COVID Model Projections

November 23, 2022

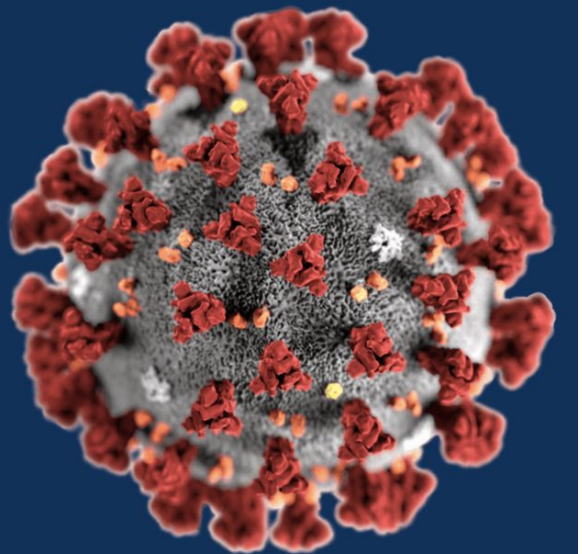
BC COVID-19 Modelling Group

@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

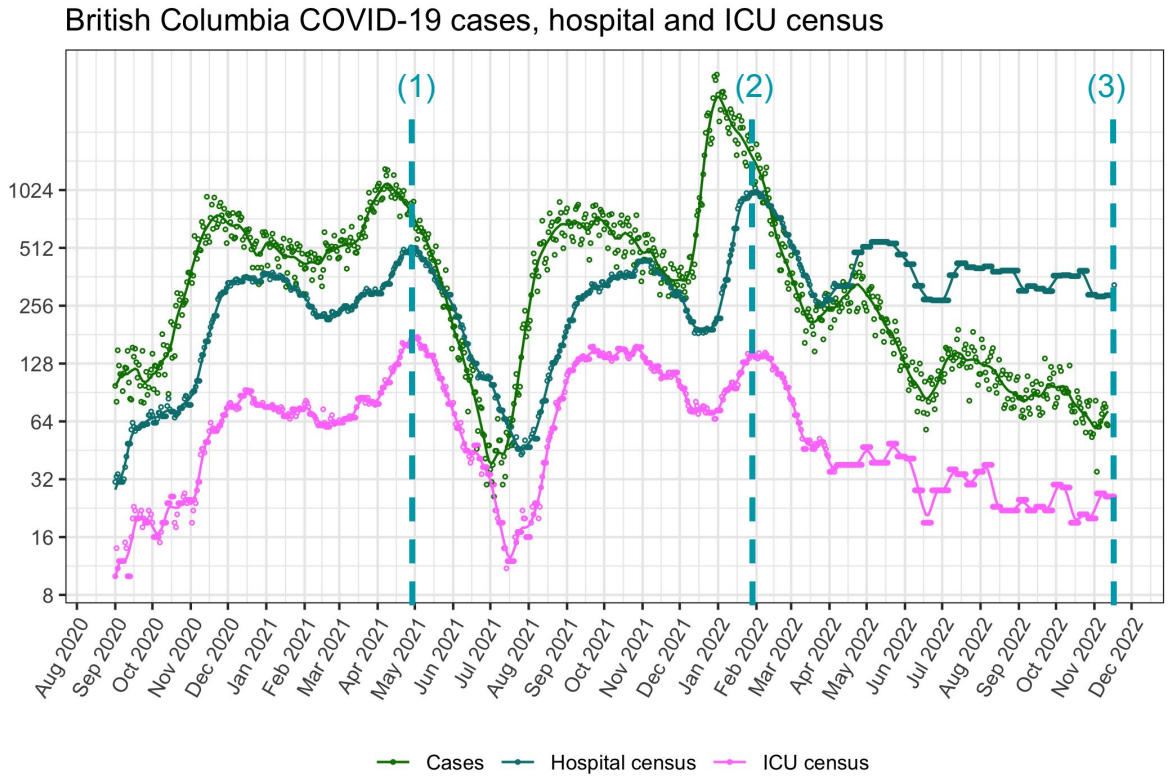
Contents of this report:

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

Summary: Omicron continues to be dominated by BA.5* variants, particularly descendants like BQ.1* that carry many mutations that reduce antibody recognition. BQ.1* has risen to an estimated current frequency of 50% in BC and in Canada. Nevertheless, case numbers are rising and falling 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



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

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 = 328

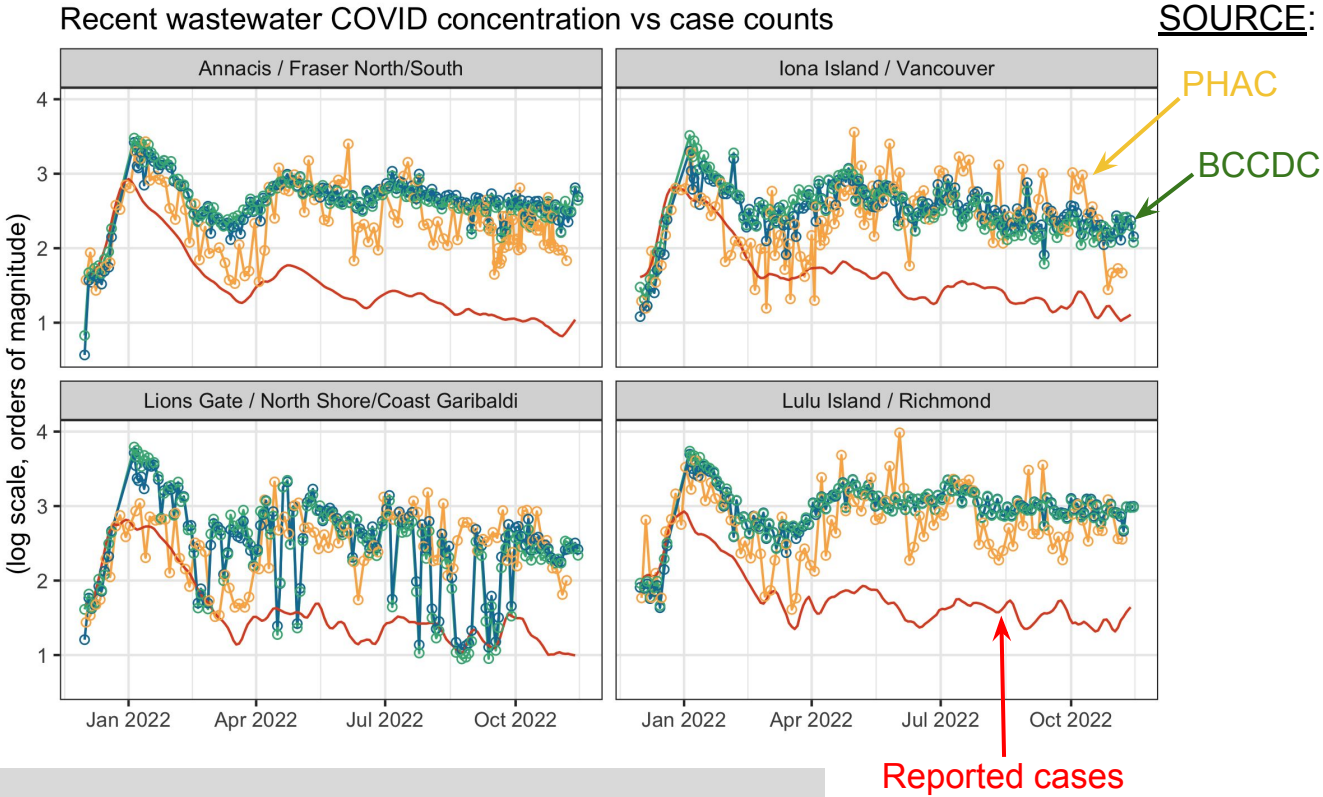
Source (J. von Bergmann) Case data from BC COVID-19 Database (http://www.bccdc.ca/health-info/diseases-conditions/covid-19/data). STL trend lines on log scale. How hospitalizations and deaths are attributed to COVID-19 changed in BC on April 2, 2022. *Reinfections with a prior lab-confirmed case are 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:

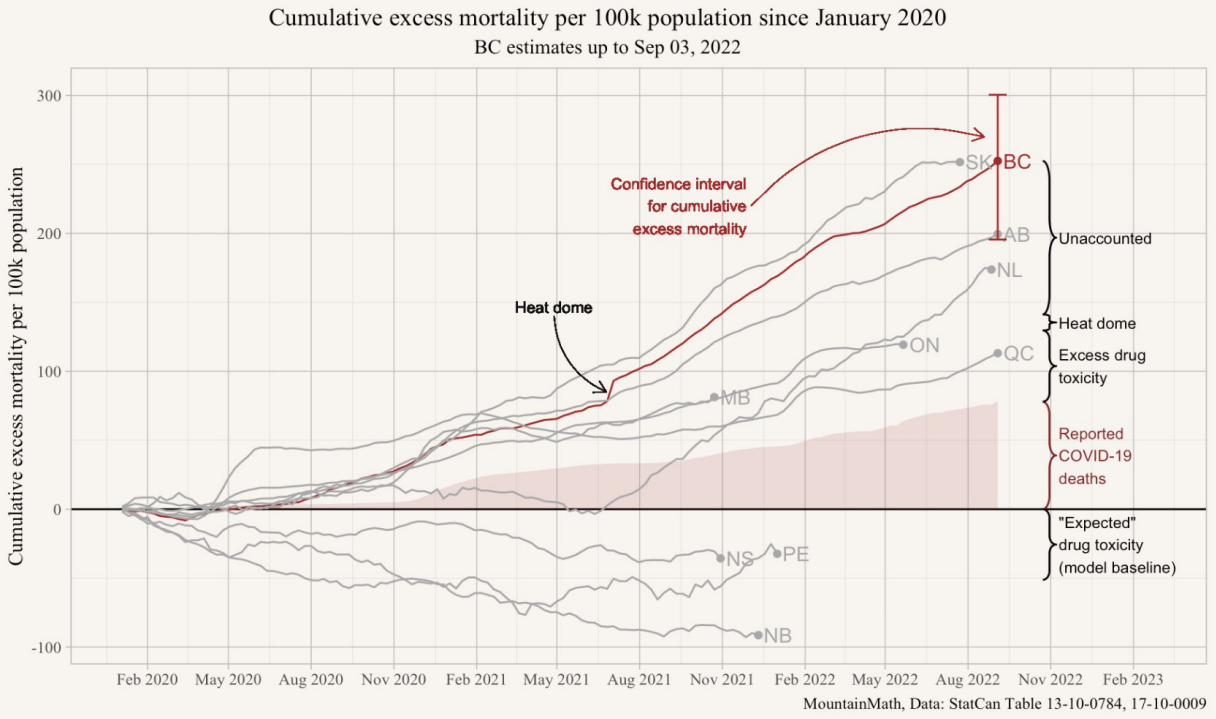
- Heights of curves are adjusted to align January through mid December 2021 to emphasize how trends differ across 2022.
- Y-axis shows the order of magnitude of virus copies (per liter in gold or blue or, adjusting for water flow, per day in green).
- Wastewater data are noisy and differ between the 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.

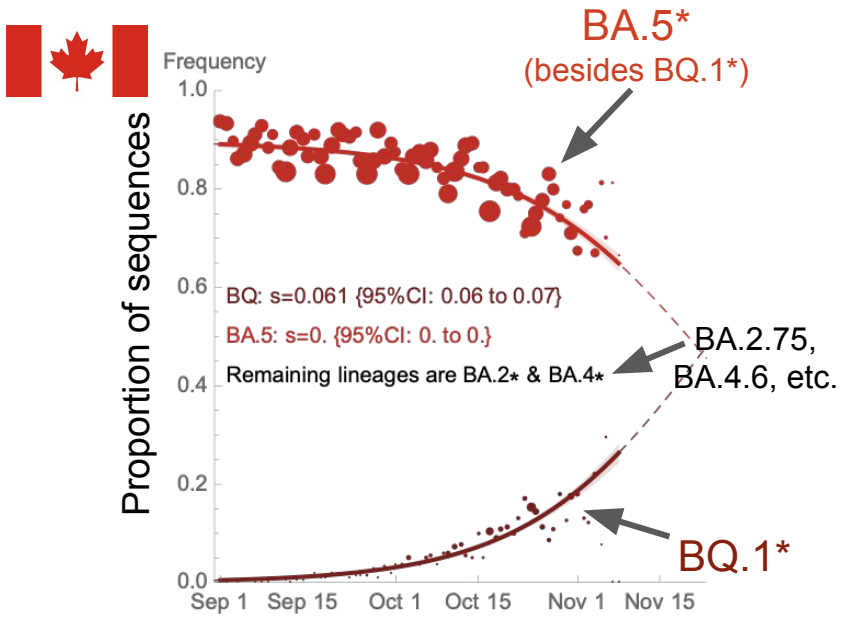
BC is likely substantially undercounting total deaths due to COVID.

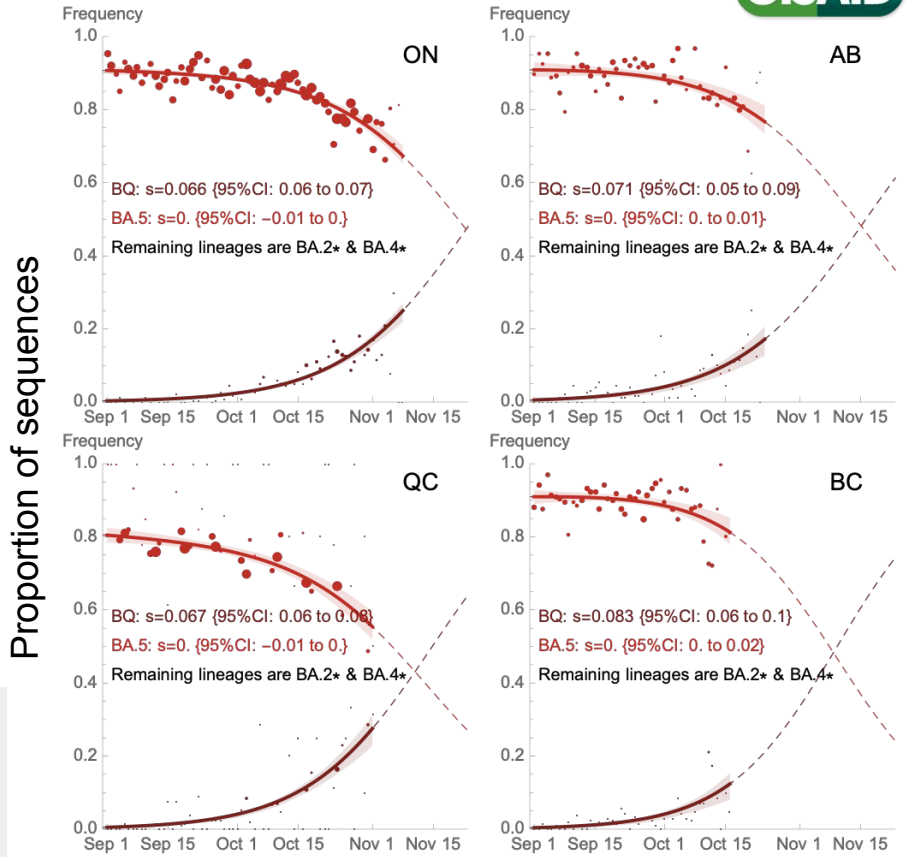
Source (J. Bergmann) Data from StatCan. The model baseline consists of “expected” deaths based on the previous four years, including drug toxicity and other causes (* indicates the levels of mortality due to drug toxicity in the four previous years). See May 19 2022 report (slide 9) for more details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



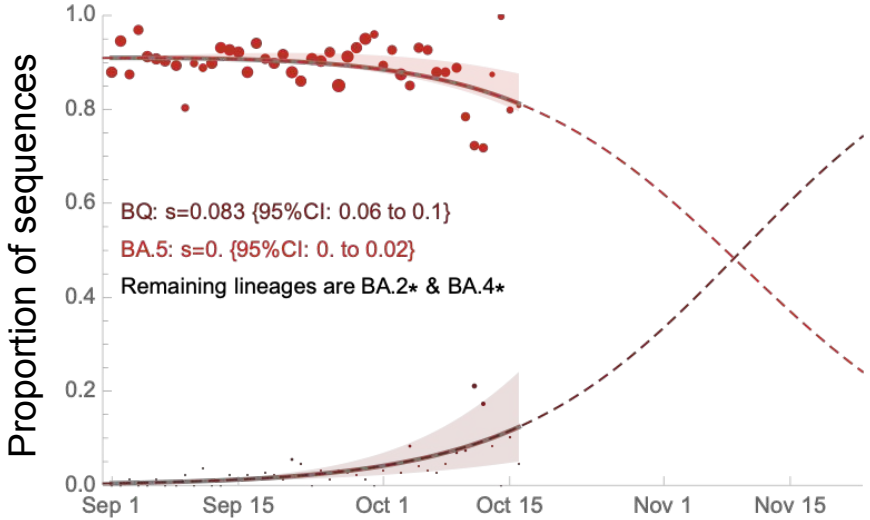


BQ.1* lineages are rising in frequency across Canada with a selective advantage of *s* ~ 6% relative to BA.5* or (BA.2*&BA.4*), leading to a current estimated frequency of ~50%.

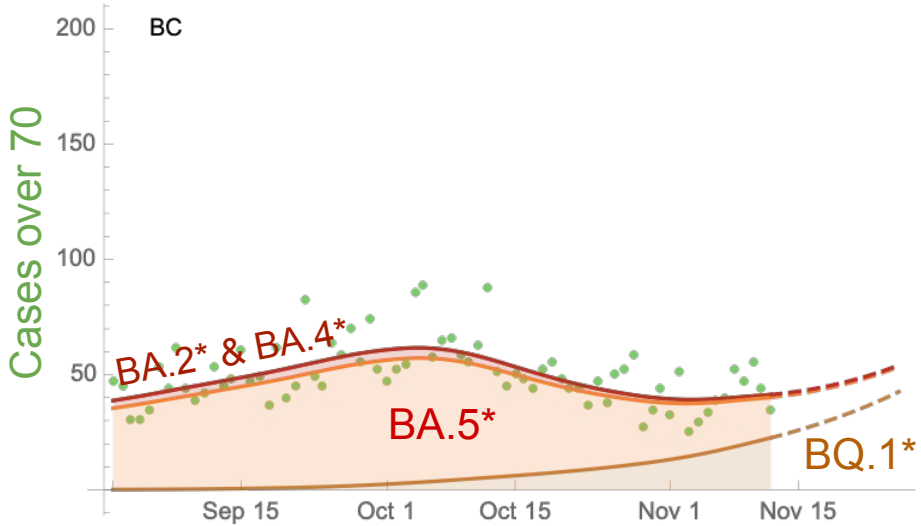
Source (S. Otto) Canadian metadata was downloaded from GISAID for the GRA clade. See Appendix for more more method details.

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.

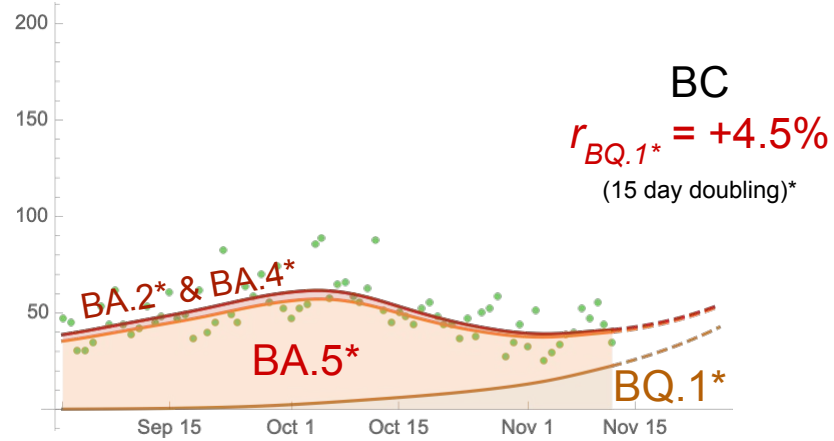


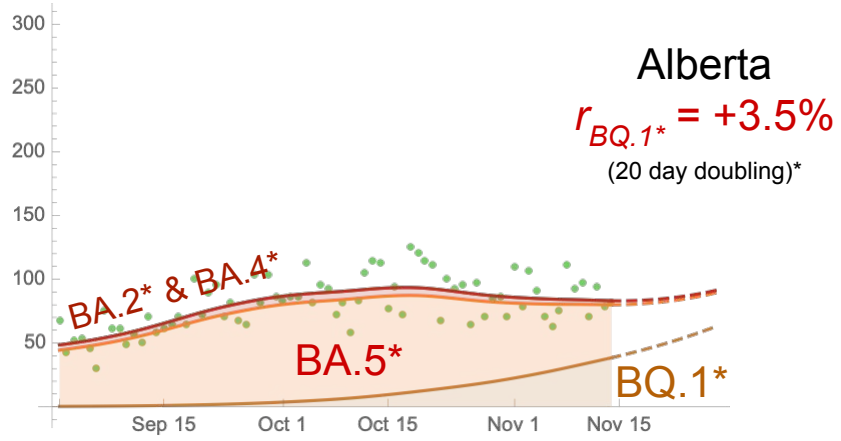
→ Despite declines in BA.5*, case counts of BQ.1* are estimated to be rising.

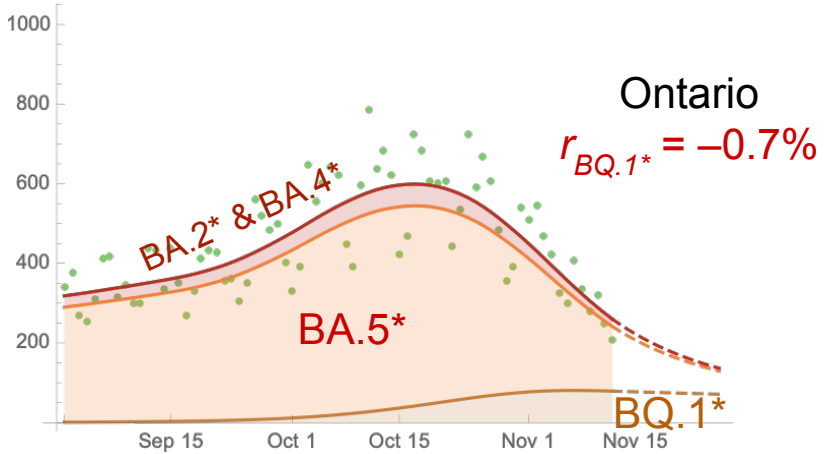
Source (S. Otto) Canadian metadata was downloaded from GISAID for the Omicron GRA clades. A model of selection was fit to the numbers of each type using maximum likelihood based on a trinomial distribution given the expected frequencies on each day. Hessian matrix used to obtain confidence intervals.

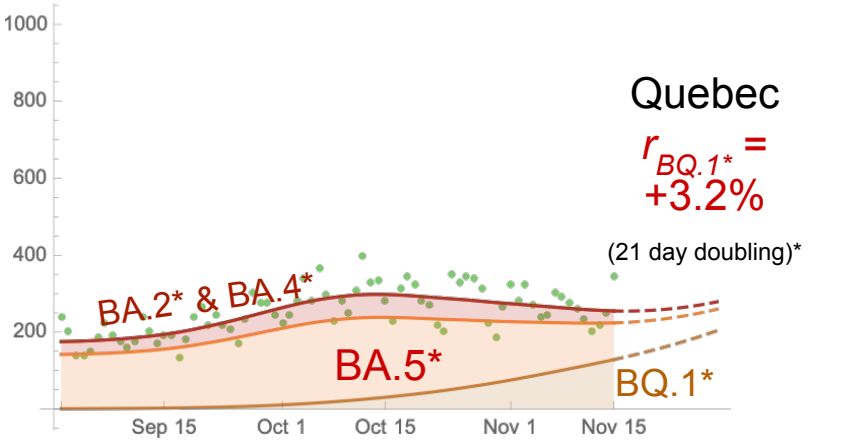
The BQ.1* Omicron Wave

Cases over 70



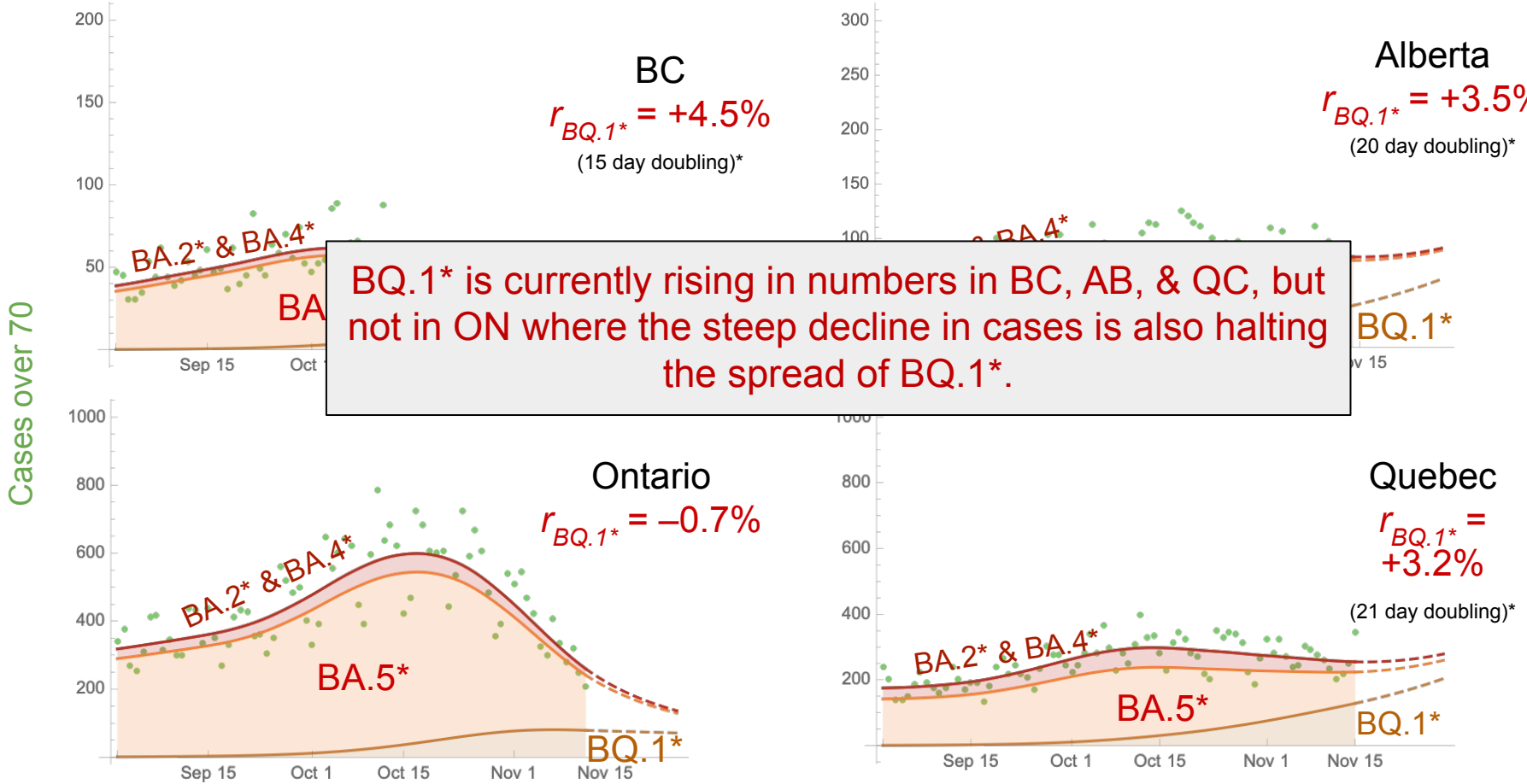






* Instantaneous estimates of growth rate, *r*, and doubling times for BQ.1*. These rates change with changing immunity and with protective health measures, both mandated and voluntary, to reduce transmission (e.g., wearing effective masks, increasing ventilation, and avoiding crowded indoor spaces)

The BQ.1* Omicron Wave

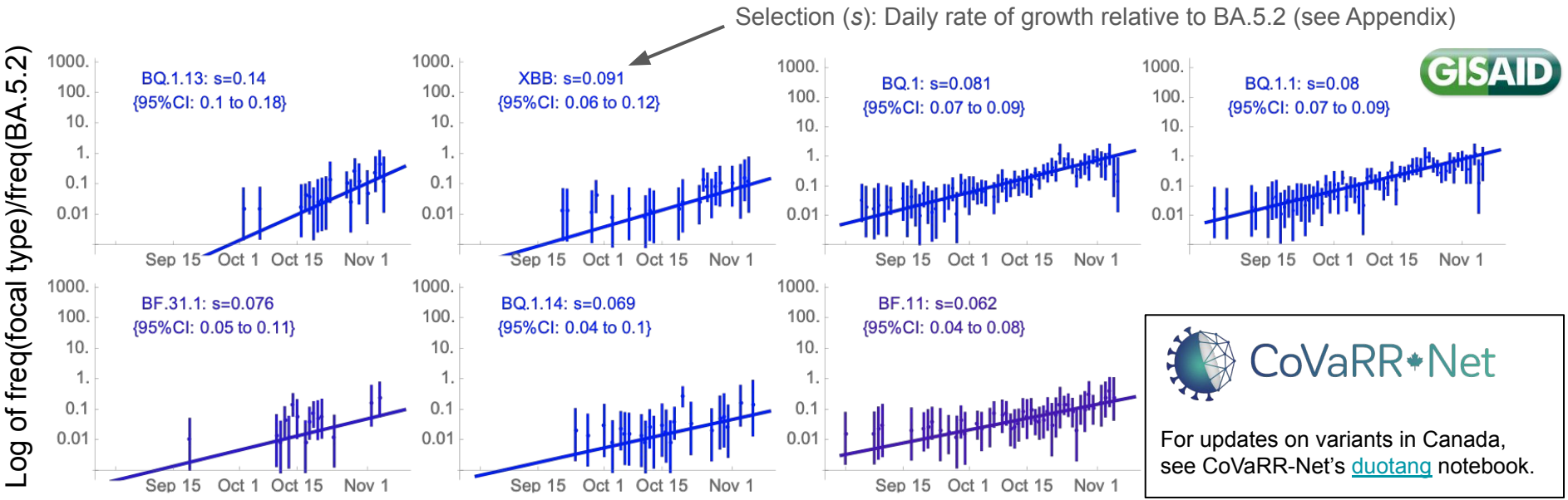


BQ.1* is currently rising in numbers in BC, AB, & QC, but not in ON where the steep decline in cases is also halting the spread of BQ.1*.

* 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

Over 200 named sub-lineages have been circulating in Canada over the last three months.
Measuring the selective advantage of each, the fastest growing sub-lineages are BQ.1 sub-lineages and the XBB recombinant lineage, with selection coefficients between *s* ~ 7-14%, which all carry mutations known to reduce recognition by antibodies in the blood (Cao et al. 2022).



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 BA.5.2 on a log scale. On this logit plot, the slope measures selection for a variant relative to BA.5.2.

Dynamic immunity and new variants

Waning immunity and vaccination

Measuring population-level immunity

As introduced in our previous two reports, population immunity parameters are estimated from hospital admission rates during the BA.2 wave (Spring 2022). The shape of the wave is used to estimate both:

- the population-level immunity at the time
- the number of new immunity-generating infections for every hospital admission

Transmission rates are assumed to be constant for each variant in 2022.

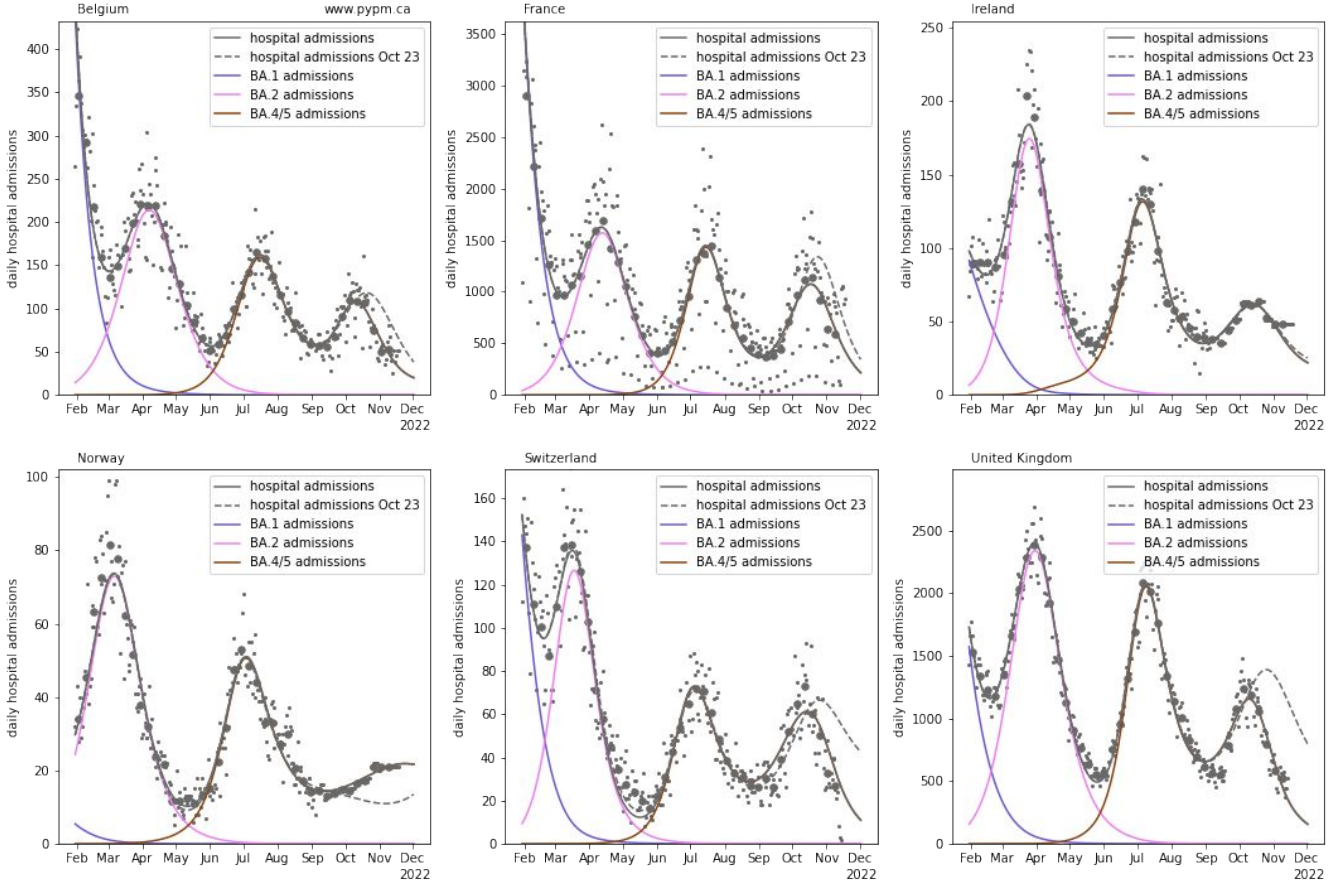
Waning of population-level immunity and the 4th Omicron wave

Our last report (October 5) used this approach to show that waning of immunity was causing the resurgence of COVID-19 in Europe, and the same effect was seen in Canadian provinces. The 4th Omicron wave (Fall) would therefore be expected due to the same strains as the 3rd wave (Summer), primarily BA.5.

Recent vaccination campaigns in Europe

Since our last report, the 4th wave peaked, as a result of additional natural and vaccination immunity. In Belgium, Switzerland, and the UK, recent rates of vaccinations have exceeded the rate of infections inferred from the model. The additional immunity from recent vaccinations are now included in the models.

Model fits to hospital admission data in Europe



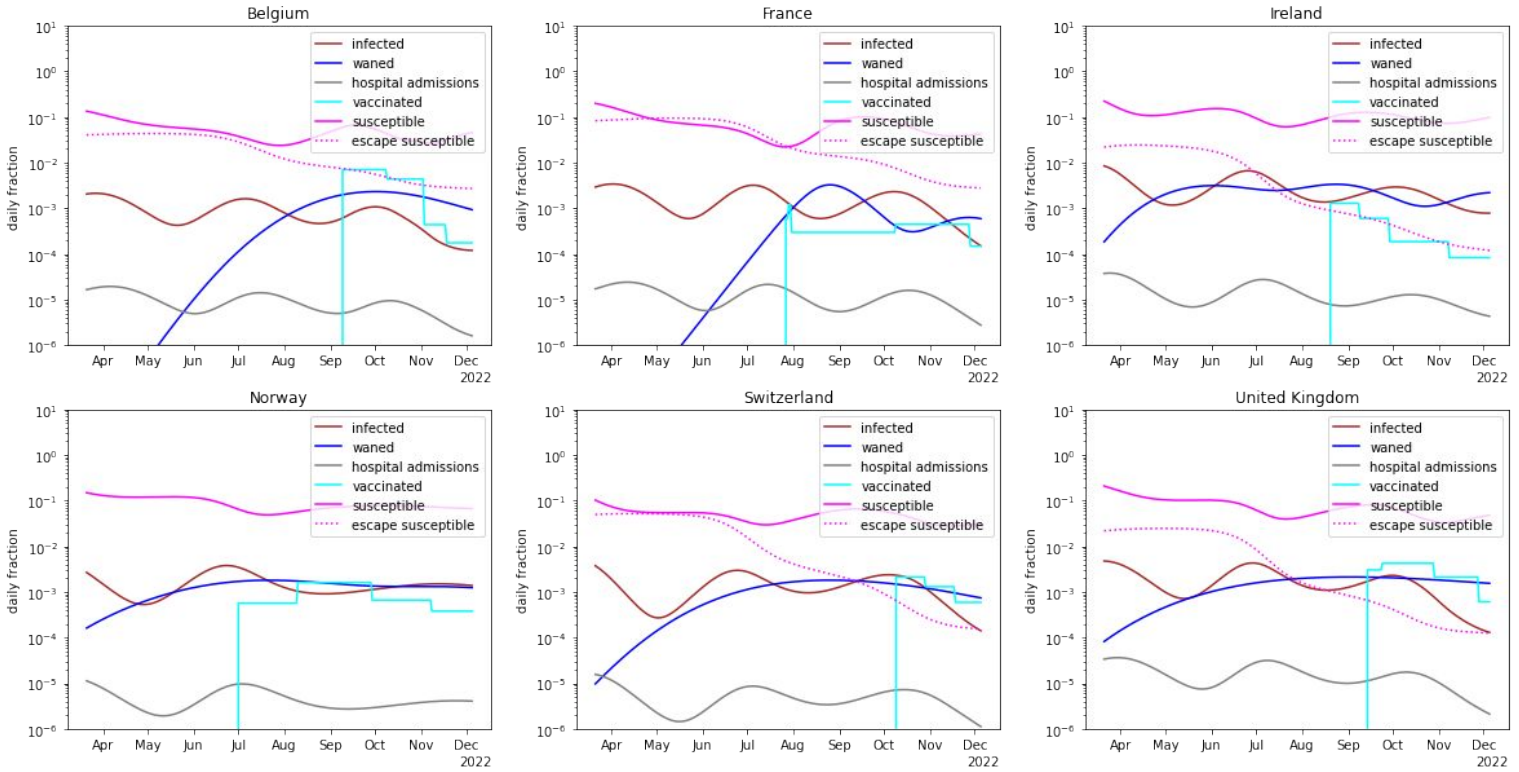
The daily (small dots) and weekly average (large dots) hospital admissions are compared to model fits (solid lines). The models have three Omicron strains (BA.1,BA.2,BA.5), each having constant transmission rate. Immunity parameters were set from the shape of the second wave (BA.2).

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

The model shown by the dashed curve was produced on October 23, prior to including the recent vaccination campaign in the model. To achieve good fits to Belgium, Swiss, and UK data, required vaccination to be included in the model.

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

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 BA.5 is estimated from the 3rd 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 cruve shows additional individuals who would be susceptible to BA.5, but not previous Omicron lineages.

Dynamic population-level immunity and new variants

Static population-level immunity (2020-2021)

In 2020 and 2021, the susceptible fraction was large and roughly constant. With this static population-level immunity, cases in a given region would grow or decline exponentially at a constant rate over substantial periods of time, corresponding to a constant growth rate, r (% per day).

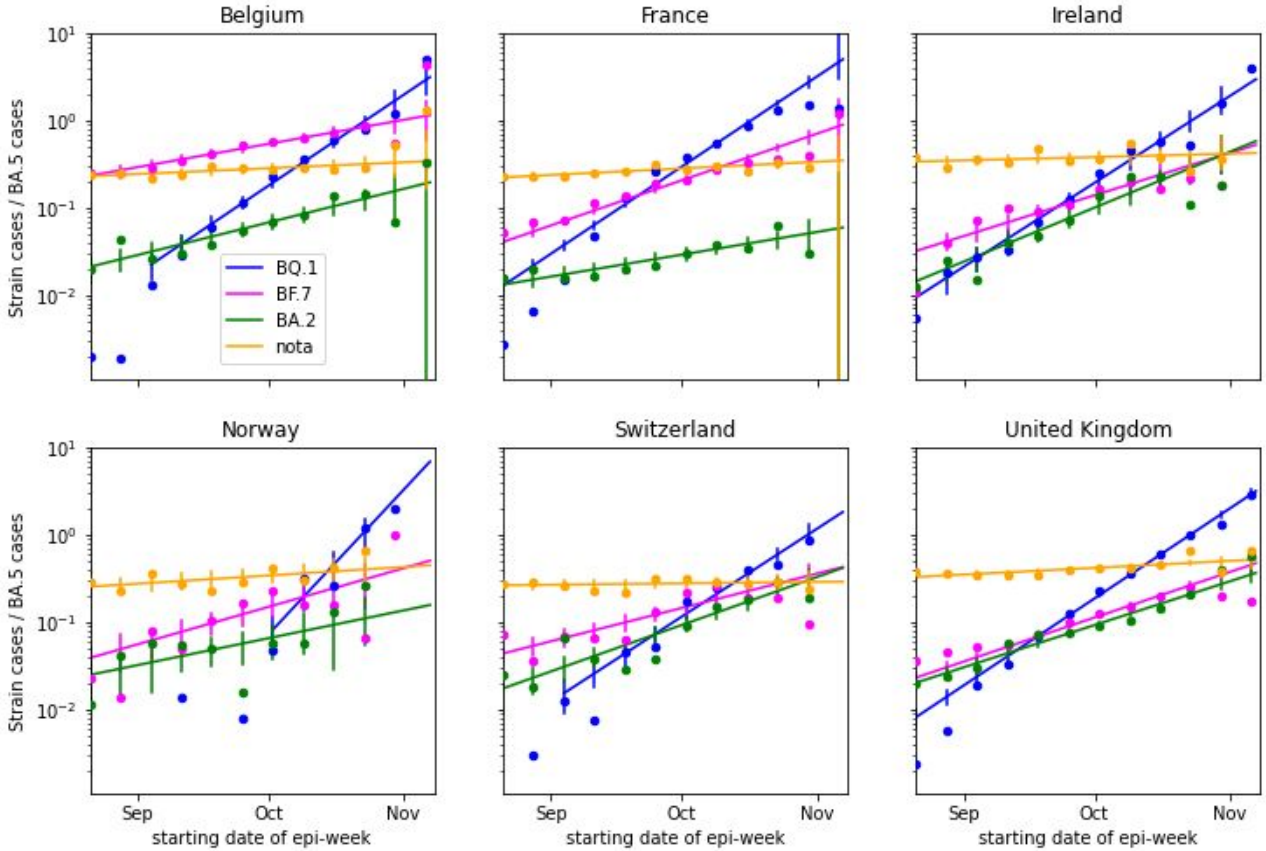
Variants of concern emerged with a faster growth rate. The ratio of new variant to original strain cases would grow exponentially with a rate given by the selection coefficient, s (% per day), being the difference of the two growth rates.

Dynamic population-level immunity (2022)

With continued vaccinations and the large number of infections from the omicron waves, the susceptible fraction is now much smaller. As a result, the growth rate, r, is no longer constant. It falls with infections and vaccinations and rises when immunity wanes.

A variant that evades immunity (thereby having a new large susceptible population) would have a growth rate that is affected less by population-level immunity dynamics. A constant selection coefficient would be a sign that population immunity is robust against the new variant.

Selection coefficient analysis for new variants



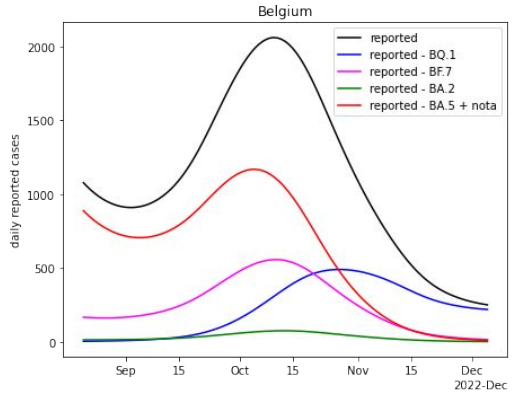
The points show the ratio of cases grouped as BQ.1*, BF.7*, BA.2* and none of the above ('nota') with respect to BA.5* cases.

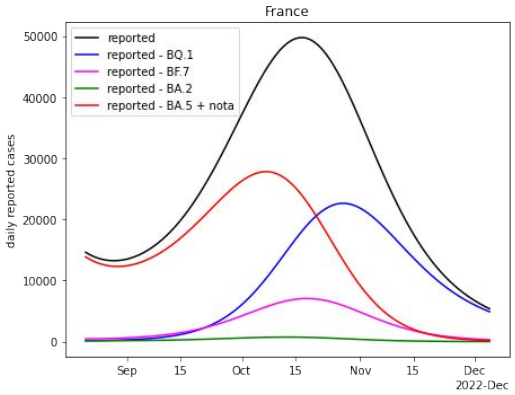
Despite highly dynamic population immunity, the ratios have roughly constant slopes, suggesting that none of these strains have significant immunity escape.

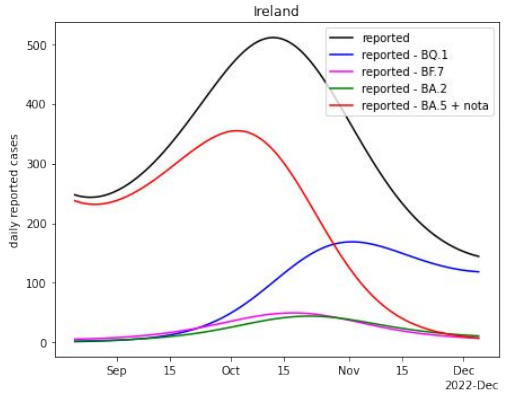
This is further illustrated in the next slide, which breaks down the recent case rates into the variant groupings, by using the fractions from these fits.

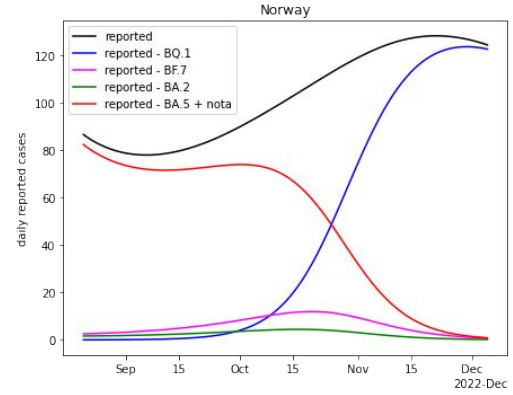
Source (D. Karlen) European metadata was downloaded from GISAID for the GRA clade.

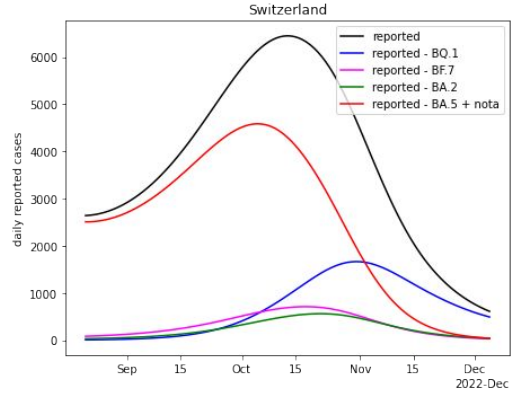
Breakdown of cases into variant groupings

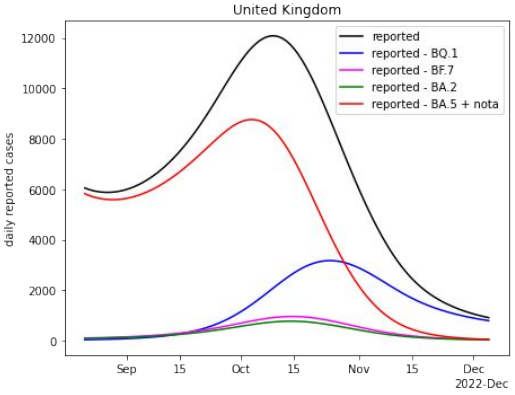










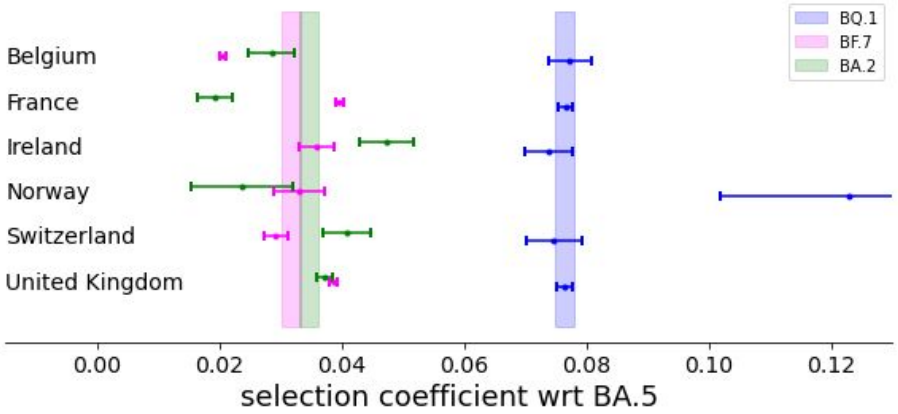


The Fall 2022 wave (cases in black) was driven largely by BA.5 (red), not by BQ.1 (blue), which peaked later. This analysis confirms our October report evaluation that the wave was due to waning.

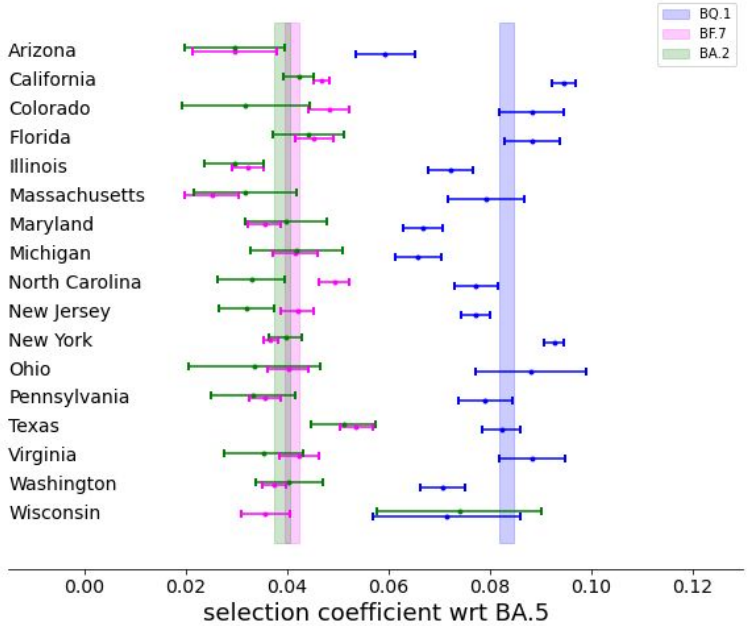
BQ.1 cases fell quickly, implying that the majority of the population retained immunity against this variant.

Source (D. Karlen) The BA.5* and the 'nota' variants that grow at the same rate are combined as the red curve. The rapidly growing BQ.1* strains were not seen as a separate wave as it peaked close to the peak of the BA.5* resurgence.

Selection coefficients for new variants: Europe and US



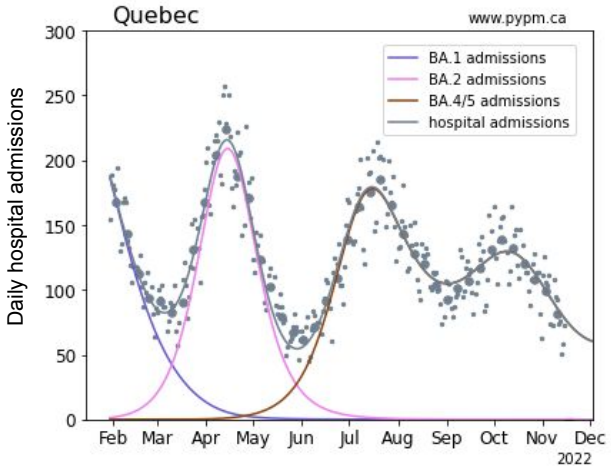
Nation	BQ.1	BF.7	BA.2	nota
Belgium	0.077 +/- 0.004	0.020 +/- 0.001	0.029 +/- 0.004	0.005 +/- 0.002
France	0.077 +/- 0.001	0.040 +/- 0.001	0.019 +/- 0.003	0.006 +/- 0.001
Ireland	0.074 +/- 0.004	0.036 +/- 0.003	0.047 +/- 0.004	0.003 +/- 0.002
Norway	0.123 +/- 0.021	0.033 +/- 0.004	0.024 +/- 0.008	0.007 +/- 0.004
Switzerland	0.075 +/- 0.005	0.029 +/- 0.002	0.041 +/- 0.004	0.001 +/- 0.002
UK	0.076 +/- 0.001	0.039 +/- 0.001	0.037 +/- 0.001	0.006 +/- 0.001

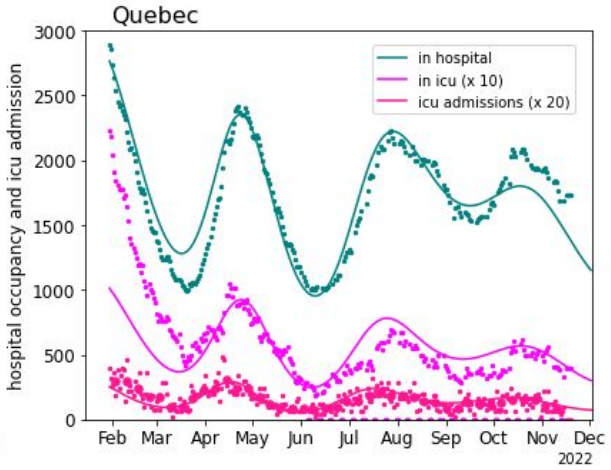


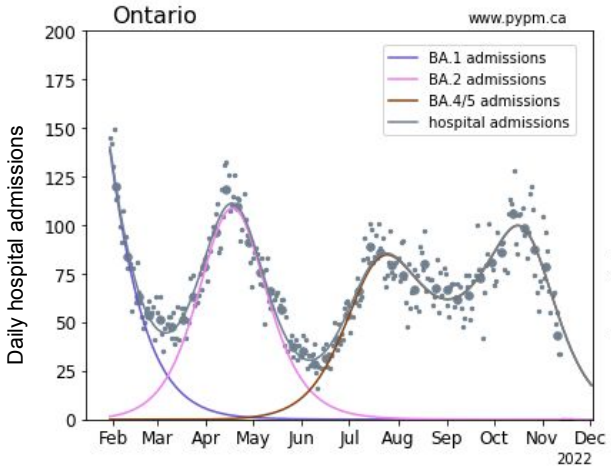
Selection coefficients estimated for Europe and US are consistent.

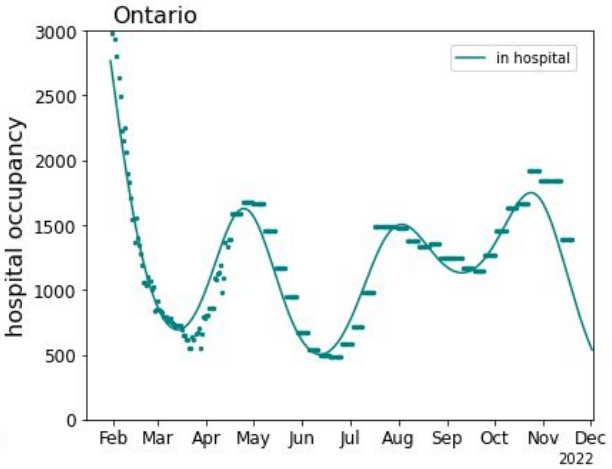
Source (D. Karlen) See www.pypm.ca. European and US metadata was downloaded from GISAID for the GRA clade.

Quebec and Ontario







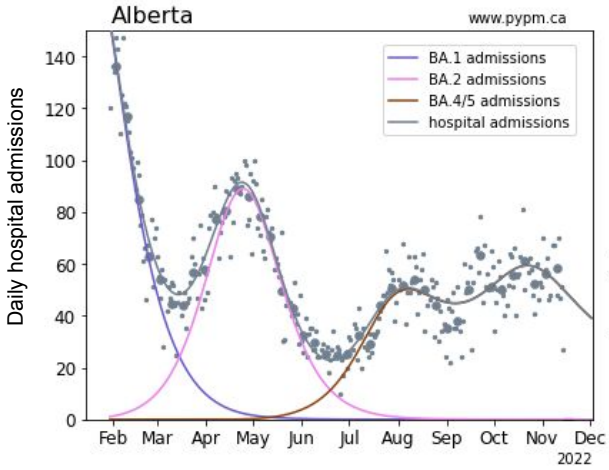


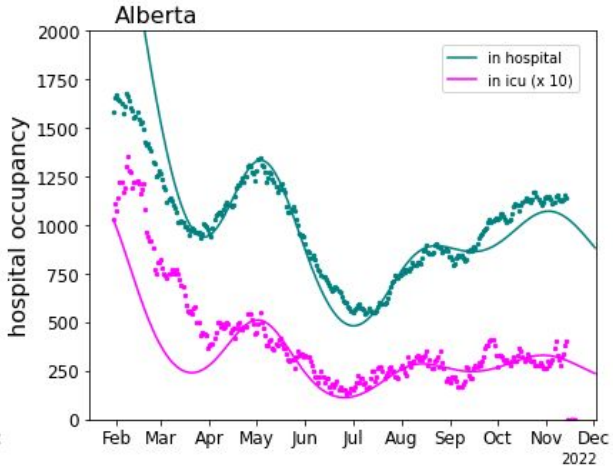
The same approach is applied to four provinces. The 4th wave due to waning is observed in each.

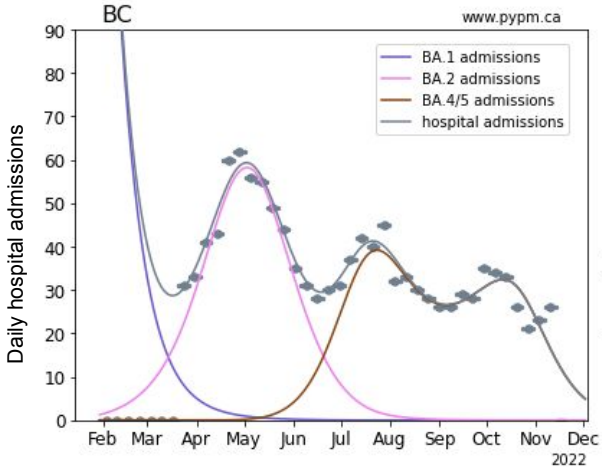
Infection rates in Quebec and Ontario are inferred to be rapidly falling, due to additional immunity from recent infections and vaccinations.

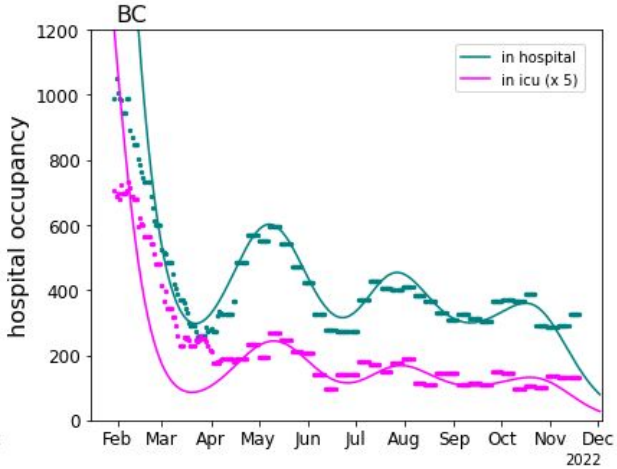
Source (D. Karlen) See www.pypm.ca.

Alberta and BC









The situation in Alberta and BC is less certain. The model predicts declining infection rates, but there is significant uncertainty in understanding waning immunity.

The uncertainty in BC is compounded by the fact that reinfections are not included in hospital admissions (grey dots).

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, as of this week.
- 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.
  - This approach indicates that it is waning of immunity, not the variants, that led to the recent fall wave.
  - This conclusion is confirmed by a separate analysis based on genomic data.

The immune evasion advantage demonstrated for BQ.1* in the lab may allow this virus to infect individuals with waning immunity sooner, but our analyses suggest that most people retain immunity to BQ.1*.

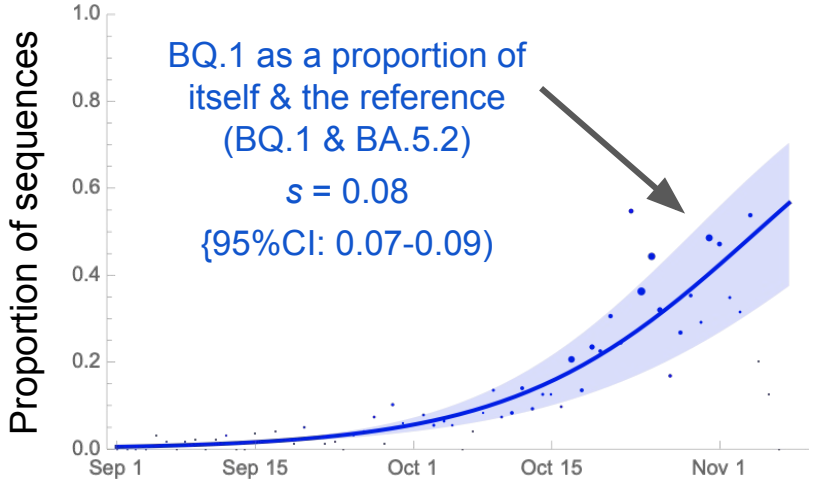
COVID-19 cases and impacts will likely rise and fall over the next few months as immunity lost through waning is offset by new immunity, gained by vaccination and/or infections.

Appendix: 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.