Supplementary Material

Supplementary Methods

Supplementary Table 1. Definitions of covariates used in the analysis.

Variable	Definition
Age	Age was determined from the Registered Persons Database. This variable was included *a priori* as hypothesized to be directly related to COVID-19 infection risk.[1]
Sex	Sex was determined from the Registered Persons Database. This variable was included *a priori* as hypothesized to be directly related to COVID-19 infection risk.[1]
Biweekly period of COVID-19 test	Based on the index date (i.e. specimen collection date, or date of severe outcome if before specimen collection date): 11 Jan 2021 to 24 Jan 2021 25 Jan 2021 to 7 Feb 2021 8 Feb 2021 to 21 Feb 2021 22 Feb 2021 to 7 Mar 2021 8 Mar 2021 to 21 Mar 2021 22 Mar 2021 to 4 Apr 2021 5 Apr 2021 to 18 Apr 2021 19 Apr 2021 to 2 May 2021 3 May 2021 to 16 May 2021 17 May 2021 to 30 May 2021 31 May 2021 to 13 Jun 2021 14 Jun 2021 to 27 Jun 2021 28 Jun 2021 to 11 Jul 2021 12 Jul 2021 to 25 Jul 2021 26 Jul 2021 to 8 Aug 2021 9 Aug 2021 to 22 Aug 2021 23 Aug 2021 to 5 Sep 2021 6 Sep 2021 to 19 Sep 2021 20 Sep 2021 to 3 Oct 2021 4 Oct 2021 to 17 Oct 2021 18 Oct 2021 to 31 Oct 2021 1 Nov 2021 to 14 Nov 2021 15 Nov 2021 to 21 Nov 2021
Chronic heart disease	Individuals were defined as having "chronic heart disease" if they had congestive heart failure (CHF), ischemic heart disease, or atrial fibrillation. The definitions for these conditions are as follows: <u>CHF:</u>[2] An ICES-derived CHF database was used to identify patients with CHF, based on 1 NACRS, DAD, SDS, or OHIP claim and a second claim (from either) in 1 year. The CHF database is limited to those aged 40 years or older. This variable was included a priori as hypothesized to be directly related to COVID-19 infection risk.[3] OHIP: 428 DAD, SDS: ICD-9: 428, ICD-10: I500, I501, I509

Variable	Definition
	Cardiac ischemic disease:[4] Any comorbidity in the past 5 years (DAD, any diagnosis field) or history of procedure in past 20 years (DAD, SDS), of the following: Comorbidity (DAD, any diagnosis in the past 5 years): Angina: ICD-10: I20 Chronic Ischemic Heart Disease: ICD-10: I25; Myocardial infarction: ICD-10: I21, I22 Procedure (DAD & SDS): Coronary Artery Bypass Grafting: CCI procedure codes: 1IJ76 CCP procedure codes: 481 Percutaneous Coronary Intervention: CCI procedure codes: 1IJ50, 1IJ54, 1IJ57GQ CCP procedure codes: 4802, 4803 Atrial fibrillation:[5] Individuals with 1 hospitalization or 4 MD visits within a year in the past 5 years with the following codes: ICD-9: 427.31, 427.32 ICD-10: I48 OHIP dxcode: 427
Chronic respiratory disease	Asthma:[6] An ICES-specific asthma database was used to identify patients with asthma, based on 2 or more ambulatory care visits and/or 1 or more hospitalizations. This variable was included a priori as hypothesized to be directly related to COVID-19 infection risk, as a result of its relationship to severe COVID-19 outcomes.[3] OHIP OHIP diagnostic code: 493 DAD ICD-9 diagnostic code: 493 ICD-10 diagnostic codes: J45, J46 Chronic obstructive pulmonary disease (COPD):[7] An ICES-specific COPD database was used to identify patients with COPD, based on 1 or more ambulatory care visits and/or 1 or more hospitalizations. The algorithm to identify COPD patients was only validated in those aged 35 years or older. This variable was included a priori as hypothesized to be directly related to COVID-19 infection risk.[3] OHIP OHIP diagnostic codes: 491, 492, 496 DAD ICD-9 diagnostic codes: 491, 492, 496

Variable	Definition
	ICD-10 diagnostic codes: J41, J42, J43, J44
Hypertension	An ICES-specific hypertension database was used to identify patients with hypertension, based on 1 or more DAD diagnoses or 2 or more OHIP diagnoses in a two-year period; or 1 OHIP diagnosis followed by an OHIP/DAD diagnosis within two years.[8] This variable was included *a priori* as hypothesized to be directly related to COVID-19 infection risk.[3] DAD, SDS: ICD-9: 401, 402, 403, 404, 405; ICD-10: I10, I11, I12, I13, I15 OHIP diagnostic codes: 401, 402, 403, 404, or 405
Diabetes	An ICES-specific diabetes database was used to identify patients with diabetes, based on 2 OHIP diagnostic codes or 1 OHIP service code or 1 DAD admission within 2 years.[9] This variable was included *a priori* as hypothesized to be directly related to COVID-19 infection risk.[3] DAD, SDS: ICD-9: 250; ICD-10: E10, E11, E13, E14 OHIP: 250 OHIP service codes: Q040, K029, K030, K045, K046
Immunocompromised (HIV, transplant, immunosuppressive therapy)	We included immunosuppressive conditions *a priori* as hypothesized to be directly related to COVID-19 infection risk.[3] <u>HIV:</u>[10] An ICES-specific HIV database was used to identify patients with HIV, based on 3 physician claims in 3 years with OHIP diagnostic codes: 042, 043 or 044 <u>Solid organ transplant recipients:</u> CORRLINK is an ICES-specific database which links CORR (Canadian Organ Replacement Register) and DAD data. This database only includes patients that have received an organ transplant and does not include dialysis patients. • For transplants before December 31, 2019: individuals are a transplant recipient if they have a treatment code of 171, where the treatment was before the index date • For transplants on/after January 1, 2020: Identify ICD-10 codes, CCI procedure codes, and OHIP feecodes from DAD, NACRS, and OHIP (codes available upon request) <u>Allogenic/autologous bone marrow transplant recipients:</u> We identified those who had a history of allogenic bone marrow transplant before the index date using the following combination of diagnostic codes: DAD: • CCP procedure codes = 53.0 • CCI procedure codes = 1WY19, 1LZ19HHU7, 1LZ19HHU8 OHIP: • Feecode = Z426 <u>Other immune disorders</u>: Individuals were identified as having disorders of the immune system based on health care encounters recorded in DAD, SDS, NACRS, and OHIP in the 2-years

Variable	Definition
	prior to index using Expanded Diagnostic Clusters from the Johns Hopkins ACG ® System Version 10.[11] <u>Any hospitalization (any diagnosis field) with the following codes</u>: • Sickle-cell disease (ICD-10 D57.0 – D57.2; D57.8 OR ICD-9 282.6); • Other immune system disorders (ICD-9 273.2, 279.0, 279.1, 279.2, 279.3, 279.8, 279.9, 289.8; ICD-10 D80, D81, D82, D83, D84, D89; OHIP dxcode 279) • Immunosuppressive therapy (>30 days (total days supplied) of oral corticosteroid in the 6 months before index date; receipt of other immunocompromising drug, including antineoplastics, in the 6 months before index date) <u>Active cancer:</u> • Any of the following treatments in the past 6 months: cancer surgery (codes available upon request), radiation (if the ICD-10 code listed was Z510 in NACRS), chemotherapy (if the ICD-10 code listed was Z511 or Z512 and any evidence of cancer diagnosis in the Ontario Cancer Registry (OCR) prior to the last treatment date) • If not any of the above, individuals still classified as having cancer if they had a cancer diagnosis in OCR in the year before the index date

Autoimmune disease	Individuals considered to have autoimmune disease if they had any of the following:
	• Rheumatoid arthritis (identified in the Ontario Rheumatoid Arthritis Database)[12,13]
	• Inflammatory bowel disease (identified in the Ontario Crohn's and Colitis Cohort)[14,15]
	• Psoriasis/psoriatic arthritis[16]
	  ○ Psoriasis: 1 hospitalization or 3 physician billings prior to index date. DAD: ICD-9: 696.1, 696.8; ICD-10: L40.0, L40.1, L40.2, L40.3, L40.4, L40.8, L40.9. OHIP: dxcode = 696
	  ○ Psoriatic arthritis: 1 hospitalization or: (3 physician billings for psoriatic arthritis + 1 billing for psoriasis [696]). DAD: ICD-9: 696.0; ICD-10: L40.5, M07.0, M07.1, M07.2, M07.3, M09.0. OHIP: dxcode = 721 (at least one of these billings must be billed by a rheumatologist).
	• Multiple sclerosis[17]
	  ○ Individuals with one hospitalization or 5 physician billings over 2 years. DAD: ICD-9: 340; ICD-10: G35. OHIP: dxcode = 340.

Chronic kidney disease (CKD)	This variable was included *a priori* as hypothesized to be directly related to COVID-19 infection risk.[3] We defined this variable as having a CKD diagnosis code in DAD, NACRS, OHIP in the past 5 years, <u>or:</u> at least 1 dialysis code in each of the 3 months prior to index.[18] OHIP: 403, 585 ICD-10: E102, E112, E132, E142, I12, I13, N08, N18, N19

Variable	Definition
	Patients who were on chronic dialysis in the year before index date, identified as those with at least 2 of any of the following codes in OHIP, DAD, or SDS separated by at least 90 days, but less than 150 days:[19] OHIP service codes: R849, G323, G325, G326, G860, G862, G865 G863, G866, G330, G331, G332, G333, G861, G082, G083, G085, G090, G091, G092, G093, G094, G095, G096, G294, G295, G864, H540, H740 DAD, SDS: CCI procedure codes: 5195, 6698 CCP procedure code: 1PZ21
Advanced liver disease (Cirrhosis or Decompensated Cirrhosis)	We included advanced liver disease *a priori* as hypothesized to be directly related to COVID-19 infection risk.[3] Defined using the Cirrhosis Algorithm 9 [from [20]]: Two or more physician visits (diagnosis code 571), or one or more hospital diagnosis of cirrhosis, using the following diagnostic codes: ICD-9 : 456.1, 571.2, 571.5 ICD-10: I85.9, I98.2, K70.3,K71.7, K74.6 Defined using the Decompensated Cirrhosis Algorithm 5 (from [20]): One or more physician visits with diagnosis code 571 and (one or more hospital diagnosis or one or more procedure), using the following diagnostic codes: ICD-9: 456.0, 456.2, 572.2, 572.3, 572.4, 782.4, 789.5l; ICD-10: I85.0, I86.4, I98.20, I98.3, K721, K729, K76.6, K76.7, R17, R18 CCI: 1.NA.13.BA-FA, 1.NA.13.BA-X7, 1.NA.13.BA-BD, 1.KQ.76GP-NR, 1.OT.52.HA CCP: 1006, 6691 OHIP: J057, Z591
Dementia	<u>Dementia (ICES cohort) definition:</u> 1 hospitalization for dementia and/or 3 ambulatory visits for dementia, each separated by at least 30 days, within 2 years and/or 1 prescription from ODB.[21] his variable was included *a priori* as hypothesized to be directly related to COVID-19 infection risk,[3] as well as a marker for healthcare access, mobility, and household-level exposures.[22,23] OHIP: 290, 331 DAD, SDS: ICD-9: 0461, 290.0, 290.1, 290.2, 290.3, 290.4, 294, 331.0, 331.1, 331.5 ICD-10: F00, F01, F02, F03, G30 ODB: 1 prescription for a cholinesterase inhibitor
Frailty	<u>Frailty:</u> Individuals were identified as having medical conditions associated with frailty based on health care encounters recorded in DAD, SDS, NACRS, and OHIP in

Variable	Definition
	the 2-years prior to index using Special Population Markers from the Johns Hopkins ACG® System Version 10.[11]
History of transient ischemic attack or acute ischemic stroke	This variable was included *a priori* as hypothesized to be directly related to COVID-19 infection risk.[3] Transient Ischemic Attack: DAD and NACRS were used to identify patients with a history of a transient ischemic attack, based on at least 1 hospitalization or ED visit with a diagnosis coded with one of the following codes: ICD-9: 435, 3623 ICD-10: G450, G451, G452, G453, G458, G459, H340 Acute Ischemic Stroke: DAD was used to identify patients with a history of acute ischemic stroke, based on at least 1 hospitalization with a main diagnosis coded with one of the following codes: ICD-9: 434, 436; ICD-10: I63, I64, H34.1
Influenza vaccine received, 2019-2020 season or 2020-2021 season	An OHIP billing with any of the following fee codes from October 1, 2019 to September 30, 2020, or October 1, 2020 up to 14 days before the index date: G590, G591, G592, Q130, Q590, Q690, Q691; or, an ODB billing with any of the following Drug Identification Numbers (DINs)/Product Identification Number (PINs) from October 1, 2019 up to September 30, 2020: 02420643, 02420783, 02432730, 02473283, or October 1, 2020 up to 14 days before the index date: 02420643, 02420783, 02432730, 02445646, 02494248, 09857645, 09857646
Public health unit region	Taken from Public Health Unit (PHU) information using postal code of residence as recorded in the Registered Persons Database and Statistics Canada Postal Code Conversion File Plus (version 7B). Regions were defined as follows: Central East: PHU 35 (Haliburton, Kawartha, Pine Ridge District Health Unit), 55 (Peterborough County—City Health Unit), 60 (Simcoe Muskoka District Health Unit) Central West: PHU 27 (Brant County Health Unit), 34 (Haldimand-Norfolk Health Unit), 36 (Halton Regional Health Unit), 37 (City of Hamilton Health Unit), 46 (Niagara Regional Area Health Unit), 65 (Waterloo Health Unit), 66 (Wellington-Dufferin-Guelph Health Unit) Durham: PHU 30 (Durham Regional Health Unit) Eastern: PHU 38 (Hastings and Prince Edward Counties Health Unit), 41 (Kingston, Frontenac and Lennox and Addington Health Unit), 43 (Leeds, Grenville and Lanark District Health Unit), 57 (Renfrew County and District Health Unit), 58 (The Eastern Ontario Health Unit) North: PHU 26 (The District of Algoma Health Unit), 47 (North Bay Parry Sound District Health Unit), 49 (Northwestern Health Unit), 56 (Porcupine Health Unit), 61 (Sudbury and District Health Unit), 62 (Thunder Bay District Health Unit), 63 (Timiskaming Health Unit) Ottawa: PHU 51 (City of Ottawa Health Unit) Peel: PHU 53 (Peel Regional Health Unit) South West: PHU 31 (Elgin-St. Thomas), 33 (Grey Bruce Health Unit), 39 (Huron County Health Unit), 40 (Chatham-Kent Health Unit), 42 (Lambton

Variable	Definition
	Health Unit), 44 (Middlesex-London Health Unit), 52 (Oxford), 54 (Perth District Health Unit), 68 (Windsor-Essex County Health Unit), 75 (Southwestern Health Unit) Toronto: PHU 95 (City of Toronto Health Unit) York: PHU 70 (York Regional Health Unit)
Dissemination area (DA)	A dissemination area (DA) is the smallest standard geographic area for which all census data are disseminated. A DA generally comprises approximately 400-700 people, but in densely populated cities may contain several thousand people. DAs cover all the territory of Canada.[24] We assigned subjects to a DA using postal code, as recorded in the Registered Persons Database.
Household income quintile	Calculated at the DA level using 2016 Census data by multiplying the median income (before-tax) by the number of households and dividing by the sum of single-person equivalent to obtain income per single person equivalent.[25] For DAs where median income was unavailable, neighbouring DAs were used to estimate income per single person equivalent. DA-based income quintiles were constructed separately for each census metropolitan area or census agglomeration (one or more adjacent municipalities integrated via commuting flows). DAs within each such area were ranked from the lowest average income per single-person equivalent to the highest, and DAs were assigned to five groups, such that each group contained approximately one-fifth the total in-scope population of each area.
Persons per dwelling quintile	Average number of persons in private households, calculated at the DA level using the 2016 Census data.[26] DAs across the province were ranked by average number of persons per household into 5 categories (quintiles), such that each group contained approximately one-fifth of the DAs.
Essential worker quintile	Calculated at the DA level, using 2016 Census data.[27] For each DA, we calculated the number of individuals ≥15 years old that were working in one of the following Census-defined work categories: 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. DAs across the province were then ranked by these percentages into quintiles, with the lowest 1/5 of DAs comprising the first quintile, and so on.
Visible minority quintile	Calculated at the DA level, using 2016 Census data.[27] An individual was marked as "self-identify as a visible minority" if they reported being one or more of the following (wording from the 2016 Census): "South Asian (e.g., East Indian, Pakistani, Sri Lankan, etc.), Chinese, Black, Filipino, Latin American, Arab, Southeast Asian (e.g., Vietnamese, Cambodian, Laotian, Thai, etc.), West Asian (e.g., Iranian, Afghan, etc.), Korean, Japanese, or Other—specify". DAs across the province were then ranked by these percentages into quintiles, with the lowest 1/5 of DAs comprising the first quintile, and so on.

Supplementary Results

Supplementary Table 2. Characteristics of individuals tested for SARS-CoV-2 between 11 January 2021 and 21 November 2021 in Ontario, Canada by study subperiod

	11 January to 4 April (Mixed wild-type SARS-CoV-2 & Alpha circulating)			5 April to 27 June (Alpha predominating)			28 June to 21 November (Delta predominating)		
Characteristics	**SARS-CoV-2 positive, n (%)[a] (N=109,282)**	**SARS-CoV-2 negative, n (%)[a] (N=1,278,180)**	**SD[b]**	**SARS-CoV-2 positive, n (%)[a] (N=109,244)**	**SARS-CoV-2 negative, n (%)[a] (N=772,026)**	**SD[b]**	**SARS-CoV-2 positive, n (%)[a] (N=42,834)**	**SARS-CoV-2 negative, n (%)[a] (N=1,384,106)**	**SD[b]**
Age (years), mean (standard deviation)	42.70 ± 17.36	46.22 ± 18.45	0.20	38.66 ± 15.32	42.38 ± 17.87	0.22	40.56 ± 16.94	45.25 ± 18.92	0.26
Age group (years)									
16-29	31,021 (28.4%)	285,287 (22.3%)	0.14	37,185 (34.0%)	221,465 (28.7%)	0.12	13,635 (31.8%)	337,067 (24.4%)	0.17
30-39	20,979 (19.2%)	239,683 (18.8%)	0.01	24,275 (22.2%)	166,698 (21.6%)	0.02	9,689 (22.6%)	285,567 (20.6%)	0.05
40-49	18,787 (17.2%)	212,902 (16.7%)	0.01	20,120 (18.4%)	130,689 (16.9%)	0.04	7,245 (16.9%)	219,098 (15.8%)	0.03
50-59	18,944 (17.3%)	221,504 (17.3%)	0.00	16,699 (15.3%)	118,852 (15.4%)	0.00	5,679 (13.3%)	202,155 (14.6%)	0.04
60-69	11,356 (10.4%)	167,006 (13.1%)	0.08	7,597 (7.0%)	71,344 (9.2%)	0.08	3,773 (8.8%)	166,802 (12.1%)	0.11
70-79	5,218 (4.8%)	90,921 (7.1%)	0.10	2,331 (2.1%)	32,129 (4.2%)	0.12	1,816 (4.2%)	103,839 (7.5%)	0.14
80+	2,977 (2.7%)	60,877 (4.8%)	0.11	1,037 (0.9%)	30,849 (4.0%)	0.20	997 (2.3%)	69,578 (5.0%)	0.14
Male sex	55,564 (50.8%)	542,163 (42.4%)	0.17	55,474 (50.8%)	343,954 (44.6%)	0.12	20,927 (48.9%)	588,226 (42.5%)	0.13
Any comorbidity	47,942 (43.9%)	625,421 (48.9%)	0.10	41,223 (37.7%)	337,720 (43.7%)	0.12	17,257 (40.3%)	657,602 (47.5%)	0.15
Number of SARS-CoV-2 tests within 3 months prior to 14 Dec 2020									
0	89,038 (81.5%)	855,438 (66.9%)	0.34	91,848 (84.1%)	542,649 (70.3%)	0.33	35,298 (82.4%)	1,040,963 (75.2%)	0.18
1	14,502 (13.3%)	220,138 (17.2%)	0.11	13,514 (12.4%)	126,574 (16.4%)	0.11	5,519 (12.9%)	223,785 (16.2%)	0.09
≥2	5,742 (5.3%)	202,604 (15.9%)	0.35	3,882 (3.6%)	102,803 (13.3%)	0.36	2,017 (4.7%)	119,358 (8.6%)	0.16
Receipt of 2019-2020 and/or 2020-2021 influenza vaccination	27,806 (25.4%)	450,393 (35.2%)	0.21	19,645 (18.0%)	209,038 (27.1%)	0.22	7,531 (17.6%)	496,415 (35.9%)	0.42
Public health unit region									
Central East	3,458 (3.2%)	90,813 (7.1%)	0.18	3,770 (3.5%)	55,295 (7.2%)	0.17	2,243 (5.2%)	93,097 (6.7%)	0.06
Central West	17,348 (15.9%)	249,992 (19.6%)	0.10	19,338 (17.7%)	153,461 (19.9%)	0.06	9,325 (21.8%)	262,936 (19.0%)	0.07
Durham	4,793 (4.4%)	57,836 (4.5%)	0.01	6,494 (5.9%)	39,854 (5.2%)	0.03	1,769 (4.1%)	62,303 (4.5%)	0.02
Eastern	2,201 (2.0%)	87,462 (6.8%)	0.24	2,051 (1.9%)	47,993 (6.2%)	0.22	1,696 (4.0%)	85,274 (6.2%)	0.10
Northern	3,240 (3.0%)	90,252 (7.1%)	0.19	2,040 (1.9%)	42,966 (5.6%)	0.20	1,831 (4.3%)	85,903 (6.2%)	0.09
Ottawa	4,940 (4.5%)	78,204 (6.1%)	0.07	5,891 (5.4%)	51,548 (6.7%)	0.05	2,175 (5.1%)	88,261 (6.4%)	0.06
Peel	20,259 (18.5%)	119,072 (9.3%)	0.27	21,375 (19.6%)	77,735 (10.1%)	0.27	4,761 (11.1%)	131,770 (9.5%)	0.05
South West	8,162 (7.5%)	150,636 (11.8%)	0.15	6,727 (6.2%)	81,626 (10.6%)	0.16	7,177 (16.8%)	170,358 (12.3%)	0.13
Toronto	33,072 (30.3%)	249,961 (19.6%)	0.25	30,447 (27.9%)	154,718 (20.0%)	0.18	7,958 (18.6%)	277,931 (20.1%)	0.04
York	11,378 (10.4%)	99,058 (7.7%)	0.09	10,632 (9.7%)	63,675 (8.2%)	0.05	3,727 (8.7%)	121,061 (8.7%)	0.00
Household income quintile									
1 (lowest)	28,172 (25.8%)	248,998 (19.5%)	0.15	26,980 (24.7%)	158,181 (20.5%)	0.10	9,138 (21.3%)	252,988 (18.3%)	0.08
2	23,403 (21.4%)	247,414 (19.4%)	0.05	23,449 (21.5%)	151,474 (19.6%)	0.05	8,301 (19.4%)	258,572 (18.7%)	0.02
3	22,585 (20.7%)	255,006 (20.0%)	0.02	23,815 (21.8%)	154,597 (20.0%)	0.04	8,724 (20.4%)	274,334 (19.8%)	0.01
4	19,158 (17.5%)	258,211 (20.2%)	0.07	19,713 (18.0%)	153,200 (19.8%)	0.05	8,547 (20.0%)	288,571 (20.8%)	0.02
5 (highest)	15,477 (14.2%)	263,098 (20.6%)	0.17	14,785 (13.5%)	151,128 (19.6%)	0.16	7,906 (18.5%)	303,840 (22.0%)	0.09
Essential workers quintile									
1 (0%–32.5%)	16,934 (15.5%)	261,556 (20.5%)	0.13	16,729 (15.3%)	157,282 (20.4%)	0.13	7,207 (16.8%)	318,975 (23.0%)	0.16
2 (32.5%–42.3%)	23,073 (21.1%)	281,797 (22.0%)	0.02	23,111 (21.2%)	168,074 (21.8%)	0.01	9,006 (21.0%)	315,765 (22.8%)	0.04
3 (42.3%–49.8%)	21,893 (20.0%)	258,482 (20.2%)	0.00	22,360 (20.5%)	154,282 (20.0%)	0.01	8,592 (20.1%)	270,630 (19.6%)	0.01
4 (50.0%–57.5%)	23,276 (21.3%)	246,452 (19.3%)	0.05	23,125 (21.2%)	148,704 (19.3%)	0.05	8,674 (20.3%)	249,869 (18.1%)	0.06
5 (57.5%–100%)	23,358 (21.4%)	221,573 (17.3%)	0.10	23,313 (21.3%)	138,650 (18.0%)	0.09	8,984 (21.0%)	220,183 (15.9%)	0.13
Persons per dwelling quintile									

1 (0–2.1)	15,437 (14.1%)	246,608 (19.3%)	0.14	14,579 (13.3%)	143,340 (18.6%)	0.14	6,935 (16.2%)	262,165 (18.9%)	0.07
2 (2.2–2.4)	13,600 (12.4%)	230,920 (18.1%)	0.16	13,676 (12.5%)	133,373 (17.3%)	0.13	7,003 (16.3%)	237,391 (17.2%)	0.02
3 (2.5–2.6)	11,766 (10.8%)	181,256 (14.2%)	0.10	11,612 (10.6%)	103,949 (13.5%)	0.09	5,534 (12.9%)	188,906 (13.6%)	0.02
4 (2.7–3.0)	25,522 (23.4%)	303,320 (23.7%)	0.01	25,776 (23.6%)	184,089 (23.8%)	0.01	10,852 (25.3%)	329,275 (23.8%)	0.04
5 (3.1–5.7)	42,141 (38.6%)	307,123 (24.0%)	0.32	42,950 (39.3%)	201,861 (26.1%)	0.28	12,125 (28.3%)	357,059 (25.8%)	0.06
Self-identified visible minority quintile									
1 (0.0%–2.2%)	7,760 (7.1%)	214,809 (16.8%)	0.30	6,956 (6.4%)	117,449 (15.2%)	0.29	5,828 (13.6%)	211,423 (15.3%)	0.05
2 (2.2%–7.5%)	10,230 (9.4%)	230,022 (18.0%)	0.25	9,703 (8.9%)	129,304 (16.7%)	0.24	6,682 (15.6%)	233,748 (16.9%)	0.03
3 (7.5%–18.7%)	14,541 (13.3%)	239,576 (18.7%)	0.15	14,905 (13.6%)	141,496 (18.3%)	0.13	7,898 (18.4%)	261,663 (18.9%)	0.01
4 (18.7%–43.5%)	24,424 (22.3%)	275,588 (21.6%)	0.02	26,080 (23.9%)	172,729 (22.4%)	0.04	10,599 (24.7%)	317,351 (22.9%)	0.04
5 (43.5%–100%)	51,581 (47.2%)	309,896 (24.2%)	0.49	50,996 (46.7%)	206,031 (26.7%)	0.42	11,456 (26.7%)	351,259 (25.4%)	0.03
Biweekly period of test									
11 Jan 2021 to 24 Jan 2021	25,871 (23.7%)	230,811 (18.1%)	0.14						
25 Jan 2021 to 7 Feb 2021	16,266 (14.9%)	194,281 (15.2%)	0.01						
8 Feb 2021 to 21 Feb 2021	11,956 (10.9%)	192,968 (15.1%)	0.12	N/A	N/A				
22 Feb 2021 to 7 Mar 2021	12,249 (11.2%)	218,548 (17.1%)	0.17						
8 Mar 2021 to 21 Mar 2021	16,179 (14.8%)	211,430 (16.5%)	0.05						
22 Mar 2021 to 4 Apr 2021	26,761 (24.5%)	230,142 (18.0%)	0.16				N/A	N/A	
5 Apr 2021 to 18 Apr 2021				42,104 (38.5%)	257,254 (33.3%)	0.11			
19 Apr 2021 to 2 May 2021				33,014 (30.2%)	187,953 (24.3%)	0.13			
3 May 2021 to 16 May 2021				19,796 (18.1%)	125,689 (16.3%)	0.05			
17 May 2021 to 30 May 2021				9,040 (8.3%)	71,117 (9.2%)	0.03			
31 May 2021 to 13 Jun 2021				3,508 (3.2%)	58,294 (7.6%)	0.19			
14 Jun 2021 to 27 Jun 2021				1,782 (1.6%)	71,719 (9.3%)	0.34			
28 Jun 2021 to 11 Jul 2021							1,187 (2.8%)	86,720 (6.3%)	0.17
12 Jul 2021 to 25 Jul 2021							1,193 (2.8%)	96,445 (7.0%)	0.20
26 Jul 2021 to 8 Aug 2021	N/A	N/A					2,123 (5.0%)	110,728 (8.0%)	0.12
9 Aug 2021 to 22 Aug 2021							5,172 (12.1%)	131,501 (9.5%)	0.08
23 Aug 2021 to 5 Sep 2021				N/A	N/A		6,480 (15.1%)	141,432 (10.2%)	0.15
6 Sep 2021 to 19 Sep 2021							6,220 (14.5%)	140,953 (10.2%)	0.13
20 Sep 2021 to 3 Oct 2021							4,934 (11.5%)	154,613 (11.2%)	0.01
4 Oct 2021 to 17 Oct 2021							4,182 (9.8%)	148,672 (10.7%)	0.03
18 Oct 2021 to 31 Oct 2021							3,241 (7.6%)	137,403 (9.9%)	0.08
1 Nov 2021 to 14 Nov 2021							5,026 (11.7%)	153,873 (11.1%)	0.02
15 Nov 2021 to 21 Nov 2021							3,076 (7.2%)	81,766 (5.9%)	0.05
COVID-19 vaccine characteristics									
Unvaccinated	108,819 (99.6%)	1,199,875 (93.9%)	0.32	107,655 (98.5%)	618,152 (80.1%)	0.63	24,816 (57.9%)	208,554 (15.1%)	0.99
Two-dose primary series vaccine schedule									
BNT162b2 only	405 (0.4%)	63,346 (5.0%)	0.29	1,228 (1.1%)	114,572 (14.8%)	0.52	11,514 (26.9%)	702,853 (50.8%)	0.51
mRNA-1273 only	58 (0.1%)	14,950 (1.2%)	0.14	333 (0.3%)	35,662 (4.6%)	0.28	2,491 (5.8%)	201,985 (14.6%)	0.29
BNT162b2 and mRNA-1273	0 (0.0%)	0 (0.0%)	0.00	<=5 (0.0%)	437 (0.1%)	0.03	2,272 (5.3%)	171,748 (12.4%)	0.25
ChAdOx1 only	0 (0.0%)	9 (0.0%)	0.00	23-27 (0.0%)	2,347 (0.3%)	0.07	748 (1.7%)	25,896 (1.9%)	0.01
ChAdOx1 and BNT162b2	0 (0.0%)	0 (0.0%)	0.00	<=5 (0.0%)	615 (0.1%)	0.04	450 (1.1%)	32,895 (2.4%)	0.10
ChAdOx1 and mRNA-1273	0 (0.0%)	0 (0.0%)	0.00	<=5 (0.0%)	241 (0.0%)	0.02	543 (1.3%)	40,175 (2.9%)	0.11
Dosing interval									
<35 days	357 (0.3%)	57,030 (4.5%)	0.27	1,054 (1.0%)	82,998 (10.8%)	0.43	3,210 (7.5%)	181,526 (13.1%)	0.19
35-55 days	106 (0.1%)	21,244 (1.7%)	0.17	410 (0.4%)	33,595 (4.4%)	0.26	5,868 (13.7%)	364,737 (26.4%)	0.32
≥56 days	0 (0.0%)	31 (0.0%)	0.01	125 (0.1%)	37,281 (4.8%)	0.31	8,940 (20.9%)	629,289 (45.5%)	0.54
Time since second dose									
7-59 days	399 (0.4%)	74,378 (5.8%)	0.32	528 (0.5%)	85,933 (11.1%)	0.47	3,658 (8.5%)	373,931 (27.0%)	0.50
60-119 days	64 (0.1%)	3,927 (0.3%)	0.06	941 (0.9%)	56,660 (7.3%)	0.33	8,122 (19.0%)	491,126 (35.5%)	0.38
120-179 days	0 (0.0%)	0 (0.0%)	0.00	120 (0.1%)	11,281 (1.5%)	0.15	5,040 (11.8%)	260,657 (18.8%)	0.20
180-239 days	0 (0.0%)	0 (0.0%)	0.00	0 (0.0%)	0 (0.0%)	0.00	842 (2.0%)	34,028 (2.5%)	0.03

≥240 days	0 (0.0%)	0 (0.0%)	0.00	0 (0.0%)	0 (0.0%)	0.00	356 (0.8%)	15,810 (1.1%)	0.03

[a]Proportion reported, unless stated otherwise.
[b]SD=standardized difference. Standardized differences of >0.10 are considered clinically relevant.
[c]The sum of counts does not equal the column total because of individuals with missing information (<1.0%) for this characteristic.
[d]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.
[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.

Supplementary Table 3. Characteristics of symptomatic individuals tested for SARS-CoV-2 between 11 January 2021 and 21 November 2021 in Ontario, Canada by study subperiod

	11 January to 4 April (Mixed wild-type SARS-CoV-2 & Alpha circulating)			5 April to 27 June (Alpha predominating)			28 June to 21 November (Delta predominating)		
Characteristics	**SARS-CoV-2 positive, n (%)[a] (N=32,504)**	**SARS-CoV-2 negative, n (%)[a] (N=171,864)**	**SD[b]**	**SARS-CoV-2 positive, n (%)[a] (N=38,592)**	**SARS-CoV-2 negative, n (%)[a] (N=111,456)**	**SD[b]**	**SARS-CoV-2 positive, n (%)[a] (N=16,184)**	**SARS-CoV-2 negative, n (%)[a] (N=327,849)**	**SD[b]**
Age (years), mean (standard deviation)	44.91 ± 18.60	42.98 ± 17.63	0.11	39.82 ± 15.88	38.71 ± 15.74	0.07	42.19 ± 17.64	40.87 ± 17.34	0.08
Age group (years)									
16-29	8,452 (26.0%)	46,176 (26.9%)	0.02	12,196 (31.6%)	37,055 (33.2%)	0.04	4,733 (29.2%)	99,076 (30.2%)	0.02
30-39	5,633 (17.3%)	37,630 (21.9%)	0.12	8,531 (22.1%)	29,118 (26.1%)	0.09	3,531 (21.8%)	80,138 (24.4%)	0.06
40-49	5,463 (16.8%)	29,270 (17.0%)	0.01	7,253 (18.8%)	19,304 (17.3%)	0.04	2,735 (16.9%)	53,951 (16.5%)	0.01
50-59	5,694 (17.5%)	26,052 (15.2%)	0.06	6,065 (15.7%)	14,341 (12.9%)	0.08	2,212 (13.7%)	40,117 (12.2%)	0.04
60-69	3,653 (11.2%)	17,658 (10.3%)	0.03	2,882 (7.5%)	6,696 (6.0%)	0.06	1,590 (9.8%)	30,039 (9.2%)	0.02
70-79	2,085 (6.4%)	9,627 (5.6%)	0.03	1,093 (2.8%)	2,569 (2.3%)	0.03	873 (5.4%)	15,893 (4.8%)	0.02
80+	1,524 (4.7%)	5,451 (3.2%)	0.08	572 (1.5%)	2,373 (2.1%)	0.05	510 (3.2%)	8,635 (2.6%)	0.03
Male sex	16,393 (50.4%)	72,898 (42.4%)	0.16	19,496 (50.5%)	49,476 (44.4%)	0.12	7,781 (48.1%)	133,279 (40.7%)	0.15
Any comorbidity	15,713 (48.3%)	82,032 (47.7%)	0.01	15,337 (39.7%)	45,966 (41.2%)	0.03	7,055 (43.6%)	144,951 (44.2%)	0.01
Number of SARS-CoV-2 tests within 3 months prior to 14 Dec 2020									
0	26,884 (82.7%)	120,237 (70.0%)	0.30	32,720 (84.8%)	79,429 (71.3%)	0.33	13,500 (83.4%)	240,124 (73.2%)	0.25
1	4,298 (13.2%)	35,753 (20.8%)	0.20	4,742 (12.3%)	22,410 (20.1%)	0.21	2,000 (12.4%)	62,514 (19.1%)	0.19
≥2	1,322 (4.1%)	15,874 (9.2%)	0.21	1,130 (2.9%)	9,617 (8.6%)	0.25	684 (4.2%)	25,211 (7.7%)	0.15
Receipt of 2019-2020 and/or 2020-2021 influenza vaccination	9,043 (27.8%)	58,143 (33.8%)	0.13	7,339 (19.0%)	27,757 (24.9%)	0.14	3,051 (18.9%)	115,598 (35.3%)	0.38
Public health unit region									
Central East	1,554 (4.8%)	18,465 (10.7%)	0.22	1,822 (4.7%)	11,723 (10.5%)	0.22	1,248 (7.7%)	31,279 (9.5%)	0.07
Central West	5,312 (16.3%)	32,883 (19.1%)	0.07	6,468 (16.8%)	22,593 (20.3%)	0.09	2,781 (17.2%)	51,298 (15.6%)	0.04
Durham	834 (2.6%)	4,667 (2.7%)	0.01	1,495 (3.9%)	4,093 (3.7%)	0.01	1,036 (6.4%)	25,988 (7.9%)	0.06
Eastern	449 (1.4%)	8,935 (5.2%)	0.22	464 (1.2%)	5,272 (4.7%)	0.21	469 (2.9%)	16,102 (4.9%)	0.10
Northern	1,306 (4.0%)	20,350 (11.8%)	0.29	834 (2.2%)	9,677 (8.7%)	0.29	638 (3.9%)	26,158 (8.0%)	0.17
Ottawa	403 (1.2%)	1,119 (0.7%)	0.06	756 (2.0%)	2,308 (2.1%)	0.01	274 (1.7%)	6,478 (2.0%)	0.02
Peel	7,400 (22.8%)	20,786 (12.1%)	0.28	10,333 (26.8%)	14,675 (13.2%)	0.35	2,573 (15.9%)	42,877 (13.1%)	0.08
South West	3,310 (10.2%)	22,490 (13.1%)	0.09	2,202 (5.7%)	11,639 (10.4%)	0.17	3,253 (20.1%)	34,132 (10.4%)	0.27
Toronto	9,005 (27.7%)	29,936 (17.4%)	0.25	10,511 (27.2%)	20,882 (18.7%)	0.20	2,588 (16.0%)	63,374 (19.3%)	0.09
York	2,804 (8.6%)	11,506 (6.7%)	0.07	3,494 (9.1%)	8,049 (7.2%)	0.07	1,270 (7.8%)	28,963 (8.8%)	0.04
Household income quintile									
1 (lowest)	8,263 (25.4%)	30,604 (17.8%)	0.19	9,095 (23.6%)	20,857 (18.7%)	0.12	3,417 (21.1%)	53,956 (16.5%)	0.12
2	6,982 (21.5%)	32,642 (19.0%)	0.06	8,636 (22.4%)	22,168 (19.9%)	0.06	3,192 (19.7%)	61,610 (18.8%)	0.02
3	6,581 (20.2%)	33,055 (19.2%)	0.03	8,704 (22.6%)	22,691 (20.4%)	0.05	3,441 (21.3%)	67,041 (20.4%)	0.02
4	5,813 (17.9%)	35,770 (20.8%)	0.07	6,891 (17.9%)	22,750 (20.4%)	0.07	3,189 (19.7%)	70,714 (21.6%)	0.05
5 (highest)	4,715 (14.5%)	38,969 (22.7%)	0.21	5,039 (13.1%)	22,412 (20.1%)	0.19	2,868 (17.7%)	73,177 (22.3%)	0.12
Essential workers quintile									
1 (0%–32.5%)	4,185 (12.9%)	32,865 (19.1%)	0.17	4,766 (12.3%)	20,158 (18.1%)	0.16	1,821 (11.3%)	63,695 (19.4%)	0.23
2 (32.5%–42.3%)	6,763 (20.8%)	38,305 (22.3%)	0.04	8,093 (21.0%)	24,455 (21.9%)	0.02	3,432 (21.2%)	79,316 (24.2%)	0.07
3 (42.3%–49.8%)	6,537 (20.1%)	35,323 (20.6%)	0.01	7,956 (20.6%)	22,917 (20.6%)	0.00	3,562 (22.0%)	68,393 (20.9%)	0.03
4 (50.0%–57.5%)	6,953 (21.4%)	33,110 (19.3%)	0.05	8,674 (22.5%)	22,351 (20.1%)	0.06	3,521 (21.8%)	61,507 (18.8%)	0.07
5 (57.5%–100%)	7,789 (24.0%)	30,930 (18.0%)	0.15	8,844 (22.9%)	20,717 (18.6%)	0.11	3,689 (22.8%)	52,784 (16.1%)	0.17
Persons per dwelling quintile									

1 (0–2.1)	4,037 (12.4%)	32,965 (19.2%)	0.19	3,990 (10.3%)	19,537 (17.5%)	0.21	2,228 (13.8%)	54,016 (16.5%)	0.08
2 (2.2–2.4)	4,072 (12.5%)	32,953 (19.2%)	0.18	4,365 (11.3%)	19,567 (17.6%)	0.18	2,627 (16.2%)	54,618 (16.7%)	0.01
3 (2.5–2.6)	3,511 (10.8%)	23,332 (13.6%)	0.08	3,694 (9.6%)	14,109 (12.7%)	0.10	1,967 (12.2%)	41,061 (12.5%)	0.01
4 (2.7–3.0)	7,884 (24.3%)	40,589 (23.6%)	0.01	9,028 (23.4%)	26,597 (23.9%)	0.01	4,189 (25.9%)	81,121 (24.7%)	0.03
5 (3.1–5.7)	12,714 (39.1%)	40,647 (23.7%)	0.34	17,247 (44.7%)	30,744 (27.6%)	0.36	5,008 (30.9%)	94,767 (28.9%)	0.04
Self-identified visible minority quintile									
1 (0.0%–2.2%)	2,545 (7.8%)	32,101 (18.7%)	0.32	2,309 (6.0%)	18,207 (16.3%)	0.33	2,205 (13.6%)	49,389 (15.1%)	0.04
2 (2.2%–7.5%)	3,275 (10.1%)	34,523 (20.1%)	0.28	3,137 (8.1%)	20,066 (18.0%)	0.30	2,580 (15.9%)	57,022 (17.4%)	0.04
3 (7.5%–18.7%)	4,380 (13.5%)	32,930 (19.2%)	0.15	4,577 (11.9%)	19,838 (17.8%)	0.17	2,876 (17.8%)	60,796 (18.5%)	0.02
4 (18.7%–43.5%)	6,677 (20.5%)	34,740 (20.2%)	0.01	7,938 (20.6%)	22,800 (20.5%)	0.00	3,574 (22.1%)	70,143 (21.4%)	0.02
5 (43.5%–100%)	15,350 (47.2%)	36,242 (21.1%)	0.57	20,372 (52.8%)	29,690 (26.6%)	0.55	4,790 (29.6%)	88,348 (26.9%)	0.06
Biweekly period of test									
11 Jan 2021 to 24 Jan 2021	5,622 (17.3%)	26,772 (15.6%)	0.05						
25 Jan 2021 to 7 Feb 2021	4,105 (12.6%)	24,104 (14.0%)	0.04						
8 Feb 2021 to 21 Feb 2021	4,023 (12.4%)	24,947 (14.5%)	0.06	N/A	N/A				
22 Feb 2021 to 7 Mar 2021	3,936 (12.1%)	30,968 (18.0%)	0.17						
8 Mar 2021 to 21 Mar 2021	5,695 (17.5%)	31,775 (18.5%)	0.03						
22 Mar 2021 to 4 Apr 2021	9,123 (28.1%)	33,298 (19.4%)	0.21						
5 Apr 2021 to 18 Apr 2021				15,326 (39.7%)	38,141 (34.2%)	0.11	N/A	N/A	
19 Apr 2021 to 2 May 2021				11,717 (30.4%)	32,024 (28.7%)	0.04			
3 May 2021 to 16 May 2021				6,748 (17.5%)	19,118 (17.2%)	0.01			
17 May 2021 to 30 May 2021				2,945 (7.6%)	8,990 (8.1%)	0.02			
31 May 2021 to 13 Jun 2021				1,243 (3.2%)	6,157 (5.5%)	0.11			
14 Jun 2021 to 27 Jun 2021				613 (1.6%)	7,026 (6.3%)	0.24			
28 Jun 2021 to 11 Jul 2021							388 (2.4%)	8,013 (2.4%)	0.00
12 Jul 2021 to 25 Jul 2021	N/A	N/A					331 (2.0%)	13,401 (4.1%)	0.12
26 Jul 2021 to 8 Aug 2021							686 (4.2%)	22,110 (6.7%)	0.11
9 Aug 2021 to 22 Aug 2021							1,834 (11.3%)	30,438 (9.3%)	0.07
23 Aug 2021 to 5 Sep 2021				N/A			2,377 (14.7%)	32,621 (10.0%)	0.14
6 Sep 2021 to 19 Sep 2021					N/A		2,330 (14.4%)	33,868 (10.3%)	0.12
20 Sep 2021 to 3 Oct 2021							1,862 (11.5%)	44,550 (13.6%)	0.06
4 Oct 2021 to 17 Oct 2021							1,687 (10.4%)	43,123 (13.2%)	0.08
18 Oct 2021 to 31 Oct 2021							1,250 (7.7%)	37,311 (11.4%)	0.12
1 Nov 2021 to 14 Nov 2021							2,117 (13.1%)	41,259 (12.6%)	0.01
15 Nov 2021 to 21 Nov 2021							1,322 (8.2%)	21,155 (6.5%)	0.07
COVID-19 vaccine characteristics									
Unvaccinated	32,472 (99.9%)	168,771 (98.2%)	0.18	38,324 (99.3%)	100,564 (90.2%)	0.42	9,700 (59.9%)	36,257 (11.1%)	1.19
Two-dose primary series vaccine schedule									
BNT162b2 only	27-31 (0.1%)	2,587 (1.5%)	0.16	209 (0.5%)	8,188 (7.3%)	0.36	4,216 (26.1%)	175,033 (53.4%)	0.58
mRNA-1273 only	<=5 (0.0%)	506 (0.3%)	0.07	53 (0.1%)	2,363 (2.1%)	0.19	931 (5.8%)	50,570 (15.4%)	0.32
BNT162b2 and mRNA-1273	0 (0.0%)	0 (0.0%)	0.00	<=5 (0.0%)	48 (0.0%)	<0.03	686 (4.2%)	42,846 (13.1%)	0.32
ChAdOx1 only	0 (0.0%)	0 (0.0%)	0.00	<=5 (0.0%)	228 (0.2%)	0.06	315 (1.9%)	5,747 (1.8%)	0.01
ChAdOx1 and BNT162b2	0 (0.0%)	0 (0.0%)	0.00	0 (0.0%)	43 (0.0%)	0.03	160 (1.0%)	7,845 (2.4%)	0.11
ChAdOx1 and mRNA-1273	0 (0.0%)	0 (0.0%)	0.00	0 (0.0%)	22 (0.0%)	0.02	176 (1.1%)	9,551 (2.9%)	0.13
Dosing interval									
<35 days	23 (0.1%)	2,205 (1.3%)	0.15	171 (0.4%)	5,371 (4.8%)	0.28	1,116 (6.9%)	38,685 (11.8%)	0.17
35-55 days	9 (0.0%)	883-887 (0.5%)	0.09	67 (0.2%)	2,929 (2.6%)	0.21	2,010 (12.4%)	102,415 (31.2%)	0.47
≥56 days	0 (0.0%)	<=5 (0.0%)	0.01	30 (0.1%)	2,592 (2.3%)	0.21	3,358 (20.7%)	150,492 (45.9%)	0.55
Time since second dose									
7-59 days	27-31 (0.1%)	2,867 (1.7%)	0.17	114 (0.3%)	6,075 (5.5%)	0.31	1,063 (6.6%)	76,999 (23.5%)	0.49
60-119 days	<=5 (0.0%)	226 (0.1%)	0.05	133 (0.3%)	3,986 (3.6%)	0.23	2,927 (18.1%)	135,846 (41.4%)	0.53
120-179 days	0 (0.0%)	0 (0.0%)	0.00	21 (0.1%)	831 (0.7%)	0.11	2,045 (12.6%)	66,667 (20.3%)	0.21
180-239 days	0 (0.0%)	0 (0.0%)	0.00	0 (0.0%)	0 (0.0%)	0.00	317 (2.0%)	7,548 (2.3%)	0.02

≥240 days	0 (0.0%)	0 (0.0%)	0.00	0 (0.0%)	0 (0.0%)	0.00	132 (0.8%)	4,532 (1.4%)	0.05

[a]Proportion reported, unless stated otherwise.
[b]SD=standardized difference. Standardized differences of >0.10 are considered clinically relevant.
[c]The sum of counts does not equal the column total because of individuals with missing information (<1.0%) for this characteristic.
[d]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.
[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.

Supplementary Table 4. Characteristics of test-positive cases with severe outcomes and symptomatic test-negative controls between 11 January 2021 and 21 November 2021 in Ontario, Canada by study subperiod

	11 January to 4 April (Mixed wild-type SARS-CoV-2 & Alpha circulating)			5 April to 27 June (Alpha predominating)			28 June to 21 November (Delta predominating)		
Characteristics	**SARS-CoV-2 positive, n (%)[a] (N=5,563)**	**SARS-CoV-2 negative, n (%)[a] (N=171,864)**	**SD[b]**	**SARS-CoV-2 positive, n (%)[a] (N=5,611)**	**SARS-CoV-2 negative, n (%)[a] (N=111,456)**	**SD[b]**	**SARS-CoV-2 positive, n (%)[a] (N=2,563)**	**SARS-CoV-2 negative, n (%)[a] (N=327,849)**	**SD[b]**
Age (years), mean (standard deviation)	63.91 ± 17.65	42.98 ± 17.63	1.19	55.71 ± 16.96	38.71 ± 15.74	1.04	58.02 ± 18.45	40.87 ± 17.34	0.96
Age group (years)									
16-29	216 (3.9%)	46,176 (26.9%)	0.67	415 (7.4%)	37,055 (33.2%)	0.68	178 (6.9%)	99,076 (30.2%)	0.63
30-39	376 (6.8%)	37,630 (21.9%)	0.44	653 (11.6%)	29,118 (26.1%)	0.38	300 (11.7%)	80,138 (24.4%)	0.34
40-49	580 (10.4%)	29,270 (17.0%)	0.19	862 (15.4%)	19,304 (17.3%)	0.05	378 (14.7%)	53,951 (16.5%)	0.05
50-59	950 (17.1%)	26,052 (15.2%)	0.05	1,335 (23.8%)	14,341 (12.9%)	0.29	453 (17.7%)	40,117 (12.2%)	0.15
60-69	1,112 (20.0%)	17,658 (10.3%)	0.27	1,162 (20.7%)	6,696 (6.0%)	0.44	509 (19.9%)	30,039 (9.2%)	0.31
70-79	1,134 (20.4%)	9,627 (5.6%)	0.45	705 (12.6%)	2,569 (2.3%)	0.40	393 (15.3%)	15,893 (4.8%)	0.35
80+	1,195 (21.5%)	5,451 (3.2%)	0.58	479 (8.5%)	2,373 (2.1%)	0.29	352 (13.7%)	8,635 (2.6%)	0.41
Male sex	3,142 (56.5%)	72,898 (42.4%)	0.28	3,054 (54.4%)	49,476 (44.4%)	0.20	1,412 (55.1%)	133,279 (40.7%)	0.29
Any comorbidity	4,471 (80.4%)	82,032 (47.7%)	0.72	3,837 (68.4%)	45,966 (41.2%)	0.57	1,753 (68.4%)	144,951 (44.2%)	0.50
Number of SARS-CoV-2 tests within 3 months prior to 14 Dec 2020									
0	4,593 (82.6%)	120,237 (70.0%)	0.30	4,923 (87.7%)	79,429 (71.3%)	0.42	2,247 (87.7%)	240,124 (73.2%)	0.37
1	657 (11.8%)	35,753 (20.8%)	0.25	514 (9.2%)	22,410 (20.1%)	0.31	230 (9.0%)	62,514 (19.1%)	0.29
≥2	313 (5.6%)	15,874 (9.2%)	0.14	174 (3.1%)	9,617 (8.6%)	0.24	86 (3.4%)	25,211 (7.7%)	0.19
Receipt of 2019-2020 and/or 2020-2021 influenza vaccination	2,423 (43.6%)	58,143 (33.8%)	0.20	1,531 (27.3%)	27,757 (24.9%)	0.05	556 (21.7%)	115,598 (35.3%)	0.30
Public health unit region									
Central East	203 (3.6%)	18,465 (10.7%)	0.28	193 (3.4%)	11,723 (10.5%)	0.28	113 (4.4%)	31,279 (9.5%)	0.20
Central West	833 (15.0%)	32,883 (19.1%)	0.11	861 (15.3%)	22,593 (20.3%)	0.13	599 (23.4%)	51,298 (15.6%)	0.20
Durham	234 (4.2%)	4,667 (2.7%)	0.08	280 (5.0%)	4,093 (3.7%)	0.06	83 (3.2%)	25,988 (7.9%)	0.21
Eastern	140 (2.5%)	8,935 (5.2%)	0.14	136 (2.4%)	5,272 (4.7%)	0.12	114 (4.4%)	16,102 (4.9%)	0.02
Northern	215 (3.9%)	20,350 (11.8%)	0.30	160 (2.9%)	9,677 (8.7%)	0.25	107 (4.2%)	26,158 (8.0%)	0.16
Ottawa	289 (5.2%)	1,119 (0.7%)	0.27	362 (6.5%)	2,308 (2.1%)	0.22	133 (5.2%)	6,478 (2.0%)	0.17
Peel	589 (10.6%)	20,786 (12.1%)	0.05	658 (11.7%)	14,675 (13.2%)	0.04	276 (10.8%)	42,877 (13.1%)	0.07
South West	388 (7.0%)	22,490 (13.1%)	0.20	390 (7.0%)	11,639 (10.4%)	0.12	456 (17.8%)	34,132 (10.4%)	0.21
Toronto	2,176 (39.1%)	29,936 (17.4%)	0.50	2,120 (37.8%)	20,882 (18.7%)	0.43	455 (17.8%)	63,374 (19.3%)	0.04
York	477 (8.6%)	11,506 (6.7%)	0.07	414 (7.4%)	8,049 (7.2%)	0.01	217 (8.5%)	28,963 (8.8%)	0.01
Household income quintile									
1 (lowest)	1,913 (34.4%)	30,604 (17.8%)	0.38	1,899 (33.8%)	20,857 (18.7%)	0.35	699 (27.3%)	53,956 (16.5%)	0.26
2	1,178 (21.2%)	32,642 (19.0%)	0.05	1,224 (21.8%)	22,168 (19.9%)	0.05	544 (21.2%)	61,610 (18.8%)	0.06
3	1,028 (18.5%)	33,055 (19.2%)	0.02	1,097 (19.6%)	22,691 (20.4%)	0.02	485 (18.9%)	67,041 (20.4%)	0.04
4	777 (14.0%)	35,770 (20.8%)	0.18	749 (13.3%)	22,750 (20.4%)	0.19	467 (18.2%)	70,714 (21.6%)	0.08
5 (highest)	648 (11.6%)	38,969 (22.7%)	0.30	603 (10.7%)	22,412 (20.1%)	0.26	356 (13.9%)	73,177 (22.3%)	0.22
Essential workers quintile									
1 (0%–32.5%)	884 (15.9%)	32,865 (19.1%)	0.09	810 (14.4%)	20,158 (18.1%)	0.10	309 (12.1%)	63,695 (19.4%)	0.20
2 (32.5%–42.3%)	1,096 (19.7%)	38,305 (22.3%)	0.06	1,031 (18.4%)	24,455 (21.9%)	0.09	520 (20.3%)	79,316 (24.2%)	0.09
3 (42.3%–49.8%)	1,051 (18.9%)	35,323 (20.6%)	0.04	1,133 (20.2%)	22,917 (20.6%)	0.01	530 (20.7%)	68,393 (20.9%)	0.00
4 (50.0%–57.5%)	1,171 (21.0%)	33,110 (19.3%)	0.04	1,186 (21.1%)	22,351 (20.1%)	0.03	560 (21.8%)	61,507 (18.8%)	0.08
5 (57.5%–100%)	1,335 (24.0%)	30,930 (18.0%)	0.15	1,410 (25.1%)	20,717 (18.6%)	0.16	624 (24.3%)	52,784 (16.1%)	0.21
Persons per dwelling quintile									

1 (0–2.1)	1,138 (20.5%)	32,965 (19.2%)	0.03	983 (17.5%)	19,537 (17.5%)	0.00	480 (18.7%)	54,016 (16.5%)	0.06
2 (2.2–2.4)	834 (15.0%)	32,953 (19.2%)	0.11	839 (15.0%)	19,567 (17.6%)	0.07	437 (17.1%)	54,618 (16.7%)	0.01
3 (2.5–2.6)	631 (11.3%)	23,332 (13.6%)	0.07	606 (10.8%)	14,109 (12.7%)	0.06	339 (13.2%)	41,061 (12.5%)	0.02
4 (2.7–3.0)	1,291 (23.2%)	40,589 (23.6%)	0.01	1,379 (24.6%)	26,597 (23.9%)	0.02	625 (24.4%)	81,121 (24.7%)	0.01
5 (3.1–5.7)	1,637 (29.4%)	40,647 (23.7%)	0.13	1,759 (31.3%)	30,744 (27.6%)	0.08	663 (25.9%)	94,767 (28.9%)	0.07
Self-identified visible minority quintile									
1 (0.0%–2.2%)	389 (7.0%)	32,101 (18.7%)	0.35	377 (6.7%)	18,207 (16.3%)	0.30	374 (14.6%)	49,389 (15.1%)	0.01
2 (2.2%–7.5%)	528 (9.5%)	34,523 (20.1%)	0.30	475 (8.5%)	20,066 (18.0%)	0.28	380 (14.8%)	57,022 (17.4%)	0.07
3 (7.5%–18.7%)	789 (14.2%)	32,930 (19.2%)	0.13	728 (13.0%)	19,838 (17.8%)	0.13	501 (19.5%)	60,796 (18.5%)	0.03
4 (18.7%–43.5%)	1,298 (23.3%)	34,740 (20.2%)	0.08	1,383 (24.6%)	22,800 (20.5%)	0.10	605 (23.6%)	70,143 (21.4%)	0.05
5 (43.5%–100%)	2,533 (45.5%)	36,242 (21.1%)	0.54	2,607 (46.5%)	29,690 (26.6%)	0.42	683 (26.6%)	88,348 (26.9%)	0.01
Biweekly period of test									
11 Jan 2021 to 24 Jan 2021	1,098 (19.7%)	26,772 (15.6%)	0.11						
25 Jan 2021 to 7 Feb 2021	790 (14.2%)	24,104 (14.0%)	0.01						
8 Feb 2021 to 21 Feb 2021	660 (11.9%)	24,947 (14.5%)	0.08	N/A	N/A				
22 Feb 2021 to 7 Mar 2021	658 (11.8%)	30,968 (18.0%)	0.17						
8 Mar 2021 to 21 Mar 2021	935 (16.8%)	31,775 (18.5%)	0.04						
22 Mar 2021 to 4 Apr 2021	1,422 (25.6%)	33,298 (19.4%)	0.15						
5 Apr 2021 to 18 Apr 2021				2,065 (36.8%)	38,141 (34.2%)	0.05	N/A	N/A	
19 Apr 2021 to 2 May 2021				1,576 (28.1%)	32,024 (28.7%)	0.01			
3 May 2021 to 16 May 2021				998 (17.8%)	19,118 (17.2%)	0.02			
17 May 2021 to 30 May 2021				524 (9.3%)	8,990 (8.1%)	0.05			
31 May 2021 to 13 Jun 2021				286 (5.1%)	6,157 (5.5%)	0.02			
14 Jun 2021 to 27 Jun 2021				162 (2.9%)	7,026 (6.3%)	0.16			
28 Jun 2021 to 11 Jul 2021							126 (4.9%)	8,013 (2.4%)	0.13
12 Jul 2021 to 25 Jul 2021							83 (3.2%)	13,401 (4.1%)	0.05
26 Jul 2021 to 8 Aug 2021	N/A	N/A					135 (5.3%)	22,110 (6.7%)	0.06
9 Aug 2021 to 22 Aug 2021							279 (10.9%)	30,438 (9.3%)	0.05
23 Aug 2021 to 5 Sep 2021							391 (15.3%)	32,621 (10.0%)	0.16
6 Sep 2021 to 19 Sep 2021				N/A	N/A		350 (13.7%)	33,868 (10.3%)	0.10
20 Sep 2021 to 3 Oct 2021							278 (10.8%)	44,550 (13.6%)	0.08
4 Oct 2021 to 17 Oct 2021							291 (11.4%)	43,123 (13.2%)	0.05
18 Oct 2021 to 31 Oct 2021							200 (7.8%)	37,311 (11.4%)	0.12
1 Nov 2021 to 14 Nov 2021							283 (11.0%)	41,259 (12.6%)	0.05
15 Nov 2021 to 21 Nov 2021							147 (5.7%)	21,155 (6.5%)	0.03
COVID-19 vaccine characteristics									
Unvaccinated	5,554 (99.8%)	168,771 (98.2%)	0.17	5,540 (98.7%)	100,564 (90.2%)	0.38	2,035 (79.4%)	36,257 (11.1%)	1.89
Two-dose primary series vaccine schedule									
BNT162b2 only	4-8 (0.1%)	2,587 (1.5%)	0.15	47 (0.8%)	8,188 (7.3%)	0.33	377 (14.7%)	175,033 (53.4%)	0.89
mRNA-1273 only	<=5 (0.0%)	506 (0.3%)	0.07	19-23 (0.4%)	2,363 (2.1%)	<0.16	66 (2.6%)	50,570 (15.4%)	0.46
BNT162b2 and mRNA-1273	0 (0.0%)	0 (0.0%)	0.00	0 (0.0%)	48 (0.0%)	0.03	40 (1.6%)	42,846 (13.1%)	0.45
ChAdOx1 only	0 (0.0%)	0 (0.0%)	0.00	<=5 (0.1%)	228 (0.2%)	<0.06	31 (1.2%)	5,747 (1.8%)	0.04
ChAdOx1 and BNT162b2	0 (0.0%)	0 (0.0%)	0.00	0 (0.0%)	43 (0.0%)	0.03	8 (0.3%)	7,845 (2.4%)	0.18
ChAdOx1 and mRNA-1273	0 (0.0%)	0 (0.0%)	0.00	0 (0.0%)	22 (0.0%)	0.02	6 (0.2%)	9,551 (2.9%)	0.22
Dosing interval									
<35 days	9 (0.2%)	2,205 (1.3%)	0.13	47 (0.8%)	5,371 (4.8%)	0.24	119 (4.6%)	38,685 (11.8%)	0.26
35-55 days	0 (0.0%)	883-887 (0.5%)	0.10	8 (0.1%)	2,929 (2.6%)	0.21	65 (2.5%)	102,415 (31.2%)	0.83
≥56 days	0 (0.0%)	<=5 (0.0%)	0.01	16 (0.3%)	2,592 (2.3%)	0.18	344 (13.4%)	150,492 (45.9%)	0.76
Time since second dose									
7-59 days	9 (0.2%)	2,867 (1.7%)	0.16	57 (1.0%)	6,075 (5.5%)	0.25	79 (3.1%)	76,999 (23.5%)	0.63
60-119 days	0 (0.0%)	226 (0.1%)	0.05	14 (0.2%)	3,986 (3.6%)	0.24	206 (8.0%)	135,846 (41.4%)	0.84
120-179 days	0 (0.0%)	0 (0.0%)	0.00	0 (0.0%)	831 (0.7%)	0.12	199 (7.8%)	66,667 (20.3%)	0.37
180-239 days	0 (0.0%)	0 (0.0%)	0.00	0 (0.0%)	0 (0.0%)	0.00	39-44 (1.5%)	7,548 (2.3%)	<0.06

≥240 days	0 (0.0%)	0 (0.0%)	0.00	0 (0.0%)	0 (0.0%)	0.00	<=5 (0.2%)	4,532 (1.4%)	<0.16

[a]Proportion reported, unless stated otherwise.
[b]SD=standardized difference. Standardized differences of >0.10 are considered clinically relevant.
[c]The sum of counts does not equal the column total because of individuals with missing information (<1.0%) for this characteristic.
[d]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.
[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.

Supplementary Table 5. Distribution of two-dose primary series vaccine regimens and dosing intervals between the study cohort (tested for SARS-CoV-2) and non-tested[a] community-dwelling Ontario population (aged ≥16 years) between 11 January 2021 to 21 November 2021

VARIABLE	Aged 16-69 years			Aged ≥70 years		
	Tested[b] (N=1,111,907)	Not tested (N=2,496,283)	SD[c]	Tested[b] (N=192,107)	Not tested (N=570,671)	SD
Two-dose primary series vaccine schedule						
BNT162b2 only	665,410 (59.8%)	1,368,572 (54.8%)	0.10	132,125 (68.8%)	403,308 (70.7%)	0.04
mRNA-1273 only	190,435 (17.1%)	432,322 (17.3%)	0.01	38,965 (20.3%)	82,713 (14.5%)	0.15
BNT162b2 and mRNA-1273	157,426 (14.2%)	407,445 (16.3%)	0.06	16,852 (8.8%)	70,270 (12.3%)	0.12
ChAdOx1 only	26,151 (2.4%)	78,356 (3.1%)	0.05	2,066 (1.1%)	6,717 (1.2%)	0.01
ChAdOx1 and BNT162b2	32,473 (2.9%)	93,258 (3.7%)	0.05	1,244 (0.6%)	4,302 (0.8%)	0.01
ChAdOx1 and mRNA-1273	40,012 (3.6%)	116,330 (4.7%)	0.05	855 (0.4%)	3,361 (0.6%)	0.02
Dosing interval (days), mean (standard deviation)						
mRNA vaccine-only schedules	53.83 ± 22.87	56.74 ± 20.79	0.13	66.83 ± 27.82	77.13 ± 20.67	0.42
ChAdOx1-containing schedules	69.99 ± 13.29	71.80 ± 12.90	0.14	76.65 ± 14.87	77.36 ± 13.60	0.05

[a]We created a comparison group of all community-dwelling individuals aged ≥16 years in Ontario who were not tested between 11 January and 21 November 2021. We used the distribution of index dates from infection study population and assigned pseudo-index dates to the comparison group to determine the vaccination status as of the pseudo-index date. This table includes individuals who completed their two-dose primary series ≥7 days before their pseudo-index date.

[b]The total number of vaccinated tested individuals (n=1,304,014) is less that the total number of vaccinated individuals in Table S2 (n=1,427,801) because vaccinated test-negative individuals who were included in >1 subperiod are only counted once in this table.

[c]SD=standardized difference. Standardized differences of >0.10 are considered clinically relevant.

Supplementary Table 6. Number of test-positive cases and test-negative controls contributing to VE estimates for two doses of any mRNA vaccine schedules in Table 1

Time since second dose (days)	Number of test-positive cases ; test-negative controls[a]								
	Any infection	Symptomatic infection	Severe outcomes	Any infection	Symptomatic infection	Severe outcomes	Any infection	Symptomatic infection	Severe outcomes
	Overall								
7-59	245,600 ; 2,528,503	81,625 ; 385,967	13,262 ; 385,967						
60-119	249,584 ; 2,534,409	83,247 ; 434,344	13,327 ; 434,344						
120-179	245,793 ; 2,272,745	82,295 ; 366,550	13,313 ; 366,550						
180-239	242,130 ; 2,060,412	80,813 ; 313,117	13,168 ; 313,117						
≥240	241,646 ; 2,042,389	80,628 ; 310,123	ǂ						
	BNT162b2 only			**mRNA-1273 only**			**Mixed mRNA vaccine regimen**		
7-59	244,442 ; 2,371,889	81,348 ; 358,618	13,220 ; 358,618	241,947 ; 2,122,693	80,667 ; 320,676	13,163 ; 320,676	241,791 ; 2,087,083	80,602 ; 317,857	13,137 ; 317,857
60-119	247,097 ; 2,354,726	82,481 ; 387,771	13,284 ; 387,771	242,597 ; 2,124,526	80,890 ; 329,836	13,150 ; 329,836	242,470 ; 2,108,319	80,868 ; 327,921	13,151 ; 327,921
120-179	244,468 ; 2,193,362	81,753 ; 346,043	13,279 ; 346,043	242,022 ; 2,076,024	80,829 ; 317,799	13,153 ; 317,799	241,883 ; 2,056,521	80,705 ; 313,892	13,139 ; 313,892
180-239	241,974 ; 2,053,096	80,739 ; 311,668	13,161 ; 311,668	241,446 ; 2,033,893	80,570 ; 307,041	13,136 ; 307,041	ǂ	ǂ	ǂ
≥240	241,616 ; 2,040,603	80,613 ; 309,668	ǂ	241,320 ; 2,028,366	80,511 ; 306,047	ǂ	ǂ	ǂ	ǂ
	Aged 16-69 years			**Aged 16-69 years with a comorbidity**			**Aged 16-69 years with no comorbidities**		
7-59	232,989 ; 2,270,979	75,714 ; 360,577	9,301 ; 360,577	87,547 ; 931,905	29,846 ; 146,180	5,891 ; 146,180	145,442 ; 1,339,074	45,868 ; 214,397	3,410 ; 214,397
60-119	236,560 ; 2,284,921	77,132 ; 405,858	9,326 ; 405,858	89,025 ; 935,538	30,437 ; 164,402	5,905 ; 164,402	147,535 ; 1,349,383	46,695 ; 241,456	3,421 ; 241,456
120-179	232,849 ; 2,051,762	76,170 ; 341,025	9,288 ; 341,025	87,636 ; 843,441	30,085 ; 140,315	5,885 ; 140,315	145,213 ; 1,208,321	46,085 ; 200,710	ǂ
180-239	229,790 ; 1,878,287	74,959 ; 293,997	9,251 ; 293,997	86,379 ; 768,492	29,565 ; 120,221	5,850 ; 120,221	143,411 ; 1,109,795	45,394 ; 173,776	ǂ
≥240	229,426 ; 1,865,701	74,825 ; 291,713	ǂ	86,189 ; 762,361	29,494 ; 119,094	ǂ	143,237 ; 1,103,340	45,331 ; 172,619	ǂ
	Aged ≥70 years			**Aged ≥70 years with a comorbidity**			**Aged ≥70 years with no comorbidities**		
7-59	12,611 ; 257,524	5,911 ; 25,390	3,961 ; 25,390	11,414 ; 234,795	5,442 ; 23,426	3,733 ; 23,426	1,197 ; 22,729	ǂ	ǂ
60-119	13,024 ; 249,488	6,115 ; 28,486	4,001 ; 28,486	11,778 ; 226,952	5,628 ; 26,119	3,774 ; 26,119	1,246 ; 22,536	487 ; 2,367	ǂ
120-179	12,944 ; 220,983	6,125 ; 25,525	4,025 ; 25,525	11,709 ; 201,034	5,632 ; 23,436	3,796 ; 23,436	1,235 ; 19,949	493 ; 2,089	ǂ
180-239	12,340 ; 182,125	5,854 ; 19,120	3,917 ; 19,120	11,161 ; 165,663	5,389 ; 17,641	3,692 ; 17,641	1,179 ; 16,462	ǂ	ǂ
≥240	12,220 ; 176,688	5,803 ; 18,410	ǂ	11,045 ; 160,435	5,338 ; 16,946	ǂ	1,175 ; 16,253	ǂ	ǂ
	Aged 16-69 years (0 prior SARS-CoV-2 tests)			**Aged 16-69 years (1 prior SARS-CoV-2 test)**			**Aged 16-69 years (≥2 prior SARS-CoV-2 tests)**		

7-59	193,665 ; 1,614,161	63,572 ; 259,928	7,978 ; 259,928	29,958 ; 384,699	9,658 ; 73,149	961 ; 73,149	9,366 ; 272,119	2,484 ; 27,500	362 ; 27,500
60-119	196,276 ; 1,652,174	64,695 ; 292,869	8,002 ; 292,869	30,562 ; 394,838	9,867 ; 82,326	967 ; 82,326	9,722 ; 237,909	2,570 ; 30,663	ǂ
120-179	193,599 ; 1,479,557	63,898 ; 244,274	7,972 ; 244,274	29,961 ; 353,458	9,723 ; 69,819	956 ; 69,819	9,289 ; 218,747	2,549 ; 26,932	ǂ
180-239	191,222 ; 1,359,076	62,939 ; 210,180	7,944 ; 210,180	29,453 ; 323,054	9,523 ; 60,097	ǂ	9,115 ; 196,157	2,497 ; 23,720	ǂ
≥240	191,009 ; 1,352,969	62,856 ; 208,874	ǂ	29,367 ; 320,613	9,485 ; 59,527	ǂ	9,050 ; 192,119	2,484 ; 23,312	ǂ
	Aged ≥70 years (0 prior SARS-CoV-2 tests)			**Aged ≥70 years (1 prior SARS-CoV-2 test)**			**Aged ≥70 years (≥2 prior SARS-CoV-2 tests)**		
7-59	10,966 ; 193,507	5,167 ; 20,166	3,406 ; 20,166	1,074 ; 32,175	515 ; 3,302	ǂ	571 ; 31,842	229 ; 1,922	179 ; 1,922
60-119	11,346 ; 192,426	5,340 ; 22,886	3,438 ; 22,886	1,115 ; 30,711	542 ; 3,592	387 ; 3,592	563 ; 26,351	233 ; 2,008	176 ; 2,008
120-179	11,287 ; 170,186	5,357 ; 20,399	3,459 ; 20,399	1,114 ; 27,354	539 ; 3,286	389 ; 3,286	543 ; 23,443	229 ; 1,840	177 ; 1,840
180-239	10,753 ; 138,340	5,108 ; 14,998	3,362 ; 14,998	1,052 ; 23,486	515 ; 2,525	ǂ	535 ; 20,299	231 ; 1,597	177 ; 1,597
≥240	10,666 ; 135,471	ǂ	ǂ	ǂ	ǂ	ǂ	ǂ	ǂ	ǂ
	Dosing interval 15-34 days			**Dosing interval 35-55 days**			**Dosing interval ≥56 days**		
7-59	242,582 ; 2,162,182	80,783 ; 319,494	13,188 ; 319,494	242,740 ; 2,176,980	80,859 ; 334,014	13,144 ; 334,014	242,858 ; 2,242,503	80,975 ; 343,643	13,188 ; 343,643
60-119	243,058 ; 2,125,620	80,917 ; 321,587	13,170 ; 321,587	244,277 ; 2,200,516	81,499 ; 356,699	13,155 ; 356,699	244,829 ; 2,261,435	81,823 ; 367,242	13,260 ; 367,242
120-179	242,061 ; 2,079,720	80,780 ; 314,194	13,166 ; 314,194	242,757 ; 2,102,547	81,062 ; 327,518	13,151 ; 327,518	243,555 ; 2,143,640	81,445 ; 336,022	13,254 ; 336,022
180-239	241,824 ; 2,048,711	80,710 ; 310,171	13,162 ; 310,171	241,563 ; 2,037,207	80,587 ; 308,239	ǂ	241,323 ; 2,027,656	80,508 ; 305,891	ǂ
≥240	241,522 ; 2,037,380	80,592 ; 308,687	ǂ	241,414 ; 2,031,588	80,532 ; 307,028	ǂ	ǂ	ǂ	ǂ
	11 Jan to 4 Apr 2021 (Mixed wild-type SARS-CoV-2 & Alpha circulating)			**5 Apr to 27 Jun 2021 (Alpha predominating)**			**28 Jun to 21 Nov 2021 (Delta predominating)**		
7-59	109,218 ; 1,274,244	32,501 ; 171,638	5,563 ; 171,638	108,158 ; 700,928	38,433 ; 106,351	5,593 ; 106,351	28,224 ; 553,331	10,691 ; 107,978	2,106 ; 107,978
60-119	108,883 ; 1,203,802	ǂ	ǂ	108,595 ; 674,766	38,457 ; 104,545	5,554 ; 104,545	32,106 ; 655,841	12,315 ; 160,802	2,219 ; 160,802
120-179	ǂ	ǂ	ǂ	107,775 ; 629,433	38,345 ; 101,395	ǂ	29,199 ; 443,437	11,478 ; 96,384	2,219 ; 96,384
180-239	ǂ	ǂ	ǂ	ǂ	ǂ	ǂ	25,656 ; 242,385	10,017 ; 43,782	2,074 ; 43,782
≥240	ǂ	ǂ	ǂ	ǂ	ǂ	ǂ	25,172 ; 224,362	9,832 ; 40,788	ǂ

[a]Each cell contains the total number of test-positive cases and test-negative controls (vaccinated and unvaccinated) that were used to calculate the corresponding VE estimate in Table S6. For each set of VE estimates in an analysis (e.g., VE estimates for 7-59, 60-119, 120-179, 180-239, and ≥240 days under the Overall header), there is only one unvaccinated group, which is included in the counts for each VE estimate. Therefore, the sum of the counts does not equal the total number of cases and controls.

ǂCounts were suppressed because they are small cell counts (≤5, which cannot be disclosed because of privacy and data obligations) or they were either 0 vaccinated test-positive cases and/or 0 vaccinated test-negative controls (this information could subsequently be used to disclose suppressed small cells in combination with other estimates in the table).

Supplementary Table 7. Number of test-positive cases and test-negative controls contributing to VE estimates for any two-dose ChAdOx1-containing schedules in Table 1

Time since second dose (days)	Number of test-positive cases ; test-negative controls[a]								
	Any infection	Symptomatic infection	Severe outcomes	Any infection	Symptomatic infection	Severe outcomes	Any infection	Symptomatic infection	Severe outcomes
	Overall								
7-59	241,565 ; 2,058,901	80,573 ; 311,158	13,141 ; 311,158						
60-119	242,123 ; 2,070,466	80,808 ; 316,898	13,151 ; 316,898						
120-179	241,947 ; 2,052,355	80,763 ; 312,132	13,144 ; 312,132						
180-239	ǂ	ǂ	ǂ						
≥240	ǂ	ǂ	ǂ						
	ChAdOx1 only			**ChAdOx1 and BNT162b2**			**ChAdOx1 and mRNA-1273**		
7-59	241,399 ; 2,035,672	80,531 ; 306,831	13,136 ; 306,831	241,368 ; 2,037,366	80,517 ; 307,528	ǂ	241,378 ; 2,039,025	80,517 ; 307,983	ǂ
60-119	241,665 ; 2,037,327	80,640 ; 308,218	13,146 ; 308,218	241,483 ; 2,041,187	80,566 ; 309,482	ǂ	241,555 ; 2,045,114	80,594 ; 310,382	ǂ
120-179	241,576 ; 2,034,809	80,637 ; 307,679	13,140 ; 307,679	241,469 ; 2,034,690	80,565 ; 307,653	ǂ	241,482 ; 2,036,018	80,553 ; 307,984	ǂ
180-239	ǂ	ǂ	ǂ	ǂ	ǂ	ǂ	ǂ	ǂ	ǂ
≥240	ǂ	ǂ	ǂ	ǂ	ǂ	ǂ	ǂ	ǂ	ǂ
	Aged 16-69 years			**Aged 16-69 years with a comorbidity**			**Aged 16-69 years with no comorbidities**		
7-59	229,352 ; 1,881,673	74,777 ; 292,714	9,254 ; 292,714	86,190 ; 771,896	29,479 ; 119,960	5,852 ; 119,960	143,162 ; 1,109,777	45,298 ; 172,754	3,402 ; 172,754
60-119	229,887 ; 1,893,146	74,999 ; 298,344	9,259 ; 298,344	86,453 ; 777,705	29,601 ; 122,833	5,856 ; 122,833	143,434 ; 1,115,441	45,398 ; 175,511	3,403 ; 175,511
120-179	229,717 ; 1,875,667	74,954 ; 293,661	9,256 ; 293,661	86,389 ; 769,214	29,583 ; 120,740	5,855 ; 120,740	143,328 ; 1,106,453	45,371 ; 172,921	3,401 ; 172,921
180-239	ǂ	ǂ	ǂ	ǂ	ǂ	ǂ	ǂ	ǂ	ǂ
≥240	ǂ	ǂ	ǂ	ǂ	ǂ	ǂ	ǂ	ǂ	ǂ
	Aged ≥70 years			**Aged ≥70 years with a comorbidity**			**Aged ≥70 years with no comorbidities**		
7-59	12,213 ; 177,228	ǂ	ǂ	11,039 ; 160,852	ǂ	ǂ	ǂ	ǂ	ǂ
60-119	12,236 ; 177,320	5,809 ; 18,554	3,892 ; 18,554	11,057 ; 160,939	5,344 ; 17,068	ǂ	ǂ	ǂ	ǂ
120-179	12,230 ; 176,688	5,809 ; 18,471	ǂ	11,053 ; 160,378	ǂ	ǂ	ǂ	ǂ	ǂ
180-239	ǂ	ǂ	ǂ	ǂ	ǂ	ǂ	ǂ	ǂ	ǂ
≥240	ǂ	ǂ	ǂ	ǂ	ǂ	ǂ	ǂ	ǂ	ǂ
	Aged 16-69 years (0 prior SARS-CoV-2 tests)			**Aged 16-69 years (1 prior SARS-CoV-2 test)**			**Aged 16-69 years (≥2 prior SARS-CoV-2 tests)**		
7-59	191,073 ; 1,371,262	62,862 ; 211,324	7,947 ; 211,324	29,367 ; 322,940	9,482 ; 59,652	ǂ	ǂ	ǂ	ǂ
60-119	191,527 ; 1,380,245	63,053 ; 215,565	7,951 ; 215,565	29,425 ; 325,158	9,508 ; 60,806	ǂ	8,935 ; 187,743	2,438 ; 21,973	ǂ
120-179	191,383 ; 1,367,008	63,011 ; 212,071	7,946 ; 212,071	29,407 ; 321,779	9,506 ; 59,840	ǂ	8,927 ; 186,880	ǂ	ǂ
180-239	ǂ	ǂ	ǂ	ǂ	ǂ	ǂ	ǂ	ǂ	ǂ
≥240	ǂ	ǂ	ǂ	ǂ	ǂ	ǂ	ǂ	ǂ	ǂ

	Aged ≥70 years (0 prior SARS-CoV-2 tests)			Aged ≥70 years (1 prior SARS-CoV-2 test)			Aged ≥70 years (≥2 prior SARS-CoV-2 tests)		
7-59	10,665 ; 136,320	ǂ	ǂ	ǂ	ǂ	ǂ	ǂ	ǂ	ǂ
60-119	10,685 ; 136,392	5,080 ; 14,776	ǂ	ǂ	ǂ	ǂ	ǂ	ǂ	ǂ
120-179	10,679 ; 135,865	5,079 ; 14,724	ǂ	ǂ	ǂ	ǂ	ǂ	ǂ	ǂ
180-239	ǂ	ǂ	ǂ	ǂ	ǂ	ǂ	ǂ	ǂ	ǂ
≥240	ǂ	ǂ	ǂ	ǂ	ǂ	ǂ	ǂ	ǂ	ǂ
	11 Jan to 4 Apr 2021 (Mixed wild-type SARS-CoV-2 & Alpha circulating)			**5 Apr to 27 Jun 2021 (Alpha predominating)**			**28 Jun to 21 Nov 2021 (Delta predominating)**		
7-59	ǂ	ǂ	ǂ	107,680 ; 621,309	ǂ	ǂ	25,066 ; 237,708	9,772 ; 41,535	2,043 ; 41,535
60-119	ǂ	ǂ	ǂ	ǂ	ǂ	ǂ	25,648 ; 252,393	10,012 ; 47,558	2,057 ; 47,558
120-179	ǂ	ǂ	ǂ	ǂ	ǂ	ǂ	25,473 ; 234,328	9,967 ; 42,797	2,050 ; 42,797
180-239	ǂ	ǂ	ǂ	ǂ	ǂ	ǂ	ǂ	ǂ	ǂ
≥240	ǂ	ǂ	ǂ	ǂ	ǂ	ǂ	ǂ	ǂ	ǂ

[a]Each cell contains the total number of test-positive cases and test-negative controls (vaccinated and unvaccinated) that were used to calculate the corresponding VE estimate in Table S8. For each set of VE estimates in an analysis (e.g., VE estimates for 7-59, 60-119, 120-179, 180-239, and ≥240 days under the Overall header), there is only one unvaccinated group, which is included in the counts for each VE estimate. Therefore, the sum of the counts does not equal the total number of cases and controls.

ǂCounts were suppressed because they are small cell counts (≤5, which cannot be disclosed because of privacy and data obligations) or they were either 0 vaccinated test-positive cases and/or 0 vaccinated test-negative controls (this information could subsequently be used to disclose suppressed small cells in combination with other estimates in the table).

Supplementary Table 8. Vaccine effectiveness of two doses of mRNA vaccines against infection caused by any SARS-CoV-2 lineage, stratified by age group, dosing interval, time since second dose, and subperiod in Ontario, Canada

Age group	Dosing interval	Time since second dose	Vaccine effectiveness (95% CI)[a] 11 January to 4 April (Mixed wild-type SARS-CoV-2 & Alpha circulating)	5 April to 27 June (Alpha predominating)	28 June to 21 November (Delta predominating)
16-69 years	15-34 days	7-59 days	89 (87, 90)	92 (91, 93)	88 (87, 89)
		60-119 days	80 (74, 84)	83 (81, 84)	83 (82, 84)
		120-179 days	-	82 (78, 86)	82 (80, 83)
		180-239 days	-	-	77 (75, 79)
		≥240 days	-	-	78 (75, 81)
	35-55 days	7-59 days	90 (88, 92)	91 (89, 93)	90 (89, 91)
		60-119 days	¶	83 (81, 85)	87 (86, 87)
		120-179 days	-	81 (67, 89)	84 (83, 85)
		180-239 days	-	-	80 (77, 82)
		≥240 days	-	-	78 (73, 81)
	≥56 days	7-59 days	¶	94 (93, 95)	91 (90, 92)
		60-119 days	-	*	87 (87, 88)
		120-179 days	-	-	83 (82, 84)
		180-239 days	-	-	75 (64, 83)
		≥240 days	-	-	¶
≥70 years	15-34 days	7-59 days	91 (87, 93)	91 (88, 92)	75 (64, 83)
		60-119 days	¶	89 (86, 91)	86 (79, 91)
		120-179 days	-	79 (57, 90)	78 (72, 83)
		180-239 days	-	-	71 (64, 76)
		≥240 days	-	-	80 (65, 89)
	35-55 days	7-59 days	80 (58, 91)	89 (83, 93)	89 (81, 94)
		60-119 days	-	88 (71, 95)	83 (77, 87)
		120-179 days	-	¶	79 (72, 84)
		180-239 days	-	-	68 (46, 81)
		≥240 days	-	-	67 (-37, 92)
	≥56 days	7-59 days	¶	89 (84, 92)	89 (86, 91)
		60-119 days	-	¶	85 (83, 86)
		120-179 days	-	-	79 (76, 82)
		180-239 days	-	-	78 (12, 95)
		≥240 days	-	-	-

[a] Models were adjusted for age (10-year age bands), sex, public health unit region, biweekly period of test, 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 influenza vaccination in current or prior influenza season, and neighbourhood-level household income, persons per dwelling, proportion of persons employed as non-health essential workers, and self-identified visible minority quintiles (unless that characteristic was used to stratify into subgroups). ¶VE estimated as 100% based on zero vaccinated test-positive cases. *VE not reported due to extremely imprecise 95% confidence interval.

Supplementary Table 9. Number of test-positive cases and test-negative controls contributing to VE estimates in Supplementary Table 10

Age group	Dosing interval	Time since second dose	Number of test-positive cases ; test-negative controls[a]		
			11 Jan to 4 Apr 2021 (Mixed wild-type SARS-CoV-2 & Alpha circulating)	5 Apr to 27 Jun 2021 (Alpha predominating)	28 Jun to 21 Nov 2021 (Delta predominating)
16-69 years	15-34 days	7-59 days	100,924 ; 1,102,429	104,713 ; 614,087	24,575 ; 244,960
		60-119 days	100,746 ; 1,065,132	105,130 ; 623,956	24,853 ; 243,940
		120-179 days	ǂ	104,643 ; 602,413	24,442 ; 230,059
		180-239 days	ǂ	ǂ	24,274 ; 211,604
		≥240 days	ǂ	ǂ	24,077 ; 205,128
	35-55 days	7-59 days	100,781 ; 1,081,515	104,659 ; 607,966	25,051 ; 304,549
		60-119 days	ǂ	104,797 ; 608,004	26,538 ; 350,552
		120-179 days	ǂ	104,559 ; 595,946	25,260 ; 266,427
		180-239 days	ǂ	ǂ	24,115 ; 205,298
		≥240 days	ǂ	ǂ	23,979 ; 200,169
	≥56 days	7-59 days	ǂ	104,621 ; 619,376	25,151 ; 336,478
		60-119 days	ǂ	ǂ	26,754 ; 378,051
		120-179 days	ǂ	ǂ	25,522 ; 280,315
		180-239 days	ǂ	ǂ	23,888 ; 196,223
		≥240 days	ǂ	ǂ	ǂ
≥70 years	15-34 days	7-59 days	8,188 ; 150,542	3,196 ; 35,158	986 ; 15,006
		60-119 days	ǂ	3,207 ; 36,303	985 ; 17,620
		120-179 days	ǂ	3,118 ; 25,293	1,039 ; 22,080
		180-239 days	ǂ	ǂ	1,076 ; 19,080
		≥240 days	ǂ	ǂ	971 ; 14,225
	35-55 days	7-59 days	8,144 ; 139,602	3,132 ; 27,192	973 ; 16,156
		60-119 days	ǂ	ǂ	1,008 ; 17,490
		120-179 days	ǂ	ǂ	1,009 ; 16,366
		180-239 days	ǂ	ǂ	974 ; 13,882
		≥240 days	ǂ	ǂ	ǂ
	≥56 days	7-59 days	ǂ	3,147 ; 33,453	1,120 ; 53,290
		60-119 days	ǂ	ǂ	1,600 ; 65,296
		120-179 days	ǂ	ǂ	1,559 ; 45,298
		180-239 days	ǂ	ǂ	ǂ
		≥240 days	ǂ	ǂ	959 ; 13,314

[a]Each cell contains the total number of test-positive cases and test-negative controls (vaccinated and unvaccinated) that were used to calculate the corresponding VE estimate in Table S10. For each set of VE estimates in an analysis (e.g., VE estimates for 7-59, 60-119, 120-179, 180-239, and ≥240 days for all dosing intervals for age group 16-69 years), there is only one unvaccinated group, which is included in the counts for each VE estimate. Therefore, the sum of the counts does not equal the total number of cases and controls.

ǂCounts were suppressed because they are small cell counts (≤5, which cannot be disclosed because of privacy and data obligations) or they were either 0 vaccinated test-positive cases and/or 0 vaccinated test-negative controls (this information could subsequently be used to disclose suppressed small cells in combination with other estimates in the table).

Supplementary Table 10. Vaccine effectiveness of two doses of mRNA vaccines against symptomatic infection caused by any SARS-CoV-2 lineage, stratified by age group, dosing interval, time since second dose, and subperiod in Ontario, Canada

Age group	Dosing interval	Time since second dose	Vaccine effectiveness (95% CI)[a] 11 January to 4 April (Mixed wild-type SARS-CoV-2 & Alpha circulating)	5 April to 27 June (Alpha predominating)	28 June to 21 November (Delta predominating)
16-69 years	15-34 days	7-59 days	94 (89, 97)	88 (83, 91)	92 (91, 93)
		60-119 days	93 (78, 98)	85 (81, 88)	89 (88, 91)
		120-179 days	-	84 (74, 90)	86 (84, 88)
		180-239 days	-	-	83 (80, 86)
		≥240 days	-	-	87 (84, 90)
	35-55 days	7-59 days	93 (86, 96)	94 (91, 97)	94 (93, 95)
		60-119 days	-	87 (82, 90)	92 (92, 93)
		120-179 days	-	82 (51, 93)	91 (90, 92)
		180-239 days	-	-	88 (85, 91)
		≥240 days	-	-	91 (87, 94)
	≥56 days	7-59 days	¶	96 (92, 97)	95 (94, 95)
		60-119 days	-	*	93 (93, 94)
		120-179 days	-	-	91 (90, 92)
		180-239 days	-	-	89 (79, 94)
		≥240 days	-	-	-
≥70 years	15-34 days	7-59 days	94 (88, 97)	93 (90, 96)	85 (70, 92)
		60-119 days	¶	96 (93, 98)	92 (85, 95)
		120-179 days	-	¶	89 (85, 93)
		180-239 days	-	-	85 (79, 89)
		≥240 days	-	-	88 (73, 94)
	35-55 days	7-59 days	¶	95 (86, 98)	96 (88, 99)
		60-119 days	-	¶	88 (82, 92)
		120-179 days	-	¶	89 (83, 93)
		180-239 days	-	-	83 (62, 92)
		≥240 days	-	-	88 (7, 98)
	≥56 days	7-59 days	¶	92 (85, 95)	94 (92, 96)
		60-119 days	-	¶	93 (92, 94)
		120-179 days	-	-	92 (90, 93)
		180-239 days	-	-	85 (-21, 98)
		≥240 days	-	-	-

[a] Models were adjusted for age (10-year age bands), sex, public health unit region, biweekly period of test, 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 influenza vaccination in current or prior influenza season, and neighbourhood-level household income, persons per dwelling, proportion of persons employed as non-health essential workers, and self-identified visible minority quintiles (unless that characteristic was used to stratify into subgroups). ¶VE estimated as 100% based on zero vaccinated test-positive cases. *VE not reported due to extremely imprecise 95% confidence interval.

Supplementary Table 11. Number of test-positive cases and test-negative controls contributing to VE estimates in Supplementary Table 12

Age group	Dosing interval	Time since second dose	Number of test-positive cases ; test-negative controls[a]		
			11 Jan to 4 Apr 2021 (Mixed wild-type SARS-CoV-2 & Alpha circulating)	5 Apr to 27 Jun 2021 (Alpha predominating)	28 Jun to 21 Nov 2021 (Delta predominating)
16-69 years	15-34 days	7-59 days	28,883 ; 155,700	36,754 ; 99,460	9,308 ; 44,676
		60-119 days	ǂ	36,791 ; 100,085	9,430 ; 47,508
		120-179 days	ǂ	36,733 ; 98,755	9,348 ; 41,885
		180-239 days	ǂ	ǂ	9,277 ; 38,748
		≥240 days	ǂ	ǂ	9,203 ; 37,891
	35-55 days	7-59 days	28,880 ; 155,070	36,731 ; 99,416	9,446 ; 60,735
		60-119 days	ǂ	36,759 ; 99,441	10,047 ; 84,184
		120-179 days	ǂ	ǂ	9,652 ; 56,259
		180-239 days	ǂ	ǂ	9,198 ; 37,479
		≥240 days	ǂ	ǂ	9,149 ; 36,341
	≥56 days	7-59 days	ǂ	36,729 ; 99,892	9,514 ; 66,071
		60-119 days	ǂ	ǂ	10,174 ; 88,246
		120-179 days	ǂ	ǂ	9,790 ; 59,594
		180-239 days	ǂ	ǂ	9,125 ; 35,212
		≥240 days	ǂ	ǂ	ǂ
≥70 years	15-34 days	7-59 days	3,609 ; 15,050	1,633 ; 3,109	596 ; 1,499
		60-119 days	ǂ	1,622 ; 3,161	599 ; 1,836
		120-179 days	ǂ	ǂ	619 ; 2,314
		180-239 days	ǂ	ǂ	637 ; 2,088
		≥240 days	ǂ	ǂ	593 ; 1,461
	35-55 days	7-59 days	ǂ	ǂ	ǂ
		60-119 days	ǂ	ǂ	613 ; 1,885
		120-179 days	ǂ	ǂ	610 ; 1,753
		180-239 days	ǂ	ǂ	593 ; 1,425
		≥240 days	ǂ	ǂ	ǂ
	≥56 days	7-59 days	ǂ	1,622 ; 3,017	638 ; 5,889
		60-119 days	ǂ	ǂ	852 ; 9,657
		120-179 days	ǂ	ǂ	859 ; 7,093
		180-239 days	ǂ	ǂ	ǂ
		≥240 days	ǂ	ǂ	ǂ

[a]Each cell contains the total number of test-positive cases and test-negative controls (vaccinated and unvaccinated) that were used to calculate the corresponding VE estimate in Table S12. For each set of VE estimates in an analysis (e.g., VE estimates for 7-59, 60-119, 120-179, 180-239, and ≥240 days for all dosing intervals for age group 16-69 years), there is only one unvaccinated group, which is included in the counts for each VE estimate. Therefore, the sum of the counts does not equal the total number of cases and controls.

ǂCounts were suppressed because they are small cell counts (≤5, which cannot be disclosed because of privacy and data obligations) or they were either 0 vaccinated test-positive cases and/or 0 vaccinated test-negative controls (this information could subsequently be used to disclose suppressed small cells in combination with other estimates in the table).

Supplementary Table 12. Vaccine effectiveness of two doses of mRNA vaccines against severe outcomes caused by any SARS-CoV-2 lineage, stratified by age group, dosing interval, time since second dose, and subperiod in Ontario, Canada

Age group	Dosing interval	Time since second dose	Vaccine effectiveness (95% CI)[a] 11 January to 4 April (Mixed wild-type SARS-CoV-2 & Alpha circulating)	5 April to 27 June (Alpha predominating)	28 June to 21 November (Delta predominating)
16-69 years	15-34 days	7-59 days	91 (71, 97)	87 (78, 92)	98 (95, 99)
		60-119 days	¶	96 (90, 99)	95 (93, 97)
		120-179 days	-	¶	97 (94, 98)
		180-239 days	-	-	98 (95, 99)
		≥240 days	-	-	99 (95, 100)
	35-55 days	7-59 days	¶	95 (85, 98)	99 (98, 100)
		60-119 days	-	98 (87, 100)	99 (99, 100)
		120-179 days	-	¶	99 (98, 100)
		180-239 days	-	-	98 (93, 99)
		≥240 days	-	-	99 (90, 100)
	≥56 days	7-59 days	¶	98 (92, 100)	99 (98, 99)
		60-119 days	-	¶	99 (99, 99)
		120-179 days	-	-	99 (98, 99)
		180-239 days	-	-	93 (51, 99)
		≥240 days	-	-	-
≥70 years	15-34 days	7-59 days	95 (89, 98)	94 (91, 97)	83 (65, 92)
		60-119 days	¶	97 (94, 99)	97 (92, 99)
		120-179 days	-	¶	90 (85, 94)
		180-239 days	-	-	91 (87, 94)
		≥240 days	-	-	94 (80, 98)
	35-55 days	7-59 days	¶	95 (84, 98)	97 (87, 99)
		60-119 days	-	¶	94 (89, 97)
		120-179 days	-	¶	91 (85, 95)
		180-239 days	-	-	93 (71, 98)
		≥240 days	-	-	¶
	≥56 days	7-59 days	¶	90 (81, 95)	97 (95, 98)
		60-119 days	-	¶	97 (96, 98)
		120-179 days	-	-	96 (94, 97)
		180-239 days	-	-	¶
		≥240 days	-	-	-

[a] Models were adjusted for age (10-year age bands), sex, public health unit region, biweekly period of test, 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 influenza vaccination in current or prior influenza season, and neighbourhood-level household income, persons per dwelling, proportion of persons employed as non-health essential workers, and self-identified visible minority quintiles (unless that characteristic was used to stratify into subgroups).

¶ VE estimated as 100% based on zero vaccinated test-positive cases.

* VE not reported due to extremely imprecise 95% confidence interval.

Supplementary Table 13. Number of test-positive cases and test-negative controls contributing to VE estimates in Supplementary Table 14

Age group	Dosing interval	Time since second dose	Number of test-positive cases ; test-negative controls[a]		
			11 Jan to 4 Apr 2021 (Mixed wild-type SARS-CoV-2 & Alpha circulating)	5 Apr to 27 Jun 2021 (Alpha predominating)	28 Jun to 21 Nov 2021 (Delta predominating)
16-69 years	15-34 days	7-59 days	ǂ	4,413 ; 99,460	1,622 ; 44,676
		60-119 days	ǂ	ǂ	1,637 ; 47,508
		120-179 days	ǂ	ǂ	1,623 ; 41,885
		180-239 days	ǂ	ǂ	ǂ
		≥240 days	ǂ	ǂ	ǂ
	35-55 days	7-59 days	ǂ	ǂ	1,620 ; 60,735
		60-119 days	ǂ	ǂ	1,627 ; 84,184
		120-179 days	ǂ	ǂ	1,621 ; 56,259
		180-239 days	ǂ	ǂ	ǂ
		≥240 days	ǂ	ǂ	ǂ
	≥56 days	7-59 days	ǂ	ǂ	1,633 ; 66,071
		60-119 days	ǂ	ǂ	1,653 ; 88,246
		120-179 days	ǂ	ǂ	1,640 ; 59,594
		180-239 days	ǂ	ǂ	ǂ
		≥240 days	ǂ	ǂ	ǂ
≥70 years	15-34 days	7-59 days	2,329 ; 15,050	1,160 ; 3,109	430 ; 1,499
		60-119 days	ǂ	1,150 ; 3,161	ǂ
		120-179 days	ǂ	ǂ	449 ; 2,314
		180-239 days	ǂ	ǂ	451 ; 2,088
		≥240 days	ǂ	ǂ	ǂ
	35-55 days	7-59 days	ǂ	ǂ	ǂ
		60-119 days	ǂ	ǂ	433 ; 1,885
		120-179 days	ǂ	ǂ	436 ; 1,753
		180-239 days	ǂ	ǂ	ǂ
		≥240 days	ǂ	ǂ	ǂ
	≥56 days	7-59 days	ǂ	1,153 ; 3,017	447 ; 5,889
		60-119 days	ǂ	ǂ	513 ; 9,657
		120-179 days	ǂ	ǂ	520 ; 7,093
		180-239 days	ǂ	ǂ	ǂ
		≥240 days	ǂ	ǂ	ǂ

[a]Each cell contains the total number of test-positive cases and test-negative controls (vaccinated and unvaccinated) that were used to calculate the corresponding VE estimate in Table S14. For each set of VE estimates in an analysis (e.g., VE estimates for 7-59, 60-119, 120-179, 180-239, and ≥240 days for all dosing intervals for age group 16-69 years), there is only one unvaccinated group, which is included in the counts for each VE estimate. Therefore, the sum of the counts does not equal the total number of cases and controls.

ǂCounts were suppressed because they are small cell counts (≤5, which cannot be disclosed because of privacy and data obligations) or they were either 0 vaccinated test-positive cases and/or 0 vaccinated test-negative controls (this information could subsequently be used to disclose suppressed small cells in combination with other estimates in the table).

Supplementary Table 14. Vaccine effectiveness of two doses any mRNA vaccines against SARS-CoV-2 infection, symptomatic SARS-CoV-2 infection, and severe outcomes between 11 January 2021 to 21 November 2021 in Ontario, Canada, by time since second dose, by various factors, including individuals with a prior SARS-CoV-2 infection

Time since second dose (days)	Vaccine effectiveness (95% CI)[a]								
	Any infection	Symptomatic infection	Severe outcomes	Any infection	Symptomatic infection	Severe outcomes	Any infection	Symptomatic infection	Severe outcomes
	Overall								
7-59	90 (89, 90)	94 (94, 94)	97 (97, 98)						
60-119	86 (86, 86)	92 (92, 93)	98 (98, 98)						
120-179	82 (82, 83)	90 (90, 91)	97 (97, 98)						
180-239	74 (72, 75)	82 (79, 84)	95 (93, 96)						
≥240	75 (73, 78)	87 (84, 89)	98 (96, 99)						
	BNT162b2 only			**mRNA-1273 only**			**Mixed mRNA vaccine schedules**		
7-59	89 (88, 89)	93 (93, 94)	98 (97, 98)	92 (91, 92)	95 (94, 96)	96 (95, 97)	91 (90, 92)	96 (95, 97)	99 (98, 99)
60-119	85 (85, 86)	92 (91, 92)	98 (98, 98)	88 (88, 89)	94 (93, 95)	99 (98, 99)	88 (87, 88)	94 (93, 94)	99 (98, 99)
120-179	81 (80, 82)	90 (89, 91)	97 (96, 97)	85 (84, 86)	91 (90, 92)	98 (97, 99)	83 (82, 85)	93 (92, 94)	99 (97, 99)
180-239	73 (71, 75)	83 (80, 85)	94 (91, 96)	75 (71, 79)	78 (72, 82)	97 (93, 99)	¶	-	-
≥240	74 (71, 77)	87 (84, 89)	98 (95, 99)	80 (71, 86)	87 (78, 92)	98 (88, 100)	¶	-	-
	Aged 16-69 years			**Aged 16-69 years with a comorbidity**			**Aged 16-69 years with no comorbidities**		
7-59	90 (90, 90)	94 (94, 95)	98 (98, 99)	90 (89, 90)	94 (93, 95)	98 (97, 98)	90 (90, 90)	94 (94, 95)	99 (99, 100)
60-119	86 (86, 86)	92 (92, 93)	99 (98, 99)	86 (85, 86)	92 (92, 93)	99 (98, 99)	86 (86, 87)	92 (92, 93)	99 (99, 99)
120-179	83 (82, 84)	91 (90, 91)	99 (98, 99)	83 (82, 84)	91 (90, 92)	98 (97, 99)	83 (82, 84)	91 (90, 92)	100 (99, 100)
180-239	74 (72, 76)	82 (80, 84)	98 (95, 99)	72 (68, 75)	81 (77, 84)	97 (93, 98)	76 (73, 78)	83 (80, 86)	99 (94, 100)
≥240	75 (72, 78)	87 (84, 89)	99 (96, 100)	77 (72, 81)	87 (83, 91)	98 (94, 100)	74 (70, 77)	87 (83, 89)	¶
	Aged ≥70 years			**Aged ≥70 years with a comorbidity**			**Aged ≥70 years with no comorbidities**		
7-59	87 (86, 88)	93 (92, 94)	95 (94, 96)	87 (85, 88)	93 (91, 94)	95 (93, 96)	90 (85, 94)	96 (90, 99)	97 (90, 99)
60-119	85 (83, 86)	93 (92, 94)	97 (96, 97)	85 (83, 86)	93 (92, 94)	97 (96, 97)	85 (79, 88)	95 (91, 97)	99 (98, 100)
120-179	77 (75, 80)	91 (90, 93)	95 (93, 96)	77 (75, 80)	91 (89, 93)	94 (93, 96)	76 (66, 83)	95 (91, 97)	99 (97, 100)
180-239	67 (61, 73)	85 (80, 89)	91 (87, 94)	67 (61, 73)	85 (79, 89)	91 (86, 94)	69 (24, 88)	95 (55, 99)	¶
≥240	79 (64, 88)	89 (77, 95)	95 (83, 98)	79 (64, 88)	89 (76, 95)	94 (81, 98)	80 (-48, 97)	94 (47, 99)	¶
	Aged 16-69 years (0 prior SARS-CoV-2 tests)			**Aged 16-69 years (1 prior SARS-CoV-2 test)**			**Aged 16-69 years (≥2 prior SARS-CoV-2 tests)**		
7-59	91 (90, 91)	95 (94, 95)	99 (98, 99)	88 (87, 89)	92 (90, 93)	97 (95, 99)	85 (84, 87)	92 (89, 94)	95 (88, 97)
60-119	87 (87, 88)	93 (93, 93)	99 (99, 99)	84 (83, 85)	90 (89, 91)	97 (95, 98)	78 (76, 80)	89 (87, 91)	100 (97, 100)
120-179	85 (84, 85)	92 (91, 92)	99 (98, 99)	80 (78, 82)	87 (84, 89)	98 (94, 99)	75 (72, 78)	84 (80, 88)	98 (94, 99)
180-239	77 (74, 79)	84 (81, 87)	96 (92, 98)	75 (70, 79)	79 (72, 84)	98 (84, 100)	72 (67, 76)	79 (73, 84)	¶
≥240	80 (77, 83)	89 (86, 92)	¶	81 (75, 86)	90 (83, 94)	¶	70 (64, 75)	82 (75, 87)	98 (89, 99)
	Aged ≥70 years (0 prior SARS-CoV-2 tests)			**Aged ≥70 years (1 prior SARS-CoV-2 test)**			**Aged ≥70 years (≥2 prior SARS-CoV-2 tests)**		
7-59	87 (86, 89)	93 (91, 94)	95 (93, 96)	88 (83, 91)	96 (92, 98)	98 (95, 100)	81 (75, 85)	87 (76, 93)	88 (75, 94)
60-119	84 (83, 86)	93 (92, 94)	97 (96, 98)	84 (79, 88)	91 (86, 95)	95 (91, 98)	84 (77, 88)	88 (77, 94)	94 (86, 98)
120-179	78 (75, 80)	92 (90, 93)	95 (94, 97)	72 (61, 80)	88 (78, 93)	91 (81, 96)	81 (70, 88)	87 (71, 94)	90 (72, 96)
180-239	63 (54, 70)	84 (77, 89)	91 (85, 94)	84 (72, 91)	93 (82, 97)	95 (84, 98)	68 (46, 81)	75 (42, 89)	82 (48, 94)
≥240	82 (62, 92)	90 (75, 96)	95 (79, 99)	83 (27, 96)	87 (-2, 98)	¶	80 (47, 93)	83 (14, 97)	88 (-12, 99)
	Dosing interval 15-34 days			**Dosing interval 35-55 days**			**Dosing interval ≥56 days**		
7-59	88 (87, 89)	92 (90, 92)	94 (93, 96)	90 (89, 90)	94 (94, 95)	99 (98, 99)	91 (90, 91)	95 (95, 95)	98 (98, 99)
60-119	83 (82, 83)	90 (88, 91)	97 (95, 98)	86 (86, 87)	93 (92, 93)	99 (98, 99)	87 (87, 88)	93 (93, 94)	98 (98, 99)
120-179	80 (79, 81)	86 (84, 88)	95 (93, 97)	84 (83, 85)	92 (91, 93)	98 (97, 99)	82 (81, 82)	91 (90, 91)	97 (97, 98)
180-239	73 (71, 75)	80 (77, 82)	95 (92, 96)	74 (71, 77)	85 (81, 88)	96 (91, 98)	72 (60, 80)	85 (74, 92)	94 (54, 99)
≥240	76 (73, 79)	86 (82, 88)	98 (95, 99)	72 (67, 77)	90 (85, 93)	98 (89, 100)	¶	-	-
	11 January to 4 April			**5 April to 27 June**			**28 June to 21 November**		

	(Mixed wild-type SARS-CoV-2 & Alpha circulating)			(Alpha predominating)			(Delta predominating)		
7-59	88 (87, 89)	92 (89, 94)	94 (89, 97)	91 (90, 92)	92 (90, 93)	94 (92, 95)	90 (89, 90)	94 (94, 94)	98 (98, 99)
60-119	81 (76, 85)	93 (79, 98)	¶	83 (82, 85)	88 (86, 90)	97 (96, 98)	87 (86, 87)	92 (92, 93)	98 (98, 99)
120-179	-	-	-	82 (78, 85)	85 (78, 91)	¶	83 (82, 83)	90 (90, 91)	97 (97, 98)
180-239	-	-	-	-	-	-	77 (75, 78)	84 (82, 86)	95 (93, 96)
≥240	-	-	-	-	-	-	78 (76, 80)	88 (86, 90)	98 (95, 99)

[a]Models were adjusted for age (10-year age bands), sex, public health unit region, biweekly period of test, 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 influenza vaccination in current or prior influenza season, and neighbourhood-level household income, persons per dwelling, proportion of persons employed as non-health essential workers, self-identified visible minority quintiles, and prior (documented) SARS-CoV-2 infection (unless that characteristic was used to stratify into subgroups).
[¶]VE estimated as 100% based on zero vaccinated test-positive cases.
[*]VE not reported due to extremely imprecise 95% confidence interval.

Supplementary Table 15. Vaccine effectiveness of two doses any ChAdOx1-containing schedule against SARS-CoV-2 infection, symptomatic SARS-CoV-2 infection, and severe outcomes between 11 January 2021 to 21 November 2021 in Ontario, Canada, by time since second dose, by various factors, including individuals with a prior SARS-CoV-2 infection

Time since second dose (days)	Vaccine effectiveness (95% CI)[a]								
	Any infection	Symptomatic infection	Severe outcomes	Any infection	Symptomatic infection	Severe outcomes	Any infection	Symptomatic infection	Severe outcomes
	Overall								
7-59	88 (87, 89)	93 (91, 94)	97 (95, 98)						
60-119	83 (82, 85)	90 (89, 92)	98 (97, 99)						
120-179	75 (73, 77)	87 (85, 89)	98 (97, 99)						
180-239	92 (68, 98)	¶	¶						
≥240	¶	¶	¶						
	ChAdOx1 only			**ChAdOx1 and BNT162b2**			**ChAdOx1 and mRNA-1273**		
7-59	82 (79, 85)	86 (80, 90)	95 (89, 98)	89 (87, 91)	95 (92, 97)	98 (94, 99)	91 (89, 93)	96 (93, 97)	99 (95, 100)
60-119	72 (69, 75)	84 (80, 86)	96 (94, 98)	88 (86, 90)	94 (92, 95)	100 (98, 100)	87 (85, 89)	93 (91, 94)	99 (98, 100)
120-179	67 (63, 71)	80 (76, 83)	97 (94, 98)	77 (73, 80)	89 (86, 91)	98 (96, 99)	80 (77, 83)	93 (91, 94)	¶
180-239	96 (69, 99)	¶	¶	*	¶	¶	¶	-	-
≥240	¶	¶	¶	-	-	-	-	-	-
	Aged 16-69 years			**Aged 16-69 years with a comorbidity**			**Aged 16-69 years with no comorbidities**		
7-59	88 (87, 90)	93 (91, 94)	98 (96, 99)	88 (86, 90)	94 (91, 96)	97 (94, 98)	88 (86, 90)	92 (90, 94)	99 (95, 100)
60-119	84 (82, 85)	91 (89, 92)	99 (98, 99)	84 (82, 86)	91 (89, 92)	98 (97, 99)	83 (81, 85)	90 (89, 92)	99 (98, 100)
120-179	75 (73, 77)	87 (85, 89)	98 (97, 99)	75 (72, 78)	87 (85, 90)	98 (96, 99)	75 (72, 78)	87 (84, 90)	100 (97, 100)
180-239	90 (60, 98)	¶	¶	80 (19, 95)	¶	¶	¶	¶	¶
≥240	¶	¶	¶	¶	-	-	¶	¶	¶
	Aged ≥70 years			**Aged ≥70 years with a comorbidity**			**Aged ≥70 years with no comorbidities**		
7-59	89 (78, 95)	97 (80, 100)	96 (73, 99)	87 (73, 94)	97 (77, 100)	96 (69, 99)	¶	¶	¶
60-119	76 (65, 83)	88 (79, 93)	93 (84, 97)	76 (65, 84)	87 (77, 93)	94 (84, 97)	72 (29, 89)	95 (57, 99)	92 (33, 99)
120-179	67 (50, 78)	86 (75, 92)	97 (88, 99)	67 (48, 79)	87 (74, 93)	97 (86, 99)	65 (-15, 89)	89 (54, 97)	¶
180-239	¶	¶	¶	¶	¶	¶	¶	¶	¶
≥240	-	-	-	-	-	-	-	-	-
	Aged 16-69 years (0 prior SARS-CoV-2 tests)			**Aged 16-69 years (1 prior SARS-CoV-2 test)**			**Aged 16-69 years (≥2 prior SARS-CoV-2 tests)**		
7-59	89 (87, 90)	93 (91, 95)	97 (95, 99)	84 (78, 88)	92 (86, 96)	¶	94 (83, 98)	94 (74, 98)	91 (29, 99)
60-119	84 (83, 85)	91 (89, 92)	99 (98, 99)	83 (79, 86)	90 (86, 93)	¶	79 (69, 86)	93 (83, 97)	92 (64, 98)
120-179	76 (74, 78)	88 (86, 89)	99 (98, 99)	71 (63, 77)	83 (75, 88)	91 (75, 97)	75 (59, 85)	93 (82, 97)	¶
180-239	88 (51, 97)	¶	¶	¶	¶	¶	¶	¶	¶
≥240	¶	¶	¶	-	-	-	-	-	-
	Aged ≥70 years (0 prior SARS-CoV-2 tests)			**Aged ≥70 years (1 prior SARS-CoV-2 test)**			**Aged ≥70 years (≥2 prior SARS-CoV-2 tests)**		
7-59	90 (77, 96)	97 (79, 100)	96 (73, 100)	*	¶	¶	¶	¶	¶
60-119	77 (66, 85)	89 (79, 94)	94 (85, 98)	70 (0, 91)	93 (41, 99)	¶	*	*	*
120-179	70 (52, 81)	90 (80, 95)	99 (90, 100)	*	*	*	¶	¶	¶
180-239	¶	-	-	¶	¶	¶	¶	¶	¶
≥240	-	-	-	-	-	-	-	-	-
	11 January to 4 April (Mixed wild-type SARS-CoV-2 & Alpha circulating)			**5 April to 27 June (Alpha predominating)**			**28 June to 21 November (Delta predominating)**		
7-59	¶	-	-	89 (84, 93)	94 (84, 97)	92 (79, 97)	89 (88, 91)	95 (93, 96)	98 (97, 99)
60-119	-	-	-	*	¶	¶	84 (83, 85)	92 (91, 93)	99 (98, 99)
120-179	-	-	-	-	-	-	76 (74, 78)	90 (88, 91)	98 (97, 99)
180-239	-	-	-	-	-	-	90 (59, 98)	¶	¶
≥240	-	-	-	-	-	-	¶	¶	¶

[a]Models were adjusted for age, sex, public health unit region, biweekly period of test, 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 influenza vaccination in current or prior influenza season, and neighbourhood-level household income, persons per dwelling, proportion of persons employed as non-health essential workers, self-identified visible minority quintiles, and prior (documented) SARS-CoV-2 infection.
[¶]VE estimated as 100% based on zero vaccinated test-positive cases.
[*]VE not reported due to extremely imprecise 95% confidence interval.

Supplementary Table 16. Vaccine effectiveness of two doses of mRNA vaccines against infection caused by any SARS-CoV-2 lineage, stratified by age group, dosing interval, time since second dose, and subperiod in Ontario, Canada, including individuals with a prior SARS-CoV-2 infection

Age group	Dosing interval	Time since second dose	Vaccine effectiveness (95% CI)[a] 11 January to 4 April (Mixed wild-type SARS-CoV-2 & Alpha circulating)	5 April to 27 June (Alpha predominating)	28 June to 21 November (Delta predominating)
16-69 years	15-34 days	7-59 days	88 (86, 89)	92 (91, 93)	88 (87, 88)
		60-119 days	80 (75, 84)	82 (81, 84)	83 (82, 84)
		120-179 days	-	82 (78, 85)	82 (80, 83)
		180-239 days	-	-	77 (74, 79)
		≥240 days	-	-	78 (75, 81)
	35-55 days	7-59 days	89 (87, 91)	91 (89, 92)	90 (89, 91)
		60-119 days	-	83 (81, 85)	87 (86, 87)
		120-179 days	-	81 (68, 89)	84 (83, 85)
		180-239 days	-	-	79 (76, 82)
		≥240 days	-	-	78 (73, 81)
	≥56 days	7-59 days	¶	93 (91, 94)	91 (90, 91)
		60-119 days	-	*	87 (87, 88)
		120-179 days	-	-	83 (82, 84)
		180-239 days	-	-	75 (64, 83)
		≥240 days	-	-	¶
≥70 years	15-34 days	7-59 days	89 (86, 91)	89 (87, 91)	74 (62, 82)
		60-119 days	¶	88 (86, 90)	85 (79, 90)
		120-179 days	-	75 (53, 86)	78 (73, 83)
		180-239 days	-	-	71 (65, 77)
		≥240 days	-	-	81 (65, 89)
	35-55 days	7-59 days	80 (61, 90)	86 (79, 90)	89 (82, 94)
		60-119 days	-	88 (72, 95)	81 (75, 86)
		120-179 days	-	¶	79 (72, 84)
		180-239 days	-	-	67 (45, 80)
		≥240 days	-	-	70 (-24, 93)
	≥56 days	7-59 days	¶	86 (80, 90)	87 (84, 89)
		60-119 days	-	¶	84 (83, 86)
		120-179 days	-	-	79 (76, 82)
		180-239 days	-	-	78 (10, 95)
		≥240 days	-	-	-

[a]Models were adjusted for age (10-year age bands), sex, public health unit region, biweekly period of test, 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 influenza vaccination in current or prior influenza season, and neighbourhood-level household income, persons per dwelling, proportion of persons employed as non-health essential workers, self-identified visible minority quintiles, and prior (documented) SARS-CoV-2 infection (unless that characteristic was used to stratify into subgroups).
[¶]VE estimated as 100% based on zero vaccinated test-positive cases.
[*]VE not reported due to extremely imprecise 95% confidence interval.

Supplementary Table 17. Vaccine effectiveness of two doses of mRNA vaccines against symptomatic infection caused by any SARS-CoV-2 lineage, stratified by age group, dosing interval, time since second dose, and subperiod in Ontario, Canada, including individuals with a prior SARS-CoV-2 infection

Age group	Dosing interval	Time since second dose	Vaccine effectiveness (95% CI)[a] 11 January to 4 April (Mixed wild-type SARS-CoV-2 & Alpha circulating)	5 April to 27 June (Alpha predominating)	28 June to 21 November (Delta predominating)
16-69 years	15-34 days	7-59 days	92 (87, 95)	88 (83, 91)	92 (91, 93)
		60-119 days	93 (79, 98)	84 (80, 87)	89 (88, 91)
		120-179 days	-	84 (74, 90)	86 (84, 88)
		180-239 days	-	-	82 (79, 85)
		≥240 days	-	-	87 (84, 90)
	35-55 days	7-59 days	92 (86, 96)	94 (90, 96)	94 (93, 95)
		60-119 days	-	87 (82, 90)	92 (92, 93)
		120-179 days	-	82 (52, 94)	91 (90, 92)
		180-239 days	-	-	88 (85, 90)
		≥240 days	-	-	91 (88, 94)
	≥56 days	7-59 days	¶	95 (92, 97)	95 (94, 95)
		60-119 days	-	*	93 (93, 94)
		120-179 days	-	-	91 (90, 92)
		180-239 days	-	-	87 (77, 93)
		≥240 days	-	-	-
≥70 years	15-34 days	7-59 days	91 (85, 95)	92 (88, 95)	85 (71, 92)
		60-119 days	¶	96 (93, 98)	90 (84, 94)
		120-179 days	-	95 (61, 99)	89 (85, 93)
		180-239 days	-		85 (79, 89)
		≥240 days	-		88 (74, 95)
	35-55 days	7-59 days	¶	95 (87, 98)	96 (88, 99)
		60-119 days	-	¶	88 (82, 92)
		120-179 days	-	¶	88 (82, 92)
		180-239 days	-	-	83 (62, 92)
		≥240 days	-	-	88 (8, 98)
	≥56 days	7-59 days	¶	92 (85, 96)	94 (92, 96)
		60-119 days	-	¶	93 (92, 94)
		120-179 days	-	-	92 (90, 93)
		180-239 days	-	-	84 (-27, 98)
		≥240 days	-	-	-

[a]Models were adjusted for age, sex, public health unit region, biweekly period of test, 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 influenza vaccination in current or prior influenza season, and neighbourhood-level household income, persons per dwelling, proportion of persons employed as non-health essential workers, self-identified visible minority quintiles, and prior (documented) SARS-CoV-2 infection.
[¶]VE estimated as 100% based on zero vaccinated test-positive cases.
[*]VE not reported due to extremely imprecise 95% confidence interval.

Supplementary Table 18. Vaccine effectiveness of two doses of mRNA vaccines against severe outcomes caused by any SARS-CoV-2 lineage, stratified by age group, dosing interval, time since second dose, and subperiod in Ontario, Canada, including individuals with a prior SARS-CoV-2 infection

Age group	Dosing interval	Time since second dose	Vaccine effectiveness (95% CI)[a] 11 January to 4 April (Mixed wild-type SARS-CoV-2 & Alpha circulating)	5 April to 27 June (Alpha predominating)	28 June to 21 November (Delta predominating)
16-69 years	15-34 days	7-59 days	88 (67, 95)	87 (78, 93)	98 (95, 99)
		60-119 days	¶	96 (90, 99)	95 (93, 97)
		120-179 days	-	¶	97 (94, 98)
		180-239 days	-	-	98 (95, 99)
		≥240 days	-	-	99 (95, 100)
	35-55 days	7-59 days	¶	95 (85, 98)	99 (98, 100)
		60-119 days	-	98 (87, 100)	99 (99, 100)
		120-179 days	-	¶	99 (98, 100)
		180-239 days	-	-	97 (92, 99)
		≥240 days	-	-	99 (90, 100)
	≥56 days	7-59 days	¶	98 (92, 100)	99 (98, 99)
		60-119 days	-	¶	99 (99, 99)
		120-179 days	-	-	99 (98, 99)
		180-239 days	-	-	93 (49, 99)
		≥240 days	-	-	-
≥70 years	15-34 days	7-59 days	95 (89, 98)	94 (90, 97)	84 (66, 92)
		60-119 days	¶	97 (94, 99)	97 (91, 99)
		120-179 days	-	¶	90 (85, 94)
		180-239 days	-	-	91 (86, 94)
		≥240 days	-	-	94 (81, 98)
	35-55 days	7-59 days	¶	95 (85, 99)	97 (87, 99)
		60-119 days	-	¶	94 (89, 97)
		120-179 days	-	¶	91 (85, 95)
		180-239 days	-	-	93 (71, 98)
		≥240 days	-	-	¶
	≥56 days	7-59 days	¶	90 (80, 95)	97 (95, 98)
		60-119 days	-	¶	97 (96, 98)
		120-179 days	-	-	96 (94, 97)
		180-239 days	-	-	¶
		≥240 days	-	-	-

[a]Models were adjusted for age (10-year age bands), sex, public health unit region, biweekly period of test, 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 influenza vaccination in current or prior influenza season, and neighbourhood-level household income, persons per dwelling, proportion of persons employed as non-health essential workers, self-identified visible minority quintiles, and prior (documented) SARS-CoV-2 infection (unless that characteristic was used to stratify into subgroups).
[¶]VE estimated as 100% based on zero vaccinated test-positive cases.
[*]VE not reported due to extremely imprecise 95% confidence interval.

Supplementary Table 19. Vaccine effectiveness of two-dose primary series against different definitions of severe outcomes[a] between 11 January to 21 November 2021 in Ontario, Canada, by time since second dose

	Vaccine effectiveness (95% CI)[b]									
Time since second dose (days)	**Hospitalization (recorded in CCM[c]) (N=12,907)**	**Death (recorded in CCM) (N=354)**	**COVID-19 as cause or contributing factor to death (recorded in CCM) (N=321)**	**Positive SARS-CoV-2 test near time of hospitalization or death (recorded in administrative data[d]) (n=16,019)**	**Positive SARS-CoV-2 test near time of hospitalization (recorded in administrative data) (N=15,279)**	**Positive SARS-CoV-2 test near time of hospitalization (U071 as most responsible diagnosis) (recorded in administrative data) (N=13,468)**	**Positive SARS-CoV-2 test near time of death (recorded in administrative data) (N=2,182)**	**Severe outcome recorded in CCM or administrative data[a] (n=18,100)**	**Hospitalization recorded in CCM or administrative data[a] (N=17,546)**	**Death recorded in CCM or administrative data[a] (N=554)**
Any two mRNA vaccine schedule										
7-59	97 (97, 98)	98 (93, 99)	¶	97 (97, 98)	97 (97, 98)	98 (98, 99)	97 (95, 98)	97 (97, 98)	97 (97, 98)	96 (92, 98)
60-119	98 (98, 99)	96 (92, 98)	98 (94, 99)	98 (98, 98)	98 (98, 99)	99 (98, 99)	98 (97, 98)	98 (98, 98)	98 (98, 98)	95 (92, 97)
120-179	97 (97, 98)	89 (78, 94)	89 (78, 95)	97 (97, 98)	98 (97, 98)	98 (97, 98)	97 (96, 98)	97 (97, 98)	97 (97, 98)	91 (84, 95)
180-239	95 (93, 96)	90 (57, 98)	89 (55, 98)	96 (94, 97)	96 (94, 97)	96 (94, 98)	95 (90, 97)	95 (93, 96)	95 (93, 96)	93 (71, 98)
≥240	98 (95, 99)	¶	¶	97 (94, 99)	98 (94, 99)	98 (94, 99)	97 (81, 100)	98 (96, 99)	98 (96, 99)	87 (1, 98)
ChAdOx1 and mRNA vaccine										
7-59	99 (96, 99)	¶	¶	98 (96, 99)	98 (96, 99)	99 (97, 100)	96 (74, 100)	98 (96, 99)	98 (96, 99)	¶
60-119	99 (98, 100)	¶	¶	99 (99, 100)	99 (99, 100)	100 (99, 100)	¶	99 (99, 100)	99 (99, 100)	¶
120-179	99 (98, 100)	¶	¶	99 (97, 99)	99 (97, 99)	99 (97, 100)	96 (86, 99)	99 (98, 100)	99 (98, 100)	¶
180-239	¶	¶	¶	¶	¶	¶	¶	¶	¶	¶
≥240	-	-	-	-	-	-	-	-	-	-
ChAdOx1 only										
7-59	94 (88, 97)	¶	¶	94 (89, 97)	95 (89, 97)	97 (92, 99)	¶	94 (88, 97)	94 (89, 97)	75 (-88, 97)
60-119	97 (95, 98)	¶	¶	96 (94, 98)	96 (94, 98)	97 (95, 98)	97 (88, 99)	96 (94, 97)	96 (94, 97)	¶
120-179	97 (94, 98)	¶	¶	96 (93, 98)	96 (93, 98)	98 (96, 99)	96 (84, 99)	97 (94, 98)	96 (94, 98)	¶
180-239	¶	¶	¶	¶	¶	¶	¶	¶	¶	¶
≥240	¶	¶	¶	¶	¶	¶	¶	¶	¶	¶

[a]The index date for severe outcomes is the earliest of specimen collection date, hospital admission, or death date. For individuals who were hospitalized then died, they would be classified in the hospitalization outcomes. If an individual died on the same day as their hospital admission, they would be classified by the most severe outcome, death.

[b]Models were adjusted for age (10-year age bands), sex, public health unit region, biweekly period of test, 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 influenza vaccination in current or prior influenza season, and neighbourhood-level household income, persons per dwelling, proportion of persons employed as non-health essential workers, and self-identified visible minority quintiles (unless characteristic was used to stratify into subgroups).

[c]CCM (Public Health Case and Contact Management) database contains information on risk factors and the clinical course (including hospitalizations, interventions, and complications) of all confirmed COVID-19 cases who meet the provincial case definition. Cause of death information is verified with the case's death certificate by the responsible public health unit when available.

[d]Severe outcomes that are recorded in administrative databases are those where a positive SARS-CoV-2 test was temporally associated with a hospitalization (14 days before or within 3 days after hospital admission) or death (30 days before or within 7 days after death [i.e., diagnosed during post-mortem]).

¶VE estimated as 100% based on zero vaccinated test-positive cases.

*VE not reported due to extremely imprecise 95% confidence interval.

Supplementary Table 20. Vaccine effectiveness of two-dose primary series against any infection, symptomatic infection, and severe outcomes caused by the Delta variant (confirmed by whole genome sequencing or mutation screening)[a] between 28 June to 21 November 2021 in Ontario, Canada, by time since second dose

	Vaccine effectiveness (95% CI)[b]		
Time since second dose (days)	**Any infection**	**Symptomatic infection**	**Severe outcomes**
Any two mRNA vaccine schedule			
7-59	91 (91, 92)	95 (94, 95)	99 (99, 99)
60-119	87 (87, 88)	93 (92, 93)	99 (98, 99)
120-179	83 (82, 84)	91 (90, 91)	98 (97, 98)
180-239	77 (75, 79)	85 (83, 87)	96 (93, 97)
≥240	78 (75, 80)	88 (85, 90)	98 (95, 99)
ChAdOx1 and mRNA vaccine			
7-59	92 (90, 93)	96 (95, 97)	99 (98, 100)
60-119	88 (87, 90)	94 (93, 95)	100 (99, 100)
120-179	80 (77, 82)	93 (91, 94)	99 (98, 100)
180-239	¶	¶	¶
≥240	-	-	-
ChAdOx1 only			
7-59	80 (74, 84)	86 (80, 91)	97 (89, 99)
60-119	69 (65, 72)	86 (84, 89)	97 (95, 98)
120-179	62 (56, 67)	82 (78, 86)	97 (95, 99)
180-239	93 (49, 99)	¶	¶
≥240	¶	¶	¶

[a]Cases were restricted to those that were confirmed to be Delta by whole genome sequencing (i.e., B.1.617) or negative for both N501Y and E484K (N501Y-/E484K-) mutations or positive for L452R mutation by mutation screening.

[b]Models were adjusted for age (10-year age bands), sex, public health unit region, biweekly period of test, 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 influenza vaccination in current or prior influenza season, and neighbourhood-level household income, persons per dwelling, proportion of persons employed as non-health essential workers, and self-identified visible minority quintiles (unless that characteristic was used to stratify into subgroups).

¶VE estimated as 100% based on zero vaccinated test-positive cases.

*VE not reported due to extremely imprecise 95% confidence interval.

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