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Research

The impact of shifting demographics, variants of concern and vaccination on outcomes during the first 3 COVID-19 waves in Alberta and Ontario: a retrospective cohort study

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Abstract

Background: In Canada, published outcome data for COVID-19 come largely from the first 2 waves of the pandemic. We examined changes in demographics and 30-day outcomes after SARS-CoV-2 infection during the first 3 pandemic waves in Alberta and Ontario; for wave 3, we compared outcomes between those infected with a variant of concern and those infected with the original "wild-type" SARS-CoV-2.

Methods: We conducted a population-based retrospective cohort study using linked health care data sets in Alberta and Ontario. We identified all-cause hospitalizations or deaths within 30 days after a positive result on a reverse transcription polymerase chain reaction test for SARS-CoV-2 in individuals of any age between Mar. 1, 2020, and June 30, 2021, with genomic confirmation of variants of concern. We compared outcomes in wave 3 (February 2021 to June 2021) with outcomes in waves 1 and 2 combined (March 2020 to January 2021) after adjusting for age, sex and Charlson Comorbidity Index score. Using wave 3 data only, we compared outcomes by vaccination status and whether or not the individual was infected with a variant of concern.

Results: Compared to those infected with SARS-CoV-2 during waves 1 and 2 (n = 372 070), we found a shift toward a younger and healthier demographic in those infected during wave 3 (n = 359 079). In wave 3, patients were more likely to be hospitalized (adjusted odds ratio [aOR] 1.57, 95% confidence interval [CI] 1.46–1.70) but had a shorter length of hospital stay (median 6 days v. 7 days, p < 0.001) and lower 30-day mortality (aOR 0.73, 95% CI 0.65–0.81). The 217 892 patients in wave 3 who were infected with a variant of concern (83.5% confirmed to have the Alpha variant, 1.7% confirmed to have the Delta variant) had a higher risk of death (Alpha: aOR 1.29, 95% CI 1.16–1.44; Delta: aOR 2.05, 95% CI 1.49–2.82) and hospitalization (Alpha: aOR 1.59, 95% CI 1.53–1.66; Delta: aOR 1.88, 95% CI 1.64–2.15) than those infected with wild-type SARS-CoV-2.

Interpretation: We observed a shift among those infected with SARS-CoV-2 toward younger patients with fewer comorbidities, a shorter length of hospital stay and lower mortality risk as the pandemic evolved in Alberta and Ontario; however, infection with a variant of concern was associated with a substantially higher risk of hospitalization or death. As variants of concern emerge, ongoing monitoring of disease expression and outcomes among vaccinated and unvaccinated individuals is important to understand the phenotypes of COVID-19 and the anticipated burdens for the health care system.

Since December 2020, the World Health Organization has recognized SARS-CoV-2 variants of concern.[1,2] Although reports from the United Kingdom, Europe and China have suggested that infections with variants of concern are more severe,[3–12] until very recently there has been a paucity of evidence from North America.[13,14]

In Canada, wave 3 of the COVID-19 pandemic occurred between February and June 2021 (www.covid19tracker.ca) and was driven by variants of concern, particularly the Alpha (B.1.1.7) and Delta (B.1.617) variants; the Gamma (P1) and Beta (B.1.351) variants were seen largely in travellers returning from regions where these were more common. The Alpha variant has been associated with higher risks of mortality (approximately 64% in a UK case–control study and 59% in a UK cohort study)[5,6] and hospitalization (52% in a UK cohort study[6] and approximately 70% in European Surveillance System data).[7] However, the UK studies[5,6] relied solely on findings from community tests; they omitted up to 70% of COVID-19 deaths, which occurred in patients diagnosed after hospital admission. In the European study,[7] less than 1%

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of specimens positive for SARS-CoV-2 were sequenced for variants. A Danish study also reported higher hospitalization rates with the Alpha variant, but this finding was based on only 128 hospitalizations (of 1235 in total), and the difference was detected only in adjusted analyses.[8]

Questions remain about disease severity and trajectories (i.e., the timing of hospitalizations or death) with variants of concern compared to the original "wild-type" SARS-CoV-2 clade in North America — crucial information for health system planners. In particular, given emerging evidence that the Delta and Omicron variants replicate more quickly, and that individuals infected with these strains have much higher viral loads, there is an urgent need to define the phenotypes of infection with variants of concern, because they rapidly become the most common circulating strain.

In this study, we examined changes in demographics and 30-day outcomes among people in Alberta and Ontario who were infected with SARS-CoV-2 over the first 15 months (3 waves) of the COVID-19 pandemic. To quantify the effect on outcomes of variants of concern, we compared event rates during wave 3 to those in waves 1 and 2, which were caused by wild-type SARS-CoV-2. Studies are ongoing to examine outcomes with newer variants of concern, such as Omicron.

Methods

Study design and setting

We conducted a retrospective cohort study in 2 of Canada's most populous provinces — Alberta and Ontario; these provinces were the first to have linkable access to province-wide SARS-CoV-2 testing data, and they include over half of the Canadian population. Health care in Canada is government-funded, with free universal access to hospital, emergency department and physician services; each province is the legal custodian of health data for its citizens.

Participants

The study population included all people of any age (outpatients and inpatients) with a positive result from a SARS-CoV-2 reverse transcription polymerase chain reaction (RT-PCR) nasopharyngeal swab between Mar. 1, 2020, and June 30, 2021, and with genomic confirmation of all screen-positive tests for variants of concern after Feb. 7, 2021.

Data sources

We linked several province-wide administrative health data sets, deterministically using encrypted unique health identifier numbers to create our study's analytical data set. Specifically, we linked RT-PCR testing data for SARS-CoV-2 from the Alberta and Ontario provincial laboratories with databases in each province that captured emergency department visits (National Ambulatory Care Reporting System), hospitalizations (Discharge Abstract Database) and COVID-19 vaccination status (see Appendix 1, available at www.cmajopen.ca/content/10/2/E400/suppl/DC1, for data sources and definitions. Vaccinations became available in both provinces in December 2020, initially for high-risk individuals only but with rapid expansion to the general adult population within 2 months as vaccine supply permitted. An individual was defined as fully vaccinated if at least 2 weeks had passed since their second dose of an approved COVID-19 vaccine; partially vaccinated if they had received at least 1 dose but did not yet meet the definition for fully vaccinated at the time of their positive SARS-CoV-2 RT-PCR test; unvaccinated).[15]

We extracted information on demographics, geographic locale and deaths from the health care insurance registry files of each province using the same deterministic linkage of unique health identifier numbers.

Definitions: cases, index dates and outcomes

For patients who were tested more than once during our study period, we examined only the data related to their first positive SARS-CoV-2 test. The index date was the date of their first positive RT-PCR test. Outcomes examined included emergency department visits, hospitalizations or deaths in the first 30 days after a positive result from an RT-PCR test.

Covariates

We identified comorbidities for each patient and generated their score on the Charlson Comorbidity Index[16] using standardized case definitions from the *International Classification of Diseases, 10th Revision*, Canadian version (previously validated in Alberta and Ontario; Appendix 1).[17] We based the identification of comorbidities on all hospitalizations in the 2 years up to and including the index date for each individual.

Statistical analysis

We have presented summary statistics, stratified according to the timing of the positive SARS-CoV-2 result (wave 1: Mar. 2020 to Oct. 2020; wave 2: Nov. 2020 to Jan. 2021; wave 3: Feb. 2021 to June 2021) and, for cases detected during wave 3, whether they were infected with a variant of concern or wild-type SARS-CoV-2. We compared outcome risks after adjusting for age, sex and Charlson Comorbidity Index score (which includes the most important of the QCovid[18] risk score factors, such as diabetes, pulmonary disease, kidney disease, heart failure, neurologic disease and cancer). We conducted all analyses using SAS version 9.4 (SAS Institute) for each province separately. We then pooled the adjusted odds ratios (aORs) for each province using meta-analysis.

Although both Alberta and Ontario used a common protocol and common case definitions for comorbidities, several potential sources of heterogeneity remained between the provinces (e.g., differences in populations, drug formulary restrictions, data capture and SARS-CoV-2 testing priorities). Therefore, as per the convention of the Canadian Network for Observational Drug Effect Studies,[19] we conducted a random effect meta-analysis using "metafor" in R package version 1.4–0 (http://CRAN.R-project.org/package=metafor). We used the restricted maximum likelihood estimator to estimate population heterogeneity because of its high efficiency compared to other estimators when the number of effect sizes is small.

Ethics approval

Ethical approval for this study was granted by the Health Research Ethics Board of the University of Alberta (Pro00101096). Signed informed consent from individual patients was waived for the Alberta data because we were analyzing de-identified health care administrative data. The use of Ontario data was authorized under section 45 of Ontario's *Personal Health Information Protection Act* and did not require review by a research ethics board.

Results

Compared to the 372 070 cases of SARS-CoV-2 infection identified in waves 1 and 2 (March 2020 to January 2021), we observed a leftward shift in age distribution for the 359 079 cases identified in wave 3 (February to June 2021; Table 1). We found a similar positivity rate across all 3 waves (5.2% of samples, overall).

Hospitalizations within 30 days of a positive result were higher in wave 3 (5.6% v. 5.4%, $p < 0.001$), a difference that remained significant after adjusting for differences in demographics and comorbidity burdens (Alberta: aOR 1.51, 95% CI 1.44–1.58; Ontario: aOR 1.63, 95% CI 1.59–1.67; pooled: aOR 1.57, 95% CI 1.46–1.70 for wave 3 v. waves 1 and 2). However, hospital lengths of stay were shorter in wave 3 (Alberta: median 5 days v. 7 days; Ontario: median 6 days v. 7 days; both $p < 0.001$) than in waves 1 and 2. Patients with SARS-CoV-2 infection during wave 3 were also less likely to die within 30 days (0.9% v. 2.2%, $p < 0.0001$) than those in waves 1 and 2, even after adjusting for their younger age and lower comorbidity burdens (Alberta: aOR 0.68, 95% CI 0.61–0.76; Ontario: aOR 0.76, 95% CI 0.72–0.80; pooled: aOR 0.73, 95% CI 0.65–0.81).

Variants of concern versus wild-type strain in wave 3

Examining wave 3 data only, we found that 310 319 (86%) of the 359 079 patients with samples that were positive for SARS-CoV-2 between February and June 2021 were screened for variants of concern. Overall, 217 892 (70.2%) of those screened were confirmed positive for a variant: 182 020 (83.5%) for the Alpha variant and 3708 (1.7%) for the Delta variant (Table 2).

After adjusting for age, sex and comorbidities, infections with either the Alpha or Delta variant were associated with higher 30-day risks of death and hospitalization than wild-type infections during wave 3 (Table 3). However, the length of hospital stay and the time between a positive test result and death were similar among patients with variants of concern and wild-type infections in wave 3. Patients who were partially or fully vaccinated had a reduced risk of all-cause hospitalization or mortality in wave 3 in both Alberta and Ontario.

Interpretation

Our data describe disease severity phenotypes for SARS-CoV-2 variants of concern in Alberta and Ontario, information that is important for public health messaging and for health system planners. We found that the mortality risk was 29% higher with Alpha variant infections in Alberta and Ontario, consistent with effect estimates from the UK and Europe.[4,5,7] However, given that wave 3 affected younger patients more than waves 1 and 2 (at least partially because of vaccination eligibility criteria), and given the increasing use of proven therapies such as corticosteroids over the course of the pandemic, we also found that the case fatality rate for those infected with SARS-CoV-2 was 27% lower in wave 3 than in the earlier waves, even though hospitalization risk increased by 57% in wave 3.

Our finding that people infected with a variant of concern were more likely to require hospitalization than those with wild-type SARS-CoV-2 was also consistent with reports from the UK and Europe (where over 80% of infections with variants of concern in wave 3 were the Alpha variant).[6–8] Our finding of even higher event rates in those infected with the Delta variant also confirmed reports from China (hazard ratio [HR] 2.98, 95%CI 1.29–6.86 for deterioration to critical status with Delta-variant infections compared to wild-type infections),[10] Scotland (85% higher risk of hospitalization with Delta-variant infections versus Alpha-variant infections)[11] and England (adjusted HRs for hospitalization with the Delta variant versus the Alpha variant: 1.94 for vaccinated patients and 2.32 for unvaccinated patients).[12] A recently published study from another group in Ontario also reported markedly higher risks of hospitalization and death in patients infected with the Delta variant (aORs of 2.08 and 2.32, respectively).[13] In the United States, the risk of hospitalization with SARS-CoV-2 infection declined in the first 6 months of 2021, but it began increasing again after the Delta variant became the predominant strain in July and August 2021.[14]

These findings suggest that communities with ongoing high transmission rates of the Delta variant will experience major potential effects on health system capacity compared to previous waves of the pandemic. In particular, we note that the 8% hospitalization risk in those infected with the Delta variant during wave 3 in Alberta and Ontario was nearly double that seen with wild-type infections in earlier waves of the pandemic.

We found that vaccination against SARS-CoV-2 was associated with reduced chances of all-cause hospitalization or death in wave 3, even after adjusting for age, sex and comorbidity burden. To that end, it is worth noting that most hospitalizations in wave 3 occurred in unvaccinated or partially vaccinated individuals: for example, 91% of those hospitalized in Alberta during wave 3 were not fully vaccinated.[20] As well, a recent US study found that vaccination was associated with a lower likelihood of hospitalization or death as a result of SARS-CoV-2 infection, and that vaccinated patients who were hospitalized had a substantially lower risk of progression to invasive mechanical ventilation.[21] Preliminary data from England has demonstrated that the elevated HR for hospitalization among vaccinated individuals who were infected with the Delta variant was not significantly different than the HR for Delta-variant versus wild-type infections in those who were unvaccinated or partially vaccinated ($p = 0.82$).[11,13,22]

Table 1 (part 1 of 2): Demographics and outcomes for those with SARS-CoV-2 infection in Alberta and Ontario — Mar. 1, 2020, to June 30, 2021

Characteristic	Wave 1 (Mar. 2020 to Oct. 2020)	Wave 2 (Nov. 2020 to Jan. 2021)	Wave 3 (Feb. 2021 to June 2021)	Total	*p* value*
No. of people with a positive SARS-CoV-2 test	100 478	271 592	359 079	731 149	–
Age, yr, *n* (%)					
< 18	10 274 (10.2)	36 367 (13.4)	66 349 (18.5)	112 990 (15.5)	< 0.0001
18–39	35 754 (35.6)	96 585 (35.6)	132 911 (37.0)	265 250 (36.3)	< 0.0001
40–65	37 986 (37.8)	103 488 (38.1)	132 022 (36.8)	273 496 (37.4)	< 0.0001
> 65	16 464 (16.4)	35 152 (12.9)	27 797 (7.7)	79 413 (10.9)	< 0.0001
Age, yr, median (IQR)					
Alberta	36 (23–51)	36 (23–52)	33 (19–47)	35 (21–49)	< 0.0001
Ontario	43 (27–60)	40 (25–57)	36 (23–52)	38 (24–55)	< 0.0001
Male, *n* (%)	48 523 (48.3)	133 329 (49.1)	182 622 (50.9)	364 474 (49.8)	< 0.0001
Rural resident, *n* (%)	4968 (4.9)	18 713 (6.9)	24 116 (6.7)	47 797 (6.5)	< 0.0001
Deprivation Index, *n* (%)					
Missing	2373 (2.4)	7409 (2.7)	8927 (2.5)	18 709 (2.6)	< 0.0001
Q1 (least deprived)	16 782 (16.7)	44 020 (16.2)	62 711 (17.5)	123 513 (16.9)	
Q2	16 809 (16.7)	47 136 (17.4)	65 702 (18.3)	129 647 (17.7)	
Q3	18 004 (17.9)	50 495 (18.6)	66 885 (18.6)	135 384 (18.5)	
Q4	18 909 (18.8)	54 169 (19.9)	69 639 (19.4)	142 717 (19.5)	
Q5 (most deprived)	27 601 (27.5)	68 363 (25.2)	85 215 (23.7)	181 179 (24.8)	
In a long-term care facility, *n* (%)	7832 (7.8)	10 202 (3.8)	826 (0.2)	18 860 (2.6)	< 0.0001
Charlson Comorbidity Index score, *n* (%)					
0/missing	90 174 (89.7)	249 436 (91.8)	334 113 (93)	673 723 (92.1)	< 0.0001
1	2278 (2.3)	4479 (1.6)	3337 (0.9)	10 094 (1.4)	
2	1526 (1.5)	2983 (1.1)	2334 (0.6)	6843 (0.9)	
3+	6500 (6.5)	14 694 (5.4)	19 295 (5.4)	40 489 (5.5)	
Specific comorbidities, *n* (%)					
COPD or asthma	804 (0.8)	1723 (0.6)	1207 (0.3)	3734 (0.5)	< 0.0001
Other chronic lung disease (non-COPD/asthma)	29 (0)	65 (0)	56 (0)	150 (0)	0.01
Congestive heart failure	1005 (1)	1813 (0.7)	1275 (0.4)	4093 (0.6)	< 0.0001
Hypertension	3100 (3.1)	5614 (2.1)	4053 (1.1)	12 767 (1.7)	< 0.0001
Diabetes mellitus	2655 (2.6)	5280 (1.9)	4231 (1.2)	12 166 (1.7)	< 0.0001
CAD (including previous MI, CABG or PCI/stent)	898 (0.9)	1996 (0.7)	1901 (0.5)	4795 (0.7)	< 0.0001
Peripheral vascular disease	218 (0.2)	424 (0.2)	335 (0.1)	977 (0.1)	< 0.0001
Cerebrovascular disease (previous stroke/TIA)	678 (0.7)	1110 (0.4)	699 (0.2)	2487 (0.3)	< 0.0001
Atrial fibrillation/flutter	1174 (1.2)	1943 (0.7)	1256 (0.3)	4373 (0.6)	< 0.0001
Ventricular arrhythmias	67 (0.1)	152 (0.1)	130 (0)	349 (0)	< 0.0001
Renal disease	489 (0.5)	988 (0.4)	725 (0.2)	2202 (0.3)	< 0.0001
Cancer	706 (0.7)	1654 (0.6)	1752 (0.5)	4112 (0.6)	< 0.0001
Peptic ulcer disease	178 (0.2)	298 (0.1)	282 (0.1)	758 (0.1)	< 0.0001
Liver disease	191 (0.2)	559 (0.2)	544 (0.2)	1294 (0.2)	< 0.0001
Dementia	1968 (2)	2602 (1)	621 (0.2)	5191 (0.7)	< 0.0001

Table 1 (part 2 of 2): Demographics and outcomes for those with SARS-CoV-2 infection in Alberta and Ontario — Mar. 1, 2020, to June 30, 2021

Characteristic	Wave 1 (Mar. 2020 to Oct. 2020)	Wave 2 (Nov. 2020 to Jan. 2021)	Wave 3 (Feb. 2021 to June 2021)	Total	*p* value*
Vaccination status, *n* (%)					
Fully vaccinated	0 (0)	8 (0)	2500 (0.7)	2508 (0.3)	< 0.0001
Partially vaccinated	0 (0)	733 (0.3)	22 378 (6.2)	23 111 (3.2)	
Unvaccinated	100 478 (100)	270 851 (99.7)	334 201 (93.1)	705 530 (96.5)	
Death					
Death within 30 days, *n* (%)	3423 (3.4)	4800 (1.8)	2639 (0.7)	10 862 (1.5)	< 0.0001
Age at death, yr, median (IQR)					
Alberta	85 (77–91)	85 (75–91)	74 (63–85)	84 (73–90)	< 0.0001
Ontario	86 (78–91)	85 (76–91)	76 (66–85)	83 (73–90)	< 0.0001
Male, *n* (%)	1604 (46.9)	2479 (51.6)	1548 (58.7)	5631 (51.8)	< 0.0001
Days to death, median (IQR)					
Alberta	7 (3–12)	8 (4–13)	9 (4–15)	8 (4–13)	0.009
Ontario	9 (5–14)	11 (7–17)	12 (6–19)	11 (6–17)	< 0.0001
All-cause hospitalization					
Hospital admission within 30 days	7036 (7)	13 025 (4.8)	20 256 (5.6)	40 317 (5.5)	< 0.0001
Age at hospitalization, yr, median (IQR)					
Alberta	63 (47–76)	65 (48–80)	54 (40–67)	59 (44–74)	< 0.0001
Ontario	68 (54–81)	70 (55–82)	60 (46–73)	64 (50–77)	< 0.0001
Male, *n* (%)	3737 (53.1)	6977 (53.6)	11 047 (54.5)	21 761 (54)	0.02
Length of stay, d, median (IQR)					
Alberta	6 (3–12)	7 (3–13)	5 (3–10)	6 (3–11)	< 0.0001
Ontario	8 (3–20)	7 (3–14)	6 (3–12)	7 (3–13)	< 0.0001

Note: CABG = coronary artery bypass graft, CAD = coronary artery disease, COPD = chronic obstructive pulmonary disease, IQR = interquartile range, MI = myocardial infarction, PCI = percutaneous coronary intervention, TIA = transient ischemic attack.
*Waves 1 and 2 versus wave 3.

However, the absolute risks for hospitalization or poor outcomes were substantially lower in those who were vaccinated, even those infected with the Delta variant.

Our data on the effectiveness of vaccination in reducing hospitalizations and deaths as a result of SARS-CoV-2 variants of concern is consistent with other recent reports.[21,23–26] Although ongoing genomic monitoring is crucial for detecting new variants of concern,[27] we believe that it is just as important to ensure continued assessment of disease severity phenotypes in different jurisdictions, in vaccinated and unvaccinated individuals, and as variants of concerns evolve.

A major strength of our study was that most specimens that were positive for SARS-CoV-2 during wave 3 in Alberta and Ontario were screened for variants of concern, and samples that screened positive underwent subsequent genomic confirmation. In contrast, very low proportions were screened and had genomic confirmation in other studies describing disease severity in variants of concern (for example, only 0.7% in the recent report from the European Surveillance System).[7]

Limitations

A limitation of our analysis was that it was based largely on Alpha-variant infections, although we did have 30-day outcome data from over 3700 individuals infected with the Delta variant.[3,6,7] As with other studies comparing variants of concern with wild-type infections, our sampling frame may have resulted in overestimates of absolute risks because minimally symptomatic or asymptomatic patients with infection were less likely to be tested (an example of collider bias).[28] However, we examined all positive community cases, which was less biased than studying only hospitalized cases (which previous studies have done), and we found that sample positivity rates were similar in all 3 waves (approximately 5%).

To the extent that the Alpha or Delta variants may have been circulating in Alberta and Ontario before screening began for variants of concern, our results may have underestimated the impact of these variants on outcomes, because events in undiagnosed infections with variants of concern would have been classified as wild-type infections. It should

Table 2 (part 1 of 2): Demographics and outcomes for those with SARS-CoV-2 infection in Alberta and Ontario by variant — Feb. 1, 2021, to June 30, 2021 (wave 3)

Characteristic	Wild-type	Alpha variant	Delta variant	Other variants	Not tested/ indeterminate	Total	*p* value
No. of people with a positive SARS-CoV-2 test	92 427	182 020	3708	32 164	48 760	359 079	–
Age, yr, *n* (%)							
< 18	19 884 (21.5)	31 875 (17.5)	702 (18.9)	5439 (16.9)	8449 (17.3)	66 349 (18.5)	< 0.0001
18–39	31 017 (33.6)	69 101 (38.0)	1409 (38.0)	12 440 (38.7)	18 944 (38.9)	132 911 (37)	
40–65	34 832 (37.7)	67 697 (37.2)	1290 (34.8)	11 652 (36.2)	16 551 (33.9)	132 022 (36.8)	
> 65	6694 (7.2)	13 347 (7.3)	307 (8.3)	2633 (8.2)	4816 (9.9)	27 797 (7.7)	
Age, yr, median (IQR)							
Alberta	32 (18–47)	33 (20–47)	32 (20–45)	35 (22–48)	NA	33 (19–47)	< 0.0001
Ontario	36 (23–54)	36 (23–52)	35 (22–52)	36 (22–52)	36 (22–53)	36 (23–52)	< 0.0001
Male, *n* (%)	47 217 (51.1)	92 315 (50.7)	1898 (51.2)	16 700 (51.9)	24 492 (50.2)	182 622 (50.9)	< 0.0001
Rural resident, *n* (%)	9317 (10.1)	9856 (5.4)	301 (8.1)	1608 (5)	3034 (6.2)	24 116 (6.7)	< 0.0001
Deprivation Index, *n* (%)							
Missing	3902 (4.2)	3231 (1.8)	69 (1.9)	482 (1.5)	1243 (2.5)	8927 (2.5)	< 0.0001
Q1 (least deprived)	15 183 (16.4)	32 650 (17.9)	589 (15.9)	5407 (16.8)	8882 (18.2)	62 711 (17.5)	
Q2	15 997 (17.3)	34 327 (18.9)	621 (16.7)	5807 (18.1)	8950 (18.4)	65 702 (18.3)	
Q3	17 047 (18.4)	34 328 (18.9)	664 (17.9)	6001 (18.7)	8845 (18.1)	66 885 (18.6)	
Q4	16 983 (18.4)	36 044 (19.8)	747 (20.1)	6576 (20.4)	9289 (19.1)	69 639 (19.4)	
Q5 (most deprived)	23 315 (25.2)	41 440 (22.8)	1018 (27.5)	7891 (24.5)	11 551 (23.7)	85 215 (23.7)	
In a long-term care facility, *n* (%)	326 (0.4)	165 (0.1)	32 (0.9)	53 (0.2)	250 (0.5)	826 (0.2)	< 0.0001
Charlson Comorbidity Index score, *n* (%)							
0/missing	87 775 (95)	169 547 (93.1)	3368 (90.8)	29 602 (92)	43 821 (89.9)	334 113 (93)	< 0.0001
1	943 (1)	1475 (0.8)	35 (0.9)	263 (0.8)	621 (1.3)	3337 (0.9)	
2	610 (0.7)	1081 (0.6)	29 (0.8)	212 (0.7)	402 (0.8)	2334 (0.6)	
3+	3099 (3.4)	9917 (5.4)	276 (7.4)	2087 (6.5)	3916 (8)	19 295 (5.4)	
Specific comorbidities, *n* (%)							
COPD or asthma	360 (0.4)	534 (0.3)	7 (0.2)	113 (0.4)	193 (0.4)	1207 (0.3)	< 0.0001
Other chronic lung disease (non-COPD/asthma)	16 (0)	23 (0)	1–5*	1–5*	10 (0)	56 (0)	0.02
Congestive heart failure	331 (0.4)	577 (0.3)	12 (0.3)	113 (0.4)	242 (0.5)	1275 (0.4)	< 0.0001
Hypertension	1001 (1.1)	1936 (1.1)	46 (1.2)	351 (1.1)	719 (1.5)	4053 (1.1)	< 0.0001
Diabetes mellitus	1124 (1.2)	1935 (1.1)	52 (1.4)	366 (1.1)	754 (1.5)	4231 (1.2)	< 0.0001
CAD (including previous MI, CABG or PCI/stent)	443 (0.5)	919 (0.5)	22 (0.6)	174 (0.5)	343 (0.7)	1901 (0.5)	< 0.0001
Peripheral vascular disease	83 (0.1)	147 (0.1)	3 (0.1)	36 (0.1)	66 (0.1)	335 (0.1)	0.008
Cerebrovascular disease (previous stroke/TIA)	185 (0.2)	312 (0.2)	8 (0.2)	54 (0.2)	140 (0.3)	699 (0.2)	< 0.0001
Atrial fibrillation/flutter	330 (0.4)	535 (0.3)	18 (0.5)	110 (0.3)	263 (0.5)	1256 (0.3)	< 0.0001
Ventricular arrhythmias	31 (0)	63 (0)	1–5*	17 (0.1)	17 (0)	130 (0)	0.5
Renal disease	181 (0.2)	348 (0.2)	1–5*	53 (0.2)	139 (0.3)	725 (0.2)	0.0002
Cancer	417 (0.5)	831 (0.5)	18 (0.5)	169 (0.5)	317 (0.7)	1752 (0.5)	< 0.0001
Peptic ulcer disease	72 (0.1)	124 (0.1)	1–5*	27 (0.1)	55 (0.1)	282 (0.1)	0.04
Liver disease	173 (0.2)	198 (0.1)	8 (0.2)	43 (0.1)	122 (0.3)	544 (0.2)	< 0.0001
Dementia	181 (0.2)	212 (0.1)	9 (0.2)	51 (0.2)	168 (0.3)	621 (0.2)	< 0.0001

Table 2 (part 2 of 2): Demographics and outcomes for those with SARS-CoV-2 infection in Alberta and Ontario by variant — Feb. 1, 2021, to June 30, 2021 (wave 3)

Characteristic	Wild-type	Alpha variant	Delta variant	Other variants	Not tested/ indeterminate	Total	*p* value
Vaccination status, *n* (%)							
Fully vaccinated	334 (0.4)	925 (0.5)	111 (3)	195 (0.6)	935 (1.9)	2500 (0.7)	< 0.0001
Partially vaccinated	3823 (4.1)	11 722 (6.4)	1010 (27.2)	2100 (6.5)	3723 (7.6)	22 378 (6.2)	
Unvaccinated	88 270 (95.5)	169 373 (93.1)	2587 (69.8)	29 869 (92.9)	44 102 (90.4)	334 201 (93.1)	
Death							
Death within 30 days, *n* (%)	532 (0.6)	1384 (0.8)	52 (1.4)	325 (1)	346 (0.7)	2639 (0.7)	< 0.0001
Age at death, yr, median (IQR)							
Alberta	75 (63–86)	74 (65–85)	72 (69–80)	66 (56–73)	NA	74 (63–85)	0.01
Ontario	79 (70–87)	75 (65–84)	73 (60–86)	74 (65–84)	78 (66–86)	76 (66–85)	< 0.0001
Male, *n* (%)	302 (56.8)	822 (59.4)	30 (57.7)	202 (62.2)	192 (55.5)	1548 (58.7)	< 0.0001
Days to death, median (IQR)							
Alberta	8 (3–14)	9 (4–17)	12 (4–18)	9 (3–14)	NA	9 (4–15)	0.4
Ontario	11 (6–17)	12 (7–19)	16 (11–21)	13 (6–20)	10 (4–16)	12 (6–19)	< 0.0001
All-cause hospitalization							
Hospital admission within 30 days	3470 (3.8)	11 552 (6.3)	295 (8)	2321 (7.2)	2618 (5.4)	20 256 (5.6)	< 0.0001
Age at hospitalization, yr, median (IQR)							
Alberta	55 (38– 69)	54 (41–66)	57 (39–69)	53 (40–62)	NA	54 (40–67)	0.3
Ontario	63 (48–77)	59 (46–71)	57 (43–70)	60 (48–72)	61 (41–75)	60 (46–73)	< 0.0001
Male, *n* (%)	1878 (54.1)	6284 (54.4)	169 (57.3)	1335 (57.5)	1381 (52.8)	11 047 (54.5)	< 0.0001
Length of stay, d, median (IQR)							
Alberta	5 (3–10)	5 (3–10)	6 (3–10)	6 (3–10)	NA	5 (3–10)	0.8
Ontario	6 (3–11)	6 (3–11)	6 (3–11)	7 (3–12)	6 (2–11)	6 (3–12)	< 0.0001

Note: CABG = coronary artery bypass graft, CAD = coronary artery disease, COPD = chronic obstructive pulmonary disease, IQR = interquartile range, MI = myocardial infarction, NA = not available, PCI = percutaneous coronary intervention, TIA = transient ischemic attack.
*Cells with values of less than 5 have been suppressed for privacy reasons.

Table 3: Outcome associations during wave 3, stratified by variant of concern and vaccination status*

	All-cause hospitalization, aOR (95% CI)			Death, aOR (95% CI)		
Variable	Alberta	Ontario	Pooled	Alberta	Ontario	Pooled
Variant of concern						
Wild-type	Reference					
Alpha variant	1.86 (1.73–2.00)	1.48 (1.41–1.56)	1.59 (1.53–1.66)	1.64 (1.32–2.04)	1.19 (1.05–1.35)	1.29 (1.16–1.44)
Delta variant	2.7 (1.91–3.81)	1.76 (1.52–2.04)	1.88 (1.64–2.15)	4.97 (2.37–10.43)	1.67 (1.17–2.38)	2.05 (1.49–2.82)
Vaccination status						
Unvaccinated	Reference					
Partially vaccinated	0.44 (0.38–0.51)	0.42 (0.39–0.44)	0.42 (0.40–0.45)	0.61 (0.46–0.81)	0.40 (0.35–0.46)	0.43 (0.38–0.49)
Fully vaccinated	0.55 (0.36–0.83)	0.18 (0.15–0.22)	0.22 (0.18–0.26)	0.98 (0.55–1.77)	0.33 (0.25–0.45)	0.41 (0.32–0.53)

Note: aOR = adjusted odds ratio, CI = confidence interval.
*Adjusted for age, sex and Charlson Comorbidity Index score.

be noted that the Public Health Agency of Canada update from Feb. 19, 2021,[29] suggested that there were very few cases of variants of concern at the national level, even 10 days after widespread screening had started in Alberta and Ontario.

The duration of the presymptomatic stage (and the frequency of asymptomatic cases) with different SARS-CoV-2 strains has not yet been described and could not be assessed using our data set. As well, our use of the index hospitalization and any hospitalizations in the previous 2 years to define comorbidities and Charlson Comorbidity Index scores likely underestimated comorbidity burdens for community-dwelling individuals who had been relatively healthy. Moreover, because we did not have access to data on in-hospital treatments, we could not adjust for the impact of therapies that have proven beneficial in the treatment of COVID-19 (such as corticosteroids[30]) when we examined trends in mortality rates. We also could not account for potential differences in uptake of public health guidance (particularly with respect to social distancing and masking guidelines) between groups over the course of the pandemic.

Conclusion

The COVID-19 pandemic has evolved over time, with more infections in younger and healthier patients and more hospitalizations (but shorter lengths of stay and fewer deaths) in wave 3 than in earlier waves. However, high community transmission rates for variants of concern will lead to correspondingly high admission rates, adversely affecting health care capacity. These data indicate that the Alpha and Delta variants are associated with substantially higher risks of hospitalization or death than the wild-type strain in Alberta and Ontario. This finding is important for individual patient counselling to address vaccine hesitancy, and for public information campaigns that reinforce the need for continued risk-reduction measures such as social distancing and masking.

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