COVID Model Projections

January 25, 2023

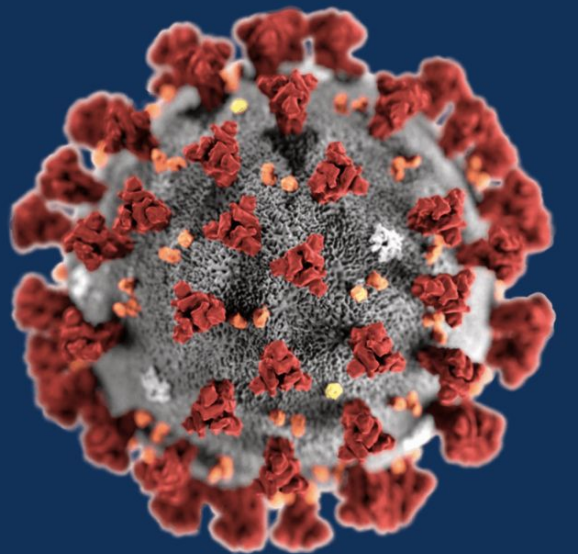
BC COVID-19 Modelling Group

@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

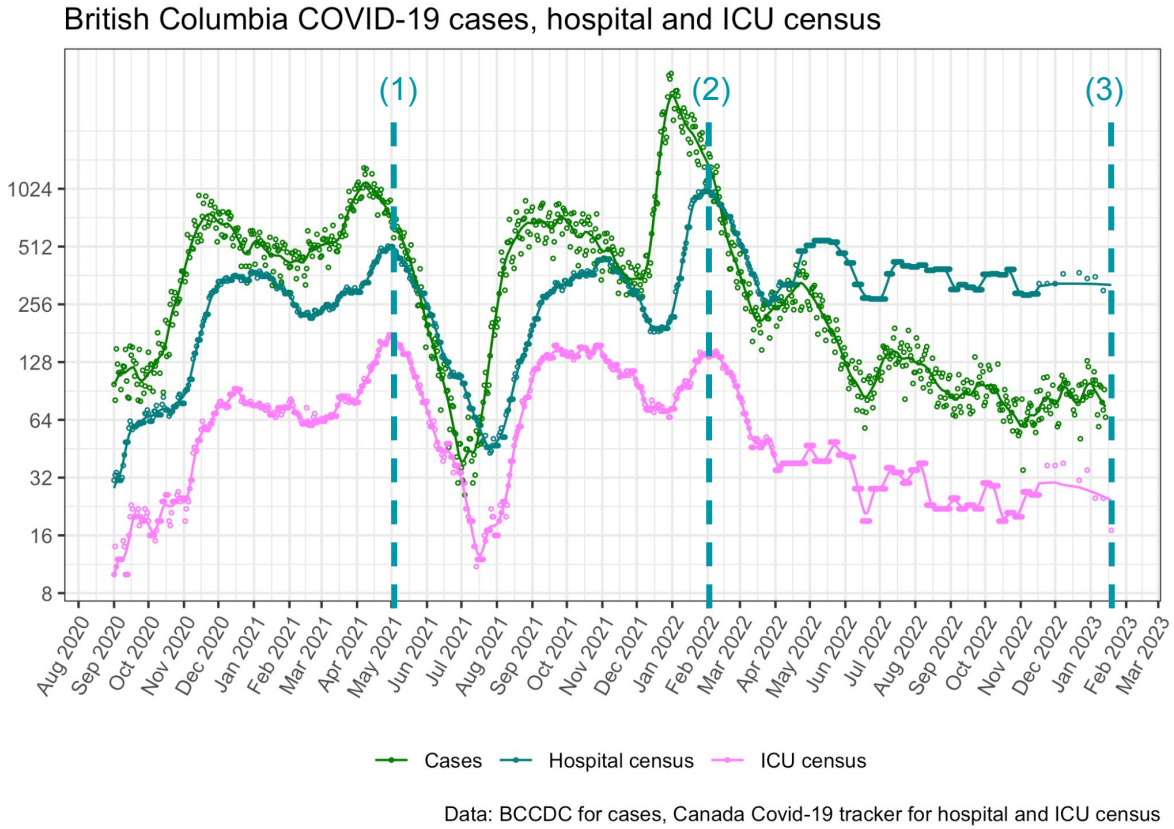
Contents of this report:

- Current COVID-19 trends in BC
- The rise of variants in Canada
  - BQ.1 and its descendants now predominate
  - XBB.1.5 is the fastest growing lineage
- Models suggest that COVID-19 levels should be less sensitive to variants that are more transmissible
- Interpretation of COVID-19 hospital admission data:
  - Evidence, particularly from Europe, for robust population-level immunity against recent variants
  - Short-term projections

Summary: SARS-CoV-2 lineages BQ.1 and XBB and their descendants, which carry several mutations reducing antibody recognition, are the fastest spreading variants in Canada. BQ.1* has risen to a current frequency of ~85% across the country. Case numbers are undergoing only modest fluctuations, reflecting the rise and fall of population-level immunity through infections, vaccinations, and waning. **Models project future declines in case numbers over the short term, with the rising tide of XBB.1.5 likely having only a modest impact.**

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.

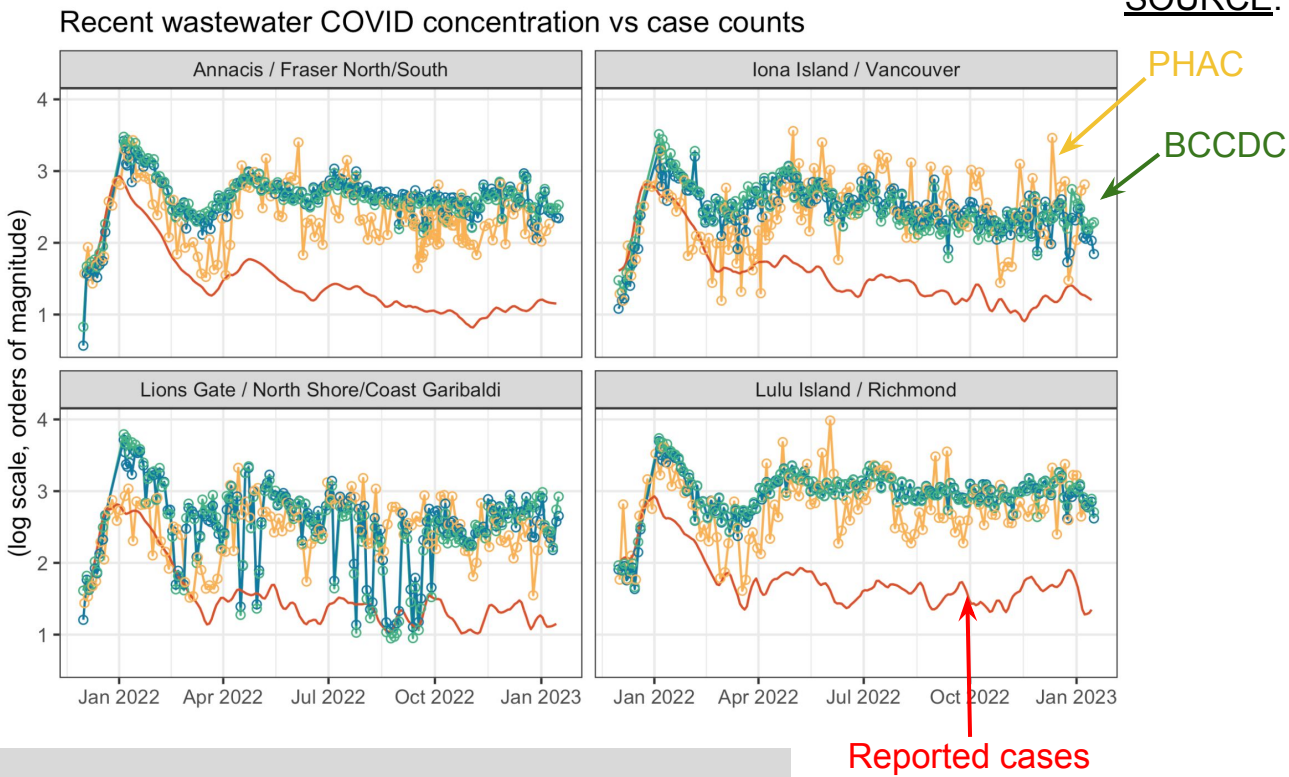
Wastewater trends in Metro Vancouver

Wastewater signals (shown on a log scale from BCCDC and PHAC) have remained flat since summer 2022, with relatively small fluctuations.

The much more dramatic drop in reported cases reflects less testing.

Notes:

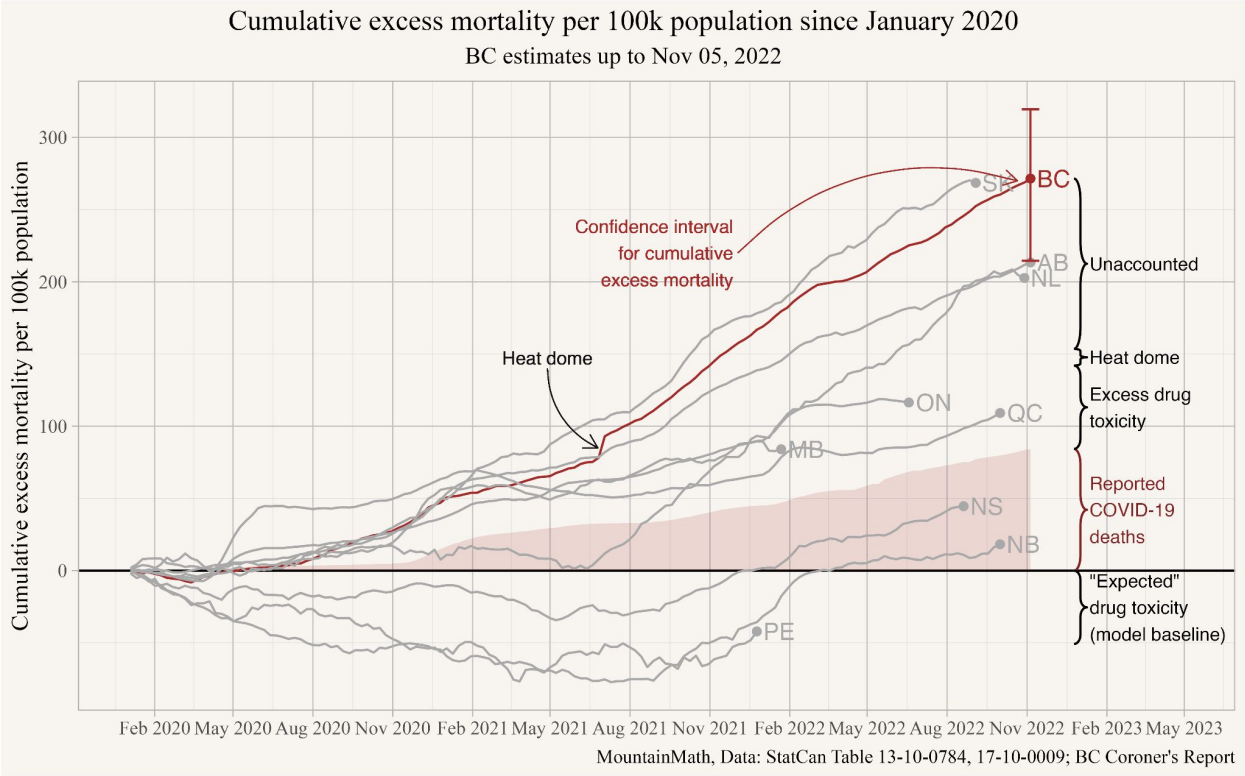
- Heights of curves are adjusted to align January through mid December 2021 to emphasize how trends differ across 2022.
- Y-axis shows the order of magnitude of virus copies (per liter in gold or blue or, adjusting for water flow, per day in green).
- Wastewater data are noisy and differ between the 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 from first infection currently used to define COVID-related deaths in BC (Xie et al.).

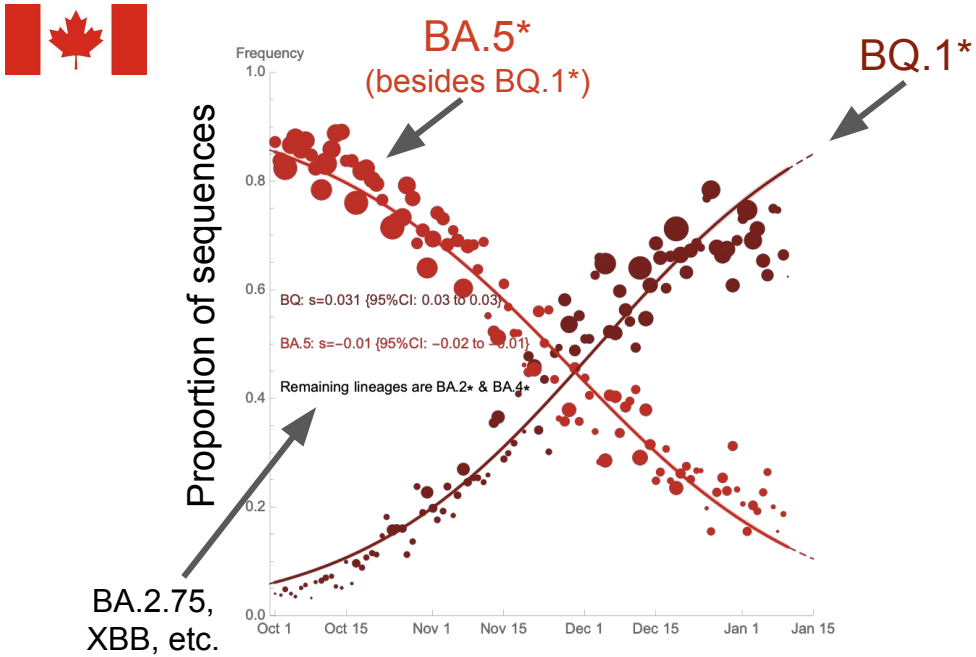
Excess death statistics indicate that BC is substantially undercounting total deaths due to COVID.

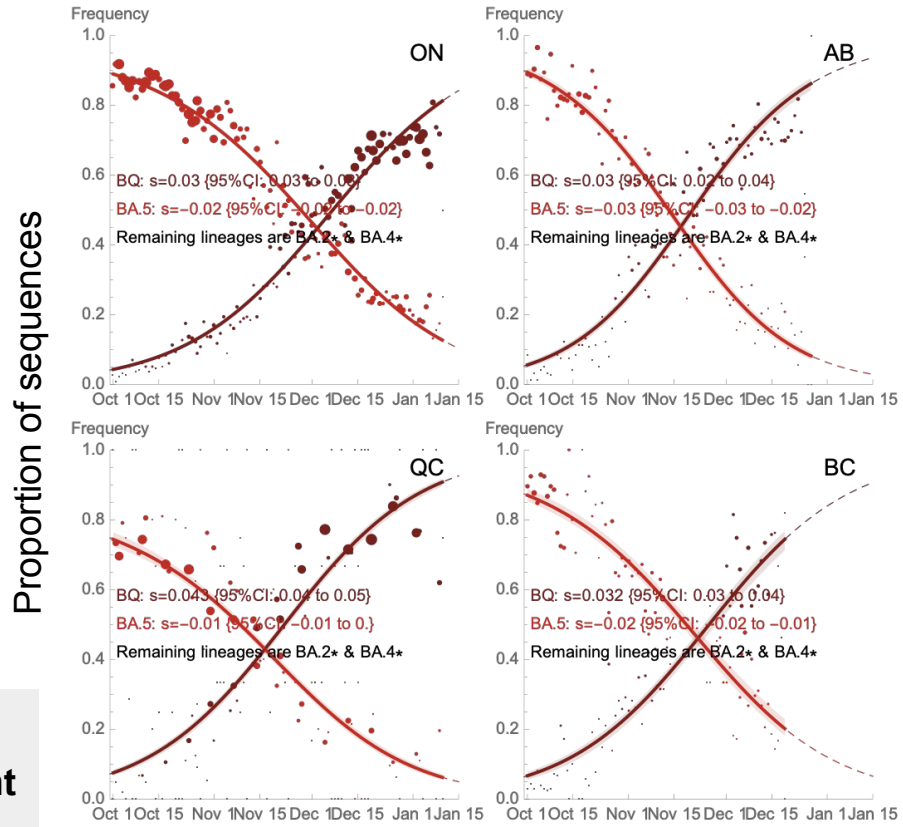
Source (J. Bergmann) Data from StatCan. The model baseline consists of "expected" deaths based on the previous four years, including drug toxicity and other causes (* indicates the levels of mortality due to drug toxicity in the four previous years). See May 19 2022 report (slide 9) for more details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

The rise of variants

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* in Canada



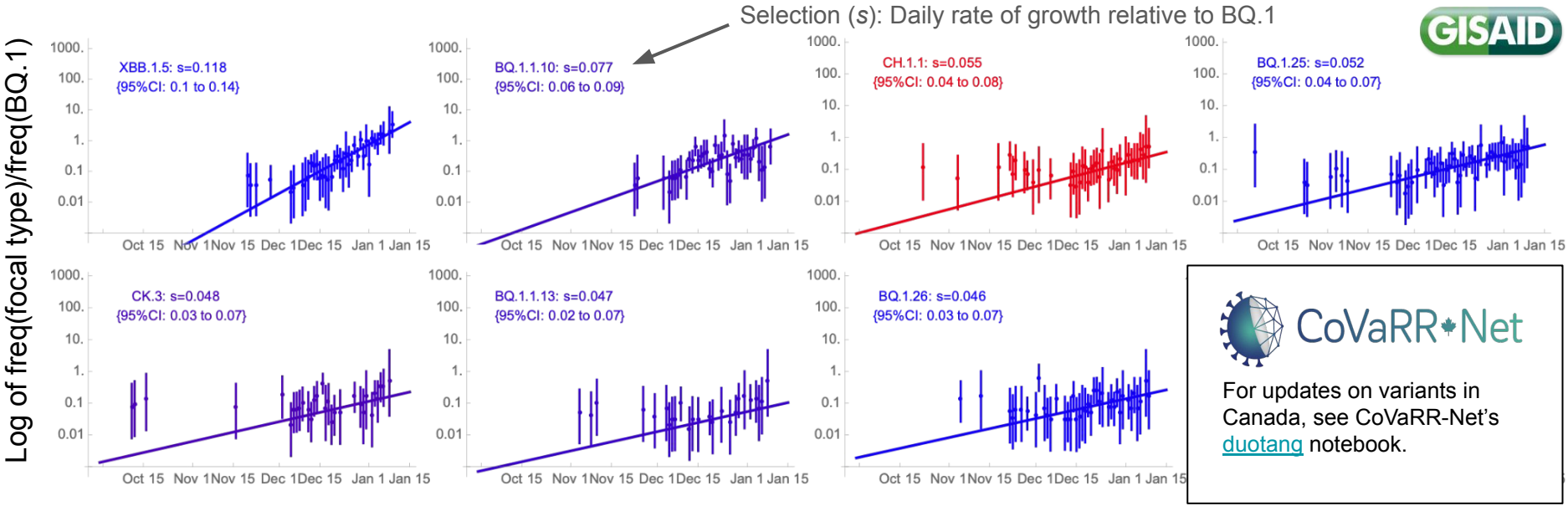


BQ.1 and its descendants (collectively called BQ.1*) have risen in frequency to >85% across Canada. Recent spread has slowed due to newly evolved lineages.

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

Recently rising variants in Canada

335 named Omicron lineages have been circulating in Canada over the last three months.
Measuring the selective advantage of each relative to BQ.1, the fastest growing lineages are the recombinant XBB.1.5 (s ~ 12%) and 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.

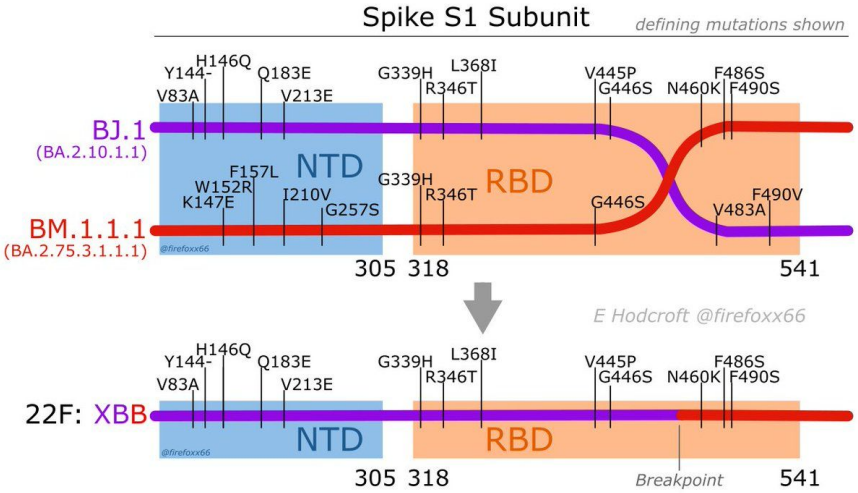
What is XBB.1.5?

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 mutational steps.

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 superior binding to ACE2 receptors and so higher transmissibility (Cao et al. 2023).

XBB.1.5 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*.

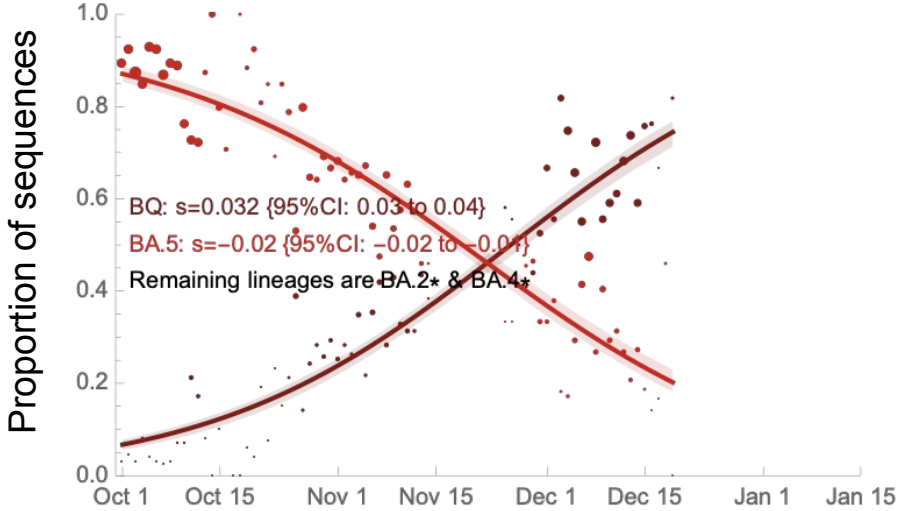
Genomic signature of recombinant origin of XBB
(from Dr. Emma Hodcroft @firefoxx66)



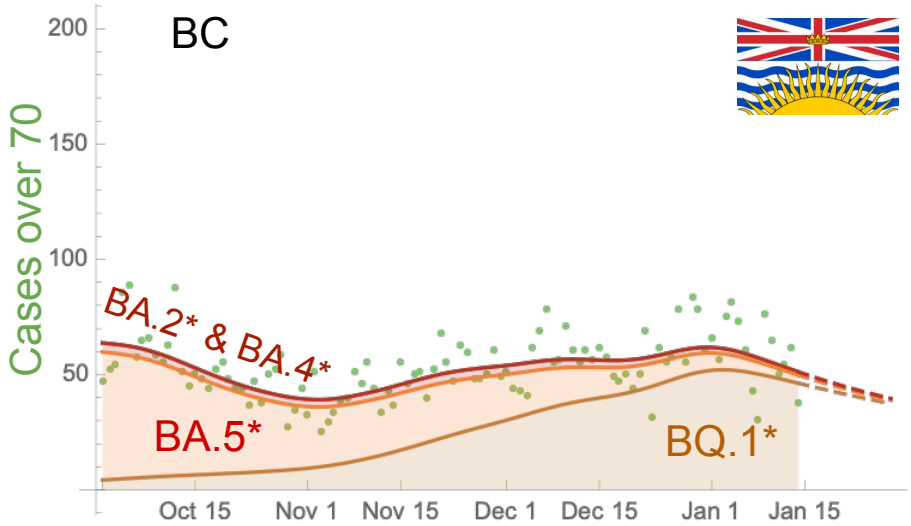
* We also don’t expect a major growth in cases, because more transmissible variants rapidly deplete the current pool of susceptible individuals, limiting the wave of cases (see also slide 18).

What does this imply for case numbers?

Fitting models of selection for the most common variants estimates changes in frequency.



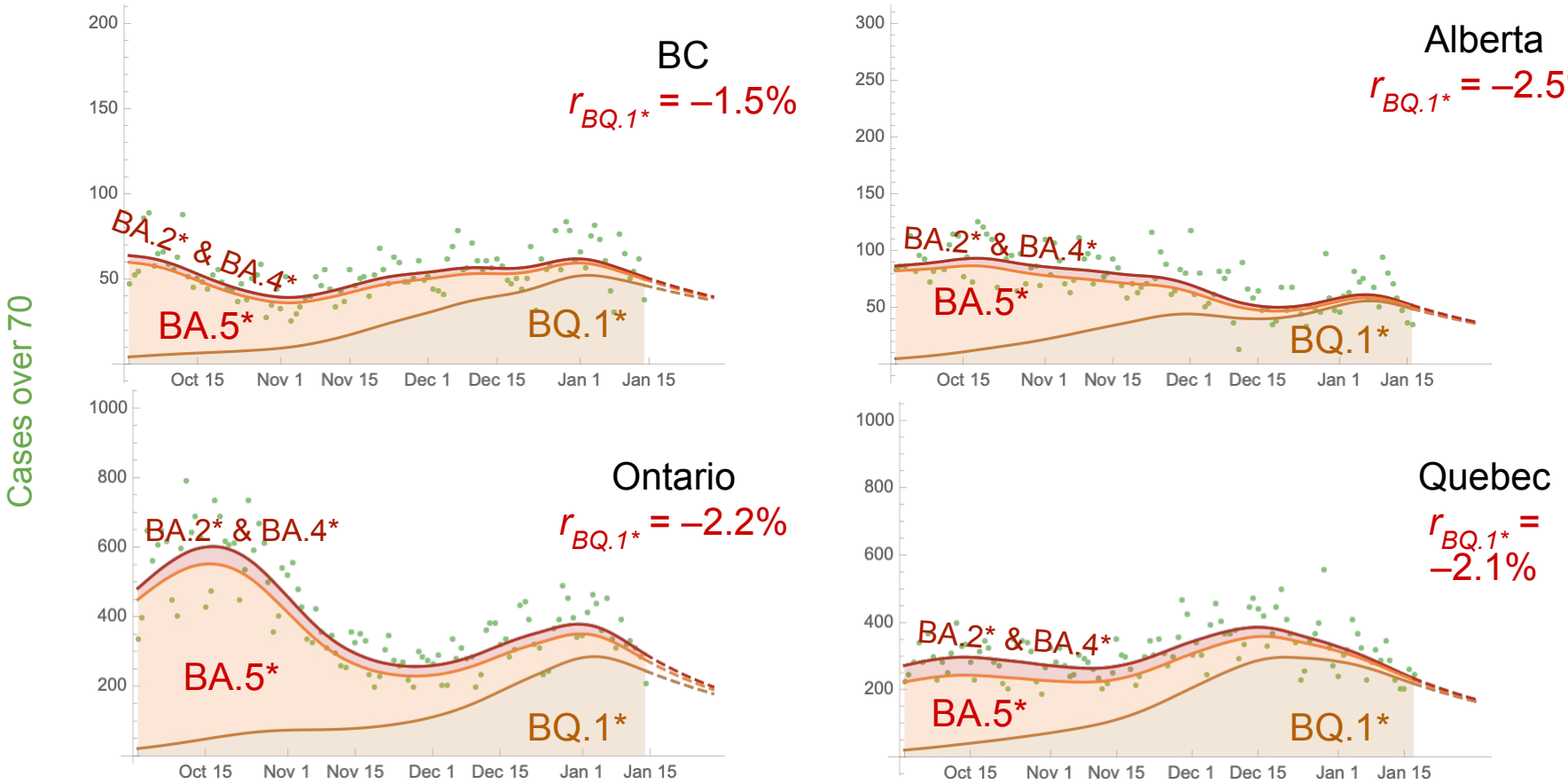
Multiplying by the # of cases in those over 70 allows us to **estimate** growth in numbers of the most common variants (avoiding extensive underreporting in younger age groups, see appendix).



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

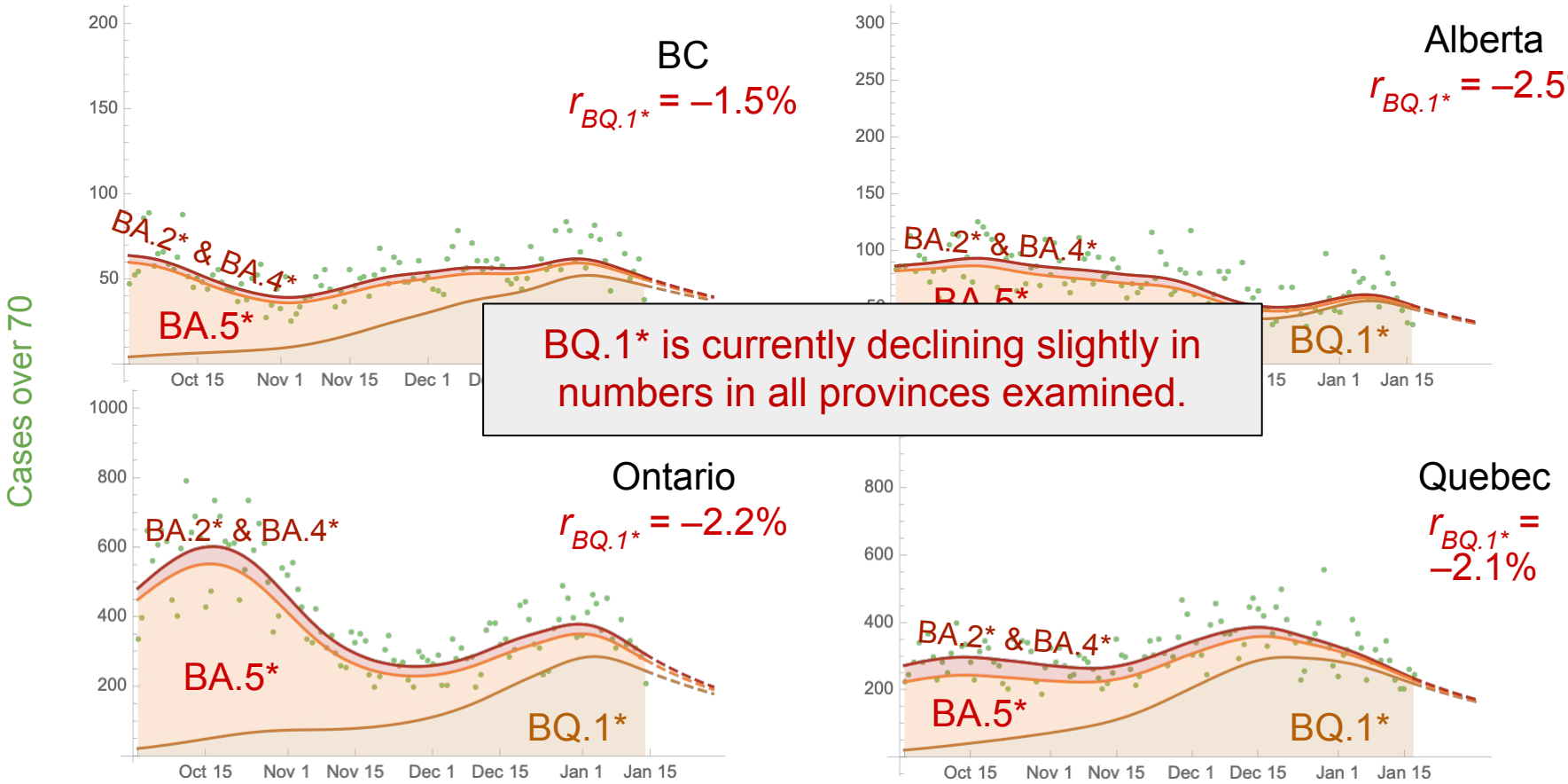
Source (S. Otto) Canadian metadata was downloaded from GISAID for the Omicron GRA clades. A model of selection was fit to the numbers of each type using maximum likelihood based on a trinomial distribution given the expected frequencies on each day. Hessian matrix used to obtain confidence intervals.

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

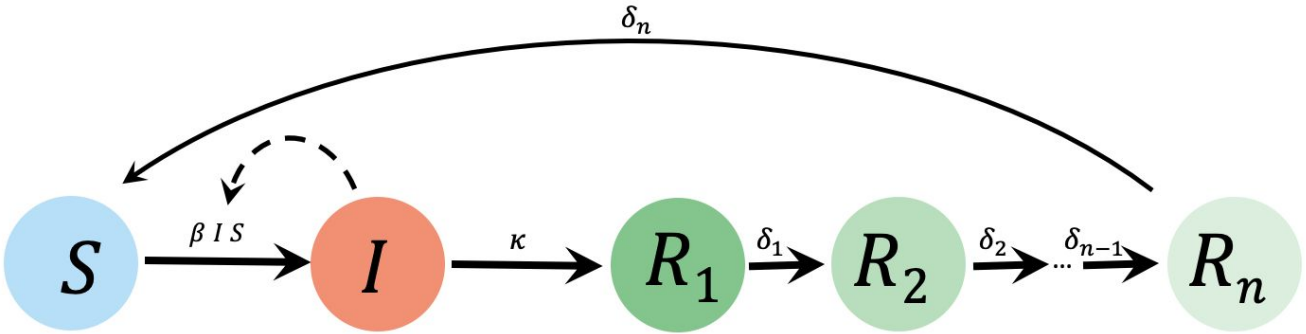


* Instantaneous estimates of growth rate, *r*, and doubling times for BQ.1*. These rates change with changing immunity and with protective health measures, both mandated and voluntary, to reduce transmission (e.g., wearing effective masks, increasing ventilation, and avoiding crowded indoor spaces)

Likely impact of new variants

The number of COVID-19 cases has undergone only modest fluctuations for 8 months (slides 5&6). 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

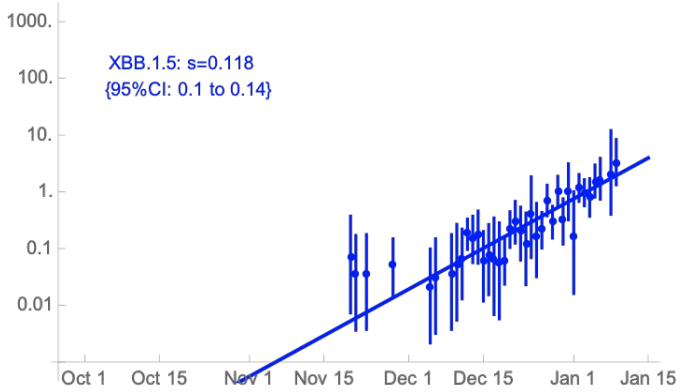
How will the spread of

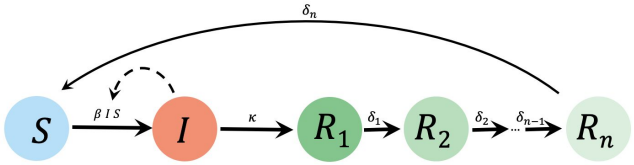
a) Immune evasive variants (e.g., BQ.1*)

or more

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

alter the level of COVID-19 cases?



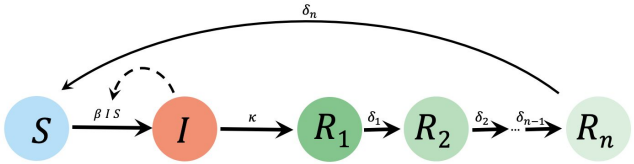


Likely impact of new variants

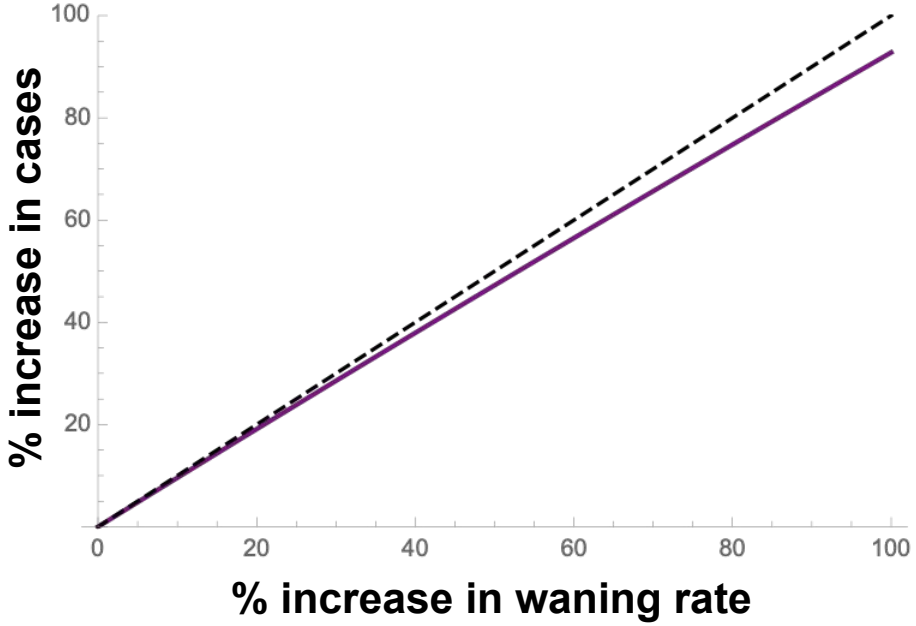
a) Immune evasive variants

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

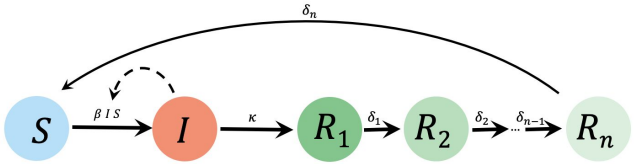


Implications of a steady state

b) Transmissible variants

Lineages, like XBB.1.5, that are more transmissible (increasing β) 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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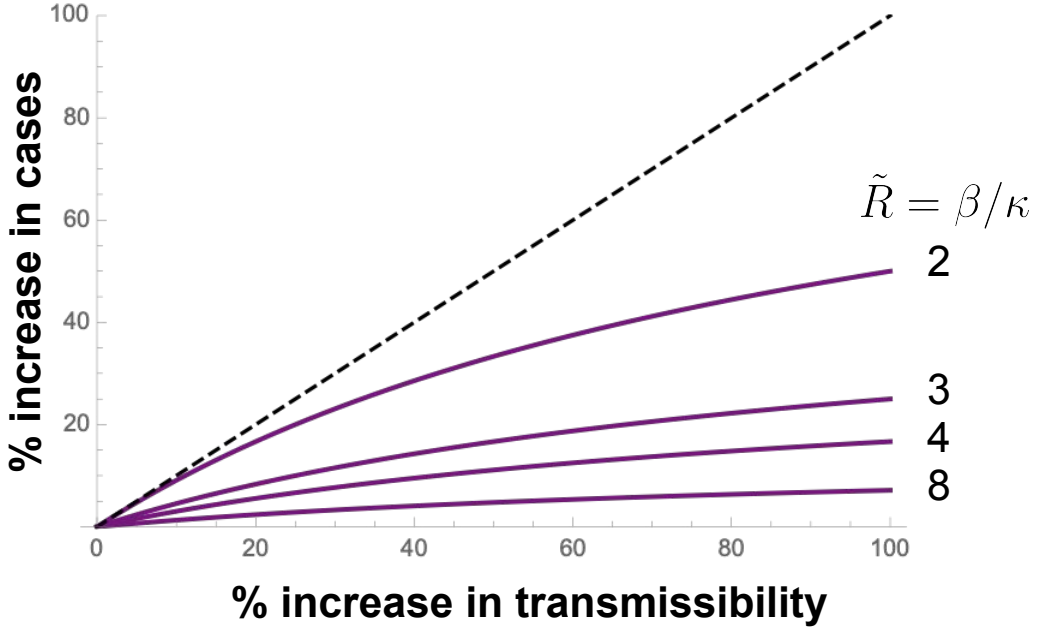


$\tilde{R} = \beta/\kappa$ is the effective reproductive number (# of new cases per infection) if everyone were susceptible today, given current measures and immune memory.

Implications of a steady state

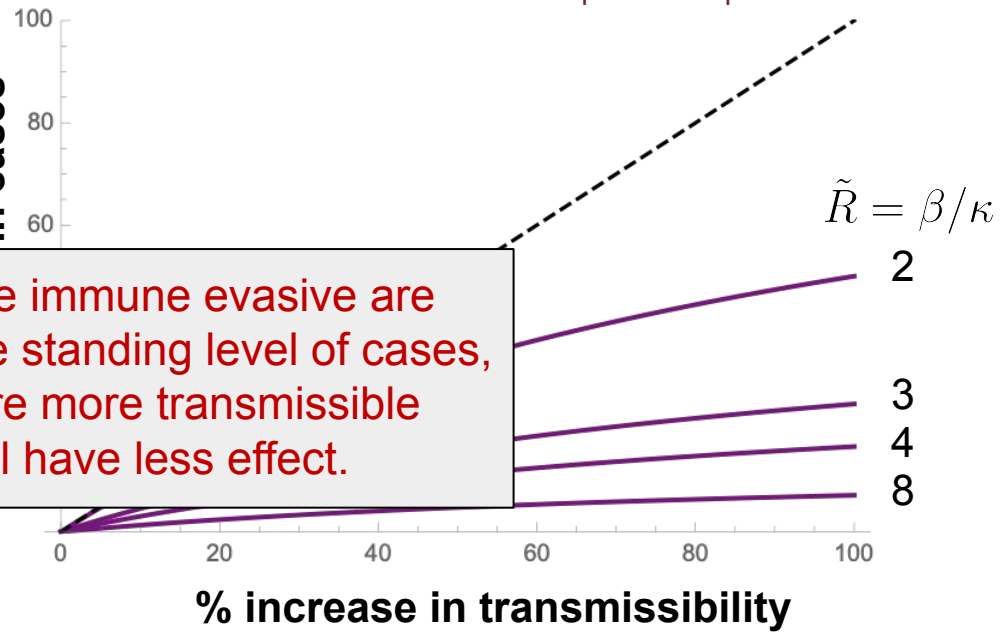
b) Transmissible variants

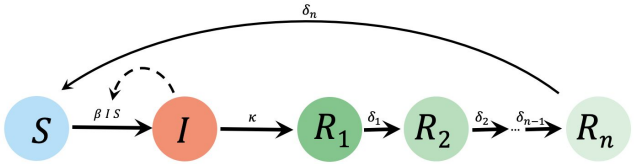
Lineages, like XBB.1.5, that are more transmissible (increasing □) rapidly deplete the susceptible and have less influence on c

Model result: If a transmission by a f state number of COVID-19 infections increases only by $\frac{c\tilde{R}-1}{c(\tilde{R}-1)}$

Variants that are more immune evasive are expected to increase the standing level of cases, while variants that are more transmissible (like XBB.1.5) will have less effect.

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





$\tilde{R} = \beta/\kappa$ 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 has been robust against the new variants.

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

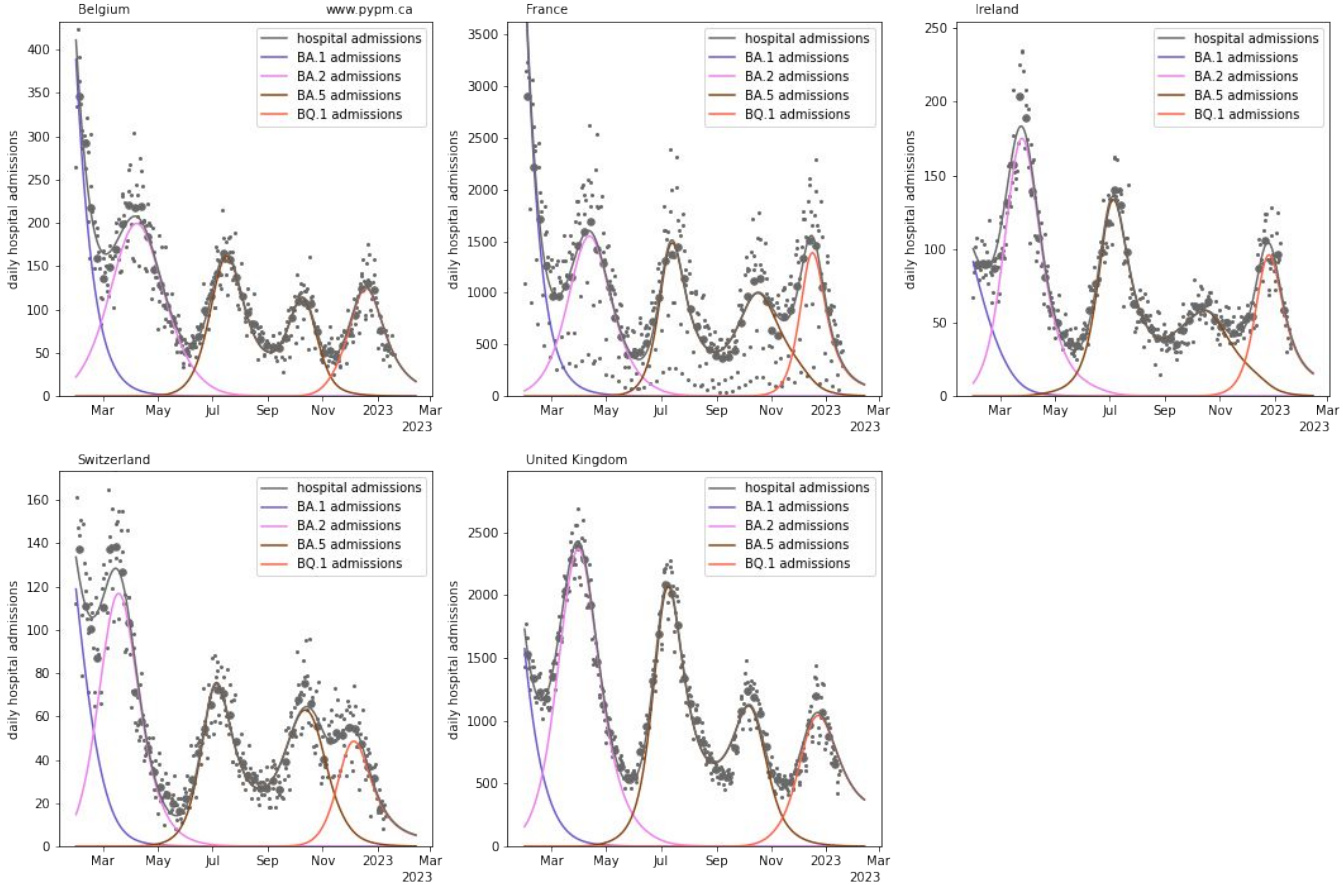
Our previous reports showed that in several European nations, waning of immunity caused the 4th Omicron wave (Fall 2022), thereby having similar strains as the 3rd wave (Summer 2022), primarily BA.5*.

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

The recent spread of BQ.1* drove a 5th Omicron wave in Europe. The timing of the emergence of new variants resulted in well separated waves, simplifying the interpretation of the data. The BQ.1* wave has now subsided in Europe. Similar projections in Canada indicate that the BQ.1* wave has peaked.

The continued rapid decline in infection rates in Europe shows that the number of people whose immunity is lost per day is not growing, unlike the situation that drove the Fall 2022 wave.

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*).

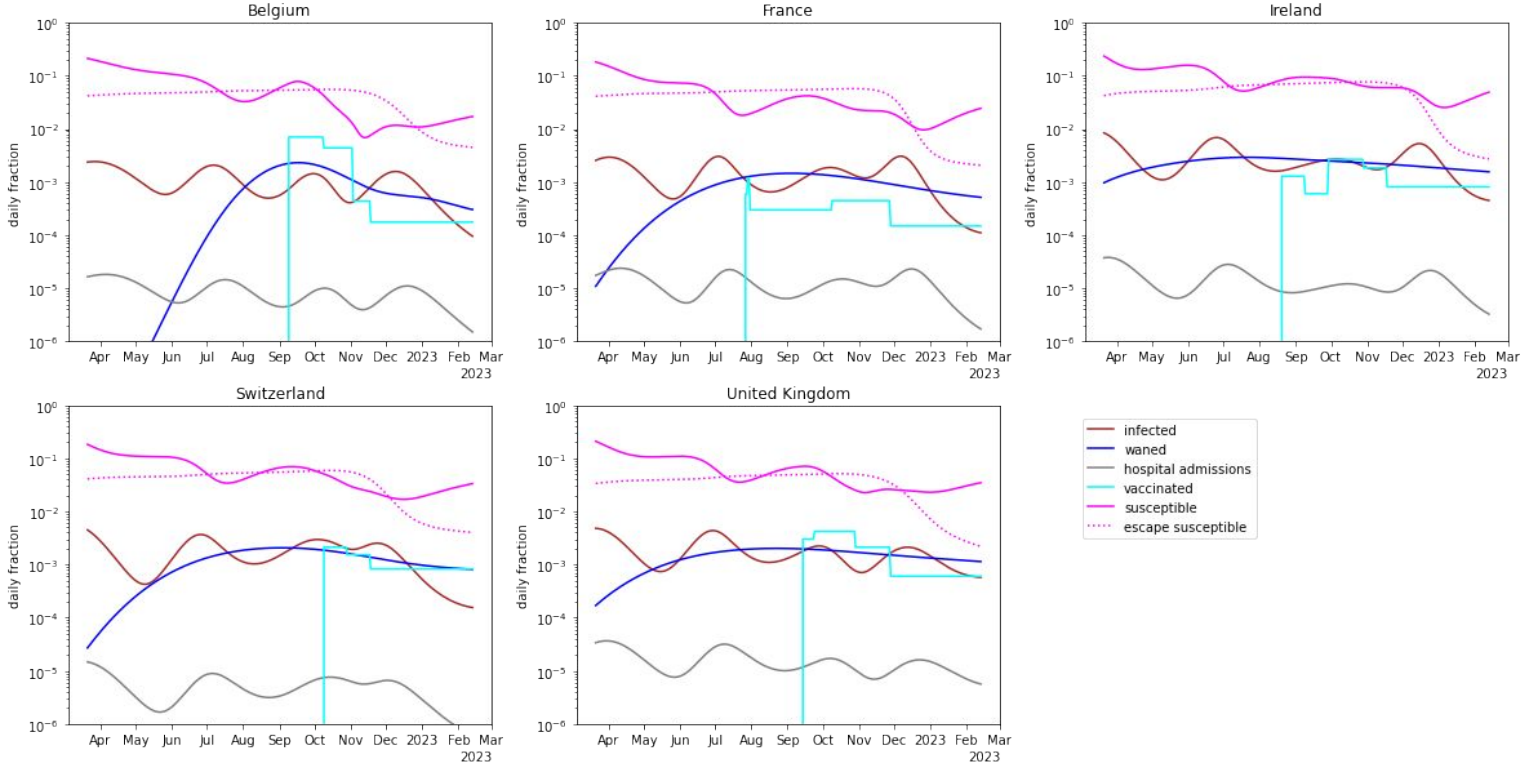
Waning is implemented as a gamma delay function, with three free parameters as described in the 5 October 2022 report.

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

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

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.

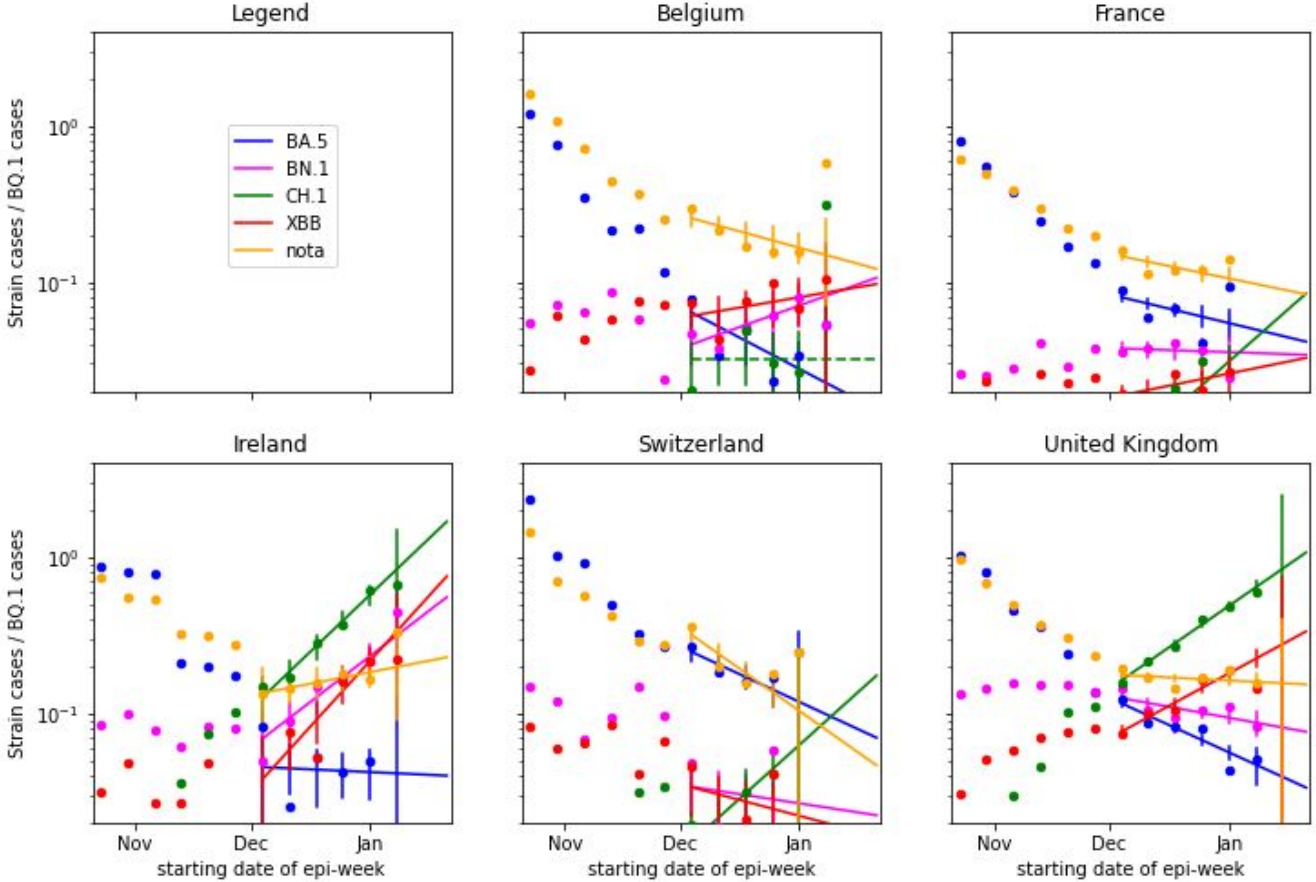
The escape fraction for BQ.1* is estimated from the 5th wave.

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

Without 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.

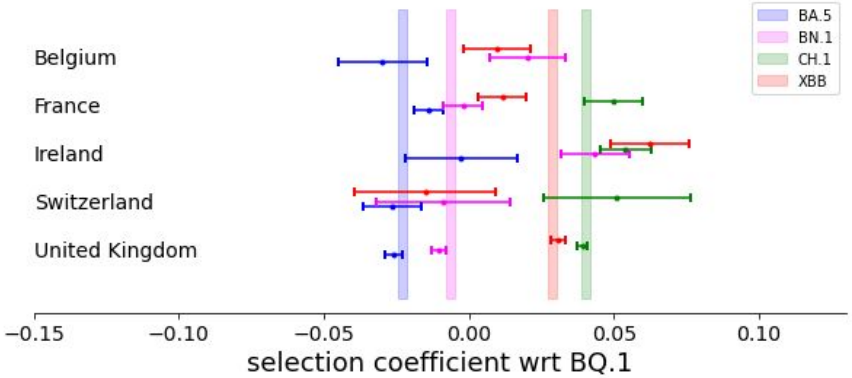
The slope of the exponential curves indicate the growth advantage of new variants compared to BQ.1*.

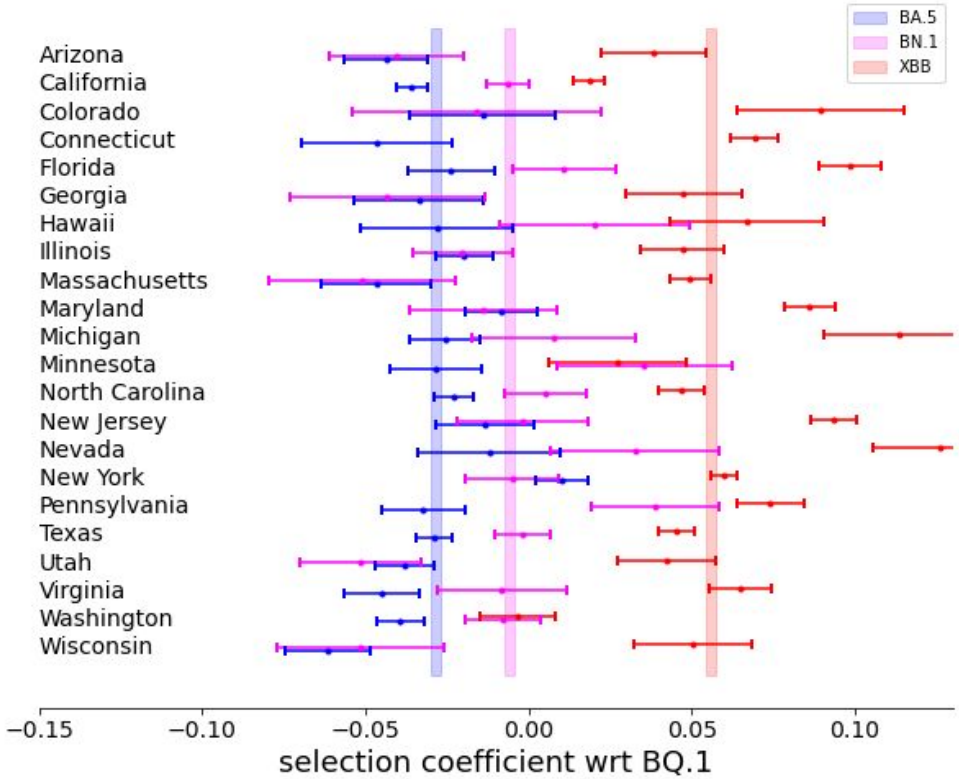
While there are new variants that grow faster than BQ.1*, a growth advantage of less than 5%/day is insufficient to lead to another Omicron wave.

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

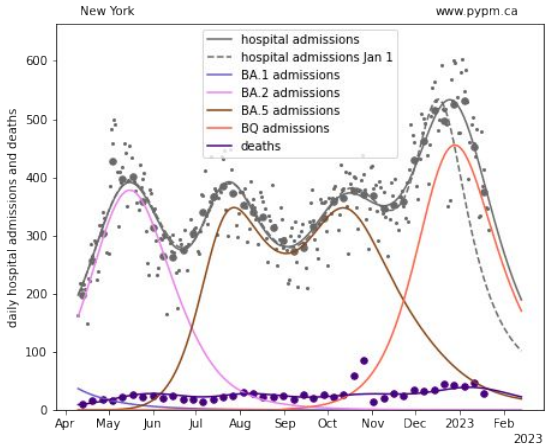


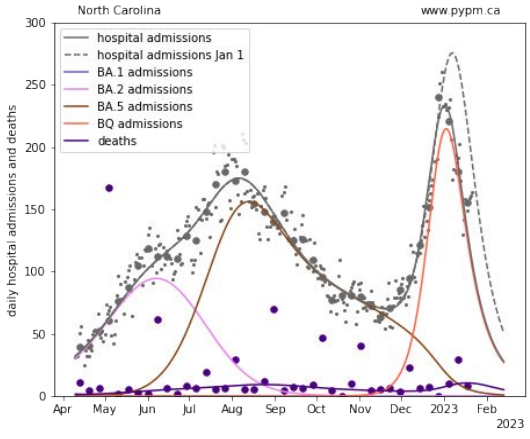


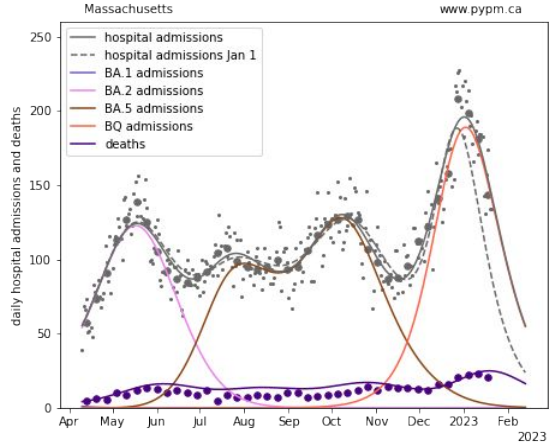
- The growth advantage of BQ.1* strains compared to BA.5* strains is diminished compared to results shown in our previous report. (Previously 8%/day, now 3%/day).
- Limited data and different mixtures of strains results in significant scatter of estimates:
  - Overall, the average selection coefficients for the different groupings are similar for Europe and US.
- Given that BQ.1* is declining at -5%/day, the existing common variants 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.

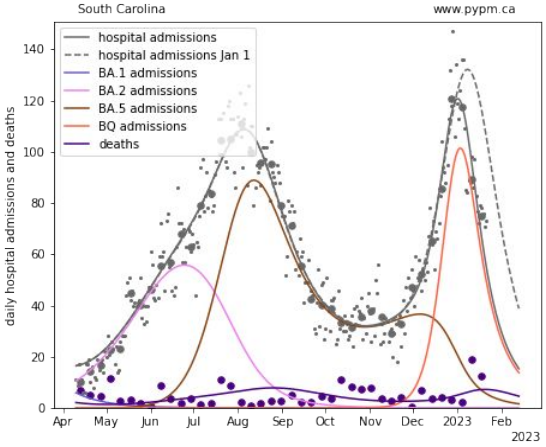
Source (D. Karlen) See www.pypm.ca. European and US metadata was downloaded from GISAID for the GRA clade.

Selected US states









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

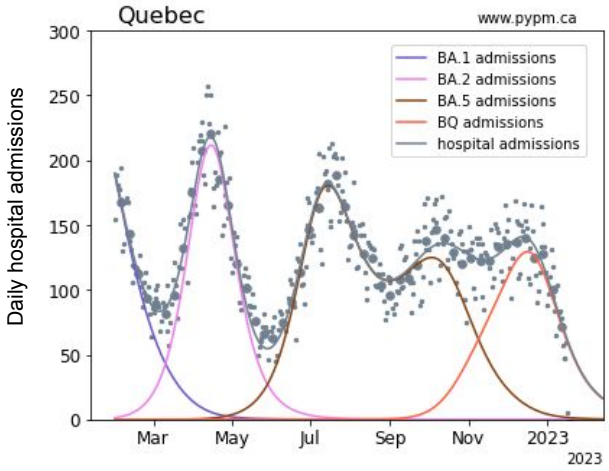
While the most recent peak in NY is a combination of BQ.1* and XBB*, this is modelled by a single additional strain

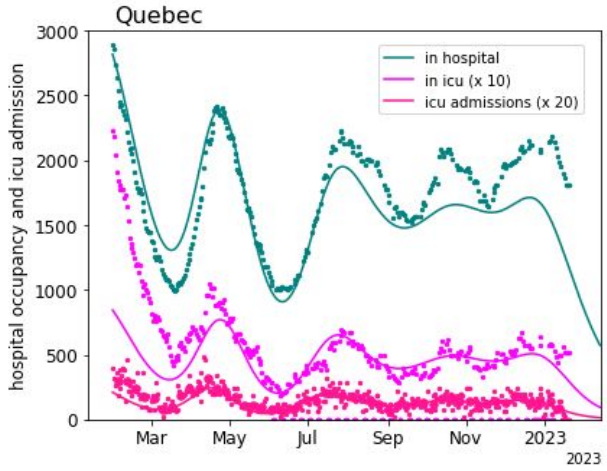
Infections are currently declining at the rate of about 5% per day, like Europe. The other common variants are therefore not likely to cause significant waves in the near future.

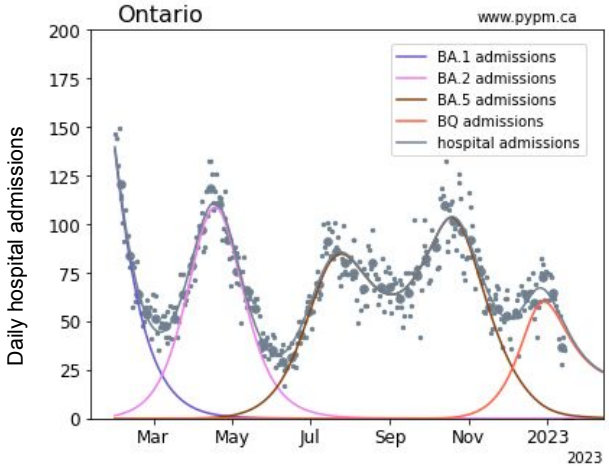
The turnaround times and amplitudes were similar to model forecasts from 1 January 2023 (dashed curves). The forecasts, made prior to data showing the turnaround in these states, assumed a small escape fraction, as seen in Europe.

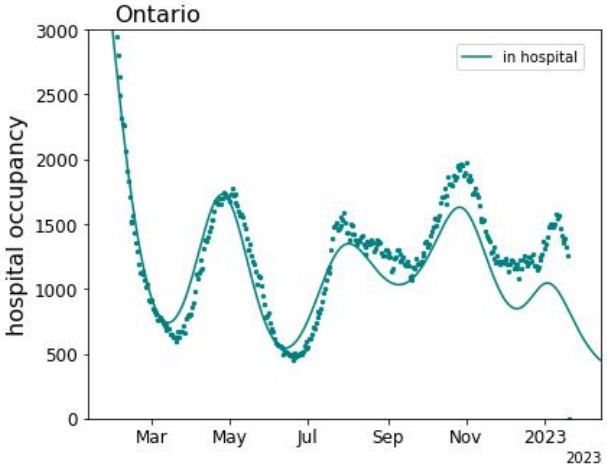
Source (D. Karlen) See www.pypm.ca.

Quebec and Ontario









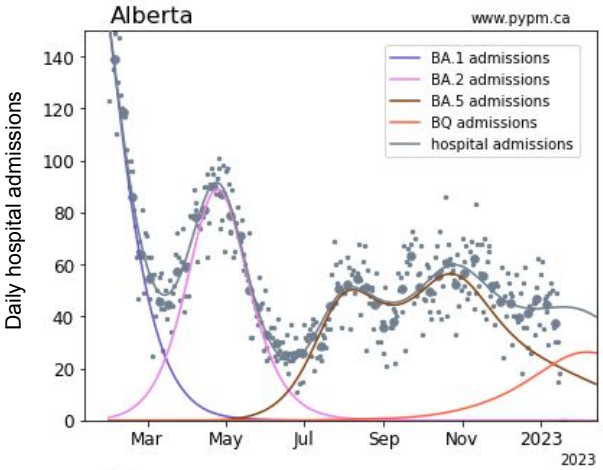
The same approach is applied to four provinces. A similar pattern is seen as in US and Europe, due to emergence of new variants and waning of immunity in Fall 2022.

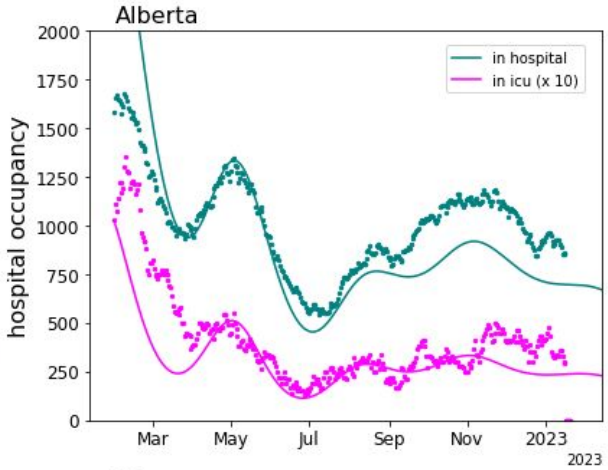
Infection rates in Quebec and Ontario are inferred to be rapidly falling, due to additional immunity from recent infections and vaccinations.

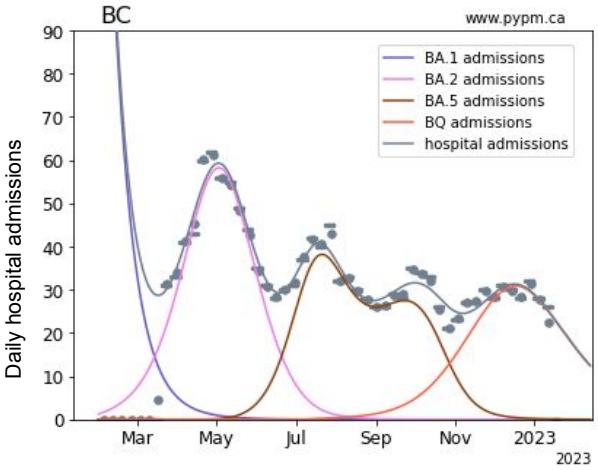
Hospital occupancy in recent months exceeds model projection assuming fixed hospital release time distributions throughout the period.

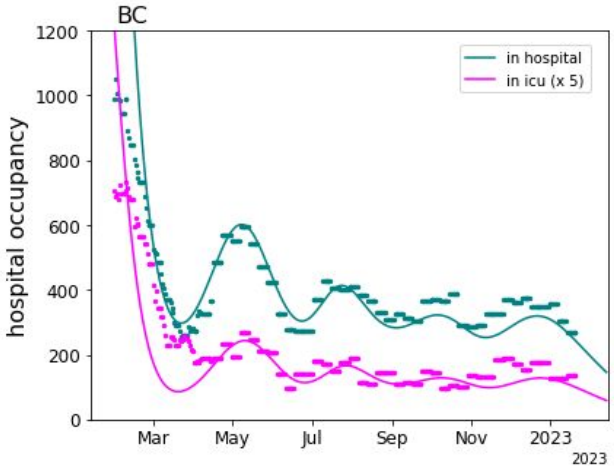
Source (D. Karlen) See www.pypm.ca.

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 over the short term.

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

Key messages

The current COVID-19 outlook

- COVID-19 has persisted at high levels in BC, with modest fluctuations, for the past 8 months.
- The main lineages in Canada are BQ.1* (a BA.5 descendant) and XBB* (a recombinant between two BA.2 sub-lineages), which carry mutations shown to better evade antibodies.
- The fastest rising variant is XBB.1.5, which is thought to be more transmissible, but not more immune evasive than its ancestor XBB (selective advantage over BQ.1 of $s \sim 12\%$/day).
- Immune evasive variants are more worrisome than more transmissible variants, because the former can lead to higher standing levels of COVID-19 disease.
- Population immunity can be estimated based on the shape of the pandemic curves, providing a way to estimate immune evasion and waning and to predict future infection and hospitalization rates.
  - BQ.1* drove a recent wave in cases but has now crested in Europe and North America.

Most people have retained immunity to BQ.1*, preventing a major wave.
Similarly, we do not expect XBB.1.5 to drive a major wave because it is not more immune evasive.

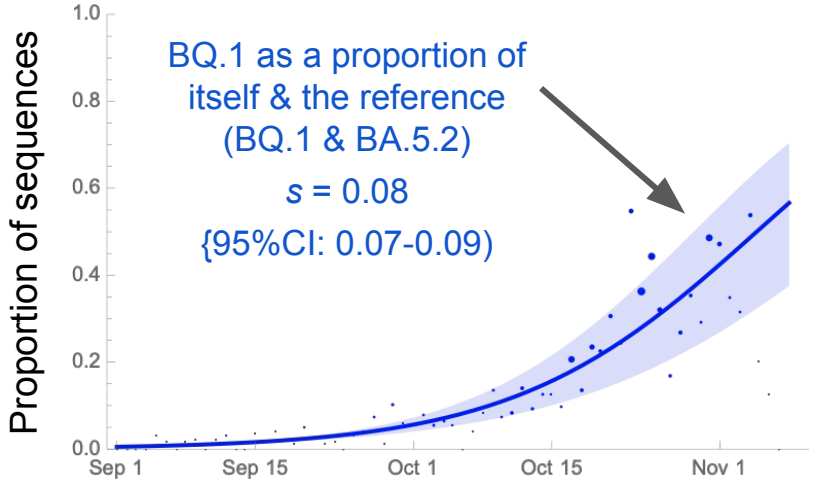
Without additional measures, COVID-19 cases are expected to ebb and flow but persist at high levels, as immunity lost through waning is offset by new immunity from infections and vaccination.

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 evade immunity or both.



* Selection 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 advantage, *s* →

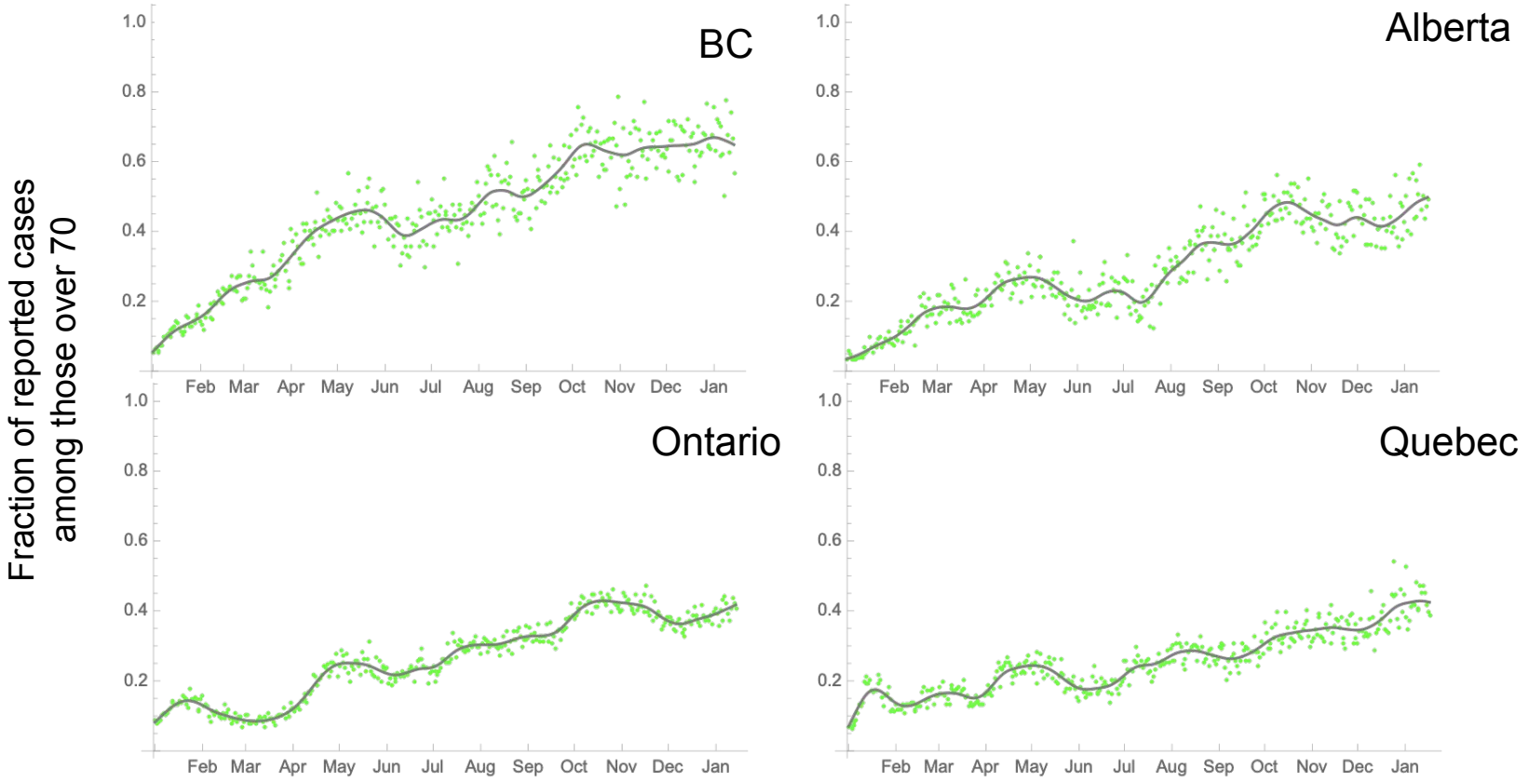
1%	2%	5%	10%	20%
69.3	34.7	13.9	6.9	3.5

← 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.

Appendix: Fraction of reported cases over 70



The fraction of reported cases in people over 70 has risen steadily across the year, suggesting that testing policies continue to change in Canada, with more and more underreporting in those under 70.