Clinical severity of Omicron SARS-CoV-2 variant relative to Delta in British Columbia, Canada: A retrospective analysis of whole genome sequenced cases

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ABSTRACT

Background:

In late 2021, the Omicron SARS-CoV-2 variant emerged and rapidly replaced Delta as the dominant variant globally. The increased transmissibility of the variant led to surges in case rates as well as increases in hospitalizations, however, the true severity of the variant remained unclear. We aimed to provide robust estimates of Omicron severity relative to Delta.

Methods:

This study was conducted using a retrospective cohort design with data from the British Columbia COVID-19 Cohort – a large provincial surveillance platform with linkage to administrative datasets. To capture the time of co-circulation with Omicron and Delta, December 2021 was chosen as the study period. We included individuals diagnosed with Omicron or Delta infection, as determined by whole genome sequencing (WGS). To assess the severity (hospitalization, ICU admission, length of stay), we conducted adjusted Cox proportional hazard models, weighted by inverse probability of treatment weights (IPTW), accounting for age, sex, underlying comorbidities, vaccination, sociodemographic status, and geographical variation.

Results:

The cohort was composed of 13,128 individuals (7,729 Omicron and 5,399 Delta). There were 419 COVID-19 hospitalizations, with 118 (22%) among people diagnosed with Omicron (crude rate=1.5% Omicron, 5.6% Delta). In multivariable IPTW analysis, Omicron was associated with a 50% lower risk of hospitalization compared to Delta (aHR=0.50; 95%CI=0·43-0.59), a 73%

lower risk of ICU admission (aHR=0.27; 95%CI=0.19-0.38), and a 5 days shorter hospital stay on average (aß=-5.03; 95% CI=-8.01, -2.05).

Conclusions:

Our analysis supports findings from other studies demonstrating lower risk of severe outcomes in Omicron-infected individuals relative to Delta.

Keywords: SARS-CoV-2; COVID-19; Omicron; Delta; severity

INTRODUCTION

Assessing the risk of severe outcomes associated with COVID-19, and identifying characteristics associated with increased risk, is critical to inform clinical and public health decision-making. In addition to well established risk factors such as older age, male sex, comorbidities and lack of immunization, previous research has identified SARS-CoV-2 variants of concern (VOC) as an important determinant of infection severity.[1–3] Indeed, each newly dominant VOC has generally been more virulent than the previous (Delta (Pangolin lineages[4] B.1.617.2 and AY.*)>Alpha (B.1.1.7 and Q.*)>wild type).

In late 2021, the Omicron SARS-CoV-2 variant (B.1.1.529 and BA.*) emerged and quickly replaced Delta as the dominant variant globally.[5] The increased transmissibility of Omicron led to much higher case rate compared to previous COVID-19 waves, and was followed by a large increase in hospitalizations. However, it was not clear whether increases in hospitalizations were the result of the sheer number of Omicron cases, increased virulence relative to Delta and/or increased identification of incidental hospitalizations (i.e., infection identified in persons hospitalized for other reasons). Promisingly, laboratory and animal studies suggested attenuated severity of infection with Omicron and reduced ability to replicate in the lower respiratory tract.[6,7] Early reports also suggest less severe infection with Omicron, although these studies were mostly conducted in South Africa, a setting very different than North America and Europe with respect to age distribution of infections and underlying pattern of protective immunity from prior infection in previous waves, potentially affecting generalizability of results.[8,9] Also, most prior studies either lacked individual-level data on VOC [10,11] or used RT-PCR S-gene target failure as a proxy for Omicron infection (as opposed to whole genome sequencing (WGS)), a

source of misclassification bias. To date, relatively few peer-reviewed studies with individual-level VOC data have been published on Omicron severity, and those published have identified a relatively wide range of reduced severity estimates relative to Delta (36-73%).[12–17] Additional analyses are therefore needed to better understand the severity of a globally dominant variant.

British Columbia (BC) has experienced over 18,000 COVID-19 hospitalizations and 2,800 deaths since the beginning of the pandemic, and is well placed to answer questions related to Omicron severity given the extent of WGS and availability of linked population-based registries. The objective of this study was to determine the clinical severity of WGS-confirmed Omicron relative to Delta during substantial co-circulation of these two variants.

METHODS

Data sources

We used data from the BC COVID-19 Cohort (BCC19C, Supplementary Table 1). The BCC19C is a surveillance platform integrating a range of COVID-19 datasets (e.g., case surveillance, laboratory tests, vaccinations) with administrative data holdings for the entire BC population (e.g., physician billings, hospitalization discharges) (Supplementary Table 2). This study was reviewed and approved by the Behavioural Research Ethics Board at the University of British Columbia (#H20-02097).

Sequencing strategy

In BC, the sequencing strategy of laboratory-confirmed COVID-19 samples has changed over time, including during our study period.[18,19] Between December 1st and December 15th, the strategy was to sequence all positive COVID-19 samples and during this time, about 80% of laboratory-confirmed positive samples were sequenced. Due to the large case load by December 15th, BC transitioned to sequencing a representative subset of positive samples (Supplementary Table 3) in addition to priority cases (outbreaks, long-term care, vaccine escape, travel-related, and hospitalization) – approximately 10-20% of all cases (Supplementary Figure 1).

Study population

We included individuals with a laboratory confirmed first time infection between December 1st and December 31st, 2021 whose SARS-CoV-2 lineage was confirmed as Delta or Omicron through WGS. We selected our study period to capture the time when Omicron first emerged and there was substantial co-circulation of Delta and Omicron (Supplementary Figure 1). Due to the small number of Delta infections and important changes to the COVID-19 diagnostic testing criteria in January 2022, we selected December 31st, 2021 as our study end date.[20]

We excluded individuals who: resided outside of Canada; were admitted to hospital greater than 2 days prior to their positive laboratory collection date; had missing information.

Exposure of interest (SARS-CoV-2 lineage)

Our exposure of interest was SARS-CoV-2 lineage, as determined by WGS. Lineage was defined as Delta (B.1.617.2, AY.*) or Omicron (B.1.1.529, BA.*). Other lineages were excluded from analysis (Supplementary Table 2).

Hospitalization due to COVID-19

We defined our primary outcome as a hospital admission date within -2 to 14 days of the positive laboratory collection date, as done by others assessing SARS-CoV-2 severity.[2,3] Hospital data sources are described in Supplementary Table2.

Secondary outcomes:

Definitions and data sources for secondary outcomes (ICU admission, LOS) are described in detail in Supplementary Table 2. In brief:

ICU admission: If an individual met the criteria of hospitalization in any hospital data source, and had a record of ICU admission associated with that hospitalization (from the same data source), then the criteria for ICU admission was met.

Length of stay (LOS): For individuals who were hospitalized within the -2 to 14-day time window, LOS was calculated as the difference between admission date and discharge date.

Mortality*:* Defined as a death within 30 days of laboratory collection date, modeling was not conducted due to small number of deaths during the study period, however counts are reported.

Analysis

We conducted Cox proportional hazards models weighted by inverse probability of treatment weights (IPTW) to examine the relationship between SARS-CoV-2 lineage and hospitalization. Individuals were followed from two days prior to lab collection date to the earliest of 14 days following lab collection date, COVID-19 death, or hospital admission. IPTW weights were calculated from a logistic regression model with VOC as the outcome and sex, age, geography, co-morbidities, neighbourhood income quintile, and vaccination status (full model only) as the independent variables. We used a doubly robust approach and adjusted for these same variables in a multivariable IPTW model. Standardized mean differences (SMDs) were computed using a threshold of 0.1 to assess success of weighting. The same methodology was applied for the secondary outcomes. Cox regression and linear regression were used to model ICU and LOS among hospitalized cases, respectively.

For all analyses, we examined an overall model and models stratified by vaccination status. Unvaccinated was defined as no record of vaccination 14 days prior to laboratory collection date. Fully vaccinated status was defined as record of two or more vaccinations (or one dose of Johnson & Johnson) at least 14 days prior to laboratory collection date. Stratified analyses excluded individuals who were partially vaccinated (only one dose 14 days prior to laboratory collection date), and individuals aged 11 and under, as no one in this age group was fully vaccinated during study period.

Covariate measurement

Age, sex, and geography of residence were extracted from the case surveillance dataset or, if missing, from the client roster of all individuals enrolled in universal health insurance. Co-morbidities were assessed using the Elixhauser index[21] and based on physician billing and hospitalization discharge data prior to lab collection date. Neighbourhood income was extracted at the level of dissemination area (DA – smallest standard unit of geography in Canada, equivalent to a street block) (Supplementary Table 2 for more details).

Sensitivity analyses

We performed sensitivity analyses to explore the impact of different potential biases. To account for potential incidental infections, we excluded people hospitalized within the 2 days prior to lab collection date and conducted an additional analysis removing individual diagnosed on same day as hospitalization. To explore the effect of sampling bias introduced by the change in sequencing strategy in mid-December, we performed an analysis limited to individuals diagnosed between Dec 15th to Dec 31st. Lastly, we also conducted another analysis adjusting for additional vaccination variables (booster within 14 days prior to lab collection and time since fully vaccinated=).

RESULTS

Study population

Overall, 41,322 people were diagnosed with laboratory confirmed SARS-CoV-2 infection between December 1st, 2021, and December 31st, 2021 (Figure 1). We excluded 27,851 (67.4%) people whose diagnostic specimen was not sequenced during this period. Overall, the sequenced

and non-sequenced populations had similar demographic distributions, although there were minor differences in geography and vaccination status (Supplementary Table 3). In addition, a higher percentage of sequenced cases were hospitalized, reflecting the targeted sequencing strategy implemented in mid-December.

Of the remaining 13,470 individuals, we excluded an additional 342 due to data incompleteness (Figure 1). Our final study population included 13,128 individuals (5,399 Delta and 7,729 Omicron) (Table 1). Most Omicron infections were BA.1 (77.5%), and the majority of Delta infections were AY.25.1 (69.1%). The majority of the cohort was fully vaccinated (n=9,310; 70.9%), while 3,266 (24.9%) was unvaccinated.

Overall, the study population was split evenly by sex (50.9% female) and half (49.1%) of participants were between the ages of 20-50 (median=33.0; IQR=25.0). There were several differences in characteristics by VOC, as reflected by the pre-weighted SMDs in Supplementary Figure 2. Omicron infections were more concentrated in the 20-40 year range and a larger proportion of individuals diagnosed with Delta were aged ≤11 years and ≥60 years. Individuals infected with Omicron were twice as likely to be fully vaccinated (87.6% vs 47.0%). Delta also had a more even geographic distribution, whereas Omicron had a greater proportion of diagnoses in more urban geographic regions (Table 1). During the study period, there were 33 deaths, with a higher case fatality rate found in those diagnosed with Delta (0.5%) compared to Omicron (0.1%).

Crude hospitalization rates

Overall, there were 419 hospitalizations in our analysis, with 301 (71.8%) occurring in people with Delta and 118 (28.2%) with Omicron (Table 1). The crude rate of hospitalization was higher for Delta (5.6%) compared to Omicron (1.5%). When stratified by vaccination status, the crude hospitalization rate for the unvaccinated was 15.0% for Delta and 3.8% for Omicron and in the vaccinated stratum was 3.0% and 1.4%, respectively. Crude hospitalization rates by sociodemographic and other covariates are presented in Supplementary Table 4.

Inverse probability treatment weights and balance

After weighting by IPTW, there was improved balance between individuals infected with Omicron and Delta across all variables (Supplementary Figure 2). In the full study population, pre-weighted standardized mean differences (SMDs) were very large for geography, vaccination status and age (SMD=1.39, 1.04 and 0.69, respectively). After weighting, all SMDs were below 0.1. Similar improvements in balance were found in each of the vaccination status strata as well, however, to a lesser degree in the unvaccinated stratum.

Risk of hospitalization among people with Delta and Omicron infection

Omicron was associated with a 50% lower risk of hospitalization (vs. Delta; aHR=0.50, 95% CI=0.43-0.59; Table 2 and Supplementary Table 4). In stratified analyses, a lower risk of hospitalization for Omicron was observed for both vaccinated and unvaccinated individuals (Table 2). However, the strength of association differed by vaccination strata. Amongst unvaccinated individuals, the risk of hospitalization for Omicron was 62% lower (vs. Delta;

aHR=0.38, 95% CI=0.30-0.49), while among vaccinated people the risk was 30% lower (vs. Delta; aHR=0.70, 95% CI=0.56-0.87).

Sensitivity analyses

Model estimates were relatively unchanged in sensitivity analyses accounting for incidental infections (aHR=0.51, 95% CI=0.43-0.60; and aHR=0.50, 95% CI=0.39-0.64 for hospitalization window of 0-14 days and 1-14 days, respectively; Supplementary Table 5) and with additional variables to adjust for booster doses and time since vaccination (aHR=0.47, 95% CI=0.40-0.55; Supplementary Table 6). Of note, in the sensitivity analysis accounting for the change in sequencing strategy in mid-December, the lower severity of Omicron relative to Delta was more pronounced (68% reduced risk of hospitalization; 95% CI=62-74%; Supplementary Table 5).

ICU admission

There was a total of 130 ICU admissions. The crude ICU admission rate was much higher for Delta (2.1%) compared to Omicron (0.2%). When stratifying by vaccination status, the crude rates for fully vaccinated individuals were 0.8% for Delta and 0.1% for Omicron and 5.4% and 0.9%, respectively, for the unvaccinated. In the Cox model, Omicron was associated with a 73% reduced risk of ICU admission (vs. Delta; aHR=0.27, 95% CI=0.19-0.38) (Table 2).

Length of Stay (LOS)

An additional eight individuals were excluded due to missing discharge dates and 32 for having died within 30 days from laboratory collection date. Length of hospital stay was higher for Delta

compared to Omicron. Median LOS for Delta was 9 (25^{th} percentile=4; 75^{th} percentile=19) and for Omicron was 4 (25^{th} percentile=2; 75^{th} percentile=8). In the IPTW multivariable linear regression model, Omicron was associated with an average LOS that was 5 days shorter compared to Delta (β-estimate=-5.03; 95% CI=-8.01, -2.05). Although weighting by IPTW significantly improved SMD balance across covariates, some SMDs remained high (Supplementary Figure 2).

DISCUSSION

In this large retrospective analysis of 7,729 and 5,399 individuals with WGS-confirmed Omicron and Delta SARS-CoV-2 infection, respectively, we identified less severe outcomes among individuals diagnosed with Omicron. In multivariable IPTW analysis, Omicron was associated with a statistically significant 50% lower risk of hospitalization relative to Delta after adjustment for age, sex, co-morbidities, vaccination status, geography, and neighbourhood income. When stratified by vaccination status, the lower risk of hospitalization with Omicron relative to Delta was less pronounced in vaccinated individuals (30% lower risk vs. 62% among unvaccinated), potentially reflecting greater vaccine protection against hospitalization for Delta with two mRNA doses.[22–25] However, fully vaccinated individuals remained at much lower risk of severe outcomes overall and crude hospitalization rates were 5-times higher for the unvaccinated compared to those fully vaccinated. Further, studies demonstrate that booster doses can increase vaccine protection against hospitalization to similarly high levels for both Omicron and Delta,[15,23–26] emphasizing the continued importance of vaccination.

Our findings are similar to studies published elsewhere. Analyses from the US, UK, Norway, Denmark and Ontario, Canada have identified a 36-73% reduced risk of hospitalization with Omicron relative to Delta.[12–17,23] Estimates from our primary (50%) and sensitivity analyses (49-68%) fall within this range. Variability between studies may be explained by differences in jurisdictional policies (e.g., diagnostic testing and sequencing strategies) and analytic approaches (e.g., outcome definitions, confounder adjustment). Unlike other studies, we included only WGS-confirmed cases and a relatively large proportion (33%) of positive SARS-CoV-2 samples were sequenced during our study period. The extent of WGS is a key strength of our study, which likely reduced the potential for misclassification that may arise from using used RT-PCR S-gene target failure as a proxy for Omicron infection. Overall, our findings suggest that the sheer number of Omicron cases led to higher numbers of hospitalizations than observed in the previous COVID-19 waves dominated by the Alpha, Gamma, and Delta variants, highlighting the importance of both transmissibility and severity from a public health perspective. Further, given that new VOCs may emerge, timely WGS of hospitalized cases may help inform prioritization of care for individuals infected with variants that are more virulent.

With respect to the impact of vaccination on disease severity, we report a lower risk of hospitalization with Omicron among both vaccinated and unvaccinated individuals, suggesting that lower Omicron severity is related to viral evolution. The lower severity of Omicron relative to Delta was less evident among vaccinated individuals, similar to other studies.[12,15,16] A potential explanation is that vaccination provides more protection against severe outcomes for Delta, leading to a smaller difference in severity. Indeed, analyses of vaccine effectiveness suggest two mRNA doses provide less protection against hospitalization for Omicron, but that

this protection increases to similarly high levels as for Delta following a booster dose.[22,24–26] While our analytic approach is not optimal compared to other designs (e.g., test-negative, RCTs) for assessing vaccine effectiveness, we identified a much higher risk of hospitalization overall among unvaccinated individuals in our analysis. These findings highlight the importance of booster doses to further reduce the severity of Omicron infection.

The reduced severity of Omicron was also apparent when assessing ICU admission and LOS, further emphasizing the lower virulence associated with this VOC. Here, Omicron was associated with a 73% lower risk of ICU admission and 5-day shorter hospital stay, on average, compared to Delta. While few deaths (n=33) were observed during our study follow up, the crude case fatality rate was higher for Delta (0.5%) compared to Omicron (0.1%), and rates were higher in the unvaccinated compared to vaccinated. The greater reduction in risk for more severe outcomes (ICU admission, mechanical ventilation) has also been observed in other analyses.[12] Others have also identified a similar reduction in LOS (3-5 days) with Omicron.[12,27]

Our study had several strengths and limitations. Strengths include the use of individual-level VOC data as opposed to time-period as a proxy, the exhaustive extent of high-quality whole genome sequences at the population-level during study period, the focus on a time period of VOC co-circulation to minimize temporal biases, the extensive data linkage to various health and data registries to measure potential confounders, and the rigorous adjustment for confounding and selection bias using IPTW. The association between Omicron and severe outcomes in our analysis is subject to some potential biases.[28,29] The population infected with Omicron was significantly different than those infected with Delta (e.g., younger age, geography), partly due to

the different stages of these respective epidemics (i.e., Delta was well established and declining, while Omicron was emerging). However, we controlled for differences between populations using IPTW, although some residual confounding likely remains. Limiting this investigation to a short period when there was co-circulation of lineages enabled the control for potential temporal effects by limiting differential exposure risks that influence transmission and could bias comparisons. The sequencing strategy changed on December 15th from sequencing the vast majority (~80%) of samples to sequencing a representative random sample and prioritizing hospitalized cases (~10-20% of cases). This led to a minority (33%) of laboratory confirmed cases being sequenced during our study period and therefore included in our analysis. Since Omicron was dominant by December 15th and there were few Delta infections, Omicron was more subject to potential selection bias. In particular, prioritization of hospitalized cases likely artificially elevated the percentage of Omicron cases who were hospitalized and overestimated the severity of Omicron (thereby underestimating the extent to which Omicron severity is lower than Delta – a conservative bias towards the null). Indeed, the lower risk of hospitalization with Omicron was more pronounced (68%) in our sensitivity analysis limited to the period after the change in sequencing strategy, although this analysis significantly reduced Delta sample size and may have introduced other biases (such as exclusion and survivorship biases) in addition to partial sampling bias. Estimates of severity are sensitive to changes in case-finding (e.g., percent of all cases identified) and therefore changes in diagnostic testing behaviors/policies/availability during the emergence of Omicron may have introduced bias. For example, less Omicron testing given the reduced availability of testing due to high demand and introduction of rapid antigen testing (not included as these were deployed at the end of the study period) would have lowered Omicron case-finding and biased results towards the null. Analyses suggest that a higher

proportion of Omicron hospitalizations are incidental,[30] another potential source of bias towards the null. Removal of individuals hospitalized on the day of testing or in the two days prior to lab collection date in sensitivity analyses to account for potential incidental hospitalizations had minimal impact on results, consistent with other studies.[13,14,17] Lack of information on undetected prior infection remains an additional limitation. In a study that attempted to adjust for under ascertainment of prior infection, the reduction of risk of hospitalization with Omicron (vs. Delta) changed from 45% to 35%.[13]

In conclusion, our analysis supports that the large numbers of incident Omicron cases rather than increased virulence mostly drove the upsurge in hospitalizations during BC's fifth wave. Our study is an important contribution to the relatively small evidence-base of peer-reviewed studies assessing Omicron severity relative to Delta, which have produced a relatively wide range of estimates.

NOTES

ROLE OF AUTHORS

SPH, JW, HS, and NZJ developed study concept and design, CR and MC contributed to the methodology. SPH conducted the analysis and JW wrote the first draft of the manuscript. YA and HVG provided statistical expertise. MK, NP, LH and JT are responsible for the laboratory-related data collection including whole genome sequencing. CR, SM, BS, HVG, and MT supported with the data interpretation. All authors contributed to writing and reviewing the paper, have approved it for submission and agree to being accountable for its content.

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DISCLAIMER

All inferences, opinions, and conclusions drawn in this manuscript are those of the authors, and do not reflect the opinions or policies of the Data Steward(s)

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CONFLICT OF INTERESTS

MK has grants and contracts with AbCellera (contract paid to institution related to support identification of SARS-CoV-2 infected individuals), Roche, Hologic (contract paid to institution related to respiratory testing), and Siemens (contract paid to institution related to SARS-CoV-2 serological testing), all of which unrelated to this study. NZJ participates in Abbvie Advisory Board meeting, reports payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events from AbbVie, and reports grants or contracts unrelated to this work from Canadian Institutes of Health Research, Michael Smith Foundation for Health Research, and Public Health Agency of Canada. HS reports grants or contracts unrelated to this work from Canadian Institutes for Health Research. NP reports grants or contracts unrelated to this work from Canadian Institutes for Health Research and Michael Smith Foundation for Health Research. All others authors declare no conflicts of interest.

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Table 1. Characteristics by study population, overall and by VOC, Dec 1st to Dec 31st, 2022

	Delta	Omicron	Overall
	(N=5,399)	(N=7,729)	(N=13,128)
Sex			
Female	2,746 (50.9%)	3,939 (51.0%)	6,685 (50.9%)
Male	2,653 (49.1%)	3,790 (49.0%)	6,443 (49.1%)
Age (years)			
Mean (SD)	34.4 (20.7)	35.0 (16.3)	34.8 (18.2)
Median (IQR)	35.0 (35.0)	32.0 (23.0)	33.0 (25.0)
Age groups			
0-4	225 (4.2%)	131 (1.7%)	356 (2.7%)
5-11	844 (15.6%)	233 (3.0%)	1,077 (8.2%)
12-19	342 (6.3%)	549 (7.1%)	891 (6.8%)
20-29	618 (11.4%)	2,390 (30.9%)	3,008 (22.9%)
30-39	982 (18.2%)	1,671 (21.6%)	2,653 (20.2%)
40-49	934 (17.3%)	1,143 (14.8%)	2,077 (15.8%)
50-59	592 (11.0%)	870 (11.3%)	1,462 (11.1%)
60-69	446 (8.3%)	459 (5.9%)	905 (6.9%)
70-79	179 (3.3%)	134 (1.7%)	313 (2.4%)
80+	237 (4.4%)	149 (1.9%)	386 (2.9%)
Health Authority			
Fraser	1,421 (26.3%)	3,297 (42.7%)	4,718 (35.9%)
Interior	1,458 (27.0%)	798 (10.3%)	2,256 (17.2%)
Northern	472 (8.7%)	132 (1.7%)	604 (4.6%)
Vancouver Coastal	826 (15.3%)	2,383 (30.8%)	3,209 (24.4%)
Vancouver Island	1,222 (22.6%)	1,119 (14.5%)	2,341 (17.8%)
Vaccination status*			
Not vaccinated	2,535 (47.0%)	731 (9.5%)	3,266 (24.9%)
Partially vaccinated	327 (6.1%)	225 (2.9%)	552 (4.2%)
Fully vaccinated	2,537 (47.0%)	6,773 (87.6%)	9,310 (70.9%)
Elixhauser comorbidity index			
0	2,285 (42.3%)	3,337 (43.2%)	5,622 (42.8%)
1	1,376 (25.5%)	2,176 (28.2%)	3,552 (27.1%)
2	782 (14.5%)	1,120 (14.5%)	1,902 (14.5%)

3+	956 (17.7%)	1,096 (14.2%)	2,052 (15.6%)
Neighbourhood income quintile			
1	981 (18.2%)	1,012 (13.1%)	1,993 (15.2%)
2	885 (16.4%)	1,172 (15.2%)	2,057 (15.7%)
3	1,094 (20.3%)	1,413 (18.3%)	2,507 (19.1%)
4	1,019 (18.9%)	1,685 (21.8%)	2,704 (20.6%)
5 (Wealthiest)	1,025 (19.0%)	1,750 (22.6%)	2,775 (21.1%)
Missing	395 (7.3%)	697 (9.0%)	1,092 (8.3%)
Hospitalizations			
No hospital admission	5,098 (94.4%)	7,611 (98.5%)	12,709 (96.8%)
Hospital admission	301 (5.6%)	118 (1.5%)	419 (3.2%)
ICU admissions			
No ICU admission	5,284 (97.9%)	7,714 (99.8%)	12,998 (99.0%)
ICU admission	115 (2.1%)	15 (0.2%)	130 (1.0%)
Deaths			
Alive	5,371 (99.5%)	7,724 (99.9%)	13,095 (99.7%)
Died	28 (0.5%)	<5 (0.1%)	33 (0.3%)

Abbreviations: ICU: Intensive care unit; IQR: interquartile range; SD: standard deviation

* Vaccination status: Fully vaccinated: Received 2nd dose (or first dose of Johnson and Johnson) at least 14 days prior to lab collection date; Unvaccinated: received no dose of any vaccine 14 days prior to lab collection date

Table 2. Multivariable IPTW regression models assessing association between VOC and severity outcomes

Hospitalizations				
Stratification****	**Variant**	**Hospitalizations (n/N)**	**Crude rate (%)**	**aHR* (95% CI)**
Full	Delta	301 / 5399	5.6%	
	Omicron	118 / 7729	1.5%	0.50 (0.43 - 0.59)
Fully Vaccinated**	Delta	75 / 2537	3.0%	
	Omicron	93 / 6772	1.4%	0.70 (0.56 - 0.87)
Unvaccinated**	Delta	216 / 1438	15%	
	Omicron	17 / 445	3.8%	0.38 (0.30 - 0.49)
ICU admissions				
Stratification	**Variant**	**ICU admissions (n/N)**	**Crude rate (%)**	**aHR (95% CI)**
Full	Delta	115 / 5399	2.1%	
	Omicron	15 / 7729	0.2%	0.27 (0.19 - 0.38)
Fully Vaccinated	Delta	21 / 2537	0.8%	
	Omicron	9 / 6772	0.1%	0.24 (0.13 - 0.44)
Unvaccinated	Delta	90 / 1438	6.3%	
	Omicron	5 / 445	1.1%	0.43 (0.29 - 0.63)
Length of stay				
Stratification	**Variant**	**N**	**Mean (SD); Median (IQR)**	**aβ (95% CI)**
Full	Delta	269	14.7 (15.9); 9 (15.0)	
	Omicron	110	8.4 (11.0); 4 (6.0)	-5.03 (-8.01 - -2.05)

Abbreviations: aβ: multivariable estimate; aHR: adjusted hazard ratio; CI: confidence interval; ICU: Intensive care unit; IQR: interquartile range; SD: standard deviation

*All models are adjusted for age, sex, geography, Elixhauser index (comorbidities), an SES (neighbourhood income quintile). The unstratified full model also adjusts for vaccination status

** Vaccination status: received 2nd dose (or first dose of Johnson and Johnson) at least 14 days prior to lab collection date; Unvaccinated: received no dose of any vaccine 14 days prior to lab collection date

*** Linear regression model

**** Partially vaccinated individuals removed from stratified analysis. Only those aged 12 and above were kept in stratified analysis.

Figure 1. Study flow diagram

Abbreviations: BC: British Columbia; LOS: length of stay

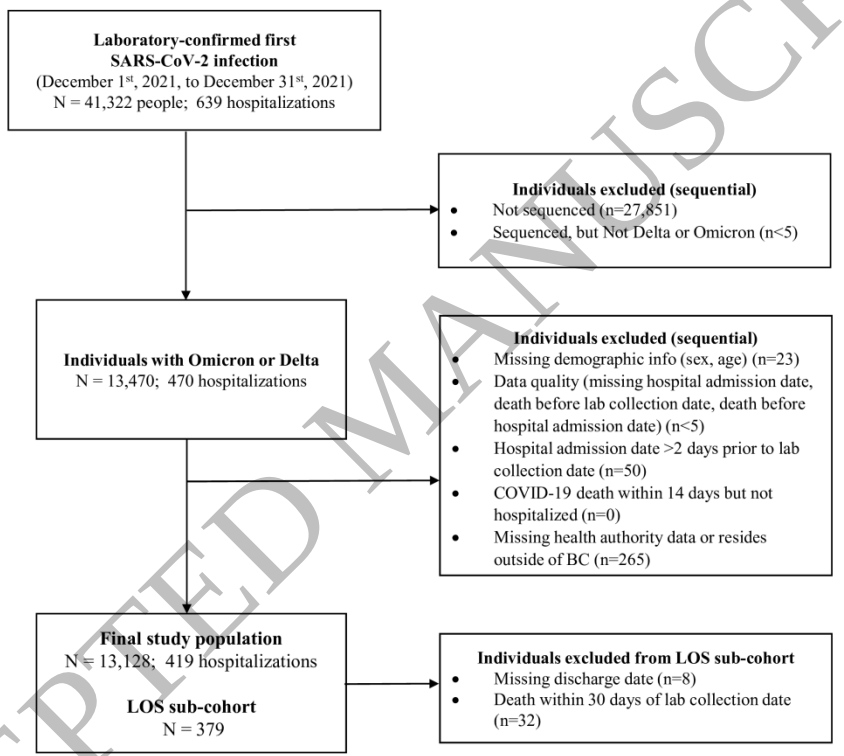

Figure 1
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