COVID Model Projections

February 17, 2022

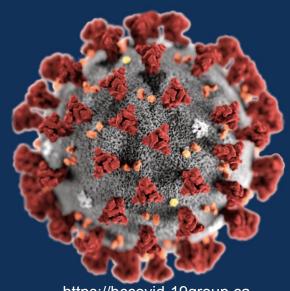
BC COVID-19 Modelling Group



About BC COVID-19 Modelling Group

The BC COVID-19 Modelling Group works on rapid response modelling of the COVID-19 pandemic, with a special focus on British Columbia and Canada.

The interdisciplinary group, working independently from Government, includes experts in epidemiology, mathematics, and data analysis from UBC, SFU, UVic, and the private sector, with support from the Pacific Institute for the Mathematical Sciences.



https://bccovid-19group.ca

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Independent and freely offered advice, using a diversity of modelling approaches.

Overview

Omicron on the decline

- Declining numbers of cases among those aged 70+ and of COVID patients in hospital provide evidence that the Omicron wave is subsiding in BC, except in Northern Health.
- BC's booster program has been highly successful (52.7% of eligible people over 12 have now been boosted) and was likely a strong contributor to taming the Omicron wave.

A cautious approach to reopening would help avoid a surge over the next month

- Omicron sub-variant BA.2 is spreading in Canada, with selection favouring BA.2 by a selection coefficient of 8% in BC per day relative to BA.1.
 - The impact of BA.2 depends strongly on when it arrives in the Omicron wave. In BC, the current frequency of BA.2 remains low, suggesting that it will extend the peak but not cause a major rise in Omicron infections.
- While Omicron is on its way out, many infections more than half typically happen on the way down from an epidemic peak, so measures such as masking, getting boosted, and avoiding poorly ventilated crowded places will continue to be important over the next month.³

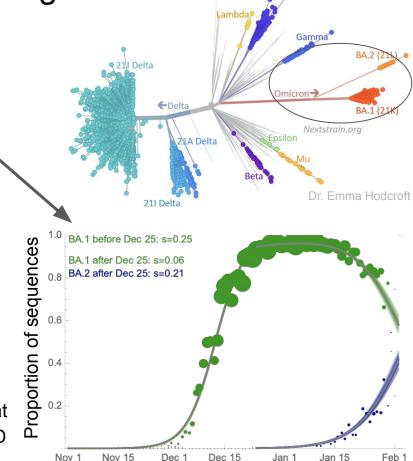
Omicron sub-lineage BA.2 is spreading in Canada

Omicron describes two major lineages, BA.1 and BA.2, which differ at a number of sites but share <u>21 changes</u> in the spike protein.

BA.1 (green) spread rapidly at first in Canada but has recently been declining due to the spread of BA.2 (blue; dot area is proportional to number of sequences).

 \rightarrow In Canada, BA.2 is spreading faster than BA.1 at a rate of s = 15% per day, similar to rates seen in Denmark and UK in our previous <u>report</u>.

Data suggests that the advantage of BA.2 over BA.1 comes from a higher inherent transmissibility (<u>UK Report</u>), not an ability to escape immunity following BA.1 infection. A <u>study</u> of neutralizing antibodies produced by individuals infected with BA.1 indicates that these antibodies neutralize BA.1 and BA.2 at nearly equal rates. A <u>UK study</u> of BA.2 cases with recent COVID found all were previously infected with Delta, not BA.1.



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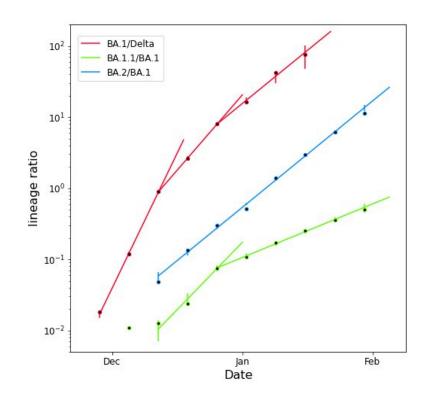
Omicron lineages in Denmark

Denmark was one of the earliest countries to see the rapid growth of Omicron cases.

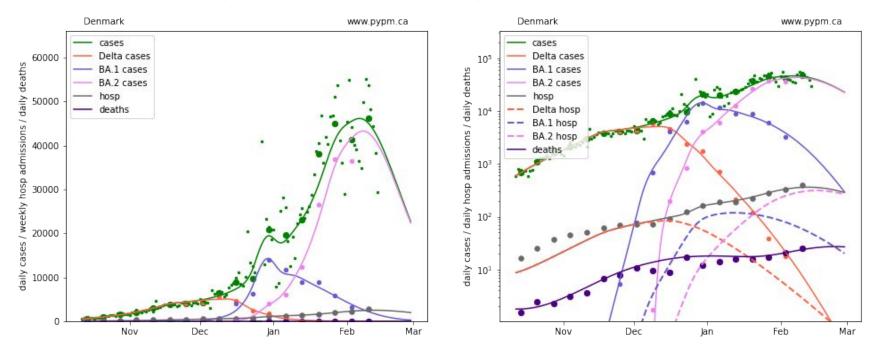
- The BA.1 growth advantage over Delta slowed significantly once it became dominant:
 - Shown in red: s = 28%/day, 16%/day, 11%/day
- The BA.2 growth advantage over BA.1 appears to be constant. Shown in blue: s = 11%/day
- BA.1.1 also shows a growth advantage over BA.1
 Shown in green: s = 14%/day, 6%/day

The changes in growth advantage occurred at the same time as a significant drop in growth rates in Denmark (and many other jurisdictions).

The lineage ratios allow hospitalization severity to be estimated for each lineage (next slide).



Omicron lineages and modelling Denmark hospitalizations



Using the lineage ratios, cases due to each lineage are inferred and fit to define a multiple-strain infection model. By fitting the model to overall hospital admission data, the relative severity of BA.2 to BA.1 infections is estimated to be about 0.7.

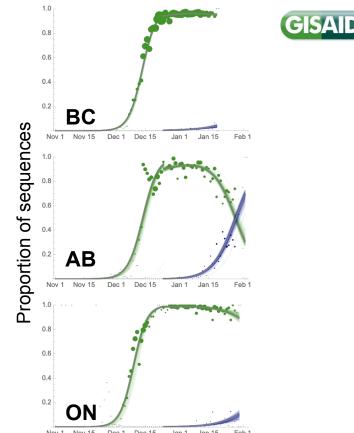
Selection on BA.1 and BA.2 by province

These plots show the proportion of BA.1 (green), BA.2 (blue), and non-Omicron (remainder) for three provinces with sufficient data about BA.2. See Appendix for details.

→ BA.2 is spreading with a selective advantage per day relative to BA.1 of 8.3% in BC [95%CI: 5-11%], 17.5% in AB [16-19%], and 11.5% in ON [9-14%].

BA.2 established earlier in Alberta, where it is now prevalent.

The estimated proportion of COVID-19 cases due to BA.2 is 30% in BC, 96% AB, 45% ON on February 17, 2022.

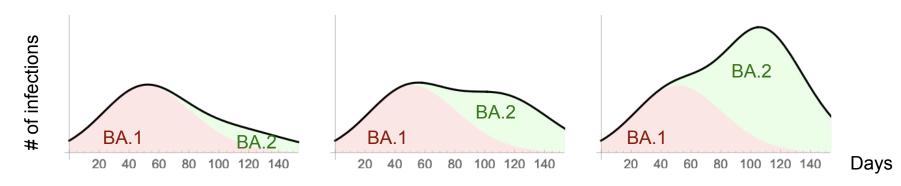


Source (S. Otto; BC COVID-19 Modelling Group) Parameters estimated by maximum likelihood based on a trinomial distribution given the expected frequencies under selection acting upon BA.1 (including BA.1.1) and BA.2, relative to non-Omicron (AY.25, AY.25.1, AY.103). Selection for BA.2 vs BA.1 can be found by subtracting BA.1's advantage over non-Omicron from BA.2's advantage over non-Omicron; Hessian matrix used to obtain confidence intervals.

How might BA.2 affect the Omicron wave?

This slide shows a simple epidemic toy model, treating individuals as either susceptible to Omicron, infected with BA.1 (red) or with BA.2 (green). Here, BA.2 spreads 15% faster than BA.1 but arrives later. Immunity provided by BA.1 infection or by boosters* protects against infection by either Omicron variant.

The impact of BA.2 depends on when it becomes common in a region. In areas where BA.2 establishes late (left), the epidemic curve is only extended slightly. In areas where, by chance, it establishes early (right), BA.2 can dominate the Omicron wave, leading to more total cases. The middle panel shows an intermediate outcome where BA.2 creates a "shoulder" in the Omicron wave.



→ The impact of BA.2 depends strongly on the timing of its introduction

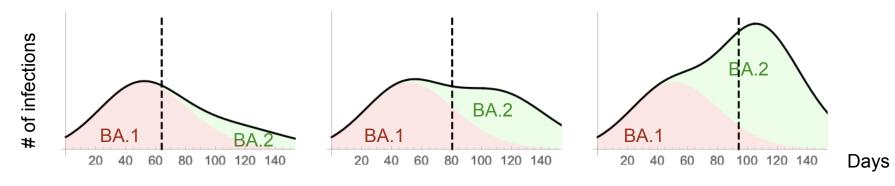
Source (S. Otto) Assumes that BA.1 initially spread at a rate of r = 0.22 per day, that BA.2 spreads at a rate of r = 0.37 per day (a 15% selective advantage of BA.2 over BA.1), infections last on average 7 days, and booster vaccinations proceeded at a rate that 52.7% of the eligible population (12+) would be vaccinated by February 14 2022 (as in BC), with 80% vaccine effectiveness against infection if boosted.

Past the peak does not mean infection risk is over

Simple epidemics (with a single variant) typically cause more infections on the way down from a peak than on the way up, a prediction that has been seen often with COVID (waves rise faster and decline slower).

Here we add dashed lines to the previous graphs to show when 50% of infections would have occurred, illustrating that many infections are yet to come in the current wave.

→ While BC remains near the Omicron peak, measures to reduce risk are important to maintain (masking, booster shots, avoiding crowded poorly ventilated areas)



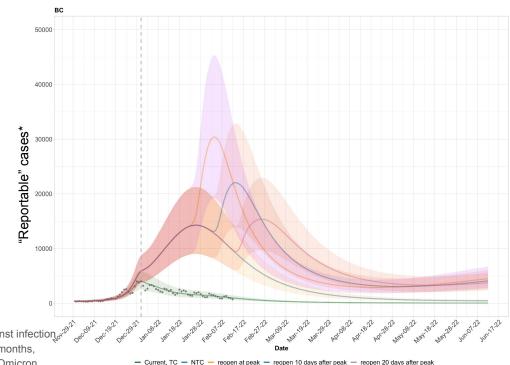
Illustrative comparisons: impact of the timing of reopening

Multi-strain model accounting for reduced testing, boosters, waning immunity and Omicron's advantage over Delta.

Here we illustrate the impact of reopening at the peak time vs 10 and 20 days later.

"Reopening": reverse the decrease in transmission that we estimate for late December 2021.

Delaying the reopening greatly reduced the peak height.



Parameters: Booster efficacy against infection 70% (Omicron); 2-dose efficacy against infection 15%, immediate protection of recovery against reinfection 90%, waning immunity 6 months, incubation period 3 days. Estimated parameters: transmission rates for Delta and Omicron, reduction in transmission late December, dispersion parameter, 2021 ascertainment fraction.

Likelihood: includes reported cases accounting for testing change; 50% Omicron ~Dec 12, 20% daily growth advantage when Omicron emerged

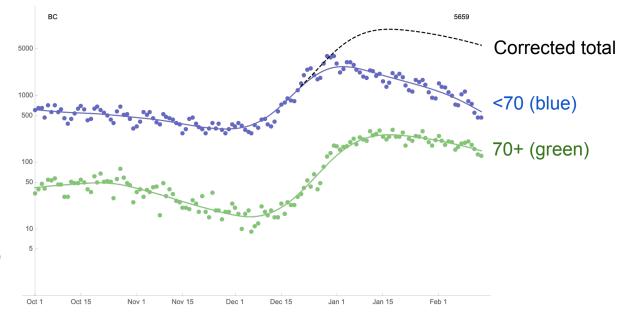
^{*} Reportable case: would have been reported, under pre-Dec 2021 testing

Age-corrected case counts: British Columbia

The black dashed curve estimates the total number of "reportable" cases, applying growth in older age cohorts (green) to correct for limited testing in younger groups (blue).

This correction suggests ~5700 reportable cases on February 14 compared to the 519* reported.

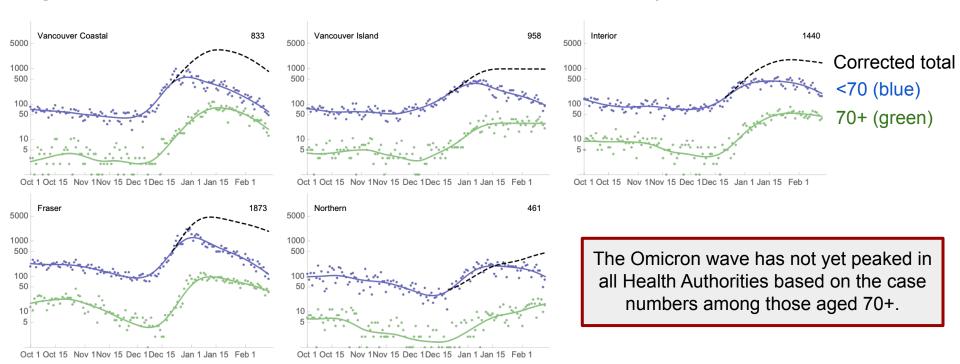
The age distribution is, however, likely to have shifted over the last month, so this total is increasingly unreliable.



→ Cases among the 70+ age group, who have been more consistently tested, are now declining significantly in BC**, although they remain high and predict continued hospital demand in the near future.

Source (S. Otto; BC COVID-19 Modelling Group) New cases per day in 10-year age groups were downloaded from the BCCDC COVID-19 data portal. Cubic spline fits to log-case data were obtained (curve) and estimates for those <70 obtained by applying the fits for those 70+, shifted up to match the projection for that age class on 21 December 2022 when testing limits were initially reached in many parts of BC. *From the daily BC Gov News reports. **Linear regression through log case counts among 70+ from last 14 days of data.

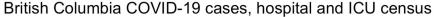
Age-corrected case counts: Health Authority

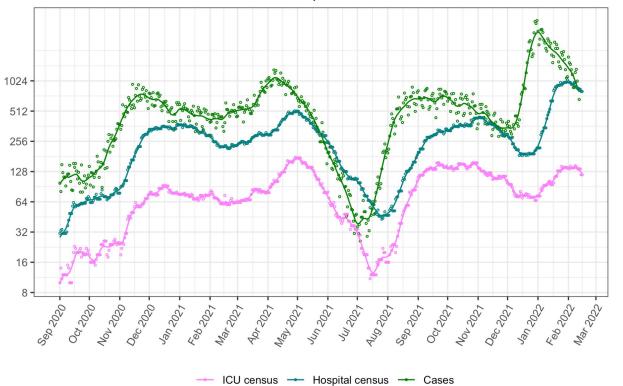


→ Significant declines among those aged 70+ are mainly observed in Vancouver Coastal and Fraser Health Authorities; cases in Northern HA is trending upwards.

Source (S. Otto) New cases per day in 10-year age groups were downloaded from the <u>BCCDC COVID-19 data portal</u>. Cubic spline fits to log-case data were obtained (curve) and estimates for those <70 obtained by applying the fits for those 70+, shifted up to match the projection for that age class on 21 December 2022 when testing limits were initially reached in many parts of the province. *Linear regression through log case counts among 70+ from last 14 days of data.

Hospital trends in BC



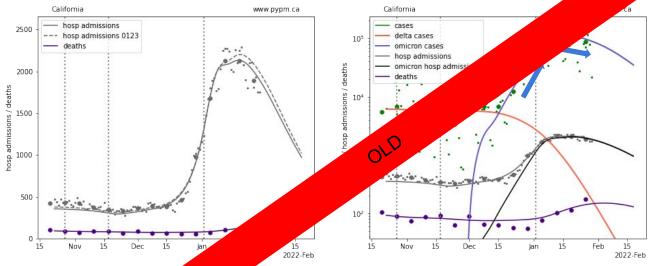


While declines in case numbers in early January largely reflected testing limitations, the number of COVID patients in hospital peaked at the end of January and is now declining.

Data: BCCDC for cases, Canada Covid-19 tracker for hospital and ICU census

Omicron infection trajectory

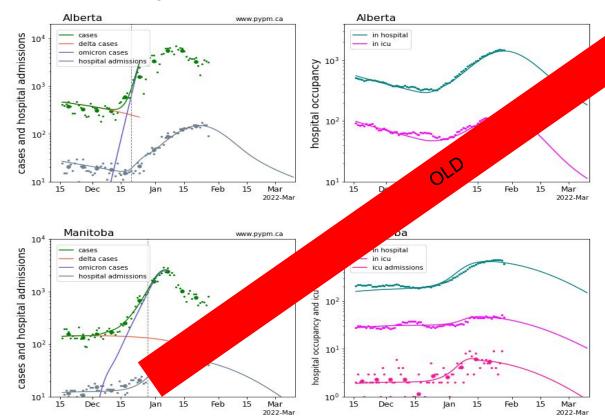
In all US states, growth rates for cases and hospital admissions reduced significantly near project.
 As a result, hospital demands have been significantly lower than earlier project.



- The left plot shows the rapid to the spital admissions in California followed by decline. The curves show model fits to these data. The model a significant reduction in transmission rate near January 1 (vertical dashed line).
- The right plot shall growth appears as straight lines.
 - the suddent of in slope is characteristic of a change in transmission rate
 - the smooth wnward bending is characteristic of growing population immunity

Omicron infection trajectory in Canada

A similar drop in growth rate is also seen in Canadian provinces (dashed vertical line

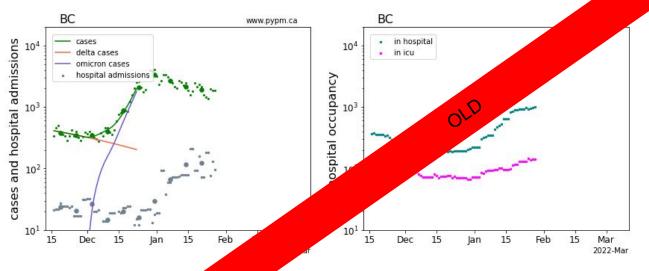


policy and testing capacity limits, cases can no longer be used in Canada to track the infection trajectory (green dots).

- Omicron growth rates can be monitored in provinces that provide reliable hospital admission data, in place of case data (left plots).
- With admission data to estimate Omicron growth rates, projections for hospital and ICU occupancy can be made (right plots).

Omicron infection trajectory in BC

Without reliable data, we cannot make reliable projections for health cannot make in BC



- Hospital admission data are posted irregularly and of poor quality (grey dots with large scatter).
- The province changed its definition for counting COVID hospital admissions in mid-January.
- Hospital occupancy appears to be leveling off (right panel).

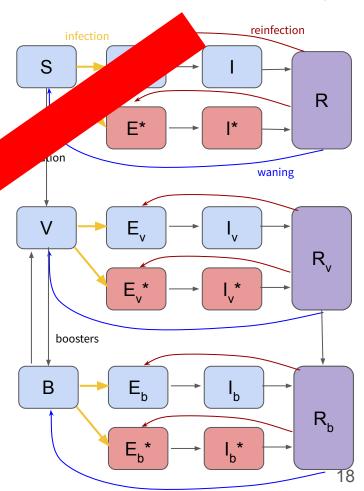
Projections in a multi-strain model

This is a model with unvaccinated, vaccinated and boosted individuals, with two strains: blue (Delta) and red (Omicron).

The model allows for reinfection, different transmissibility and efficacy for Omicrowaning of immunity.

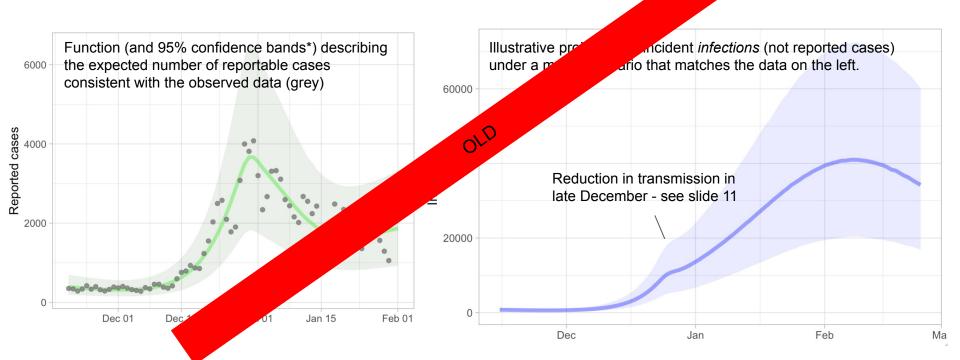
Approach: Fit to reported the pout adjust the fraction of infection are reported to mirror changes in the pout adjust are reported to over 70 as a line at the pout adjust are reported to mirror changes in the pout adjust are reported to mirror changes in the pout adjust are reported to mirror changes in the pout adjust are reported to mirror changes in the pout adjust are reported to mirror changes in the pout adjust are reported to mirror changes in the pout adjust are reported to mirror changes in the pout adjust are reported to mirror changes in the pout adjust are reported to mirror changes in the pout adjust are reported to mirror changes in the pout adjust are reported to mirror changes in the pout adjust are reported to mirror changes in the pout adjust are reported to mirror changes in the pout adjust are reported to mirror changes in the pout and pout adjust are reported to over 70 as a line and pout adjust are reported to a pout adjust and pout adjust are reported to a pout adjust and pout adjust are reported to a pout adjust and pout adjust are reported to a pout adjust and pout adjust are reported to a pout adjust and pout adjust and pout adjust are reported to a pout adjust and pout adjust and pout adjust are reported to a pout adjust and pout adjust and pout adjust are reported to a pout adjust and pout adjust and pout adjust are reported to a pout adjust and pout adj

Source: SFU MAGPIE group. Boosters are ongoing in the model at a rate matching BC's reported levels in late December.



Reported cases and infections

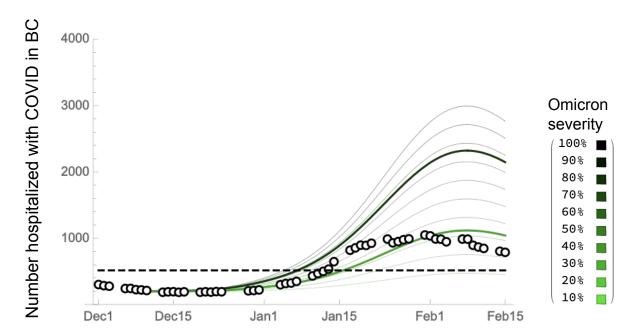
Reported cases declined in January, but inferred infections are only now particles are considerable uncertainty about the peak size and timing

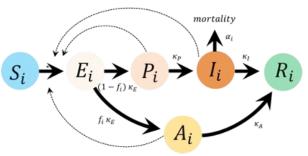


Source (SFU MAGPIE group; C. Colijn). Data used: reported cases; 50% Omicron by Dec 12; early growth advantage of Omicron 20% per day; test positivity in the private sector (slide 6); reporting in <70 and 70+ (slide 9). Fitted parameters: transmission parameters for the strains, strength of transmission reduction in late December. 19 *Assuming case data is distributed according to a negative binomial.

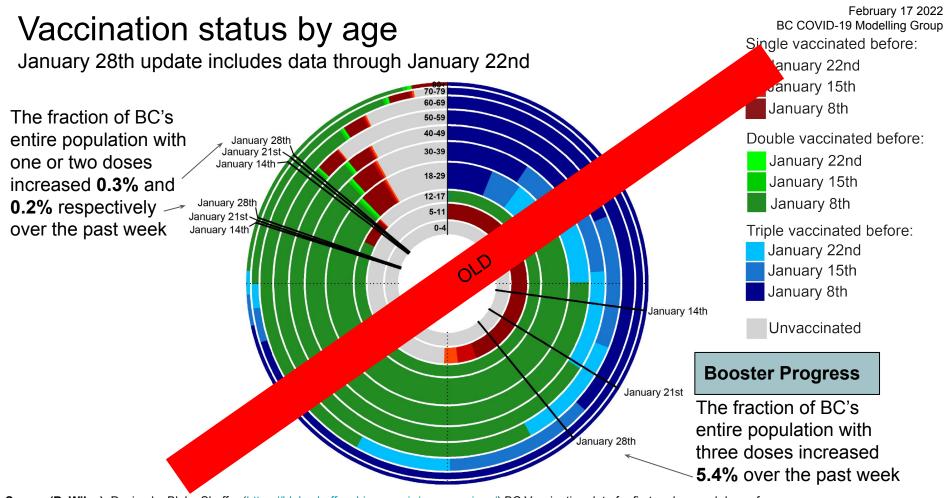
Age-based model: Hospital projections with Omicron

Compared to the model explored in the 19th January 2022 report, the number of COVID patients in hospital tracked the low severity scenario with Omicron and peaked earlier.





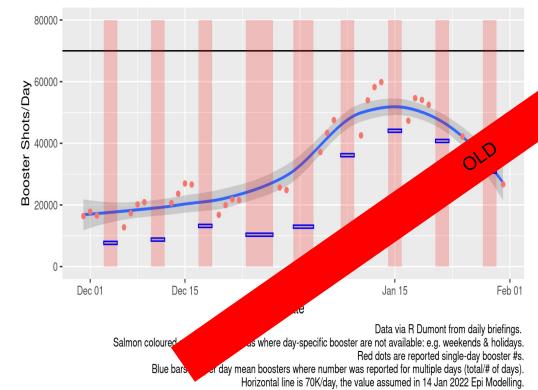
Severity: Varied from 0.1 (light green) to 0.9 (light black) for the risk of hospitalization per case for Omicron relative to previous variants for unvaccinated individuals. Estimated of 76% from Ferguson et al. is thicker black curve; estimate of 33% from UK Technical Briefing is thicker green curve.



Source (B. Wiley). Design by Blake Shaffer (https://blakeshaffer.shinyapps.io/app_vaccines/) BC Vaccination data for first and second doses from https://blakeshaffer.shinyapps.io/app_vaccines/) BC Vaccination data for first and second doses from https://blakeshaffer.shinyapps.io/app_vaccines/) BC Vaccination data for first and second doses from https://blakeshaffer.shinyapps.io/app_vaccines/) BC Vaccination data for first and second doses from https://blakeshaffer.shinyapps.io/app_vaccines/) BC Vaccination data for first and second doses from https://blakeshaffer.shinyapps.io/app_vaccines/) BC Vaccination data for first and second doses from https://blakeshaffer.shinyapps.io/app_vaccines/) BC Vaccination data for first and second doses from https://blakeshaffer.shinyapps.io/app_vaccines/) BC Vaccination data for first and second doses from https://blakeshaffer.shinyapps.io/app_vaccines/https://blakeshaffer.shinyapps.io/app_vaccines/https://blakeshaffer.shinyapps.io/app_vaccines/https://blakeshaffer.shinyapps.io/app_vaccines/https://blakeshaffer.shinyapps.io/app_vaccines/https://blakeshaffer.shinyapps.io/app_vaccines/https://

Booster Shot Progress





Boosters have been for the substantially increase protection and hospitalization of Omicron.

BC PHC bor boosters was 70K/day (see horizontal line).

dots show reported boosters/day.

Blue curve shows smoothed trend in boosters/day. Now trending down and <30K/day.

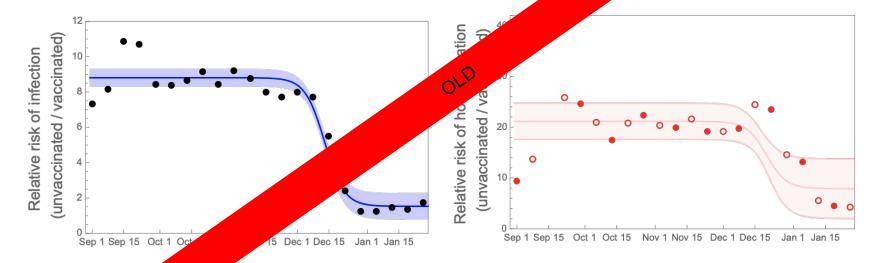
Blue horizontal bars are estimated boosters/day for days when booster #s are reported for a period of several days rather than a single day. Estimate gives boosters provided over period /# days in period.

Note that weekend boosters are typically less than adjacent weekdays (red dots).

Changing immunity with Omicron

The risk of COVID-19 for an unvaccinated person relative to a fully vaccinated person has declined to the spread of Omicron in BC. Being unvaccinated increased the relative risk of infection by an average of 8.8 declined to only 1.5-fold with Omicron (left). The risk of hospitalization has fallen less, from the spread of Omicron, but this has declined to only 1.5-fold with Omicron (left). The risk of hospitalization has fallen less, from the spread of Omicron to 7.9 (right).

[Relative risks are for an average person (age corrected) and do not reflect patterns in specific types and dates of vaccination.]



Source (S. Otto) Risks for an unit procedure of person relative to a fully vaccinated person (age corrected) were obtained from the daily <u>BC Gov News</u> reports. Because risk of infection is calculated across the past week, we use data from only one day per week (Wednesday) and fit $a(1-p_t) + b p_t$, where p_t is the frequency of Omicron (inferred by D. Karlen in Dec 22 report, slide 7). Risk of hospitalization is calculated over the past two weeks of data, so we fit to a model of Omicron frequency seven days ago $a(1-p_{t,7}) + b p_{t,7}$ to account for the lag in hospitalizations, using data from every other week (analysing solid and hollow points separately) and averaging the results.

Key messages

State of the Omicron wave in BC:

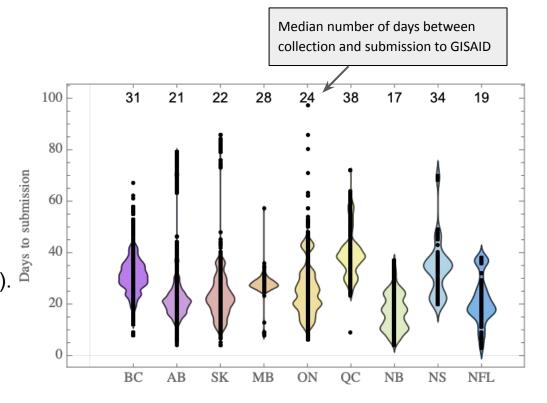
- Cases in individuals >70 in age are now declining significantly in BC, although this largely reflects declines in Vancouver Coastal Health and Fraser Health, with rising trends continuing in Northern Health.
- Declines in the number of people hospitalized with COVID is a strong indicator that many parts of BC are now past the Omicron peak.
- The biggest source of uncertainty over the next few weeks is whether a further surge will occur because:
 - The reopening on 16 February 2022 could increase transmission rates more than the current rate of decline
 - The selective advantage of BA.2 could allow it to spread further, despite growing immunity in BC
- What is certain is that Omicron remains prevalent in BC, and we should expect many more infections, even if infection rates are declining.
- → Measures to reduce risk are important to maintain while Omicron remains prevalent (masking, booster shots, avoiding crowded poorly ventilated areas)

Appendix: Timely contributions of genomic data

This plot shows delays in uploading sequence data to <u>GISAID</u> for samples collected in Canada since November 1, 2021 (relevant to Omicron).

Across Canada, the median delay is 28 days between collection and submission, not including the sequences that have yet to be uploaded. This is greatly improved over the 88 days found earlier (Kalia et al.).

New Brunswick is the leader of the pack, comparing favourably to international standards (e.g., <u>UK at 16 days</u>).



→ Delays in submitting data make it challenging to detect the spread of variants such as BA.1 and BA.2 and their impact on public health.



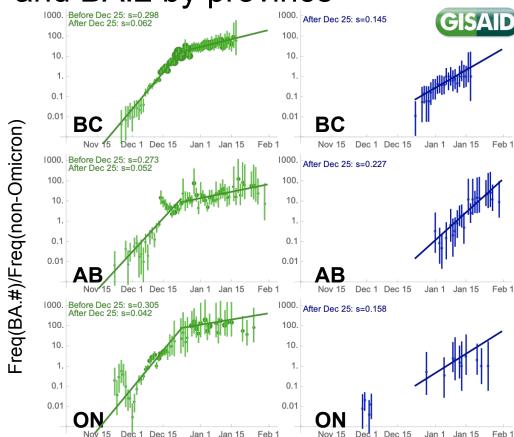
Appendix: Selection on BA.1 and BA.2 by province

The relative frequency of BA.1 (green) or BA.2 (blue) to non-Omicron is shown on the right for the three provinces with enough data on BA.2.

Fits (lines) were obtained by maximum likelihood and give estimates of selection for BA.1 and BA.2 relative to non-Omicron.

Selection favoring Omicron (mostly BA.1) was stronger before measures were taken to slow its spread (late December).

→ Recently, BA.2 is spreading with a selective advantage per day relative to BA.1 of 8.3% in BC [95%CI: 5-11%], 17.5% in AB [16-19%], and 11.5% in ON [9-14%].



Source (S. Otto; BC COVID-19 Modelling Group) Parameters estimated by maximum likelihood based on a trinomial distribution given the expected frequencies under selection acting upon BA.1 (including BA.1.1) and BA.2, relative to non-Omicron (AY.25, AY.25.1, AY.27, AY.103). Selection for BA.2 vs BA.1 can be found by subtracting BA.1's advantage over non-Omicron from BA.2's; Hessian matrix used to obtain confidence intervals.

Appendix: Selection coefficient for BA.2 wrt BA.2

Selection coefficient analysis

For an exponential process, the expected number of cases reported over a period of m = 7 days commencing on day d is

$$E[N(d)] = \int_{d}^{d+m} n_0 e^{rt} dt = \frac{n_0}{r} e^{rd} (e^{rm} - 1)$$

For two exponential processes (1 and 2), the ratio of the daily cases is given by

$$r(d, s, d_0) = \frac{E[N_2(d)]}{E[N_1(d)]} = a \exp(r_2 - r_1)d = a \exp(sd) = \exp(s(d - d_0))$$

where a is a constant, d is an integer day number, and s is the selection coefficient $s = r_2 - r_1$. The constant a defines the relative prevalence for the commencing on day 0. A more suitable parameterization specifies the time d_0 for which the two have equal prevalence.

There are other strains in the samples and the sampling fraction can change with time. The problem can be considered to be a binomial proconsidering the omicron samples.

The probability for an omicron case to be type 2 is:

$$p_2(d, s, d_0) = \frac{E[N_2(d)]}{E[N_1(d) + N_2(d)]} = \frac{1}{1 + 1/r(d, s, d_0)}$$

To estimate s, use maximum likelihood. This is a binomial problem, with $n = n_1 + n_2$ trials each day.

$$\ln \mathcal{L}(s, d_0) = c + \sum_{d} \left[n_2(d) \ln p_2(d, s, d_0) + n_1(d) \ln(1 + d) \right]$$

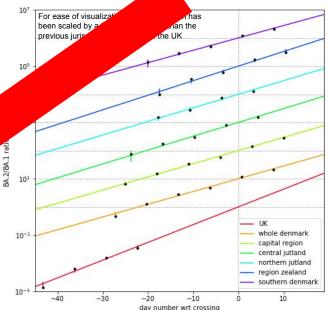
No analytic solution, so find the estimates and uncertainty numerically.

Data from <u>UK</u> and <u>regions of</u> <u>Denmark</u> analyzed:

- s: selection coefficient
- d0: days after 12/5/2021 when BA.2 becomes the dominant Omicron Jin

68% statistical uncertaint

egion	s	d0
UK	0.145 ± 0.001	64.3 ± 0.2
whole denmark	0.104 ± 0.001	34.3 ± 0.1
capital region	0.108 ± 0.007	32.0 ± 0.0
central jutland	0.113 ± 0.003	37.8 ± 0.0
northern jutland	0.111 ± 0.002	38.7 ± 0.4
region zealand	0.119 ± 0.004	31.5 ± 0.1
southern denmark	0.101 ± 0.003	34.1 ± 0.2



Selection coefficient of BA.2 relative to BA.1 is consistent across Denmark and somewhat smaller than in UK.

BA.2 will become the dominant Omicron lineage in the UK about 30 days later than in Denmark.