COVID Model Projections

January 25, 2023

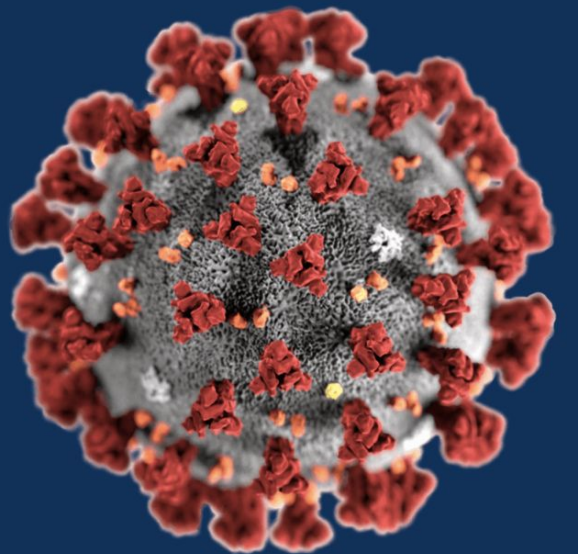
BC COVID-19 Modelling Group

@bcCOVID19group

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

Contents of this report:

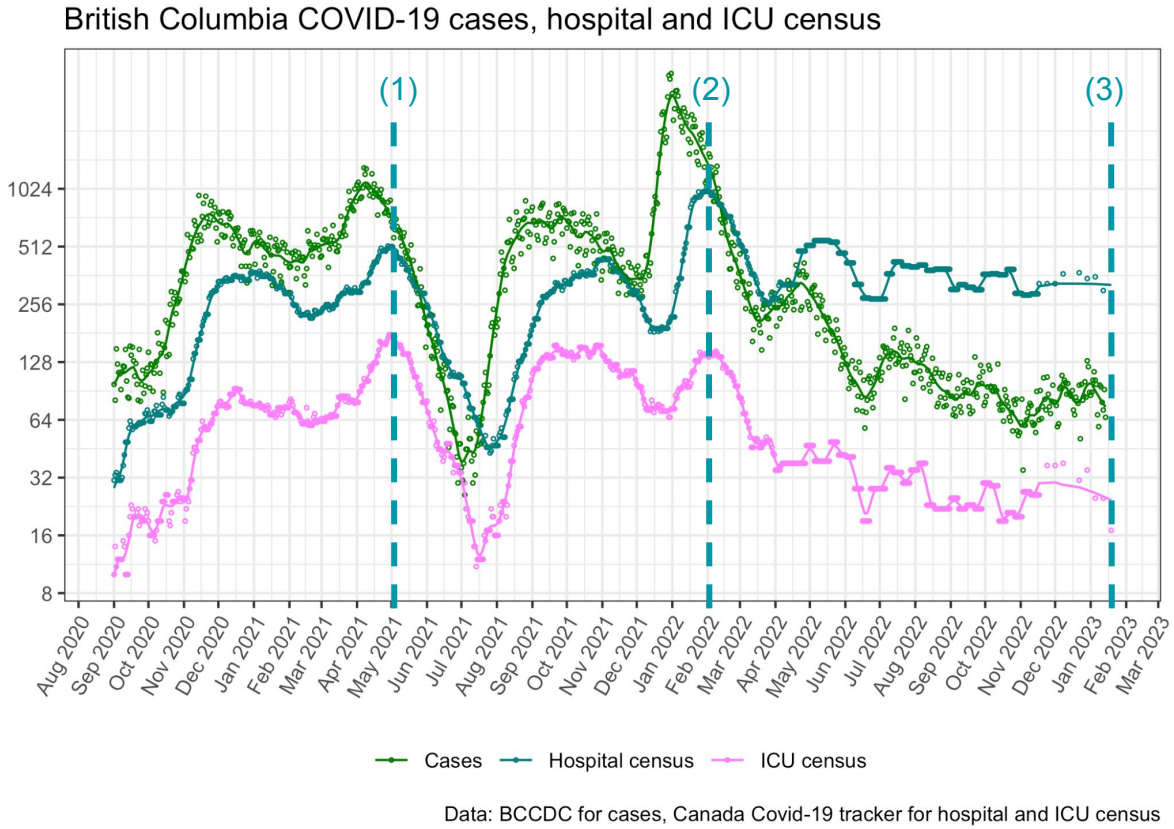
- Current COVID-19 trends in BC
- The rise of BQ.1
  - soon to become dominant in Canada
  - already dominant in Europe - we analyze data fr to peek into our future
- Interpretation of COVID-19 hospital admission
  - Evidence for waning of immunity
  - Short-term projections

OLD

Summary: Omicron con be dominated by BA.5* variants, particularly descendants like BQ.1* that car utations that reduce antibody recognition. BQ.1* has risen to an estimated cu ency of 50% in BC and in Canada. Nevertheless, case numbers are rising and f in a manner that depends less on these variants and more on population-level immunity and the waning of this immunity. **This is good news, suggesting that population-level immunity is largely protective against BQ.1* as well.**

Current COVID-19 trends in BC

Hospital trends in BC



The number of people in hospital and the number in ICU have remained at similar levels for months. By contrast, reported case numbers have declined sharply because of limited testing*.

Number in hospital with COVID-19:

Pre-Omicron

(1) Highest = 515 (28 April 2021)

Omicron wave:

(2) Highest = 1038 (31 January 2022)

(3) Current = 268

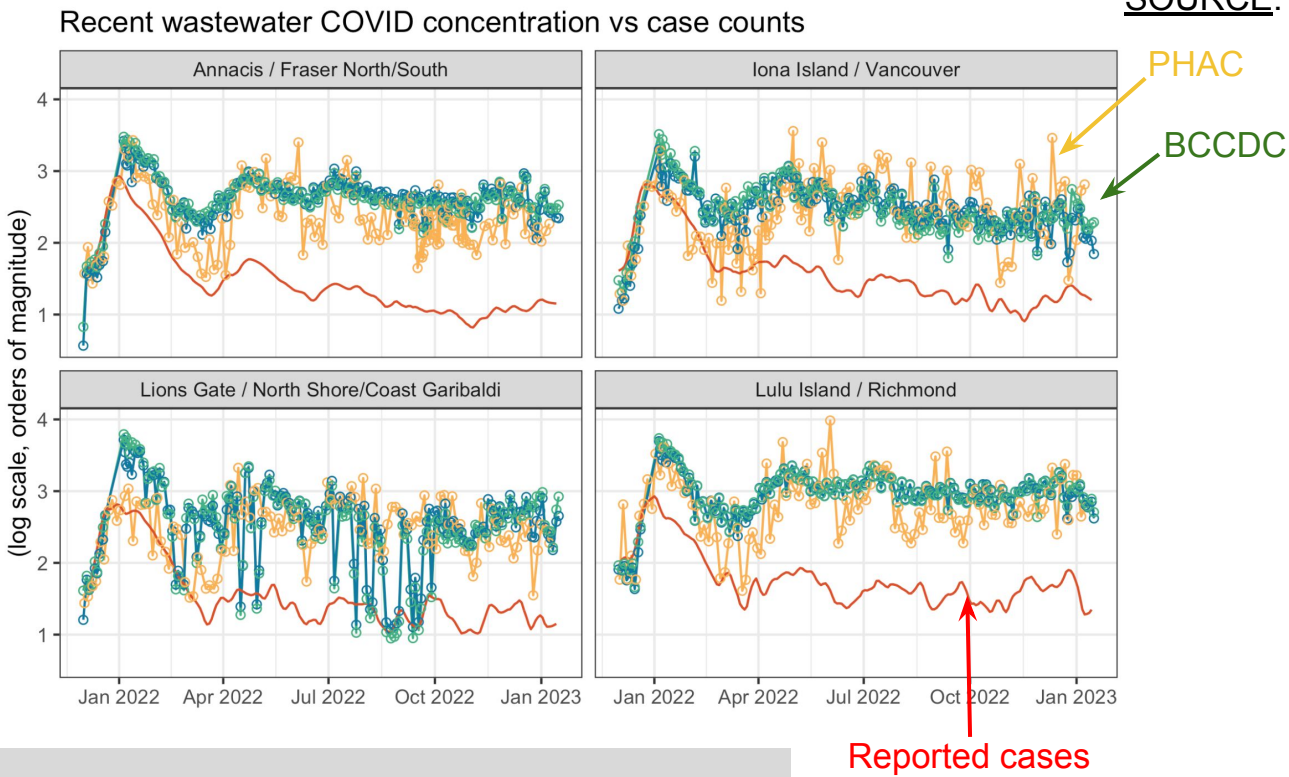
Source (J. von Bergmann) Case data from BC COVID-19 Database (http://www.bccdc.ca/health-info/diseases-conditions/covid-19/data). STL trend lines on log scale. How hospitalizations and deaths are attributed to COVID-19 changed in BC on April 2, 2022. *Reinfections with a prior lab-confirmed case are currently not counted in BC for reported case numbers, hospital admissions, or deaths, but they are included in hospital censuses as shown here.

Wastewater trends in Metro Vancouver

Wastewater signals (shown on a log scale from BCCDC and PHAC) have declined much less than reported cases, with only a slight decline in COVID-19 signals in wastewater since June.

Notes:

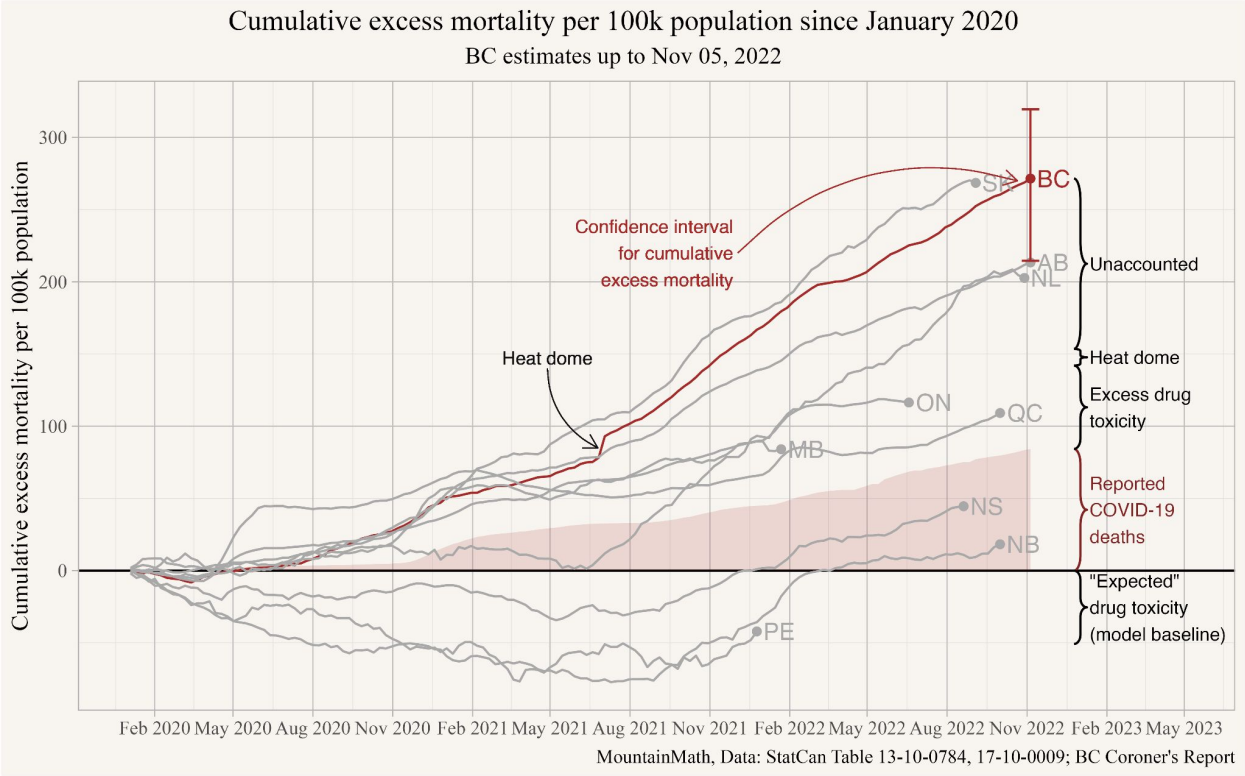
- Heights of curves are adjusted to align January through mid December 2021 to emphasize how trends differ across 2022.
- Y-axis shows the order of magnitude of virus copies (per liter in gold or blue or, adjusting for water flow, per day in green).
- Wastewater data are noisy and differ between the source labs for reasons that are not fully understood.



Check out UBC's Wastewater Tracker too!!

Source (J. Bergmann) Data from BCCDC & Metro Vancouver from Testing for the COVID-19 VIrus in Wastewater and from PHAC's COVID-19 Wastewater Dashboard.

Excess mortality update



Excess mortality accounts for all causes of mortality above those expected based on previous years, but a large fraction are unaccounted for.

What about the unaccounted deaths?

COVID-19 can cause a heightened health risk long after the 30-days currently used in BC to define COVID-related deaths (e.g., Xie et al.).

Deaths that are caused by COVID reinfections are also missing, if previous infection was officially recorded in BC.

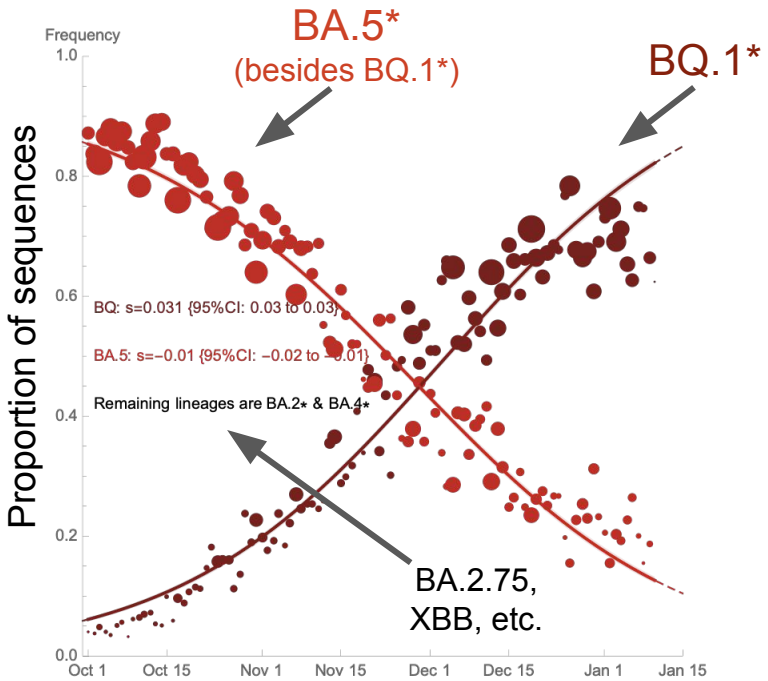
BC is likely substantially undercounting total deaths due to COVID.

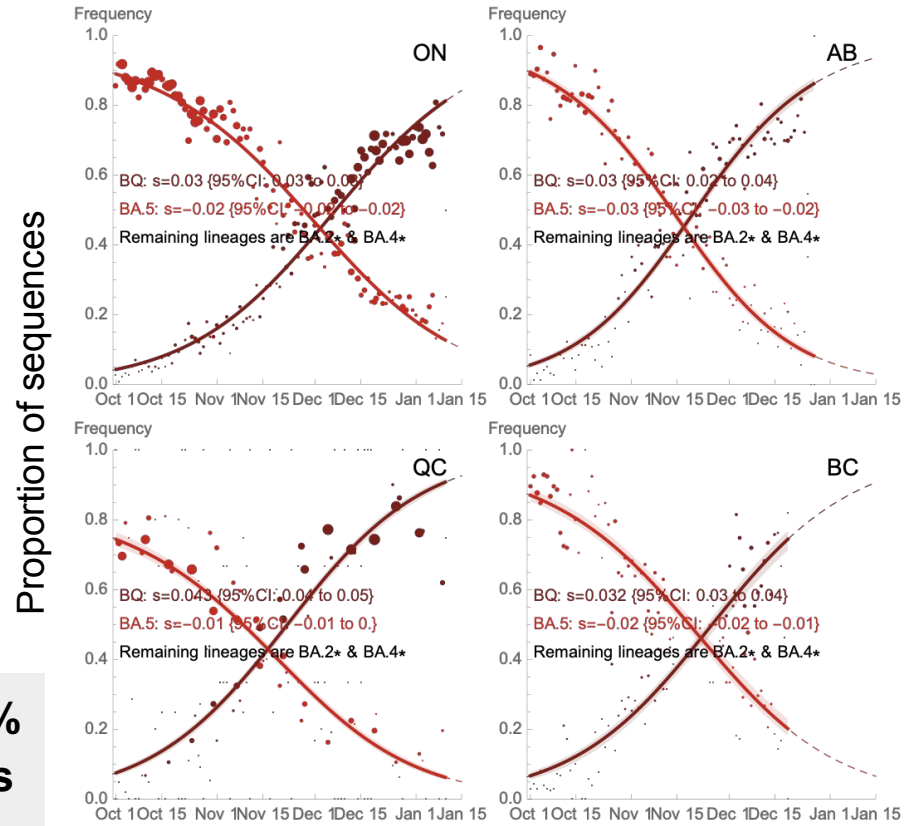
Source (J. Bergmann) Data from StatCan. The model baseline consists of "expected" deaths based on the previous four years, including drug toxicity and other causes (* indicates the levels of mortality due to drug toxicity in the four previous years). See May 19 2022 report (slide 9) for more details on excess deaths.

The rise of BQ.1

In this report, we separate out BQ.1 and its descendants (collectively called BQ.1*) from all of the other lineages that descend from BA.5 (collectively called BA.5*)

Spread of BQ.1* sub-lineages in Canada



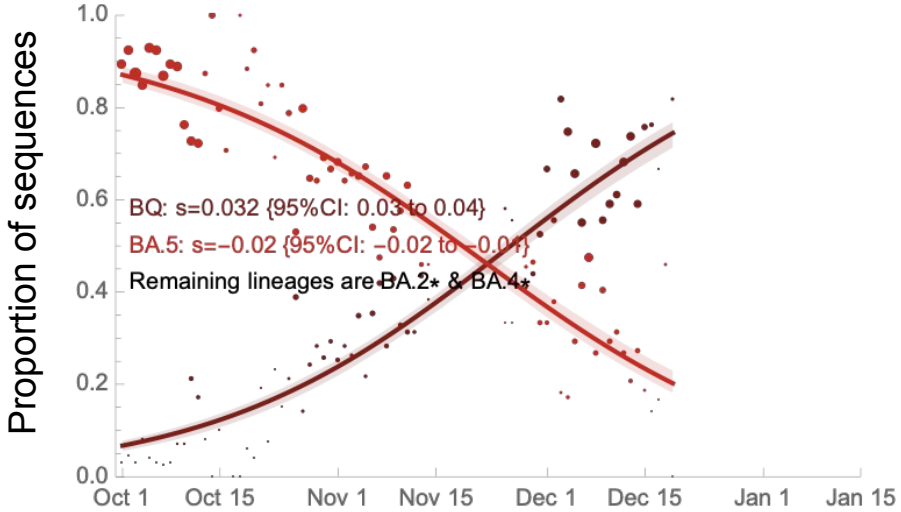


BQ.1* lineages have risen in frequency to >85% across Canada, although its recent spread has slowed due to newly evolved BA.2* lineages.

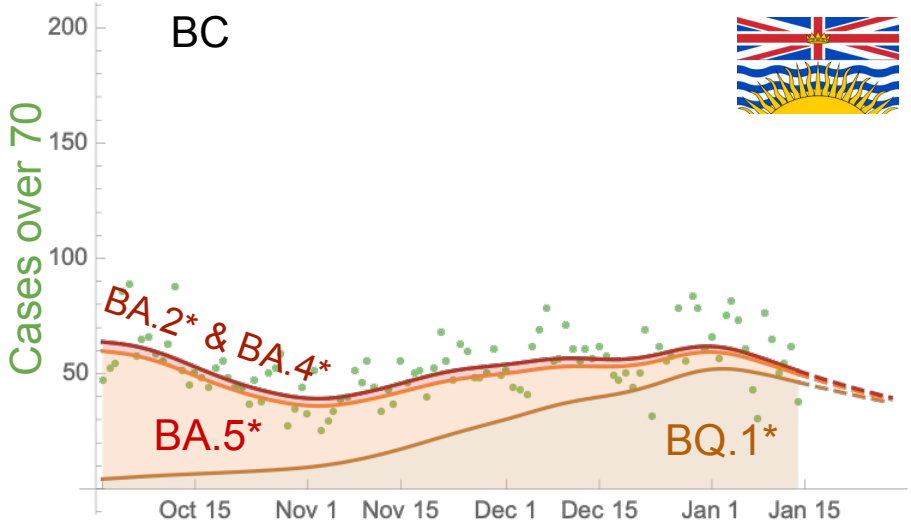
Source (S. Otto) Canadian metadata was downloaded from GISAID for the GRA clade. See Appendix for more more method details.

What does this imply for case numbers?

Fitting models of selection allows us to estimate frequency changes among variants.



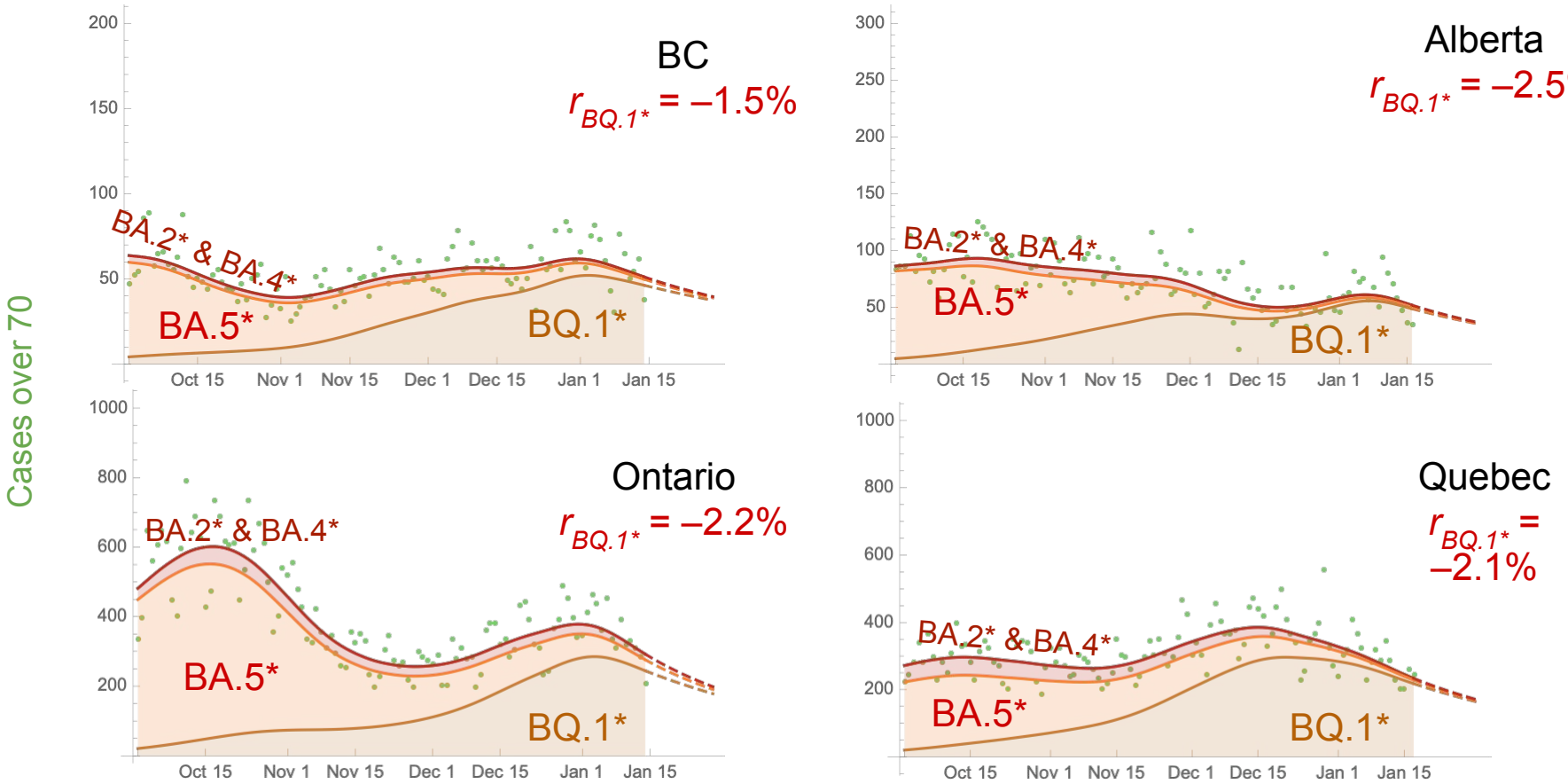
Multiplying by the # of cases in those over 70 allows us to **estimate** growth in numbers of each Omicron sublineage, while reducing extent of underreporting.



→ Despite spread in frequency of BQ.1*, case counts have remained steady.

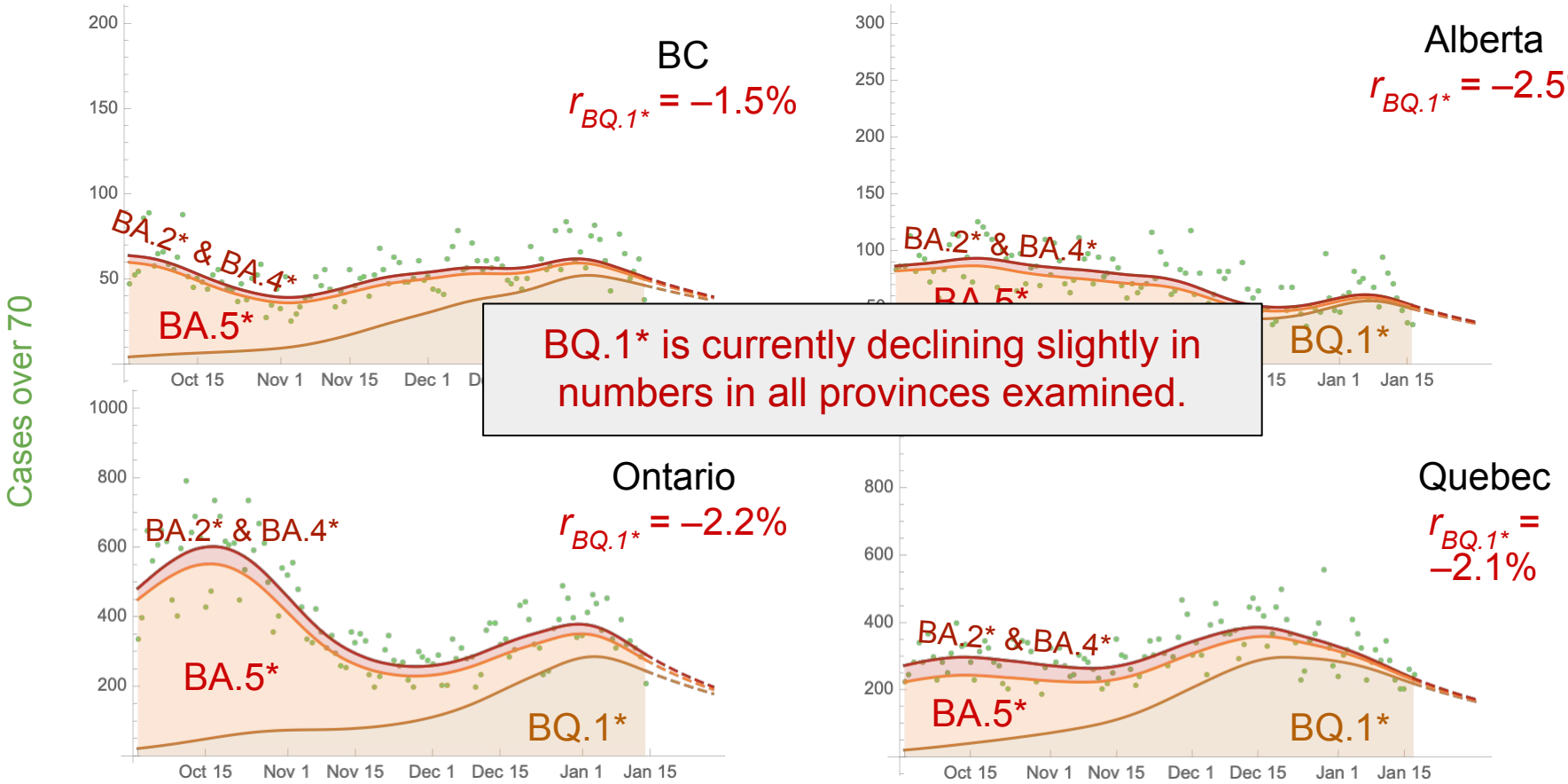
Source (S. Otto) Canadian metadata was downloaded from GISAID for the Omicron GRA clades. A model of selection was fit to the numbers of each type using maximum likelihood based on a trinomial distribution given the expected frequencies on each day. Hessian matrix used to obtain confidence intervals.

The BQ.1* Omicron Wave



* Instantaneous estimates of growth rate, *r*, and doubling times for BQ.1*. These rates change with changing immunity and with protective health measures, both mandated and voluntary, to reduce transmission (e.g., wearing effective masks, increasing ventilation, and avoiding crowded indoor spaces)

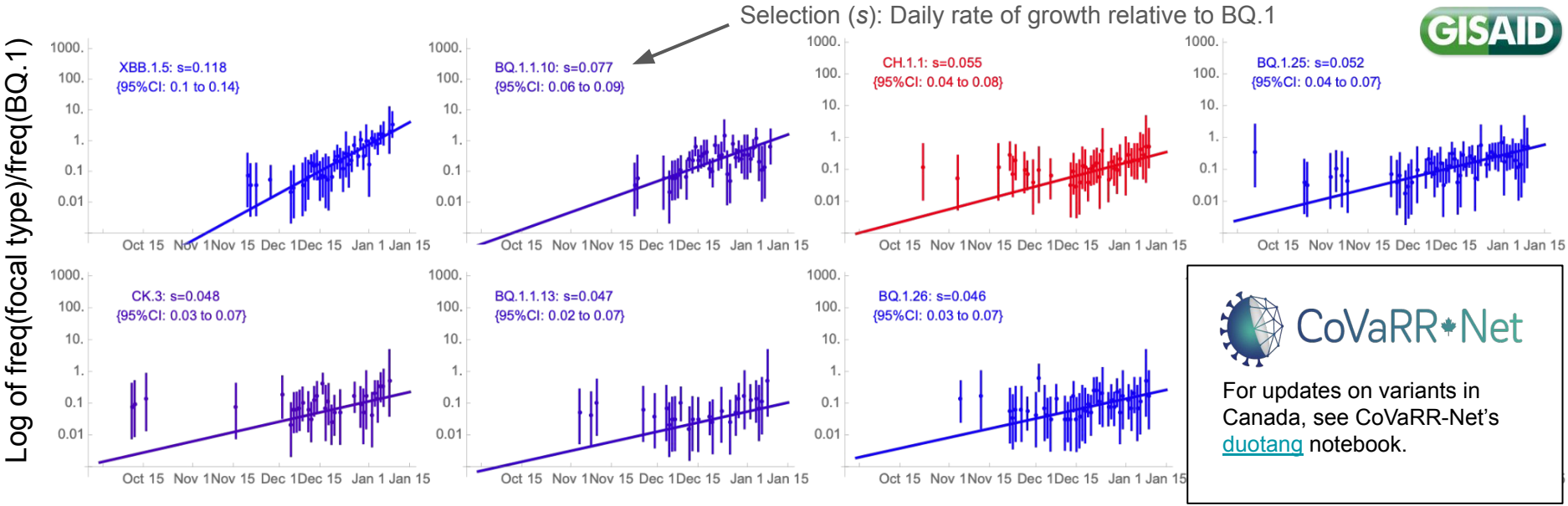
The BQ.1* Omicron Wave



* Instantaneous estimates of growth rate, *r*, and doubling times for BQ.1*. These rates change with changing immunity and with protective health measures, both mandated and voluntary, to reduce transmission (e.g., wearing effective masks, increasing ventilation, and avoiding crowded indoor spaces)

Spread of Omicron sub-lineages in Canada

335 named sub-lineages have been circulating in Canada over the last three months.
Measuring the selective advantage of each relative to BQ.1, the fastest growing lineage is the recombinant XBB.1.5 (s ~ 12%), followed by BQ.1.1.10 (s ~ 8%).



CoVaRR-Net

For updates on variants in Canada, see CoVaRR-Net's duotang notebook.

Source (S. Otto) Canadian metadata was downloaded from GISAID for the Omicron GRA clades. Each lineage is plotted separately relative to BQ.1 on a log scale. On this logit plot, the slope measures selection for a variant relative to BQ.1.

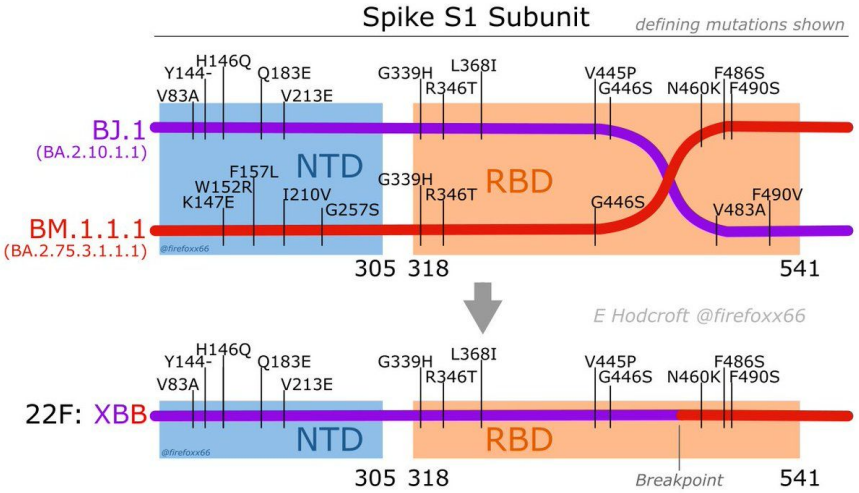
What is XBB.1.5?

XBB.1.5 is a descendant of XBB, a recombinant lineage between two BA.2* lineages. XBB.1.5 carries a change in the spike protein (S:F486P) that is rare because the change from phenylalanine (F) to proline (P) requires two mutations.

All XBB and BQ.* lineages have strong immune evasion properties relative to BA.5*, but what gives XBB.1.5 the edge is thought to be higher transmissibility due to its superior binding to ACE2 receptors on our cells (Cao et al. 2023).

It is sometimes called “Kraken”, but this suggests that it is a much riskier lineage than it likely is. There is no evidence that it causes different symptoms or is more severe.

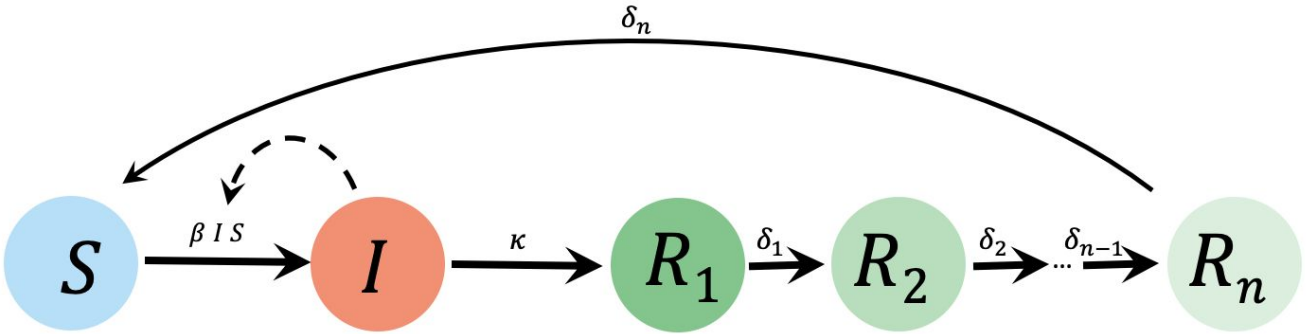
Genomic signature of recombinant origin of XBB
(from Dr. Emma Hodcroft @firefoxx66)



Likely impact of new variants

COVID-19 in Canada has remained at a roughly constant level for nearly 9 months (see slide 5). This suggests that the disease is approaching steady state, reflecting a balance between new infections depleting the pool of susceptible individuals and waning of immunity replenishing that pool.

Models can help us explore the factors that affect the steady-state level of COVID-19 (e.g., new variants).



Infection

(From susceptible to infectious)

Waning

(green classes represent degrees of waning, e.g., spike-antibody concentrations)

Likely impact of new variants

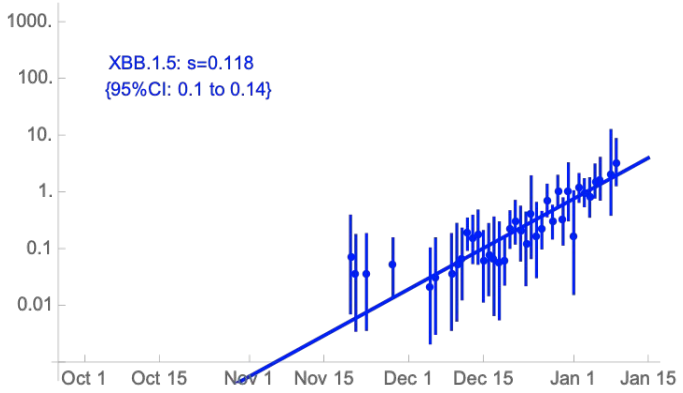
How will the spread of

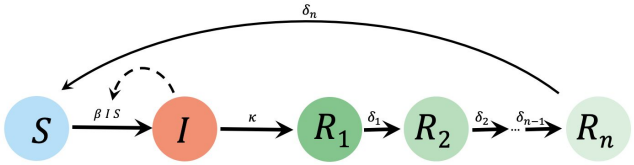
a) Immune evasive variants (e.g., BQ.1*)

or more

a) Transmissible variants (e.g., XBB.1.5)

alter the steady-state level of COVID-19?



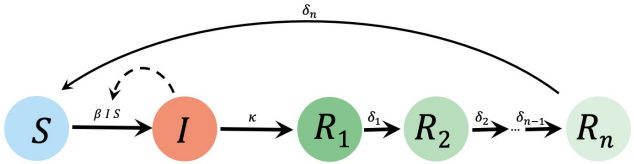


Likely impact of new variants

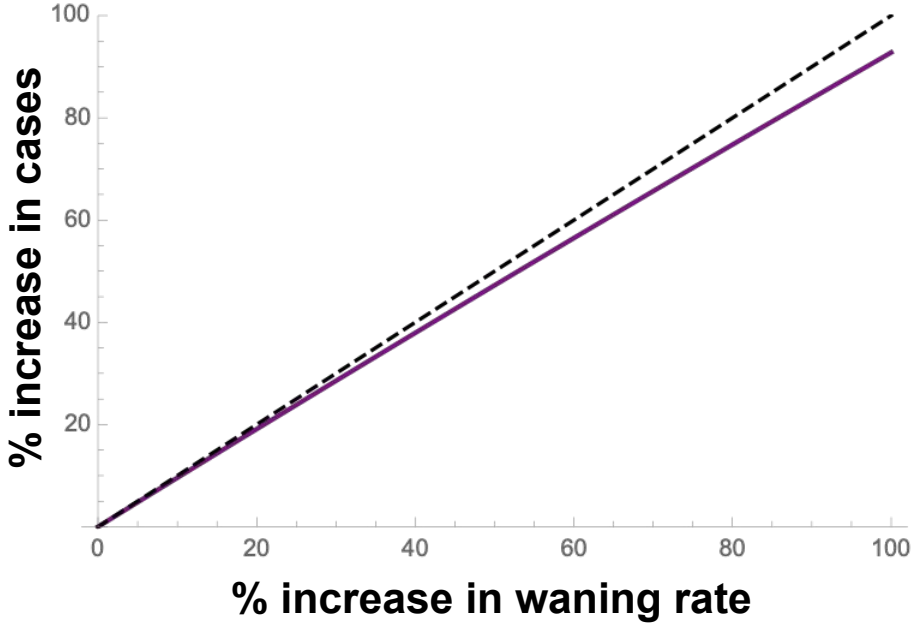
a) Immune evasive variants

Variants that are more immune evasive are able to infect individuals earlier.

Model result: If a variant reduces the time until susceptibility by a factor *c*, the steady-state number of COVID-19 infections increases by a similar amount.



Dashed: Proportional effect (1:1 line)
Purple: Model prediction

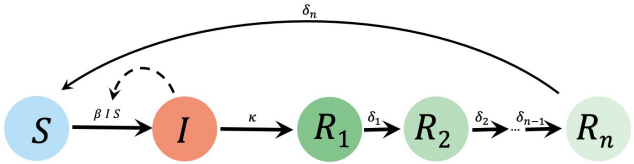


Implications of a steady state

b) Transmissible variants

Lineages, like XBB.1.5, that are more transmissible (increasing □) rapidly deplete the susceptible pool and have less influence on cases.

Model result: If a variant increases transmission by a factor *c*, the steady state number of COVID-19 infections increases only by $\frac{c\tilde{R}-1}{c(\tilde{R}-1)}$



Dashed: Proportional effect (1:1 line)
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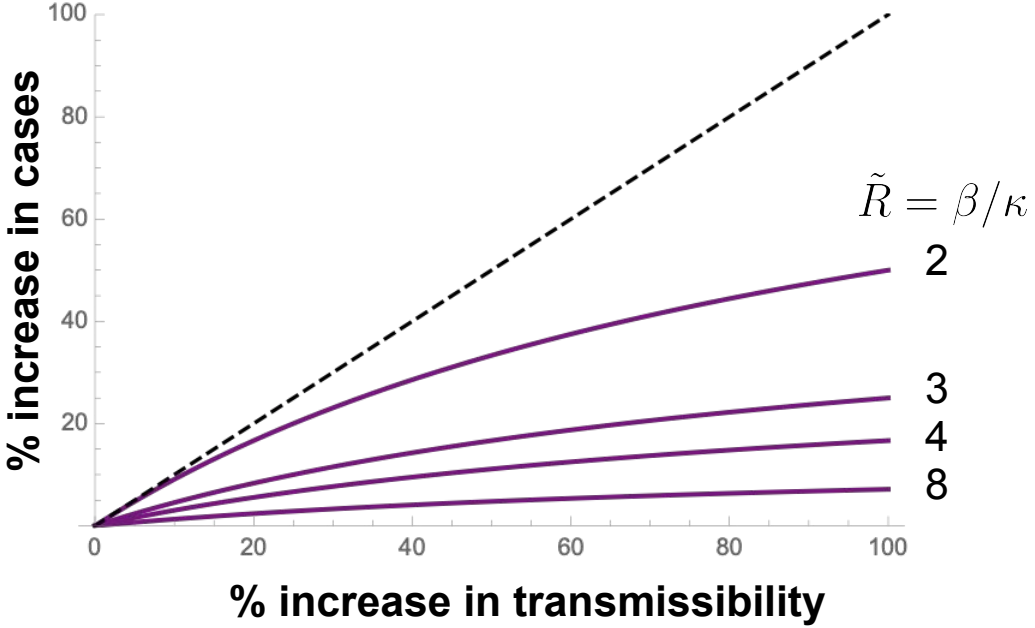


$\tilde{R} = \beta/\kappa$ is the effective reproductive number (# of new cases per infection) if everyone were susceptible today, given current measures and prior exposure.

Immunity against recent variants

Population immunity and the omicron waves

Despite new omicron variants emerging with improved transmission, the corresponding waves have been generally smaller than the preceding waves

This provides direct evidence that population-level immunity is robust against a new variant.

In our previous report, we showed data that indicated the BQ.1* variants did not substantially evade population immunity and therefore the magnitudes of their waves were not expected to be substantial.

Waning of population-level immunity and the 4th Omicron wave

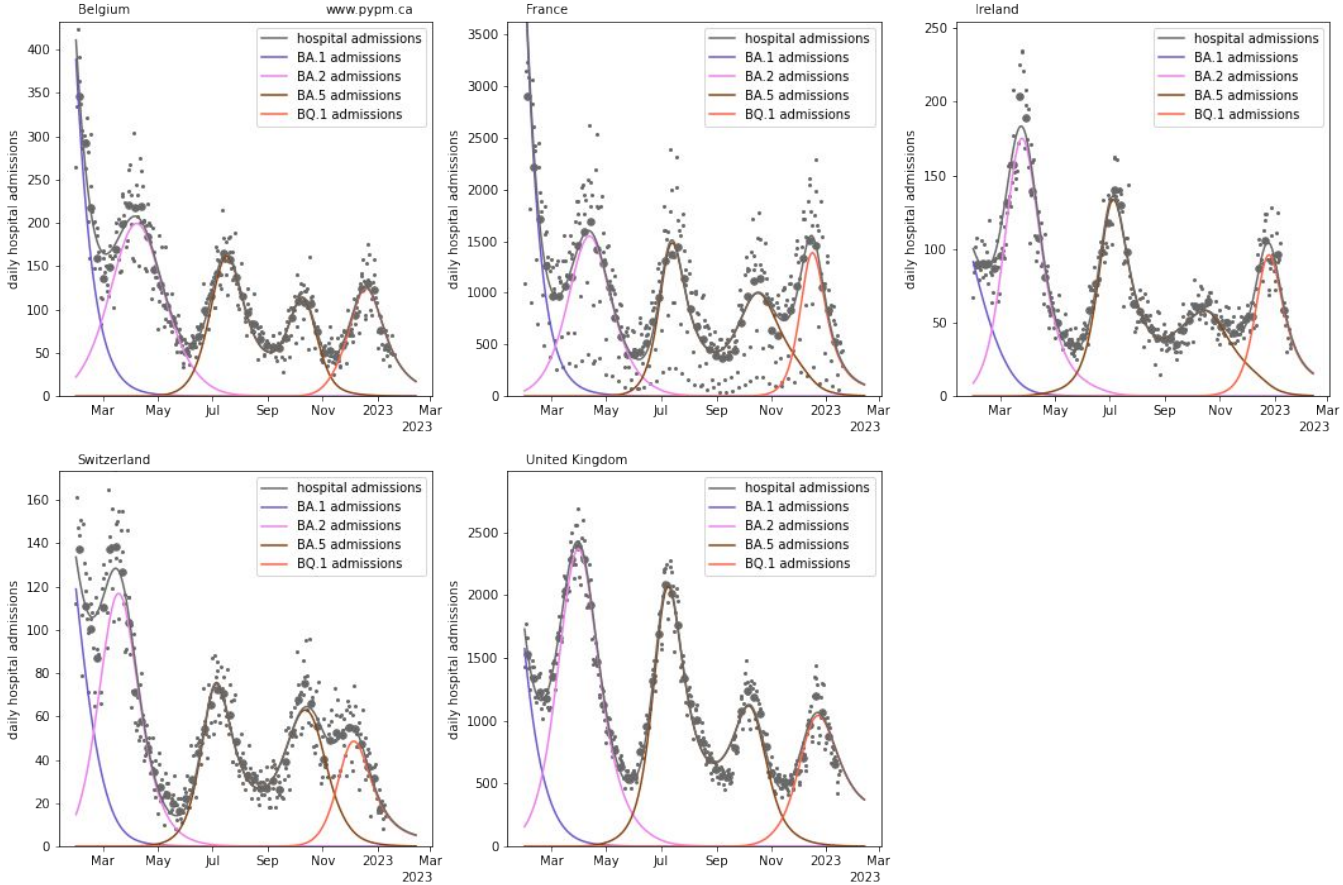
Our previous reports showed that in several European nations, waning of immunity caused the 4th Omicron wave (Fall 2022), thereby having similar strains as the 3rd wave (Summer 2022), primarily BA.5.

Peaking of the 5th Omicron wave, primarily due to BQ.1* variants

Since our last report, the 5th omicron wave peaked in Europe, thanks to robust population-level immunity. The timing of the emergence of new variants resulted in well separated waves, simplifying the interpretation of the data. We can infer that the BQ.1* will not cause a substantial new wave in Canada.

The continued rapid decline in infection rates in Europe shows that waning rates are not growing, unlike the situation after the 3rd wave. A second BQ.1* wave is not expected.

Model fits to hospital admission data in Europe



The daily (small dots) and weekly average (large dots) hospital admissions are compared to model fits (solid lines). The models have four strains (for BA.1, BA.2, BA.5, and BQ.1), each having constant transmission rate. Immunity parameters were set from the shape of the second wave (BA.2).

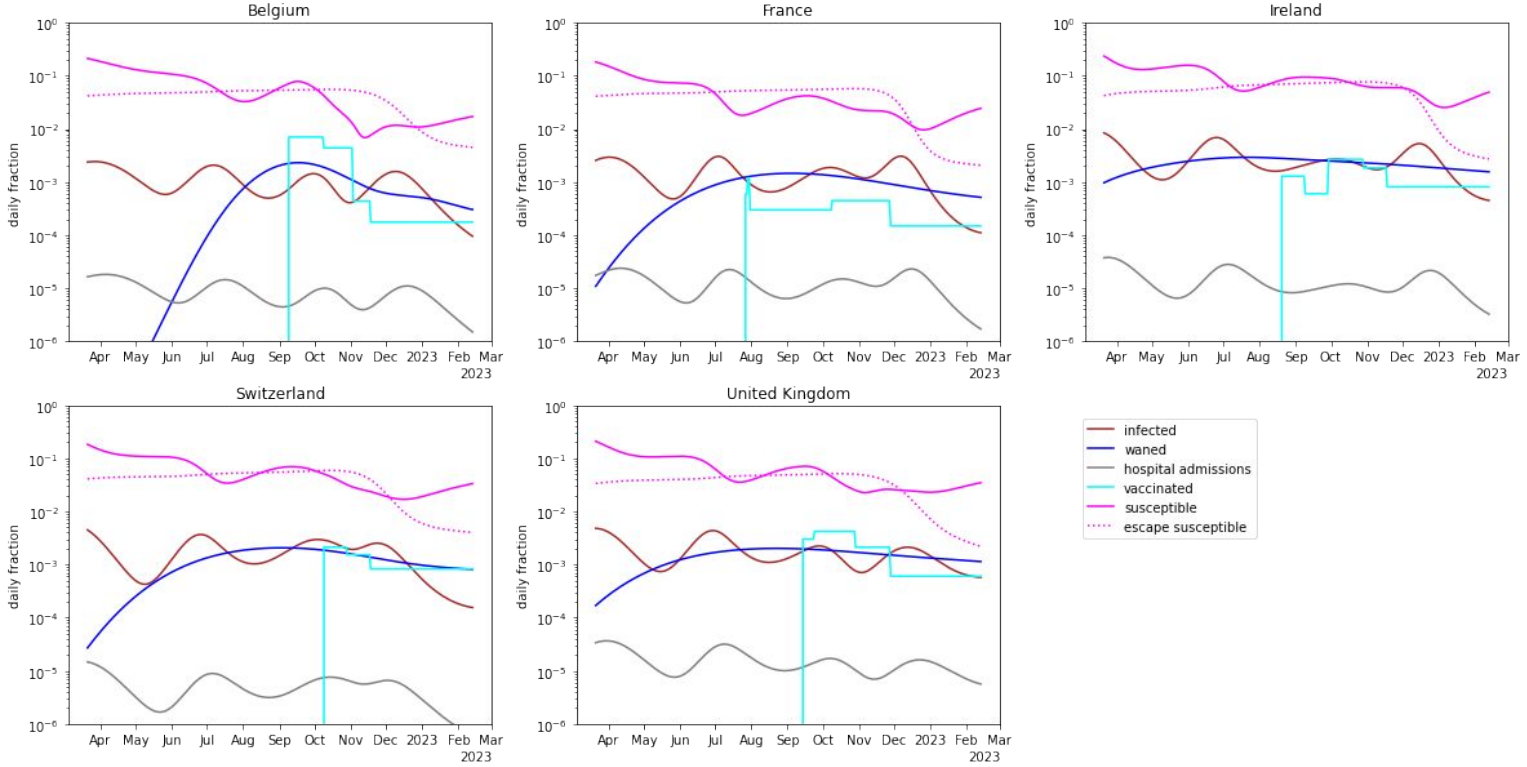
Waning is implemented as a gamma delay function, with three free parameters as described in the October 5 report.

Infections are currently declining at the rate of about 5% per day.

Norway has stopped reporting hospital admission data since mid-November 2022, and therefore is no longer included in these analyses.

Source (D. Karlen) See www.pypm.ca. Hospital admission data from European COVID-19 Forecast Hub, Our World in Data, GOV.UK, and geohive.ie

Inferred immunity dynamics



The analysis estimates the initial susceptible fraction and the ratio of infections to hospital admissions from the shape of the BA.2 wave.

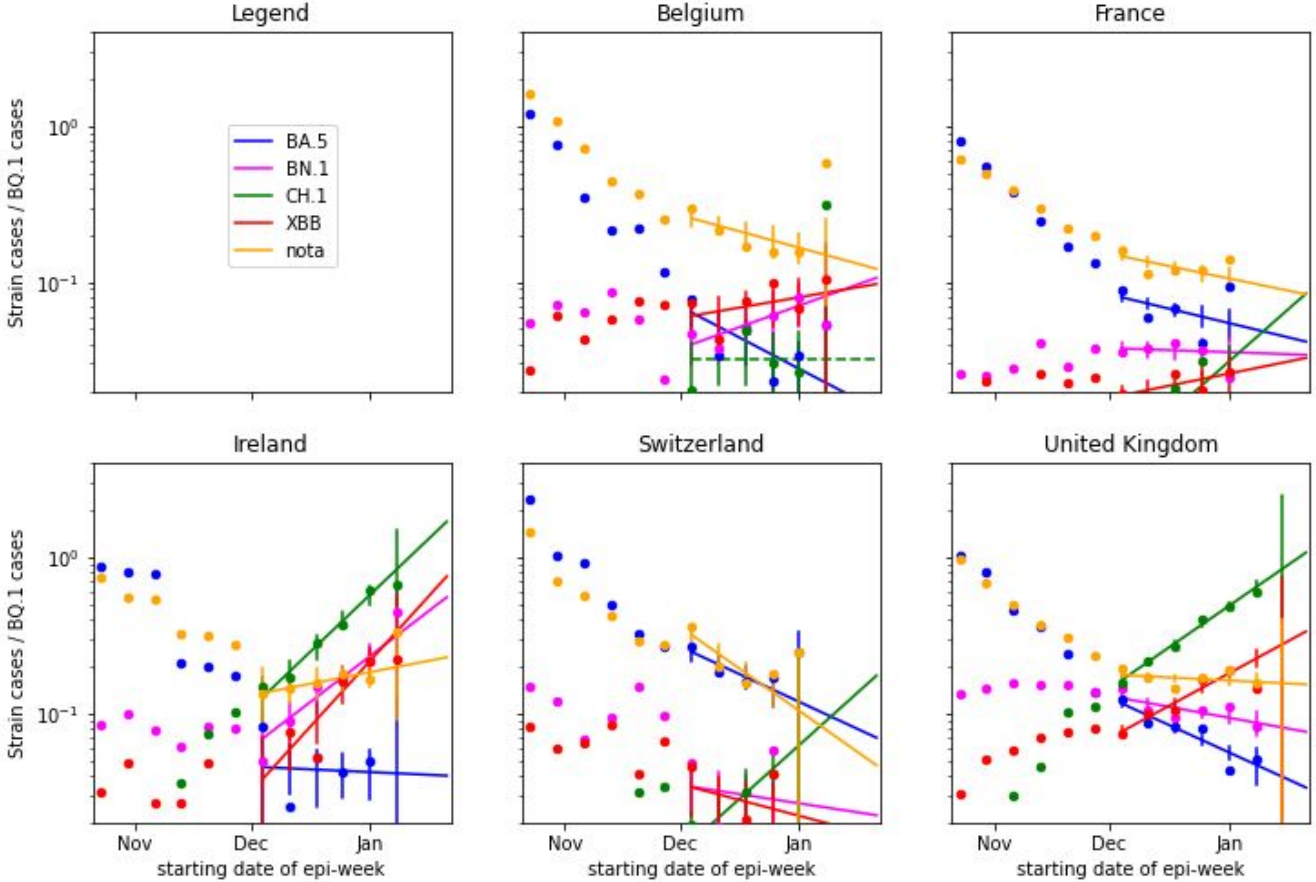
The escape fraction for BQ.1 is estimated from the 5th wave.

Waning parameters are estimated from the data following the peak of the 3rd wave.

In absence of significant vaccination, future infection rates are largely driven by the waning rates.

Source (D. Karlen) See www.pypm.ca. Data from ECDC vaccine tracker. The dashed pink curve shows additional individuals who would be susceptible to BQ.1*, but not previous Omicron lineages. Fits to the data find that this escape fraction is about 5%.

Selection coefficient analysis for new variants



The points show the ratio of weekly cases grouped as BA.5*, BN.1*, CH.1*, XBB* and none of the above ('nota') with respect to BQ.1* cases.

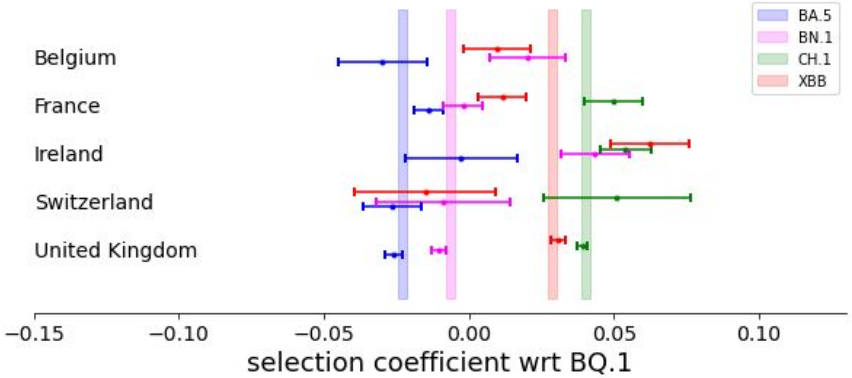
The slope of the exponential curves indicate the growth advantage of new variants compared to BQ.1.

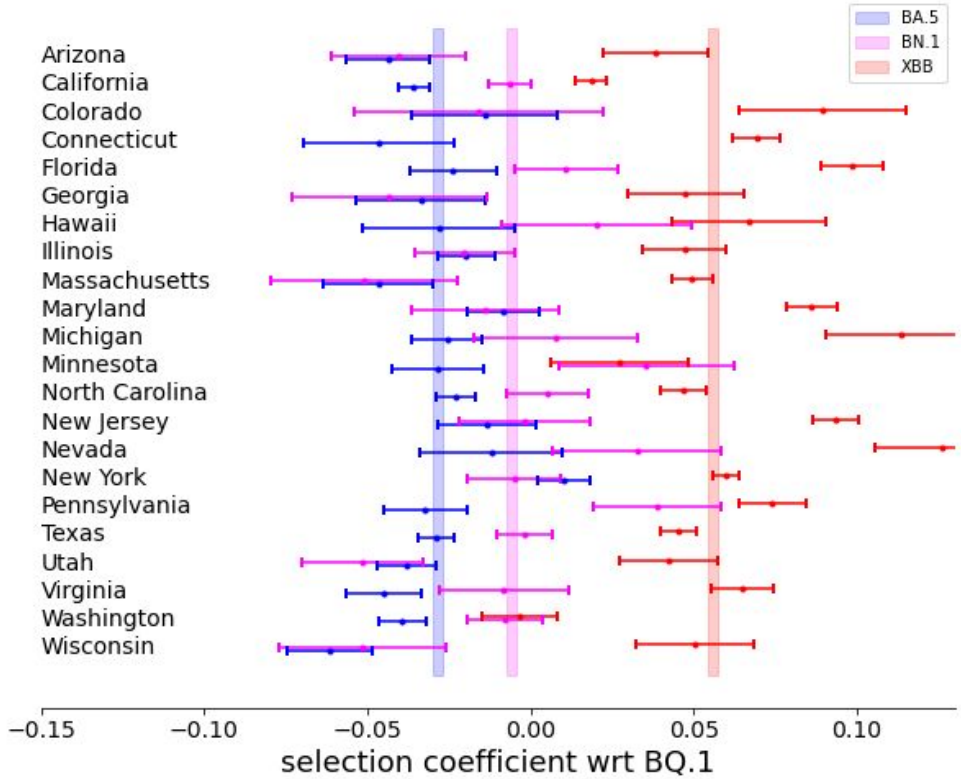
While there are new variants that grow faster than BQ.1, a growth advantage of less than 5%/day is insufficient to lead to another Omicron wave.

The next slide shows growth advantage estimates.

Source (D. Karlen) European metadata was downloaded from GISAID for the GRA clade.

Selection coefficients for new variants: Europe and US

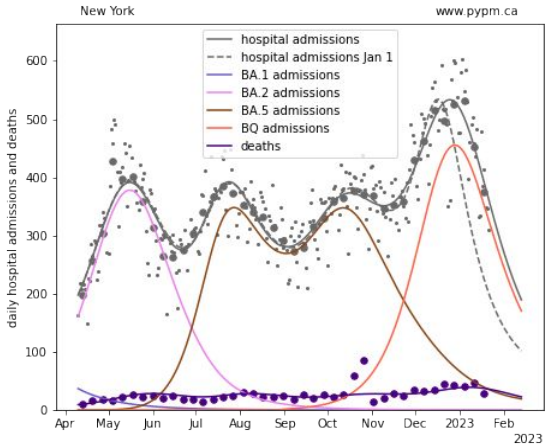


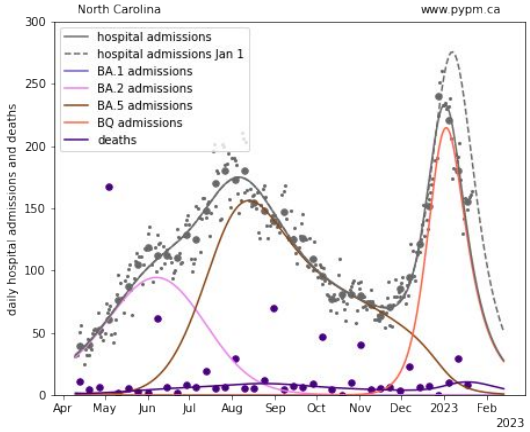


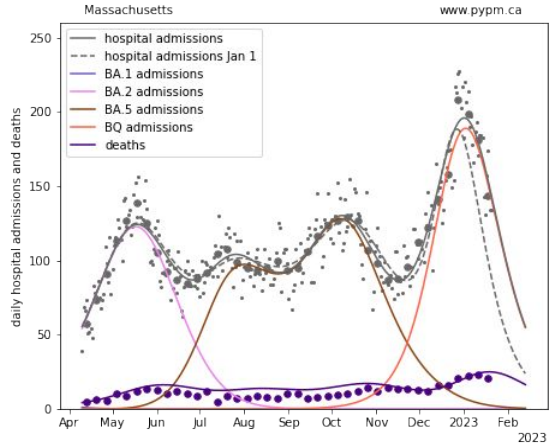
- The growth advantage of BQ.1* strains compared to BA.5* strains is diminished compared to results shown in our previous report. (Previously 8%/day, now 3%/day).
- Limited data and different mixtures of strains results in significant scatter of estimates:
  - Overall, the average selection coefficients for the different groupings wrt BQ.1* are similar for Europe and US.
- Given that BQ.1* is declining at -5%/day, XBB* and CH.1* are not likely to produce significant waves in Europe.
- Some US states (particularly NY) have mostly XBB* cases. CH.1* currently has low prevalence in the US.

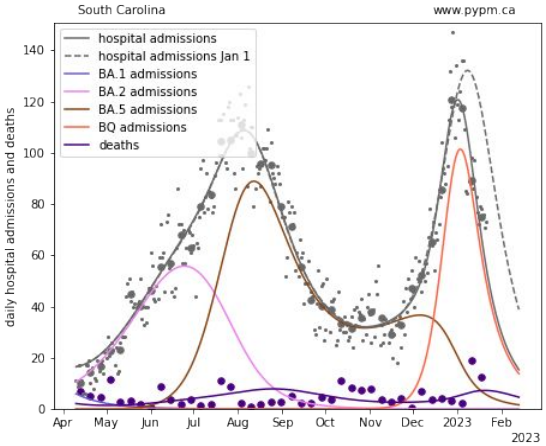
Source (D. Karlen) See www.pypm.ca. European and US metadata was downloaded from GISAID for the GRA clade.

Selected US states









Unlike Europe, the 4 Omicron peaks following BA.1 are generally not well separated in US states.

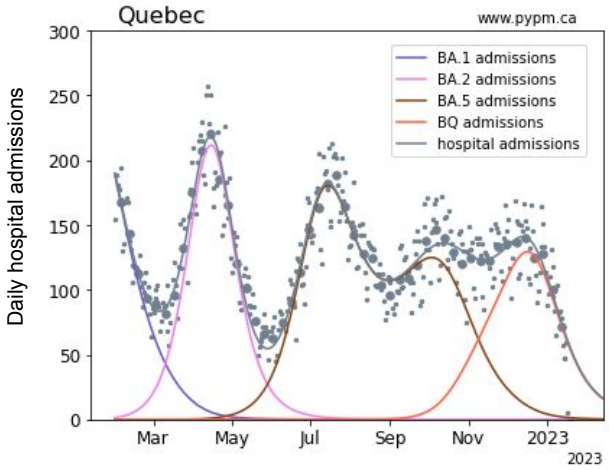
While the most recent peak in NY is a combination of BQ.1 and XBB, this is modelled by a single additional strain

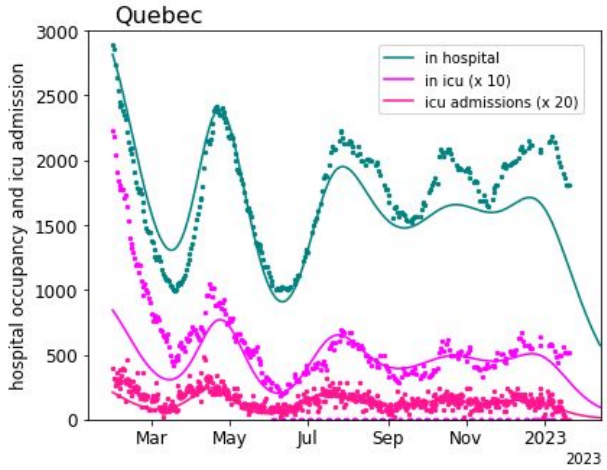
Infections are currently declining at the rate of about 5% per day, like Europe. The new variants (XBB and CH.1) are therefore not likely to cause significant waves in US states.

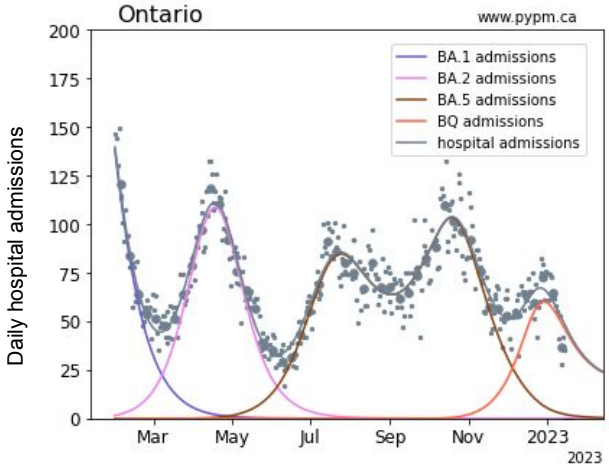
The turnaround times and amplitudes were similar to model forecasts from January 1 (shown by dashed curves). The forecasts, made prior to data showing the turnaround in these states, assumed a small escape fraction, as seen in Europe.

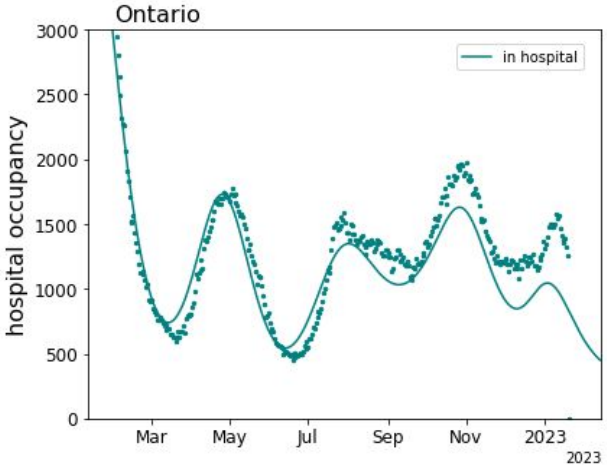
Source (D. Karlen) See www.pypm.ca.

Quebec and Ontario









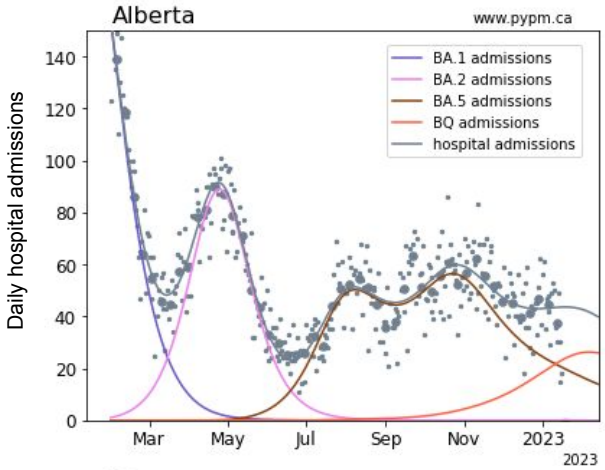
The same approach is applied to four provinces. A similar pattern is seen as in US and Europe, due to emergence of new variants and waning of immunity in Fall.

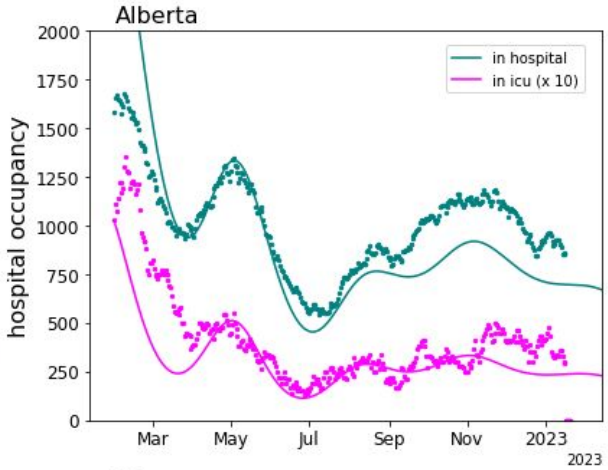
Infection rates in Quebec and Ontario are inferred to be rapidly falling, due to additional immunity from recent infections and vaccinations.

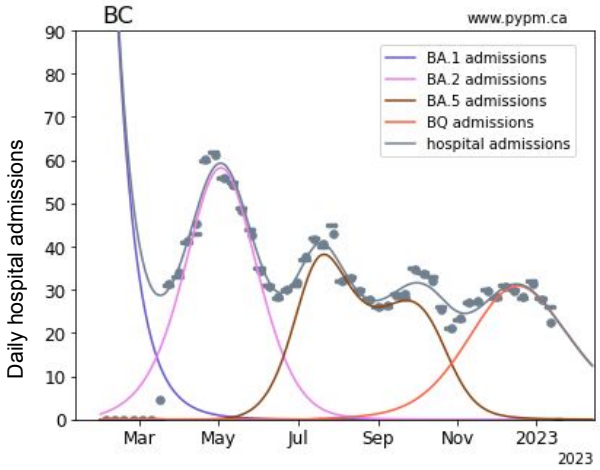
Hospital occupancy in recent months exceeds model projection assuming fixed hospital release time distributions throughout the period.

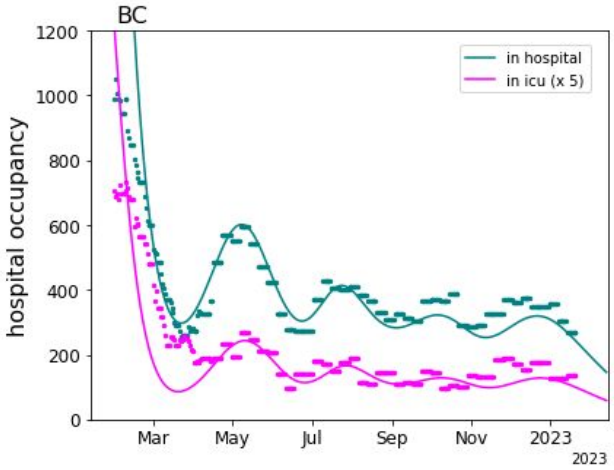
Source (D. Karlen) See www.pypm.ca.

Alberta and BC









The interpretation of recent data from Alberta and BC is less clear, as the waves are less distinct.

Based on data from other jurisdictions, it appears likely that hospital admissions will continue to decline.

Source (D. Karlen) See www.pypm.ca.

Key messages

The current COVID-19 outlook

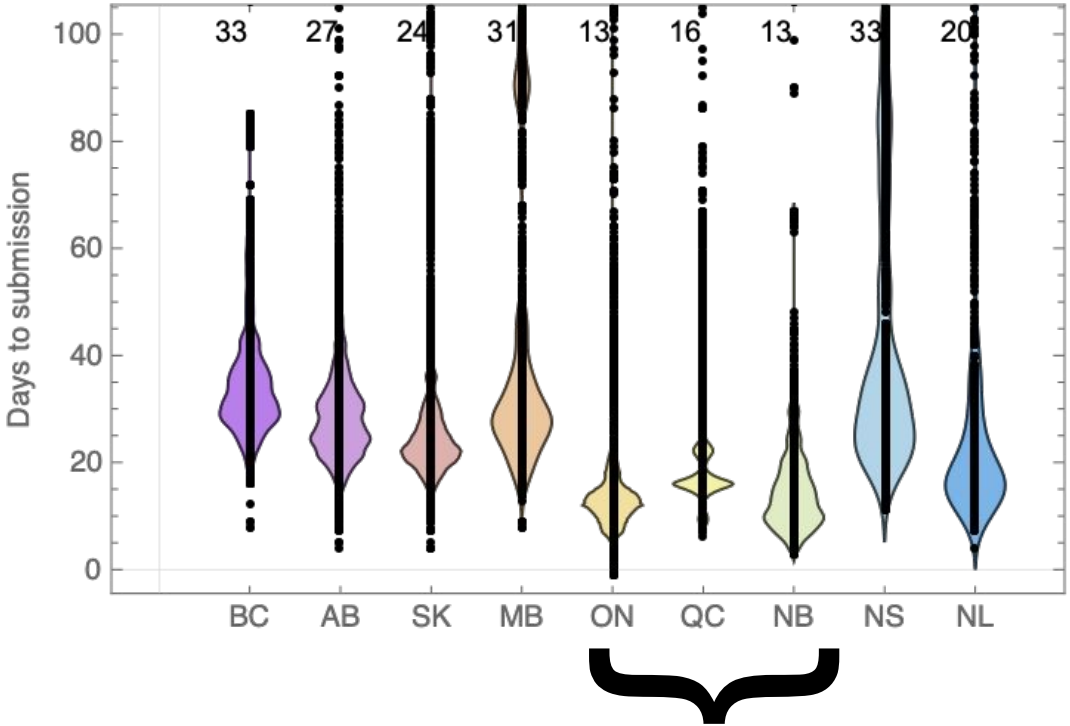
- COVID-19 has persisted at high levels in BC ever since BA.5 started to rise in June 2022
- The main lineages spreading in Canada are BQ.1* (a BA.5 descendant) and XBB* (a recombinant between two BA.2 sub-lineages). These carry mutations shown to better evade antibodies
- BQ.1* is estimated to account for 50% of sequences in BC and in Canada this week.
- Population immunity can be estimated based on the shape of the epidemic curves, providing a way to estimate immune evasion and waning and to predict future cases and hospitalization rates.
  - This approach indicates that it is waning of immunity to the variants, that led to the recent fall wave.
  - This conclusion is confirmed by a separate analysis based on genomic data.

OLD

The immune evasion advantage demonstrated for BQ.1* [in the lab](#) may allow this variant to infect individuals with waning immunity sooner, but our results suggest that most people retain immunity to BQ.1*.

COVID-19 cases and impacts will likely rise and fall over the next few months as immunity lost through waning is offset by new immunity, gained by vaccination and/or infections.

Appendix: Genomic data sharing



GISAID

Median # of days from sample collection to posting on GISAID (for Omicron).

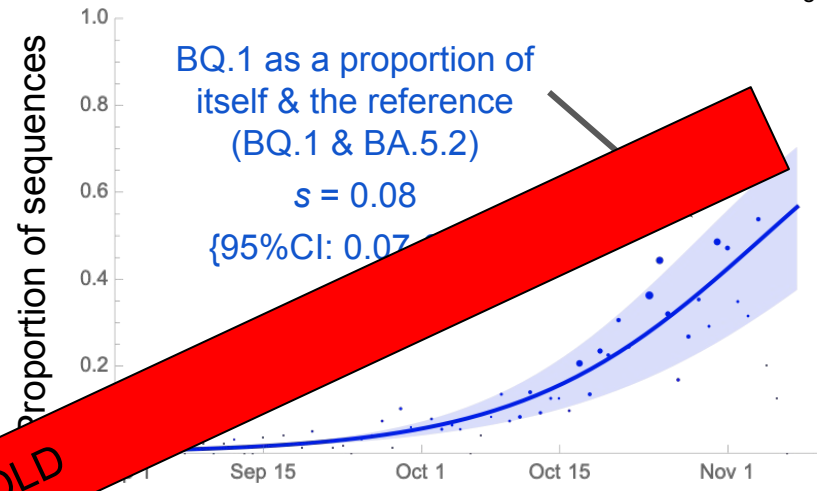
Excellent pipelines in some provinces (~ two week turn-around times) enable more accurate real-time projections.

Appendix: Interpreting selection

What is selection ("*s*") and what does it mean?

s measures the selective advantage per day of a variant relative to a reference strain (e.g., measuring the rate of spread of BQ.1 relative to BA.5.2)*.

This selective advantage may reflect a higher transmission rate or a greater ability to evad immunity or both.



OLD

ection per day, *s*, satisfies $p_T = \mathrm{Exp}(s\,T)\,p_0 / (1-p_0+\mathrm{Exp}(s\,T)\,p_0)$ where p_T is the frequency of a lineage of interest on day T, considering only itself and the reference (e.g., the # of BQ.1 divided by the # of BQ.1 and BA.5.2). *s* is estimated from the numbers of sequences over time by maximizing the likelihood of observing the data (see methods).

Daily selective advantag

1%	2%	5%	10%	20%
69.3	34.7	13.9	6.9	3.5

Days to double in **frequency** relative to reference strain

Alpha vs Wuhan

BA.5 vs BA.2

Omicron vs Delta

Source (S. Otto): BC sequences for Omicron (GRA clade) were downloaded from GISAID. More details on these methods are described on the CoVaRR-Net site.