COVID Model Projections

November 23, 2022

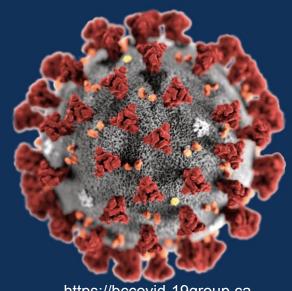
BC COVID-19 Modelling Group



About BC COVID-19 Modelling Group

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

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



https://bccovid-19group.ca

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

Overview

Contents of this report:

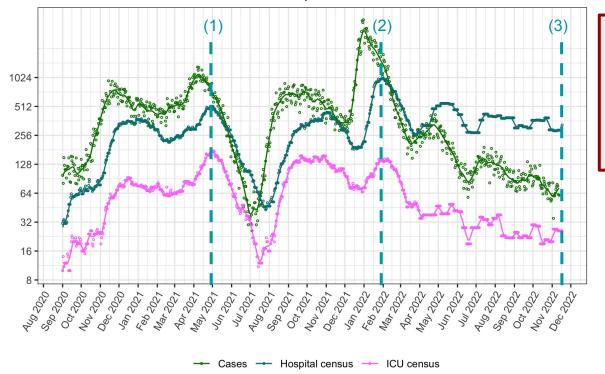
- Current COVID-19 trends in BC
- The rise of BQ.1
- Interpretation of COVID-19 hospital admission data:
 - Evidence for waning of immunity
 - Short-term projections

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

British Columbia COVID-19 cases, 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

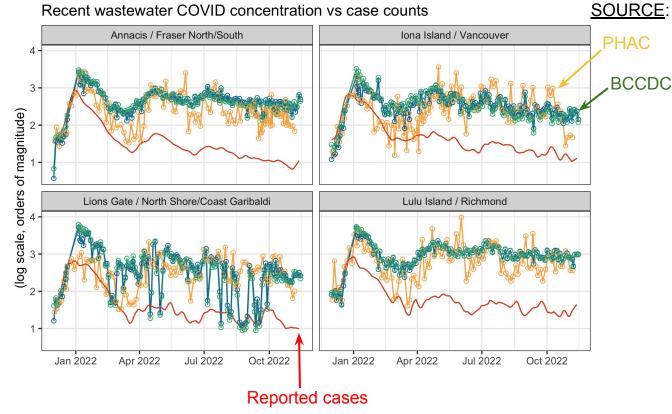
Data: BCCDC for cases, Canada Covid-19 tracker for hospital and ICU census

Wastewater trends in Metro Vancouver

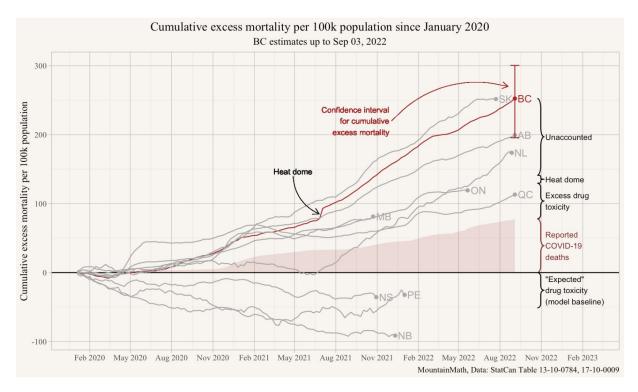
Wastewater signals (shown on a log scale from BCCDC and PHAC) have declined much less than reported cases, with only a slight decline in COVID-19 signals in wastewater since June.

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.



Excess mortality update



Source (J. Bergmann) Data from <u>StatCan</u>. 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 <u>May 19 2022</u> report (slide 9) for more details on excess deaths.

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

There are more unaccounted deaths than counted in the official COVID-19 death toll since the start of the pandemic this accounted for in official statistics.

What about the unaccounted deaths?

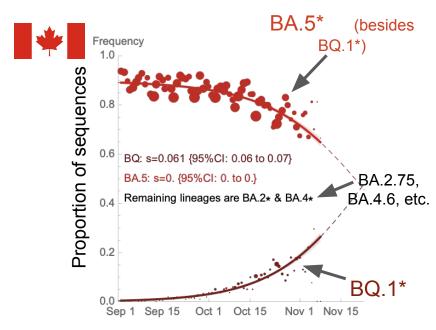
COVID-19 can cause a heightened health risk long after the 30-days currently used in <u>BC</u> to define COVID-related deaths.

For example, Xie et al. studied US veterans and found a 55% higher risk of a major cardiovascular event (e.g., heart attack) in the year after COVID

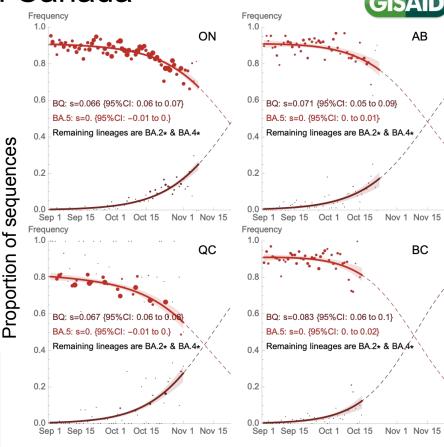
BC is likely substantially undercounting

The rise of BQ.1

Spread of BQ.1* sub-lineages in Canada



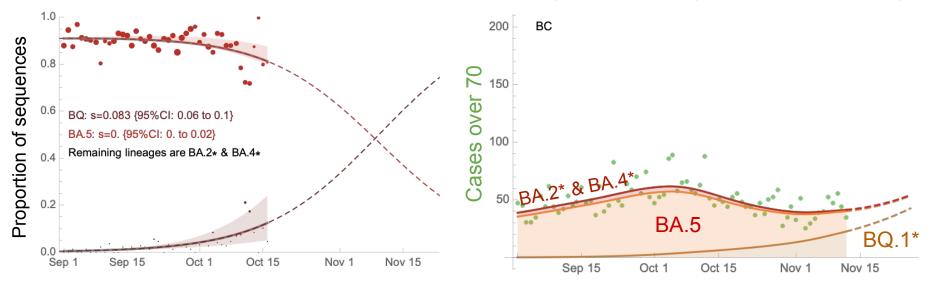
BQ.1* lineages are rising in frequency across Canada with a selective advantage of $s \sim 6\%$ relative to BA.5* or (BA.2*&BA.4*), leading to a current estimated frequency of ~50%.



What does this imply for case numbers?

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

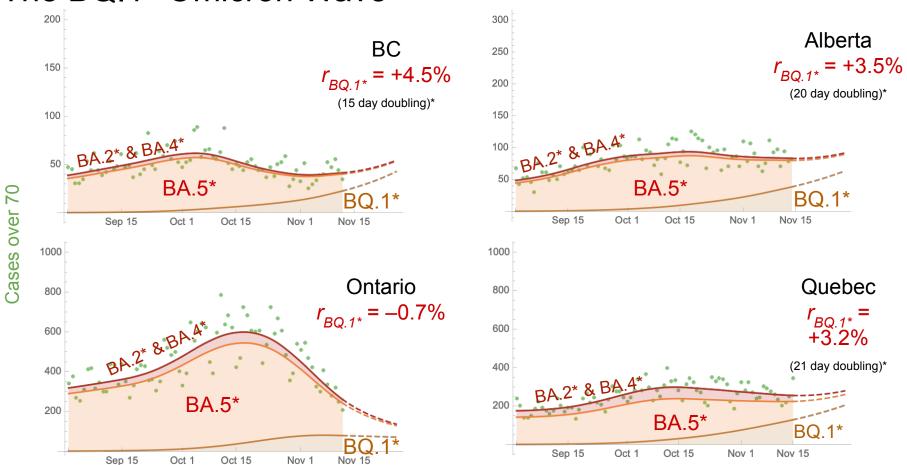
Multiplying by the # of cases in those over 70 allows us to **estimate** growth in numbers of each Omicron sublineage, while reducing extent of underreporting.



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

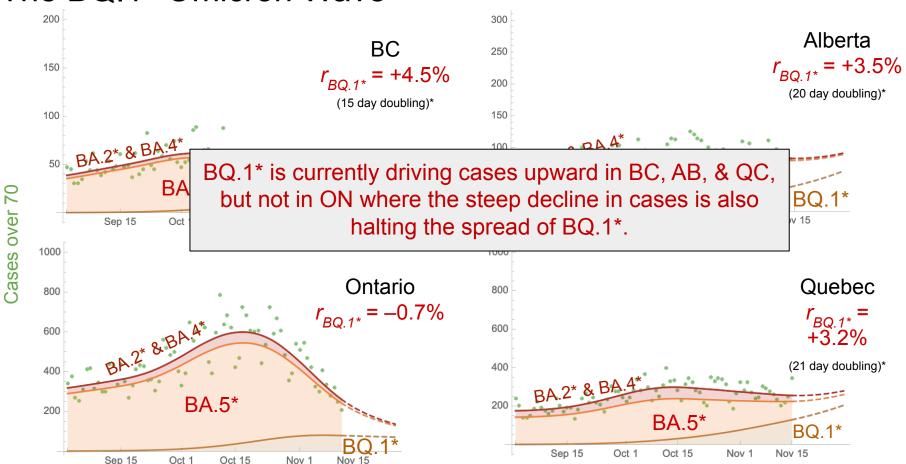
Source (S. Otto) Canadian metadata was downloaded from GISAID for the Omicron GRA clades. A model of selection was fit to the numbers of each type 10 using maximum likelihood based on a trinomial distribution given the expected frequencies on each day. Hessian matrix used to obtain confidence intervals.

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

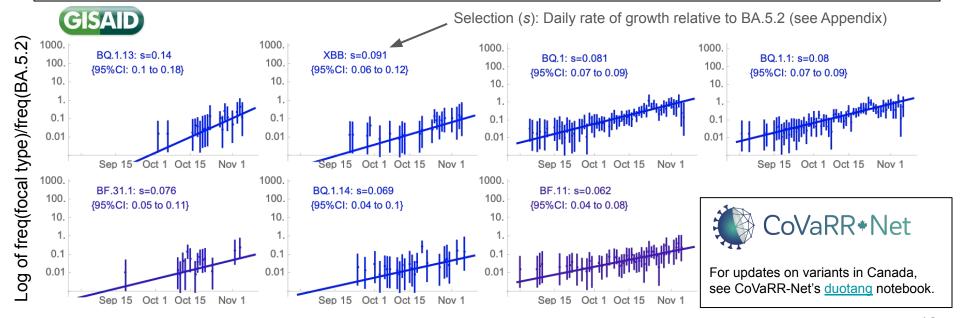


^{*} Instantaneous estimates of growth rate, *r*, and doubling times for BQ.1*. These rates change with changing immunity and with protective health measures, both mandated and voluntary, to reduce transmission (e.g., wearing effective masks, increasing ventilation, and avoiding crowded indoor spaces)

Spread of Omicron sub-lineages in Canada

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 $s \sim 7-14\%$, which all carry mutations known to reduce recognition by antibodies (<u>Cao et al. 2022</u>).



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

Dynamic immunity and new variants

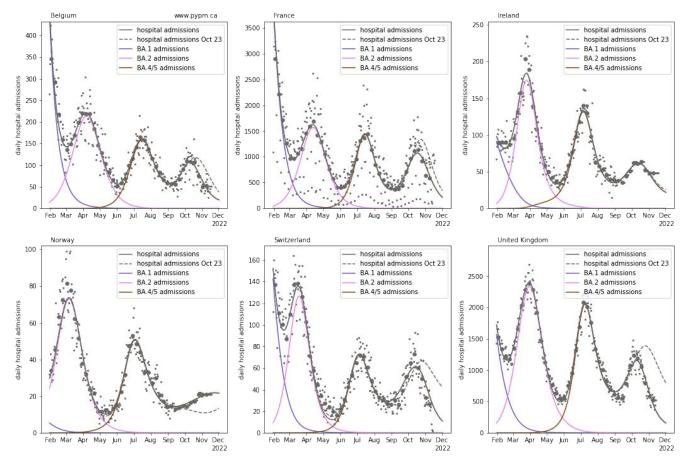
Waning immunity and vaccination

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

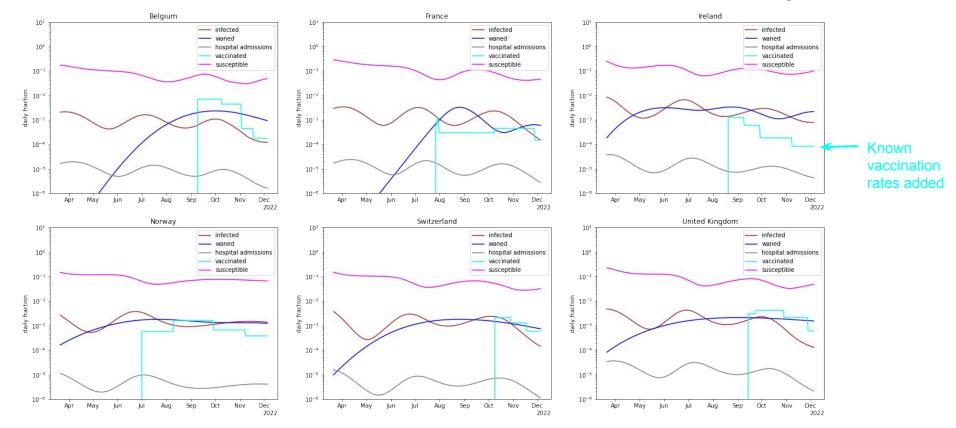


The daily (small dots) and weekly average (large dots) hospital admissions are compared to model fits (solid lines). The models have three Omicron strains (BA.1,BA.2,BA.5), each having constant transmission rate. Immunity parameters were set from the shape of the second wave (BA.2).

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.

Recent vaccination rates, and inferred infection and waning rates



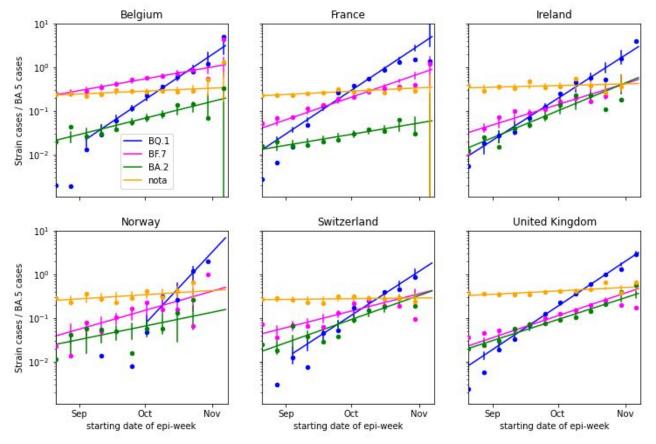
Dynamic population-level immunity and new variants

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 <u>highly dynamic</u> 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

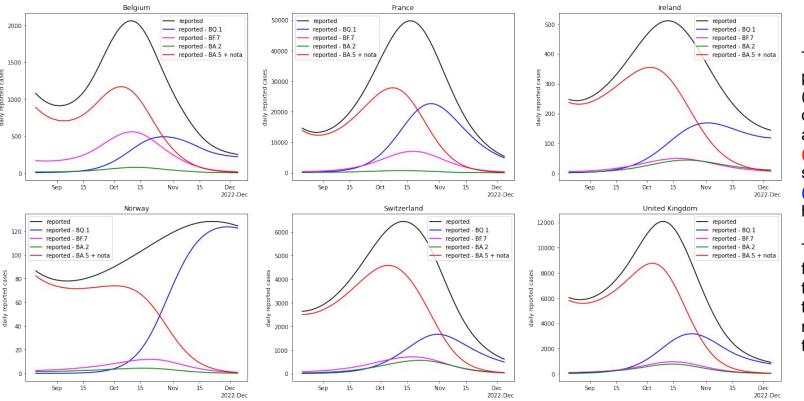


The points show the ratio of cases identified as BQ.1*, BF.7*, BA.2* and none of the above ('nota') with respect to BA.5* cases.

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

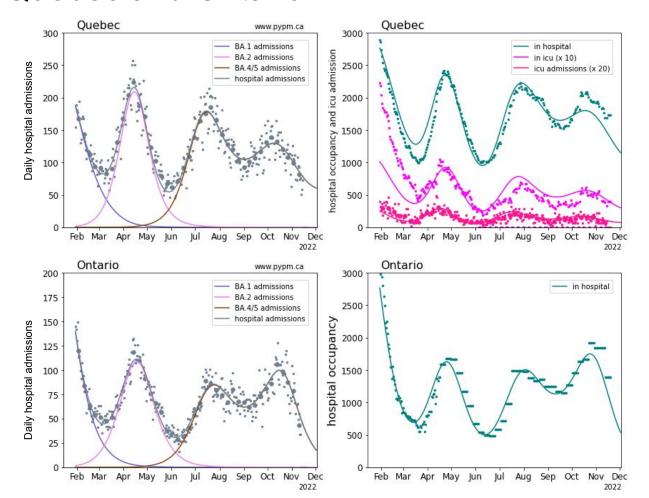


The second BA.5 peak in fall 2022 (cases in black) is driven largely by another BA.5 wave (red), not by the spread of BQ.1 (blue), which happens later.

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.

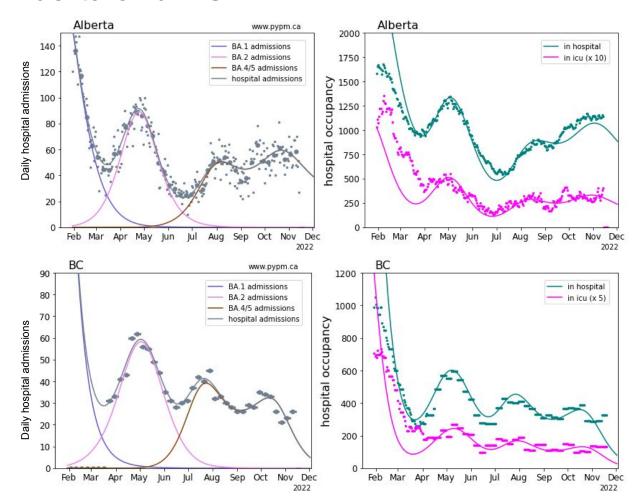
Quebec and Ontario



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.

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).

Key messages

Waves are now being driven more by waning than by variants

- While a large BA.5, and specifically BA.5.2, is the predominant variant across Canada.
- Some sub-variants of BA.5 (e.g., BF.7), as well as sub-variants of BA.2 (esp. BA.2.75 types) and BA.4 (esp. BA.4.6), carry mutations known to better evade antibodies in blood samples and show signs of rising in frequency, but the growth advantages of these sub-variants over BA.5.2 are currently small in Canada.
- 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.

The growth in COVID-19 will reverse once the immunity lost through waning is offset by new immunity, gained by vaccination and/or new infections.

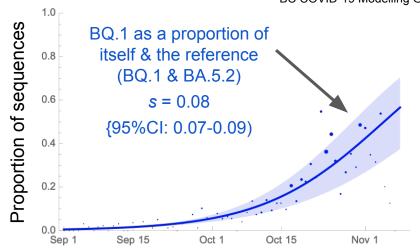
Underreporting the impacts of COVID make it challenging for the public to have a full understanding of current risks. Current infection rates are ~100-fold underreported based on two different serology datasets.

Appendix: Interpreting selection

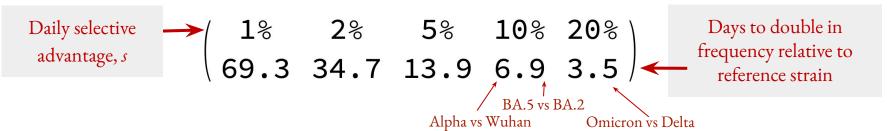
What is selective ("s") and what does it mean?

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)*.

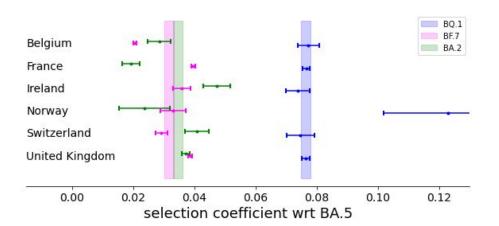
This selective advantage may reflect a higher transmission rate or a greater ability to evade immunity or both.



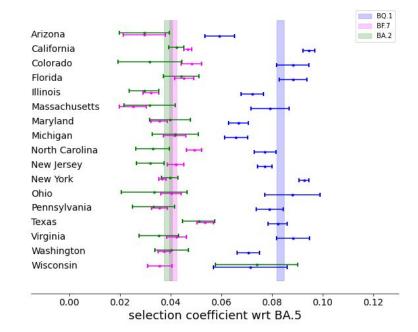
* Selection per day, s, satisfies $p_T = \exp(s T) p_0 / (1 - p_0 + \exp(s T) p_0)$ where p_T is the frequency of a lineage of interest on day T, considering only itself and the reference (e.g., the # of BQ.1 divided by the # of BQ.1 and BA.5.2). s is estimated from the numbers of sequences over time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



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