COVID Model Projections

November 23, 2022

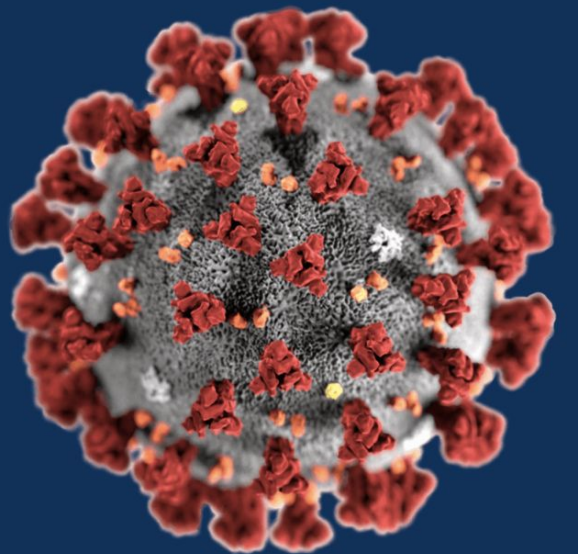
BC COVID-19 Modelling Group

@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

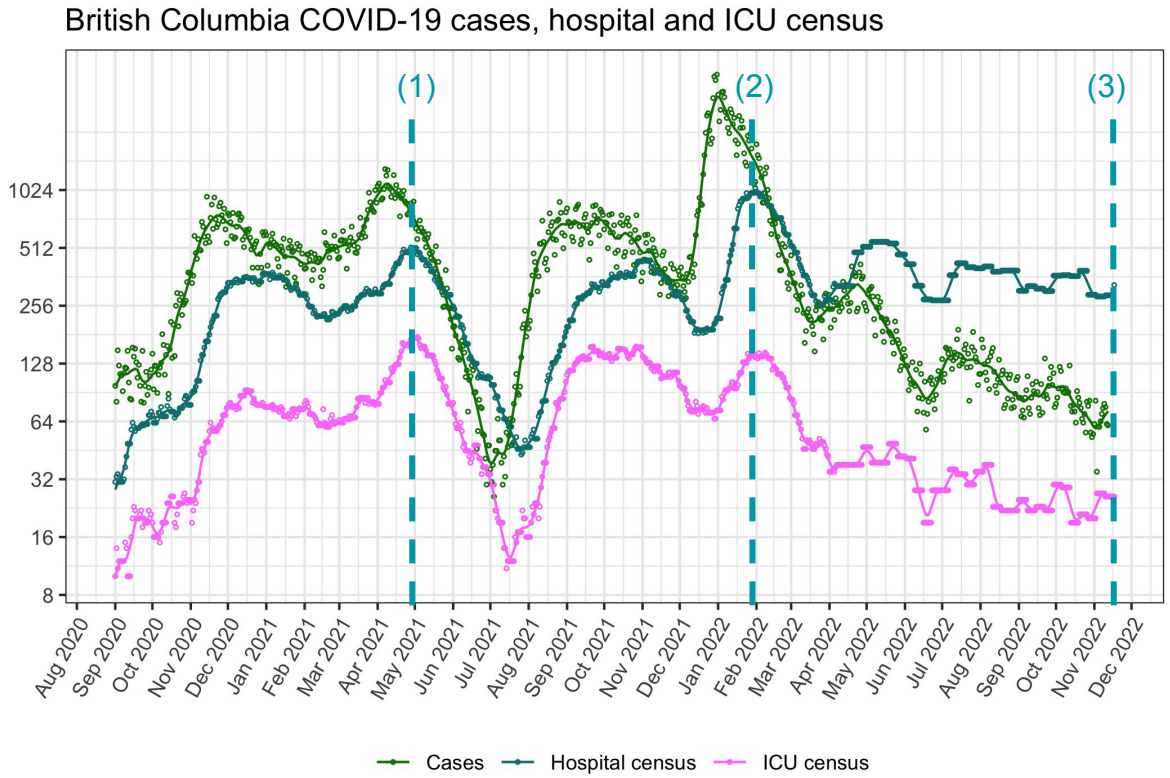
Contents of this report:

- Current COVID-19 trends in BC
- The rise of BQ.1
- 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 in Canada 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 = 328

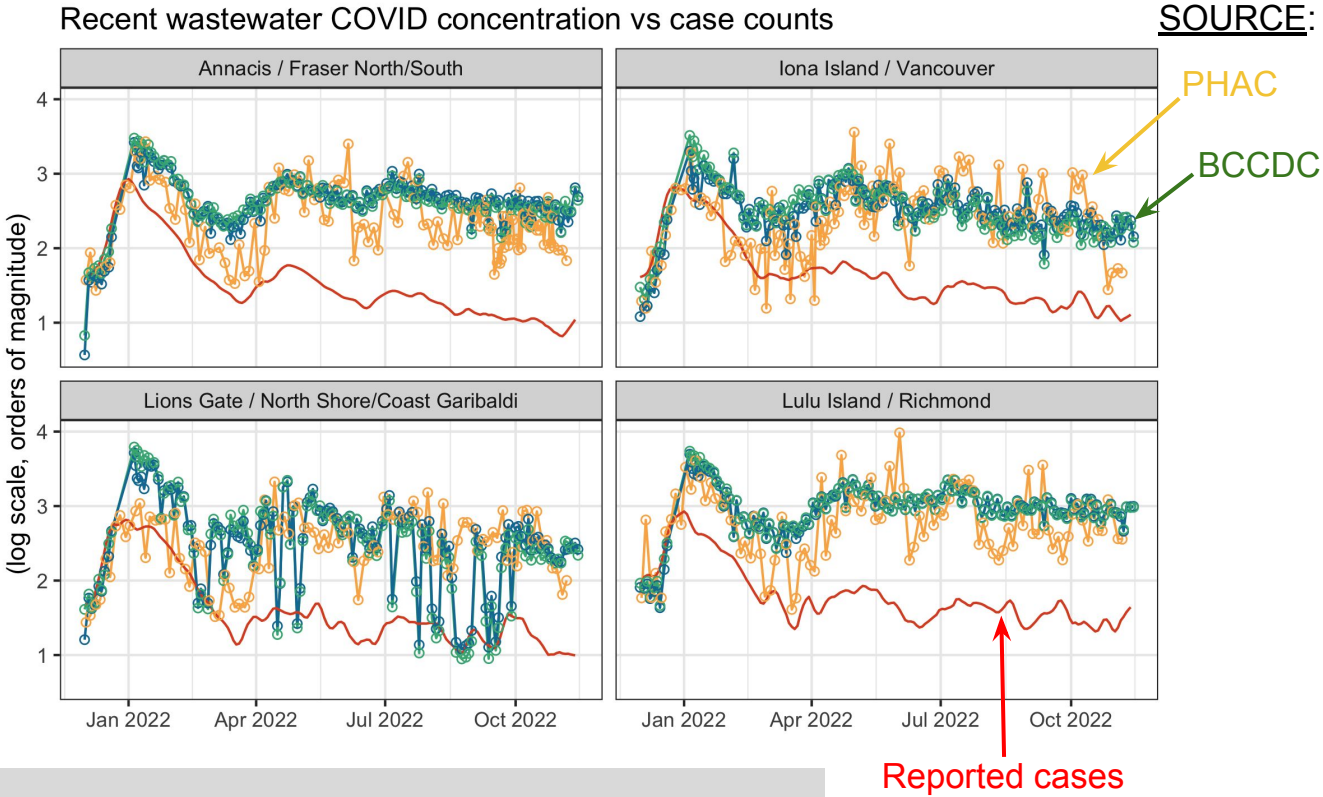
Source (J. von Bergmann) Case data from BC COVID-19 Database (http://www.bccdc.ca/health-info/diseases-conditions/covid-19/data). STL trend lines on log scale. How hospitalizations and deaths are attributed to COVID-19 changed in BC on April 2, 2022. *Reinfections with a prior lab-confirmed case are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

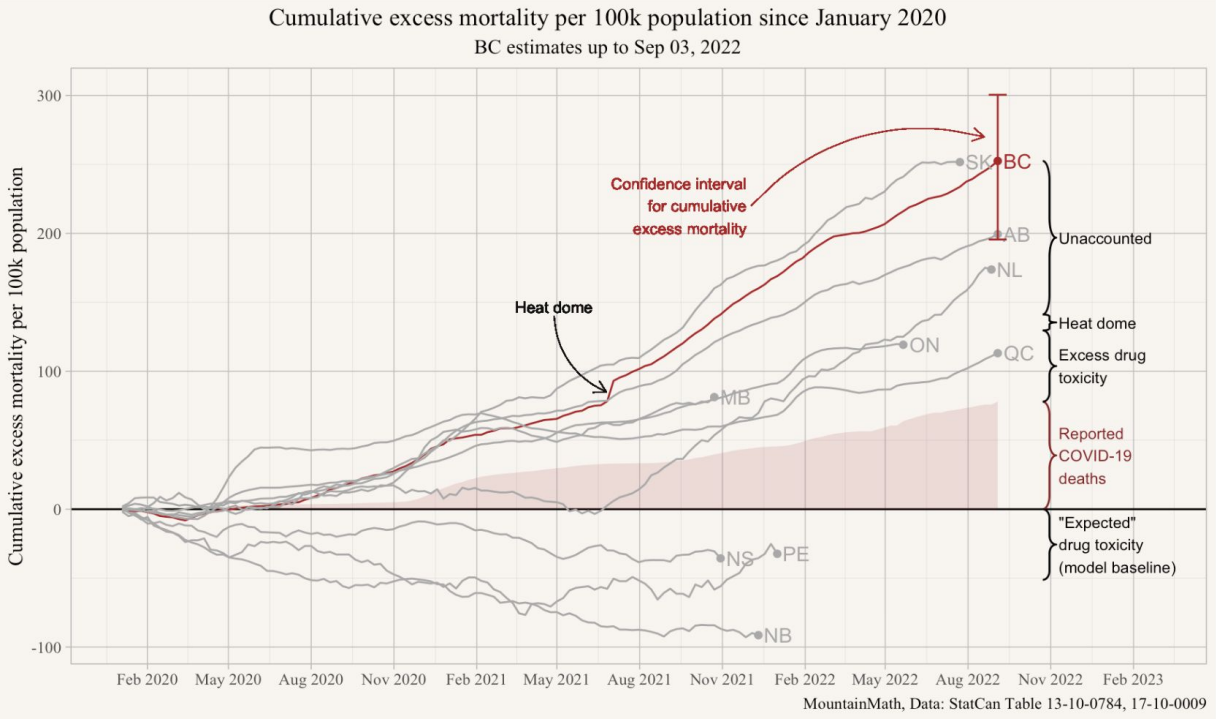
- Heights of curves are adjusted to align in December 2021 to emphasize how trends differ across 2022.
- Y-axis shows the order of magnitude of virus copies (per liter in gold or blue or, adjusting for water flow, per day in green).
- Wastewater data are noisy and differ between the source labs for reasons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

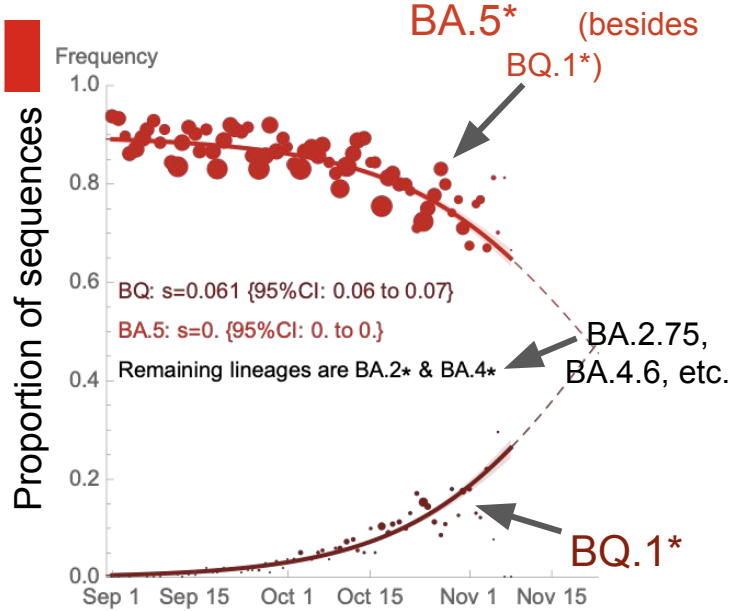
Deaths that are caused by COVID reinfections are also missing, if previous infection was officially recorded in BC.

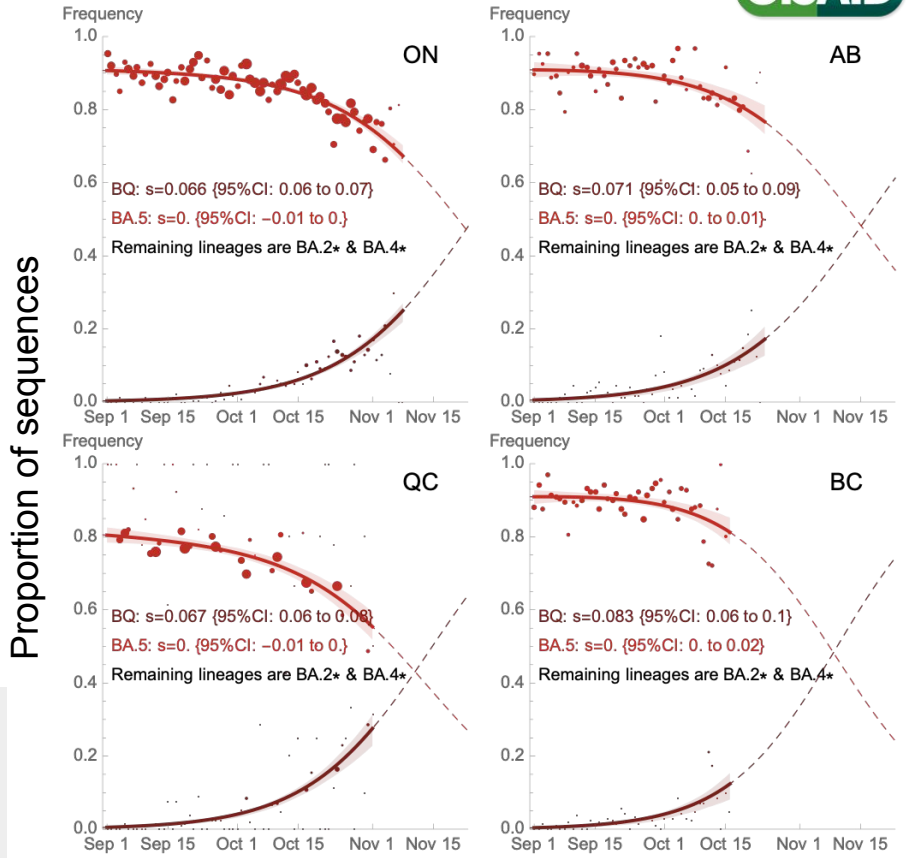
BC is likely substantially undercounting total deaths due to COVID.

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

Spread of BQ.1* sub-lineages in Canada



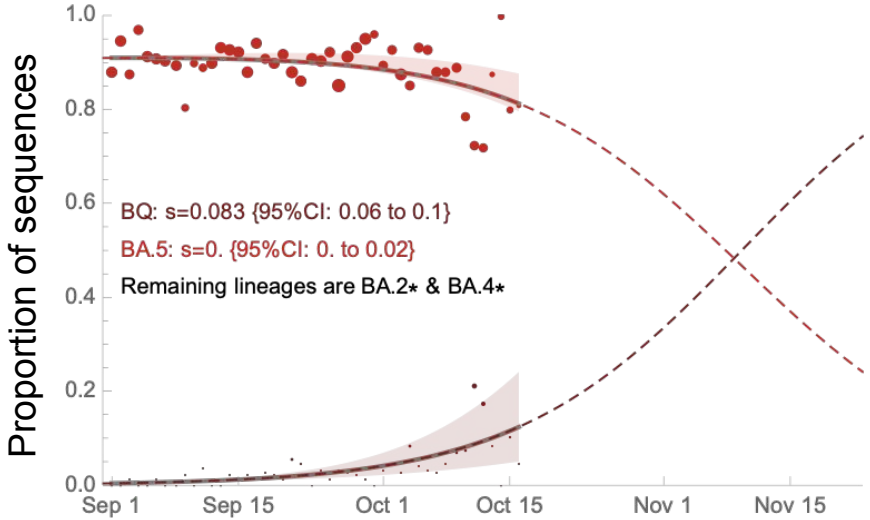


BQ.1* lineages are rising in frequency across Canada with a selective advantage of *s* ~ 6% relative to BA.5* or (BA.2*&BA.4*), leading to a current estimated frequency of ~50%.

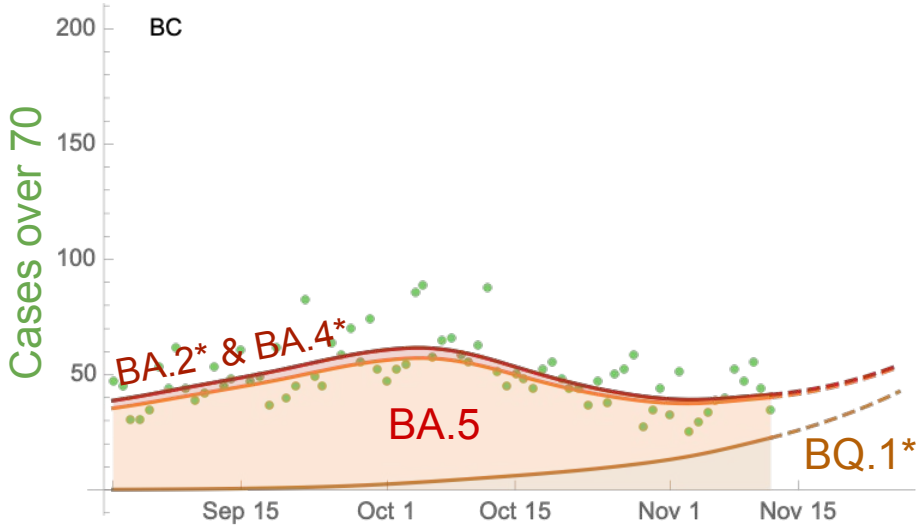
Source (S. Otto) Canadian metadata was downloaded from GISAID for the GRA clade. See Appendix for more more method details.

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.

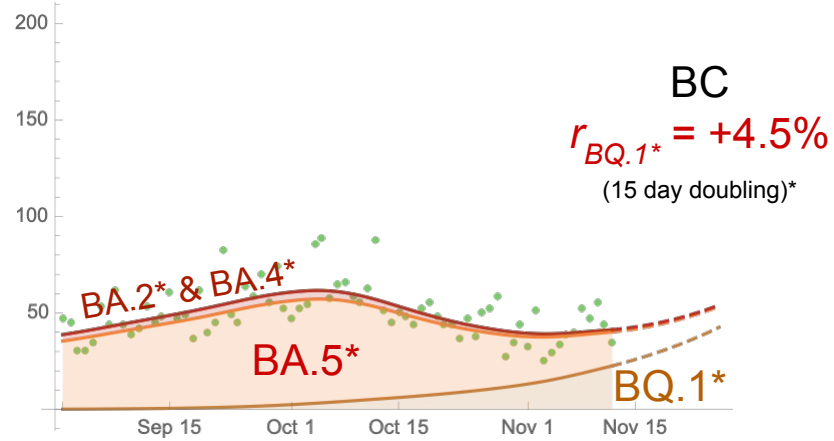


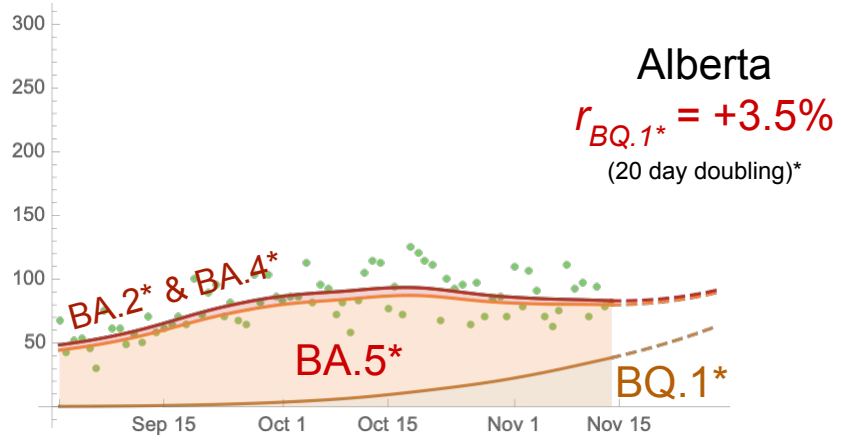
→ BQ.1 case counts are estimated to be rising, despite overall downward trend.

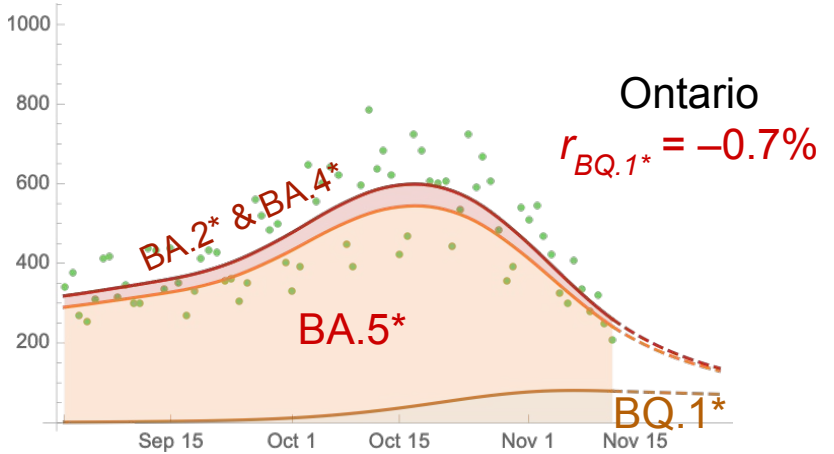
Source (S. Otto) Canadian metadata was downloaded from GISAID for the Omicron GRA clades. A model of selection was fit to the numbers of each type using maximum likelihood based on a trinomial distribution given the expected frequencies on each day. Hessian matrix used to obtain confidence intervals.

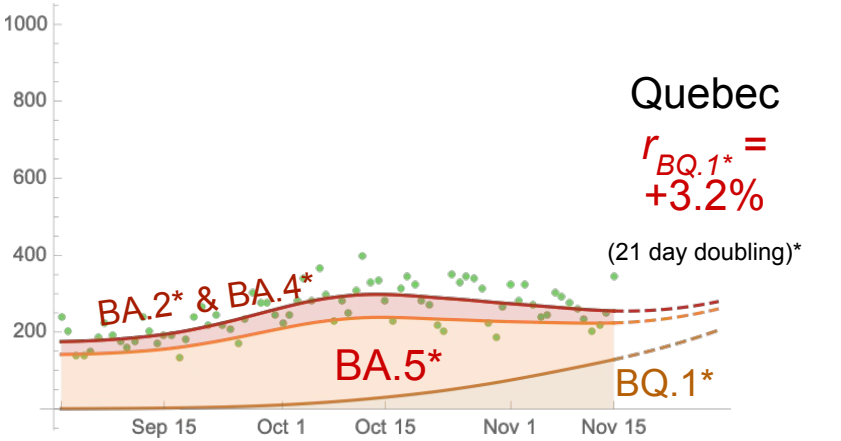
The BQ.1* Omicron Wave

Cases over 70



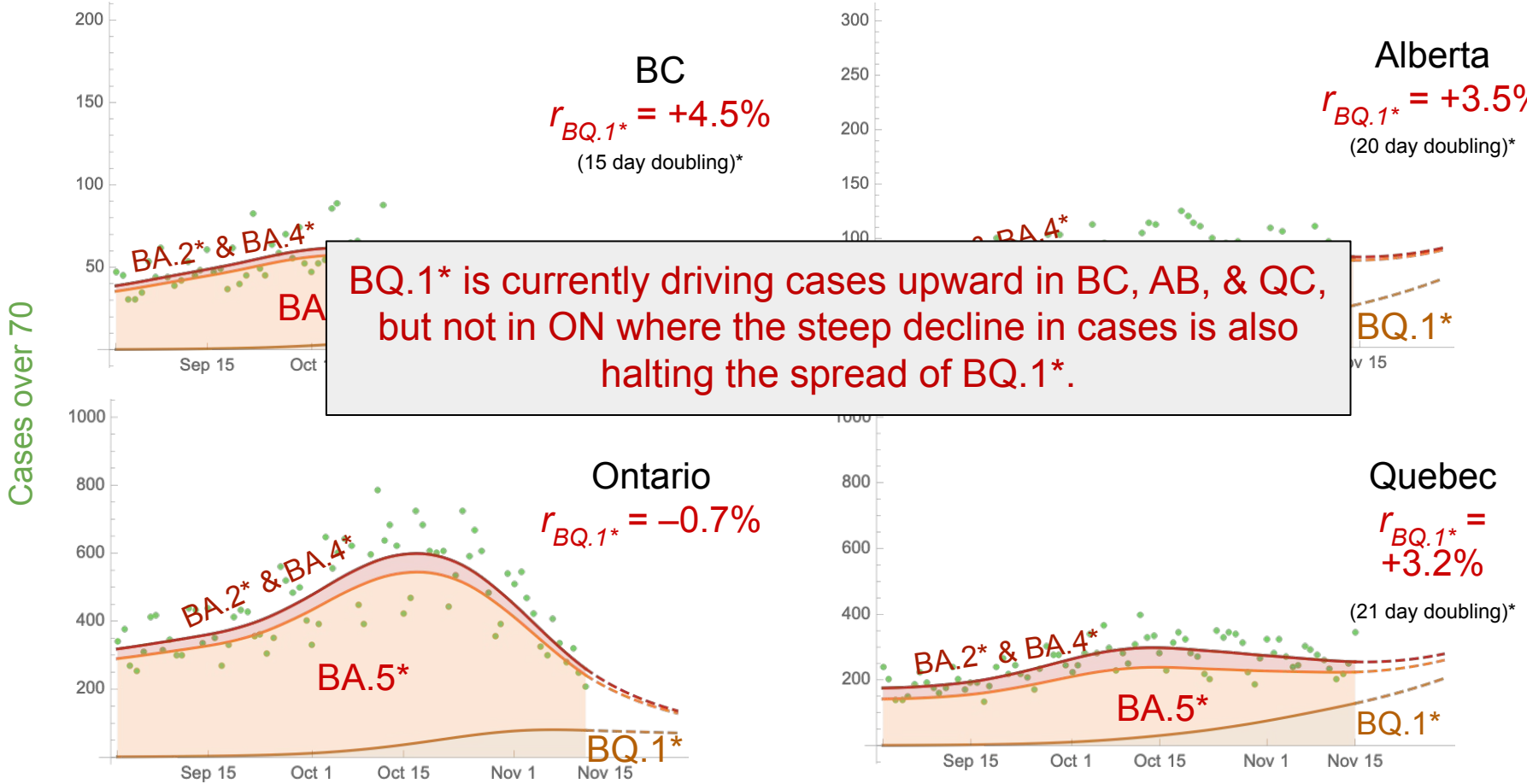






* Instantaneous estimates of growth rate, *r*, and doubling times for BQ.1*. These rates change with changing immunity and with protective health measures, both mandated and voluntary, to reduce transmission (e.g., wearing effective masks, increasing ventilation, and avoiding crowded indoor spaces)

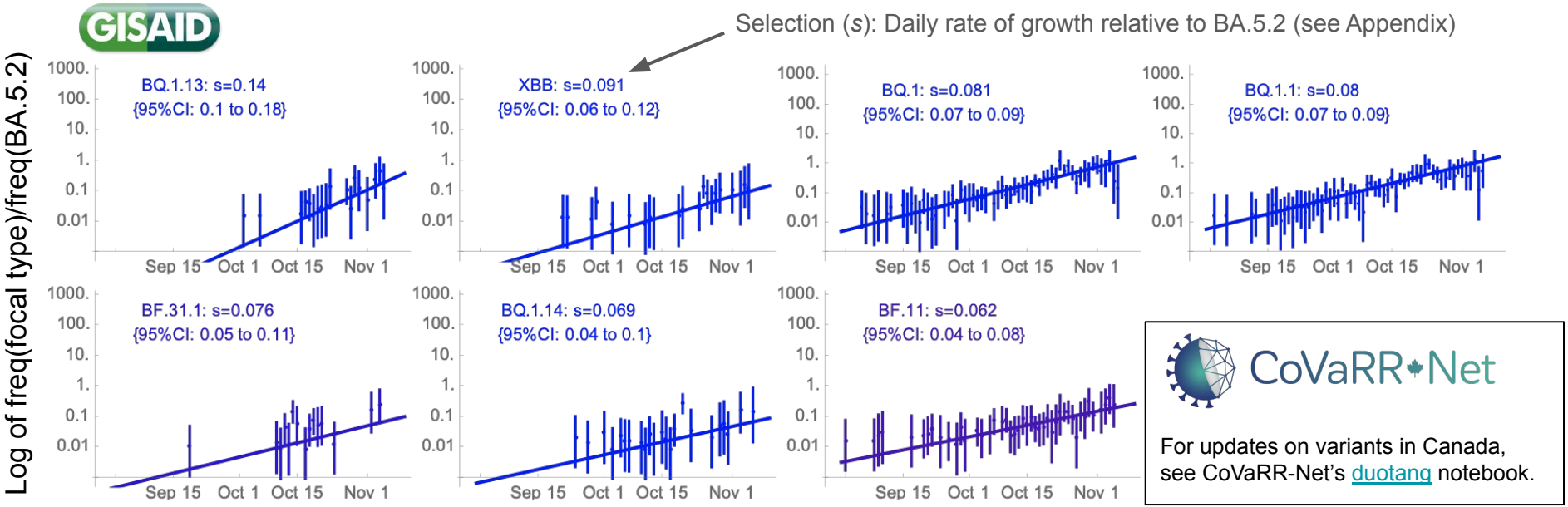
The BQ.1* Omicron Wave



* 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 (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

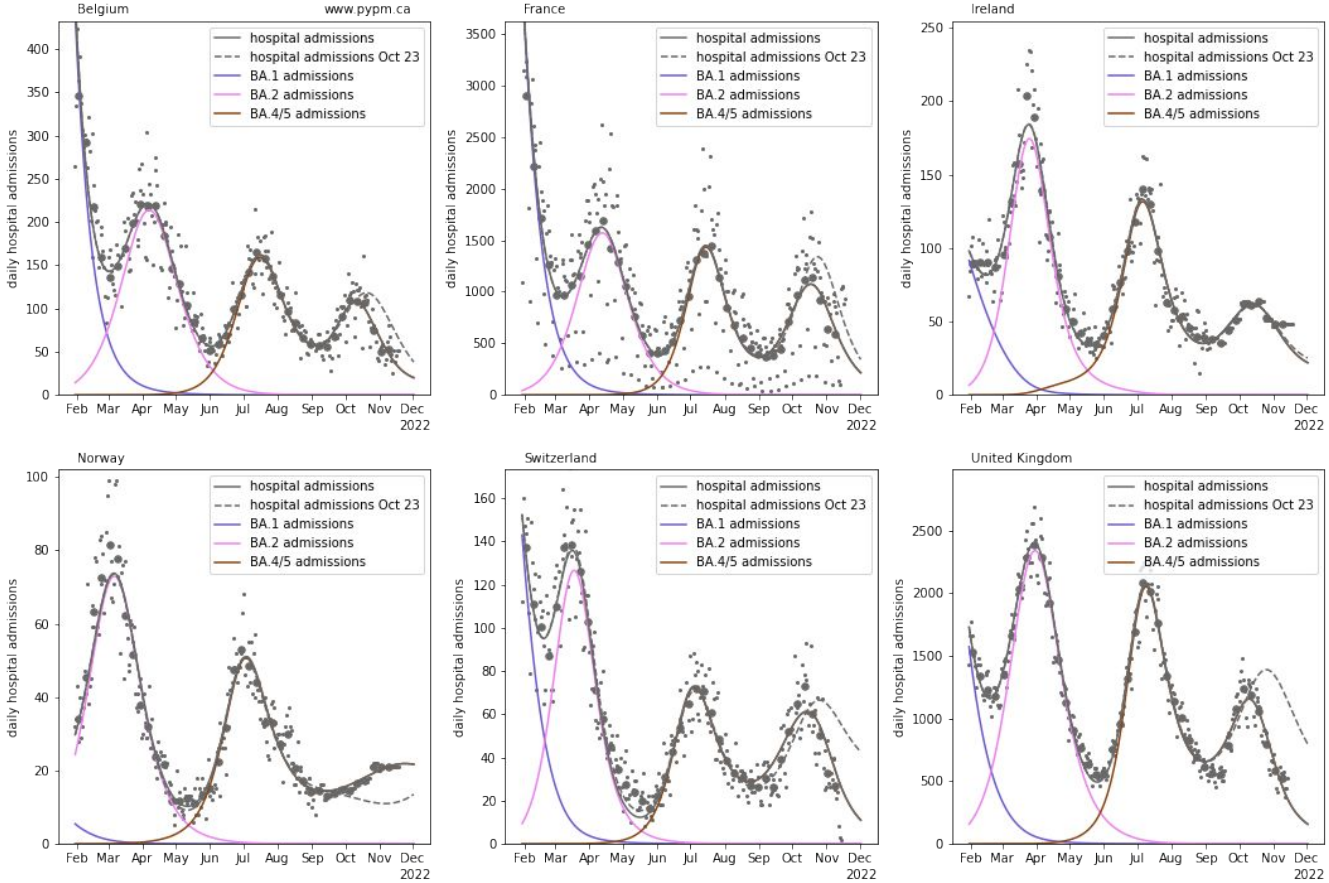
Waning immunity and vaccination

Approach: Population-level immunity dynamics can be deduced directly from data. Both the initial immunity and the rate that immunity grows are determined by the rise and fall of the BA.2 wave. Given underreporting of cases, only hospital admission data are used, and the number of new immunity-generating infections per hospital admission is inferred. Transmission is constant for each main variant.

Our last report used this approach to show that waning of immunity was causing a resurgence of COVID-19 in Europe and in Canadian provinces. This resurgence involved the same variant (BA.5) in both the 3rd (mid-summer 2022) and 4th (fall 2022) Omicron waves and so was driven by waning, not new variants.

Since our last report, the resurgence due to waning has petered out, as a result of the additional natural and vaccination immunity. The additional immunity from recent vaccinations are now included in the models.

Model fits to hospital admission data in Europe



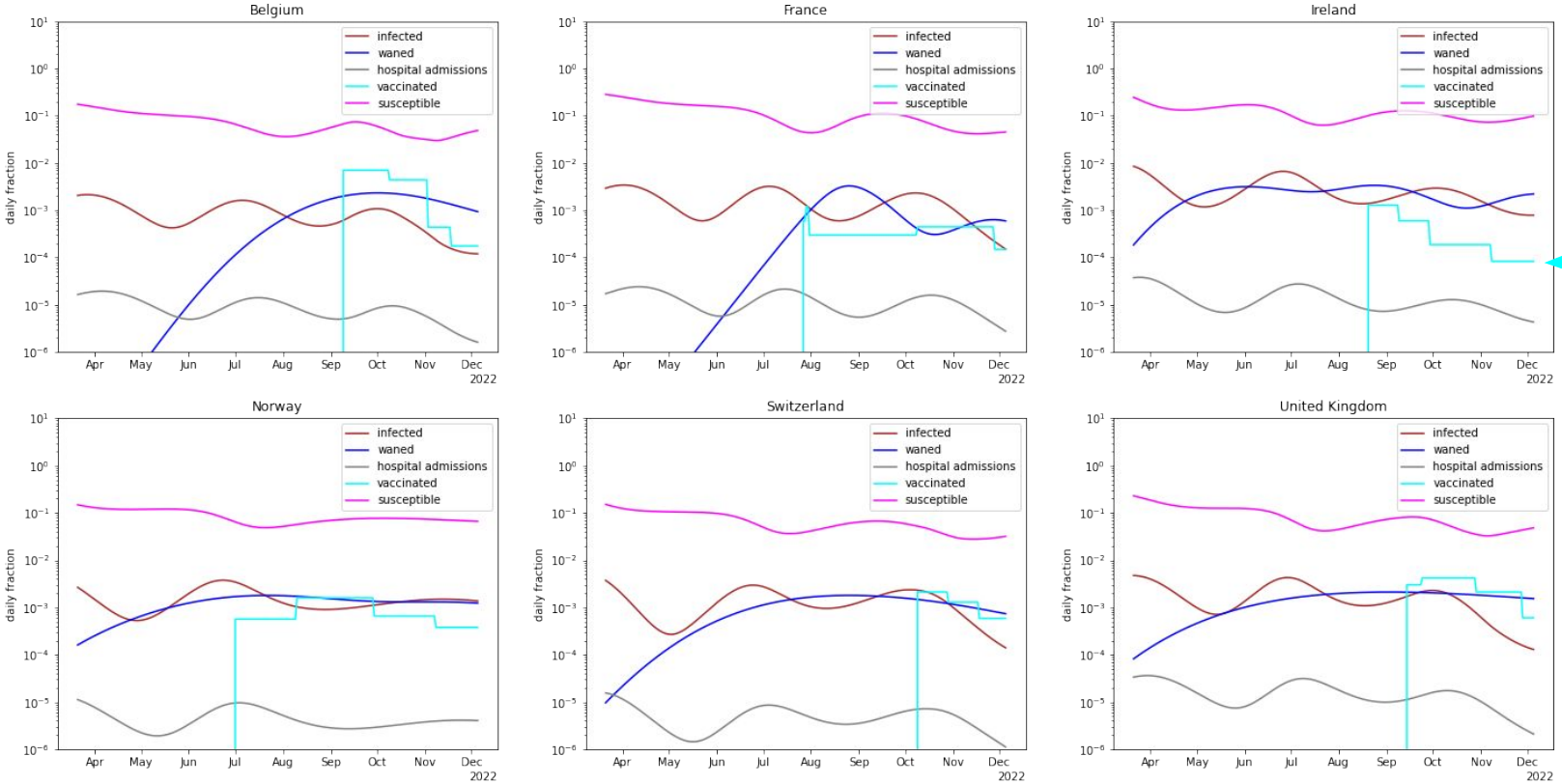
The daily (small dots) and weekly average (large dots) hospital admissions are compared to model fits (solid lines). The models have three Omicron strains (BA.1,BA.2,BA.5), each having constant transmission rate. Immunity parameters were set from the shape of the second wave (BA.2).

Waning is implemented as a gamma delay function, with three free parameters in the fits.

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, the model required vaccination to be included.

Source (D. Karlen) See www.pypm.ca. Data from European COVID-19 Forecast Hub and Our World in Data

Recent vaccination rates, and inferred infection and waning rates



Known vaccination rates added

Source (D. Karlen) See www.pypm.ca. Data from ECDC vaccine tracker.

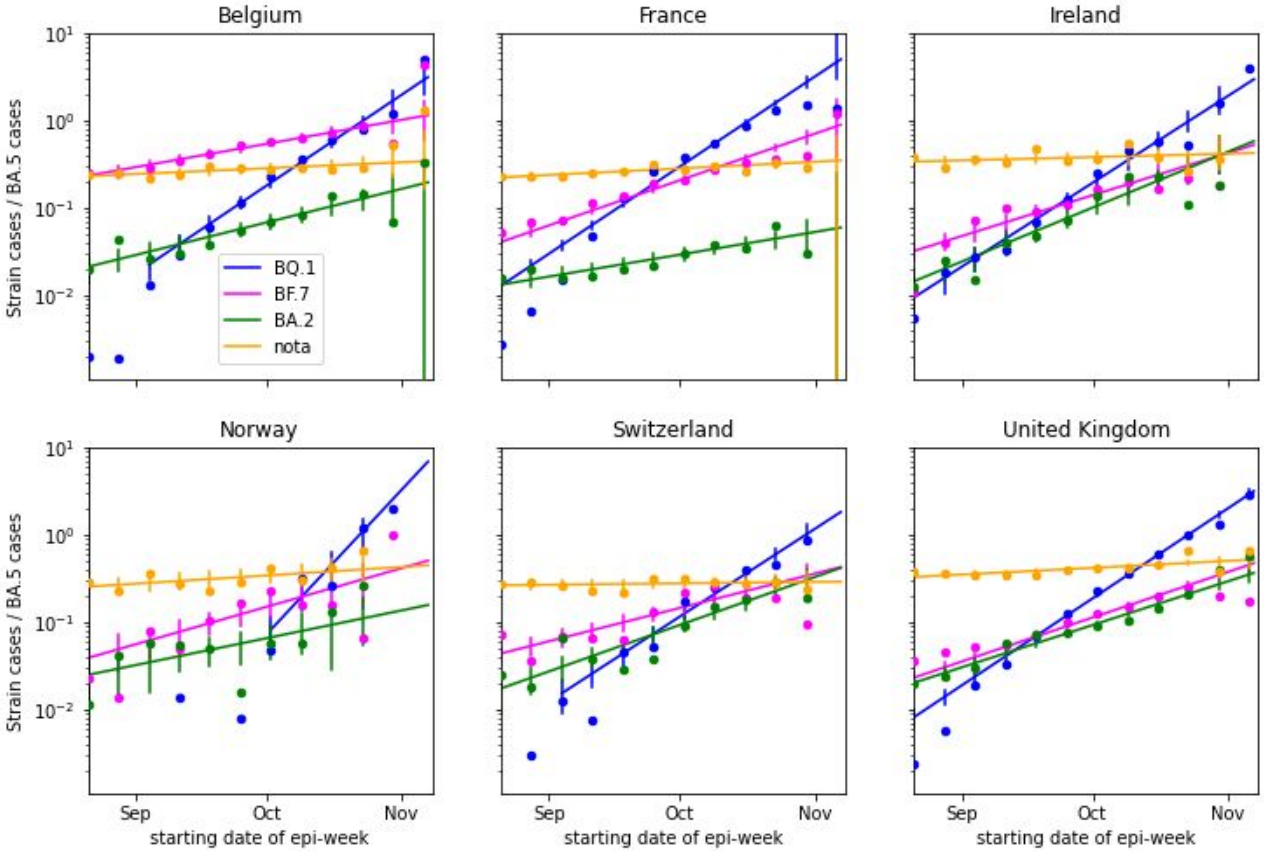
Dynamic population-level immunity and new variants

With large numbers of infections and vaccinations, the susceptible fraction is now much smaller in these European countries and in Canada (estimated by the pink curves at ~10-20%, compared to the largely susceptible population during the first two years of the pandemic). As immune protection wanes (blue curves), this generates highly dynamic population-level susceptibility and infection rates.

That is, the daily growth rate of COVID-19, *r*, is not constant but rises with waning and falls with infections and vaccinations.

As illustrated in the next slide, variants are rising and falling similarly over time, so that their relative frequencies change at a constant rate over time (constant selection). This suggests that the variants have similar pools of susceptible individuals and that variants like BQ.1 do not substantially evade immunity.

Selection coefficient analysis for new variants

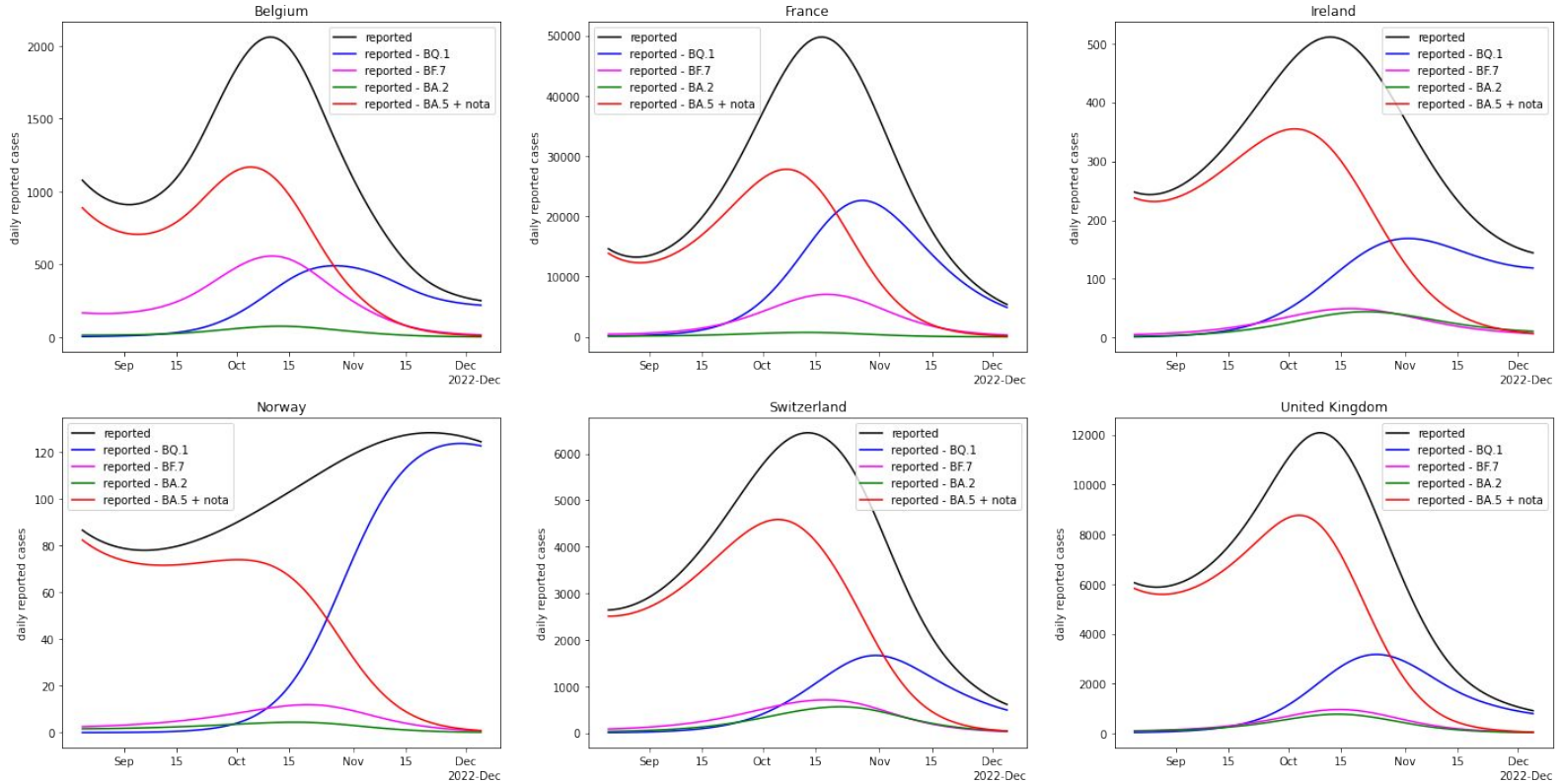


The points show the ratio of cases identified as BQ.1*, BF.7*, BA.2* and none of the above ('nota') with respect to BA.5* cases.

The roughly constant slopes (selection coefficients are given in the Appendix) suggest that none of these strains have significant immunity escape.

This is further illustrated in the next slide, which breaks down the recent rates of cases into these variant groupings.

Breakdown of cases into variant groupings

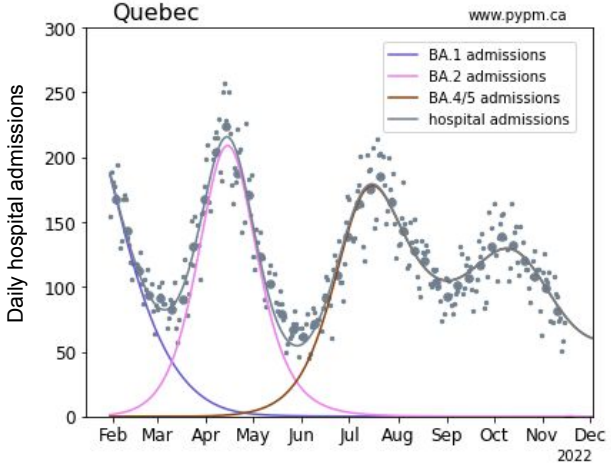


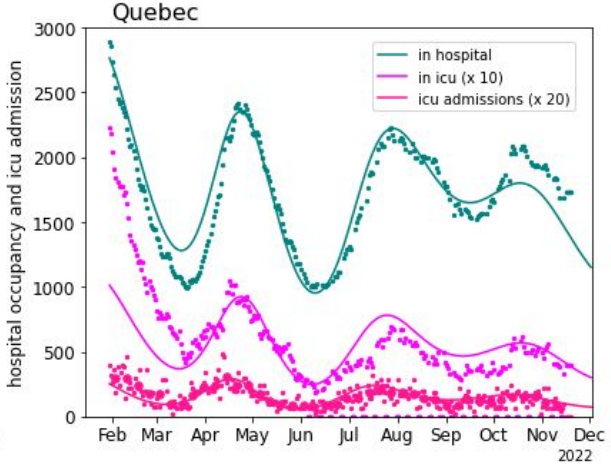
The second BA.5 peak in fall 2022 (cases in black) is driven largely by another BA.5 wave (red), not by the spread of BQ.1 (blue), which happens later.

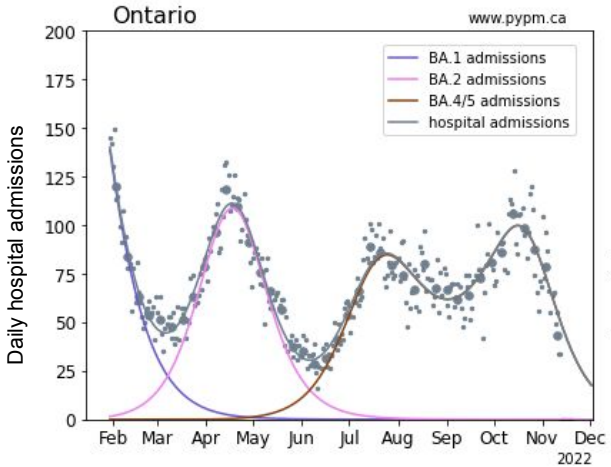
The BQ.1 sub-wave fell quickly, implying that the majority of the population retained immunity to this variant.

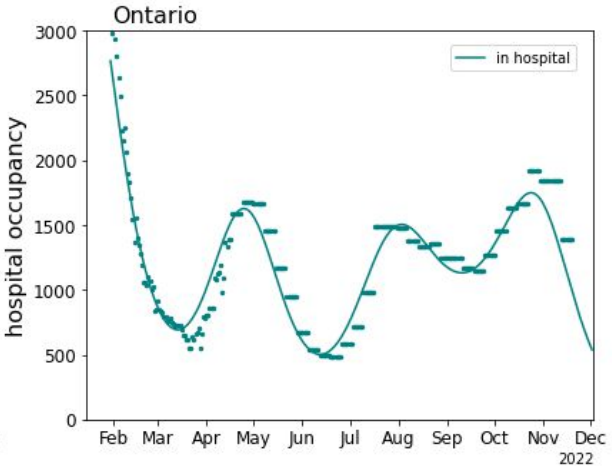
Source (D. Karlen) The BA.5* and the 'nota' variants that grow at the same rate are combined as the red curve. The rapidly growing BQ.1* strains are not seen as a separate wave as it peaked close to the peak of the BA.5* resurgence.

Quebec and Ontario







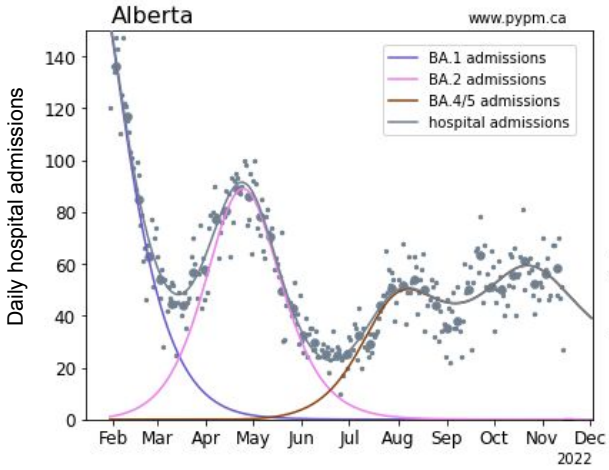


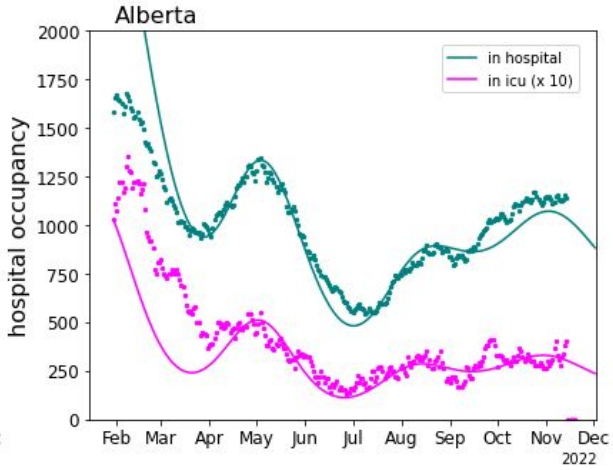
The same approach is applied to four provinces.

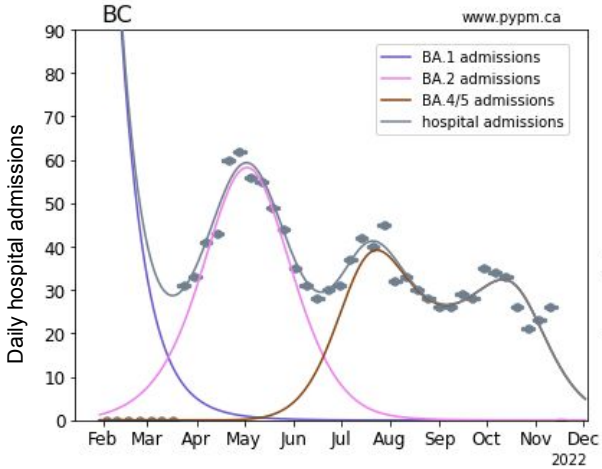
Quebec and Ontario show rapidly falling infection rates, due to additional immunity from recent infections and vaccinations.

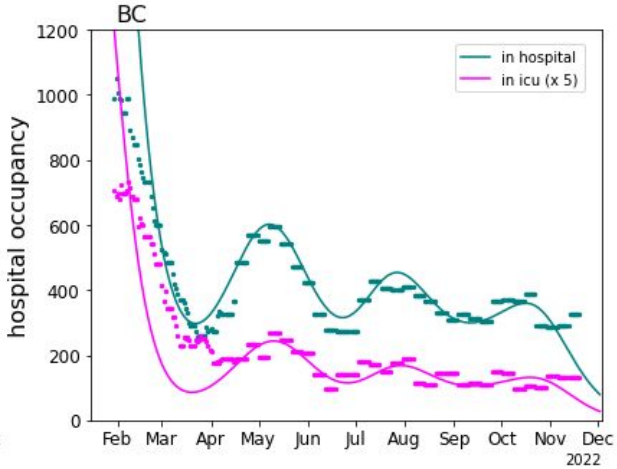
Source (D. Karlen) See www.pypm.ca.

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 and the current situation with new variants.

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 the BA.5 started to rise in June 2022.
- There have been over 200 named COVID-19 sub-lineages circulating in Canada over the last three months, but the main ones spreading 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 in blood samples.
- 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 wave.

Recent COVID peak was driven more by waning than by variants

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.

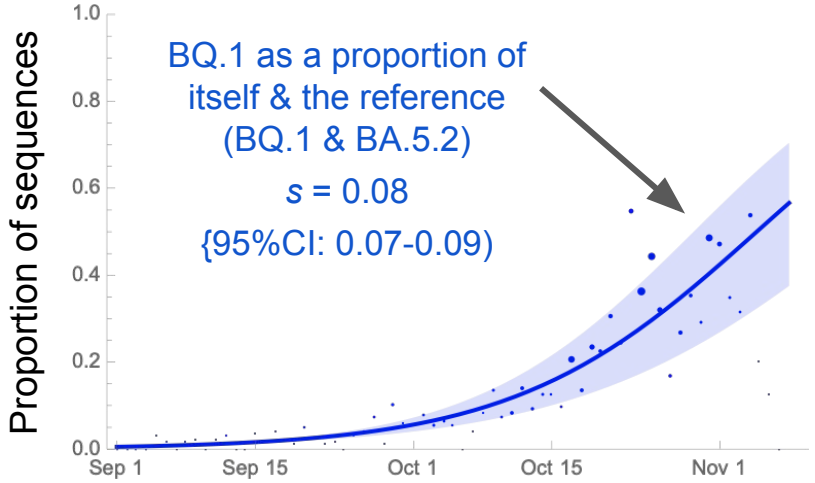
The immune evasion advantage demonstrated for BQ.1* in the lab (Cao et al.) may allow this virus to infect individuals with waning immunity sooner, but models suggest that most people retain immunity to BQ.1*.

Appendix: Interpreting selection

What is selective ("*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* →

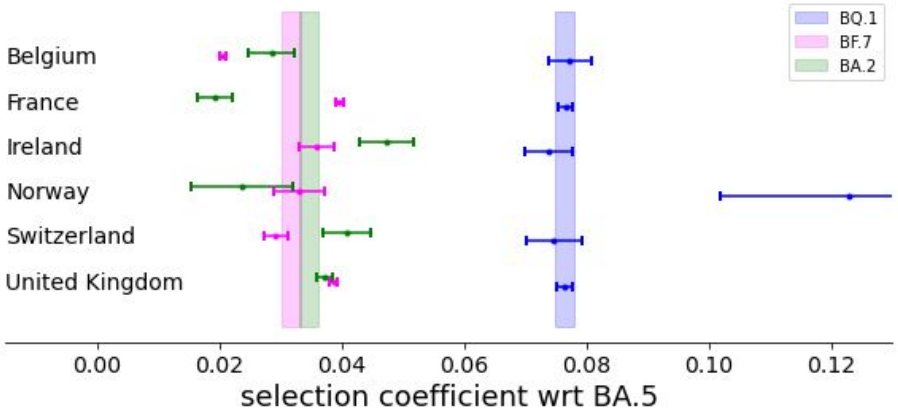
1%	2%	5%	10%	20%
69.3	34.7	13.9	6.9	3.5

← Days to double in frequency relative to reference strain

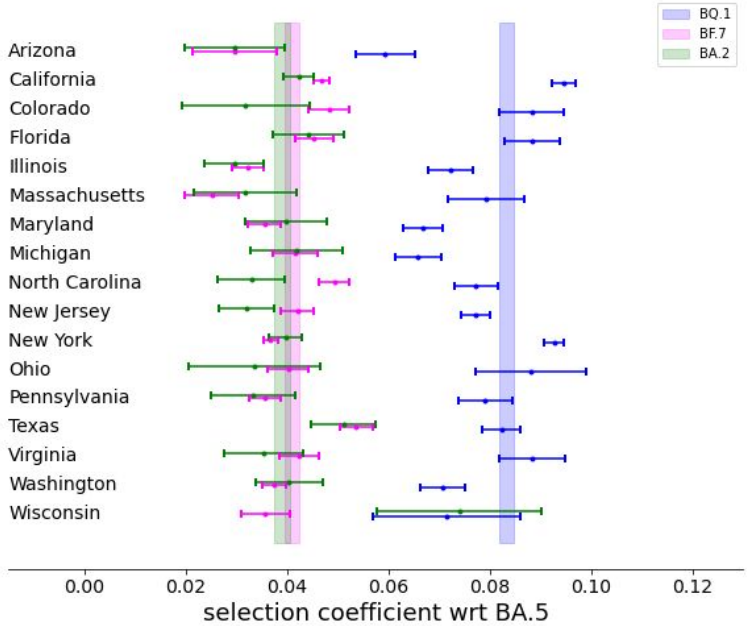
Alpha vs Wuhan
BA.5 vs BA.2
Omicron vs Delta

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.

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



Consistent selection coefficients for Europe and US

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