COVID Model Projections

July 13, 2022

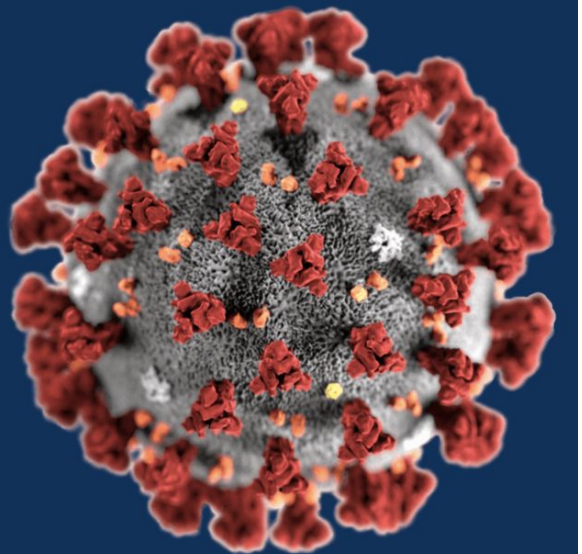
BC COVID-19 Modelling Group

@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

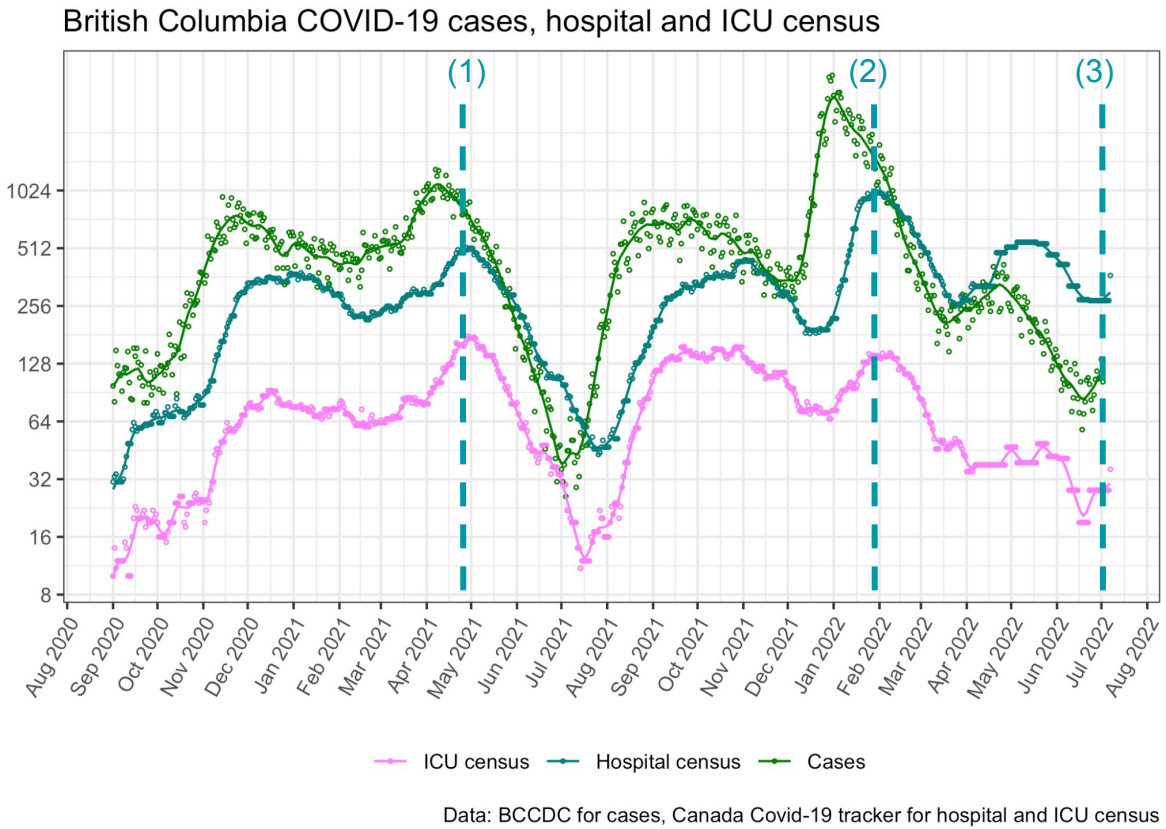
Contents of this report:

- Current COVID-19 trends in BC
- The rise of Omicron BA.4 & BA.5
- Implications of the spread of BA.4 & BA.5 for COVID-19 cases
- Interpretation of COVID-19 hospital admission data: Short-term projections
- Impact of the BA.5 wave

Summary: The next Omicron wave has started in BC and across Canada and is being caused by a faster rate of spread by the BA.5 variant. The number of infections and severe cases leading to hospitalization are expected to rise through July. The height of the BA.5 wave and its impact are challenging to predict.

Current COVID-19 trends in BC

Hospital trends in BC



Reported case numbers are rising, while the number of people in hospital and ICU are no longer declining in BC
(see Appendix for data on admissions and deaths).

Number in hospital with COVID-19:

Pre-Omicron
- (1) Highest = 515 (28 April 2021)

Omicron wave:
- (2) Highest = 1038 (31 January 2022)
- (3) Current = 369

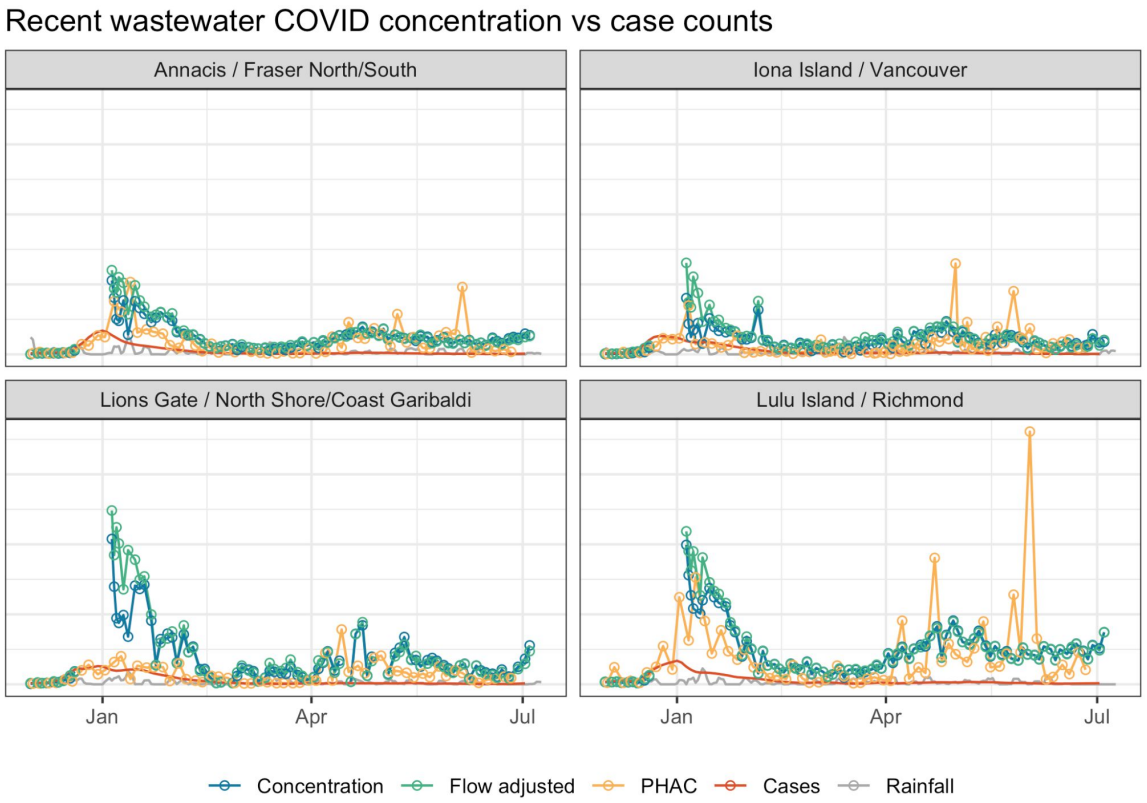
Source (J. von Bergmann) Case data from BC COVID-19 Database (http://www.bccdc.ca/health-info/diseases-conditions/covid-19/data). STL trend lines on log scale. How hospitalizations and deaths are attributed to COVID-19 changed in BC on April 2, 2022.

Wastewater trends in Metro Vancouver

Wastewater signals are also showing signs of a rising number of Omicron infections.

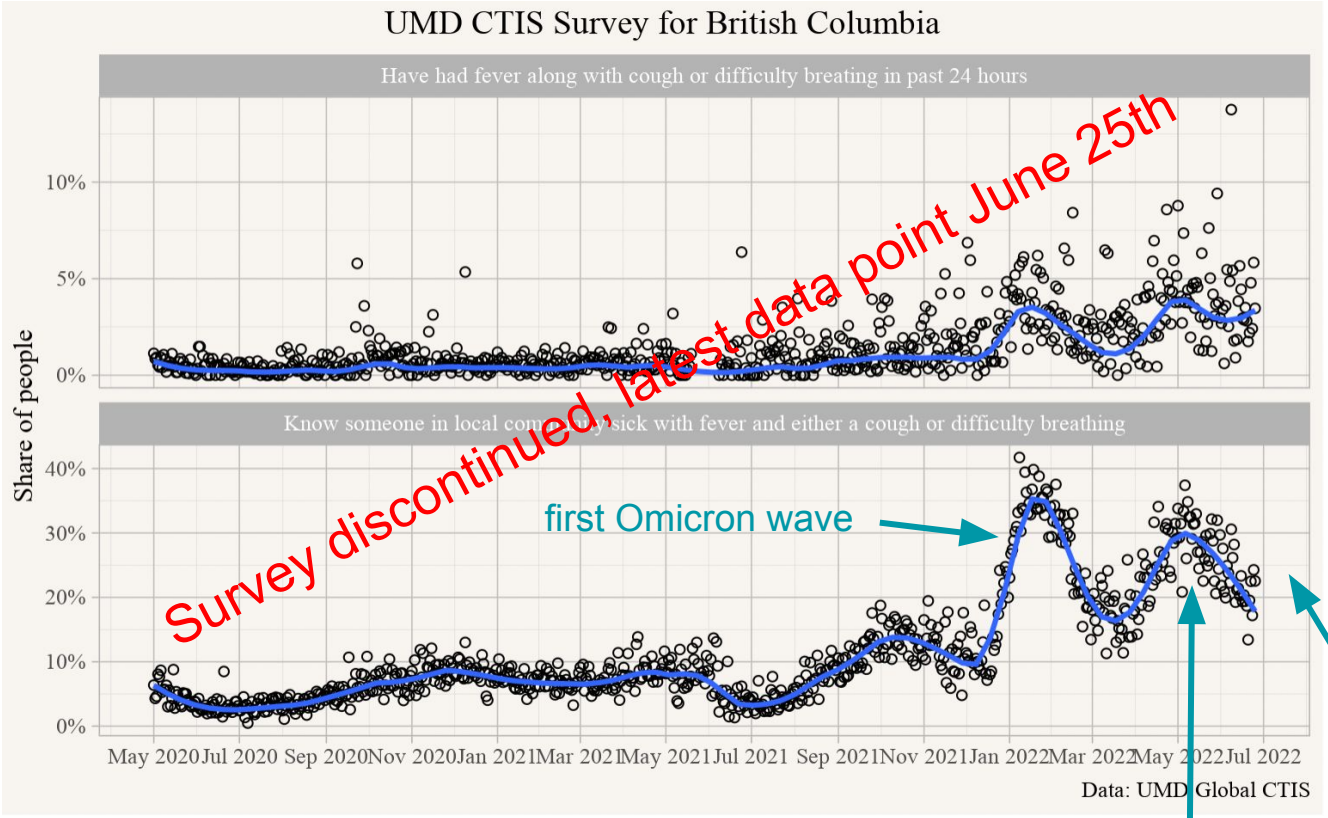
But wastewater data are noisy and best contribute to a joint estimate of infections, along with data on reported cases and hospital admissions.

We request that the province provide the raw data for wastewater and updated hospital admissions across time for a **more timely and unbiased estimate of current COVID-19 infections**.



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

Survey of COVID-19 trends in Metro Vancouver



The COVID-19 Trends and Impact survey, in collaboration with Facebook, was an alternative source of information as individuals shared information about their infections (top) or about others who are infected (bottom) with COVID-19*.

Unfortunately, this social-media data on infections is no longer being collected.

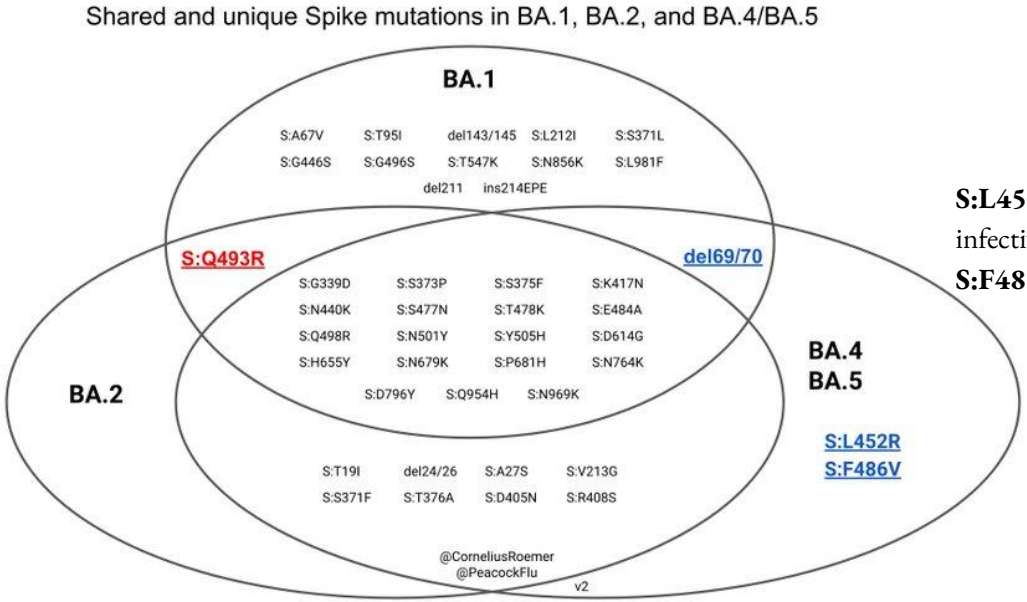
Source (J. Bergmann) Data from COVID-19 Trends and Impact survey.

The Rise of Omicron BA.4 & BA.5

Omicron lineages BA.4 and BA.5

What is driving this rise in cases? The more rapid spread of BA.4 and particularly BA.5.

BA.4 and BA.5 are sub-lineages of Omicron that share many mutations with BA.2 (diagram shows shared mutations in the spike protein). The additional changes in spike ("S:") have previously been associated with increased infectivity and immune evasion.



S:L452R - increased ACE2 binding and infectivity; reduced antibody recognition

S:F486R - a key site for evasion of antibodies

Tegally et al. (2022)

Source: Diagram of spike mutations distinguishing Omicron lineages from Cornelius Roemer.

Omicron Sub-Lineages

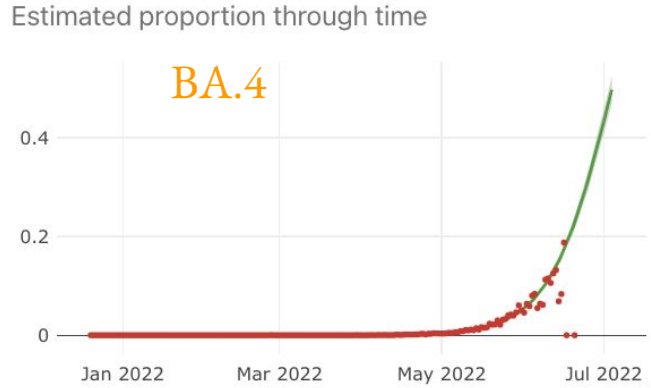
covSPECTRUM
Enabled by data from GISAID

Global proportion

Early data from South Africa suggests an 8% per day selective advantage for BA.4 and 12% for BA.5 (Tegally et al. 2022), relative to BA.2. Similar rates of spread are observed across the United States (see Appendix).

Faster spread may result from a combination of **higher inherent transmissibility** and **immune evasion** (Khan et al. 2022; Hachmann et al.).

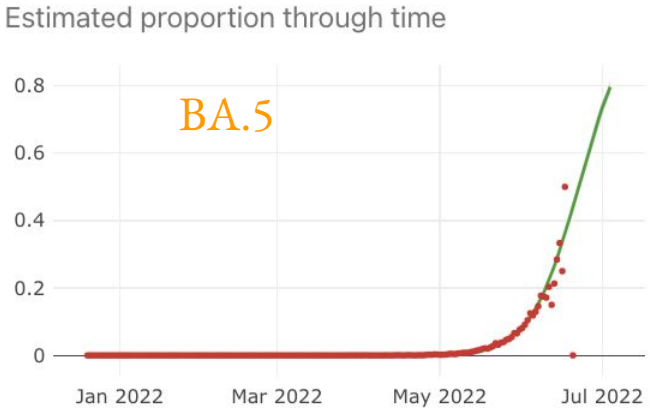
Together, BA.4 & BA.5 comprise ~80% of global sequences [July 8 covSPECTRUM]



s = 9% per day

83% per week
Current adv.

79-86%
Confidence int.



s = 12% per day

122% per week
Current adv.

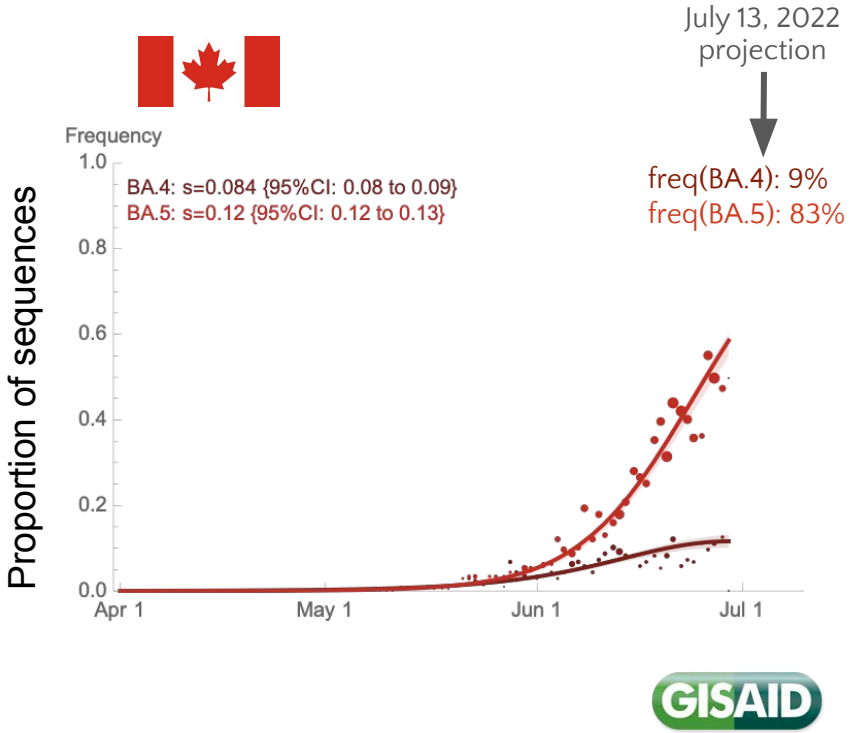
117-126%
Confidence int.

Spread of Omicron sub-lineages in Canada

→ BA.4 is spreading rapidly at a rate of s=8.4% per day relative to BA.2#

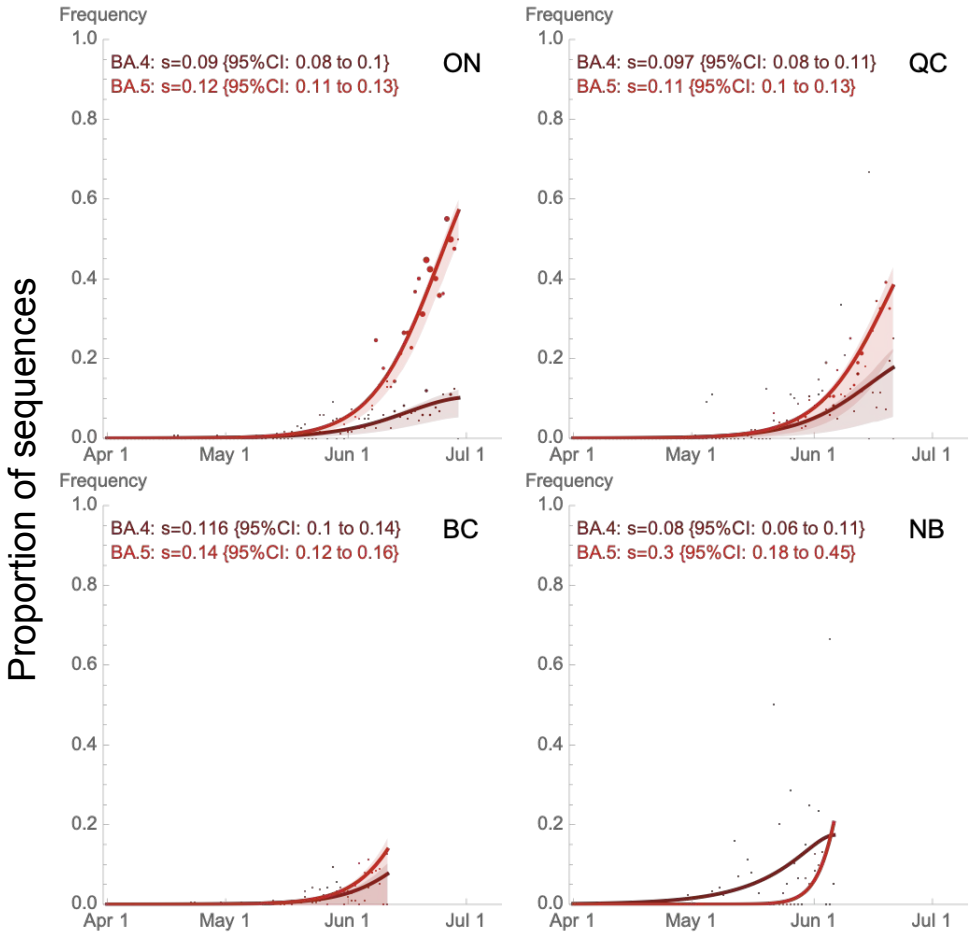
→ BA.5 is spreading even faster with s=12% per day relative to BA.2#

These lineages now dominate the COVID-19 picture in Canada, with BA.5 predicted to account for >80% of cases today.

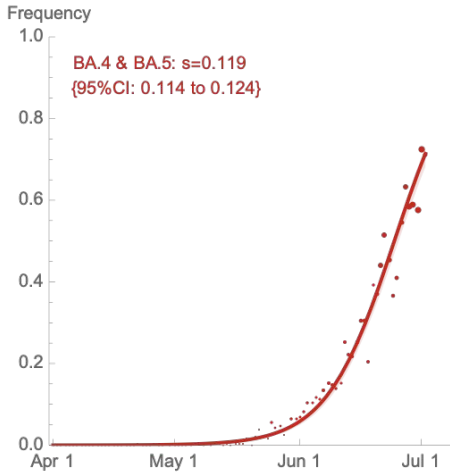


Source (S. Otto) Canadian metadata was downloaded from GISAID for the Omicron GRA clades (Alberta sequences were removed as AB first identifies variants and preferentially sequences some subtypes). A model of selection was fit to the numbers of each type using maximum likelihood based on a trinomial distribution given the expected frequencies on each day. Hessian matrix used to obtain confidence intervals.

Spread of Omicron sub-lineages in Canada



Alberta analysed separately (based on PCR typing combining recent S:69/70del as BA.4 & BA.5)



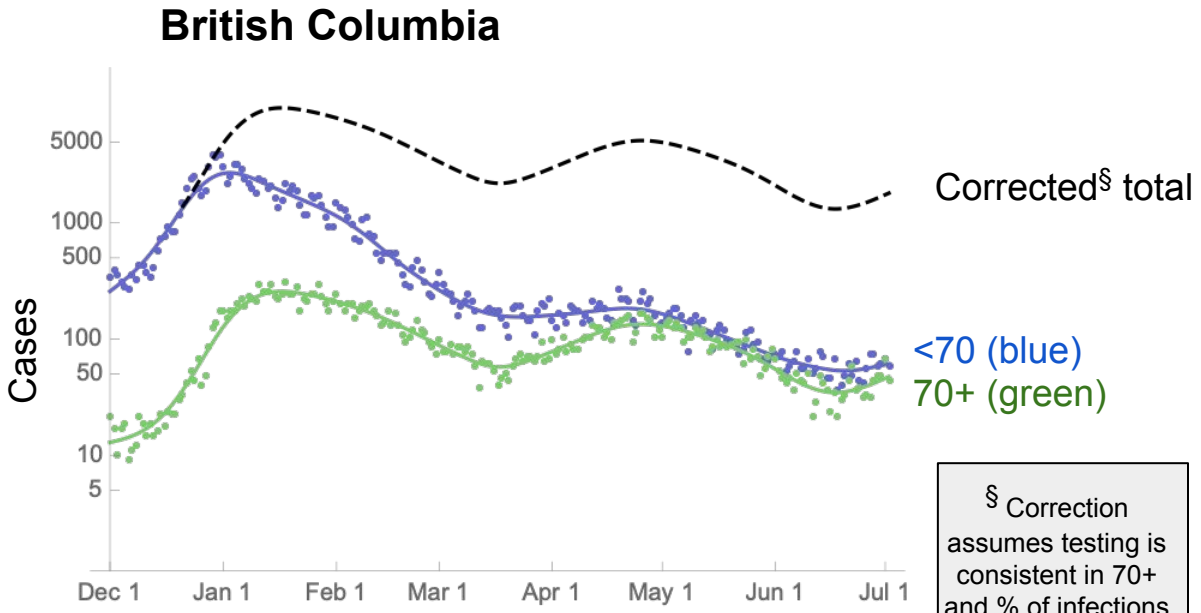
Provinces show similar estimates of selective spread where data are sufficient.

Implications of the spread of BA.4 & BA.5 for COVID-19 cases

What does this imply for case numbers?

We can use case numbers reported in individuals aged 70+ (green) to assess trends, as this age group has been more consistently tested.

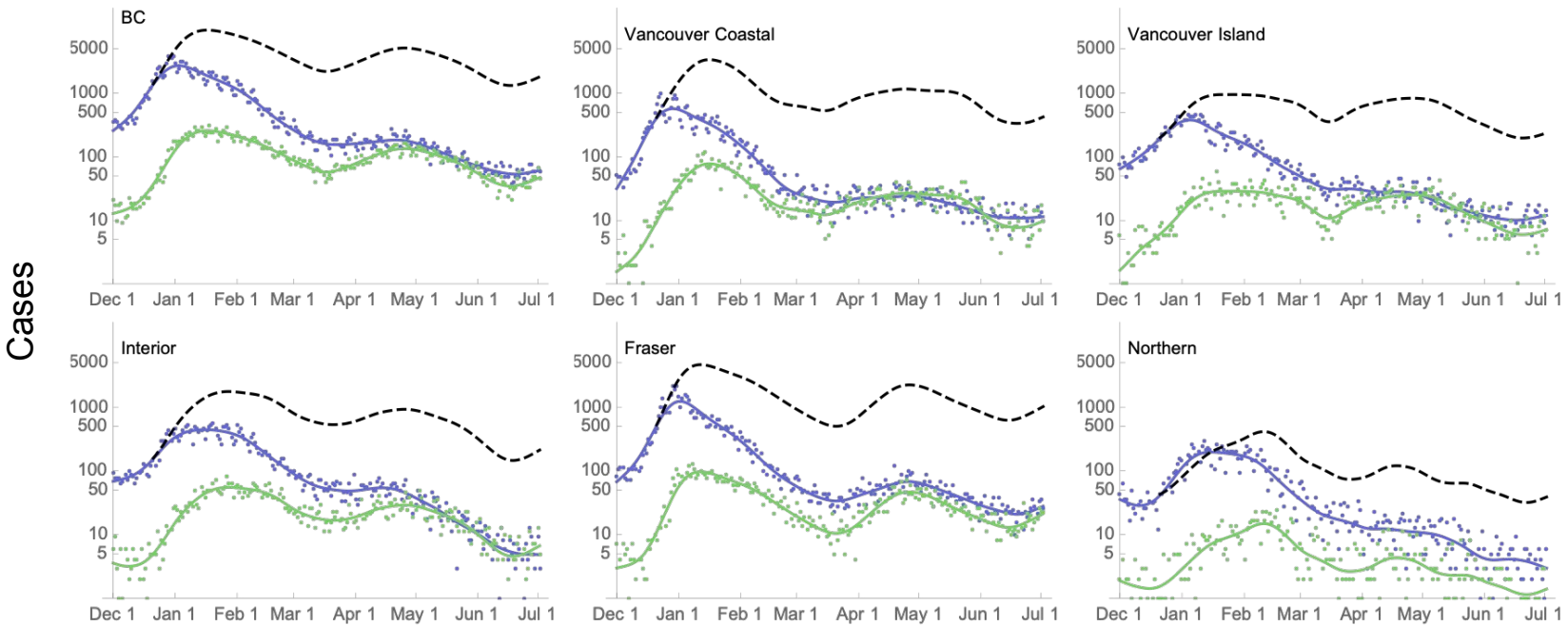
Cases among those 70+ in age are rising **significantly***.



§ Correction assumes testing is consistent in 70+ and % of infections in this age class has been stable.

Source (S. Otto) New cases per day in 10-year age groups were downloaded from the **BCCDC COVID-19 data portal**. Cubic spline fits to log-case data were obtained (curves) for those 70+ (green) or <70 (blue). *Linear regression through log case counts among 70+ from last 14 days of data.

BC: Age-corrected case counts

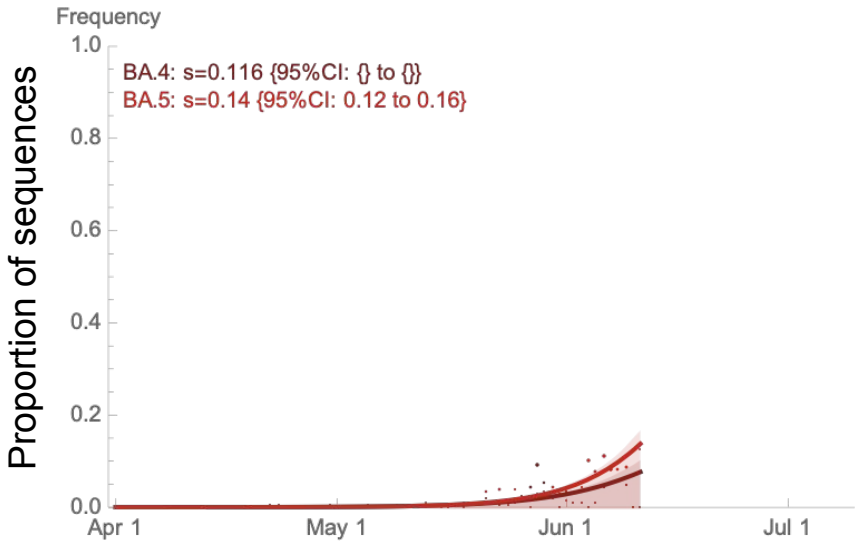


→ Reported cases among those aged 70+ (green) are rising across the province. Black curves provide a rough guide of total cases, had testing continued in all age groups§.

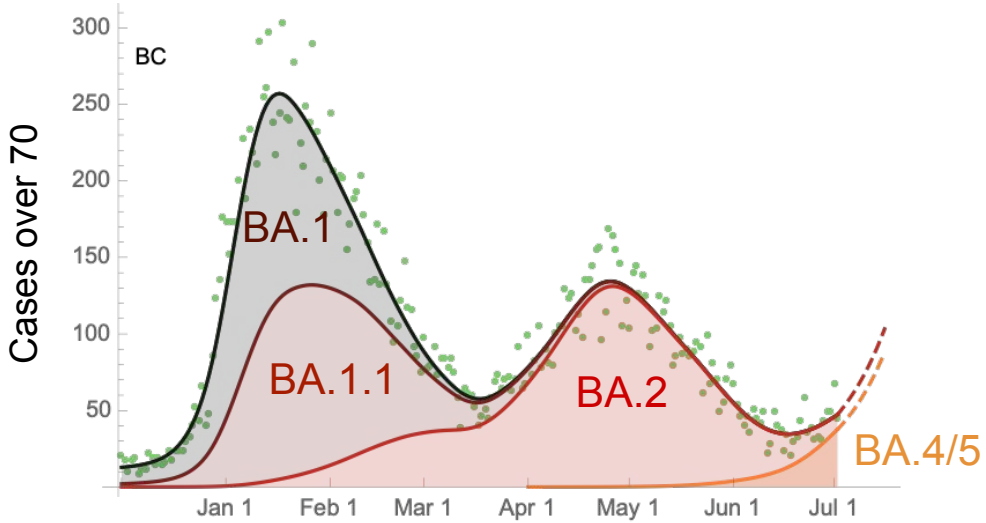
Source (S. Otto) New cases per day in 10-year age groups were downloaded from the **BCCDC COVID-19 data portal**. Cubic spline fits to log-case data were obtained (curve) and estimates for those <70 obtained by applying the fits for those 70+, shifted up to match the projection for that age class on 21 December 2022 when testing limits were initially reached in many parts of the province.

What does this imply for case numbers?

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



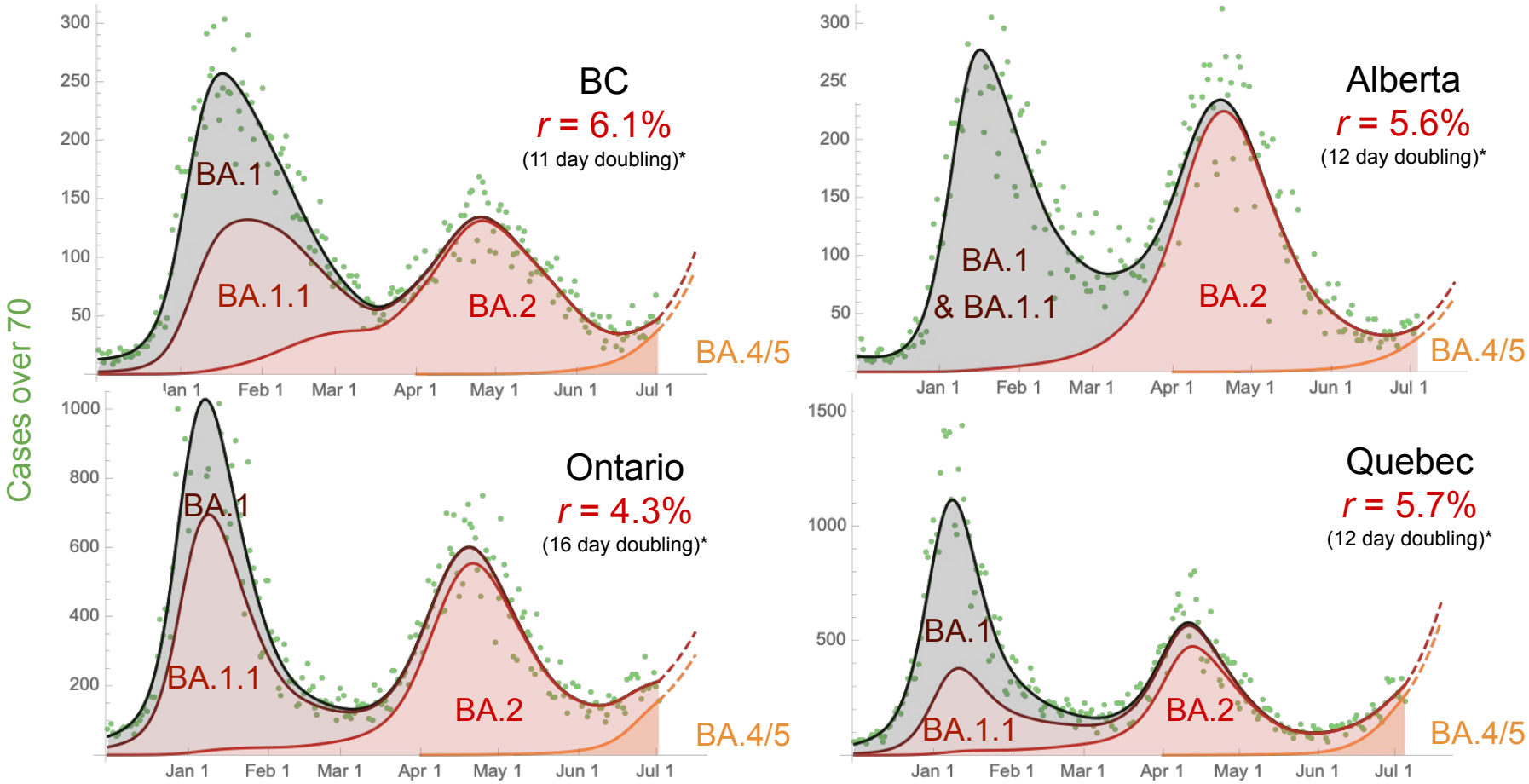
Multiplying by the # of cases in those over 70 allows us to **estimate** growth in numbers of each Omicron sublineage.



→ While numbers of BA.1 and BA.2 are declining, **estimated numbers of BA.4 & BA.5 (grouped together) are rising (*r* = +6.1%) in British Columbia.**

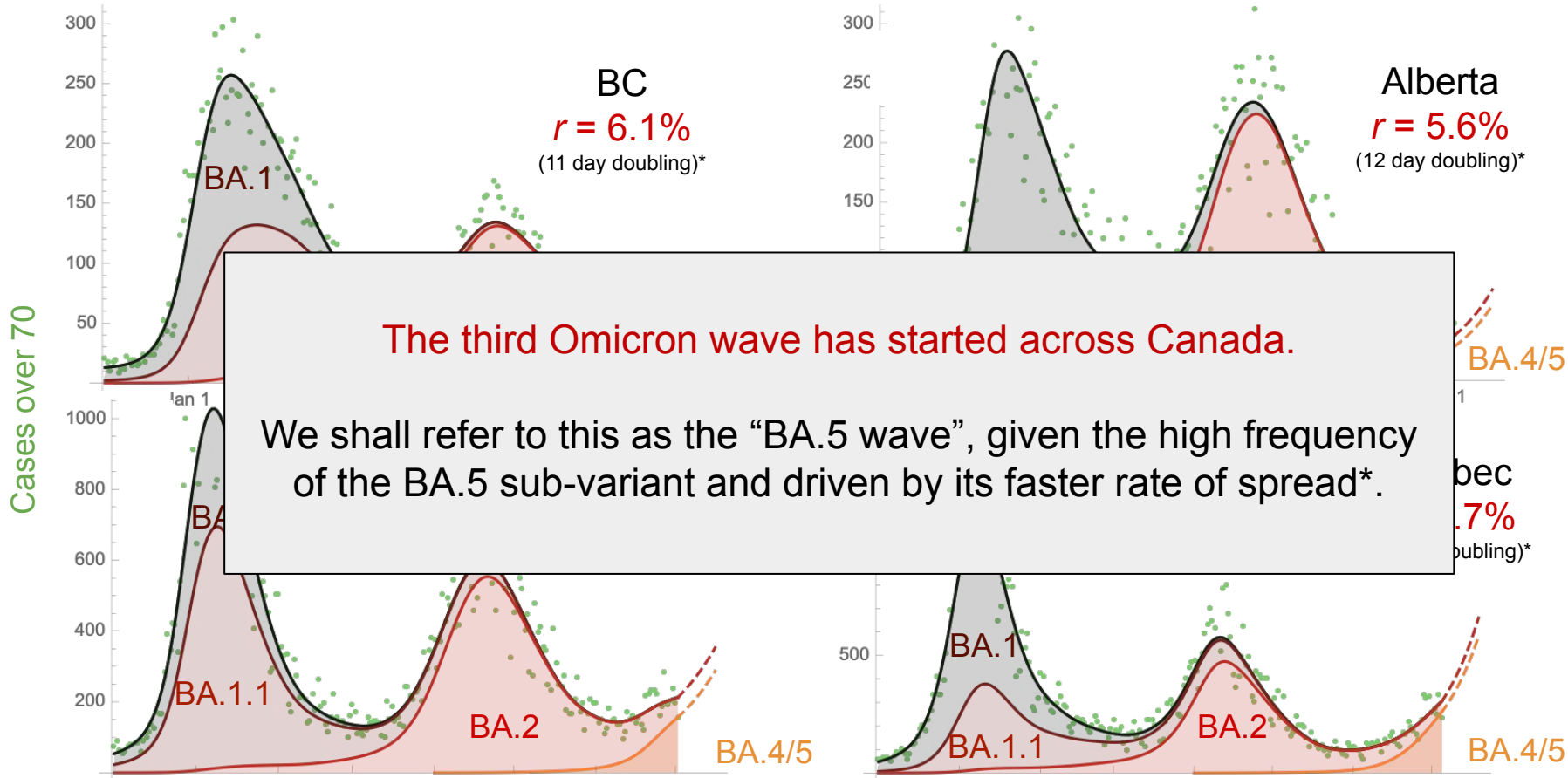
Source (S. Otto) Canadian metadata was downloaded from GISAID for the Omicron GRA clades. A model of selection was fit to the numbers of each type using maximum likelihood based on a trinomial distribution given the expected frequencies on each day. Hessian matrix used to obtain confidence intervals.

The Third Omicron Wave



* Instantaneous estimates of growth rate, *r*, and doubling times for BA.4 & BA.5 (mainly BA.5). 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 Third Omicron Wave

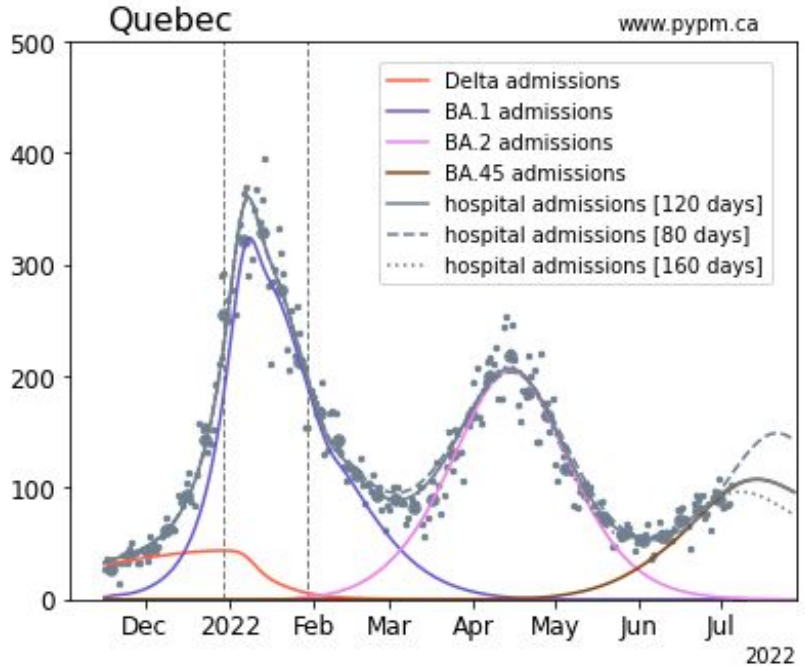


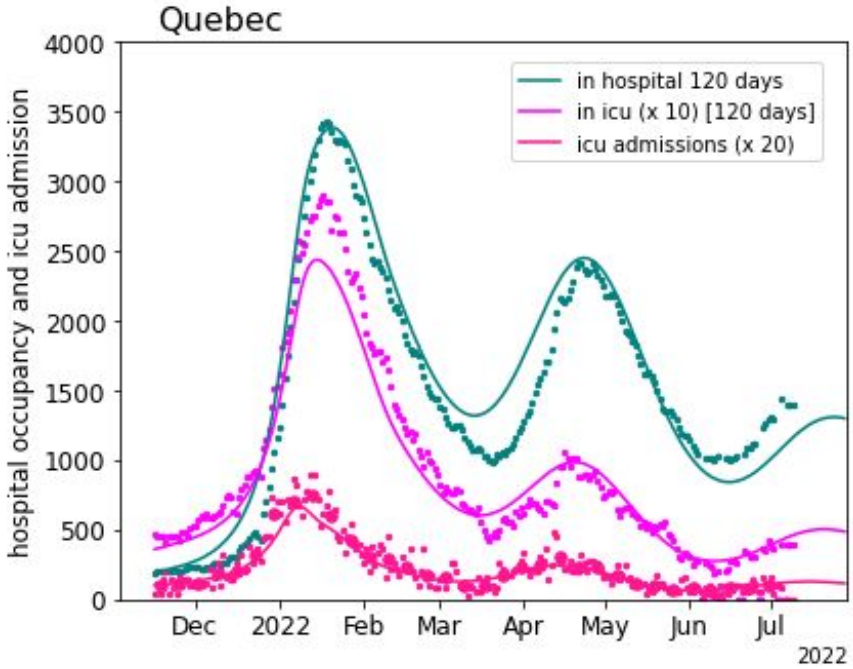
*We predicted that the BA.5 wave would drive a rise in cases around the beginning of July, as observed. These predictions were presented to the Variants of Concern Leadership Group Meeting on June 28, 2022 involving Federal and Provincial Public Health officials (summarized on Twitter).

Interpretation of COVID-19 hospital admission data: Short-term projections

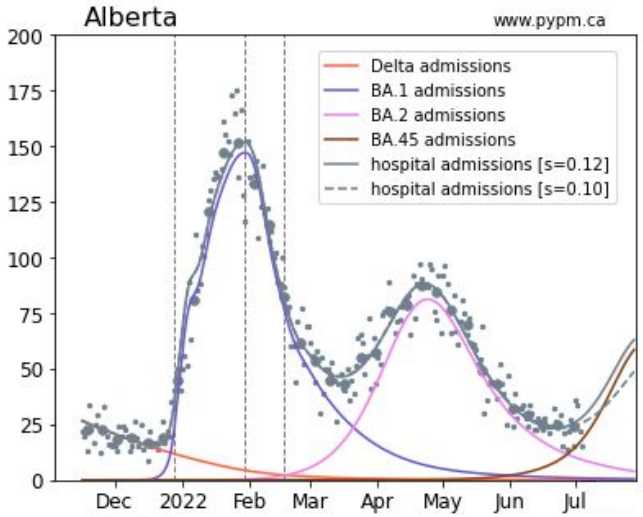
Hospital admissions: Quebec

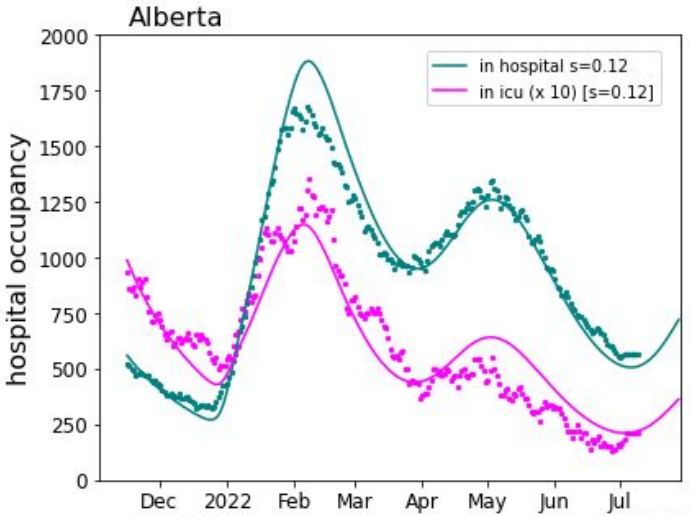
The pypm model was fit to COVID-19 hospital admission data to characterize transmission and population immunity. The model now includes BA.4 and BA.5 (combined and labelled as BA.45). In order to fit recent data, it is necessary to reduce immunity gained from Omicron infections. The effect is modelled with shorter mean waning times (80, 120, 160 days shown).

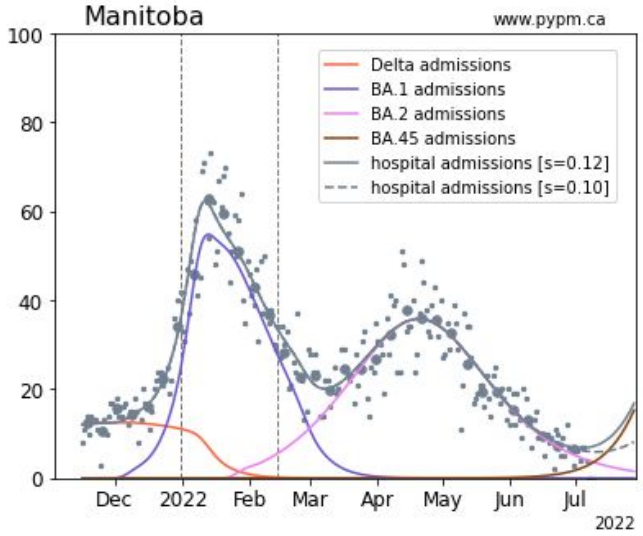


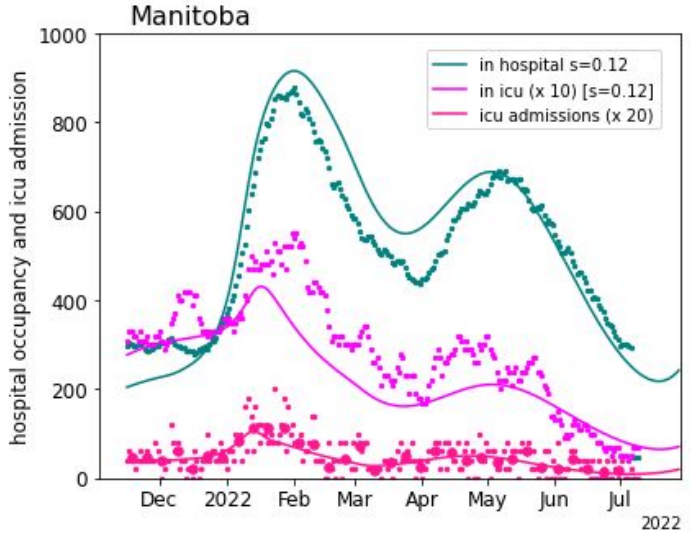


Source (D. Karlen) As in previous reports, the model has no age structure. Three Omicron strains are included with all evading 80% of natural immunity from previous strains and 80% of 2 dose vaccinations. Booster doses are assumed to provide 80% effectiveness against infection. Omicron infections are assumed to produce symptoms with a probability of 60% of that for previous strains. The probability that symptoms lead to hospitalization is 45% of that for previous strains. Vertical lines show fitted dates for transmission rate changes. The larger dots show weekly averages. Fit selection coefficient for BA.45 wrt BA.2 is 0.12 per/day.









Alberta and Manitoba Projections

BA.4 & BA.5 are dominant about one month later than in Quebec.

Omicron natural immunity waning set at a mean of 120 days in these models.

Two selection coefficients shown (0.12 and 0.1).

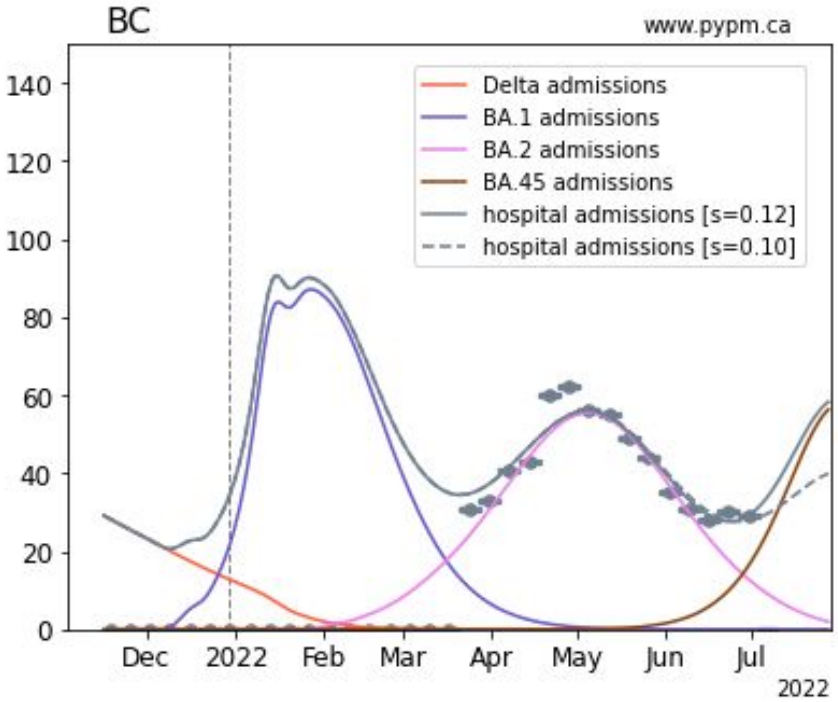
Hospital and ICU occupancy curves (right figures) assume no changes to length of hospital stays over period shown.

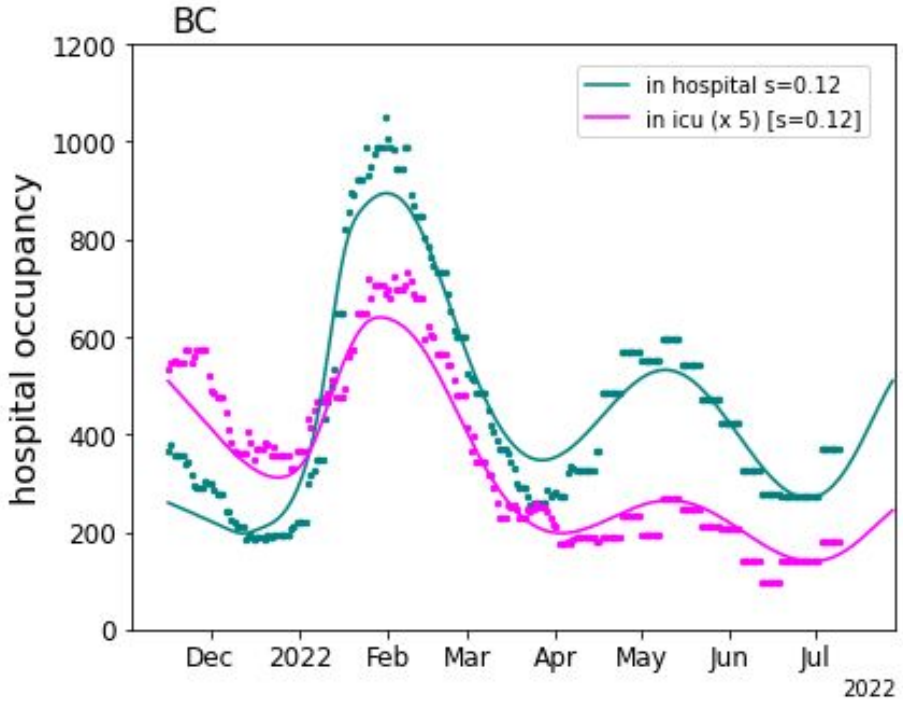
Hospital admissions expected to start growing in the near future.

Hospital projection for BC

Model is fit to corrected hospital admission data from BCCDC weekly reports (available since mid-March)

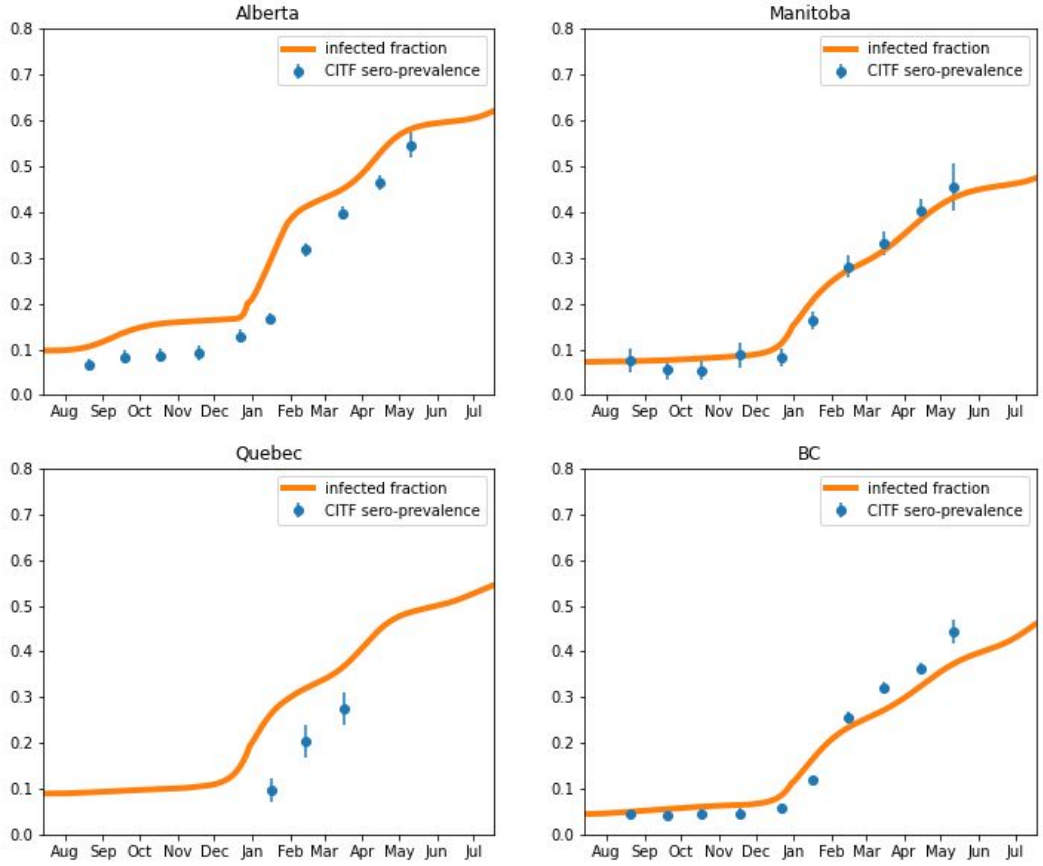
- Our assessment in our May 18 report that hospital admission had peaked was correct.





Source (D. Karlen) As in previous reports, the model has no age structure. Three Omicron strains are included with all evading 80% of natural immunity from previous strains and 80% of 2 dose vaccinations. Booster doses are assumed to provide 80% effectiveness against infection. Omicron infections are assumed to produce symptoms with a probability of 60% of that for previous strains. The probability that symptoms lead to hospitalization is 35% of that for previous strains. Vertical lines show fitted dates for transmission rate changes. The larger dots show weekly average. Mean Omicron natural immunity waning is set at 120 days.

Infected fraction of the population (models vs data)



A significant contribution to population immunity has come from Omicron infections.

Figures on the left compare model estimates of the fraction of the population ever infected by COVID-19 (yellow curves) to data collected by the CITF representing infection rates in blood donors.

Models for Alberta and Quebec appear to have higher infected fractions than seen in data.

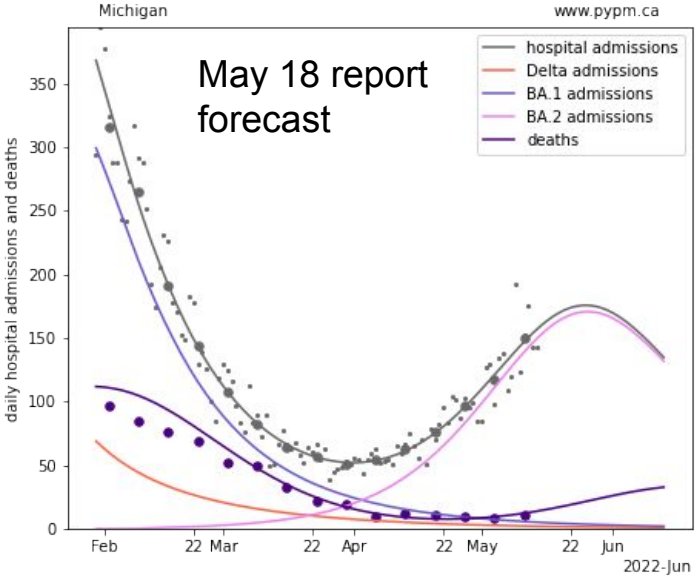
Source (D. Karlen) Model curves are from the updated models shown in the previous pages.

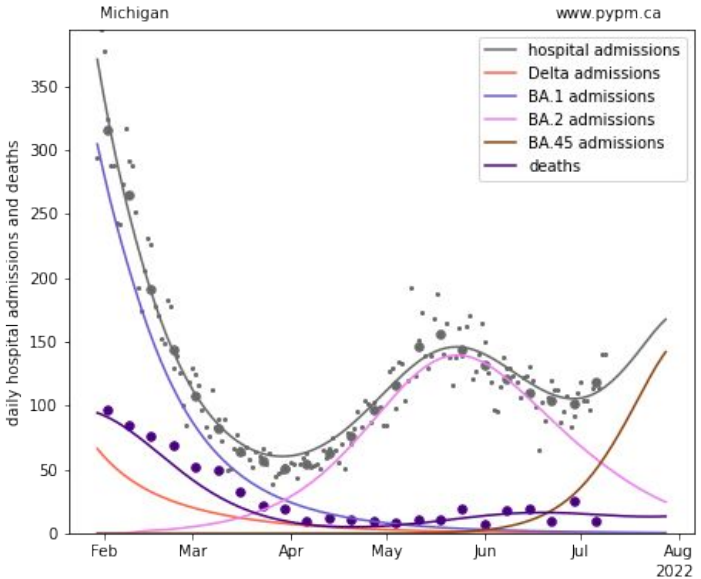
Hospital projections in the USA

Unlike BC, AB, MB, and QC, in most US states, BA.4/5 arrived while BA.2 was still growing

See www.pypm.ca for each state. Some states, like Michigan, have a distinct wave for BA.4/5.

- Left: Michigan forecast from May 18 report. Correctly predicted the BA.2 turnover, confirming immunity model.
- Right: Current Michigan forecast incorporates new strains.





Source (D. Karlen) As in previous reports, the model has no age structure. Omicron strains evade 80% of natural immunity from previous strains and 80% of 2 dose vaccinations. Booster doses are assumed to provide 80% effectiveness against infection. Omicron infections are assumed to produce symptoms with a probability of 60% of that for previous strains. The probability that symptoms lead to hospitalization is 30% of that for previous strains. No transmission rate changes occur during the period shown. Non-exponential behaviour (turn-overs) are due to growth in immunity. The larger dots show weekly averages. See: https://pypm.github.io/home/docs/studies/usa20220710/

Impact of the BA.5 wave

The Third Omicron Wave

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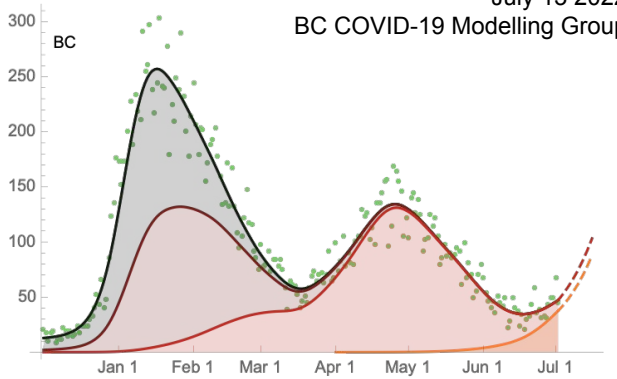


The **height and impact of the BA.5 wave are challenging to predict**, depending on the interplay of several factors.

1. **Antibody levels** caused by the combination of vaccines and previous Omicron infections
2. **Efficacy of neutralizing antibodies** preventing infection against BA.4 & BA.5
3. **Risk-reduction measures** preventing infections via NPI measures and boosters

} Infections

The subsequent **impact on severe disease**, hospitalizations, and deaths depends on:

4. **Ability to clear infections** due to existing cellular & humoral immunity
5. **Virulence** of BA.4 & BA.5

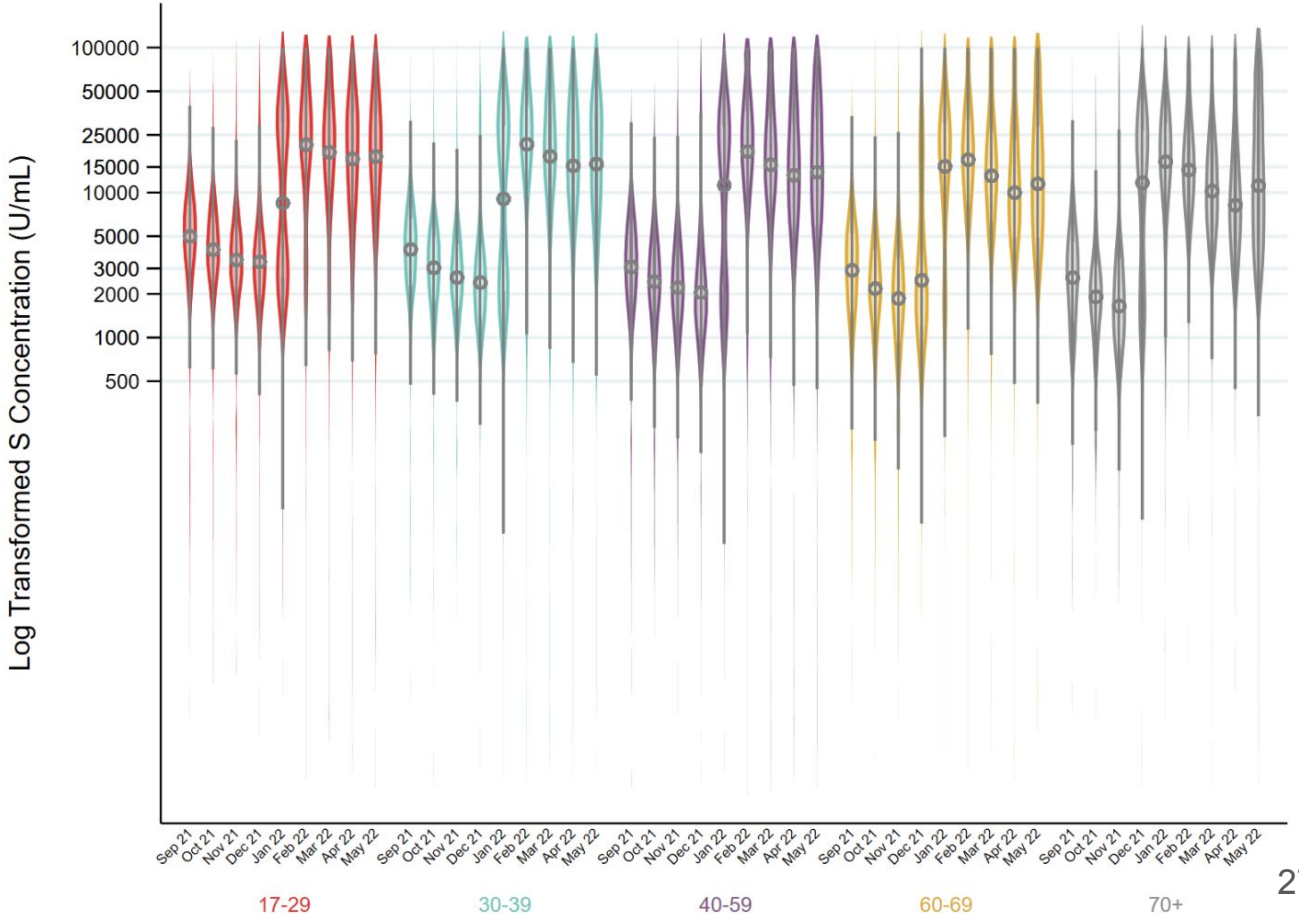
} Disease

Factors determining the impact of the BA.5 wave

1. Antibody levels

The COVID-19 Immunity Task Force & Canadian Blood Services data finds high standing levels of spike antibodies among adults in all age groups in Canada (blood donations through mid-May 2022), protecting against infection.

Good news



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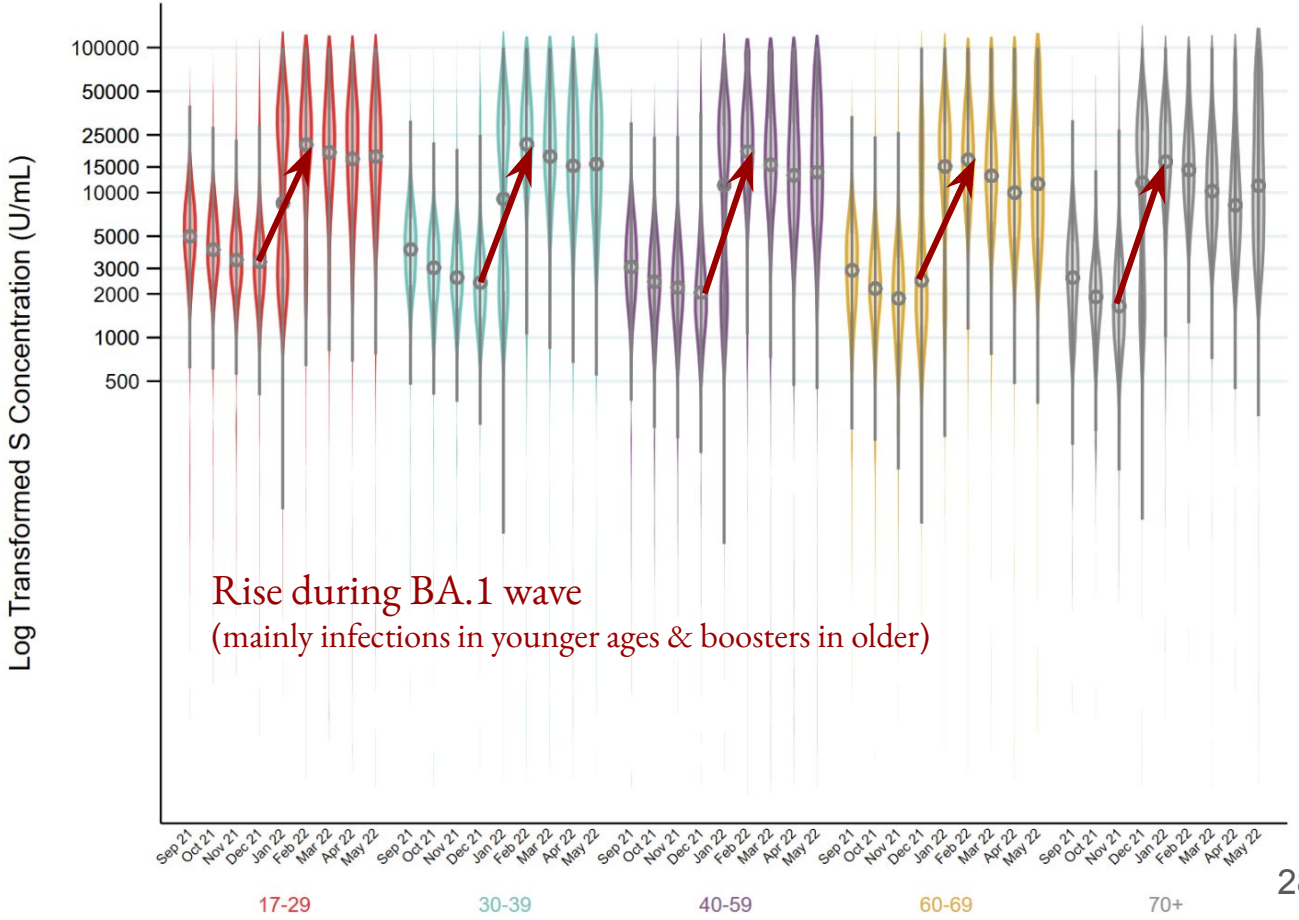

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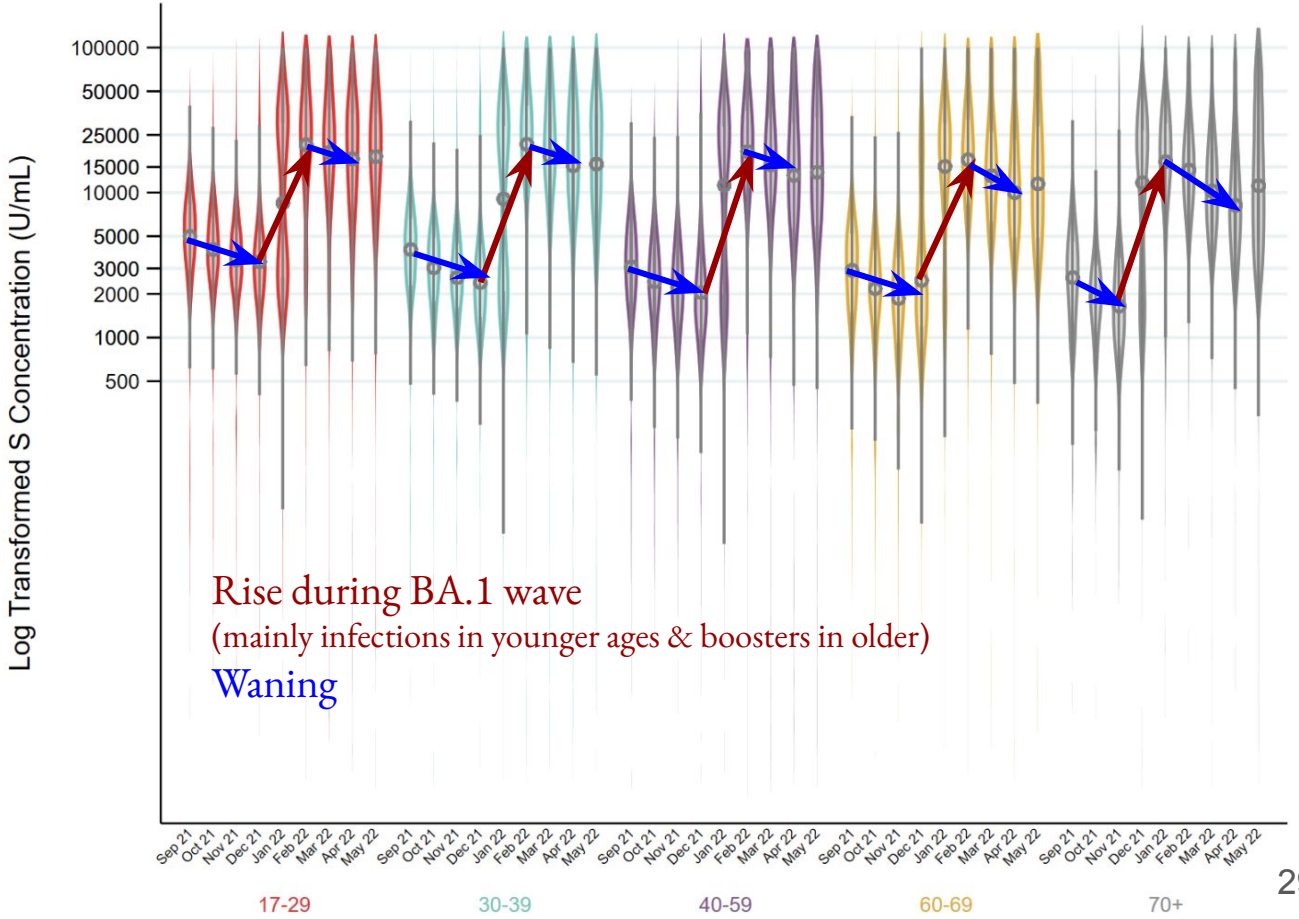

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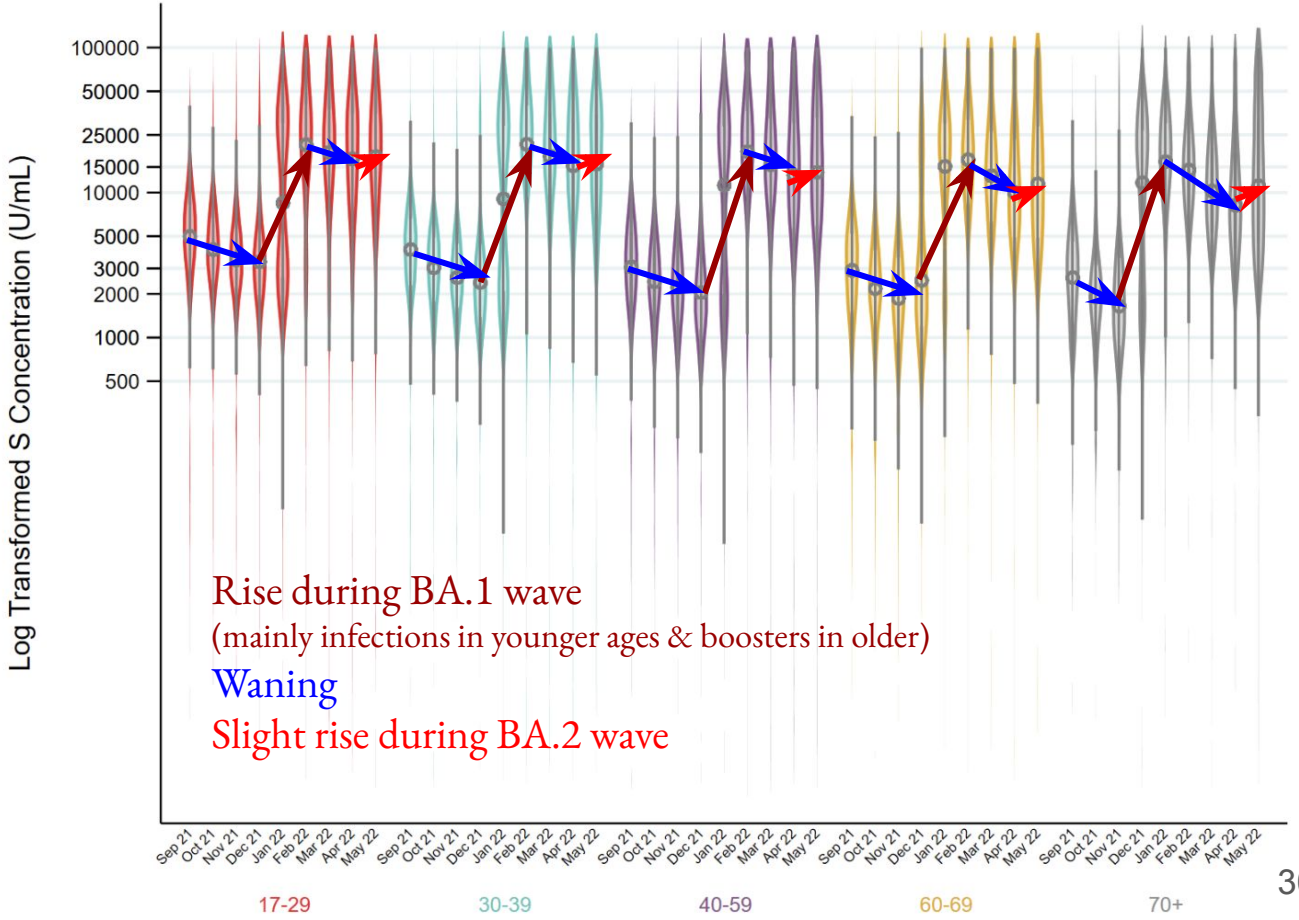
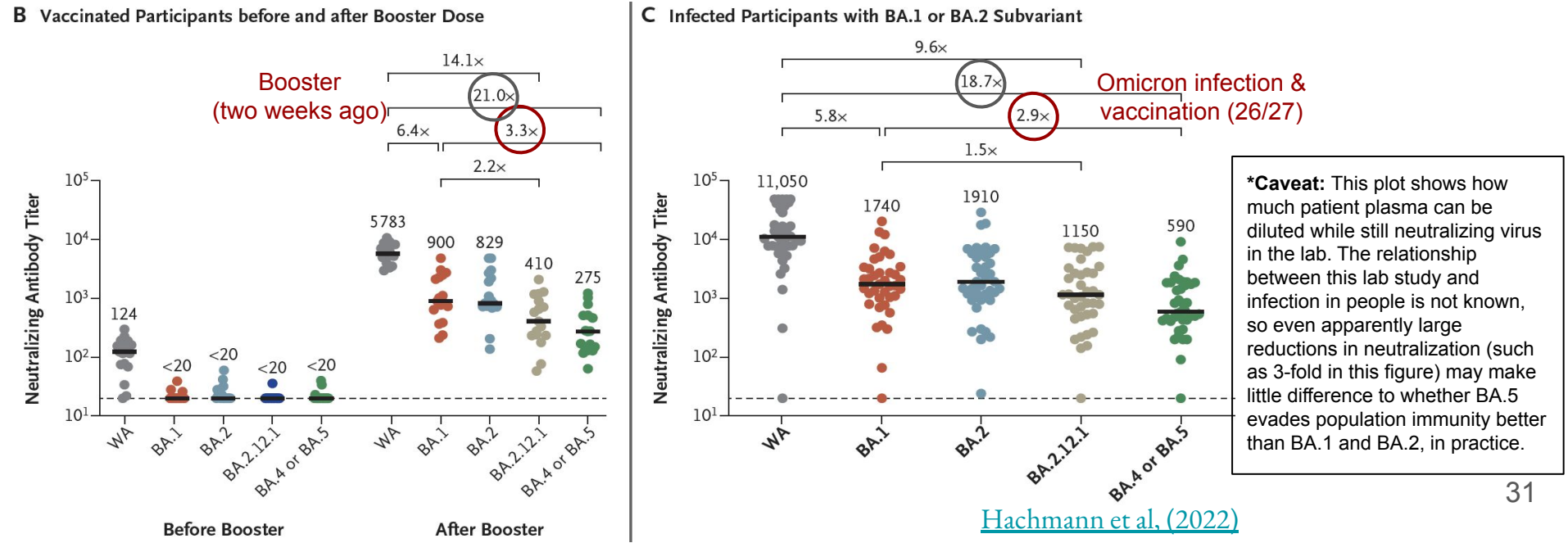


Factors determining the impact of the BA.5 wave

2. Efficacy of neutralizing antibodies: Lab studies suggest that the ability of these antibodies to neutralize SARS-CoV-2 and prevent infection is substantially compromised for BA.4 & BA.5.

- Circled numbers show protection from boosters (left) and recent infections on top of vaccines (right) against BA.4/5 relative to BA.1 (red: ~3-fold less) or relative to the Wuhan strain (gray: ~20-fold less), based on lab assays*.



***Caveat:** This plot shows how much patient plasma can be diluted while still neutralizing virus in the lab. The relationship between this lab study and infection in people is not known, so even apparently large reductions in neutralization (such as 3-fold in this figure) may make little difference to whether BA.5 evades population immunity better than BA.1 and BA.2, in practice.

Hachmann et al, (2022)

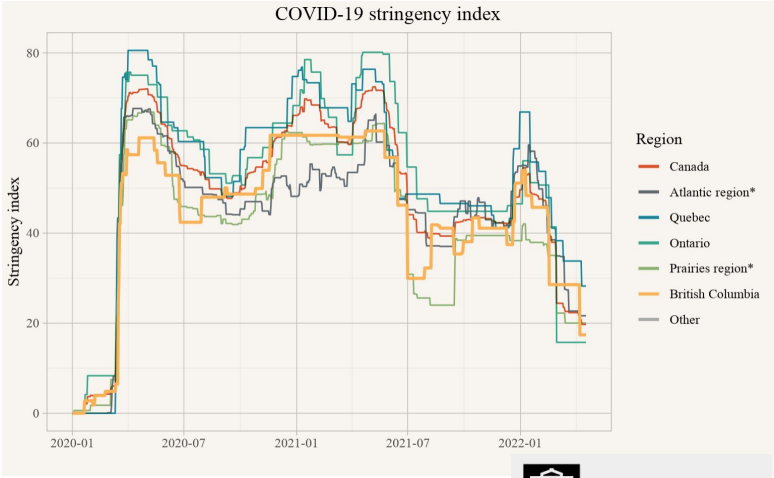
Factors determining the impact of the BA.5 wave

3. Risk-reduction measures:

Risk-reduction behaviours (such as effective masking and seeking well-ventilated spaces) reduce individual risk.

Risk-reducing behaviour can have more effect during the upswing of a wave, rather than during a downturn, because each infection averted prevents more subsequent infections during this phase of the wave.

The stringency of public health measures are at their lowest level since the pandemic began, with little appetite to mandate protections. However, collective public efforts are powerful. For example, mask-wearing behaviour has been shown to have more to do with social expectations and norms than with mandates (Leech et al. 2022).

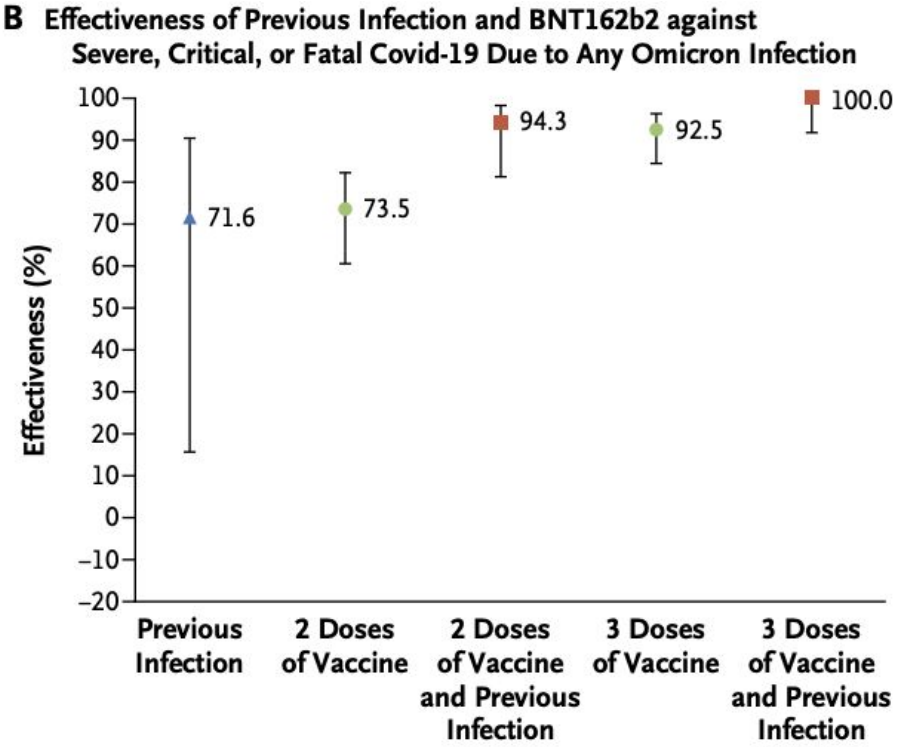


Factors determining the impact of the BA.5 wave

4. Clearing infections: Vaccines protect against severe disease by building memory T and B cells that make more antibodies and kill infected cells once virus is detected.

Altarawneh et al. studied protection against severe disease caused by Omicron BA.1 and BA.2. Relative to unvaccinated people, they found that people who had a primary (two-dose) vaccine series were ~3x less likely to experience severe disease. This relative level of protection rose to ~10x with a (at the time) recent booster dose, or with vaccines plus infection.

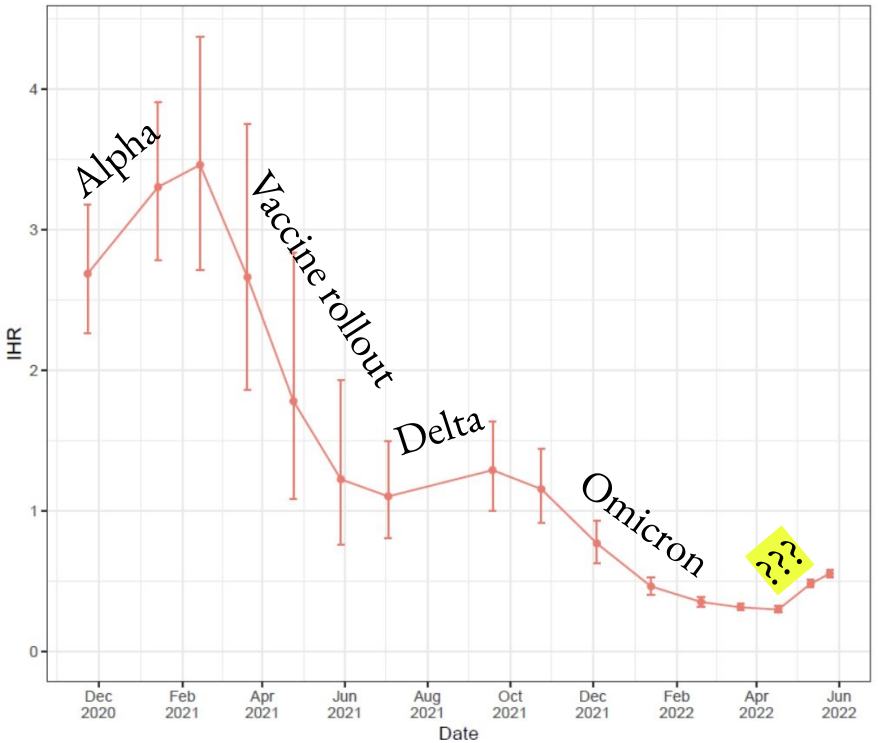
We don't yet have comparable data for BA.5.



Factors determining the impact of the BA.5 wave

5. Virulence: The relative severity of BA.5 is not known. Early indications from other countries suggest it is similar to, but potentially slightly more severe than, BA.1 and BA.2.

- In its 43 technical briefing, the UK Health Security Agency reported a recent uptick in their modelled estimates of hospitalization rate per infection (IHR) over time. This may be due to slightly increased intrinsic severity of BA.5 or population factors such as waning immunity.
- South African scientists reported a slightly (but not significantly) higher hospitalization rate per BA.5 case compared to previous Omicron sub-variants (hazard ratio 1.12; 95% CI 0.93-1.34)

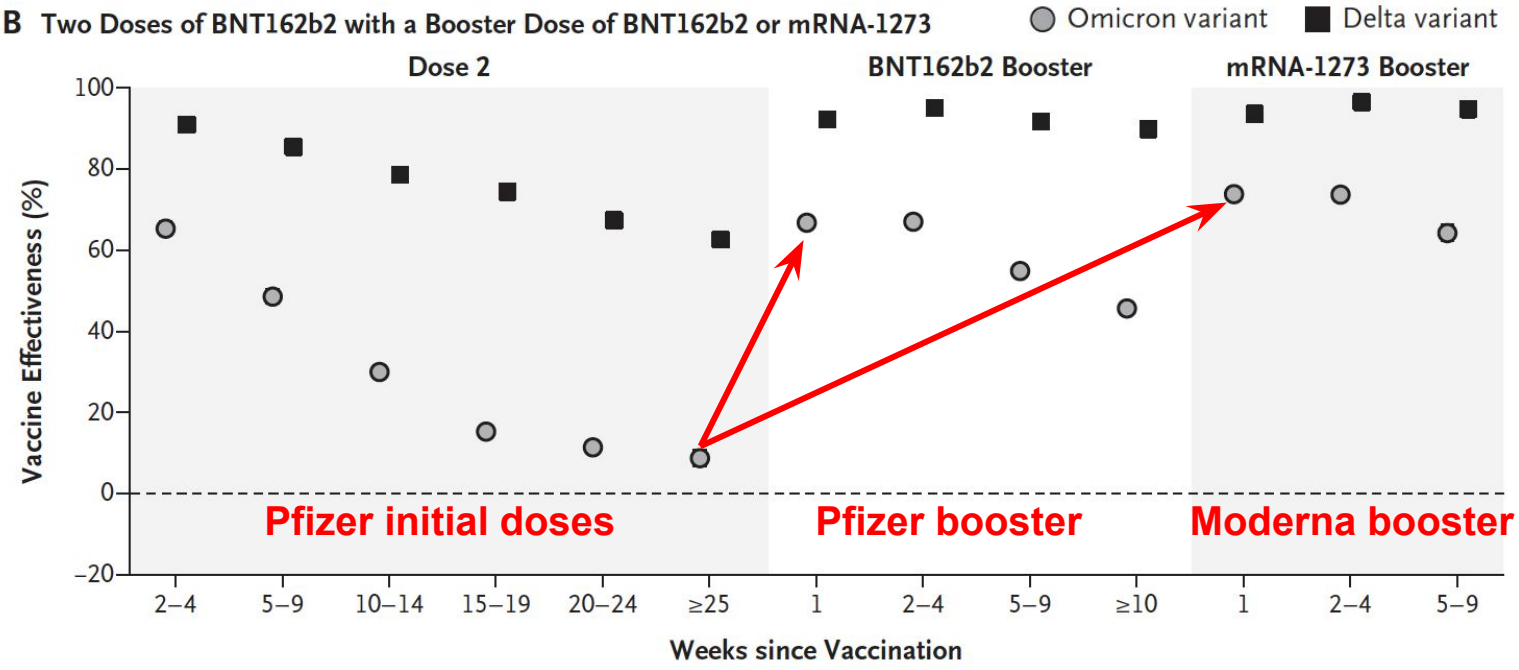


43 technical briefing, UK Health Security Agency

Lowering the BA.5 wave

Is it too late to get a booster to avoid COVID-19 during the BA.5 wave? No!

Data on boosters show that antibody levels rise quickly – within a week – after a booster. This figure shows how quickly vaccine effectiveness against symptomatic disease with Omicron (BA.1) rebounds following boosting (Andrews et al.).



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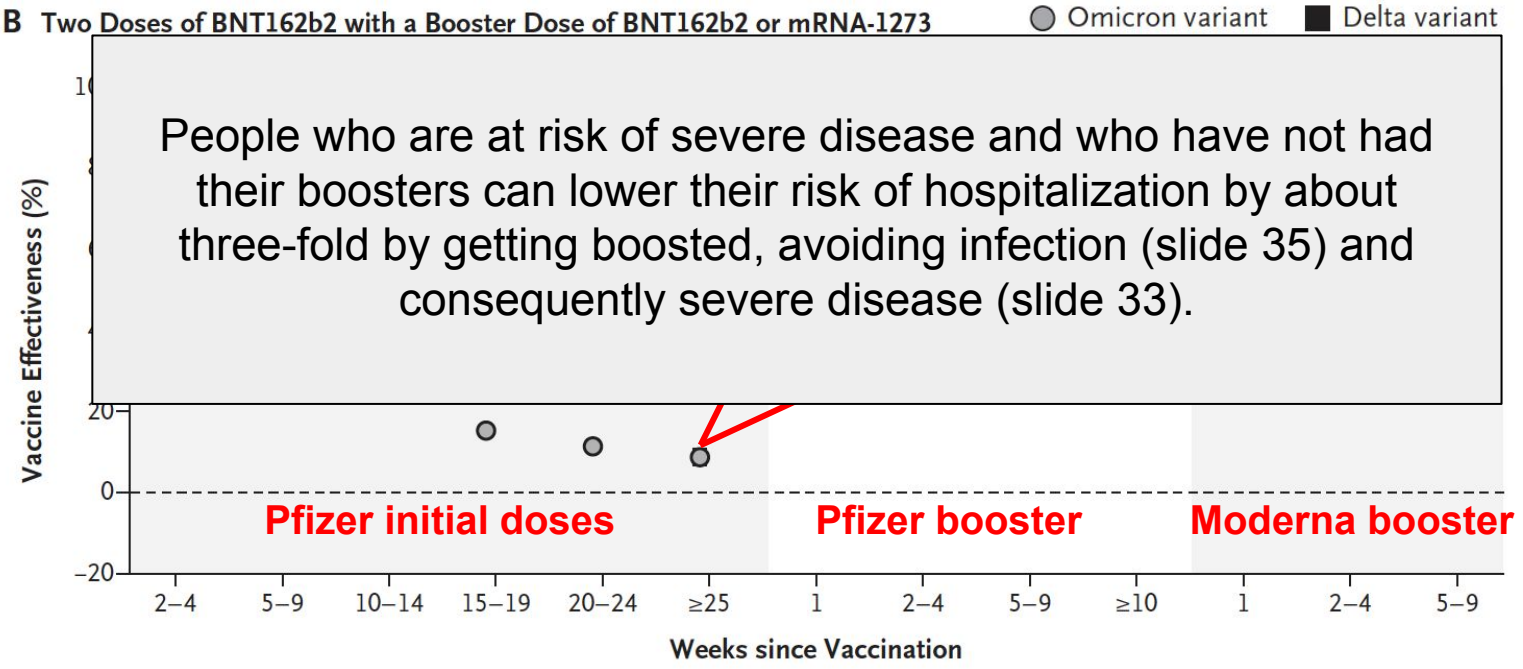


People who are at risk of severe disease and who have not had their boosters can lower their risk of hospitalization by about three-fold by getting boosted, avoiding infection (slide 35) and consequently severe disease (slide 33).

Key messages

The next Omicron wave has started in BC and across Canada.

This wave is driven by the spread of sub-variant BA.5, which is predicted to represent >80% of cases, as of this week.

- The selective advantage of BA.5 over BA.2 has been high and similar across provinces, states, and countries (s ~ 12% per day).

As correctly predicted in our previous reports, the BA.2 wave was smaller than the BA.1 wave, despite its transmission advantage over BA.1.

- The lower peak was due to enhanced immunity from boosters & natural immunity from BA.1 infections.

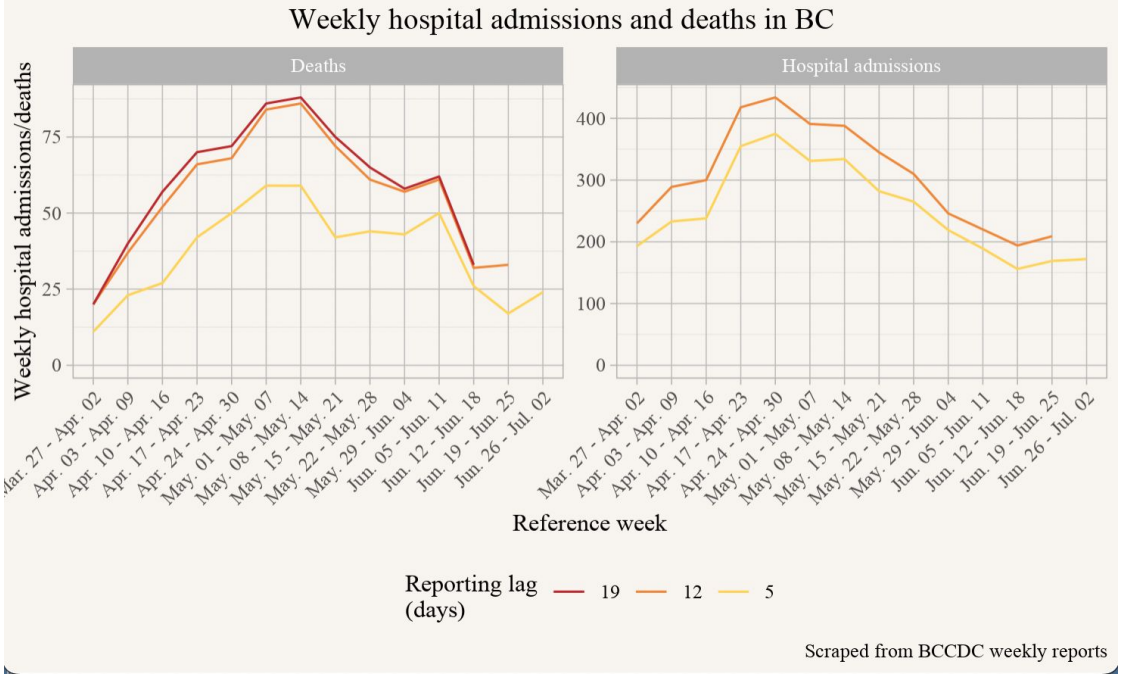
With waning immunity and increased potential for BA.5 to evade immunity, hospital admissions are expected to return to growth in BC and Alberta, as observed already in Ontario, Quebec (slide 20), and in several states (see pypm analyses).

Projections about the impact of the BA.5 wave on severe cases, hospitalizations, and death are difficult given uncertainty in population-level immunity to the new variants and about the risk reduction measures that will be taken.

Appendix: Hospital admissions and deaths in BC

Hospital admissions data and deaths are reported weekly in BC but suffer major data lags

- When first reported, only data up to 5 days prior are included
- Data are substantially underreported when first reported (revised in the following weeks)



Updated the next week (and the week after)

Value initially reported

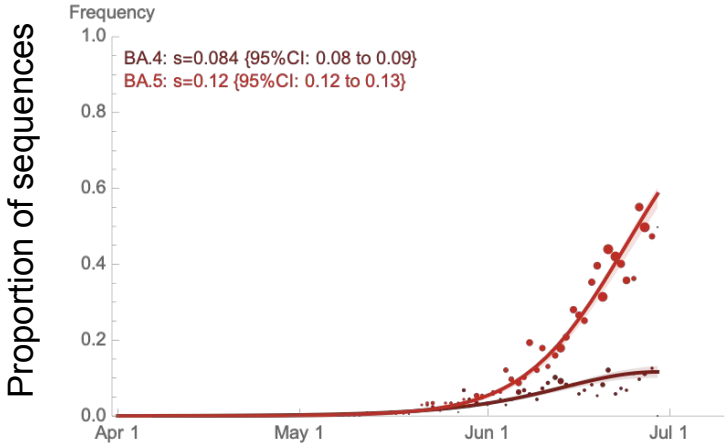
BC hospital admissions are revised upwards by ~20% and deaths substantially more (sometimes doubling!) when updated.

Appendix: Interpreting selection (again)

What is "*s*" and what does it mean to be modest?

s measures the selective advantage per day relative to a reference strain (e.g., measuring the rate of spread of BA.5 relative to BA.2)*.

By modest, we mean that a strain will take about a month to double in relative frequency.



* Selection per day, *s*, satisfies $X_T = \text{Exp}(s\,T)\,X_0$ where X_T is the frequency of a lineage of interest relative to the frequency of a reference strain on day T (e.g., X_T = freq(BA.5)/freq(BA.2)). *s* is estimated from the numbers of sequences of the two types over time by maximizing the likelihood of observing the data (see link).

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

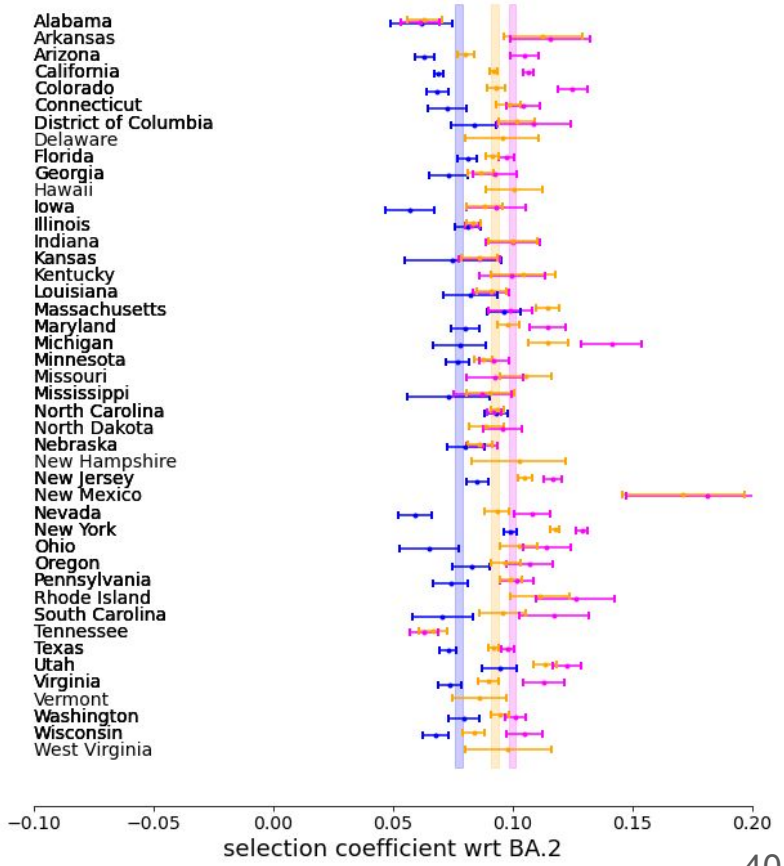
BA.5 vs BA.2
Alpha vs Wuhan
Omicron vs Delta

Source (S. Otto): BC sequences for Omicron (GRA clade) were downloaded from GISAID on 16 May 2022. See methods at the CoVaRR-Net Modelling Resources link

Appendix: Spread of BA.4 and BA.5 in the USA

BA.5 is spreading at a faster rate (pink) than BA.4 (blue) across the United States. Estimates obtained by combining the BA.4 and BA.5 are shown in orange.

The **selection coefficients** shown here measure the rate of exponential growth in the frequency of a strain of interest (e.g., BA.5) relative to a reference strain (here BA.2) (see previous slide).



Source: Dean Karlen. *GISAID 6 July 2022