infection was defined as a PCR-positive swab collected in the absence of reported respiratory tract symptoms, such as during a survey or a random testing campaign (data sources in Methods).

For comparison, vaccine effectiveness against Beta infection was also estimated over the same period 23 March 2021 to 7 September 2021. Beta cases were also ascertained using RT–qPCR genotyping of randomly collected clinical samples (Methods)[1,3]. Effectiveness against Beta infection was estimated for BNT162b2 at 18.9% (95% CI, −1.8–35.4%) 14 or more days after only one dose and at 74.3% (95% CI, 70.3–77.7%) 14 or more days after the second dose (Table 6). The corresponding effectiveness measures for mRNA-1273 were 66.3% (95% CI, 55.8–74.2%) and 80.8% (95% CI, 69.0–88.2%), respectively. Estimated effectiveness against any Beta-induced severe[11], critical[11] or fatal[12] COVID-19 disease was >90% for both vaccines (Table 6).

In comparing estimates for Beta to those for Delta, it must be noted that the median PCR diagnosis date was 15 April 2021 for Beta cases, but was 2 August 2021 for Delta cases. Beta dominated transmission earlier in the study, whereas Delta dominated transmission later in the study[1–5]. From 1 August 2021 to 7 September 2021, 83.6% of the RT–qPCR-genotyped cases were Delta cases (Methods).

Discussion

BNT162b2 and mRNA-1273 vaccines both showed robust effectiveness (≥90%) against Delta-related hospitalization and fatality, in line with studies from the United Kingdom[13,14], United States[15–18] and Israel[19]. Despite many breakthrough infections, particularly for BNT162b2, there were limited instances of severe or critical disease among vaccinated individuals. In BNT162b2 fully vaccinated individuals, only 15 severe disease cases, 2 critical disease cases and 1 COVID-19 death were due to Delta. For mRNA-1273, only 1 severe disease case and no critical or fatal disease cases were reported.

Notably, estimated BNT162b2 or mRNA-1273 effectiveness against Delta infection 14 or more days after the first dose or 14 or more days after the second dose, were comparable. Recent evidence pointed to considerable waning of vaccine effectiveness over time, particularly for BNT162b2 (refs. [14,20–23]). The high effectiveness against Alpha and Beta in Qatar in our previous studies (≥75%)[4,5,24,25] as well as against Beta in this study (Table 6) were estimated when most residents in Qatar were recently vaccinated with BNT162b2 or mRNA-1273. Conversely, effectiveness against Delta was estimated here after several months have passed since the second vaccine dose for a large proportion of residents. This unexpectedly low effectiveness against Delta in fully vaccinated individuals could be therefore reflecting gradual waning of vaccine protection.

This observation is consistent with the pattern seen in reported effectiveness estimates against Delta elsewhere. Our estimate of 51.9% in BNT162b2 fully vaccinated individuals is lower than that reported in the United Kingdom[14,26,27] and Canada[28], where effectiveness was estimated at >75%, but similar to that reported in Israel[19] and the United States[18,29–31], where effectiveness was estimated between 39% and 66%. The delay in administering the second dose in the United Kingdom and Canada led to most persons being fully vaccinated ~3 months more recently than in Israel, the United States and Qatar, where vaccinated persons received their second dose 3 weeks after the first dose. The lower effectiveness in Israel, the United States and Qatar may therefore signal waning of vaccine protection in those who were fully vaccinated by the end of 2020 or early in 2021, as also suggested in a recent analysis of waning of BNT162b2 protection over time in Qatar[23]. Notably, mass vaccination in Qatar started shortly after that in Israel and the United States.

Another potential explanation pertains to the gradual easing of public health restrictions in Qatar in the last few months, at a time when Delta incidence has been slowly increasing. With more restrictions eased based on vaccination status, which is implemented through a mandatory mobile app (the Ehteraz app), vaccinated individuals may have had higher social contact rates than unvaccinated persons and may have adhered less strictly to safety measures, such as masks, due to their perception of lower risk[32–34]. Such risk compensation may even increase over time after completing the second dose, resulting in further normalization of behavior[33–35]. Vaccinated persons may therefore have higher risk of exposure to the virus than unvaccinated individuals, leading to increased infection incidence among those vaccinated, thereby reducing the observed real-world vaccine effectiveness.

Higher effectiveness against infection with Delta after the second dose was estimated for mRNA-1273 compared to BNT162b2 ($P=0.009$), in line with studies indicating a stronger induced immune response and protection for mRNA-1273 (refs. [5,36–38]).

This study found higher vaccine effectiveness for more serious COVID-19 disease (greater protection against symptomatic or severe infections), as observed earlier for BNT162b2 and mRNA-1273 effectiveness against the Alpha and Beta variants[4,5,24,28].

This study has limitations. With the relatively small number of severe and critical disease cases and fatal cases in Qatar's young population[9,39], some of the effectiveness estimates against hospitalization and death had wide 95% confidence intervals. Data on comorbid conditions were not available to be included in the analysis. With the young population of Qatar[9,10], the part of the population with serious comorbid conditions is small. In the national list of vaccine prioritization, there were only 19,800 individuals of all age groups with serious comorbid conditions. Accordingly, our findings may not apply to settings where the elderly population constitutes a considerable part of the population.

Data on occupation were not available to study investigators. The matching by nationality may have controlled in part for the occupational risk, considering the labor force structure in Qatar[40–42]. Infection incidence and vaccination were broadly distributed across the country's neighborhoods or areas and population social substrata. Therefore, it is not likely that the results could be explained by clustering of vaccination or infection in specific geographies or social strata.

Vaccine effectiveness was investigated using a test-negative case–control study design[43,44], rather than a randomized clinical trial design or a cohort study design that followed vaccinated and unvaccinated cohorts. However, the cohort study design applied to the same population of Qatar previously resulted in similar findings to the test-negative case–control study design[4,5,45] (Extended Data Fig. 4), supporting the reliability of the test-negative case–control study design that has been of wide application for vaccine effectiveness studies of respiratory tract infections[43,44].

In conclusion, both the BNT162b2 and mRNA-1273 vaccines are highly effective in preventing hospitalization and death due to infection with the Delta variant. However, effectiveness against infection was considerably lower than that against serious COVID-19 disease, particularly for the BNT162b2 vaccine. The reasons for the inferior protection against infection remain to be determined and may not necessarily relate to immune evasion by the Delta variant. The lower effectiveness may reflect some waning of vaccine protection over time[23] or higher risk of exposure to the virus among vaccinated individuals compared to unvaccinated individuals, due to higher social contact rate and less adherence to safety measures. These findings indicate the need for more follow-up of vaccinated cohorts to investigate waning of vaccine immunity and for studies that investigate the effect of risk compensation on biasing vaccine effectiveness estimates.

Online content

Any methods, additional references, Nature Research reporting summaries, source data, extended data, supplementary information, acknowledgements, peer review information; details of author contributions and competing interests; and statements of data and code availability are available at https://doi.org/10.1038/s41591-021-01583-4.

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Methods

Hamad Medical Corporation and Weill Cornell Medicine-Qatar Institutional Review Boards approved the study with waiver of informed consent. A STROBE checklist is included in Supplementary Table 2.

Data sources, study population and study design. This study was conducted in the resident population of Qatar. COVID-19 laboratory testing, vaccination, clinical infection data and related demographic details were extracted from the integrated, nationwide, digital-health information platform at Hamad Medical Corporation, the main public healthcare provider and the nationally designated provider for all COVID-19 healthcare needs. This platform hosts the national, federated SARS-CoV-2 databases. Data access was provided by the Ministry of Public Health for analyses to inform the national COVID-19 response. These databases include complete information for PCR testing, vaccinations, hospitalizations and demographic characteristics from epidemic onset.

Almost all vaccinations were provided at no cost in Qatar rather than abroad, through the universal public healthcare system for all nationals and residents of Qatar. In occasional episodes of vaccination abroad, details were still incorporated into the health system upon arrival to Qatar (at airport), for compliance with national regulations and to take advantage of travel-related privileges, such as quarantine exemption[25].

All PCR tests in Qatar, irrespective of test-center location, are classified with respect to 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). Only 9% of residents of Qatar are aged ≥50 years and 89% are incomers from over 150 countries[9,10]. Most of these expatriates are male craft and manual workers[9,40,41].

We estimated vaccine effectiveness using a test-negative, case–control study design, a widely used design for appraising influenza vaccine effectiveness[43,44]. This design controls for potential bias due to infection misclassification or to healthcare-seeking differentials between vaccinated and unvaccinated individuals[43,44]. To maximize statistical power, all cases (PCR-positive individuals with confirmed SARS-CoV-2 Delta infection) and controls (PCR-negative individuals) in Qatar, between 23 March 2021 and 7 September 2021, were included in the study.

To adjust for underlying differences in the risk of exposure to infection[9,40–42], we exact-matched cases and controls in a one-to-five ratio by sex, 5-year age group, nationality, reason for PCR testing and calendar week of PCR test. By virtue of having many more PCR-negative tests than PCR-positive tests, it was generally possible to find exact PCR-negative matches for most age groups for the PCR-positive Delta cases included in this study.

For each case, we considered the first PCR-positive test with confirmed Delta infection during the study from 23 March 2021 to 7 September 2021. After excluding all other PCR tests on individuals with infection, we considered the first PCR-negative test for each control during this period. This yielded an independent sample of unique cases and controls. This strategy was used to control for potential bias due to repeat testing in PCR-positive individuals seeking to check for infection clearance or bias arising from repeat testers among controls (persons with a higher level of healthcare-seeking behavior and presumably lower risk of infection).

PCR tests conducted for pre-travel or at the port of entry were excluded from analysis. This type of testing could possibly be affected by different test-seeking behavior among those vaccinated versus unvaccinated individuals given travel-related benefits extended only to vaccinated individuals, such as exemption from quarantine[25].

We estimated effectiveness against Delta (B.1.617.2) documented infection (defined as a PCR-positive test with the Delta variant irrespective of the reason for the test or presence of symptoms) and against related severe, critical or fatal disease. Classification of case severity (acute care hospitalizations)[11], criticality (ICU hospitalizations)[11] and fatality[12] was per WHO classification using individual chart reviews (details below).

We reviewed all PCR testing records for vaccinated and unvaccinated individuals. We excluded individuals with mixed vaccinations or with a vaccine record other than BNT162b2 or mRNA-1273. Every Delta case fulfilling the inclusion criteria, regardless of vaccination status and that could be matched to one or more controls was retained for the analysis. Infection and vaccination statuses were both ascertained at the time of PCR test. Each hospitalized individual underwent an infection severity assessment every 3 d from hospital admission up to discharge or death. Hospitalized individuals were classified according to their worst outcome (death[12]), followed by critical disease[11] and severe disease[11] (details below).

COVID-19 severity, criticality and fatality classification. WHO defines severe COVID-19 as a SARS-CoV-2-infected individual with 'oxygen saturation of <90% on room air and/or respiratory rate of >30 breaths min^{-1} in adults and children >5 years old (or ≥60 breaths min^{-1} in children <2 months old or ≥50 breaths min^{-1} in children 2–11 months old or ≥40 breaths min^{-1} 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)'[11]. Detailed criteria are in the WHO technical report[11].

Critical COVID-19 is defined as a SARS-CoV-2-infected individual 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 noninvasive) or vasopressor therapy'[11]. Detailed criteria are in the WHO technical report[11].

COVID-19 death is defined 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 (for example, 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 (such as cancer) and should be counted independently of preexisting conditions that are suspected of triggering a severe course of COVID-19'. Detailed criteria are in the WHO technical report[12].

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) and tested with real-time RT–qPCR using TaqPath COVID-19 Combo kits (Thermo Fisher Scientific) on an ABI 7500 FAST (Thermo Fisher); tested directly on the Cepheid GeneXpert system using the Xpert Xpress SARS-CoV-2 (Cepheid); or loaded directly into a Roche cobas 6800 system and assayed with a cobas SARS-CoV-2 Test (Roche). 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.

Tests were performed at the HMC Central Laboratory or Sidra Medicine Laboratory, following standardized protocols.

Classification of infections by variant type. Viral genome sequencing and multiplex RT–qPCR were used to screen for variants[46] in randomly collected positive clinical samples[1–3], supplemented by deep wastewater sequencing[1,47]. The latter is used to compare the distribution of variants in wastewater to that in clinical samples collected from patients with SARS-CoV-2.

Ascertainment of Delta (B.1.617.2) and Beta (B.1.351) cases in this study was through weekly RT–qPCR genotyping of positive clinical samples[1,3]. From 23 March 2021 to 7 September 2021, RT–qPCR genotyping identified 6,005 (35.5%) Beta (B.1.351)-like cases, 3,658 (21.6%) Alpha (B.1.1.7)-like cases, 7,218 (42.6%) 'other' variant cases and 51 (0.3%) B.1.375-like or B.1.258-like cases in 16,932 randomly collected specimens[1,3]. Since RT–qPCR genotyping started on 23 March 2021, the proportion of all diagnosed infections in Qatar that have been RT–qPCR genotyped is 12.0%, with the proportion of infections genotyped increasing with time, especially in the summer of 2021.

RT–qPCR genotyping accuracy was contrasted against results of Sanger sequencing of the receptor-binding domain 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 Alpha-like, 186 Beta-like and 23 'other' variants), PCR genotyping results for Alpha-like, Beta-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.

Within the 'other' variant category, Sanger sequencing and/or Illumina sequencing of the receptor-binding domain of SARS-CoV-2 spike gene on 728 random samples, between 23 March 2021 and 7 September 2021, confirmed that 701 (96.3%) were Delta cases and 17 (2.3%) were other variant cases, with 10 (1.4%) samples failing lineage assignment.[6,8] Consequently, a Delta infection was proxied as any 'other' case based on the RT–qPCR-based variant screening result.

Statistical analysis. Study samples were described using frequency distributions and measures of central tendency. The odds ratio (and 95% CI, comparing odds of vaccination among cases to that among controls), was estimated using conditional logistic regression factoring the matching in the study design. This analytical approach was implemented to reduce potential bias due to variation in epidemic phase[43,48], gradual vaccination roll-out[43,48] and other confounders[9,40–42,49,50]. CIs did not factor multiplicity. Interactions were not examined. Vaccine effectiveness at different time frames and its associated 95% CI were then estimated using[43,44]:

$$\text{Vaccine effectiveness} = 1 - \text{odds ratio of vaccination among cases versus controls}$$

In each time-since-vaccination stratum, for first and second doses, we analyzed only those vaccinated in this specific time-since-vaccination stratum and those unvaccinated (our reference group). Accordingly, the sample size for cases (and controls) varied in the different time-since-vaccination analyses. As we used a test-negative study design, some individuals were tested PCR-positive or PCR-negative after their first dose and before the second dose. This allowed us to estimate effectiveness after only the first vaccination dose.

A sensitivity analysis was implemented to control for previous infection and health worker status in the conditional logistic regression, because health workers are potentially at higher risk of infection exposure and were prioritized for vaccination.

Additional analyses were performed to estimate vaccine effectiveness stratified by age (<50 versus ≥50 years of age). We also estimated vaccine effectiveness against symptomatic infection, defined as a PCR-positive swab collected based on clinical suspicion (symptoms indicative of a respiratory tract infection) and against asymptomatic infection, defined as a PCR-positive swab collected in the absence of

reported respiratory tract infection symptoms (during a survey or a random testing campaign). For comparison, vaccine effectiveness was further estimated against the Beta variant, the only other variant with an appreciable incidence concurrent with the Delta incidence[1–3].

A two-sided P value derived from logistic regression analyses was used to compare effectiveness of both vaccines with $P < 0.05$ showing statistical significance. Statistical analyses were conducted in STATA/SE version 17.0 (ref. [51]).

Reporting Summary. Further information on research design is available in the Nature Research Reporting Summary linked to this article.

Data availability

The dataset of this study is the property of the Qatar Ministry of Public Health and was provided to the researchers through a restricted-access agreement that prevents sharing the dataset with a third party or publicly for preservation of confidentiality of patient data. Access to this dataset is at the discretion of the Qatar Ministry of Public Health. Access to the dataset may be granted following a direct application for data access to Her Excellency the Minister of Public Health (https://www.moph.gov.qa/english/Pages/default.aspx). Aggregate data are available within the manuscript and its supplementary information.

Code availability

Standard epidemiological analyses were conducted using standard commands in STATA/SE 17.0 (ref. [51]). The commands/code are accessible at https://github.com/IDEGWCMQ/Delta/blob/main/Code.do.

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Author contributions

P.T. and M.R.H. conducted the multiplex RT–qPCR variant screening and viral genome sequencing. H.C. co-designed the study, performed statistical analyses and co-wrote the first draft of the article. L.J.A. conceived and co-designed the study, led statistical analyses and co-wrote the first draft of the article. H.Y., F.M.B. and H.A.K. conducted viral genome sequencing. All authors contributed to data collection and acquisition, database development, discussion and interpretation of results and to writing the manuscript. All authors read and approved the final manuscript.

Competing interests

The authors declare no competing interests.

Additional information

Extended data is available for this paper at https://doi.org/10.1038/s41591-021-01583-4.

Supplementary information The online version contains supplementary material available at https://doi.org/10.1038/s41591-021-01583-4.

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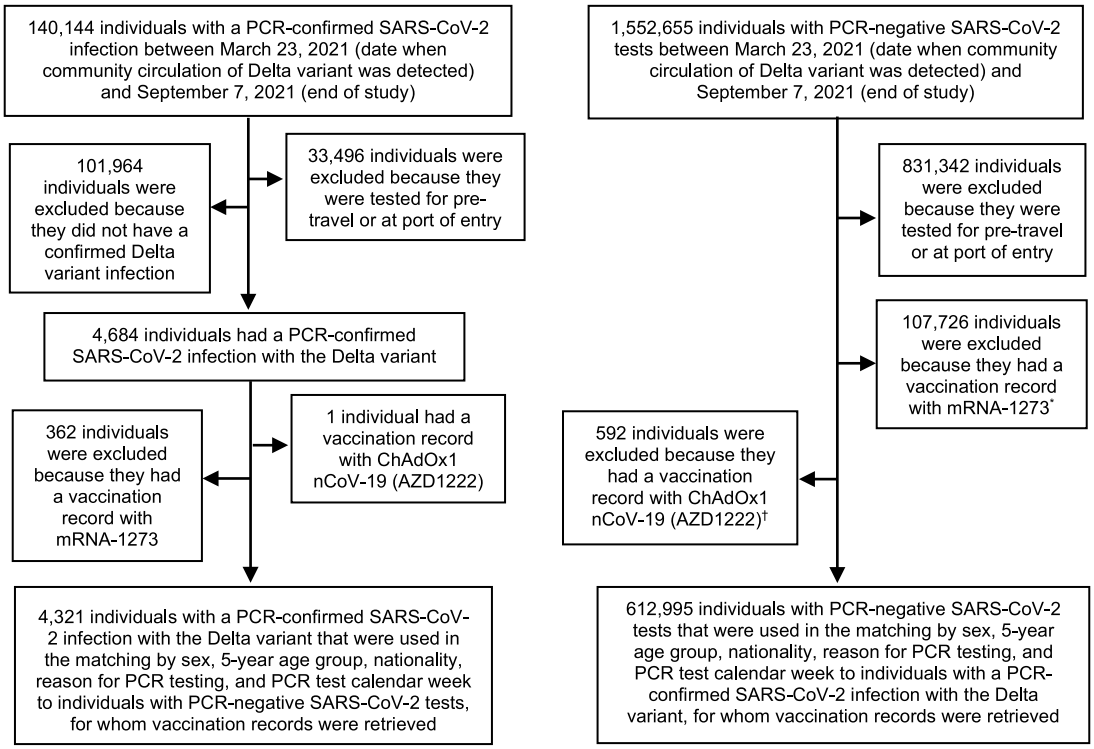
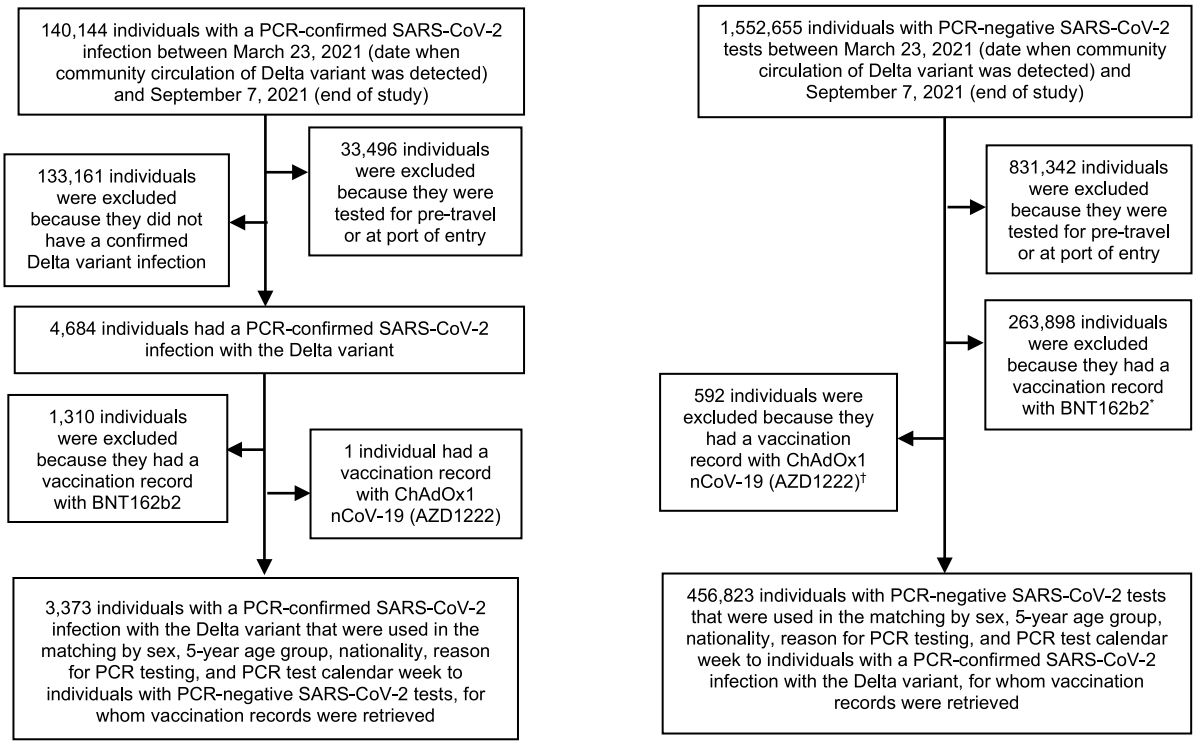
Peer review information *Nature Medicine* thanks Ben Lopman and the other, anonymous, reviewer(s) for their contribution to the peer review of this work. Alison Farrell was the primary editor on this article and managed its editorial process and peer review in collaboration with the rest of the editorial team.



*Sample includes 41 persons who had another vaccination with mRNA-1273
†Sample includes 1 person who had another vaccination with BNT162b2 and 1 person who had another vaccination with mRNA-1273

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). Thus, the number of cases (and controls) varied across time-since-vaccination analyses.

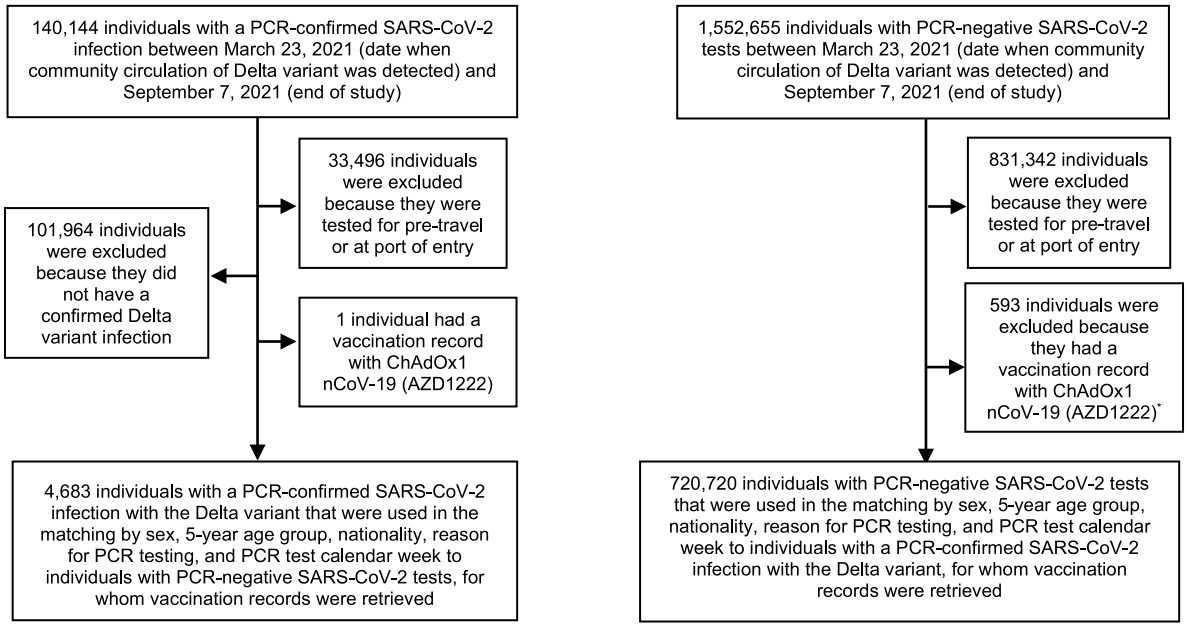
Extended Data Fig. 1 | Population selection process for investigating BNT162b2 vaccine effectiveness. Flowchart describing the population selection process for investigating BNT162b2 vaccine effectiveness against infection with the SARS-CoV-2 Delta variant.



*Sample includes 41 persons who had another vaccination with BNT162b2
†Sample includes 1 person who had another vaccination with BNT162b2 and 1 person who had another vaccination with mRNA-1273

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). Thus, the number of cases (and controls) varied across time-since-vaccination analyses.

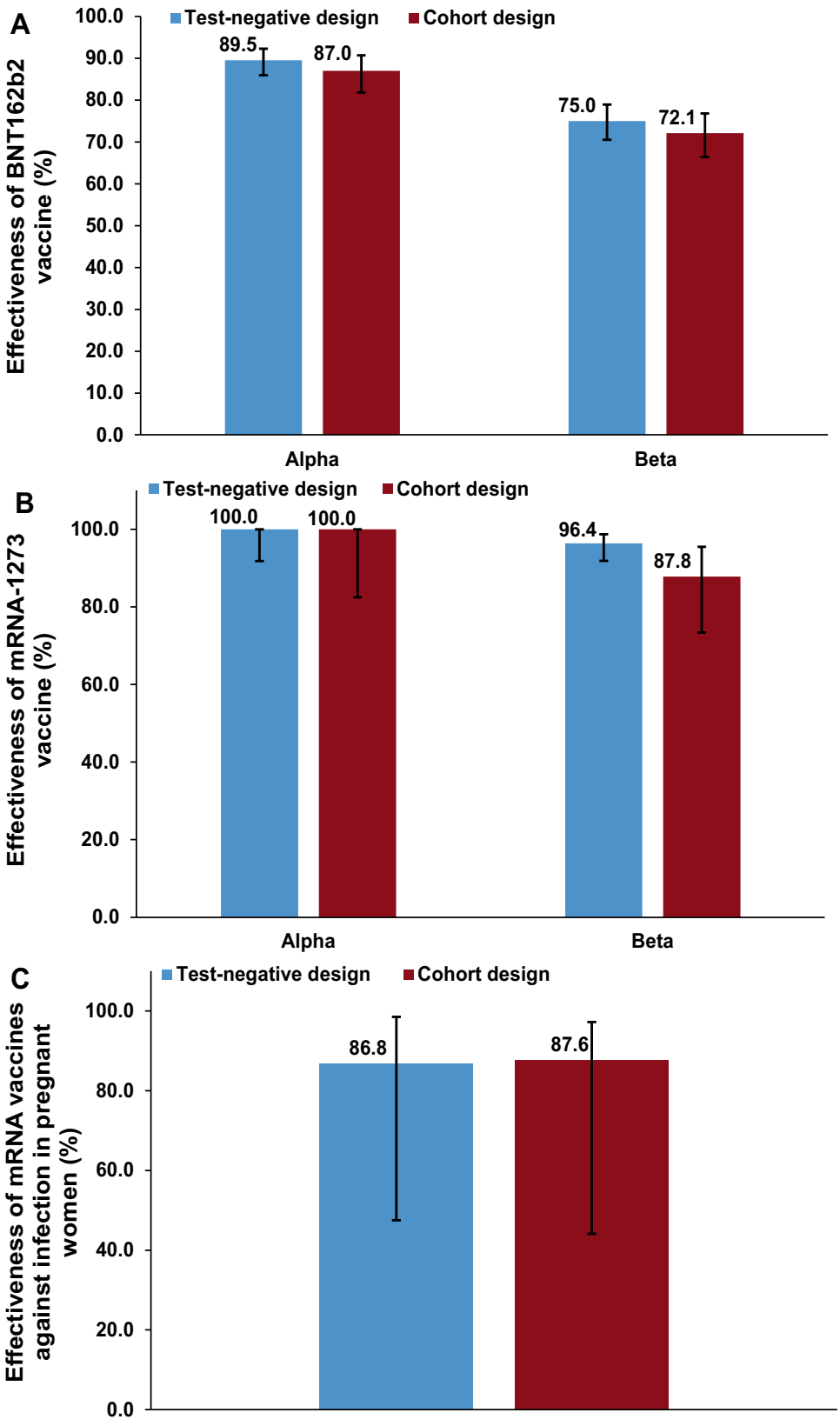
Extended Data Fig. 2 | Population selection process for investigating mRNA-1273 vaccine effectiveness. Flowchart describing the population selection process for investigating mRNA-1273 vaccine effectiveness against infection with the SARS-CoV-2 Delta variant.



*Sample includes 1 person who had another vaccination with BNT162b2 and 1 person who had another vaccination with mRNA-1273

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). Thus, the number of cases (and controls) varied across time-since-vaccination analyses.

Extended Data Fig. 3 | Population selection process for investigating the BNT162b2 and mRNA-1273 vaccines effectiveness. Flowchart describing the population selection process for investigating the BNT162b2 and mRNA-1273 vaccines effectiveness against infection with the SARS-CoV-2 Delta variant.



Extended Data Fig. 4 | See next page for caption.

Extended Data Fig. 4 | Comparison of vaccine effectiveness estimates using the test-negative case-control study design versus the cohort study design in previous assessments of vaccine effectiveness in Qatar. Effectiveness of A) BNT162b2 vaccine against each of the SARS-CoV-2 Alpha (independent samples of n = 20,195 PCR-positive cases and n = 20,195 PCR-negative controls) and Beta (independent samples of n = 23,718 PCR-positive cases and n = 23,718 PCR-negative controls) variants, B) mRNA-1273 vaccine against each of the SARS-CoV-2 Alpha (independent samples of n = 25,034 PCR-positive cases and n = 25,034 PCR-negative controls) and Beta (independent samples of n = 52,442 PCR-positive cases and n = 52,442 PCR-negative controls) variants and C) BNT162b2 or mRNA-1273 vaccines against any SARS-CoV-2 infection in pregnant women (independent samples of n = 386 PCR-positive cases and n = 834 PCR-negative controls). Data are presented as effectiveness point estimates with error bars indicating the corresponding 95% confidence intervals.

nature research

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Our web collection on statistics for biologists contains articles on many of the points above.

Software and code

Policy information about availability of computer code

Data collection	Data were available to authors through .csv files downloaded from the CERNER database system.
Data analysis	Analyses were conducted in STATA/SE 17.0. The commands/code are accessible using URL: https://github.com/IDEGWCMQ/Delta/blob/main/Code.do

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The dataset of this study is a property of the Qatar Ministry of Public Health that was provided to the researchers through a restricted-access agreement that prevents sharing the dataset with a third party or publicly for preservation of confidentiality of patient data. Access to this dataset is at the discretion of the Qatar Ministry of Public Health. Access to the dataset can be considered through a direct application for data access to Her Excellency the Minister of Public Health (https://www.moph.gov.qa/english/Pages/default.aspx). Aggregate data are available within the manuscript and its supplementary information.

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Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	Coronavirus Disease 2019 (COVID-19) laboratory testing, vaccination, clinical infection data, and related demographic details were extracted from the integrated nationwide digital-health information platform that hosts the national, federated SARS-CoV-2 databases. These databases are complete and have captured all SARS-CoV-2-related data since epidemic onset. The data is based on a national cohort that includes every single individual tested using PCR in Qatar. Sample size varied depending on the definition used for cases [PCR-positive swab regardless of the reason for PCR testing or presence of symptoms with the Delta (B.1.617.2) variant, as well as severe, critical, or fatal COVID-19 disease due to Delta infection] and controls (PCR-negative swab). Cases and controls were matched one-to-five by sex, 5-year age group, nationality, reason for SARS-CoV-2 polymerase chain reaction (PCR) testing, and calendar week of PCR test. 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). Thus, the number of cases (and controls) varied across time-since-vaccination analyses. Given that the sample sizes were based on national cohorts with only individuals that do not fit the eligibility criteria excluded, the sample size for each sub-study can be considered sufficient. Detailed sample sizes can be found in Extended Data 1-3.
Data exclusions	Exclusion criteria were specified for cases and controls in each study group a priori. For each vaccine effectiveness study, PCR-positive individuals (cases) were excluded if they did not have a PCR confirmed infection with the Delta variant. Only the first PCR-positive test with confirmed Delta infection during the study, January 1, 2021 to September 7, 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. Additionally, cases and controls were excluded if they received a different vaccine from that under study.
Replication	For replication, additional analyses were conducted to estimate vaccine effectiveness after 1) adjusting for prior infection and health worker status in conditional logistic regression analyses, 2) restricting the analysis to either symptomatic infection (defined as a PCR-positive test conducted because of clinical suspicion due to presence of symptoms compatible with a respiratory tract infection) or asymptomatic infection (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), and 3) stratifying the analysis by age (<50 versus >=50 years). All analyses confirmed/reproduced estimates of vaccine effectiveness obtained in the main analysis.
Randomization	Not applicable as this is an observational case-control study where individuals are aware of both their infection status and their vaccination status. However, to ensure control confounding, cases and controls were matched one-to-five by sex, 5-year age group, nationality, reason for SARS-CoV-2 polymerase chain reaction (PCR) testing, and calendar week of PCR test. To ensure that vaccine effectiveness estimates were not biased, conditional logistic regression analyses were applied and a sensitivity analysis was conducted by additionally adjusting for prior infection and health worker status in conditional logistic regression analyses.
Blinding	Not applicable as this is an observational study case-control study where individuals are aware of both their infection status and their vaccination status.

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☒	☐ Clinical data
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Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☒	☐ Flow cytometry
☒	☐ MRI-based neuroimaging

Human research participants

Policy information about studies involving human research participants

Population characteristics	The demographic characteristics of the different study populations can be found in Tables 1 and 2.
Recruitment	This is a retrospective study where COVID-19 laboratory testing, vaccination, clinical infection data, and related demographic details were extracted from the integrated nationwide digital-health information platform that hosts the national, federated SARS-CoV-2 databases. These databases are complete with no missing information for PCR testing, COVID-19 vaccinations, COVID-19 hospitalizations, and basic demographic details, and have captured all SARS-CoV-2-related data since epidemic onset. Cases and controls were defined based on analysis for these data. Cases were defined as a PCR-positive swab or presence of symptoms with the B.1.617.2 variant, as well as against severe, critical, or fatal COVID-19 disease due to Delta infection. While controls were defined as a PCR-negative swab. Classification of COVID-19 case severity (acute-care hospitalizations), criticality (ICU hospitalizations), and fatality, followed the World Health Organization guidelines, and assessments were made by trained medical personnel using individual chart reviews. All records of PCR testing for those vaccinated and unvaccinated during the study duration were examined.
Ethics oversight	The study was approved by the Hamad Medical Corporation and Weill Cornell Medicine-Qatar Institutional Review Boards with waiver of informed consent.

Note that full information on the approval of the study protocol must also be provided in the manuscript.