COVID Model Projections

October 5, 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.

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Overview

Contents of this report:

- Current COVID-19 trends in BC
- The persistent Omicron BA.5 wave
- Interpretation of COVID-19 hospital admission data: Short-term projections

Summary: The BA.5-driven Omicron wave persists with high rates of infection. The prolonged nature of the BA.5 wave is consistent with waning of immunity from infections and vaccinations early in the year. Future projections predict a rise in cases, even without new variants, which are better able to evade immunity. Underreporting of cases is extremely high, with ~100-fold more infections currently than reported cases.

Current COVID-19 trends in BC

Hospital trends in BC

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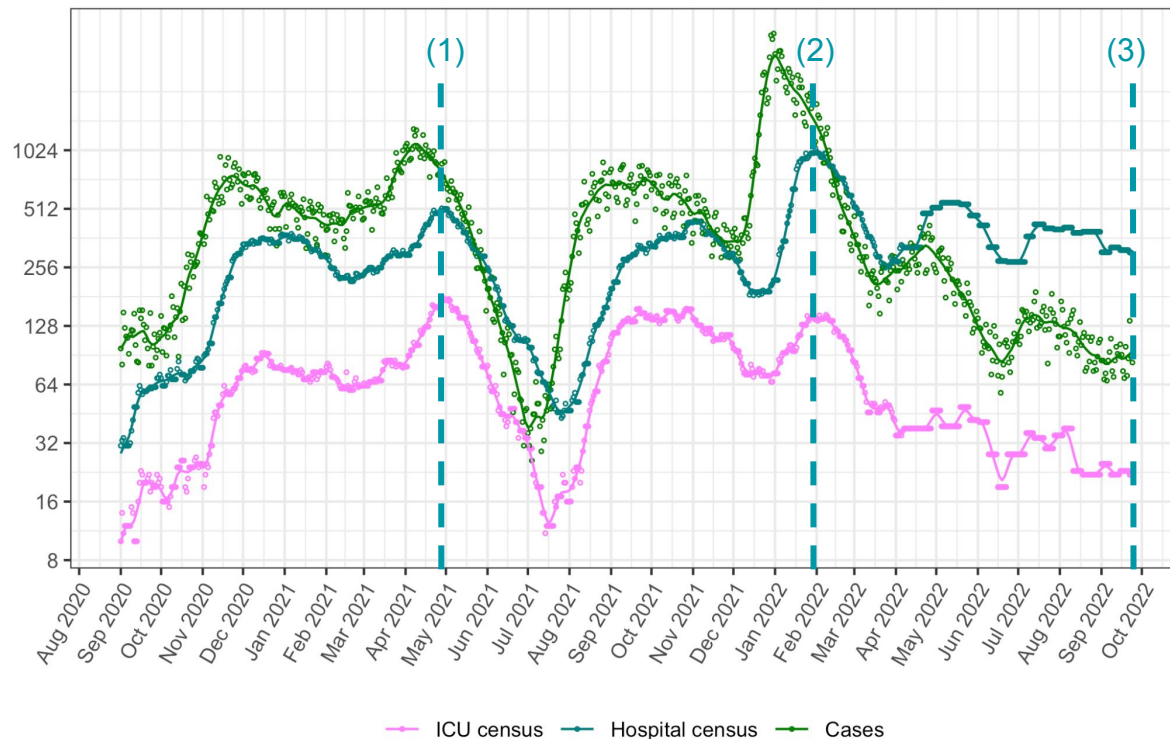
Data: BCCDC for cases, Canada Covid-19 tracker for hospital and ICU census

Reported case numbers, the number of people in hospital and the number in ICU have remained at similar levels for three months (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 = 367

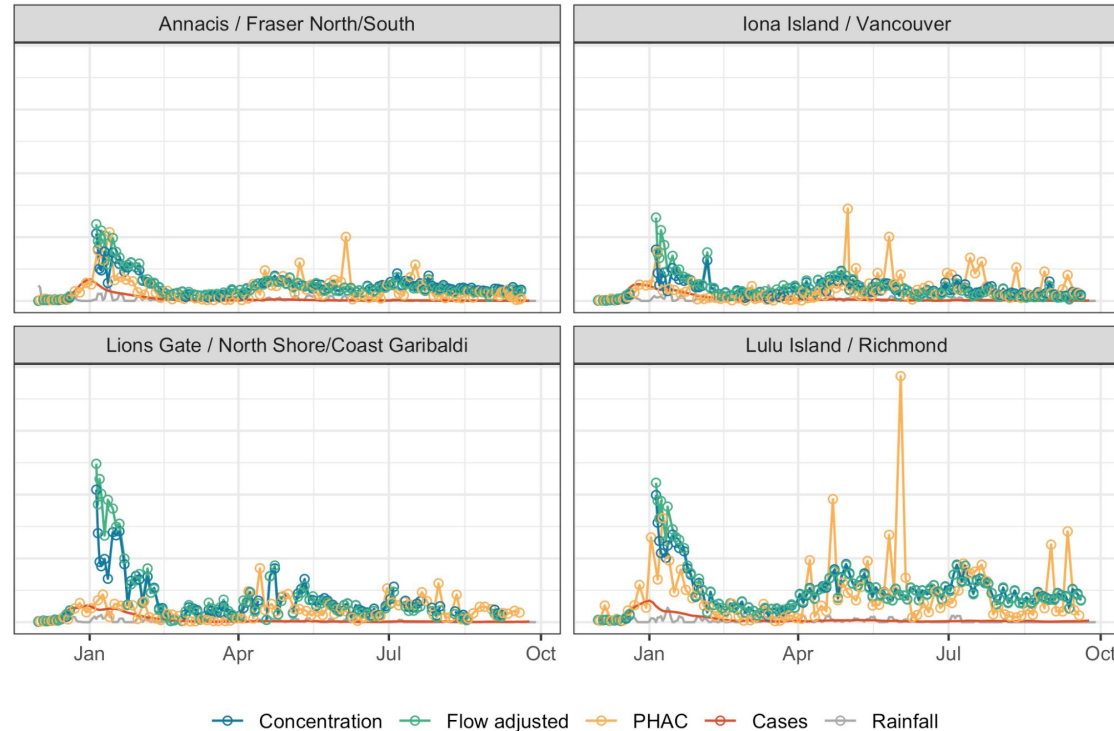**Source (J. von Bergmann)** Case data from BC COVID-19 Database (http://www.bccdc.ca/health-info/diseases-conditions/covid-19/data). STL trend lines on log scale. How hospitalizations and deaths are attributed to COVID-19 changed in BC on April 2, 2022.

Wastewater trends in Metro Vancouver

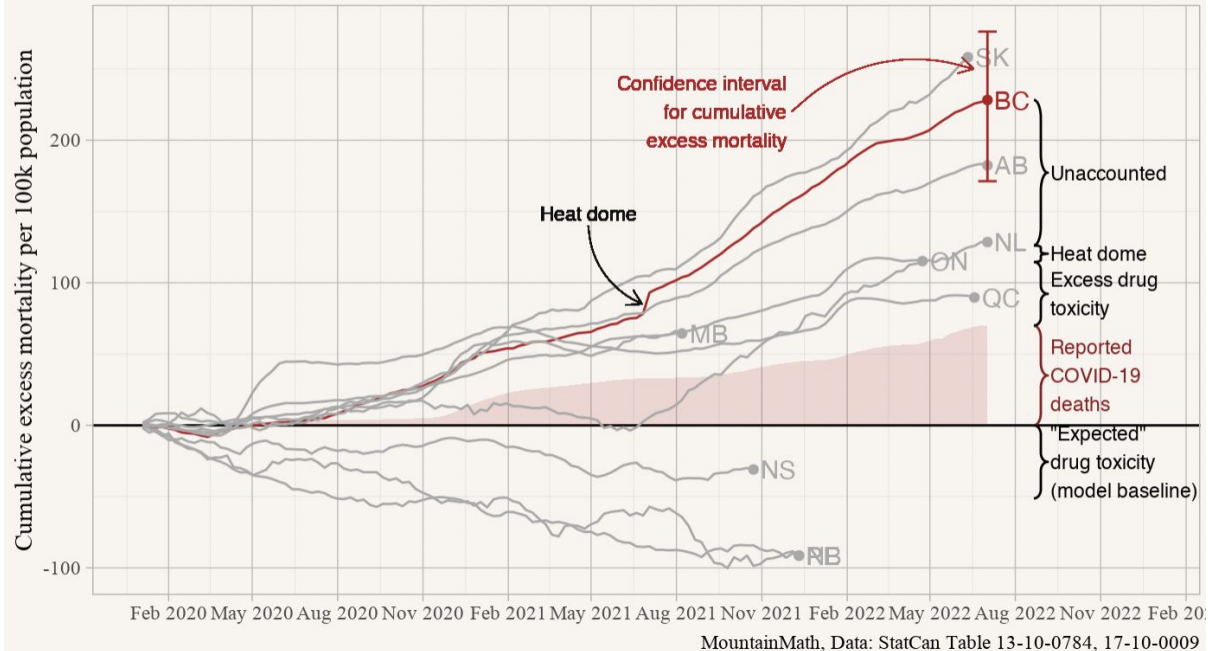Wastewater signals also showing signs of persistent numbers of Omicron infections.

BC announced plans to scale up the number of wastewater sites across the province* and has promised better data accessibility (to date, access to the raw data needed to model trends is not available).

Recent wastewater COVID concentration vs case counts

Source (J. Bergmann) Data from Metro Vancouver's Testing for the COVID-19 VIrus in Wastewater. *Adding Comox, Victoria, Nanaimo (VIHA), Kelowna, Nelson, Kamloops (IHA), and Prince George, Terrace, Fort St John, Prince Rupert (pending ongoing discussions, NHA)

Excess mortality update

Cumulative excess mortality per 100k population since January 2020
BC estimates up to Jul 02, 2022

MountainMath, Data: StatCan Table 13-10-0784, 17-10-0009

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.

Excess mortality accounts for all causes of mortality above those expected based on previous years.

Only half of BC's excess mortality since the start of the pandemic is 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 BC 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.

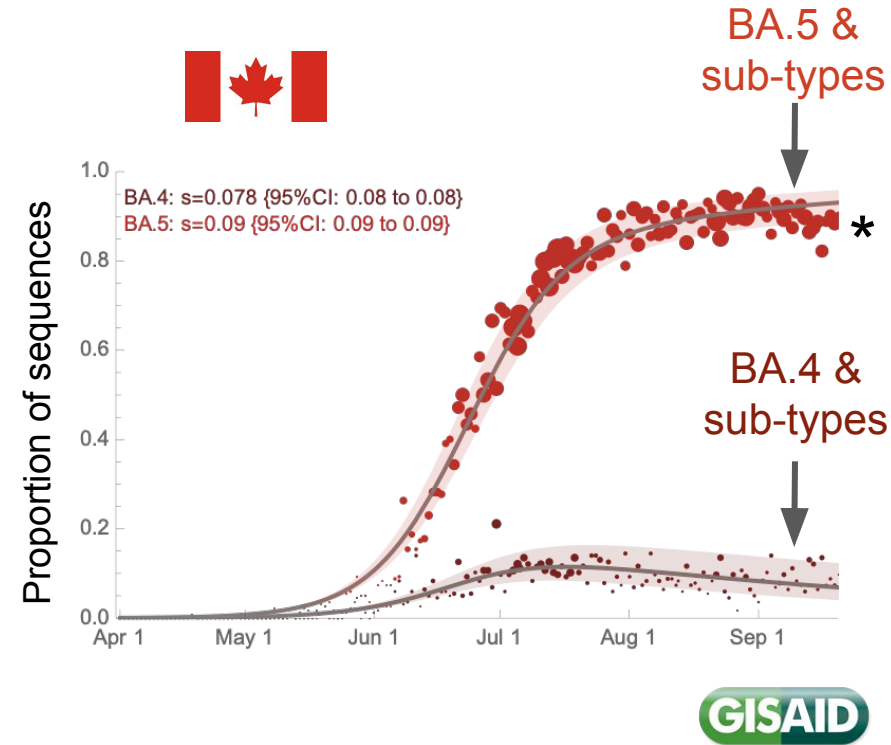BC is likely substantially undercounting total deaths due to COVID.

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BA.5 predominates across Canada

Spread of Omicron sub-lineages in Canada

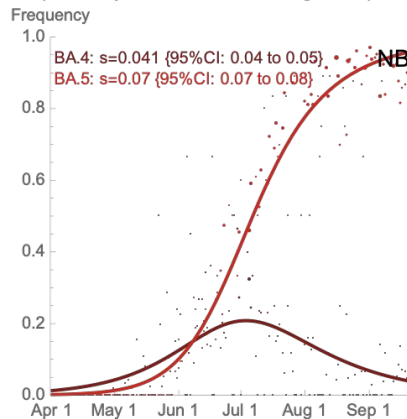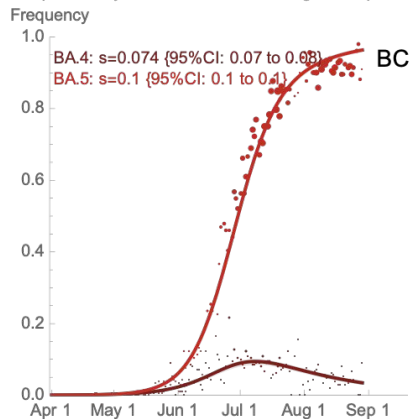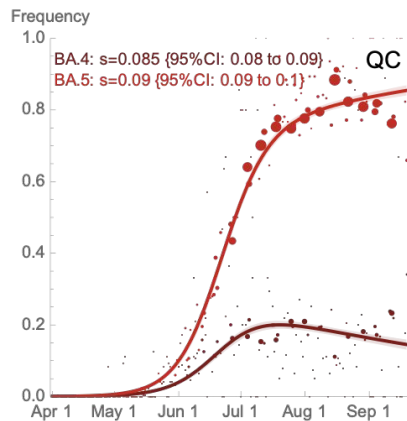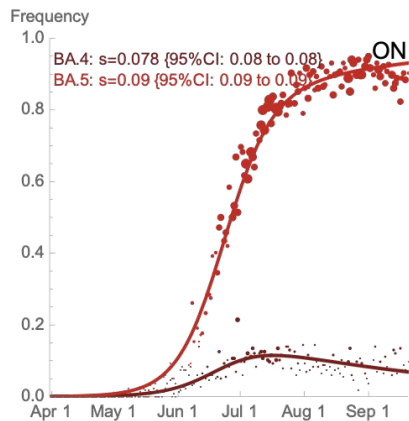→ BA.5 (and it's many sub-types, including BE.# and BF.#) are now predominant across Canada.

* BA.5 has fallen slightly in frequency in the last two weeks, due to variants of BA.2 (especially BA.2.75 sub-types) and BA.4 (especially BA.4.6 sub-types) that have acquired mutations allowing them to better evade immunity.
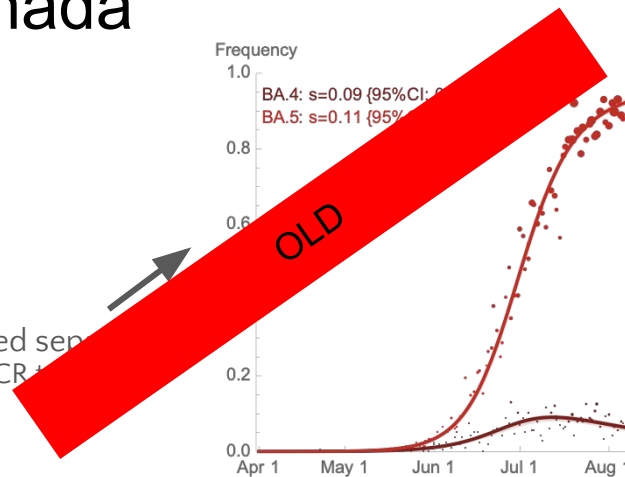

BA.5 & sub-types

BA.4 & sub-types

BA.4: s=0.078 {95%CI: 0.08 to 0.08}
BA.5: s=0.09 {95%CI: 0.09 to 0.09}

GISAID

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Spread of Omicron sub-lineages in Canada

Proportion of sequences

ON
BA.4: s=0.078 {95%CI: 0.08 to 0.08}
BA.5: s=0.09 {95%CI: 0.09 to 0.09}

QC
BA.4: s=0.085 {95%CI: 0.08 to 0.09}
BA.5: s=0.09 {95%CI: 0.09 to 0.1}

BC
BA.4: s=0.074 {95%CI: 0.07 to 0.08}
BA.5: s=0.1 {95%CI: 0.1 to 0.1}

NB
BA.4: s=0.041 {95%CI: 0.04 to 0.05}
BA.5: s=0.07 {95%CI: 0.07 to 0.08}

OLD

BA.4: s=0.09 {95%CI:
BA.5: s=0.11 {95%

Alberta analysed sequences
based on PCR t

Provinces show similar trends, with BA.5# dominating but recently declining.

Source (S. Otto) Canadian metadata was downloaded from GISAID (see previous slide). Alberta data were based on PCR and analyzed separately (*recent BA.1 are undifferentiated, as stated on AB Variants site, and are dropped)
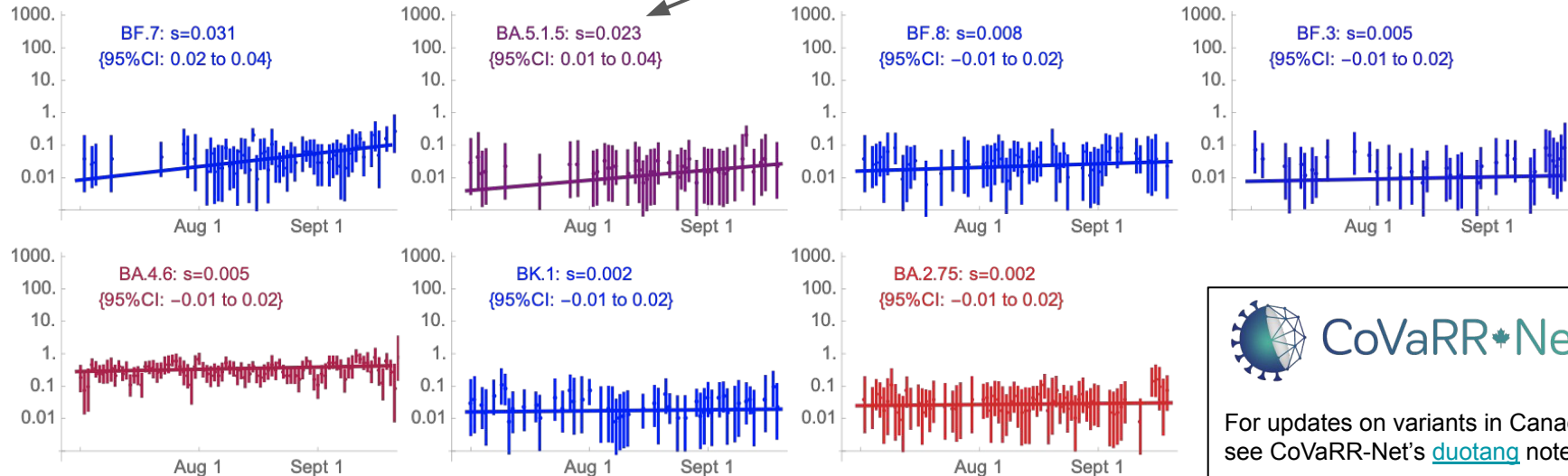
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Spread of Omicron sub-lineages in Canada

BA.5.2 is now the most common Omicron lineage in Canada. Sub-variants growing relative to BA.5.2 are shown below. Some of these (BF.7, BA.4.6, BA.2.75) have mutations predicted to increase immune evasion (next slide), but currently exhibit only a modest growth advantage (s = 0–3% per day).

Selection (s): Daily rate of growth relative to BA.5.2

BF.7: s=0.031 {95%CI: 0.02 to 0.04}

BA.5.1.5: s=0.023 {95%CI: 0.01 to 0.04}

BF.8: s=0.008 {95%CI: −0.01 to 0.02}

BF.3: s=0.005 {95%CI: −0.01 to 0.02}

BA.4.6: s=0.005 {95%CI: −0.01 to 0.02}

BK.1: s=0.002 {95%CI: −0.01 to 0.02}

BA.2.75: s=0.002 {95%CI: −0.01 to 0.02}

Log of freq(focal type)/freq(BA.5.2)

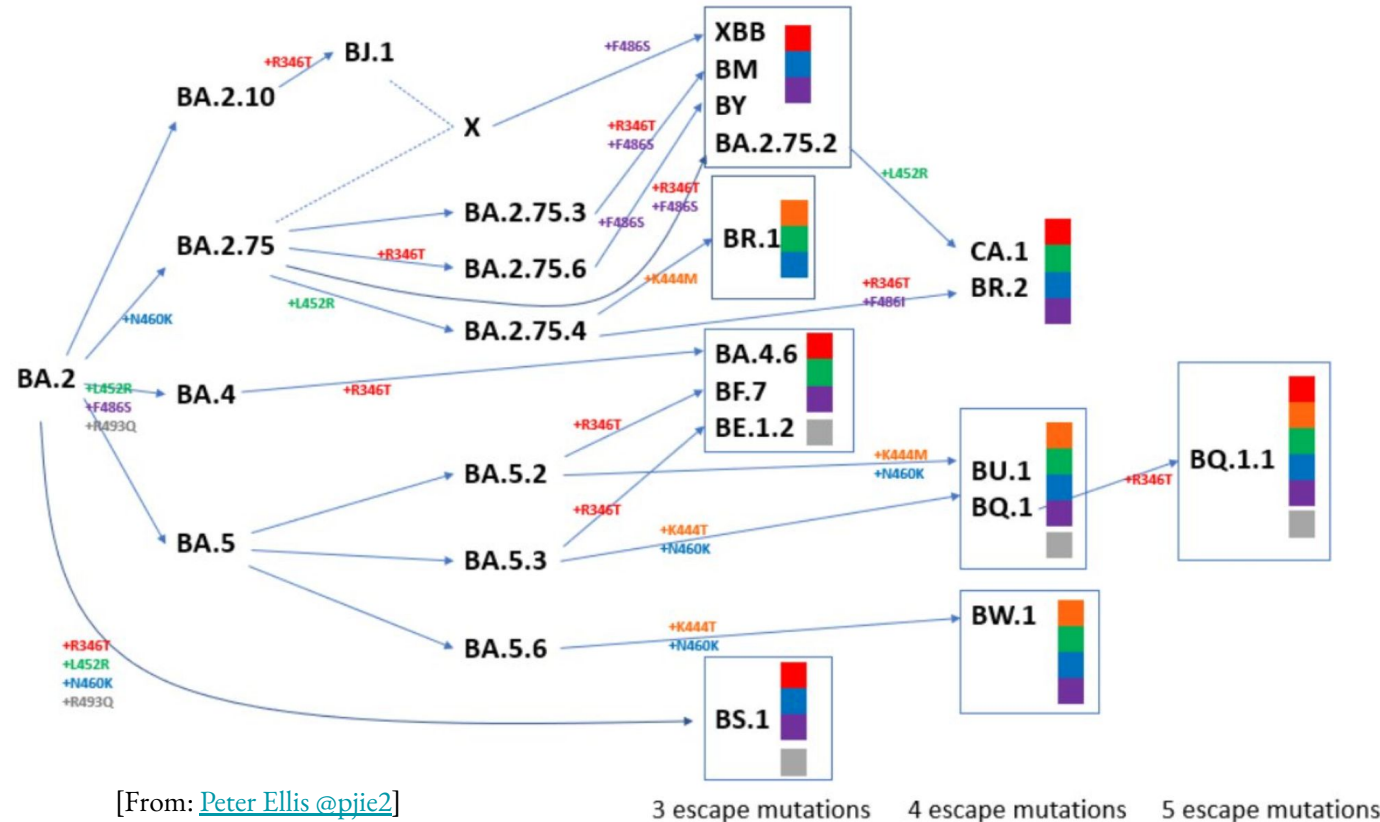For updates on variants in Canada, see CoVaRR-Net's duotang notebook.

Source (S. Otto) See previous page. 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.

Omicron sub-lineages are evolving to evade immunity

Identical mutations (colour) are accumulating in many different Omicron lineages.

These mutations are less well neutralized by existing antibodies (Cao et al.).

Such parallel evolution is evidence of selection favouring viruses better able to evade our immune responses.

[From: Peter Ellis @pjie2]

3 escape mutations   4 escape mutations   5 escape mutations

Illustration tracks five mutations in spike known to better evade antibodies (R346T, K444T, L452R, and N460K) or better bind ACE2 (R493Q) (Cao et al.).
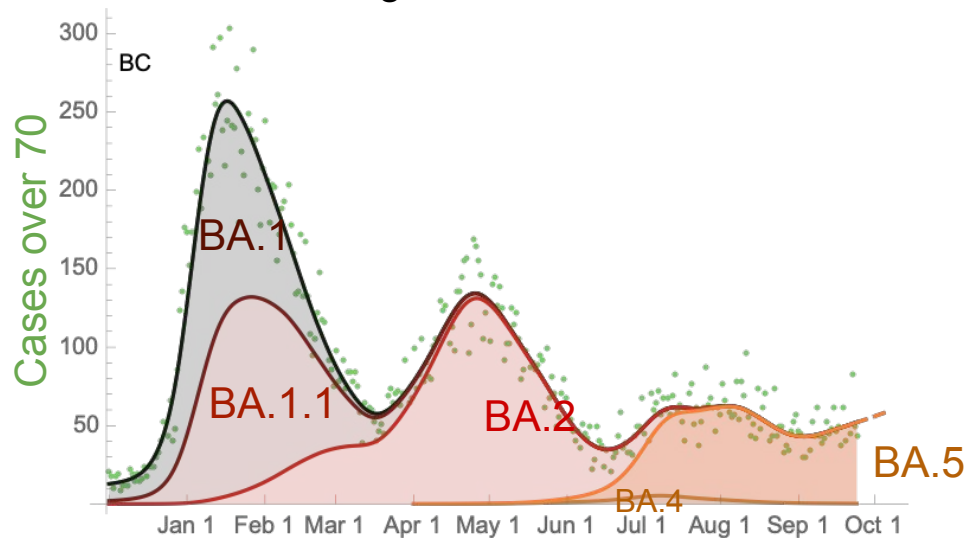
What does this imply for case numbers?

Fitting models of selection allows us to estimate frequency changes among variants.
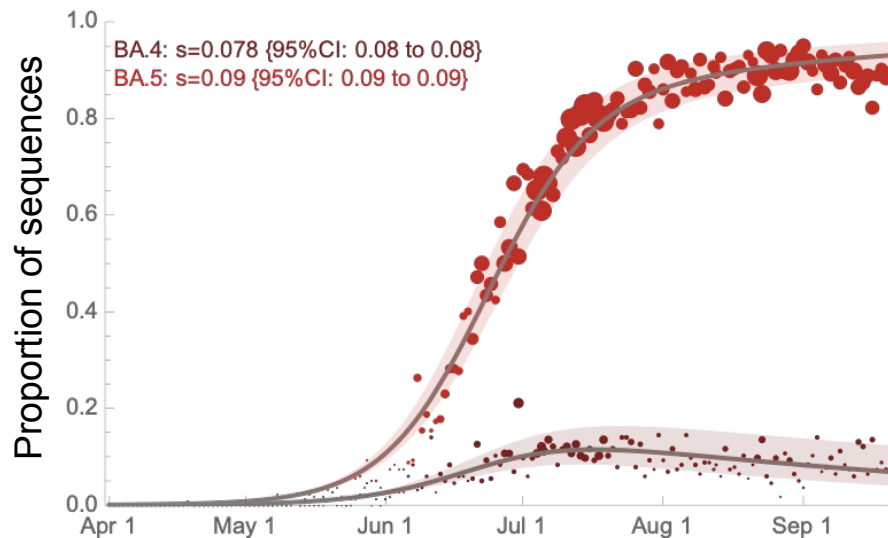
Multiplying by the # of cases in those over 70 allows us to **estimate** growth in numbers of each Omicron sublineage.

→ **The BA.5 wave shows no signs of falling. The persistence is likely due to waning of immunity from infections and vaccines early in the year.**
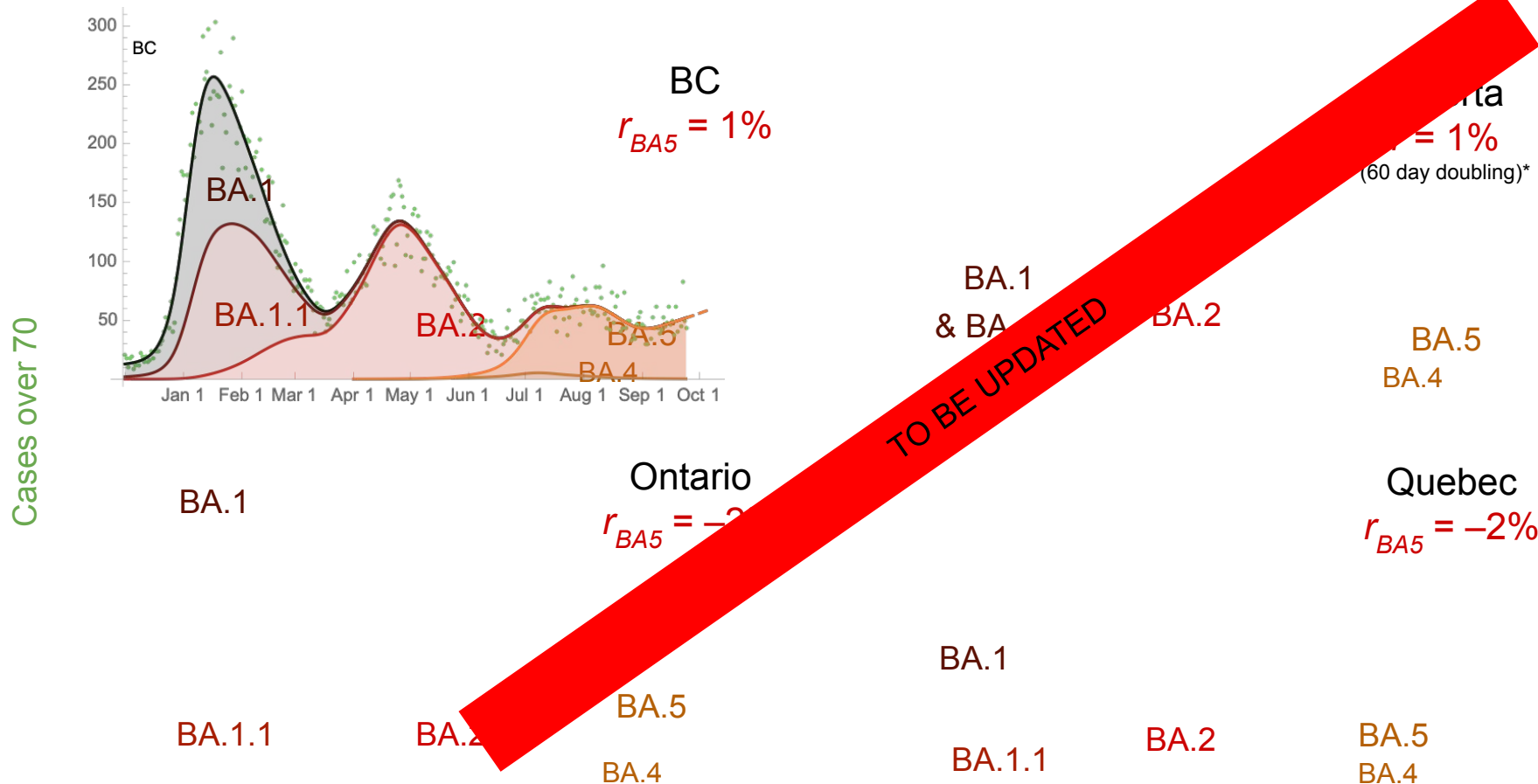
Source (S. Otto) Canadian metadata was downloaded from GISAID for the Omicron GRA clades. A model of selection was fit to the numbers of each type using maximum likelihood based on a trinomial distribution given the expected frequencies on each day. Hessian matrix used to obtain confidence intervals.

The Third Omicron Wave

BC

Cases over 70

BA.1

BA.1.1

BA.2

BA.5

BA.4

Jan 1 Feb 1 Mar 1 Apr 1 May 1 Jun 1 Jul 1 Aug 1 Sep 1 Oct 1

BC
$r_{BA5} = 1\%$

Alberta
$r = 1\%$
(60 day doubling)*

BA.1
& BA

BA.2

TO BE UPDATED

BA.5
BA.4

Ontario
$r_{BA5} = -2$

Quebec
$r_{BA5} = -2\%$

BA.1

BA.1

BA.1.1   BA.2

BA.5

BA.4

BA.1.1   BA.2

BA.5
BA.4

* 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)

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The Third Omicron Wave

BC
$r_{BA5} = 0\%$

Alberta
$r = 1\%$
(60 day doubling)*

Cases over 70

BA.1

ON

BA.1.

BA.2

BA.5

BA.4

BA.1

BA.1.1

BA.2

BA.5

BA.4

bec
−2%

BA5

The BA.5 wave is near... its peak across Canada.

Infection risks remain... but are likely to decline through August.

OLD

Jan 1   Feb 1   Mar 1   Apr 1   May 1   Jun 1   Jul 1   Aug 1

Jan 1   Feb 1   Mar 1   Apr 1   May 1   Jun 1   Jul 1   Aug 1
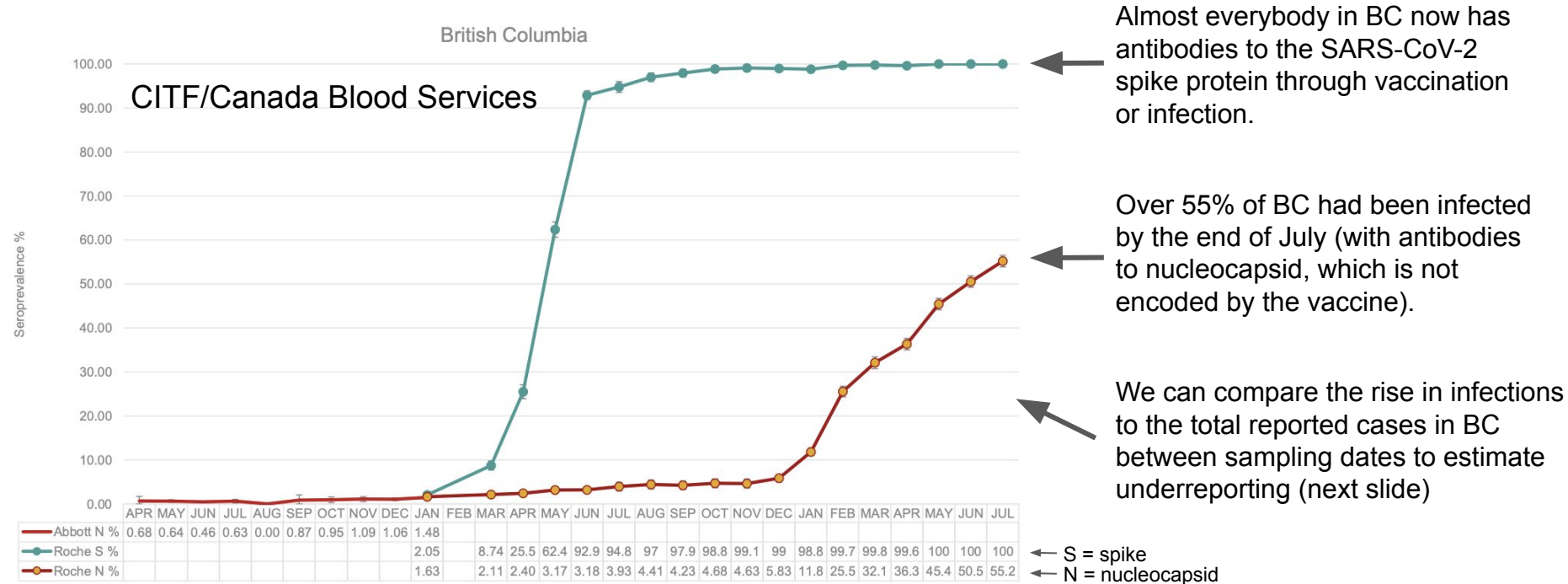
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* Instantaneous estimates of growth rate, r, and doubling times for BA.4 & BA.5 (mainly BA.5). These rates change with changing immunity and with protective health measures, both mandated and voluntary, to reduce transmission (e.g., wearing effective masks, increasing ventilation, and avoiding crowded indoor spaces)
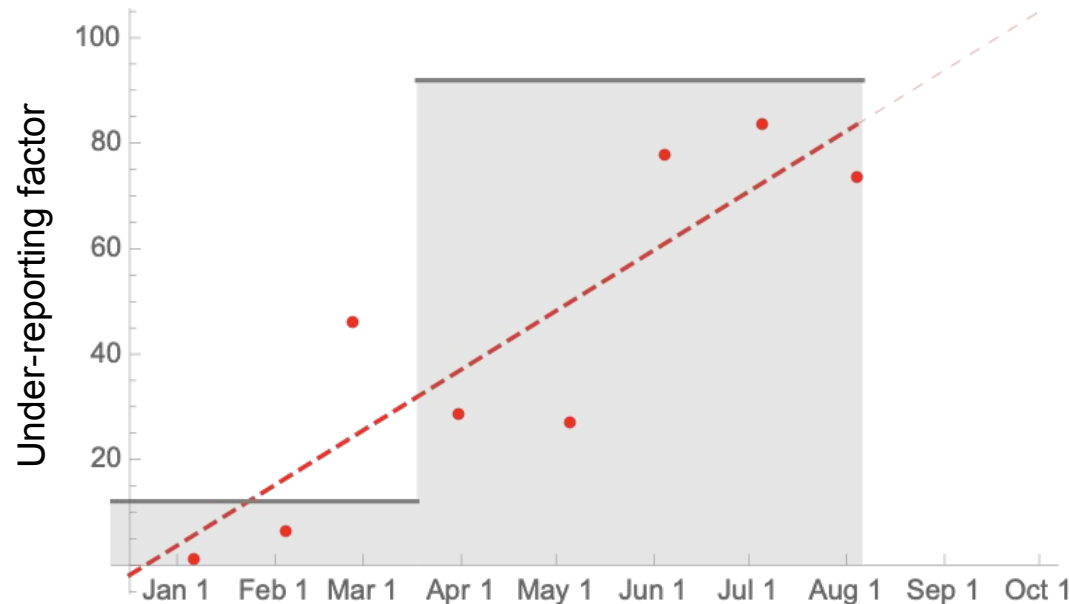
How much are cases under-reported in BC?

Antibodies in blood samples allow infection rates to be estimated and compared to reported case counts in BC.

We compare data from the CITF/Canada Blood Services survey to a recent BCCDC study by Skowronski et al.

British Columbia

CITF/Canada Blood Services

Almost everybody in BC now has antibodies to the SARS-CoV-2 spike protein through vaccination or infection.

Over 55% of BC had been infected by the end of July (with antibodies to nucleocapsid, which is not encoded by the vaccine).

We can compare the rise in infections to the total reported cases in BC between sampling dates to estimate underreporting (next slide)

	APR	MAY	JUN	JUL	AUG	SEP	OCT	NOV	DEC	JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	SEP	OCT	NOV	DEC	JAN	FEB	MAR	APR	MAY	JUN	JUL
Abbott N %	0.68	0.64	0.46	0.63	0.00	0.87	0.95	1.09	1.06	1.48																		
Roche S %										2.05		8.74	25.5	62.4	92.9	94.8	97	97.9	98.8	99.1	99	98.8	99.7	99.8	99.6	100	100	100
Roche N %										1.63		2.11	2.40	3.17	3.18	3.93	4.41	4.23	4.68	4.63	5.83	11.8	25.5	32.1	36.3	45.4	50.5	55.2

← S = spike
← N = nucleocapsid

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How much are cases under-reported in BC?

Underreporting of cases in BC is currently ~100 fold.

Similar estimates of current under-reporting based on the two serology studies:

- 106-fold if we use CITF Blood donor data to estimate the rise in frequency of past infections among BC blood donors relative to the frequency of total reported cases since the previous month (red dots, dashed shows a linear fit to today*).
- 92-fold based on lower mainland blood samples drawn for lab analyses between March and August (gray regions; Skowronski et al. 2022)

Note that serology data is noisy and that both sets of blood donors are a non-representative subset of the BC population.

Source (S. Otto) Red dots show the change in number of blood donors infected since the last month versus the total number of reported cases. The mean underreporting over this entire time period is 43-fold (66-fold after 1 April 2022). The linear fit (red line) shows a significant positive slope, consistent with a rise in underreporting, although the true rise in the unreported fraction of infections is almost certainly not linear.

COVID-19 infection rates if corrected

Estimated number of infections per day is ~10000, much greater than reported cases (~100 per day),
an estimate that includes only infections leading to an immune response (seropositive) and ignores reinfections.
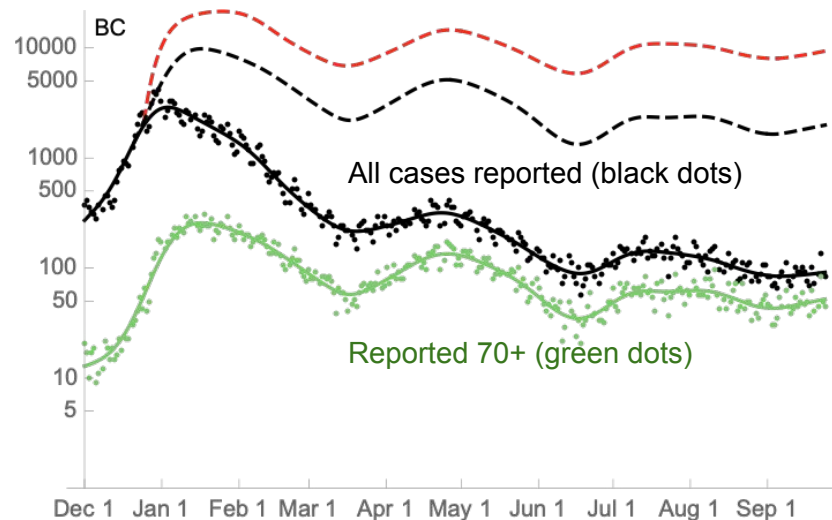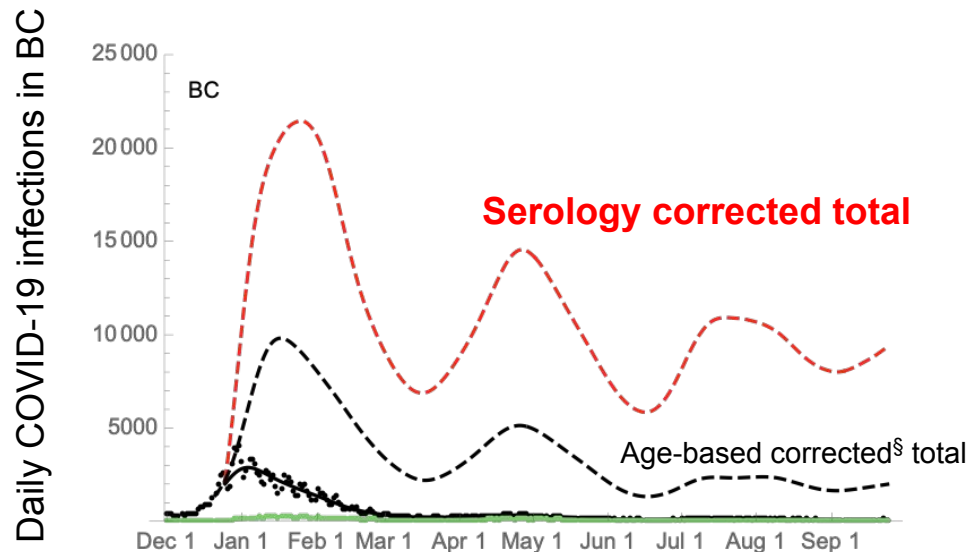
§ Age-based correction assumes testing is consistent in 70+
and % of infections in this age class has been stable.

Source (S. Otto) Multiplies the cases reported per day fit by a cubic spline (black solid curve) by the underreporting factor (from linear fit red line on previous slide).

Waning immunity and
the resurgence of COVID-19

Determining Population-level Immunity

The spread of COVID-19 in 2022 is greatly influenced by population-level immunity.

- For example, the turn around in the growth of BA.2 infections happened because of the increasing immunity primarily from new BA.2 infections (and not because of changes to public health measures or personal behaviour).

As introduced in our previous report (August 17), population immunity dynamics are deduced directly from population-level data. No assumptions are made for immunity effectiveness, waning, or a "reporting fraction". Immunity and the rate of new infections are determined by the rise and fall of the BA.2 wave. Hospital admission data are used, and the "reporting fraction" is inferred as the fraction of immunity generating infections that lead to hospitalization. Transmission rates are assumed to be constant.

- The approach fits hospital admission data well, with relatively few parameters:
  - Two parameters for each strain, and the hospitalization/infection ratio
- **New:** waning of immunity is necessary in the models to fit recent data
  - Changes in transmission rate cannot produce the observed effect.
  - **The resurgence of COVID-19 is due primarily to waning of immunity.**

Spread of disease in a highly immune population

- In 2020 and 2021, the infection rate could remain constant or grow or decline exponentially
  - New infections did not significantly change the susceptible fraction of the population, because the number of new infections each day represented a very small fraction of the population
  - If the number of new infections on a given day exceeded the number of people who recovered or removed from circulation (therefore increasing the number of infectious people), the infection rate would grow exponentially.
  - If it was less, the infection rate would decline exponentially. If it was just right, the infection rate would remain constant
- In 2022, the susceptible fraction of the population is much smaller. If immunity is robust, new infections can significantly reduce the susceptible fraction, so that the number of new infections each day r

European nations with distinct BA.2 and BA.4/5 waves
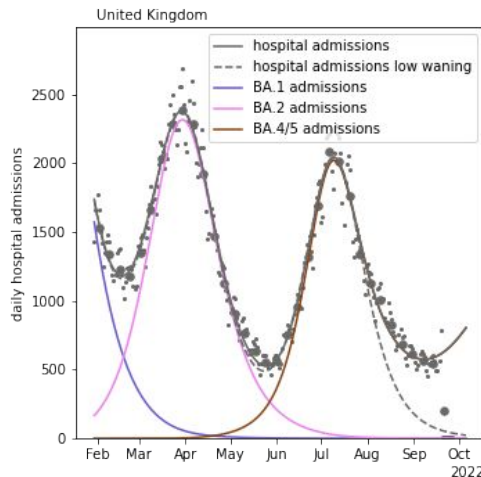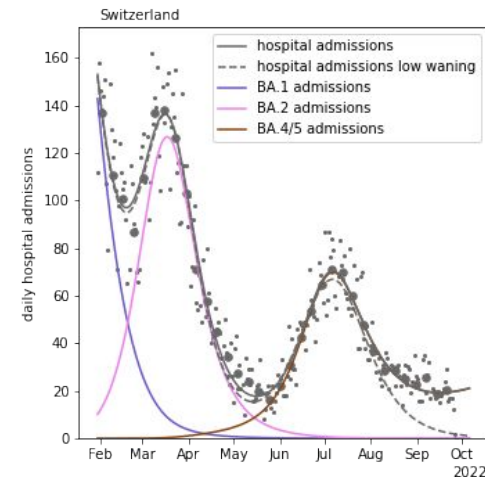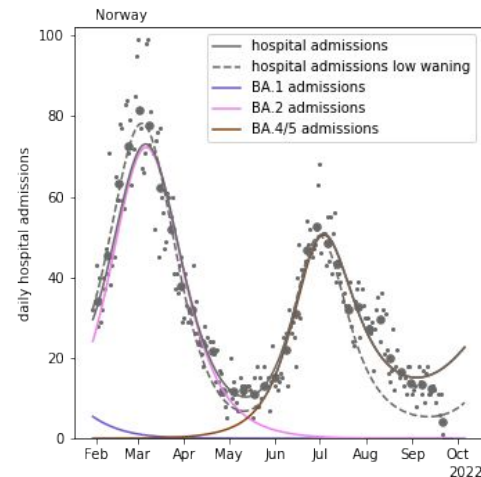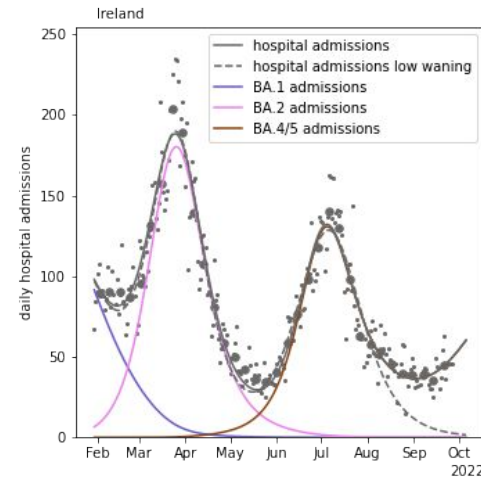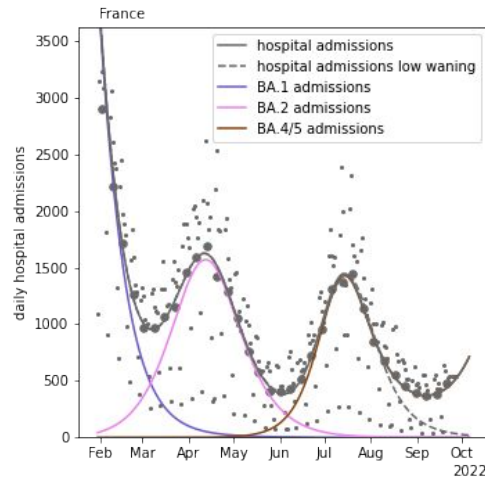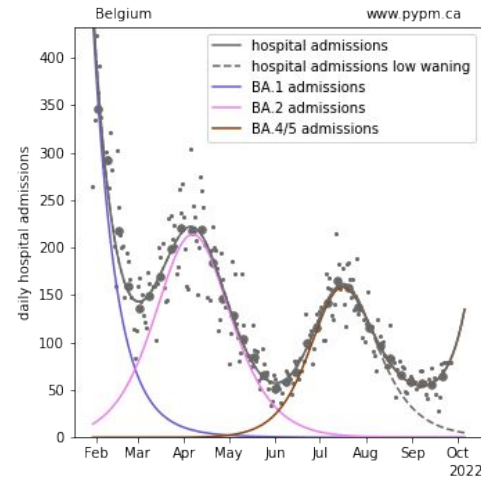
During the fall of the BA.1 wave, population immunity was very high. This led to a much smaller wave for BA.2, despite its higher transmission rate.

The shape of the BA.2 wave helps reveal:
  (A) population immunity going into that wave
  (B) the rate at which immunity grew (i.e., the number of infections that provide immunity per hospitalization)

The model allows BA.4/5 to partially escape from immunity and now includes waning of immunity. August 17 models (with very little waning) no longer fit data, as shown by dashed curves.

Source (D. Karlen) Data from
European COVID-19 Forecast Hub

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Immunity escape and waning

The table shows model parameters estimated from fits to data from Europe. A substantial fraction of the population immunity is found to wane, with mean waning times of 7-11 months.

Country	$\alpha_{4/5}$	f_esc$_{4/5}$	wane_frac	wane_delay
Belgium	3.0	0.046	0.70	342
France	2.8	0.057	0.38	276
Ireland	1.5	0.086	0.61	201
Norway	2.2	0.000	0.50	298
Switzerland	3.0	0.015	0.25	201
UK	2.3	0.030	0.41	241

- $\alpha_{4/5}$: transmission rate for BA.4/5
- f_esc$_{4/5}$: additional susceptible fraction of immunized population available to BA.4/5 (partial escape from immunity)
- wane_frac: fraction of the population immunity that wanes
- wane_delay: mean waning time (days)

Source (D. Karlen) As in previous reports, each pypm model represents a homogeneous population that produces a similar time history of hospital admissions as the jurisdiction under study. Three Omicron strains are included. For this study, immunity of the population is modelled only by infections, by adjusting the magnitude of the BA.1 wave, the two BA.2 parameters (transmission rate and timing), and the hospitalization fraction to reproduce the observed BA.2 wave. The models include waning (with a Gamma delay having mean as shown in table and standard deviation of 60 days).

Quebec and Alberta
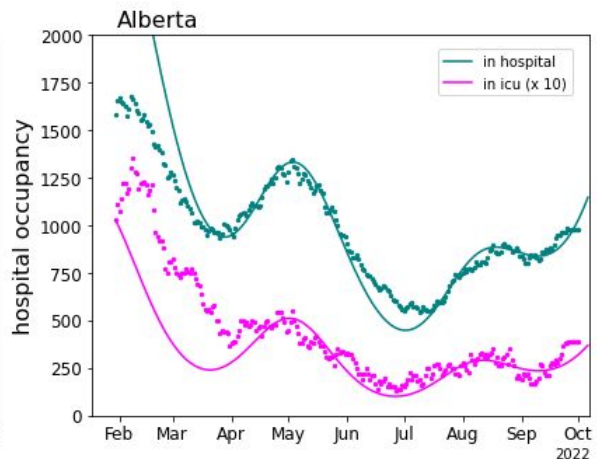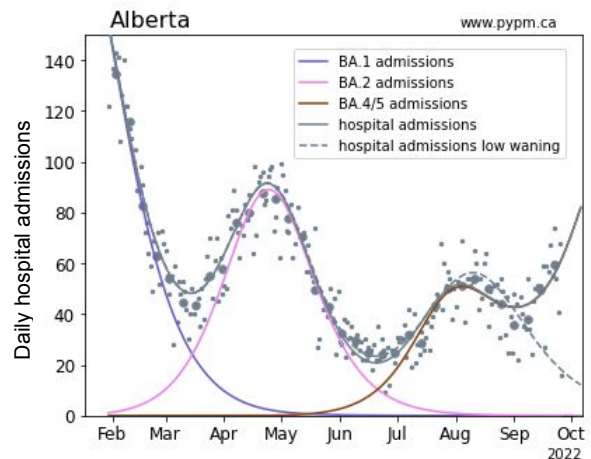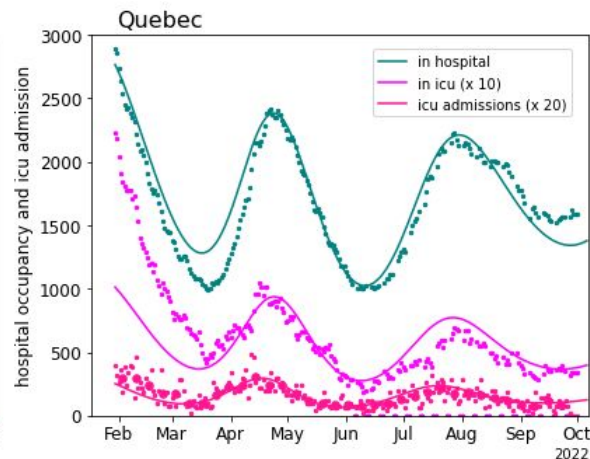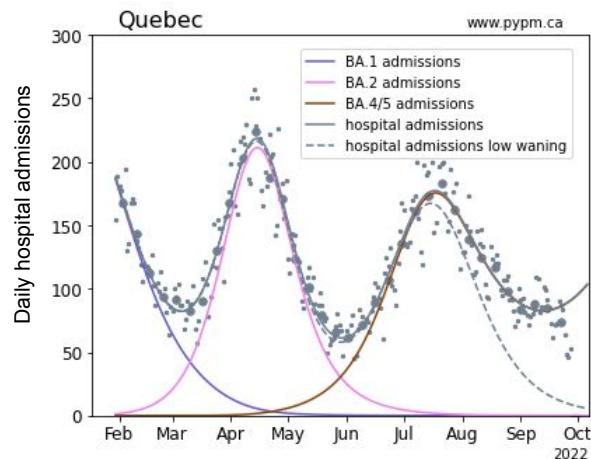
The same approach is applied to three provinces. The dashed curves show model fits from our last report (with very little waning included).

In Quebec, the decline of hospital admissions has reached a plateau, much like Europe. This may be followed by a return to growth.

In Alberta, hospital admissions are clearly growing, unlike other jurisdictions.

Distributions for length of stay in hospital and ICU are adjusted to fit recent data.

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

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BC
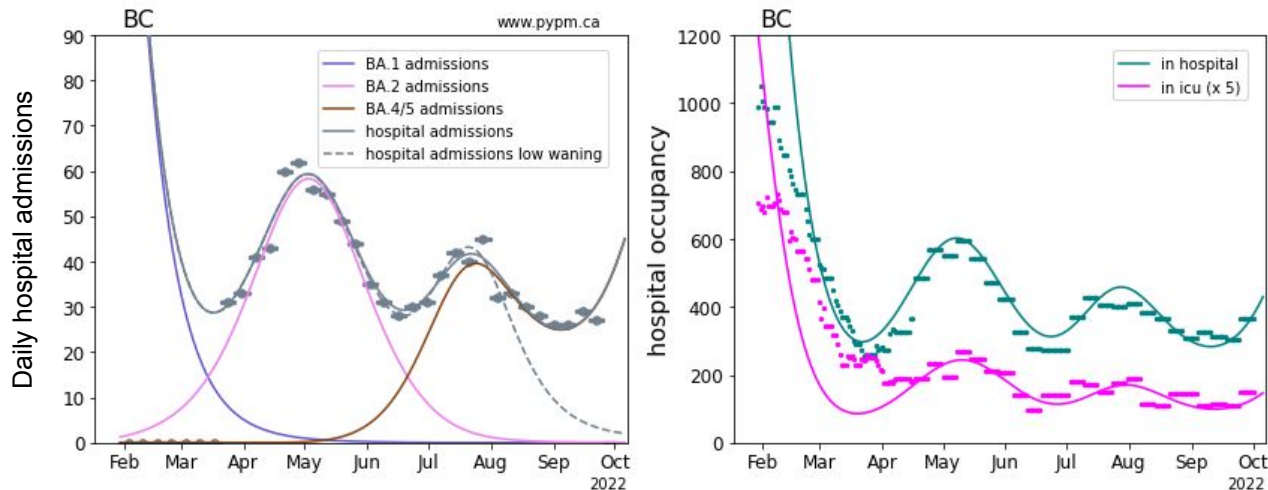
The decline in hospital admissions in BC appears to have reached a plateau and the data suggest that a return to growth may be starting, just as seen elsewhere.

Model fits are very sensitive to the recent data, and may change with revisions to hospital admission data.

The approach is challenging to apply for BC data, given lack of comparable data prior to mid-March when weekly reports started.

Immunity escape and waning

The escape and waning parameter estimates differ significantly from those for European nations. A large escape fraction best fits Quebec data (resulting in a smaller transmission rate). Alberta and Quebec models have a much larger waning fraction than those for Europe.

Province	$\alpha_{4/5}$	f_esc$_{4/5}$	wane_frac	wane_delay
Alberta	2.8	0.01	1.00	308
BC	3.8	0.00	0.35	304
Quebec	1.0	0.21	0.93	252

The BCCDC sawtooth

Figure to be added

Victoria Times Colonist (September 15, 2022):
The latest COVID-19 numbers from the British Columbia Centre for Disease Control show the number of people admitted to hospital with the illness is **declining**.The weekly report says 142 people were hospitalized during the week of Sept. 4 to 10, down from 180 admissions during the previous week.

What is the bivalent vaccine used in Canada?

"Bivalent" refers to having two types: the current Moderna bivalent vaccine available in Canada encodes the spike protein from both the original (Wuhan) and Omicron (BA.1) variants.

Getting the bivalent vaccine boosts immunity and broadens the diversity of antibodies in the bloodstream to better recognize Omicron, priming your immune system to neutralize the virus and avoid infection*.

Moderna's bivalent (Wuhan & BA.1) boosts neutralizing antibodies that recognize BA.1 by a geometric mean factor of 1.75 more than boosting with the original vaccine (see plot).

Neutralizing antibodies that recognize BA.5 are also raised by a factor of 1.68, indicating a benefit across multiple Omicron lineages (Chalkias et al. 2022).
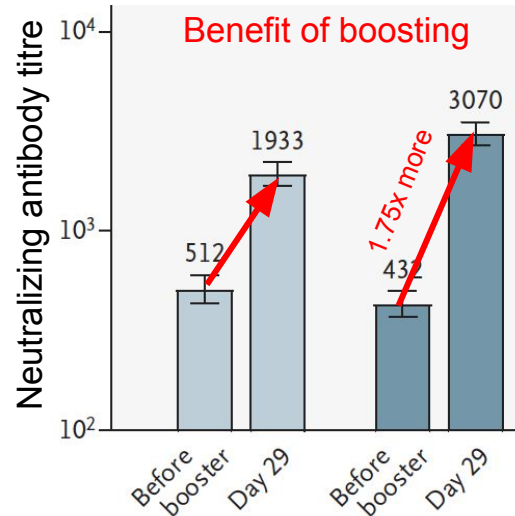
Moderna vaccine: Original   Bivalent

Both the original vaccine and the bivalent help, but the bivalent helps more against Omicron.

Note: The BA.5 & Wuhan bivalent approved in the United States has been tested in mice but not yet in humans (learn more from CoVaRR-Net).

*These neutralizing antibodies wane over the course of months. Once a person is infected, memory cells that recognize SARS-CoV-2 are stimulated, allowing vaccinated and previously infected people to clear infections more efficiently, reducing (but not eliminating) the risk of severe disease.

Key messages

The third Omicron wave, driven by BA.5, has not fallen and shows signs of rising again.

○ 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.
○ Population immunity can be estimated based on the shape of the pandemic curves, providing a way to estimate immune evasion and predict future infection and hospitalization rates.

The third Omicron wave is predicted to rise further due to waning immunity, unless counterbalanced by an uptake of vaccines.

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: 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)
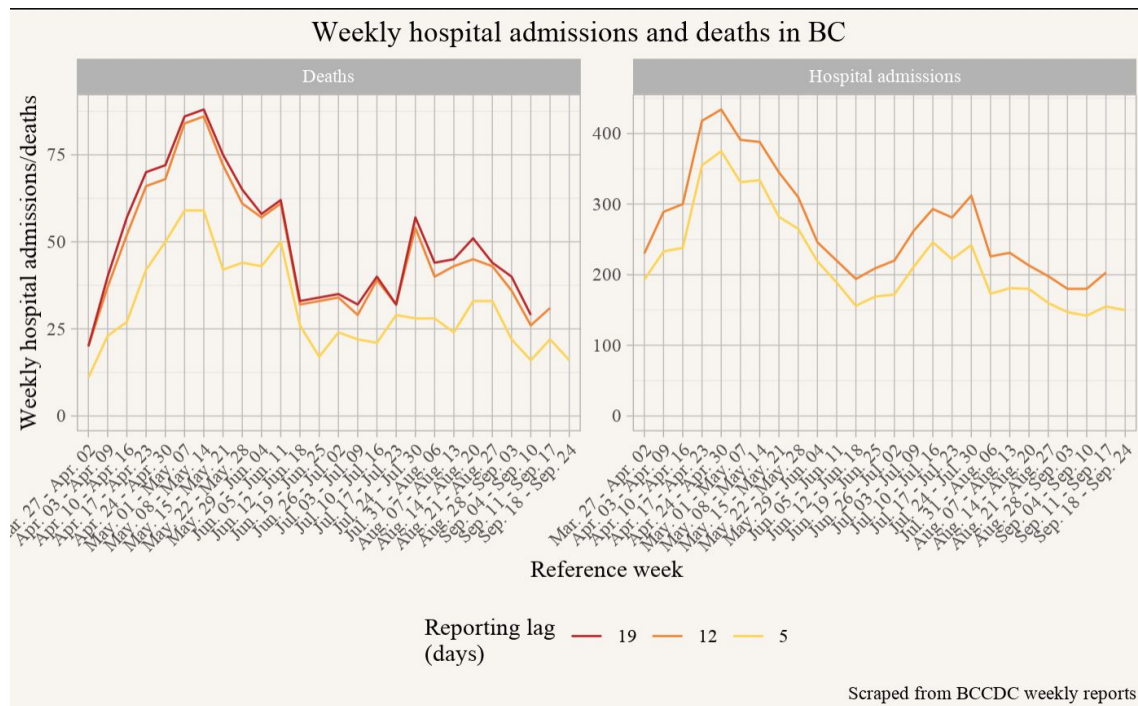
Updated the next week
(and the week after)

Value initially reported

BC hospital admissions are revised upwards by ~20% and deaths substantially more when updated.

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