Supplementary Appendix

Supplement to: Accorsi EK, Britton A, Shang N, et al. Effectiveness of homologous and heterologous Covid-19 boosters against omicron. N Engl J Med. DOI: 10.1056/NEJMc2203165

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

Supplementary Appendix

Table of Contents

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Conflict of Interest Disclosures

There are no disclosures to report for Dr. Accorsi, Dr. Britton, Dr. Shang, Dr. Fleming-Dutra, Dr. Link-Gelles, Mr. Smith, Dr. Derado, Dr. Miller, Dr. Schrag, or Dr. Verani.

Supplementary Methods

Methods for vaccine effectiveness analyses using the *Increasing Community Access to Testing* (ICATT) platform have been previously described in depth.[1-3] Relevant methods sections are included again in this supplement for reference.

Study protocol approval

This activity was determined to be public health surveillance as defined in 45 CFR 46.102(l) (US Department of Health and Human Services, Title 45 Code of Federal Regulations 46, Protection of Human Subjects); thus, it was not submitted for institutional review board approval and informed consent was not needed.

Data source

Data from the *Increasing Community Access to Testing* (ICATT) platform were used. ICATT is a Department of Health and Human Services (HHS) program that contracts with four commercial pharmacy chains to facilitate drive-through SARS-CoV-2 testing nationally.[1-4] No-cost testing is available to anyone regardless of symptom or exposure status, and sites were selected to address COVID-19 health disparities by increasing access in racially and ethnically diverse communities and areas with moderate-to-high social vulnerability.[4] During the analysis period, contracted pharmacy chains did not all capture data on booster doses. This analysis was therefore limited to a single pharmacy chain which collected data on booster doses and provided 93.5% of tests platform-wide for adults aged ≥18 years during the analysis period.

Individuals registered online in advance for SARS-CoV-2 testing at a drive-through pharmacy site.[1-3] At the time of registration, individuals could select their desired test type (rapid nucleic acid amplification test [NAAT] performed by the pharmacy versus send-out laboratory-based NAAT). Individuals then answered a questionnaire (available in English or Spanish) to self-report demographic information (including race and ethnicity selected from fixed categories, shown in **Table S1**), COVID-19-like illness symptoms (fever, cough, shortness of breath, recent loss of sense of smell or taste, muscle pain, fatigue, chill, headache, sore throat, congestion or runny nose, vomiting, or diarrhea; reported to HHS as asymptomatic or symptomatic with ≥1 symptom), and vaccination status.[1-3] Race and ethnicity were collected as part of the HHS COVID-19 laboratory reporting requirements.[5] Self-reported COVID-19 vaccination data included number of doses received up to 4, and for each dose, vaccine product and month and year received. For doses reported in the same month or the month before test registration, the individual was asked whether the most recent dose was administered at least two weeks before test date.[2,3] Reporting of vaccination status was neither mandatory nor verified. Test registrants were also asked to self-report underlying health conditions, including immunocompromising conditions (defined in the questionnaire as "immunocompromising medications, solid organ or blood stem cell transplant, HIV, or other immunocompromising conditions"), and whether they had previously tested positive for SARS-CoV-2 (within 90 days and/or >90 days before test registration);[2,3] answers were not verified.

Nasal swabs were self-collected at drive-through sites and tested for SARS-CoV-2 either onsite by the pharmacy with the IDNow (Abbott Diagnostics Scarborough, Inc.) rapid NAAT or sent out for processing at contracted laboratories (using the TaqPath COVID-19 Combo Kit [Thermo Fischer Scientific, Inc.] or COVID-19 RT-PCR Test [Laboratory Corporation of America]).[3,4] De-identified questionnaire data,

specimen collection date, test type, test result, testing site location, and testing site census tract social vulnerability index (SVI)[6] were reported to HHS with an approximately 3-day lag.

Study design

A test-negative, case-control analysis[7] was conducted to estimate VE of four vaccination regimens ([1] Ad26.COV2.S, [2] Ad26.COV2.S/Ad26.COV2.S, [3] Ad26.COV2.S/mRNA, [4] mRNA/mRNA/mRNA; mRNA vaccine doses were either BNT162b2 [Pfizer-BioNTech] or mRNA-1273 [Moderna]) against symptomatic infection. This analysis used rapid and laboratory-based NAATs from adults aged ≥18 years self-reporting ≥1 COVID-19-like illness symptom tested at the pharmacy chain from January 2, 2022, to March 23, 2022. The unit of analysis was tests; unique identifiers for individuals were not available. Cases were defined as those with positive SARS-CoV-2 NAAT, and controls were those with negative SARS-CoV-2 NAAT. Tests from individuals which met any of the following criteria were excluded: indeterminate test results, missing assay type, reported an immunocompromising condition (as COVID-19 vaccine recommendations differ for these individuals)[8], missing data on sex or testing site census tract SVI, unknown vaccination status, receipt of a vaccination regimen other than the regimens of interest, receipt of the last vaccine dose within two weeks of the test date, vaccination before the month of the ACIP recommendation for primary or booster dose, receipt of a booster dose <2 or <5 months after the primary series for Ad26.COV2.S and mRNA primary series, respectively, or inconsistent vaccination information (e.g., reported receipt of vaccine but missing dose dates, reported no vaccine receipt but vaccine doses reported). In addition, we excluded tests from individuals reporting any prior positive test result (i.e., within 90 days and/or >90 days prior to testing). Prior SARS-CoV-2 infection could impact estimation of VE in multiple ways, including through infection-induced immunity providing protection to

the unvaccinated, which could bias VE towards the null, and through hybrid immunity in persons who had both infection-induced and vaccine-induced immunity.[3] Prior positives within the last 90 days might also represent recent prior infection with a non-Omicron variant or an at-home test during the same illness episode.

Exposure

The exposures of interest were four vaccination regimens ([1] Ad26.COV2.S, [2] Ad26.COV2.S/ Ad26.COV2.S, [3] Ad26.COV2.S/mRNA, [4] mRNA/mRNA/mRNA). Cases and controls were considered unvaccinated if tests were from individuals who received no COVID-19 vaccine before the SARS-CoV-2 test. Cases and controls were considered vaccinated if tests were from individuals who reported receiving the last dose of one of the four vaccination regimens ≥2 weeks before the SARS-CoV-2 test.

Outcome

The outcome measure was symptomatic SARS-CoV-2 infection determined by positive NAAT in a person reporting COVID-19-like illness.

Statistical analysis

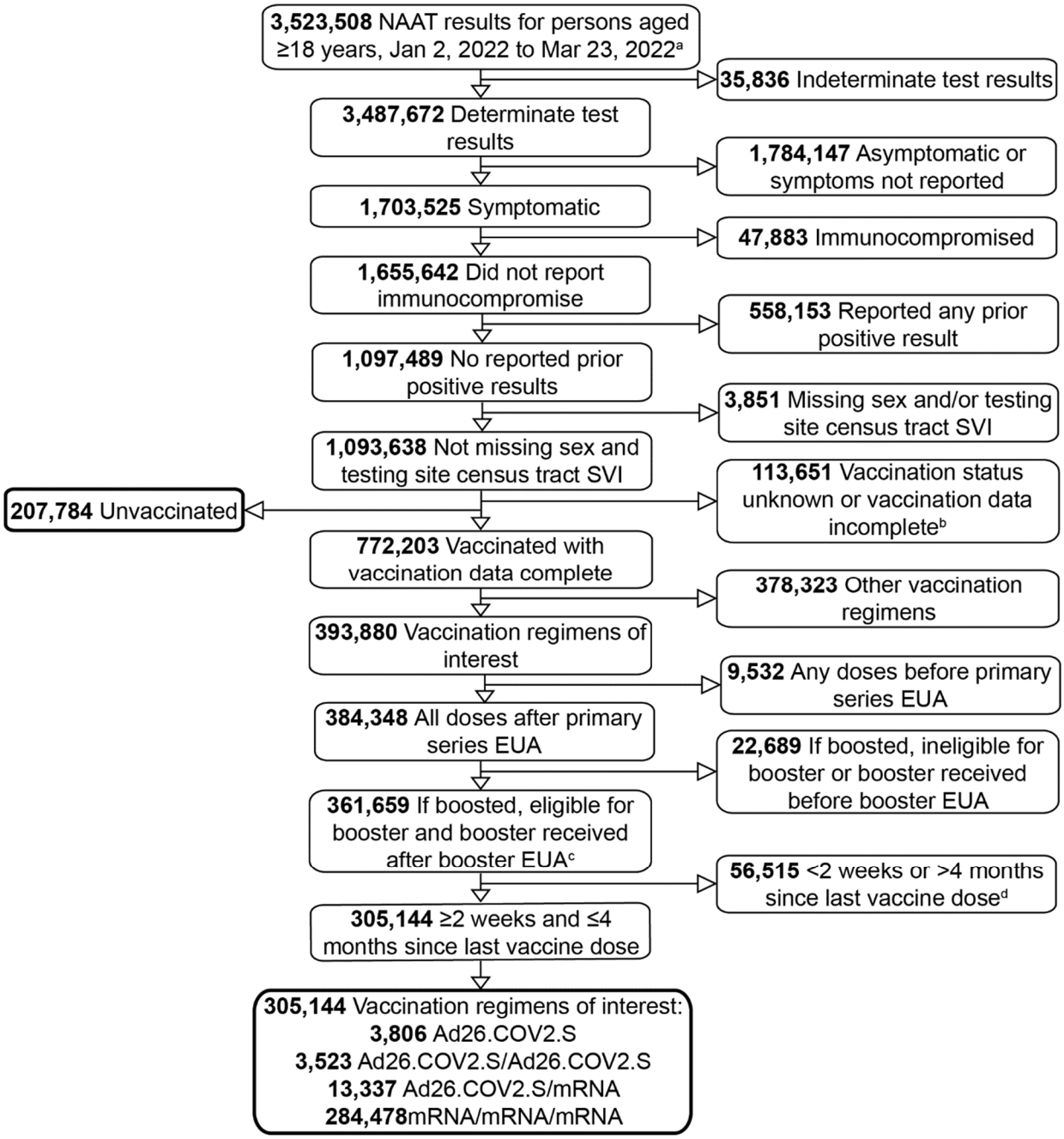
Associations between symptomatic SARS-CoV-2 infection and vaccination were estimated by comparing the odds of prior vaccination with a regimen of interest ([1] Ad26.COV2.S, [2] Ad26.COV2.S/ Ad26.COV2.S, [3] Ad26.COV2.S/mRNA, [4] mRNA/mRNA/mRNA) versus no vaccination in cases versus controls using multivariable logistic regression. The odds ratio (OR) was used to estimate the vaccine effectiveness (VE), where VE = (1 – OR) x 100%. Regression models were adjusted for the number of

days between the start of the analysis period and test date (as a continuous variable with linear and quadratic terms), age group (18-24, 25-34, 35-44, 45-54, 55-64, ≥65 years), sex, race, ethnicity, testing site HHS region, testing site census tract SVI (dichotomized as 0-<0.5 and ≥0.5-1), and number of underlying chronic conditions (0, 1, or ≥2) to control for possible confounding. Unknown race and ethnicity were coded as categorical levels within each variable to retain those tests in regression models.

We explored including test type (rapid vs laboratory-based NAAT) as a covariate in the model to assess the possibility test type (selected by the test registrant) could be a confounder associated both with likelihood of vaccination and likelihood of infection. However, VE estimates did not change when adjusting for test type. We therefore elected not to include test type in the model and report results of the two test types as a single outcome (with a positive or negative result).

VE was estimated at 14 days to 1 month and 2 to 4 months since receipt of the last vaccine dose. Since only vaccination month and year but not exact calendar dates of each dose were reported, months since last dose was calculated as the difference between the month and year of testing and the month and year of the last vaccine dose (at least 2 weeks after the dose).[2,3] The range of possible days after last dose for 14 days to 1 month since receipt of the last dose was 14-60 days and for 2 to 4 months since receipt of the last dose was 30-150 days (assuming 30 days per month). No adjustments were made for multiple comparisons.

Figure S1. Criteria for test inclusion in an analysis of the effectiveness of four vaccination regimens ([1] Ad26.COV2.S, [2] Ad26.COV2.S/Ad26.COV2.S, [3] Ad26.COV2.S/mRNA, [4] mRNA/mRNA/mRNA) against symptomatic SARS-CoV-2 Omicron infection among adults aged ≥18 years tested in the *Increasing Community Access to Testing* platform, January 2, 2022–March 23, 2022.



EUA=Emergency Use Authorization; NAAT=nucleic acid amplification test; SVI=Social vulnerability index

Data from the *Increasing Community Access to Testing* (ICATT) platform were used from adults aged ≥ 18 years tested from January 2, 2022 to March 23, 2022. During the analysis period, ICATT contracted four pharmacy chains which used different versions of the registration questionnaire and not all captured data on booster doses. This analysis was limited to a single chain which collected data on booster doses and performed 93.5% of tests platform-wide for adults during the analysis period. Nasal swabs were self-collected at drive-through sites and tested for SARS-CoV-2 either onsite with the IDNow (Abbott Diagnostics Scarborough, Inc.) rapid NAAT or at contracted laboratories using laboratory-based NAAT (TaqPath COVID-19 Combo Kit [Thermo Fischer Scientific, Inc] or COVID-19 RT-PCR Test [Laboratory Corporation of America]).

[a] 164 tests were removed because of reported ages older than 100 years.

[b] Individuals self-reported COVID-19 vaccination status at test registration, including the number of doses (up to four), product, and month and year of receipt for each vaccine dose. For doses received in the same month or the month prior to testing, registrants were asked whether the dose was received at least two weeks before testing. Vaccination data were considered incomplete if the number of doses reported did not match the products and dates reported.

[c] Persons who received a booster were considered to have been eligible for that booster if at least 2 or 5 months had elapsed between the last dose of the primary series and the booster dose for Ad26.COV2.S and mRNA primary series, respectively.

[d] Analysis was limited to tests from persons with ≤4 months since last dose due to limited sample size for heterologous regimens at >4 months since last dose.

Table S1. Characteristics of included tests in an analysis of the effectiveness of four vaccination regimens ([1] Ad26.COV2.S, [2] Ad26.COV2.S/Ad26.COV2.S, [3] Ad26.COV2.S/mRNA, [4] mRNA/mRNA/mRNA) against symptomatic SARS-CoV-2 Omicron infection among adults aged ≥18 years tested in the *Increasing Community Access to Testing* platform, January 2, 2022–March 23, 2022.

	Cases (SARS-CoV-2 Positive) (n = 187838)	**Controls (SARS-CoV-2 Negative) (n = 325090)**	**Ad26.COV2.S (n = 3806)**	**Ad26.COV2.S/Ad26.COV2.S (n = 3523)**	**Ad26.COV2.S/ mRNA (n = 13337)**	**mRNA/ mRNA/ mRNA (n = 284478)**	**Unvaccinated (n = 207784)**	**Overall (n = 512928)**
SARS-CoV-2 test result								
Positive	187838 (100.0%)	NA	1878 (49.3%)	1518 (43.1%)	4097 (30.7%)	76175 (26.8%)	104170 (50.1%)	187838 (36.6%)
Negative	NA	325090 (100.0%)	1928 (50.7%)	2005 (56.9%)	9240 (69.3%)	208303 (73.2%)	103614 (49.9%)	325090 (63.4%)
Vaccination regimens and status[a,b]								
Ad26.COV2.S	1878 (1.0%)	1928 (0.6%)	3806 (100.0%)	NA	NA	NA	NA	3806 (0.7%)
Ad26.COV2.S/Ad26.COV2.S	1518 (0.8%)	2005 (0.6%)	NA	3523 (100.0%)	NA	NA	NA	3523 (0.7%)
Ad26.COV2.S/ mRNA	4097 (2.2%)	9240 (2.8%)	NA	NA	13337 (100.0%)	NA	NA	13337 (2.6%)
mRNA/mRNA/ mRNA	76175 (40.6%)	208303 (64.1%)	NA	NA	NA	284478 (100.0%)	NA	284478 (55.5%)
Unvaccinated	104170 (55.5%)	103614 (31.9%)	NA	NA	NA	NA	207784 (100.0%)	207784 (40.5%)
Age group (years)								
18-24	26181 (13.9%)	40664 (12.5%)	499 (13.1%)	196 (5.6%)	1226 (9.2%)	20179 (7.1%)	44745 (21.5%)	66845 (13.0%)
25-34	48902 (26.0%)	79015 (24.3%)	1198 (31.5%)	448 (12.7%)	3169 (23.8%)	55068 (19.4%)	68034 (32.7%)	127917 (24.9%)
35-44	37357 (19.9%)	62863 (19.3%)	846 (22.2%)	596 (16.9%)	3085 (23.1%)	53271 (18.7%)	42422 (20.4%)	100220 (19.5%)
45-54	27181 (14.5%)	46416 (14.3%)	636 (16.7%)	695 (19.7%)	2408 (18.1%)	43395 (15.3%)	26463 (12.7%)	73597 (14.3%)
55-64	24620 (13.1%)	47173 (14.5%)	472 (12.4%)	964 (27.4%)	2430 (18.2%)	50948 (17.9%)	16979 (8.2%)	71793 (14.0%)
65+	23597 (12.6%)	48959 (15.1%)	155 (4.1%)	624 (17.7%)	1019 (7.6%)	61617 (21.7%)	9141 (4.4%)	72556 (14.1%)

	Cases (SARS-CoV-2 Positive) (n = 187838)	Controls (SARS-CoV-2 Negative) (n = 325090)	Ad26.COV2.S (n = 3806)	Ad26.COV2.S/Ad26.COV2.S (n = 3523)	Ad26.COV2.S/ mRNA (n = 13337)	mRNA/ mRNA/ mRNA (n = 284478)	Unvaccinated (n = 207784)	Overall (n = 512928)
Sex								
Female	101924 (54.3%)	203570 (62.6%)	1747 (45.9%)	1939 (55.0%)	7860 (58.9%)	179559 (63.1%)	114389 (55.1%)	305494 (59.6%)
Male	85914 (45.7%)	121520 (37.4%)	2059 (54.1%)	1584 (45.0%)	5477 (41.1%)	104919 (36.9%)	93395 (44.9%)	207434 (40.4%)
Race[c]								
American Indian or Alaska Native	1958 (1.0%)	2865 (0.9%)	43 (1.1%)	27 (0.8%)	80 (0.6%)	1935 (0.7%)	2738 (1.3%)	4823 (0.9%)
Asian	9563 (5.1%)	21326 (6.6%)	109 (2.9%)	197 (5.6%)	1088 (8.2%)	25464 (9.0%)	4031 (1.9%)	30889 (6.0%)
Black or African American	23444 (12.5%)	37903 (11.7%)	391 (10.3%)	347 (9.8%)	787 (5.9%)	19192 (6.7%)	40630 (19.6%)	61347 (12.0%)
Native Hawaiian or Other Pacific Islander	1067 (0.6%)	1681 (0.5%)	37 (1.0%)	13 (0.4%)	42 (0.3%)	1011 (0.4%)	1645 (0.8%)	2748 (0.5%)
White	134858 (71.8%)	235195 (72.3%)	2844 (74.7%)	2648 (75.2%)	10278 (77.1%)	216440 (76.1%)	137843 (66.3%)	370053 (72.1%)
Not Reported	16948 (9.0%)	26120 (8.0%)	382 (10.0%)	291 (8.3%)	1062 (8.0%)	20436 (7.2%)	20897 (10.1%)	43068 (8.4%)
Ethnicity[c]								
Hispanic/Latino	29361 (15.6%)	43622 (13.4%)	466 (12.2%)	485 (13.8%)	1677 (12.6%)	34342 (12.1%)	36013 (17.3%)	72983 (14.2%)
Not Reported	15244 (8.1%)	24226 (7.5%)	427 (11.2%)	302 (8.6%)	886 (6.6%)	19202 (6.7%)	18653 (9.0%)	39470 (7.7%)
HHS Region[d]								
South Atlantic	45619 (24.3%)	70312 (21.6%)	772 (20.3%)	858 (24.4%)	2562 (19.2%)	61831 (21.7%)	49908 (24.0%)	115931 (22.6%)
East North Central	33925 (18.1%)	68706 (21.1%)	744 (19.5%)	687 (19.5%)	3087 (23.1%)	59942 (21.1%)	38171 (18.4%)	102631 (20.0%)

	Cases (SARS-CoV-2 Positive) (n = 187838)	**Controls (SARS-CoV-2 Negative) (n = 325090)**	**Ad26.COV2.S (n = 3806)**	**Ad26.COV2.S/Ad26.COV2.S (n = 3523)**	**Ad26.COV2.S/ mRNA (n = 13337)**	**mRNA/ mRNA/ mRNA (n = 284478)**	**Unvaccinated (n = 207784)**	**Overall (n = 512928)**
West South Central	28154 (15.0%)	44405 (13.7%)	504 (13.2%)	437 (12.4%)	1502 (11.3%)	35192 (12.4%)	34924 (16.8%)	72559 (14.1%)
Mountain	18173 (9.7%)	31040 (9.5%)	436 (11.5%)	326 (9.3%)	1233 (9.2%)	28752 (10.1%)	18466 (8.9%)	49213 (9.6%)
East South Central	19979 (10.6%)	26582 (8.2%)	356 (9.4%)	244 (6.9%)	793 (5.9%)	19844 (7.0%)	25324 (12.2%)	46561 (9.1%)
West North Central	14559 (7.8%)	27648 (8.5%)	300 (7.9%)	251 (7.1%)	1534 (11.5%)	23735 (8.3%)	16387 (7.9%)	42207 (8.2%)
Pacific	12143 (6.5%)	22304 (6.9%)	284 (7.5%)	280 (7.9%)	948 (7.1%)	21545 (7.6%)	11390 (5.5%)	34447 (6.7%)
Mid-Atlantic	9602 (5.1%)	20741 (6.4%)	265 (7.0%)	322 (9.1%)	805 (6.0%)	20189 (7.1%)	8762 (4.2%)	30343 (5.9%)
New England	5072 (2.7%)	11401 (3.5%)	136 (3.6%)	109 (3.1%)	784 (5.9%)	11803 (4.1%)	3641 (1.8%)	16473 (3.2%)
Puerto Rico	612 (0.3%)	1951 (0.6%)	9 (0.2%)	9 (0.3%)	89 (0.7%)	1645 (0.6%)	811 (0.4%)	2563 (0.5%)
Site census tract social vulnerability index (SVI)[e]								
0 - < 0.5 (less vulnerable)	84502 (45.0%)	161922 (49.8%)	1661 (43.6%)	1759 (49.9%)	7484 (56.1%)	156181 (54.9%)	79339 (38.2%)	246424 (48.0%)
0.5 - 1.0 (more vulnerable)	103336 (55.0%)	163168 (50.2%)	2145 (56.4%)	1764 (50.1%)	5853 (43.9%)	128297 (45.1%)	128445 (61.8%)	266504 (52.0%)
Test Type								
Laboratory-based NAAT[f]	74243 (39.5%)	122213 (37.6%)	1312 (34.5%)	1380 (39.2%)	5824 (43.7%)	123842 (43.5%)	64098 (30.8%)	196456 (38.3%)
Rapid NAAT[g]	113595 (60.5%)	202877 (62.4%)	2494 (65.5%)	2143 (60.8%)	7513 (56.3%)	160636 (56.5%)	143686 (69.2%)	316472 (61.7%)
Underlying chronic conditions[h]								
No conditions	117737 (62.7%)	188735 (58.1%)	2574 (67.6%)	1789 (50.8%)	8200 (61.5%)	152087 (53.5%)	141822 (68.3%)	306472 (59.7%)
One condition	40433 (21.5%)	75800 (23.3%)	787 (20.7%)	874 (24.8%)	3026 (22.7%)	70403 (24.7%)	41143 (19.8%)	116233 (22.7%)
Two or more conditions	29668 (15.8%)	60555 (18.6%)	445 (11.7%)	860 (24.4%)	2111 (15.8%)	61988 (21.8%)	24819 (11.9%)	90223 (17.6%)

	Cases (SARS-CoV-2 Positive) (n = 187838)	**Controls (SARS-CoV-2 Negative) (n = 325090)**	**Ad26.COV2.S (n = 3806)**	**Ad26.COV2.S/Ad26.COV2.S (n = 3523)**	**Ad26.COV2.S/ mRNA (n = 13337)**	**mRNA/ mRNA/ mRNA (n = 284478)**	**Unvaccinated (n = 207784)**	**Overall (n = 512928)**
High blood pressure	34864 (18.6%)	66927 (20.6%)	495 (13.0%)	1024 (29.1%)	2406 (18.0%)	71081 (25.0%)	26785 (12.9%)	101791 (19.8%)
Overweight	26335 (14.0%)	59622 (18.3%)	451 (11.8%)	749 (21.3%)	2500 (18.7%)	60982 (21.4%)	21275 (10.2%)	85957 (16.8%)
Smoking	22298 (11.9%)	38484 (11.8%)	490 (12.9%)	509 (14.4%)	1269 (9.5%)	30406 (10.7%)	28108 (13.5%)	60782 (11.9%)
Diabetes	13314 (7.1%)	24752 (7.6%)	176 (4.6%)	384 (10.9%)	875 (6.6%)	26937 (9.5%)	9694 (4.7%)	38066 (7.4%)
Heart condition	9570 (5.1%)	19018 (5.9%)	105 (2.8%)	240 (6.8%)	530 (4.0%)	19992 (7.0%)	7721 (3.7%)	28588 (5.6%)
Lung disease or asthma	7895 (4.2%)	19354 (6.0%)	135 (3.5%)	195 (5.5%)	664 (5.0%)	17784 (6.3%)	8471 (4.1%)	27249 (5.3%)
Kidney disease	757 (0.4%)	1377 (0.4%)	12 (0.3%)	18 (0.5%)	52 (0.4%)	1411 (0.5%)	641 (0.3%)	2134 (0.4%)
Liver disease	363 (0.2%)	739 (0.2%)	6 (0.2%)	12 (0.3%)	24 (0.2%)	656 (0.2%)	404 (0.2%)	1102 (0.2%)
Detailed vaccination history[a,b]								
Unvaccinated	104170 (55.5%)	103614 (31.9%)	NA	NA	NA	NA	207784 (100.0%)	207784 (40.5%)
BNT162b2 & BNT162b2 & BNT162b2	44302 (23.6%)	111281 (34.2%)	NA	NA	NA	155583 (54.7%)	NA	155583 (30.3%)
mRNA-1273 & mRNA-1273 & mRNA-1273	26065 (13.9%)	78937 (24.3%)	NA	NA	NA	105002 (36.9%)	NA	105002 (20.5%)
BNT162b2 & BNT162b2 & mRNA-1273	2942 (1.6%)	9998 (3.1%)	NA	NA	NA	12940 (4.5%)	NA	12940 (2.5%)
mRNA-1273 & mRNA-1273 & BNT162b2	2715 (1.4%)	7670 (2.4%)	NA	NA	NA	10385 (3.7%)	NA	10385 (2.0%)
Ad26.COV2.S & mRNA-1273	2043 (1.1%)	4865 (1.5%)	NA	NA	6908 (51.8%)	NA	NA	6908 (1.3%)
Ad26.COV2.S & BNT162b2	2054 (1.1%)	4375 (1.3%)	NA	NA	6429 (48.2%)	NA	NA	6429 (1.3%)

	Cases (SARS-CoV-2 Positive) (n = 187838)	**Controls (SARS-CoV-2 Negative) (n = 325090)**	**Ad26.COV2.S (n = 3806)**	**Ad26.COV2.S/Ad26.COV2.S (n = 3523)**	**Ad26.COV2.S/ mRNA (n = 13337)**	**mRNA/ mRNA/ mRNA (n = 284478)**	**Unvaccinated (n = 207784)**	**Overall (n = 512928)**
Ad26.COV2.S	1878 (1.0%)	1928 (0.6%)	3806 (100.0%)	NA	NA	NA	NA	3806 (0.7%)
Ad26.COV2.S & Ad26.COV2.S	1518 (0.8%)	2005 (0.6%)	NA	3523 (100.0%)	NA	NA	NA	3523 (0.7%)
BNT162b2 & mRNA-1273 & BNT162b2	54 (<0.1%)	121 (<0.1%)	NA	NA	NA	175 (0.1%)	NA	175 (<0.1%)
BNT162b2 & mRNA-1273 & mRNA-1273	36 (<0.1%)	133 (<0.1%)	NA	NA	NA	169 (0.1%)	NA	169 (<0.1%)
mRNA-1273 & BNT162b2 & BNT162b2	35 (<0.1%)	91 (<0.1%)	NA	NA	NA	126 (<0.1%)	NA	126 (<0.1%)
mRNA-1273 & BNT162b2 & mRNA-1273	26 (<0.1%)	72 (<0.1%)	NA	NA	NA	98 (<0.1%)	NA	98 (<0.1%)
Days from January 2, 2022 until testing								
Median (IQR)	22.0 (19.0)	26.0 (27.0)	24.0 (19.0)	24.0 (22.0)	25.0 (24.0)	25.0 (24.0)	24.0 (23.0)	24.0 (24.0)
Min, Max	1.0, 80.0	1.0, 80.0	1.0, 80.0	1.0, 80.0	1.0, 80.0	1.0, 80.0	1.0, 80.0	1.0, 80.0
Months between primary series and testing[i]								
Median (IQR)	10.0 (1.0)	10.0 (2.0)	3.0 (2.0)	10.0 (1.0)	10.0 (1.0)	10.0 (2.0)	NA	10.0 (2.0)
Min, Max	0.0, 14.0	0.0, 15.0	0.0, 4.0	2.0, 13.0	2.0, 13.0	5.0, 15.0	NA	0.0, 15.0
Missing (no primary series)	104170 (55.5%)	103614 (31.9%)	NA	NA	NA	NA	207784 (100.0%)	207784 (40.5%)

	Cases (SARS-CoV-2 Positive) (n = 187838)	Controls (SARS-CoV-2 Negative) (n = 325090)	Ad26.COV2.S (n = 3806)	Ad26.COV2.S/Ad26.COV2.S (n = 3523)	Ad26.COV2.S/ mRNA (n = 13337)	mRNA/ mRNA/ mRNA (n = 284478)	Unvaccinated (n = 207784)	Overall (n = 512928)
Months between booster dose and testing[i]								
Median (IQR)	2.0 (2.0)	2.0 (2.0)	NA	2.0 (2.0)	2.0 (2.0)	2.0 (2.0)	NA	2.0 (2.0)
Min, Max	0.0, 4.0	0.0, 4.0	NA	0.0, 4.0	0.0, 4.0	0.0, 4.0	NA	0.0, 4.0
Missing (no booster)	106048 (56.5%)	105542 (32.5%)	3806 (100.0%)	NA	NA	NA	207784 (100.0%)	211590 (41.3%)
Months between primary series and booster dose[j]								
Median (IQR)	7.0 (1.0)	8.0 (1.0)	NA	8.0 (1.0)	8.0 (1.0)	7.0 (1.0)	NA	7.0 (1.0)
Min, Max	2.0, 13.0	2.0, 13.0	NA	2.0, 12.0	2.0, 12.0	5.0, 13.0	NA	2.0, 13.0
Missing (no primary series or no booster)	106048 (56.5%)	105542 (32.5%)	3806 (100.0%)	NA	NA	NA	207784 (100.0%)	211590 (41.3%)

IQR=interquartile range; NA=not applicable; NAAT=Nucleic acid amplification test; SVI=Social vulnerability index

[a] Cases and controls were considered vaccinated if tests were from persons who reported receiving the most recent vaccine dose ≥2 weeks before their SARS-CoV-2 test date.

[b] Individuals self-reported COVID-19 vaccination status at test registration, including the number of doses (up to four), product, and month and year of receipt for each vaccine dose. For doses received in the same month or the month prior to testing, registrants were asked whether the dose was received at least two weeks before testing. Vaccination reporting was neither mandatory nor verified.

[c] Race and ethnicity were self-reported from fixed categories provided at test registration. The question regarding race was required on the questionnaire, and registrants were only able to select one category or select “Decline to answer”, which was coded as unknown race. Unknown race (n=43,068) and

ethnicity (n=39,470) were coded as categorical levels within each variable to retain those tests in regression models.

[d] Regions defined as: East North Central (Illinois, Indiana, Michigan, Ohio, and Wisconsin), South Atlantic (Delaware, Florida, Georgia, Maryland, North Carolina, South Carolina, Virginia, Washington, DC, and West Virginia), West South Central (Arkansas, Louisiana, Oklahoma, and Texas), Mountain (Arizona, Colorado, Idaho, Montana, Nevada, New Mexico, Utah, and Wyoming), East South Central (Alabama, Kentucky, Mississippi, and Tennessee), West North Central (Iowa, Kansas, Minnesota, Missouri, Nebraska, North Dakota, and South Dakota), Mid-Atlantic (New Jersey, New York, and Pennsylvania), Pacific (Alaska, California, Hawaii, Oregon, and Washington), New England (Connecticut, Maine, Massachusetts, New Hampshire, Rhode Island, and Vermont), and Puerto Rico.

[e] Testing site census tract SVI was an available variable in ICATT data. SVI is assigned for all US census tracts by CDC/ATSDR (Agency for Toxic Substances and Disease Registry) based on US Census data. Higher SVI indicates greater social vulnerability.

[f] Laboratory-based NAAT was performed by contract laboratories on self-collected nasal swabs using either the TaqPath COVID-19 Combo Kit (Thermo Fischer Scientific, Inc) or COVID-19 RT-PCR Test (Laboratory Corporation of America). Data regarding specimen collection date, test type and test results were directly reported by the pharmacy to ICATT.

[g] Rapid NAAT was performed onsite by the pharmacy on self-collected nasal swabs using IDNow (Abbott Diagnostics Scarborough, Inc.). Data regarding specimen collection date, test type and test results were directly reported by the pharmacy to ICATT.

[h] Test registrants were asked to report whether a healthcare worker had ever diagnosed them with heart conditions; high blood pressure; overweight or obesity; diabetes; current or former smoker;

kidney failure or end stage renal disease; cirrhosis of the liver; or chronic lung disease, such as COPD, moderate to severe asthma, cystic fibrosis, or pulmonary embolism.

[i] Months between the primary series or booster dose and testing were calculated as the difference between the month and year of testing and the month and year of the last primary series dose or booster dose, respectively. Tests from participants with <2 weeks between the date of the last dose and the date of testing were excluded.

[j] For all boosted regimens ([2]Ad26.COV2.S/Ad26.COV2.S, [3]Ad26.COV2.S/mRNA, [4]mRNA/mRNA/mRNA) tests were excluded if <2 or <5 months for Ad26.COV2.S and mRNA primary series, respectively, had elapsed between the last dose of the primary series and the booster dose. For Ad26.COV2.S we did not limit by months since primary series receipt; however, tests with 14 days to 1 month since primary series receipt were not eligible for a booster dose unlike those with ≥2 months.

Table S2. Representativeness of included SARS-CoV-2 tests in vaccine effectiveness analysis of adults aged ≥ 18 years tested in the *Increasing Community Access to Testing* platform, January 2, 2022–March 23, 2022.

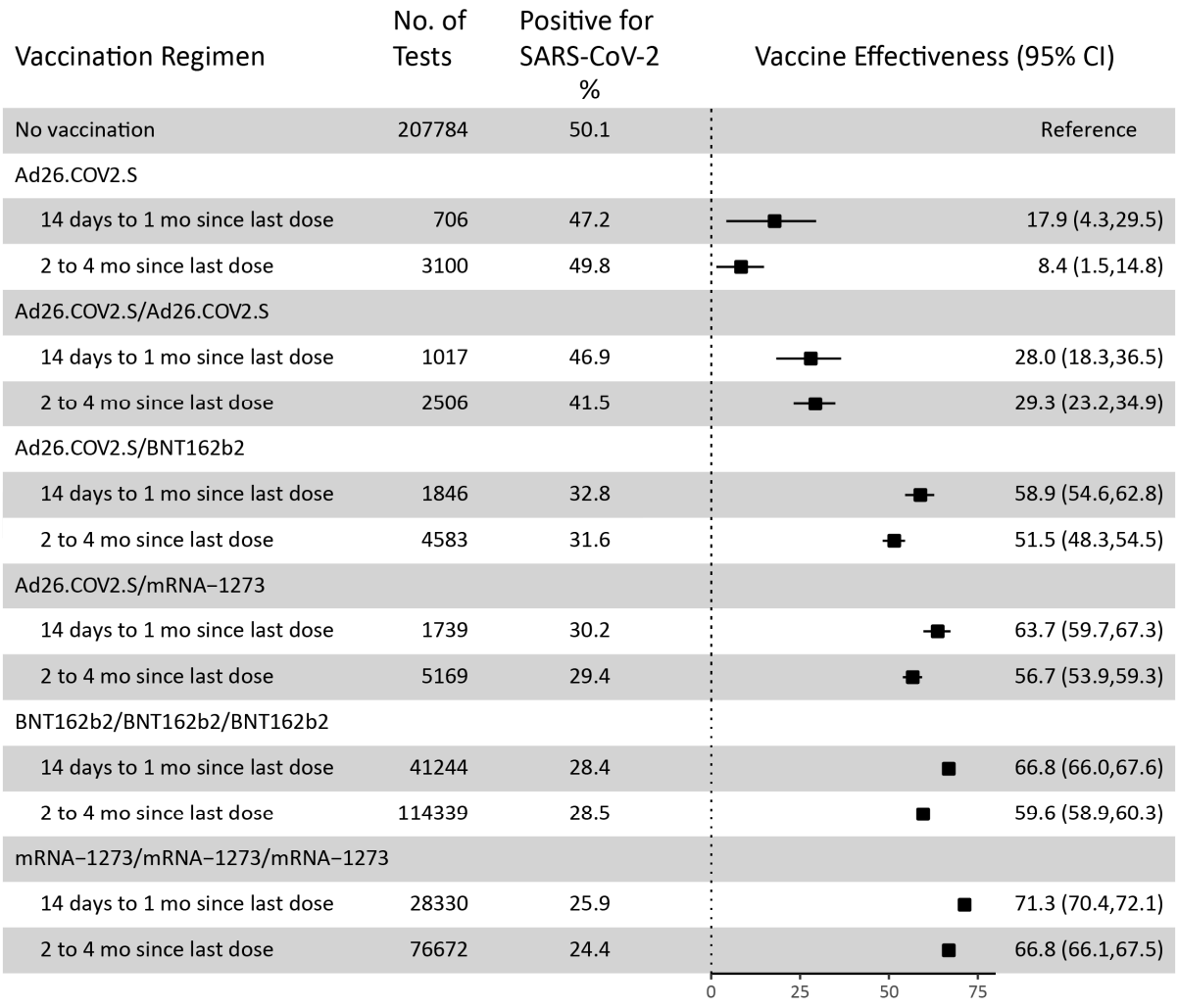
Category	Details
Disease under investigation	Symptomatic SARS-CoV-2 infection[a] defined as ≥1 COVID-19-like illness symptom (fever, cough, shortness of breath, recent loss of sense of smell or taste, muscle pain, fatigue, chill, headache, sore throat, congestion or runny nose, vomiting, diarrhea).
Special considerations related to:	
Sex	Rates of SARS-CoV-2 infection are similar among those of male and female sex. In data on cumulative COVID-19 cases reported by U.S. states and territories to CDC as of March 4, 2022, 53.7% of all reported cases in adults 18 and older for which sex was known were from those of female sex[b], while the U.S. population aged ≥ 18 years is 51.3% female.[c]
Age	Rates of symptomatic SARS-CoV-2 infection in different age groups have been dynamic throughout the pandemic. The estimated rate of symptomatic infection per 100,000 population between February 2020 and September 2021 was highest among adults 18-49 years of age and lowest among adults ≥65 years of age.[d]
Race or ethnic group	COVID-19 has disproportionately affected persons from racial and ethnic minority groups, putting them at increased risk of SARS-CoV-2 infection. CDC identifies race and ethnicity as risk markers for other factors that affect health, including socioeconomic status, access to health care, and increased occupational exposure to the virus, e.g., frontline, essential, and critical infrastructure workers.[e] In data on cumulative COVID-19 cases reported by U.S. states and territories to CDC as of March 4, 2022, the risk of SARS-CoV-2 infection after adjusting for age was 1.5 times higher in non-Hispanic American Indian or Alaska Natives persons than in non-Hispanic White persons, 1.5 times higher in Hispanic or Latino persons than non-Hispanic White persons, and 1.1 times higher in non-Hispanic Black or African American persons than non-Hispanic White persons.[e]
Geography	Geographic differences in COVID-19 case rates have been observed both globally by country and within the U.S. by urban-rural classification[f] and region.[g]
Other considerations	The CDC/ATSDR Social Vulnerability Index (SVI) uses 15 variables from the US Census to identify socially vulnerable communities that may need support before, during, and after public health emergencies. County-level SVI is associated with COVID-19 case rates, but the association is dynamic. At times during the pandemic, counties with high SVI have had higher COVID-19 case rates, while at other times counties with low SVI have had higher COVID-19 case rates.[h,i,j,k]
Overall representativeness of this study	The outcome of symptomatic SARS-CoV-2 infection in this analysis likely reflects mild disease as it is defined as ≥1 COVID-19-like illness symptom. No clinical assessment was performed at the time of testing. The tests included in this

	study were more frequently from individuals reporting female sex than the general U.S. population (in this analysis 59.6% of tests for which sex was not missing were from those reporting female sex; 51.3% of the U.S population is female).[l] ICATT did not collect information on gender identity. Included tests were more frequently from individuals aged 18-24 years (13.1% of tests in the analysis vs 11.8% of the U.S. population ≥ 18 years), 25-34 (25.0% vs 18.0%), and 35-44 (19.5% vs 16.3%). Tests were less frequently from individuals aged 45-54 (14.3% of tests in the analysis vs 16.0% of the U.S. population), 55-64 (14.0% vs 16.6%), and ≥65 years (14.1% vs 21.2%). Reporting of race and ethnicity was required by ICATT test sites (options included American Indian or Alaska Native, Asian, Black or African American, Native Hawaiian or Other Pacific Islander, White, or decline to answer; Hispanic or Latino, Non-Hispanic or Latino, or decline to answer). The questionnaire used by the pharmacy chain included in this analysis did not give the option to report multiple races and these individuals may have been misclassified or chosen to decline reporting race. Among included tests for which race was not missing, the distribution of reported race and ethnicity was similar to that of the U.S. population aged ≥18 years (American Indian or Alaska Native: 1.0% in the analysis vs 1.2% in the U.S. population; Asian: 6.6% vs 6.2%; Black or African American: 13.0% vs 13.2%; Native Hawaiian or Other Pacific Islander: 0.6% vs 0.2%; White: 78.8% vs 79.1%; Hispanic or Latino ethnicity: 15.4% vs 16.4%).[l,m] This analysis was limited to testing sites in the U.S. The geographic distribution of tests was similar to the distribution of the U.S. population (tests included from 49 states [all except North Dakota], Washington, DC and Puerto Rico). ICATT testing sites are not available in U.S. territories other than Puerto Rico. Urban-rural differences were not assessed in this study.

a. The outcome of this study was symptomatic SARS-CoV-2 infection. Other COVID-19 outcomes—such as hospitalization and death, may have different relationships with these categories.
b. CDC. COVID-19 Case Surveillance Public Use Data. Website: https://data.cdc.gov/Case-Surveillance/COVID-19-Case-Surveillance-Public-Use-Data/vbim-akqf. Updated 3/4/22. Accessed 4/6/22.
c. U.S. Census Bureau. 2016-2020 American Community Survey 5-Year Estimates: ACS Demographic and Housing Estimates. Website: https://data.census.gov/cedsci/table?q=2020%20ACS&tid=ACSDP5Y2020.DP05. Accessed 3/30/22.
d. CDC. Estimated rates of COVD-19 disease outcomes per 100,000 by age group—United States, February 2020-September 2021. Website: https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/burden.html. Updated 11/16/21. Accessed 3/24/22.
e. CDC. Risk for COVID-19 Infection, Hospitalization, and Death By Race/Ethnicity. Website: https://www.cdc.gov/coronavirus/2019-ncov/covid-data/investigations-discovery/hospitalization-death-by-race-ethnicity.html. Updated 3/10/22. Accessed 3/24/22.
f. Duca LM, Coyle J, McCabe C, et al. COVID-19 Stats: COVID-19 incidence, by urban-rural classification — United States, January 22–October 31, 2020. *Morb. Mortal. Wkly. Rep.* 69, 2020 (2020).

g. Ferguson JM, Justice AC, Osborne TF, et al. Geographic and temporal variation in racial and ethnic disparities in SARS-CoV-2 positivity between February 2020 and August 2021 in the United States. *Sci Rep* 12, 273 (2022). https://doi.org/10.1038/s41598-021-03967-5
h. ATSDR. Innovative Uses of SVI During COVID-19. Website: https://www.atsdr.cdc.gov/placeandhealth/project_snapshots/svitool_covid.html?msclkid=ccb486b1aebc11ecac9c44d283148e13#anchor_1630441079427. Updated: 8/31/21. Accessed 4/6/22.
i. Barry V, Dasgupta S, Weller DL, et al. Patterns in COVID-19 Vaccination Coverage, by Social Vulnerability and Urbanicity - United States, December 14, 2020-May 1, 2021. MMWR Morb Mortal Wkly Rep. 2021 Jun 4;70(22):818-824. doi: 10.15585/mmwr.mm7022e1.
j. Thakore N, Khazanchi R, Orav EJ, and Ganguli I. Association of Social Vulnerability, COVID-19 vaccine site density, and vaccination rates in the United States. Healthc (Amst). 2021 Dec; 9(4):100583. doi: 10.1016/j.hjdsi.2021.100583.
k. Neelon B, Mutiso F, Mueller NT, et al. Spatial and temporal trends in social vulnerability and COVID-19 incidence and death rates in the United States. PLoS One. 2021 Mar 24;16(3):e0248702. doi: 10.1371/journal.pone.0248702.
l. U.S. Census Bureau, Population Division. Annual Estimates of the Resident Population by Sex, Age, Race, and Hispanic Origin for the United States: April 1, 2010 to July 1, 2019 (NC-EST2019-ASR6H. Website: https://www.census.gov/data/tables/time-series/demo/popest/2010s-national-detail.html. Accessed 4/6/2022.
m. Percentages of the U.S. population by race based on 2019 estimates of population 18 and older reporting a single race. Those reporting 2 or more races were not included as ICATT does not allow reporting of more than 1 race category.

Figure S2. Vaccine effectiveness (VE) against symptomatic Omicron infection for vaccination regimens by mRNA COVID-19 vaccine product among adults aged ≥18 years tested in the *Increasing Community Access to Testing* platform, January 2 2022 to March 23, 2022**.**



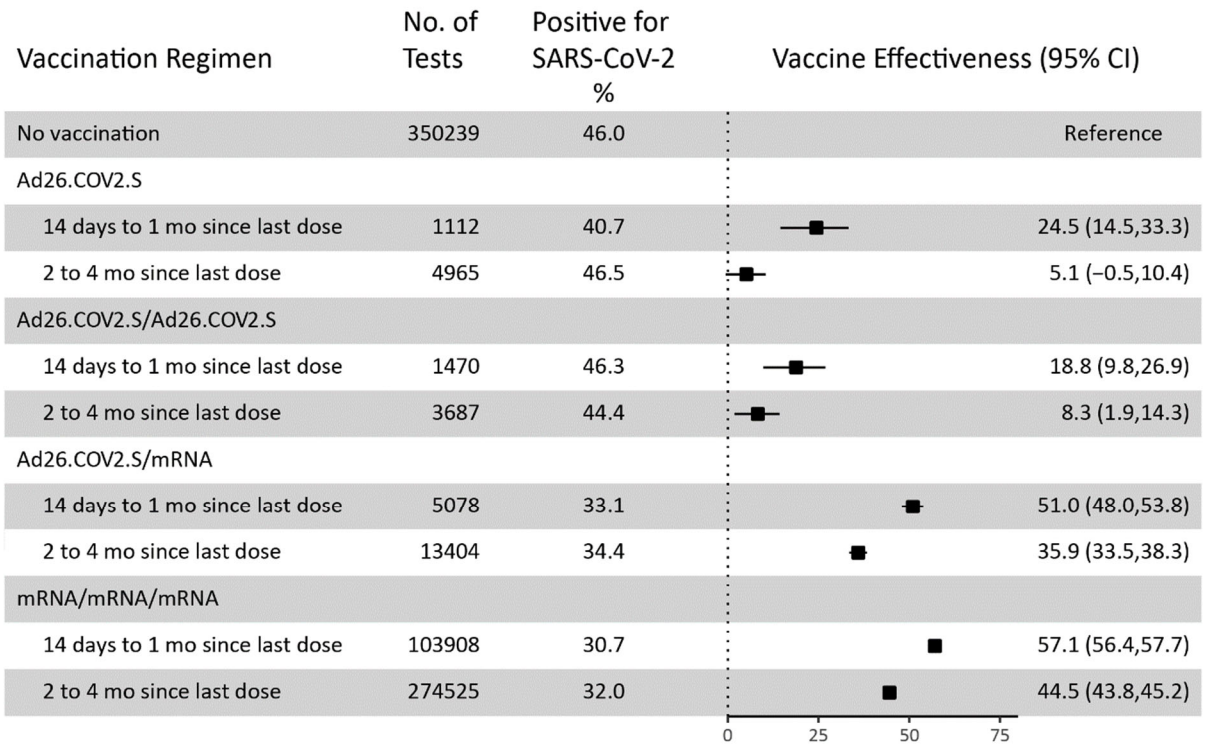
VE was estimated using logistic regression comparing each vaccination regimen against no vaccination, where VE = (1-odds ratio) x 100%. Regression models were adjusted for the number of days between the start of the analysis period and test date (as a continuous variable with linear and quadratic terms), age group (18-24, 25-34, 35-44, 45-54, 55-64, ≥65 years), sex, race, ethnicity, testing site HHS region, testing site census tract social vulnerability index (SVI, dichotomized as 0-<0.5 and ≥0.5-1), and number of underlying chronic conditions (0, 1, or ≥2) to control for possible confounding (**Table S1**). No

adjustment was made for multiplicity. Months since last dose was calculated as the difference between the month and year of testing and the month and year of the last vaccine dose. Tests from participants with <2 weeks between the date of the last dose and the date of testing were excluded. For all boosted regimens tests were excluded if <2 or <5 months for Ad26.COV2.S and mRNA primary series, respectively, had elapsed between the last dose of the primary series and the booster dose. To estimate VE of Ad26.COV2.S over time we did not limit by months since primary series receipt (i.e., eligibility for boosting).

Sensitivity analysis

To assess the effect of prior SARS-CoV-2 test positivity on our results, we conducted a sensitivity analysis including all tests regardless of whether the individual reported any prior positive test result (**Figure S3**). With the exception of Ad26.COV2.S at 14 days to 1 month since last dose, all point estimates for VE were higher in the main analysis compared to the sensitivity analysis, indicative of including tests from individuals reporting prior infection biasing estimates of VE towards less protection. Overall trends remained similar in the sensitivity analysis, supporting our main finding that a single booster dose of mRNA COVID-19 vaccine in Ad26.COV2.S primary series recipients provides protection close to that of 3 mRNA vaccine doses. These results can also help us understand the additional protection provided by vaccination as prior SARS-CoV-2 infection becomes more common in the U.S. population. A limitation of this sensitivity analysis is that prior infection status is self-reported and individuals might choose not to report prior infection, may not be aware of having been previously infected, or may not accurately recall dates of infection. If there was differential accuracy in the ascertainment or reporting of prior infection between unvaccinated and vaccinated individuals, it is possible that there might still be confounding by prior infection that this sensitivity analysis cannot account for.

Figure S3. Sensitivity analysis of vaccine effectiveness (VE) against symptomatic SARS-CoV-2 Omicron infection for four vaccination regimens among adults aged ≥18 years tested in *the Increasing Community Access to Testing* platform, January 2, 2022 to March 23, 2022 including all tests regardless of self-report of prior SARS-CoV-2 infection.



VE was estimated using logistic regression comparing each vaccination regimen against no vaccination, where VE = (1-odds ratio) x 100%. Regression models were adjusted for the number of days between the start of the analysis period and test date (as a continuous variable with linear and quadratic terms), age group (18-24, 25-34, 35-44, 45-54, 55-64, ≥65 years), sex, race, ethnicity, testing site HHS region, testing site census tract social vulnerability index (SVI, dichotomized as 0-<0.5 and ≥0.5-1), and number of underlying chronic conditions (0, 1, or ≥2) to control for possible confounding (**Table S1**). No adjustment was made for multiplicity. Months since last dose was calculated as the difference between the month and year of testing and the month and year of the last vaccine dose. Tests from participants with <2 weeks between the date of the last dose and the date of testing were excluded. For all boosted

regimens tests were excluded if <2 or <5 months for Ad26.COV2.S and mRNA primary series, respectively, had elapsed between the last dose of the primary series and the booster dose. To estimate VE of Ad26.COV2.S over time we did not limit by months since primary series receipt (i.e., eligibility for boosting).

Table S3. Logistic regression model coefficients for main analysis (**Figure 1** model), 14 days to 1 month since last vaccine dose

	Estimate	Std. Error	z value	Pr(>|z|)
(Intercept)	-0.26122	0.03942	-6.62658	3.44E-11
vaccination_statusjanssen	-0.19657	0.078051	-2.51851	0.011785
vaccination_statusjanssen_janssen	-0.32774	0.064334	-5.09442	3.5E-07
vaccination_statusjanssen_mrna	-0.94842	0.036928	-25.6829	1.8E-145
vaccination_statusmrna_mrna	-1.16761	0.010005	-116.707	0
age_group25-34	0.119161	0.011665	10.21532	1.69E-24
age_group35-44	0.173422	0.012821	13.52648	1.09E-41
age_group45-54	0.236935	0.014466	16.37844	2.73E-60
age_group55-64	0.265808	0.01608	16.53055	2.21E-61
age_group65+	0.243857	0.019842	12.29027	1.02E-34
genderMale	0.273183	0.007985	34.21348	1.5E-256
raceAsian	0.026205	0.041799	0.626914	0.530716
raceBlack or African American	-0.26395	0.038007	-6.9447	3.79E-12
raceMissing	0.018392	0.038983	0.471812	0.637061
raceNative Hawaiian or Other Pacific Islander	-0.15577	0.060102	-2.59181	0.009547
raceWhite	0.020407	0.036865	0.553557	0.579882
ethnicityMissing	-0.03687	0.017268	-2.13497	0.032764
ethnicityNot Hispanic/Latino	-0.05567	0.012072	-4.61189	3.99E-06
SVI_binbelow_0.5	-0.01169	0.008191	-1.42779	0.153352
regionEast South Central	0.26203	0.015081	17.37455	1.29E-67
regionMid-Atlantic	0.006904	0.020061	0.344138	0.730742
regionMountain	0.14238	0.016223	8.776559	1.69E-18
regionNew England	0.042421	0.026665	1.590899	0.111632
regionPacific	0.172101	0.018878	9.116242	7.78E-20
regionPuerto Rico	-0.79663	0.068969	-11.5506	7.33E-31
regionSouth Atlantic	0.236912	0.012378	19.13933	1.19E-81
regionWest North Central	0.043529	0.016775	2.594904	0.009462
regionWest South Central	0.102348	0.013724	7.457493	8.82E-14
risk_conditions_catone	-0.09002	0.010245	-8.78707	1.54E-18
risk_conditions_cattwo+	-0.16891	0.012744	-13.2541	4.27E-40
poly(days_since_start, 2)1	-284.659	2.738702	-103.94	0
poly(days_since_start, 2)2	-172.776	2.792373	-61.8744	0

Table S4. Logistic regression model coefficients for main analysis (**Figure 1** model), 2 to 4 months since last vaccine dose

	Estimate	Std. Error	z value	Pr(>|z|)
(Intercept)	-0.34063	0.035767	-9.52349	1.67E-21
vaccination_statusjanssen	-0.08755	0.037145	-2.3569	0.018428
vaccination_statusjanssen_janssen	-0.34566	0.042198	-8.19132	2.58E-16
vaccination_statusjanssen_mrna	-0.78281	0.02323	-33.6978	6.2E-249
vaccination_statusmrna_mrna	-0.98864	0.007903	-125.103	0
age_group25-34	0.104423	0.011148	9.367137	7.45E-21
age_group35-44	0.17533	0.011968	14.65043	1.34E-48
age_group45-54	0.240165	0.013133	18.28772	1.04E-74
age_group55-64	0.281819	0.013753	20.49132	2.57E-93
age_group65+	0.284365	0.014205	20.01906	3.76E-89
genderMale	0.305416	0.00672	45.44705	0
raceAsian	0.051664	0.036868	1.401338	0.161113
raceBlack or African American	-0.22722	0.034636	-6.56009	5.38E-11
raceMissing	-0.00439	0.035399	-0.12407	0.901257
raceNative Hawaiian or Other Pacific Islander	-0.13166	0.05508	-2.39032	0.016834
raceWhite	0.01236	0.03353	0.368624	0.712408
ethnicityMissing	-0.05318	0.015103	-3.52137	0.000429
ethnicityNot Hispanic/Latino	-0.07522	0.010646	-7.06546	1.6E-12
SVI_binbelow_0.5	-0.023	0.00685	-3.35779	0.000786
regionEast South Central	0.261289	0.013024	20.06139	1.61E-89
regionMid-Atlantic	0.020908	0.016288	1.283636	0.199269
regionMountain	0.171568	0.013207	12.99081	1.38E-38
regionNew England	-0.00188	0.02145	-0.08778	0.93005
regionPacific	0.161639	0.015633	10.33943	4.67E-25
regionPuerto Rico	-0.56076	0.056107	-9.99448	1.61E-23
regionSouth Atlantic	0.226711	0.01031	21.98859	3.7E-107
regionWest North Central	0.040101	0.013884	2.888407	0.003872
regionWest South Central	0.125012	0.011755	10.63483	2.05E-26
risk_conditions_catone	-0.1094	0.008457	-12.9351	2.85E-38
risk_conditions_cattwo+	-0.16929	0.009824	-17.2328	1.51E-66
poly(days_since_start, 2)1	-312.112	2.723247	-114.61	0
poly(days_since_start, 2)2	-162.687	2.670003	-60.9315	0

Table S5. Logistic regression model coefficients for sub-analysis by mRNA COVID-19 vaccine product (**Figure S2** model), 14 days to 1 month since last vaccine dose

	Estimate	Std. Error	z value	Pr(>|z|)
(Intercept)	-0.26295	0.039426	-6.66952	2.57E-11
vaccination_status_janssen	-0.19671	0.078052	-2.52019	0.011729
vaccination_status_janssen_janssen	-0.32877	0.064334	-5.11026	3.22E-07
vaccination_status_janssen_pfizer	-0.88814	0.050726	-17.5086	1.23E-68
vaccination_status_janssen_moderna	-1.0138	0.053271	-19.0309	9.46E-81
vaccination_status_pfizer_pfizer	-1.10328	0.012499	-88.2694	0
vaccination_status_moderna_moderna	-1.24815	0.014932	-83.586	0
vaccination_status_other*	-1.22078	0.025886	-47.1602	0
age_group25-34	0.120318	0.011664	10.3151	6.02E-25
age_group35-44	0.174456	0.01282	13.60759	3.61E-42
age_group45-54	0.237965	0.014467	16.4492	8.5E-61
age_group55-64	0.267604	0.016086	16.63582	3.83E-62
age_group65+	0.24988	0.019872	12.57429	2.92E-36
genderMale	0.273088	0.007986	34.19714	2.7E-256
raceAsian	0.019927	0.041811	0.476605	0.633643
raceBlack or African American	-0.26519	0.038012	-6.97638	3.03E-12
raceMissing	0.018048	0.038987	0.462929	0.643415
raceNative Hawaiian or Other Pacific Islander	-0.15587	0.060108	-2.59308	0.009512
raceWhite	0.020396	0.036871	0.553174	0.580144
ethnicityMissing	-0.03551	0.017271	-2.05582	0.0398
ethnicityNot Hispanic/Latino	-0.05381	0.012075	-4.45658	8.33E-06
SVI_binbelow_0.5	-0.01284	0.008193	-1.56714	0.117082
regionEast South Central	0.260879	0.015082	17.29708	4.95E-67
regionMid-Atlantic	0.005304	0.020063	0.264384	0.791484
regionMountain	0.14276	0.016227	8.797894	1.39E-18
regionNew England	0.046568	0.02669	1.744794	0.081021
regionPacific	0.172905	0.018883	9.15652	5.36E-20
regionPuerto Rico	-0.79435	0.068988	-11.5142	1.12E-30
regionSouth Atlantic	0.235925	0.01238	19.05684	5.77E-81
regionWest North Central	0.042545	0.016777	2.535953	0.011214
regionWest South Central	0.103054	0.013727	7.507214	6.04E-14
risk_conditions_catone	-0.08972	0.010247	-8.75575	2.03E-18
risk_conditions_cattwo+	-0.16763	0.01275	-13.1478	1.75E-39
poly(days_since_start, 2)1	-284.779	2.738732	-103.982	0
poly(days_since_start, 2)2	-172.748	2.792617	-61.8587	0

* The “other” category of vaccination status included mixed BNT162b2 and mRNA-1273 regimens that were originally included in the 3 mRNA doses group.

Table S6. Logistic regression model coefficients for sub-analysis by mRNA COVID-19 vaccine product (**Figure S2** model), 2 to 4 months since last vaccine dose

	Estimate	Std. Error	z value	Pr(>|z|)
(Intercept)	-0.33976	0.035782	-9.49518	2.2E-21
vaccination_status_twojanssen	-0.08785	0.037142	-2.36536	0.018013
vaccination_status_twojanssen_janssen	-0.34669	0.042193	-8.21683	2.09E-16
vaccination_status_twojanssen_pfizer	-0.72352	0.033045	-21.8951	2.9E-106
vaccination_status_twojanssen_moderna	-0.83728	0.031775	-26.3501	5.1E-153
vaccination_status_twopfizer_pfizer	-0.90676	0.008998	-100.776	0
vaccination_status_twomoderna_moderna	-1.10366	0.01063	-103.828	0
vaccination_status_twoother	-1.08128	0.020254	-53.3849	0
age_group25-34	0.105301	0.011146	9.447039	3.49E-21
age_group35-44	0.176762	0.011967	14.77025	2.28E-49
age_group45-54	0.241249	0.013134	18.36866	2.34E-75
age_group55-64	0.283746	0.013759	20.62238	1.73E-94
age_group65+	0.291	0.014243	20.43125	8.82E-93
genderMale	0.30535	0.006723	45.41876	0
raceAsian	0.042768	0.036887	1.159434	0.246279
raceBlack or African American	-0.23192	0.034651	-6.6929	2.19E-11
raceMissing	-0.00686	0.035415	-0.19363	0.846464
raceNative Hawaiian or Other Pacific Islander	-0.1357	0.055083	-2.46361	0.013754
raceWhite	0.010734	0.033546	0.319973	0.748989
ethnicityMissing	-0.05085	0.015107	-3.36622	0.000762
ethnicityNot Hispanic/Latino	-0.07257	0.010649	-6.81483	9.44E-12
SVI_binbelow_0.5	-0.02538	0.006855	-3.70317	0.000213
regionEast South Central	0.259296	0.013027	19.90481	3.7E-88
regionMid-Atlantic	0.017932	0.016294	1.100519	0.271106
regionMountain	0.170481	0.013213	12.90217	4.38E-38
regionNew England	0.003012	0.021475	0.140255	0.888458
regionPacific	0.161744	0.015642	10.34024	4.63E-25
regionPuerto Rico	-0.56091	0.056114	-9.9958	1.59E-23
regionSouth Atlantic	0.226982	0.010315	22.00569	2.5E-107
regionWest North Central	0.037449	0.013889	2.696268	0.007012
regionWest South Central	0.126416	0.011761	10.74887	6E-27
risk_conditions_catone	-0.10954	0.008462	-12.945	2.51E-38
risk_conditions_cattwo+	-0.16998	0.009831	-17.2914	5.46E-67
poly(days_since_start, 2)1	-310.804	2.724578	-114.074	0
poly(days_since_start, 2)2	-162.501	2.670261	-60.8557	0

Table S7. Logistic regression model coefficients for sensitivity analysis (**Figure S3** model), 14 days to 1 month since last vaccine dose

	Estimate	Std. Error	z value	Pr(>|z|)
(Intercept)	-0.51907	0.030756	-16.877	6.64E-64
vaccination_statusjanssen	-0.28039	0.063283	-4.43074	9.39E-06
vaccination_statusjanssen_janssen	-0.20851	0.053531	-3.89506	9.82E-05
vaccination_statusjanssen_mrna	-0.71321	0.030636	-23.28	7.1E-120
vaccination_statusmrna_mrna	-0.84548	0.008176	-103.415	0
age_group25-34	0.098826	0.009112	10.84567	2.09E-27
age_group35-44	0.145324	0.010038	14.47723	1.69E-47
age_group45-54	0.221266	0.011306	19.57147	2.71E-85
age_group55-64	0.276505	0.012631	21.89035	3.2E-106
age_group65+	0.28821	0.015853	18.17995	7.44E-74
genderMale	0.297428	0.006286	47.3134	0
raceAsian	0.049848	0.033044	1.50855	0.131414
raceBlack or African American	-0.25016	0.029666	-8.4325	3.38E-17
raceMissing	0.052096	0.030464	1.710063	0.087254
raceNative Hawaiian or Other Pacific Islander	-0.09295	0.04781	-1.94404	0.051891
raceWhite	0.058648	0.028757	2.039418	0.041408
ethnicityMissing	-0.00507	0.01373	-0.36939	0.711835
ethnicityNot Hispanic/Latino	-0.01279	0.009255	-1.38215	0.166927
SVI_binbelow_0.5	-0.01328	0.006437	-2.06252	0.039158
regionEast South Central	0.274037	0.011873	23.08042	7.3E-118
regionMid-Atlantic	-0.00952	0.01633	-0.58304	0.55987
regionMountain	0.11263	0.012936	8.706431	3.14E-18
regionNew England	0.101365	0.022405	4.524156	6.06E-06
regionPacific	0.246605	0.015526	15.88284	8.33E-57
regionPuerto Rico	-0.50801	0.055762	-9.11026	8.22E-20
regionSouth Atlantic	0.266122	0.009697	27.44321	8.4E-166
regionWest North Central	0.025654	0.013532	1.895872	0.057977
regionWest South Central	0.118392	0.010623	11.1445	7.62E-29
risk_conditions_catone	-0.08734	0.008099	-10.7847	4.06E-27
risk_conditions_cattwo+	-0.15149	0.010099	-15.0003	7.31E-51
poly(days_since_start, 2)1	-356.236	2.744519	-129.799	0
poly(days_since_start, 2)2	-219.163	2.760733	-79.3856	0

Table S8. Logistic regression model coefficients for sensitivity analysis (**Figure S3** model), 2 to 4 months since last vaccine dose

	Estimate	Std. Error	z value	Pr(>|z|)
(Intercept)	-0.57004	0.028068	-20.3094	1.06E-91
vaccination_statusjanssen	-0.05248	0.029404	-1.78491	0.074276
vaccination_statusjanssen_janssen	-0.08628	0.03446	-2.50389	0.012284
vaccination_statusjanssen_mrna	-0.44542	0.019159	-23.2483	1.5E-119
vaccination_statusmrna_mrna	-0.58948	0.006312	-93.3864	0
age_group25-34	0.081412	0.008701	9.356261	8.26E-21
age_group35-44	0.138956	0.00938	14.81481	1.18E-49
age_group45-54	0.22002	0.010288	21.38505	1.8E-101
age_group55-64	0.289212	0.01083	26.70347	4.3E-157
age_group65+	0.314594	0.011337	27.75014	1.7E-169
genderMale	0.324279	0.00534	60.72981	0
raceAsian	0.074312	0.029143	2.549923	0.010775
raceBlack or African American	-0.21133	0.027186	-7.77355	7.63E-15
raceMissing	0.045781	0.027834	1.644821	0.100007
raceNative Hawaiian or Other Pacific Islander	-0.06405	0.043872	-1.4599	0.144318
raceWhite	0.052083	0.026321	1.978759	0.047843
ethnicityMissing	-0.02958	0.012069	-2.45089	0.01425
ethnicityNot Hispanic/Latino	-0.03228	0.008194	-3.93911	8.18E-05
SVI_binbelow_0.5	-0.01796	0.005443	-3.30011	0.000966
regionEast South Central	0.274845	0.010356	26.54045	3.3E-155
regionMid-Atlantic	-0.01605	0.013421	-1.1955	0.231893
regionMountain	0.133638	0.010663	12.53303	4.92E-36
regionNew England	0.007679	0.01821	0.421693	0.673249
regionPacific	0.211083	0.012919	16.33837	5.26E-60
regionPuerto Rico	-0.28904	0.04473	-6.46186	1.03E-10
regionSouth Atlantic	0.265304	0.00817	32.47426	2.5E-231
regionWest North Central	0.018977	0.011324	1.675821	0.093773
regionWest South Central	0.158441	0.009149	17.31769	3.46E-67
risk_conditions_catone	-0.09989	0.006751	-14.7964	1.55E-49
risk_conditions_cattwo+	-0.17501	0.007903	-22.1461	1.1E-108
poly(days_since_start, 2)1	-355.822	2.582462	-137.784	0
poly(days_since_start, 2)2	-209.348	2.556232	-81.8972	0

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