Effectiveness of COVID-19 vaccines against Omicron or Delta infection

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ABSTRACT

Background

The incidence of SARS-CoV-2 infection, including among those who have received 2 doses of COVID-19 vaccines, has increased substantially since Omicron was first identified in the province of Ontario, Canada.

Methods

Applying the test-negative design to linked provincial data, we estimated vaccine effectiveness against infection (irrespective of symptoms or severity) caused by Omicron or Delta between November 22 and December 19, 2021. We included individuals who had received at least 2 COVID-19 vaccine doses (with at least 1 mRNA vaccine dose for the primary series) and used multivariable logistic regression to estimate the effectiveness of two or three doses by time since the latest dose.

Results

We included 3,442 Omicron-positive cases, 9,201 Delta-positive cases, and 471,545 test-negative controls. After 2 doses of COVID-19 vaccine, vaccine effectiveness against Delta infection declined steadily over time but recovered to 93% (95%CI, 92-94%) ≥7 days after receiving an mRNA vaccine for the third dose. In contrast, receipt of 2 doses of COVID-19 vaccines was not protective against Omicron. Vaccine effectiveness against Omicron was 37% (95%CI, 19-50%) ≥7 days after receiving an mRNA vaccine for the third dose.

Conclusions

Two doses of COVID-19 vaccines are unlikely to protect against infection by Omicron. A third dose provides some protection in the immediate term, but substantially less than against Delta. Our results may be confounded by behaviours that we were unable to account for in our analyses. Further research is needed to examine protection against severe outcomes.

INTRODUCTION

The World Health Organization declared Omicron a Variant of Concern on November 26, 2021 due to its highly transmissible nature and risk of immune evasion.[1] In Ontario, Canada, the first detected case of Omicron was identified on November 22, 2021; within weeks, Omicron accounted for the majority of new cases. Despite very high 2-dose COVID-19 vaccine coverage (88% among those aged ≥12 years by mid-December),[2] the rate of cases among fully vaccinated individuals increased substantially during this period.[3]

While reduced neutralizing antibodies against Omicron following second and third doses of mRNA vaccines has been established,[4-9] real-world data evaluating vaccine performance against Omicron infection are more limited,[10-12] particularly in a North American context. The objective of this study was to estimate vaccine effectiveness (VE) against infection caused by Omicron or Delta in Ontario.

METHODS

Study population, setting, and design

We used the test-negative design and linked provincial data to estimate VE. We included all individuals aged ≥18 years with provincial health insurance who had a reverse transcription real-time polymerase chain reaction (PCR) test for SARS-CoV-2 between November 22 and December 19, 2021.

We excluded: long-term care residents; individuals who had received only 1 dose of COVID-19 vaccine or who had received their second dose <7 days prior to being tested; individuals who had received 2 doses of ChAdOx1 (AstraZeneca Vaxzevria, COVISHIELD) because VE for that schedule is known to be lower; those who had received non-Health Canada authorized vaccine(s); and those who received the Janssen (Johnson & Johnson) vaccine (which, while approved for use in Canada, was largely unavailable and very rarely used).

Data sources

We linked provincial SARS-CoV-2 laboratory testing, reportable disease, COVID-19 vaccination, and health administrative databases using unique encoded identifiers and analyzed them at ICES, a not-for-profit provincial research institute (www.ices.on.ca).

Outcomes

We identified individuals with confirmed SARS-CoV-2 infections using provincial reportable disease data. We included confirmed COVID-19 cases irrespective of symptoms or severity. The specimen

collection date was used as the index date. For individuals who tested negative for SARS-CoV-2 during the study period and were considered as controls, we randomly selected one negative test to use as the index date. To ensure that negative tests were not associated with recent illness, we excluded controls who tested positive for SARS-CoV-2 within the past 90 days.

Positive specimens identified through whole genome sequencing as B.1.1.529 lineage or found to have S-gene Target Failure (SGTF; a proxy measure for Omicron resulting from the amino acid 69-70 spike deletion that does not occur with Delta) were considered Omicron infections, and specimens sequenced as B.1.617 lineage, found to be negative for SGTF, or collected prior to December 3 (when the prevalence of Omicron was <5%) and had no SGTF information, were considered Delta infections. As of December 6, 2021, all specimens with a positive PCR result were re-tested using Thermofisher Taqpath™ COVID-19 PCR to identify SGTF. Prior to this date, SGTF specimens were only identified if the particular testing laboratory used the Taqpath™ platform. Between December 6 and 20, all SGTF-positive specimens with cycle threshold (Ct) values ≤30 also underwent whole genome sequencing (WGS). In Ontario, the estimated sensitivity of SGTF relative to WGS for detecting Omicron among samples with Ct ≤30 was 99.5% and the specificity was 99.8%.[13]

COVID-19 vaccination

To date, Ontario has primarily used 3 products (BNT162b2 [Pfizer-BioNTech Comirnaty], mRNA-1273 [Moderna Spikevax], and ChAdOx1) in its COVID-19 vaccination program. Due to fluctuating vaccine supplies, both varying dosing intervals and mixed vaccine schedules were employed. Using a centralized province-wide vaccine registry to identify receipt of COVID-19 vaccines, we classified individuals depending on whether they had received 2 or 3 doses of vaccine and the timing of these doses relative to the index date. We considered the following vaccine schedules for the primary 2-dose series: receipt of at least 1 mRNA vaccine (since a mixed schedule consisting of ChAdOx1 and an mRNA vaccine has previously been demonstrated to have similar VE as 2 mRNA vaccines),[14] receipt of any combination of 2 mRNA vaccines, and receipt of 2 doses of BNT162b2. For the third dose, we considered receipt of any mRNA vaccine and also compared receipt of BNT162b2 with mRNA-1273. All comparisons used those who had not yet received any doses (i.e., “unvaccinated”) by the testing date as the reference group.

Third dose eligibility in Ontario began in August 2021 and expanded gradually.[15] Initially, only moderately or severely immunocompromised individuals were eligible to receive a third dose as part of an extended primary series. Shortly thereafter, third doses (i.e., ‘boosters’) were provided to residents of higher-risk congregate settings for older adults (e.g., long-term care homes, high-risk retirement

homes). In early October, older adults living in other congregate care settings, including all remaining retirement homes, became eligible. All individuals aged ≥70 years and healthcare workers became eligible on November 6, followed by individuals aged ≥50 years on December 13 and individuals aged ≥18 years on December 18. The standard interval for third dose eligibility was generally ≥168 days following the second dose but was shortened to ≥84 days on December 15.

Covariates

From various databases, we obtained information on each individual's age, sex, public health unit region of residence, number of SARS-CoV-2 PCR tests during the 3 months prior to December 14, 2020 (as a proxy for healthcare worker status based on the start date of the provincial COVID-19 vaccine program), past SARS-CoV-2 infection >90 days prior to testing date, comorbidities associated with increased risk of severe COVID-19, influenza vaccination status during the 2019/2020 and/or 2020/2021 influenza seasons (as a proxy for health behaviours), and neighbourhood-level information on median household income, proportion of the working population employed as non-health essential workers, mean number of persons per dwelling, and proportion of the population who self-identify as a visible minority. These databases and definitions have been fully described elsewhere.[16]

Statistical analysis

For both Omicron and Delta infections, we calculated means (continuous variables) and frequencies (categorical variables) and compared test-positive cases and test-negative controls using standardized differences.

We used multivariable logistic regression to estimate odds ratios comparing the odds of vaccination in each "time since latest dose" interval among cases with the odds among controls, while adjusting for all listed covariates and a categorical variable for week of test. VE was calculated using the formula VE=(1-OR)x100%. For both Omicron and Delta infections, we estimated VE by vaccine schedule and time since latest dose.

All analyses were conducted using SAS Version 9.4 (SAS Institute Inc., Cary, NC). All tests were two-sided and used $p<0.05$ as the level of statistical significance.

RESULTS

Between November 22 and December 19, 2021, we included 3,442 Omicron-positive cases, 9,201 Delta-positive cases, and 471,545 test-negative controls. Compared to controls, Omicron cases were: substantially younger (mean age 34.9 years vs. 45.0 years); more likely to be male; less likely to have

any comorbidities; less likely to have had multiple prior SARS-CoV-2 tests; less likely to have received an influenza vaccine during the previous 2 influenza seasons; more likely to have occurred during the latter half of the study period; less likely to have previously tested positive for SARS-CoV-2; more likely to have received 2 doses of COVID-19 vaccines; and less likely to have received a third dose (Table 1).

In contrast, Delta cases were more similar to controls than Omicron cases in some respects (e.g., age, comorbidities) but were more different in others, such as being more likely to have occurred during the initial half of the study period, far more likely to be unvaccinated (33.1% vs. 7.5%), and less likely to have received 2 or 3 doses.

After 2 doses of COVID-19 vaccines (with at least 1 mRNA vaccine), VE against Delta declined steadily over time from 84% (95%CI, 81-86%) 7-59 days after the second dose to 71% (95%CI, 66-75%) ≥240 days after the second dose, but recovered to 93% (95%CI, 92-94%) ≥7 days after receiving an mRNA vaccine for the third dose (Table 2; Figure 1). In contrast, receipt of 2 doses of COVID-19 vaccines was not protective against Omicron infection at any point in time, and VE was –38% (95%CI, –61%, –18%) 120-179 days and –42% (95%CI, –69%, –19%) 180-239 days after the second dose. VE against Omicron was 37% (95%CI, 19-50%) ≥7 days after receiving an mRNA vaccine for the third dose.

Findings were consistent for any combination of 2 mRNA vaccines and 2 doses of BNT162b2 for the primary series (Table S1, Figure S1).

DISCUSSION

Our results demonstrate that the effectiveness of 2 doses of COVID-19 vaccines against infection (irrespective of symptoms or severity) is substantially lower for Omicron than Delta, and that VE against Omicron infection was only 37% ≥7 days following a third dose. We also observed negative VE against Omicron among those who had received 2 doses compared to unvaccinated individuals.

Early estimates of VE against the Omicron variant are available from several countries, including England, Scotland, Denmark, and South Africa. In a test-negative study conducted in England, Andrews et al. found substantial waning of VE after 2 doses, and lower VE against symptomatic infection from Omicron than Delta at each time point following 2 or 3 doses.[10 17] While lower than for Delta, VE against Omicron was restored to ~70% in the 4 weeks following a third dose and subsequently waned. Similar to those findings, our results show a marked reduction in 2-dose effectiveness against Omicron infection relative to Delta, followed by increased effectiveness after a third dose. While the pattern of our results were similar, our absolute estimates were lower. Our results

align more closely with recent Danish data, where VE was estimated for both BNT162b2 and mRNA-1273 vaccines between November 20 and December 12, 2021.[12] In both Ontario and Denmark, VE was estimated against any infection; these estimates are expected to be lower than against symptomatic infection. In the Danish study, there was no significant protection against Omicron infection beyond 31 days after the second dose of BNT162b2, with significant negative VE estimates 91-150 days after the second dose. We also observed a pattern of non-existent, or even negative VE in Ontario. However, VE in Denmark (available for BNT162b2 only) recovered to 55% in the first 30 days following a third dose. The Danish estimates are also aligned with other study results from England,[11] where an estimated VE of 0-20% against symptomatic infection was observed for those with 2 doses of BNT162b2 and 55-80% for those with 3 doses, and from Scotland,[18] where relative VE against Omicron following a third dose was estimated at 56-57% in the 2 weeks following a third dose compared to those who had received 2 vaccine doses ≥25 weeks before the symptom onset date. Finally, a study from South Africa estimated VE against infection at 33% in the Omicron period compared to 77% in the pre-Omicron period.[19]

Direct comparisons to other jurisdictions are challenging[20] due to differences in study methodology, outcome definitions (i.e., symptomatic infection vs. any infection), vaccination policies (i.e., homologous vs. heterologous vaccine schedules, third dose eligibility criteria, product-specific policies), population age structures, and public health measures that were in place during the study period (e.g., vaccine certificates, mask mandates[21]). Despite this, the general trends across the studies are similar, demonstrating substantially lower VE against Omicron infection than for previous SARS-CoV-2 variants.

The behaviour of individuals who are vaccinated, and the policies that apply to this group, may differ from those who are unvaccinated such that “vaccinated” status could be associated with an increased risk of exposure. In Ontario, a vaccine certificate system was introduced in the fall of 2021, such that only individuals who have received 2 doses of vaccine are permitted to travel by air and rail, and to enter restaurants, bars, gyms, and large cultural and sporting events. Younger adults may be more likely to frequent such venues and have more social contacts[22] (and Omicron cases in our study were younger). As such, the exposure risk of vaccinated individuals may be higher than unvaccinated individuals since vaccination is a requirement to participate in these social activities. This may explain the negative VE following 2 doses observed for Omicron during this early study period. In earlier work, we noted negative VE in the first week following the second dose against previous variants, in keeping with the hypothesis that a mistaken belief in immediate protection post-vaccination may lead to premature behaviour change. However, other hypotheses should also be considered, including the

possibility that antigenic imprinting could impact the immune response to Omicron.[23] Ontario has experienced a lower cumulative incidence of reported infections and has attained higher vaccine coverage, and thus has a potentially dissimilar distribution of infection-induced versus vaccine-induced immunity, than other countries that have estimated VE against Omicron to date.[24]

In addition to the potential that behavioural patterns differ by age, the characteristics of individuals who received specific products may differ due to a preferential recommendation in Ontario of BNT162b2 for young adults.[25 26] This may be another contributing factor in observed differences in VE across products (i.e., higher VE for mRNA-1273 than BNT162b2) in other studies.[17 27 28]

Although prior studies have demonstrated reduced neutralizing antibodies against Omicron relative to other variants following receipt of 2 mRNA vaccines[4-7 9] (but with potent neutralization following a third dose[29 30]), CD8+ cytotoxic T cells are less impacted by mutations in the Omicron variant and are likely to continue to provide protection against severe disease.[30 31] To date, little real-world data on protection against hospitalization are available. In South Africa, effectiveness against hospitalization was reduced from 93% in the pre-Omicron period to 70% in the Omicron period.[19 32] In England, VE against hospitalization due to Omicron also appears to be better maintained relative to infection with Omicron.[11] Further data on effectiveness of 2 or 3 doses against severe outcomes are needed.

Our analysis has several limitations. First, we were unable to differentiate individuals who received a third dose as part of an extended primary series (i.e., severely or moderately immunocompromised individuals) as well as those who were eligible for a third dose earlier (e.g., residents of retirement homes). As such, the proportion of our sample with a third dose may reflect these highly vulnerable populations, and thus VE may be lower than for the general population due to underlying comorbidities, for example. Second, due to sample size constraints, we were unable to provide age-specific VE estimates. Third, we were unable to estimate effectiveness against severe outcomes, due to the lag between infection and hospitalization or death. Fourth, there may be residual confounding that was not accounted for in our analysis. This includes an inability to control for previous undocumented infections, which may be differential by vaccination status, as well as confounding due to behavioural patterns. For example, if vaccinated individuals have more exposure to SARS-CoV-2, our VE estimates are likely underestimated.[21] Last, changes in testing patterns, including increased use of rapid antigen tests (which are not captured in our data) and decreased PCR testing availability, may have impacted our estimates, but the direction of any resulting bias is uncertain.

Our findings have potentially important implications for proof of vaccination requirements. If the goal of these policies is to protect against infection then individuals who have received 2 doses of

mRNA vaccines may no longer be considered fully vaccinated. However, if the primary goal of these policies is to protect against severe illness and impact on the health system, further data will be needed to determine the number of doses required to provide adequate protection against severe outcomes caused by Omicron. Our work adds to an emerging body of research that suggests that immunization status cannot be simply dichotomized, and that protection is instead based on a variety of factors such as type of vaccine received, age of recipient, time since latest dose, and circulating variant.

Conclusions

Two doses of COVID-19 vaccines are unlikely to protect against Omicron infection. While VE against Omicron infection is substantially lower than against Delta infection, a third dose of mRNA vaccine affords some level of protection against Omicron infection in the immediate term. However, the duration of this protection and effectiveness against severe disease are uncertain. Additional tools beyond the currently available vaccines, such as public health measures, antivirals, and updated vaccines, are likely needed to protect against Omicron infection.

Ethics approval

ICES is a prescribed entity under Ontario's Personal Health Information Protection Act (PHIPA). Section 45 of PHIPA authorizes ICES to collect personal health information, without consent, for the purpose of analysis or compiling statistical information with respect to the management of, evaluation or monitoring of, the allocation of resources to or planning for all or part of the health system. Projects that use data collected by ICES under section 45 of PHIPA, and use no other data, are exempt from REB review. The use of the data in this project is authorized under section 45 and approved by ICES' Privacy and Legal Office.

Data availability

The dataset from this study is held securely in coded form at ICES. While legal data sharing agreements between ICES and data providers (e.g., healthcare organizations and government) prohibit ICES from making the dataset publicly available, access may be granted to those who meet pre-specified criteria for confidential access, available at www.ices.on.ca/DAS (email: das@ices.on.ca).

Code availability

The full dataset creation plan and underlying analytic code are available from the authors upon request, understanding that the computer programs may rely upon coding templates or macros that are unique to ICES and are therefore either inaccessible or may require modification.

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Author contributions

S.A.B, H.C., and J.C.K. designed the study. H.C. obtained the data and conducted all analyses (data set and variable creation and statistical modelling). S.A.B. and J.C.K. drafted the manuscript. All authors contributed to the analysis plan, interpreted the results, critically reviewed and edited the manuscript, approved the final version, and agreed to be accountable for all aspects of the work.

Competing interests

K.W. is CEO of CANImmunize and serves on the data safety board for the Medicago COVID-19 vaccine trial. The other authors declare no conflicts of interest.

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Table 1. Characteristics of study subjects tested for SARS-CoV-2 between 22 November and 19 December 2021 in Ontario, Canada

	SARS-CoV-2 negative, n (%)[a]	Omicron, n (%)[a]	SD[b]	Delta, n (%)[a]	SD[b]
Total	471,545	3,442	N/A	9,201	N/A
Subject characteristics					
Age (years), mean (standard deviation)	45.04 ± 17.66	34.87 ± 13.71	0.64	43.76 ± 16.30	0.08
Age group (years)					
18–29	104,897 (22.2%)	1,528 (44.4%)	0.48	2,002 (21.8%)	0.01
30–39	106,181 (22.5%)	742 (21.6%)	0.02	2,215 (24.1%)	0.04
40–49	83,328 (17.7%)	638 (18.5%)	0.02	1,901 (20.7%)	0.08
50–59	74,452 (15.8%)	351 (10.2%)	0.17	1,396 (15.2%)	0.02
60–69	52,441 (11.1%)	117 (3.4%)	0.3	941 (10.2%)	0.03
70–79	30,559 (6.5%)	49 (1.4%)	0.26	528 (5.7%)	0.03
≥80	19,687 (4.2%)	17 (0.5%)	0.25	218 (2.4%)	0.10
Male sex	202,843 (43.0%)	1,695 (49.2%)	0.13	4,529 (49.2%)	0.12
Any comorbidity[c]	215,267 (45.7%)	1,220 (35.4%)	0.21	3,986 (43.3%)	0.05
Number of SARS-CoV-2 tests within 3 months prior to 14 Dec 2020					
0	351,505 (74.5%)	2,600 (75.5%)	0.02	7,519 (81.7%)	0.17
1	80,508 (17.1%)	651 (18.9%)	0.05	1,248 (13.6%)	0.10
≥2	39,532 (8.4%)	191 (5.5%)	0.11	434 (4.7%)	0.15
Receipt of 2019-2020 and/or 2020-2021 influenza vaccination	162,615 (34.5%)	890 (25.9%)	0.19	2,142 (23.3%)	0.25
Public health unit region[d]					
Central East	31,437 (6.7%)	122 (3.5%)	0.14	875 (9.5%)	0.1
Central West	86,882 (18.4%)	780 (22.7%)	0.10	1,701 (18.5%)	0
Durham	20,988 (4.5%)	233 (6.8%)	0.10	304 (3.3%)	0.06
Eastern	38,635 (8.2%)	376 (10.9%)	0.09	713 (7.7%)	0.02
North	31,375 (6.7%)	35 (1.0%)	0.30	847 (9.2%)	0.09
Ottawa	32,836 (7.0%)	309 (9.0%)	0.07	475 (5.2%)	0.08
Peel	42,643 (9.0%)	442 (12.8%)	0.12	873 (9.5%)	0.02
South West	57,132 (12.1%)	122 (3.5%)	0.32	1,537 (16.7%)	0.13
Toronto	90,349 (19.2%)	746 (21.7%)	0.06	1,304 (14.2%)	0.13
York	37,420 (7.9%)	255 (7.4%)	0.02	532 (5.8%)	0.09
Household income quintile[d, e]					
1 (lowest)	82,944 (17.6%)	377 (11.0%)	0.19	1,811 (19.7%)	0.05
2	86,939 (18.4%)	465 (13.5%)	0.13	1,702 (18.5%)	0
3	92,991 (19.7%)	653 (19.0%)	0.02	1,853 (20.1%)	0.01
4	99,462 (21.1%)	771 (22.4%)	0.03	1,939 (21.1%)	0
5 (highest)	107,161 (22.7%)	1,153 (33.5%)	0.24	1,846 (20.1%)	0.06
Essential workers quintile[d, f]					
1 (0%–32.5%)	111,693 (23.7%)	1,201 (34.9%)	0.25	1,605 (17.4%)	0.15
2 (32.5%–42.3%)	107,392 (22.8%)	943 (27.4%)	0.11	1,980 (21.5%)	0.03
3 (42.3%–49.8%)	92,534 (19.6%)	584 (17.0%)	0.07	1,868 (20.3%)	0.02
4 (50.0%–57.5%)	84,326 (17.9%)	416 (12.1%)	0.16	1,816 (19.7%)	0.05
5 (57.5%–100%)	72,486 (15.4%)	272 (7.9%)	0.23	1,834 (19.9%)	0.12
Persons per dwelling quintile[d, g]					
1 (0–2.1)	91,000 (19.3%)	522 (15.2%)	0.11	1,665 (18.1%)	0.03
2 (2.2–2.4)	81,998 (17.4%)	423 (12.3%)	0.14	1,650 (17.9%)	0.01
3 (2.5–2.6)	66,496 (14.1%)	453 (13.2%)	0.03	1,389 (15.1%)	0.03
4 (2.7–3.0)	112,978 (24.0%)	912 (26.5%)	0.06	2,216 (24.1%)	0
5 (3.1–5.7)	115,770 (24.6%)	1,102 (32.0%)	0.17	2,172 (23.6%)	0.02
Self-identified visible minority quintile[d, h]					
1 (0.0%–2.2%)	75,821 (16.1%)	310 (9.0%)	0.21	1,742 (18.9%)	0.08
2 (2.2%–7.5%)	83,649 (17.7%)	514 (14.9%)	0.08	1,889 (20.5%)	0.07
3 (7.5%–18.7%)	92,075 (19.5%)	805 (23.4%)	0.09	1,832 (19.9%)	0.01

	SARS-CoV-2 negative, n (%)[a]	Omicron, n (%)[a]	SD[b]	Delta, n (%)[a]	SD[b]
4 (18.7%–43.5%)	105,666 (22.4%)	946 (27.5%)	0.12	1,867 (20.3%)	0.05
5 (43.5%–100%)	111,237 (23.6%)	841 (24.4%)	0.02	1,780 (19.3%)	0.10
Week of test					
22 November to 28 November 2021	98,419 (20.9%)	12 (0.3%)	0.71	3,359 (36.5%)	0.35
29 November to 5 December 2021	111,195 (23.6%)	55 (1.6%)	0.70	3,237 (35.2%)	0.26
6 December to 12 December 2021	126,583 (26.8%)	1,123 (32.6%)	0.13	1,530 (16.6%)	0.25
13 December to 19 December 2021	135,348 (28.7%)	2,252 (65.4%)	0.79	1,075 (11.7%)	0.43
Prior positive SARS-CoV-2 test	20,279 (4.3%)	33 (1.0%)	0.21	24 (0.3%)	0.27
COVID-19 vaccine characteristics					
Unvaccinated	35,264 (7.5%)	176 (5.1%)	0.10	3,046 (33.1%)	0.67
Received 2-dose primary series only (with at least 1 mRNA vaccine)	389,573 (82.6%)	3,102 (90.1%)	0.22	5,946 (64.6%)	0.42
Received BNT162b2 for third dose	38,730 (8.2%)	148 (4.3%)	0.16	180 (2.0%)	0.29
Received mRNA-1273 for third dose	7,978 (1.7%)	16 (0.5%)	0.12	29 (0.3%)	0.14
Time since second dose					
7-59 days	14,288 (3.0%)	63 (1.8%)	0.08	204 (2.2%)	0.05
60-119 days	34,741 (7.4%)	214 (6.2%)	0.05	562 (6.1%)	0.05
120-179 days	282,977 (60.0%)	2,257 (65.6%)	0.12	4,342 (47.2%)	0.26
180-239 days	47,282 (10.0%)	522 (15.2%)	0.16	635 (6.9%)	0.11
≥240 days	10,285 (2.2%)	46 (1.3%)	0.06	203 (2.2%)	0
Time since third dose					
No third dose (i.e., only 2 doses)	389,573 (82.6%)	3,102 (90.1%)	0.22	5,946 (64.6%)	0.42
0-6 days	10,208 (2.2%)	50 (1.5%)	0.05	71 (0.8%)	0.12
7-59 days	32,528 (6.9%)	108 (3.1%)	0.17	117 (1.3%)	0.29
≥60 days	3,972 (0.8%)	6 (0.2%)	0.09	21 (0.2%)	0.08

[a]Proportion reported, unless stated otherwise.

[b]SD=standardized difference. Standardized differences of >0.10 are considered clinically relevant. Comparison of Omicron-positive cases with SARS-CoV-2-negative controls, and Delta-positive cases with SARS-CoV-2-negative controls.

[c]Comorbidities include chronic respiratory diseases, chronic heart diseases, hypertension, diabetes, immunocompromising conditions due to underlying diseases or therapy, autoimmune diseases, chronic kidney disease, advanced liver disease, dementia/frailty and history of stroke or transient ischemic attack.

[d]The sum of counts does not equal the column total because of individuals with missing information (<1.0%) for this characteristic.

[e]Household income quintile has variable cut-off values in each city/Census area to account for cost of living. A dissemination area (DA) being in quintile 1 means it is among the lowest 20% of DAs in its city by income.

[f]Percentage of people in the area working in the following occupations: sales and service occupations; trades, transport and equipment operators and related occupations; natural resources, agriculture, and related production occupations; and occupations in manufacturing and utilities. Census counts for people are randomly rounded up or down to the nearest number divisible by 5, which causes some minor imprecision.

[g]Range of persons per dwelling.

[h]Percentage of people in the area who self-identified as a visible minority. Census counts for people are randomly rounded up or down to the nearest number divisible by 5, which causes some minor imprecision.

Table 2. Vaccine effectiveness against infection by Omicron or Delta among adults aged ≥18 years by time since latest dose

Doses	Vaccine products	Days since latest dose	SARS-CoV-2 negative controls, n	Omicron-positive cases, n	Vaccine effectiveness against Omicron (95% CI)	Delta-positive cases, n	Vaccine effectiveness against Delta (95% CI)
First 2 doses	≥1 mRNA vaccine	7-59	14,288	63	6 (-25, 30)	204	84 (81, 86)
		60-119	34,741	214	-13 (-38, 8)	562	81 (79, 82)
		120-179	282,977	2,257	-38 (-61, -18)	4,342	80 (79, 81)
		180-239	47,282	522	-42 (-69, -19)	635	74 (72, 76)
		≥240	10,285	46	-16 (-62, 17)	203	71 (66, 75)
Third dose	Any mRNA vaccine	0-6	10,208	50	2 (-35, 29)	71	88 (85, 90)
		≥7	36,500	114	37 (19, 50)	138	93 (92, 94)
	BNT162b2	0-6	8,461	42	2 (-39, 30)	64	87 (83, 90)
		≥7	30,269	106	34 (16, 49)	116	93 (91, 94)
	mRNA-1273	0-6	1,747	8	5 (-94, 54)	7	93 (86, 97)
		≥7	6,231	8	59 (16, 80)	22	93 (90, 96)

Figure 1. Vaccine effectiveness against infection by Omicron or Delta among adults aged ≥18 years by time since latest dose