Effectiveness of COVID-19 vaccines against variants of concern, Canada

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ABSTRACT:

Objectives: To estimate the effectiveness of BNT162b2 (Pfizer-BioNTech), mRNA-1273 (Moderna), and ChAdOx1 (AstraZeneca) vaccines against symptomatic SARS-CoV-2 infection and severe outcomes (COVID-19 hospitalization or death) caused by the Alpha (B.1.1.7), Beta (B.1.351), Gamma (P.1), and Delta (B.1.617.2) variants of concern (VOCs) during December 2020 to May 2021.

Methods: We conducted a test-negative design study using linked population-wide vaccination, laboratory testing, and health administrative databases in Ontario, Canada.

Results: Against symptomatic infection caused by Alpha, vaccine effectiveness with partial vaccination (≥14 days after dose 1) was higher for mRNA-1273 than BNT162b2 and ChAdOx1. Full vaccination (≥7 days after dose 2) increased vaccine effectiveness for BNT162b2 and mRNA-1273 against Alpha. Protection against symptomatic infection caused by Beta/Gamma was lower with partial vaccination for ChAdOx1 than mRNA-1273. Against Delta, vaccine effectiveness after partial vaccination tended to be lower than against Alpha for BNT162b2 and mRNA-1273, but was similar to Alpha for ChAdOx1. Full vaccination with BNT162b2 increased protection against Delta to levels comparable to Alpha and Beta/Gamma. Vaccine effectiveness against hospitalization or death caused by all studied VOCs was generally higher than for symptomatic infection after partial vaccination with all three vaccines.

Conclusions: Our findings suggest that even a single dose of these 3 vaccine products provide good to excellent protection against symptomatic infection and severe outcomes caused by the 4 currently circulating variants of concern, and that 2 doses are likely to provide even higher protection.

INTRODUCTION

SARS-CoV-2 variants of concern (VOC) are more transmissible and have the potential for increased disease severity and decreased vaccine effectiveness.[1] Few studies have reported the effectiveness of COVID-19 vaccines against infection or severe outcomes caused by VOCs.[2-5] All four VOCs, Alpha (B.1.1.7), Beta (B.1.351), Gamma (P.1), and Delta (B.1.617.2), have been circulating at various times in Canada, where a delayed second-dose strategy was implemented due to vaccine supply constraints.

We aimed to estimate the effectiveness of BNT162b2 (Pfizer-BioNTech), mRNA-1273 (Moderna), and ChAdOx1 (AstraZeneca) vaccines against symptomatic SARS-CoV-2 infection and severe outcomes (COVID-19 hospitalization or death) caused by the Alpha, Beta, Gamma, and Delta variants during December 2020 to May 2021.

METHODS

We employed a test-negative design to compare vaccination status between test-positive individuals (with symptomatic infection or a severe outcome) and symptomatic but test-negative individuals.[6] We included community-dwelling Ontarians aged ≥16 years who had symptoms consistent with, or a severe outcome attributable to, COVID-19, and who were tested for SARS-CoV-2 between 14 December 2020 and 30 May 2021. We excluded individuals who tested positive for SARS-CoV-2 prior to their selected index date.

Data sources and definitions

Various datasets were linked using unique encoded identifiers and analyzed at ICES. Details have been described previously.[7]

Vaccination status

We obtained information regarding COVID-19 vaccination status, including vaccine product, date of administration, and dose number, from COVaxON, a centralized COVID-19 vaccine information system in Ontario.

COVID-19 testing and identification of variants

Data on laboratory-confirmed SARS-CoV-2 infection detected by real-time reverse transcription polymerase chain reaction (RT-PCR) were collected from the Ontario Laboratories Information System (OLIS) for both individuals who tested positive (treated as cases) and individuals who tested negative (treated as controls). We used specimen collection date as the index date because symptom onset date was inconsistently available in OLIS. We used the first positive test for cases with multiple positive tests, and a randomly selected negative test for controls with multiple negative tests.

We obtained information on variants from the Public Health Case and Contact Management system (CCM), which contains results of screening tests for mutations and whole genome sequencing to assign SARS-CoV-2 lineage or variant of concern (VOC). All RT-PCR positive specimens with cycle threshold values ≤35 were screened for N501Y and E484K mutations by multiplex RT-PCR (VOC PCR).[8]

At the beginning of 2021, whole genome sequencing was performed on specimens that had specific mutations detected by VOC PCR to confirm they were VOCs. From 3 February 2021,

specimens with the N501Y mutation, and from 22 March 2021, specimens with the E484K mutation, and cycle threshold values ≤30 were sequenced for surveillance purposes.[8,9] A subset of RT-PCR-positive specimens without any mutations detected by VOC PCR were also selected for sequencing for surveillance purposes.[8] Additionally, VOC PCR testing and sequencing were performed for specific indications such as recent travellers, partially or fully vaccinated individuals, cases of suspected reinfection, or to support investigations of outbreaks and potential super-spreading events.[10] Ontario started sequencing 10% and 50% of VOC PCR-screened specimens on 2 May 2021 and 30 May 2021, respectively.

In addition to those classified into SARS-CoV-2 lineages based on sequencing, we considered specimens positive for the N501Y mutation and negative for the E484K mutation as the Alpha variant. We classified specimens positive for both N501Y and E484K mutations as the Beta or Gamma variants since both variants have the E484K mutation and insufficient numbers of specimens were sequenced to permit estimation of vaccine effectiveness for Beta and Gamma separately. We classified specimens collected after 1 April 2021 that were negative for both N501Y and E484K (N501Y-/E484K-) mutations as either probable, possible, or unlikely Delta cases based on the probability that it was Delta. To do this, we created a logistic regression model of the probability a N501Y-/E484K- case was Delta based on the date of specimen collection and the forward sortation area (geographical unit based on the first three characters of the postal code) ranked on the cumulative incidence of laboratory-confirmed SARS-CoV-2 cases between 23 January 2020 and 28 March 2021 and grouped into deciles.[11] For each decile, we examined the trajectories of the daily counts of N501Y-/E484K- specimens between 1 April 2021 and 30 May 2021 to estimate the probability that a N501Y-/E484K- specimen represented the Delta variant. We classified specimens with >75% probability of being a Delta variant case to

be 'probable Delta' variant cases, those with 25-75% probability to be 'possible Delta' variant cases, and those with <25% probability to be 'unlikely Delta' variant cases. Our approach correlates well with sequencing results (n=538) for the province indicating a rapid increase in the proportion of N501Y-/E484K- cases being identified as the Delta variant from mid-March to mid-May 2021 (unpublished results). We grouped the probable Delta cases with those identified through sequencing together.

We classified specimens with no lineage information and N501Y-/E484K- specimens collected prior to 1 April 2021 as non-VOC. We also grouped the 'unlikely Delta' cases with the non-VOC specimens.

Outcomes

For vaccine effectiveness against symptomatic infection, individuals who were symptomatic and tested positive for SARS-CoV-2 in OLIS were considered as cases. For severe outcomes, test-positive individuals who had a hospitalization or death up to 13 June 2021 (regardless of the presence of any symptoms recorded at the time of RT-PCR testing) were identified from CCM and considered as cases. Individuals who were symptomatic but only had tests negative for SARS-CoV-2 in OLIS were considered as controls for both outcomes. However, for severe outcomes, we excluded symptomatic test-negative individuals who later tested positive between 31 May 2021 and 13 June 2021.

Covariates

We obtained information on the following covariates from administrative databases: age and sex from the Ontario Registered Persons Database (RPDB); postal code and Public Health Unit of

residence from the RPDB and Statistics Canada Postal Code Conversion File Plus (version 7B); the number of SARS-CoV-2 RT-PCR tests for each individual during the 3 months prior to 14 December (a proxy for individuals who are at increased risk of exposure to SARS-CoV-2 infection and undergo frequent testing), and biweekly (weekly for Delta) period of RT-PCR test to account for the temporal viral activity and regional vaccine roll-out created using testing information from OLIS; comorbidities[12] associated with increased risk of severe COVID-19 identified from various databases using validated algorithms and commonly used diagnostic codes described previously;[13] influenza vaccination status during the 2019/2020 and/or 2020/2021 influenza season determined from physician and pharmacist billing claims in the Ontario Health Insurance Plan and Ontario Drug Benefit databases, respectively; and information on median neighbourhood income, proportion of the working population employed as non-health essential workers, average number of persons per dwelling, and proportion of the population who self-identify as a visible minority obtained from 2016 Census data. These covariates have been described in detail previously.[7]

Statistical analyses

We used multivariable logistic regression models to estimate the odds ratio comparing the odds of vaccination in test-positive cases with the odds of vaccination among test-negative controls, adjusting for the aforementioned covariates that are associated with COVID-19 and vaccine uptake.[12 14 15] We calculated vaccine effectiveness using the following formula: Vaccine effectiveness = 1 – (odds ratio) x 100%.

We estimated vaccine effectiveness against SARS-CoV-2 infection and severe COVID-19 outcomes (hospitalization or death) caused by non-VOC (i.e., non-Alpha/Beta/Gamma/Delta)

SARS-CoV-2, Alpha, Beta/Gamma, and Delta variants stratified by vaccine product (BNT162b2, mRNA-1273, and ChAdOx1) and number of doses received. For individuals who had received only 1 dose (i.e., partial vaccination) by the index date, we calculated vaccine effectiveness ≥14 days after the first dose. For individuals who had received 2 doses (i.e., full vaccination), we calculated vaccine effectiveness ≥7 days after the second dose.

When estimating vaccine effectiveness against the Beta/Gamma and Delta variants, we restricted test-negative controls to individuals who were tested from 11 January 2021 and 11 April 2021 onwards, respectively, corresponding to the dates of initial confirmation of these variants in Ontario.

RESULTS

Over the study period, we identified 421,073 symptomatic community-dwelling individuals who were tested for SARS-CoV-2, with 28,705 (6.8%) positive for non-VOC SARS-CoV-2 and 40,828 (9.7%) positive for a VOC (Table 1). We identified 14,168 individuals with a COVID-19 hospitalization or death (Table 2).

Against symptomatic infection caused by Alpha, vaccine effectiveness with partial vaccination (≥14 days after dose 1) was higher for mRNA-1273 (83%; 95% confidence interval [CI], 80–86%) than BNT162b2 (66%; 95% CI, 64–68%) and ChAdOx1 (64%; 95% CI, 60–68%) (Table 3). Full vaccination (≥7 days after dose 2) increased vaccine effectiveness for BNT162b2 (89%; 95% CI, 86–91%) and mRNA-1273 (92%; 95% CI, 86–96%) against Alpha, but could not be reliably estimated for ChAdOx1 due to inadequate sample size. Protection against symptomatic infection caused by Beta/Gamma was lower with partial vaccination for ChAdOx1 (48%; 95%CI, 28–63%) than mRNA-1273 (77%; 95%CI, 69–92%), and was

intermediate for BNT162b2 (60%; 95%CI, 52–67%). Against Delta, vaccine effectiveness after partial vaccination tended to be lower than against Alpha for BNT162b2 (56% vs. 66%) and mRNA-1273 (72% vs. 83%), but was similar to Alpha for ChAdOx1 (67%). Full vaccination with BNT162b2 increased protection against Delta (87%; 95% CI, 64–95%) to levels comparable to Alpha (89%; 95% CI, 86–91%) and Beta/Gamma (84%; 95% CI, 69–92%).

Vaccine effectiveness against hospitalization or death caused by all studied VOCs was generally higher than for symptomatic infection after partial vaccination with all three vaccines (Table 3). In particular, against Delta, vaccine effectiveness against severe outcomes after 1 dose of BNT162b2, mRNA-1273, and ChAdOx1 was 78% (95% CI, 65–86%), 96% (95% CI, 72–99%), and 88% (95% CI, 60–96%), respectively. Full vaccination was associated with vaccine effectiveness estimates in the mid-90s against Alpha and Beta/Gamma for BNT162b2 and against Alpha for mRNA-1273.

DISCUSSION

We estimated that partial vaccination with BNT162b2 and mRNA-1273 were >55% and >70% effective, respectively, against symptomatic infection by currently circulating VOCs in Canada. Partial vaccination with ChAdOx1 prevents nearly half of symptomatic infections by Beta/Gamma variants, and is >60% effective against Alpha and Delta variants. Full vaccination with mRNA vaccines substantially improves vaccine effectiveness. Effectiveness of partial vaccination was substantially higher against hospitalization or death than symptomatic infection caused be all VOCs except for mRNA-1273 against the Alpha variant; full vaccination further improved effectiveness against severe outcomes.

Our vaccine effectiveness estimates against symptomatic COVID-19 infection with Alpha and Beta/Gamma variants after partial vaccination with mRNA or ChAdOx1 vaccines are similar to the vaccine effectiveness estimates against SARS-CoV-2 infection with these variants in British Columbia[16] but higher than the vaccine effectiveness estimates after partial vaccination against SARS-CoV-2 infection or symptomatic COVID-19 reported recently from Qatar[3], England[4] and Scotland[2]. Our estimates after partial vaccination are also higher than the estimates for severe, critical, or fatal disease in Qatar [3] but comparable with the estimates for hospitalization in England[5] caused by the Alpha variant. Similarly, we estimated higher vaccine effectiveness against symptomatic COVID-19 with the Delta variant after partial vaccination with mRNA or ChAdOx1 vaccines than the effectiveness against symptomatic or asymptomatic infections reported in other studies.[2 4] Against hospitalization with the Delta variant, our vaccine effectiveness after partial vaccination was lower for BNT162b2 and higher for ChAdOx1 than other studies.[5] However, after full vaccination, our estimates against both outcomes for all VOCs were comparable with the effectiveness reported in previous studies.[2-5]

There are some limitations of our study. First, VOC classification in this study relied on a combination of mutation screening and whole genome sequencing, and the criteria for sequencing evolved over the course of the pandemic. Our definition of Delta specimens relied largely on a proxy measure of a N501Y-/E484K- result on mutation screening and a combination of date and geographic location, which were used to infer probable Delta variant specimens. Thus, a small proportion of specimens designated as Delta may have been non-VOC specimens. Second, since vaccine effectiveness is likely impacted by age, the interval between most recent vaccination and index date, vaccine product, and VOC, and given that the eligibility criteria for vaccination (e.g., initial prioritization of older age groups), the availability of certain vaccine

products, and the distribution of circulating VOCs all varied over time, comparisons of vaccine effectiveness estimates between combinations of vaccine products and VOCs should be made with caution. However, we adjusted for relevant covariates and restricted the periods of vaccine effectiveness estimation for Beta/Gamma and Delta variants to correspond with their initial confirmation in Ontario. Third, it is possible that we may have missed some of the severe outcomes if they were not recorded in CCM, such as when severe outcomes occur after completion of case follow-up or when cases volumes exceed public health system capacity and public health investigation of each laboratory-confirmed case is not possible. Fourth, we used specimen collection data as the index date because of lack of available data on symptom onset date in OLIS, which precluded us from restricting the study population to individuals who tested within 10 days of symptom onset. Thus, we may have underestimated vaccine effectiveness by increasing the risk of false-negative cases by extending the interval between symptom onset and testing. Last, despite our best efforts to adjust for potential confounders and the use of the test-negative design, these results may nonetheless be susceptible to residual confounding given to the observational nature of the study.

Our real-world vaccine effectiveness estimates suggest that even a single dose of these 3 vaccine products provide good to excellent protection against symptomatic infection and severe outcomes caused by the 4 currently circulating VOCs, and that 2 doses are likely to provide even higher protection.

Conflicts of interest

KW 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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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 statement

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). 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.

Disclaimers

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Tables:

Table 1. Characteristics of symptomatic test-positive cases (by variants) and test-negative controls tested for SARS-CoV-2 between 14 December 2020 and 30 May 2021 in Ontario, Canada

Characteristic	SARS-CoV-2-positive symptomatic cases				SARS-CoV-2-negative symptomatic controls, n (%)* (N=351,540)
	Non-VOC, n (%)* (N=28,705)	Alpha, n (%)* (N=36,832)	Beta/Gamma, n (%)* (N=3,005)	Delta, n (%)* (N=991)	
BNT162b2 (Pfizer-BioNTech)					
Received 1 dose only	506 (1.8)	3,905 (10.6)	305 (10.1)	277 (28.0)	34,790 (9.9)
Received 2 doses	18 (0.1)	92 (0.2)	9 (0.3)	6 (0.6)	6,914 (2.0)
mRNA-1273 (Moderna)					
Received 1 dose only	91 (0.3%)	695 (1.9)	58 (1.9)	56 (5.7)	7,814 (2.2)
Received 2 doses	≤5 (0.0)	12 (0.0)	0 (0.0)	≤5 (≤0.5)	1,522 (0.4)
ChAdOx1 (AstraZeneca)					
Received 1 dose only	25 (0.1%)	647 (1.8)	62 (2.1)	22 (2.2)	5,919 (1.7)
Received 2 doses	0 (0.0%)	≤5 (0.0)	0 (0.0)	0 (0.0)	25 (0.0)
Age (years), mean (standard deviation)	43.0 (17.5)	40.8 (16.0)	41.9 (16.4)	39.3 (15.6)	43.1 (17.7)
Age group (years)					
16–29	8,124 (28.3)	10,965 (29.8)	840 (28.0)	327 (33.0)	94,113 (26.8)
30–39	5,251 (18.3)	7,667 (20.8)	592 (19.7)	245 (24.7)	77,537 (22.1)
40–49	4,941 (17.2)	7,020 (19.1)	588 (19.6)	162 (16.3)	59,197 (16.8)
50–59	5,124 (17.9)	6,228 (16.9)	528 (17.6)	141 (14.2)	53,154 (15.1)
60–69	3,012 (10.5)	3,228 (8.8)	293 (9.8)	69 (7.0)	36,048 (10.3)
70–79	1,397 (4.9)	1,263 (3.4)	115 (3.8)	35 (3.5)	19,075 (5.4)
≥80	856 (3.0)	461 (1.3)	49 (1.6)	12 (1.2)	12,416 (3.5)
Male sex	13,928 (48.5)	18,261 (49.6)	1,511 (50.3)	499 (50.4)	148,313 (42.2)
Public health unit region†					
Central East	1,319 (4.6)	1,772 (4.8)	186 (6.2)	20 (2.0)	36,869 (10.5)
Central West	4,812 (16.8)	5,259 (14.3)	376 (12.5)	105 (10.6)	65,145 (18.5)

Characteristic	SARS-CoV-2-positive symptomatic cases				SARS-CoV-2-negative symptomatic controls, n (%)* (N=351,540)
	Non-VOC, n (%)* (N=28,705)	Alpha, n (%)* (N=36,832)	Beta/Gamma, n (%)* (N=3,005)	Delta, n (%)* (N=991)	
Durham	662 (2.3)	1,402 (3.8)	99 (3.3)	9-13 (0.9-1.3)	11,642 (3.3)
Eastern	397 (1.4)	313 (0.8)	37 (1.2)	0 (0.0)	18,844 (5.4)
North	1,388 (4.8)	451 (1.2)	32 (1.1)	17 (1.7)	37,813 (10.8)
Ottawa	196 (0.7)	328 (0.9)	23 (0.8)	≤5 (≤0.5)	4,410 (1.3)
Peel	6,787 (23.6)	11,079 (30.1)	947 (31.5)	564 (56.9)	45,302 (12.9)
South West	6,626 (23.1)	1,565 (4.2)	82 (2.7)	34 (3.4)	46,857 (13.3)
Toronto	4,977 (17.3)	10,578 (28.7)	946 (31.5)	206 (20.8)	60,882 (17.3)
York	1,412 (4.9)	3,903 (10.6)	264 (8.8)	31 (3.1)	22,275 (6.3)
Biweekly period of test					
14 Dec 2020 to 27 Dec 2020	4,153 (14.5)	≤5 (0.0)	0 (0.0)	0 (0.0)	26,368 (7.5)
28 Dec 2020 to 10 Jan 2021	6,866 (23.9)	5-9 (0.0-0.0)	0 (0.0)	0 (0.0)	25,779 (7.3)
11 Jan 2021 to 24 Jan 2021	4,812 (16.8)	61 (0.2)	7 (0.2)	0 (0.0)	25,565 (7.3)
25 Jan 2021 to 7 Feb 2021	3,214 (11.2)	146 (0.4)	18 (0.6)	0 (0.0)	23,193 (6.6)
8 Feb 2021 to 21 Feb 2021	2,517 (8.8)	335 (0.9)	41 (1.4)	0 (0.0)	23,539 (6.7)
22 Feb 2021 to 7 Mar 2021	2,074 (7.2)	602 (1.6)	58 (1.9)	0 (0.0)	29,474 (8.4)
8 Mar 2021 to 21 Mar 2021	2,121 (7.4)	1,459 (4.0)	238 (7.9)	0 (0.0)	31,458 (8.9)
22 Mar 2021 to 4 Apr 2021	1,493 (5.2)	5,103 (13.9)	426 (14.2)	0 (0.0)	34,787 (9.9)
5 Apr 2021 to 18 Apr 2021	1,250 (4.4)	11,160 (30.3)	928 (30.9)	≤5 (≤0.5)	42,224 (12.0)
19 Apr 2021 to 2 May 2021	184 (0.6)	9,505 (25.8)	760 (25.3)	107-111 (10.8-11.2)	40,289 (11.5)
3 May 2021 to 16 May 2021	16-20 (0.1-0.1)	5,873 (15.9)	384 (12.8)	397 (40.1)	30,140 (8.6)
17 May 2021 to 30 May 2021	≤5 (0.0)	2,578 (7.0)	145 (4.8)	482 (48.6)	18,724 (5.3)
Number of tests in previous 3 months					
0	23,426 (81.6)	30,799 (83.6)	2,533 (84.3)	844 (85.2)	250,351 (71.2)
1	3,731 (13.0)	4,919 (13.4)	388 (12.9)	118 (11.9)	69,784 (19.9)
≥2	1,548 (5.4)	1,114 (3.0)	84 (2.8)	29 (2.9)	31,405 (8.9)

Characteristic	SARS-CoV-2-positive symptomatic cases				SARS-CoV-2-negative symptomatic controls, n (%)* (N=351,540)
	Non-VOC, n (%)* (N=28,705)	Alpha, n (%)* (N=36,832)	Beta/Gamma, n (%)* (N=3,005)	Delta, n (%)* (N=991)	
Any comorbidity‡	12,640 (44.0)	14,861 (40.3)	1,202 (40.0)	342 (34.5)	163,911 (46.6)
Receipt of 2019-2020 and/or 2020-2021 influenza vaccination	7,492 (26.1)	8,482 (23.0)	749 (24.9)	234 (23.6)	114,976 (32.7)
Neighbourhood income quintile†, §					
1 (lowest)	6,517 (22.7)	7,955 (21.6)	600 (20.0)	230 (23.2)	62,119 (17.7)
2	5,746 (20.0)	8,171 (22.2)	739 (24.6)	227 (22.9)	67,623 (19.2)
3	6,063 (21.1)	8,301 (22.5)	688 (22.9)	328 (33.1)	69,464 (19.8)
4	5,524 (19.2)	6,960 (18.9)	539 (17.9)	149 (15.0)	72,904 (20.7)
5 (highest)	4,692 (16.3)	5,257 (14.3)	425 (14.1)	55 (5.5)	77,721 (22.1)
Essential workers quintile†, ¶					
1 (0%–32.5%)	3,118 (10.9)	4,802 (13.0)	392 (13.0)	64 (6.5)	65,531 (18.6)
2 (32.5%–42.3%)	5,789 (20.2)	8,169 (22.2)	580 (19.3)	144 (14.5)	78,487 (22.3)
3 (42.3%–49.8%)	6,025 (21.0)	7,592 (20.6)	659 (21.9)	198 (20.0)	72,765 (20.7)
4 (50.0%–57.5%)	6,247 (21.8)	8,139 (22.1)	652 (21.7)	273 (27.5)	68,865 (19.6)
5 (57.5%–100%)	7,249 (25.3)	7,919 (21.5)	707 (23.5)	310 (31.3)	63,262 (18.0)
Persons per dwelling quintile†, **					
1 (0–2.1)	3,578 (12.5)	3,207 (8.7)	233 (7.8)	65 (6.6)	65,751 (18.7)
2 (2.2–2.4)	4,200 (14.6)	3,481 (9.5)	272 (9.1)	90 (9.1)	66,049 (18.8)
3 (2.5–2.6)	3,405 (11.9)	3,391 (9.2)	258 (8.6)	70 (7.1)	47,111 (13.4)
4 (2.7–3.0)	7,002 (24.4)	8,753 (23.8)	706 (23.5)	166 (16.8)	83,176 (23.7)
5 (3.1–5.7)	10,237 (35.7)	17,784 (48.3)	1,518 (50.5)	598 (60.3)	86,720 (24.7)
Self-identified visible minority quintile†, ††					
1 (0.0%–2.2%)	3,026 (10.5)	1,656 (4.5)	151 (5.0)	27 (2.7)	64,481 (18.3)
2 (2.2%–7.5%)	3,945 (13.7)	2,663 (7.2)	249 (8.3)	38 (3.8)	68,949 (19.6)
3 (7.5%–18.7%)	4,402 (15.3)	4,053 (11.0)	330 (11.0)	70 (7.1)	65,066 (18.5)

Characteristic	SARS-CoV-2-positive symptomatic cases				SARS-CoV-2-negative symptomatic controls, n (%)* (N=351,540)
	Non-VOC, n (%)* (N=28,705)	Alpha, n (%)* (N=36,832)	Beta/Gamma, n (%)* (N=3,005)	Delta, n (%)* (N=991)	
4 (18.7%–43.5%)	5,802 (20.2)	7,362 (20.0)	540 (18.0)	153 (15.4)	70,010 (19.9)
5 (43.5%–100%)	11,253 (39.2)	20,887 (56.7)	1,720 (57.2)	701 (70.7)	80,410 (22.9)

*Proportion reported, unless stated otherwise.

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

‡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.

§Neighbourhood 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.

¶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.

**Range of persons per dwelling.

††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. Characteristics of test-positive cases with severe outcomes (hospitalization or death) between 14 December 2020 and 13 June 2021 in Ontario, Canada

Characteristics	Non-VOC, n (%)* (N=6,327)	Alpha, n (%)* (N=6,896)	Beta/Gamma, n (%)* (N=780)	Delta, n (%)* (N=165)	SARS-CoV-2-negative symptomatic controls, n (%)* (N=351,240)
BNT162b2 (Pfizer-BioNTech)					
Received 1 dose only	107 (1.7)	1,122 (16.3)	127 (16.3)	50 (30.3)	34,747 (9.9)
Received 2 doses	≤5 (≤0.1)	26 (0.4)	≤5 (≤0.6)	≤5 (≤3.0)	6,910 (2.0)
mRNA-1273 (Moderna)					
Received 1 dose only	74 (1.2)	211 (3.1)	18 (2.3)	≤5 (≤3.0)	7,806 (2.2)
Received 2 doses	≤5 (≤0.1)	17 (0.2)	≤5 (≤0.6)	≤5 (≤3.0)	1,520 (0.4)
ChAdOx1 (AstraZeneca)					
Received 1 dose only	≤5 (≤0.1)	142 (2.1)	13 (1.7)	≤5 (3.0)	5,916 (1.7)
Received 2 doses	0 (0.0)	≤5 (0.1)	0 (0.0)	0 (0.0)	25 (0.0)
Age (years), mean (standard deviation)	69.8 (17.3)	60.5 (17.4)	62.6 (15.8)	55.6 (19.0)	43.1 (17.7)
Age group (years)					
16–29	167 (2.6)	342 (5.0)	23 (2.9)	17 (10.3)	94,012 (26.8)
30–39	278 (4.4)	568 (8.2)	39 (5.0)	20 (12.1)	77,465 (22.1)
40–49	399 (6.3)	874 (12.7)	90 (11.5)	27 (16.4)	59,139 (16.8)
50–59	757 (12.0)	1,420 (20.6)	170 (21.8)	31 (18.8)	53,123 (15.1)
60–69	1,137 (18.0)	1,422 (20.6)	181 (23.2)	30 (18.2)	36,027 (10.3)
70–79	1,428 (22.6)	1,225 (17.8)	155 (19.9)	21 (12.7)	19,064 (5.4)
≥80	2,161 (34.2)	1,045 (15.2)	122 (15.6)	19 (11.5)	12,410 (3.5)
Male sex	167 (2.6)	342 (5.0)	23 (2.9)	17 (10.3)	148,187 (42.2)
Public health unit region†					
Central East	205 (3.2)	225 (3.3)	42 (5.4)	≤5 (≤3.0)	36,858 (10.5)
Central West	1,298 (20.5)	846 (12.3)	68 (8.7)	27 (16.4)	65,060 (18.5)
Durham	224 (3.5)	391 (5.7)	24 (3.1)	10 (6.1)	11,632 (3.3)

Characteristics	Non-VOC, n (%)* (N=6,327)	Alpha, n (%)* (N=6,896)	Beta/Gamma, n (%)* (N=780)	Delta, n (%)* (N=165)	SARS-CoV-2-negative symptomatic controls, n (%)* (N=351,240)
Eastern	119 (1.9)	142 (2.1)	23 (2.9)	0 (0.0)	18,842 (5.4)
North	199 (3.1)	113 (1.6)	12 (1.5)	≤5 (≤3.0)	37,774 (10.8)
Ottawa	224 (3.5)	370 (5.4)	76 (9.7)	6 (3.6)	4,407 (1.3)
Peel	518 (8.2)	842 (12.2)	91 (11.7)	47 (28.5)	45,240 (12.9)
South West	715 (11.3)	314 (4.6)	24 (3.1)	≤5 (≤3.0)	46,825 (13.3)
Toronto	2,240 (35.4)	3,030 (43.9)	365 (46.8)	60 (36.4)	60,839 (17.3)
York	562 (8.9)	586 (8.5)	53 (6.8)	≤5 (≤3.0)	22,263 (6.3)
Biweekly period of test					
14 Dec 2020 to 27 Dec 2020	1,274 (20.1)	≤5 (≤0.1)	0 (0.0)	0 (0.0)	26,352 (7.5)
28 Dec 2020 to 10 Jan 2021	1,644 (26.0)	8-12 (0.1-0.2)	0 (0.0)	0 (0.0)	25,765 (7.3)
11 Jan 2021 to 24 Jan 2021	1,265 (20.0)	14 (0.2)	≤5 (≤0.6)	0 (0.0)	25,553 (7.3)
25 Jan 2021 to 7 Feb 2021	813 (12.8)	49 (0.7)	≤5 (≤0.6)	0 (0.0)	23,182 (6.6)
8 Feb 2021 to 21 Feb 2021	407 (6.4)	114 (1.7)	7-15 (0.9-1.9)	0 (0.0)	23,527 (6.7)
22 Feb 2021 to 7 Mar 2021	307 (4.9)	151 (2.2)	35 (4.5)	0 (0.0)	29,460 (8.4)
8 Mar 2021 to 21 Mar 2021	285 (4.5)	428 (6.2)	97 (12.4)	0 (0.0)	31,436 (9.0)
22 Mar 2021 to 4 Apr 2021	196 (3.1)	1,150 (16.7)	128 (16.4)	0 (0.0)	34,763 (9.9)
5 Apr 2021 to 18 Apr 2021	117 (1.8)	2,009 (29.1)	237 (30.4)	≤5 (≤3.0)	42,186 (12.0)
19 Apr 2021 to 2 May 2021	14-18 (0.2-0.3)	1,583 (23.0)	155 (19.9)	10-14 (6.1-8.5)	40,262 (11.5)
3 May 2021 to 16 May 2021	≤5 (≤0.1)	974 (14.1)	66 (8.5)	71 (43.0)	30,105 (8.6)
17 May 2021 to 30 May 2021	0 (0.0)	411 (6.0)	45 (5.8)	79 (47.9)	18,649 (5.3)
Number of tests in previous 3 months					
0	4,760 (75.2)	5,983 (86.8)	678 (86.9)	143 (86.7)	250,128 (71.2)
1	831 (13.1)	683 (9.9)	74 (9.5)	17-21 (10.3-12.7)	69,731 (19.9)
≥2	736 (11.6)	230 (3.3)	28 (3.6)	≤5 (≤3.0)	31,381 (8.9)
Any comorbidity‡	5,486 (86.7)	5,142 (74.6)	600 (76.9)	109 (66.1)	163,783 (46.6)

Characteristics	**Non-VOC, n (%)[*] (N=6,327)**	**Alpha, n (%)[*] (N=6,896)**	**Beta/Gamma, n (%)[*] (N=780)**	**Delta, n (%)[*] (N=165)**	**SARS-CoV-2-negative symptomatic controls, n (%)[*] (N=351,240)**
Receipt of 2019-2020 and/or 2020-2021 influenza vaccination	3,140 (49.6)	2,622 (38.0)	336 (43.1)	50 (30.3)	114,917 (32.7)
Neighbourhood income quintile[†, §]					
1 (lowest)	2,082 (32.9)	2,277 (33.0)	253 (32.4)	46 (27.9)	62,056 (17.7)
2	1,378 (21.8)	1,514 (22.0)	190 (24.4)	46 (27.9)	67,556 (19.2)
3	1,149 (18.2)	1,344 (19.5)	148 (19.0)	44 (26.7)	69,402 (19.8)
4	929 (14.7)	939 (13.6)	104 (13.3)	18 (10.9)	72,840 (20.7)
5 (highest)	766 (12.1)	783 (11.4)	83 (10.6)	10 (6.1)	77,679 (22.1)
Essential workers quintile[†, ¶]					
1 (0%–32.5%)	999 (15.8)	1,110 (16.1)	143 (18.3)	21 (12.7)	65,503 (18.6)
2 (32.5%–42.3%)	1,233 (19.5)	1,329 (19.3)	142 (18.2)	25 (15.2)	78,412 (22.3)
3 (42.3%–49.8%)	1,223 (19.3)	1,364 (19.8)	161 (20.6)	32 (19.4)	72,701 (20.7)
4 (50.0%–57.5%)	1,287 (20.3)	1,416 (20.5)	150 (19.2)	34 (20.6)	68,798 (19.6)
5 (57.5%–100%)	1,551 (24.5)	1,638 (23.8)	182 (23.3)	52 (31.5)	63,197 (18.0)
Persons per dwelling quintile[†, **]					
1 (0–2.1)	1,462 (23.1)	1,197 (17.4)	147 (18.8)	20 (12.1)	65,700 (18.7)
2 (2.2–2.4)	967 (15.3)	985 (14.3)	92 (11.8)	20 (12.1)	65,995 (18.8)
3 (2.5–2.6)	741 (11.7)	739 (10.7)	103 (13.2)	17 (10.3)	47,073 (13.4)
4 (2.7–3.0)	1,421 (22.5)	1,748 (25.3)	193 (24.7)	26 (15.8)	83,114 (23.7)
5 (3.1–5.7)	1,695 (26.8)	2,184 (31.7)	243 (31.2)	81 (49.1)	86,626 (24.7)
Self-identified visible minority quintile[†, ††]					
1 (0.0%–2.2%)	516 (8.2)	339 (4.9)	52 (6.7)	≤5 (≤3.0)	64,435 (18.3)
2 (2.2%–7.5%)	731 (11.6)	501 (7.3)	57 (7.3)	≤5 (≤3.0)	68,908 (19.6)
3 (7.5%–18.7%)	1,056 (16.7)	847 (12.3)	98 (12.6)	17 (10.3)	65,016 (18.5)
4 (18.7%–43.5%)	1,536 (24.3)	1,708 (24.8)	184 (23.6)	37 (22.4)	69,950 (19.9)

Characteristics	**Non-VOC, n (%)[*] (N=6,327)**	**Alpha, n (%)[*] (N=6,896)**	**Beta/Gamma, n (%)[*] (N=780)**	**Delta, n (%)[*] (N=165)**	**SARS-CoV-2-negative symptomatic controls, n (%)[*] (N=351,240)**
5 (43.5%–100%)	2,454 (38.8)	3,462 (50.2)	387 (49.6)	101 (61.2)	80,308 (22.9)

[*] Proportion reported, unless stated otherwise.

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

[‡] 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.

[§] Neighbourhood 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.

[¶] 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.

[**] Range of persons per dwelling.

[††] 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 3. Vaccine effectiveness against Alpha (B.1.1.7), Beta (B.1.351)/Gamma (P.1), and Delta (B.1.617.2) variants of concern by outcome, vaccine product, and number of doses received for those tested for SARS-CoV-2 between 14 December 2020 and 30 May 2021 in Ontario, Canada.

Outcome	Adjusted VE* (95% CI)			
	Non-VOC	Alpha	Beta/Gamma†	Delta‡
Symptomatic infection				
BNT162b2 (Pfizer-BioNTech)				
≥14 days after dose 1 only§	61 (54, 68)	66 (64, 68)	60 (52, 67)	56 (45, 64)
≥7 days after dose 2	93 (88, 96)	89 (86, 91)	84 (69, 92)	87 (64, 95)
mRNA-1273 (Moderna)				
≥14 days after dose 1 only§	54 (28, 70)	83 (80, 86)	77 (63, 86)	72 (57, 82)
≥7 days after dose 2	89 (65, 96)	92 (86, 96)	-¶	-¶
ChAdOx1 (AstraZeneca)				
≥14 days after dose 1 only§	67 (38, 82)	64 (60, 68)	48 (28, 63)	67 (44, 80)
≥7 days after dose 2	-**	-**	-¶	-¶
Hospitalization or death				
BNT162b2 (Pfizer-BioNTech)				
≥14 days after dose 1 only§	68 (54, 78)	80 (78, 82)	77 (69, 83)	78 (65, 86)
≥7 days after dose 2	96 (82, 99)	95 (92, 97)	95 (81, 99)	-¶
mRNA-1273 (Moderna)				
≥14 days after dose 1 only§	57 (28, 75)	79 (74, 83)	89 (73, 95)	96 (72, 99)
≥7 days after dose 2	96 (70, 99)	94 (89, 97)	-¶	-¶
ChAdOx1 (AstraZeneca)				
≥14 days after dose 1 only§	-¶	85 (81, 88)	83 (66, 92)	88 (60, 96)
≥7 days after dose 2	-¶	-**	-¶	-¶

*Adjusted for age, sex, public health unit region, period of test (weekly period for Delta, and bi-weekly period for non-VOC and other VOCs), number of SARS-CoV-2 tests in the 3 months prior to 14 December 2020, presence of any comorbidity that increase the risk of severe COVID-19, receipt of 2019/2020 and/or 2020/2021 influenza vaccination, and Census dissemination area-level quintiles of neighbourhood household income, proportion of persons employed as non-health essential workers, persons per dwelling, and proportion of self-identified visible minorities

†RT-PCR testing date for both test-positive cases and test-negative controls restricted to 11 January 2021 to 30 May 2021 for the Beta/Gamma variants

‡RT-PCR testing date for both test-positive cases and test-negative controls restricted to 11 April 2021 to 30 May 2021 for the Delta variant

§Excludes individuals who received dose 2

¶VE estimated as 100% based on zero vaccinated test-positive cases
**VE not reported due to extremely imprecise 95% confidence intervals