COVID Model Projections

August 17, 2022

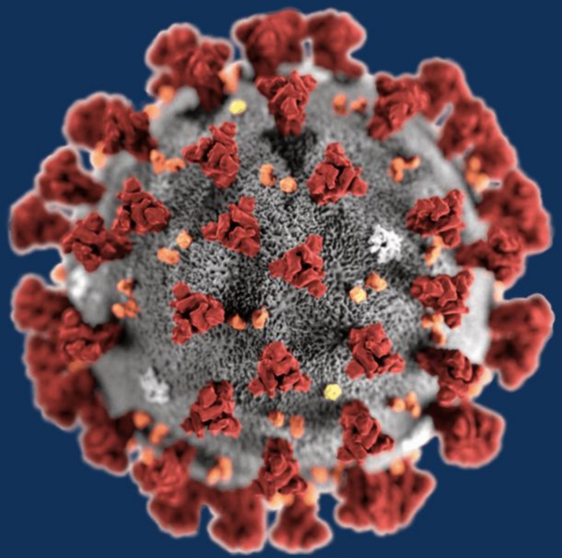
BC COVID-19 Modelling Group

@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

<u>Contributors to report</u>

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

Overview

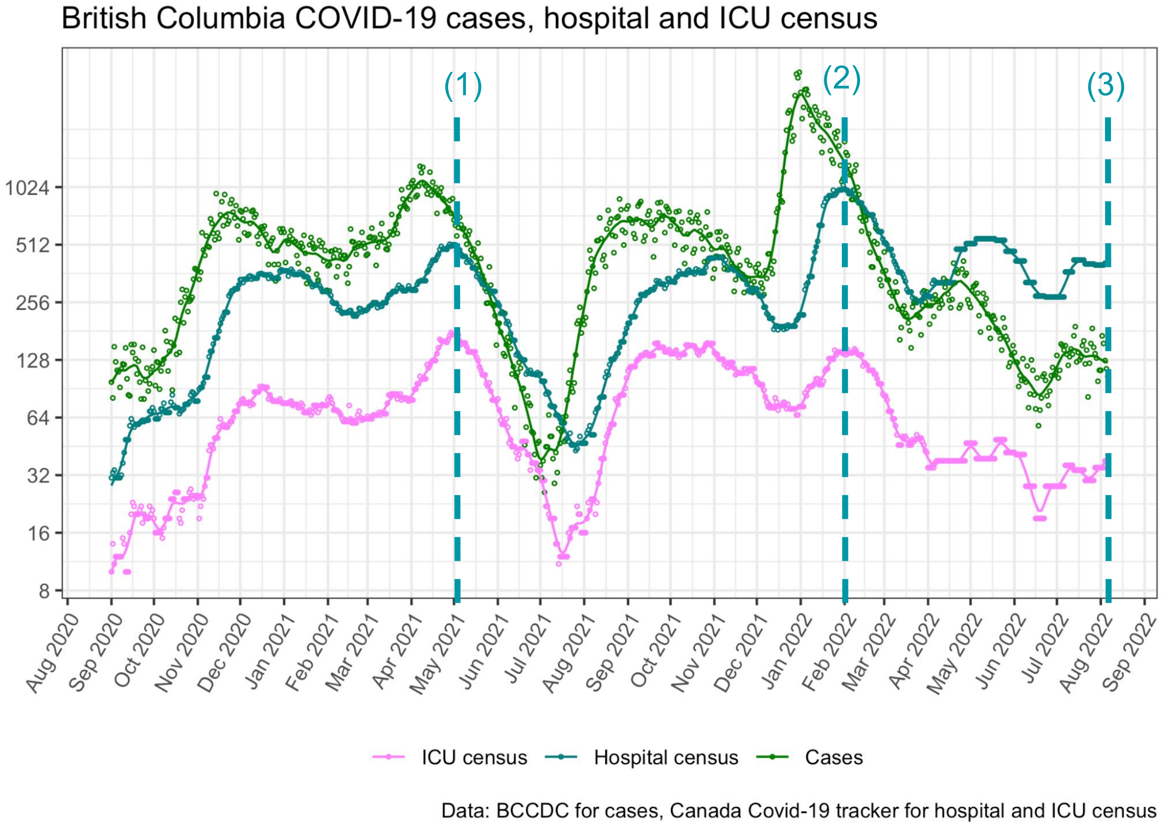
Contents of this report:

- Current COVID-19 trends in BC
- The rise and fall of Omicron BA.4 & BA.5
- Interpretation of COVID-19 hospital admission data: Short-term projections

Summary: The BA.5-driven Omicron wave has crested in BC and across much of Canada. Underreporting of cases is extremely high, with ~100-fold more infections currently than reported cases. The shape of the waves provides information about immunity within a population, helping to make better projections for the spread of COVID-19 in highly immunized populations.

Current COVID-19 trends in BC

Hospital trends in BC



Reported case numbers, the number of people in hospital and the number in ICU are stable or declining slightly 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)

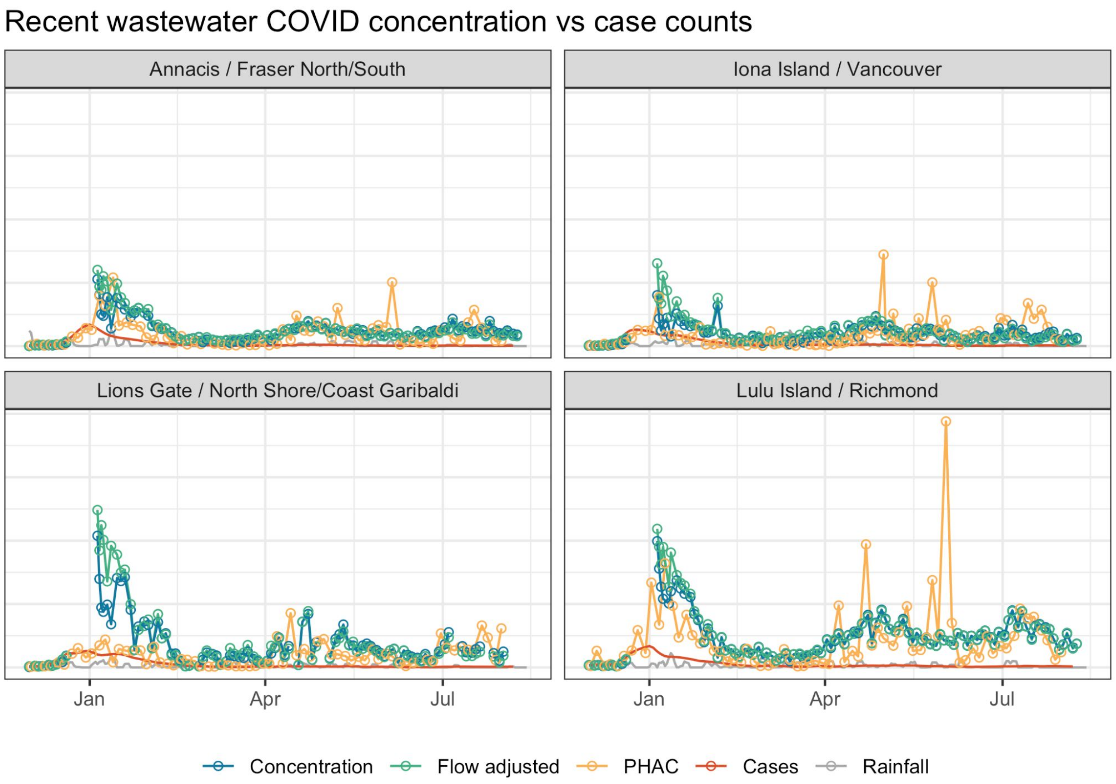
(3) Current = 385

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

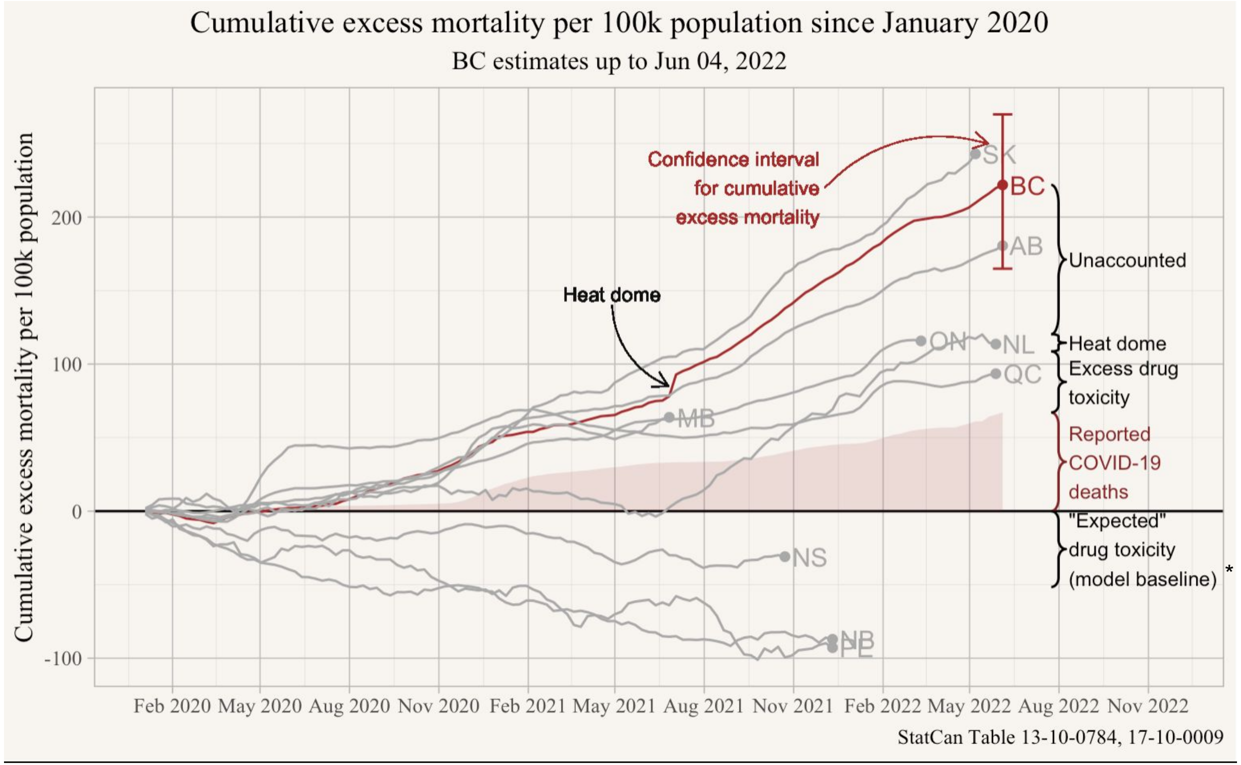
Wastewater signals are also showing signs of a stable or declining number of Omicron infections.

We have not received access to the raw data on wastewater to be able to statistically model and forecast the **current number of COVID-19 infections**.



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

Excess mortality



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.

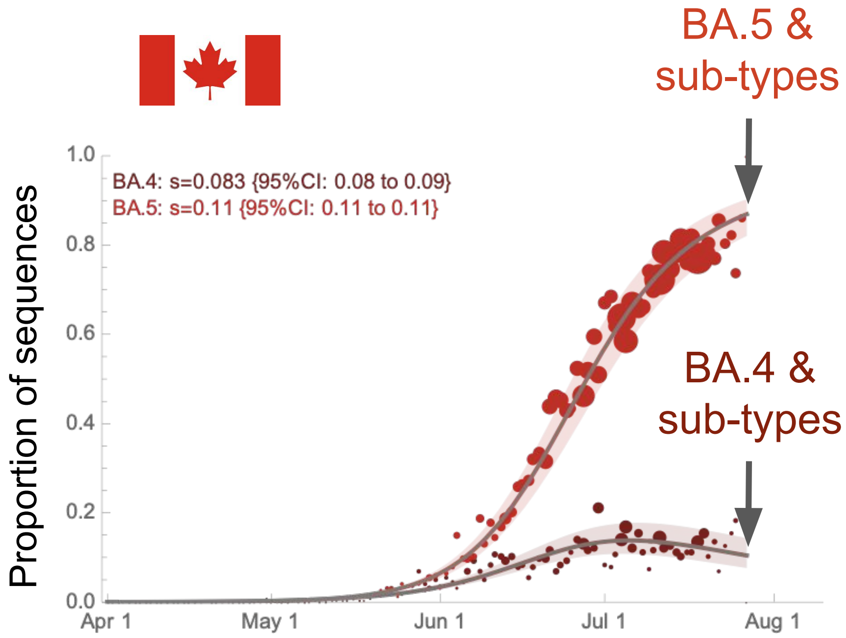
BC is likely substantially undercounting deaths due to COVID.

BA.5 predominates across Canada

Spread of Omicron sub-lineages in Canada

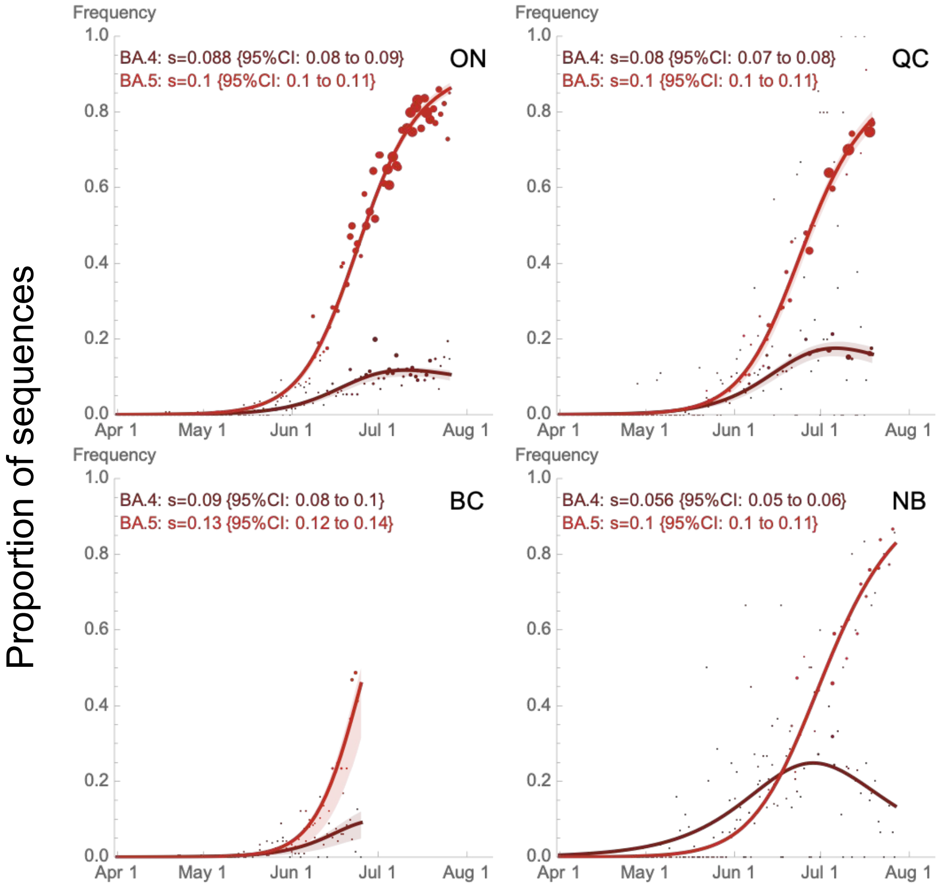
→ BA.5 (and it's many sub-types, including BE.# and BF.#) are now predominant across Canada.

BA.5 has differentiated into many sub-types carrying distinct mutations, 28 of which are present in Canada. Once there are so many sub-types that a lineage would have four decimals in its name, it is renamed by the Pangolin group (e.g., BA.5.3.1.1 became BE.1 and BA.5.2.1.1 became BF.1.

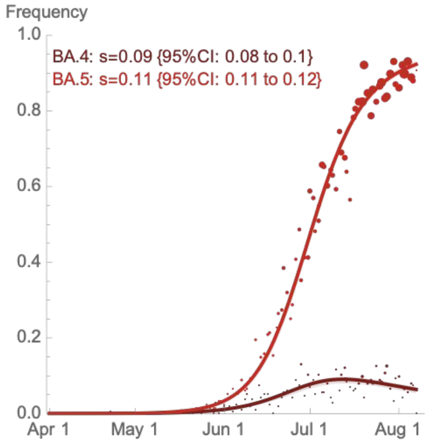


Source (S. Otto) Canadian metadata was downloaded from GISAID for the Omicron GRA clades (Alberta sequences were removed as AB first identifies variants and preferentially sequences some subtypes). A model of selection was fit to the numbers of each type using maximum likelihood based on a trinomial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

Spread of Omicron sub-lineages in Canada

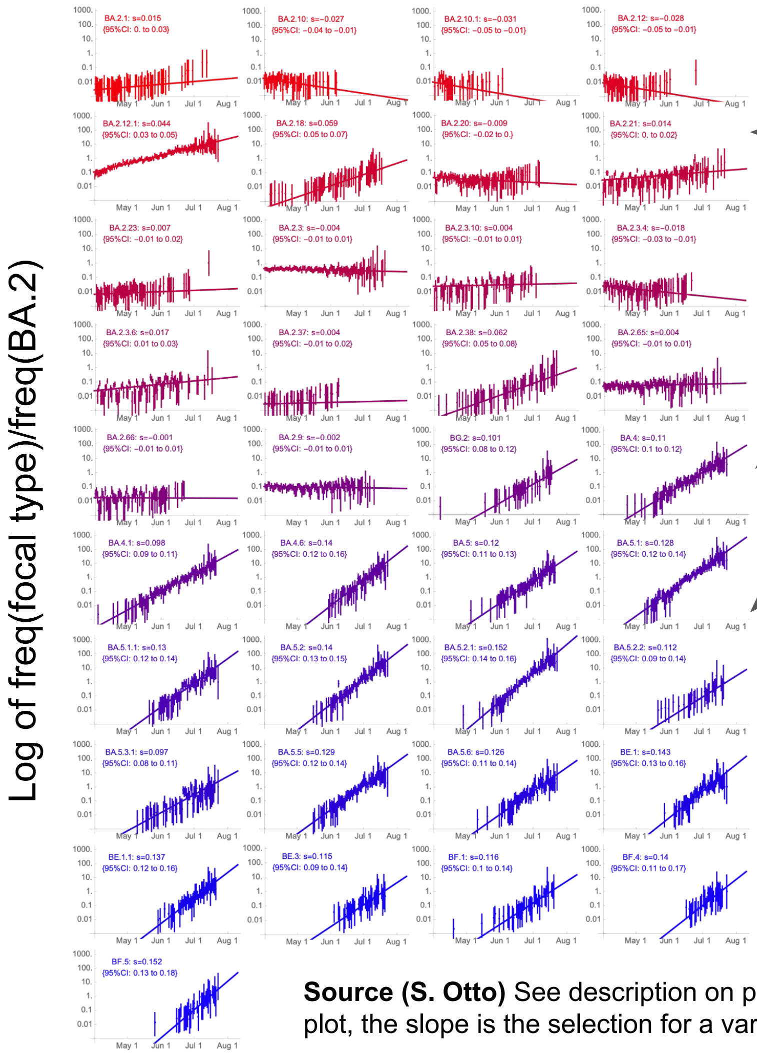


Alberta analysed separately based on PCR typing:



Provinces show similar trends, with BA.5# now dominating.

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)



BA.2 sub-types

BA.4 & sub-types

BA.5 & sub-types

We are tracking the spread of different variants across the country.

Some sub-lineages of BA.5 (e.g., BA.5.2, BE.# & BF.#) are growing slightly faster (steeper slopes in graphs to the left), but no lineage is showing substantially faster growth than BA.5.

For updates on variants in Canada, see CoVaRR-Net's duotang:
https://covarr-net.github.io/duotang/duotang.html

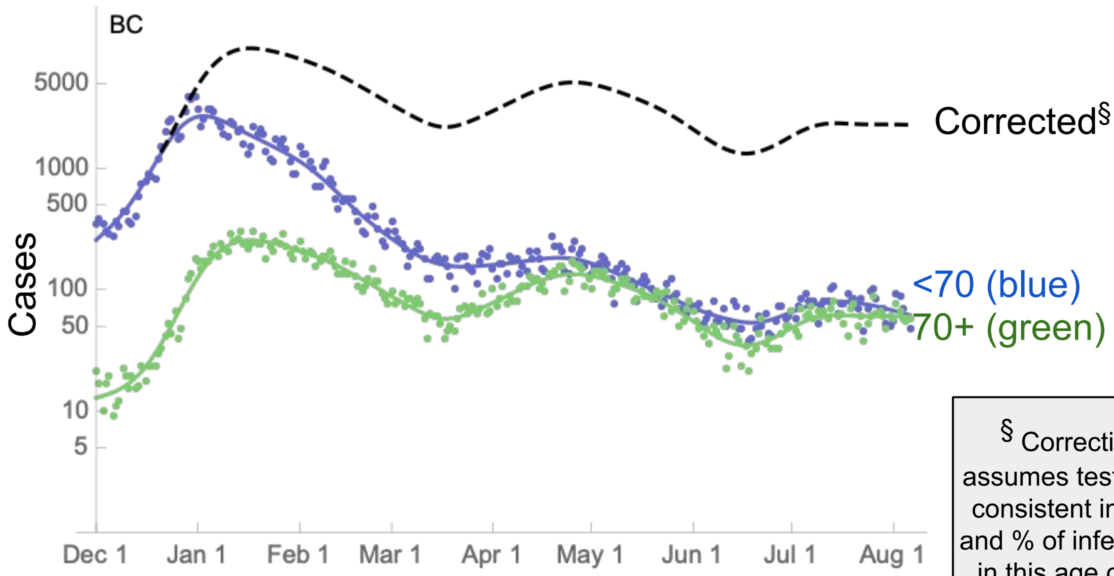
Source (S. Otto) See description on previous page, each lineage is plotted separately relative to BA.2 on a log scale. On this logit plot, the slope is the selection for a variant relative to the reference, here BA.2.

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 currently stable*.

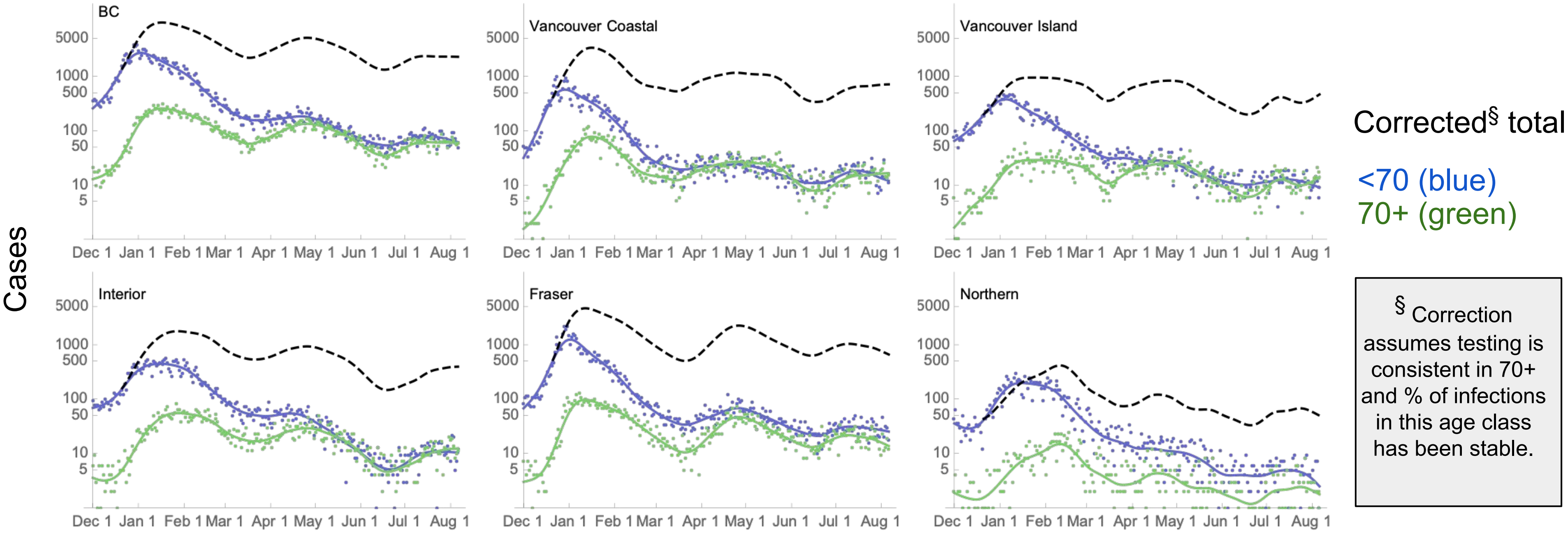
British Columbia



§ 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 is not significant.

BC: Age-corrected case counts



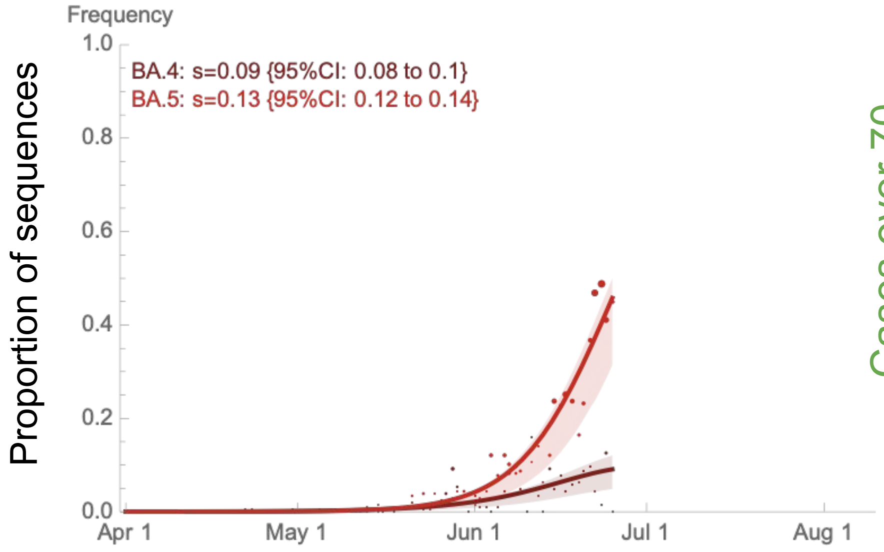
§ Correction assumes testing is consistent in 70+ and % of infections in this age class has been stable.

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

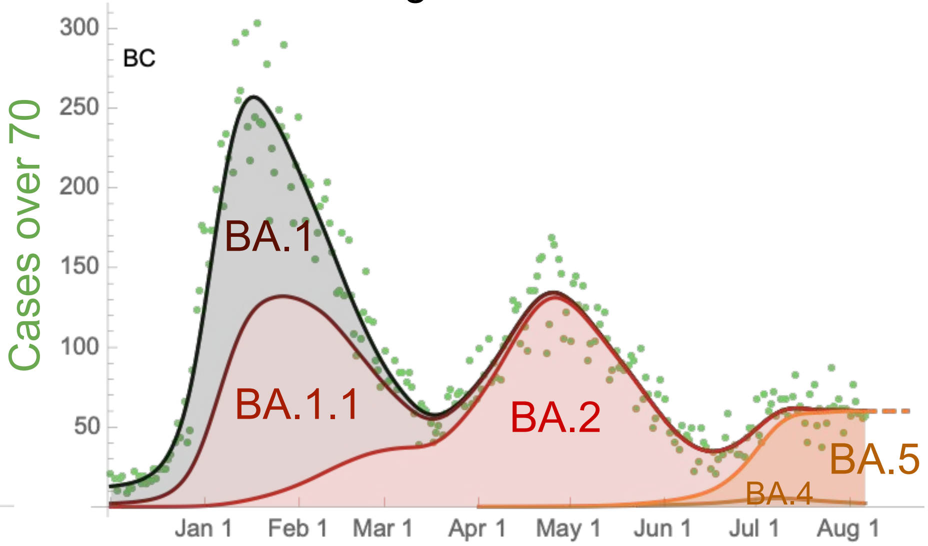
Source (S. Otto) New cases per day in 10-year age groups were downloaded from the BCCDC COVID-19 data portal. Cubic spline fits to log-case data were obtained (curve) and estimates for those <70 obtained by applying the fits for those 70+, shifted up to match the projection for that age class on 21 December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

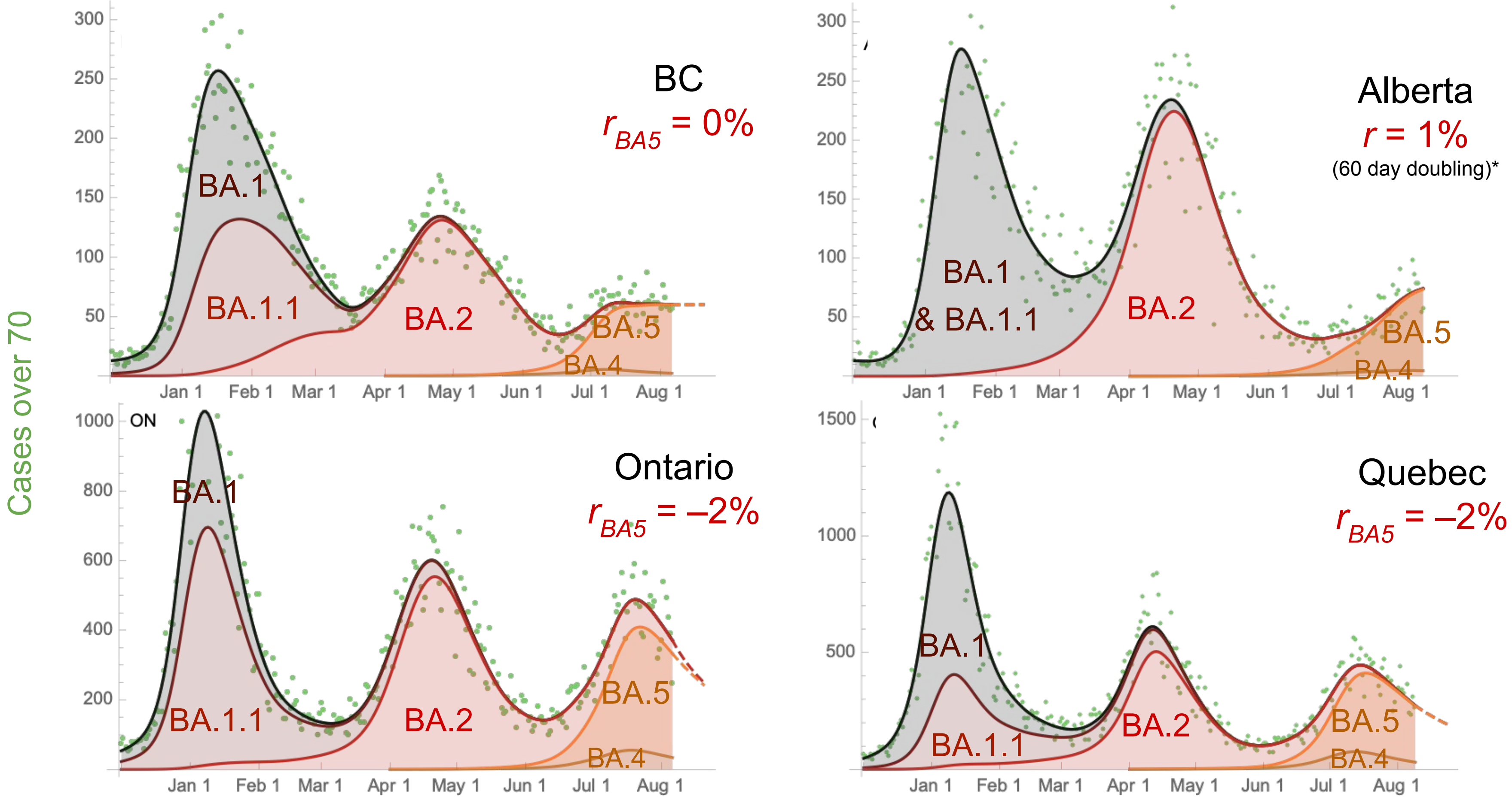


→ Estimated numbers of BA.5 have peaked.

BA.5# sub-lineages with faster growth rates may prolong this peak.

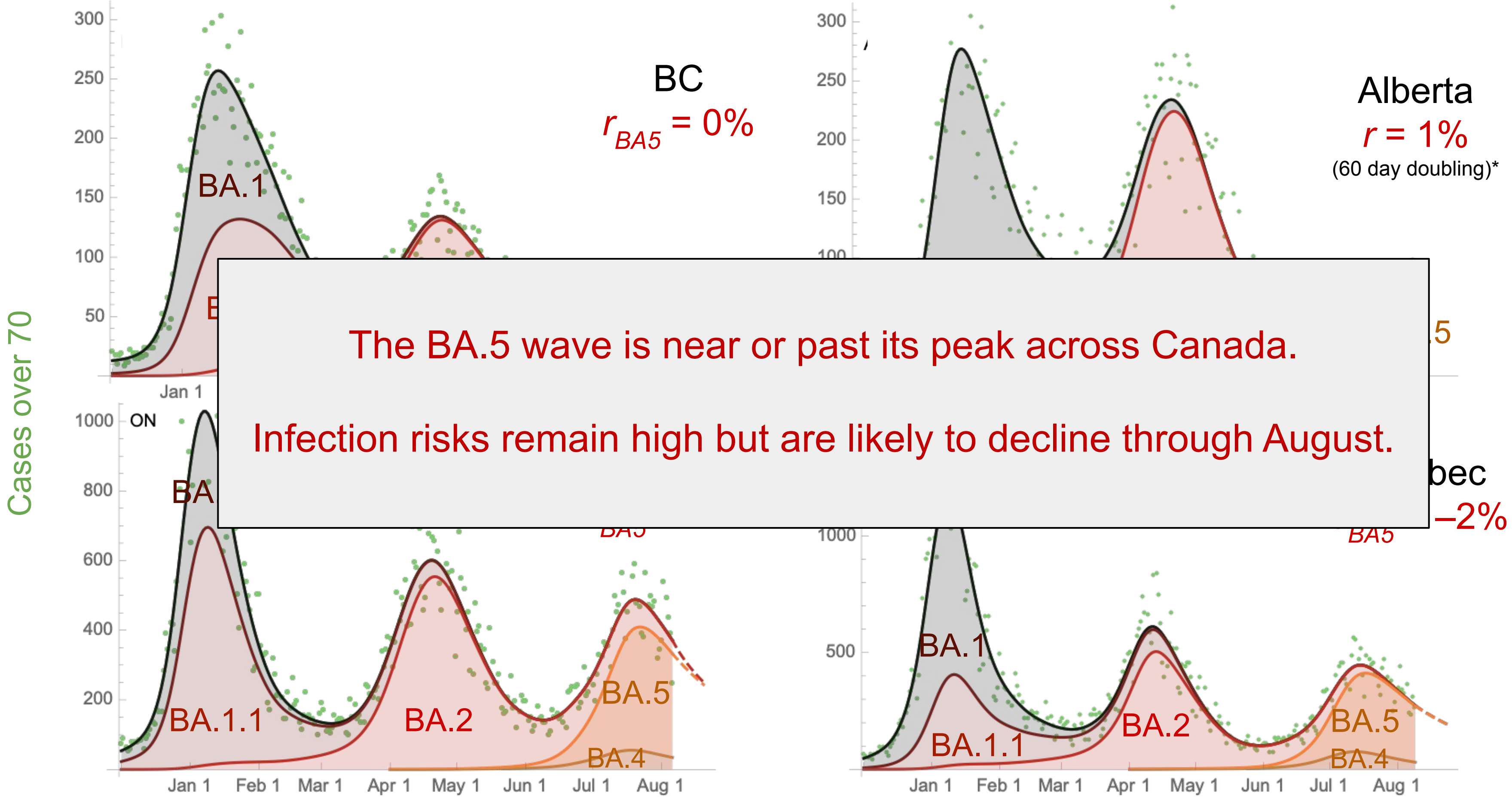
Source (S. Otto) Canadian metadata was downloaded from GISAID for the Omicron GRA clades. A model of selection was fit to the numbers of each type using maximum likelihood based on a trinomial distribution given the expected frequencies on each day. Hessian matrix used to obtain confidence intervals.

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



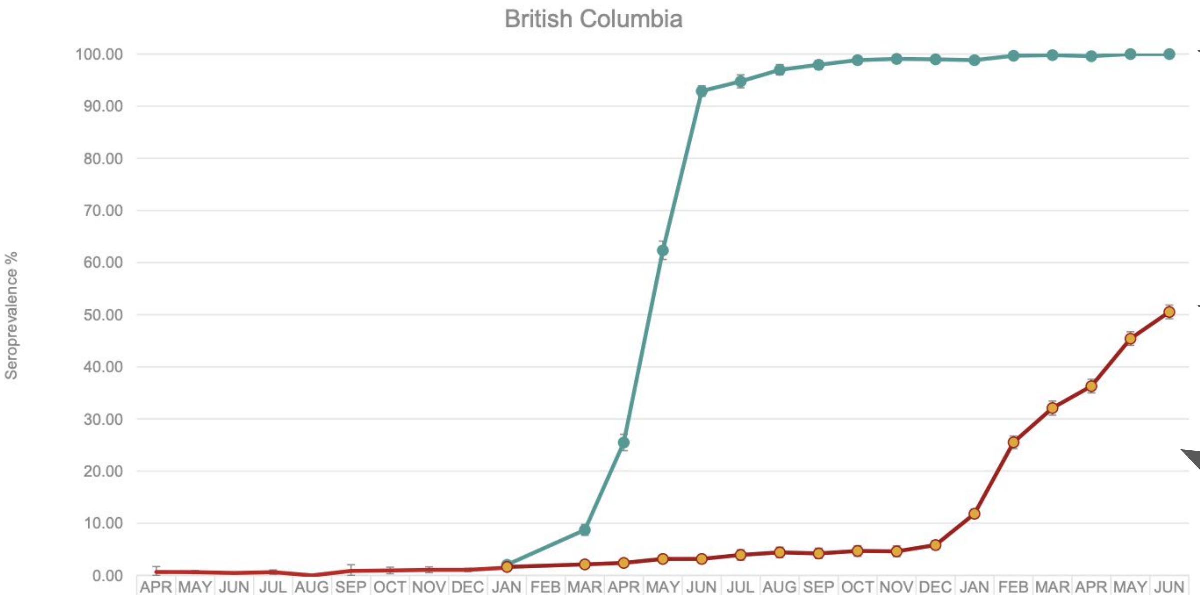
The BA.5 wave is near or past its peak across Canada.

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

* 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?

To judge the current risk of infection in BC, we need to estimate the number of unreported cases. We can use data from the CITF & Canada Blood Services survey on antibodies to SARS-CoV-2.



	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
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
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

S = spike
N = nucleocapsid

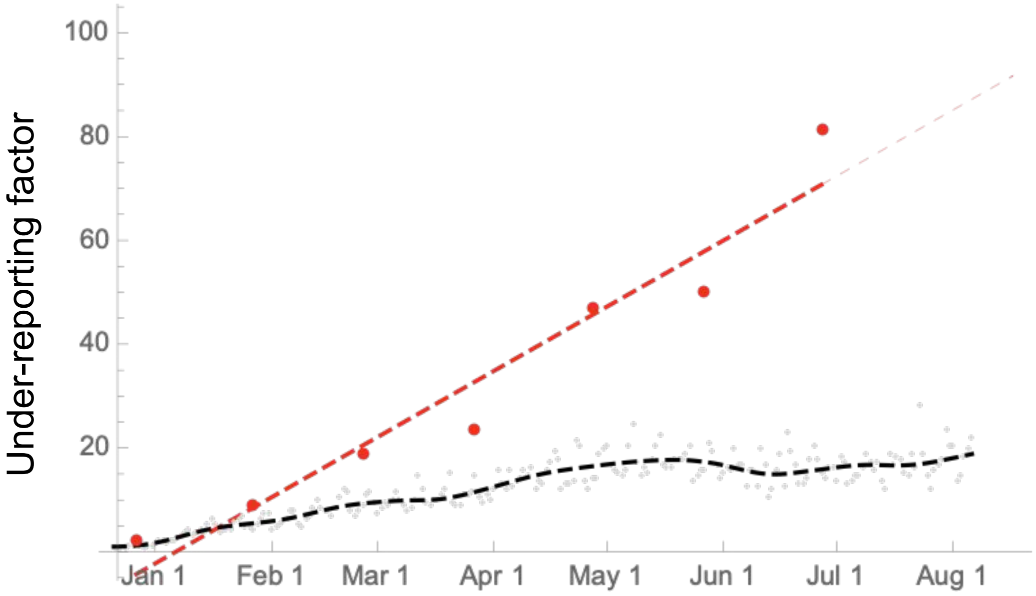
Almost everybody in BC now has antibodies to the SARS-CoV-2 spike protein through vaccination or infection.

Over 50% of BC had been infected by the end of June (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)

Source Figure from CITF Report #23.

How much are cases under-reported in BC?



Underreporting of cases in BC is currently ~100 fold.

- 91-fold if we use CITF serology data to estimate the rise in frequency of past infections among blood donors relative to the frequency of total reported cases since the previous month (red dots, dashed shows a linear fit*). Note that the serology data is noisy and that blood donors are a non-representative subset of the population.
- 20-fold if we assume that the % of infections in the 70% age class has been stable, ignoring under-reporting in this age class (black curve)
- 160-fold if we correct cases among those >70 by the overall underreporting estimated in BC by Skowronski et al. (2020)

Source (S. Otto) Black dots are the age-corrected totals from slide 12 divided by the total number of cases reported for BC (black curve shows the smoothed fit). 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 33-fold (60-fold after 1 April 2022). The linear fit (red line) shows a significant positive slope, consistent with a rise in underreporting. The estimated underreporting from the linear model is 72-fold on 1 July 2022 and would be 91-fold today, although the true rise in the unreported fraction of infections is almost certainly not linear.

Novel approach for modeling population immunity dynamics of the Omicron waves

Projections and Population-level Immunity

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

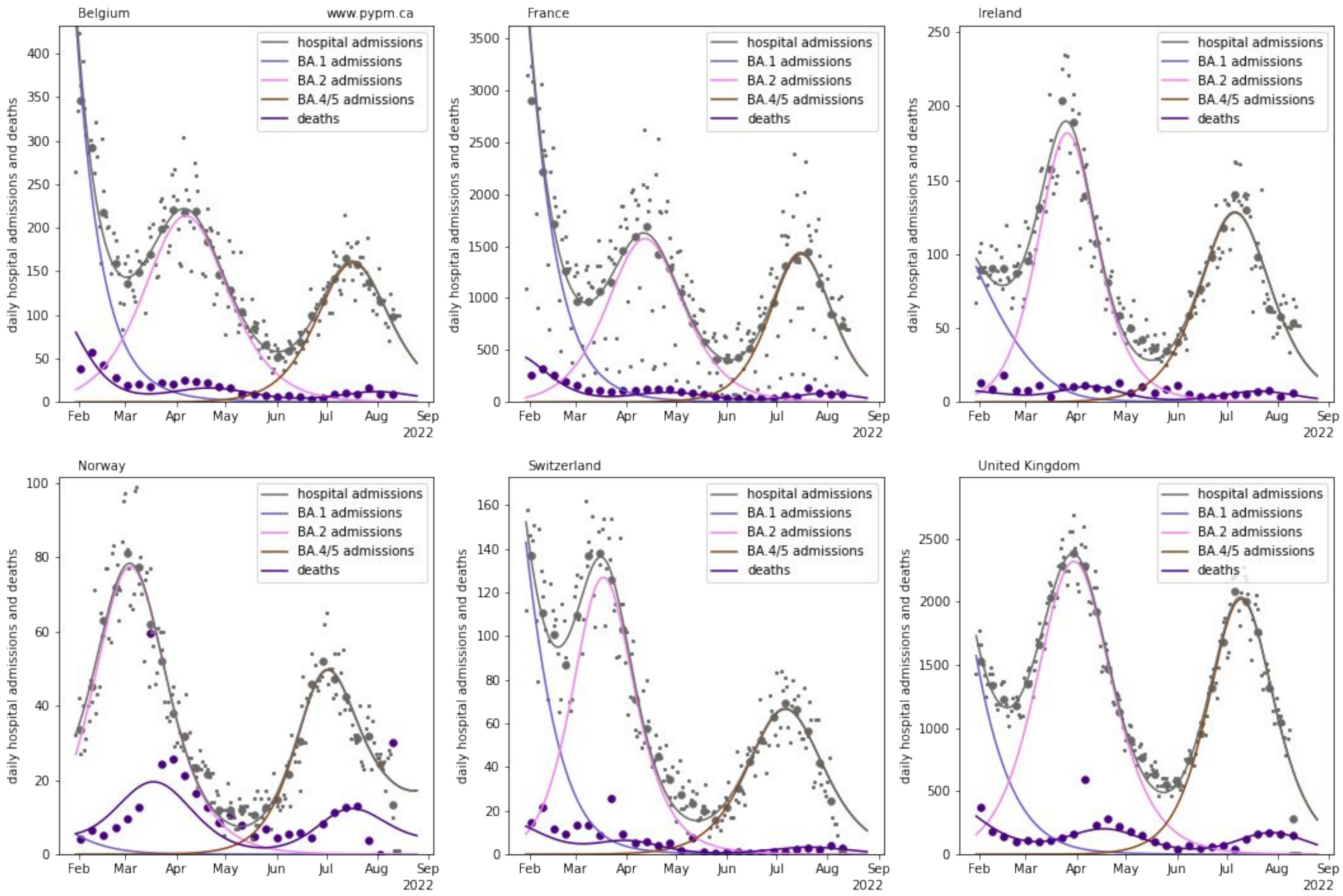
- For example, the turn around in the growth of BA.2 infections happened because of the increasing immunity primarily from new BA.2 infections (and not because of changes to public health measures or personal behaviour).

Estimating population-level immunity by modeling past infections and vaccination is difficult, due to uncertainty in immunity effectiveness, waning, and reporting fraction.

The next slide shows the results of a new approach. Population immunity dynamics are deduced directly from population-level data. No assumptions need to be made for immunity effectiveness, waning, or a “reporting fraction” since immunity and the rate of new infections are determined by the rise and fall of the BA.2 wave. In this study, hospital admission data are used, and so the “reporting fraction” is the fraction of 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

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, which is necessary to fit data.

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

BA.2 and BA.4/5 waves and immunity

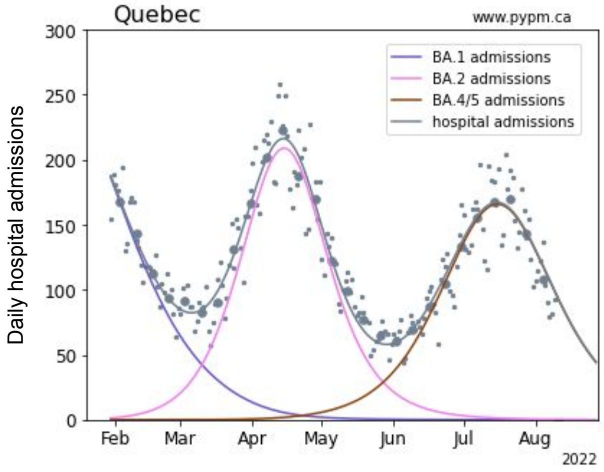
In these simple models, 20%-40% of the population were susceptible prior to the BA.2 wave. Following the BA.2 wave, this declined to only 5-10% susceptible to BA.2. An additional susceptible population must be added to fit the BA.4/5 wave (escape fraction).

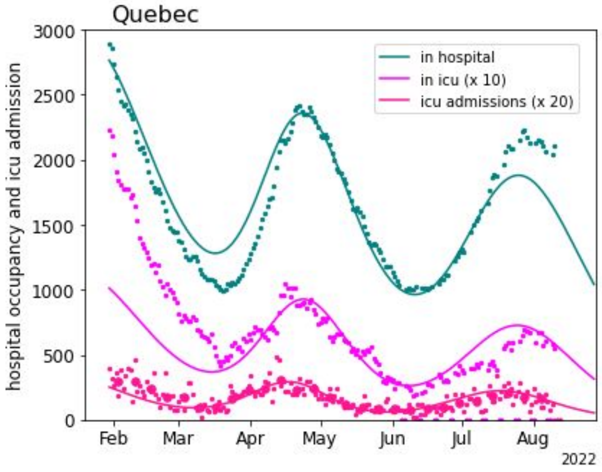
		BA.2		BA.4/5		
Country	**f_hosp**	**s_2**	**f_susc_2**	**$s_{4/5}$**	**$f\_susc_{4/5}$**	**$f\_escape_{4/5}$**
Belgium	0.012	0.11	0.17	0.12	0.05	0.05
France	0.009	0.12	0.23	0.13	0.06	0.10
Ireland	0.006	0.12	0.43	0.13	0.08	0.35
Norway	0.003	0.11	0.39	0.13	0.10	0.06
Switzerland	0.004	0.12	0.24	0.12	0.05	0.15
United Kingdom	0.010	0.11	0.32	0.13	0.08	0.16

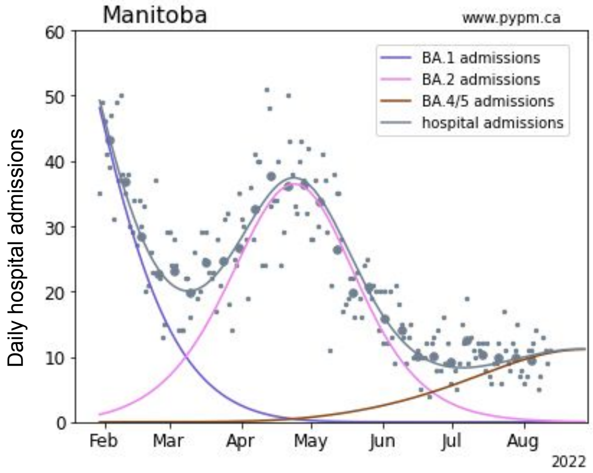
- f_hosp: fraction of infections that lead to immunity that also lead to hospitalization
- s_2: selection coefficient for BA.2 wrt BA.1/day
- f_susc_2: susceptible fraction of population when BA.2 became dominant
- $s_{4/5}$: selection coefficient for BA.4/5 wrt BA.2
- $f\_susc_{4/5}$: susceptible fraction of population when BA.4/5 became dominant
- $f\_escape_{4/5}$: additional susceptible fraction of population available to BA.4/5 (partial escape from immunity)

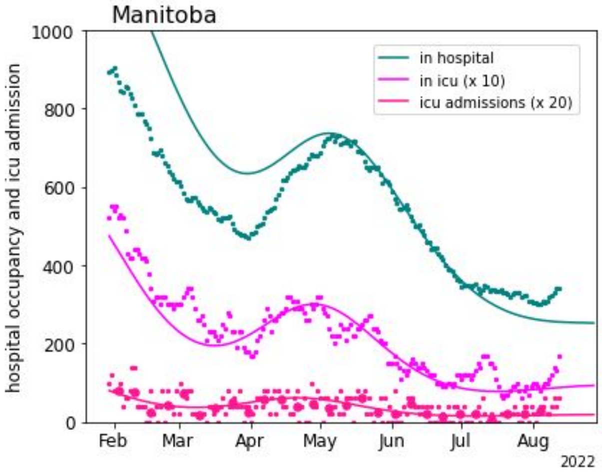
Source (D. Karlen) As in previous reports, each pypm model represents a homogeneous population that produces a similar time history of hospital admissions as the jurisdiction under study. Three Omicron strains are included. For this study, immunity of the population is modelled only by infections, by 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. Only the model for Norway includes waning (with a Gamma delay having mean and standard deviation of 12 and 2 months respectively). More data are required to establish evidence for waning.

Quebec and Manitoba









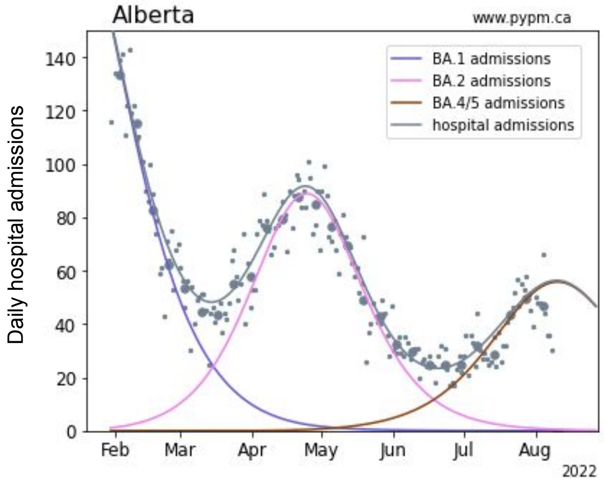
The same approach is applied to four provinces.

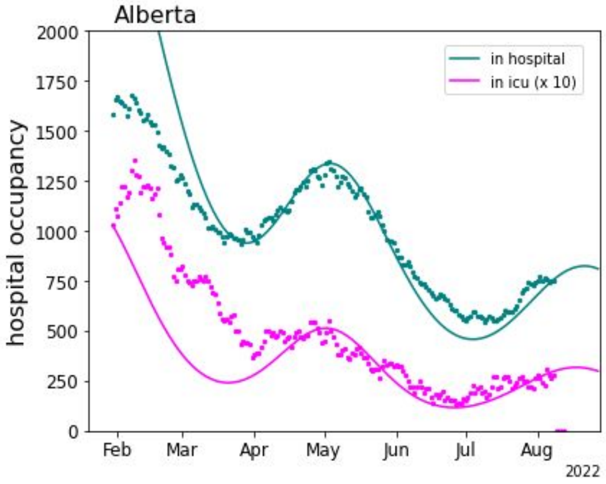
In Quebec, the third omicron wave peaked in July, like many European nations.

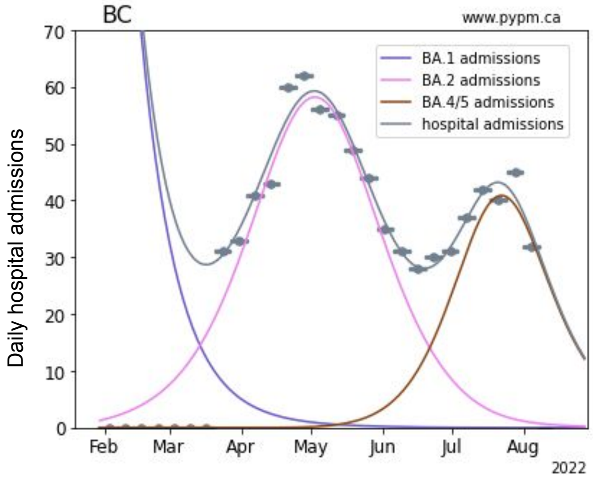
In Manitoba, the BA.4/5 wave appears significantly smaller and peaks later than other jurisdictions.

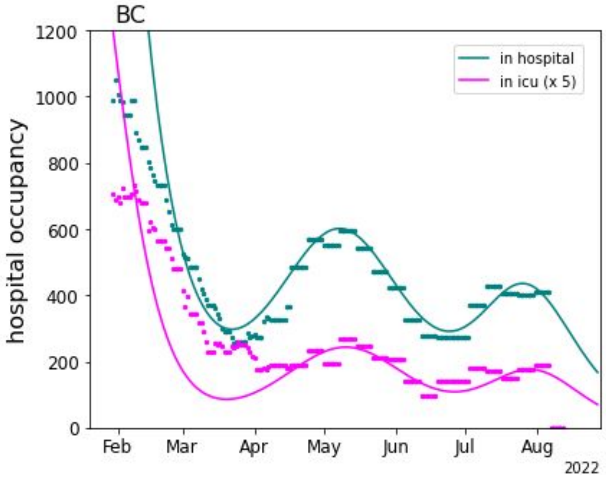
Distributions for length of stay in hospital and ICU are adjusted to fit recent data (constant through entire period).

Alberta and BC









The peak in hospital admissions in Alberta and BC appear to have been reached, or soon will be reached.

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.

The turnover in BC is faster than expected, forcing the model to assign a very small susceptible population for the BA.4/5 wave. The last data point is corrected for typical undercounting (see appendix).

BA.2 and BA.4/5 waves and immunity

Like models for Europe, 20%-40% of the population remained susceptible prior to the BA.2 wave. Following the BA.2 wave, this reduced to only 5-15%. The estimated selection coefficients (difference in daily growth rates) are somewhat lower than found from European nations, but consistent with estimates from genomic data, shown on page 10.

		BA.2		BA.4/5		
Province	**f_hosp**	**s_2**	**f_susc_2**	**$s_{4/5}$**	**$f\_susc_{4/5}$**	**$f\_escape_{4/5}$**
BC	0.007	0.11	0.19	0.11	0.06	0.02
Alberta	0.006	0.11	0.32	0.10	0.09	*
Manitoba	0.008	0.10	0.40	0.08	0.15	*
Quebec	0.004	0.12	0.36	0.12	0.07	0.36

* without an established peak in BA.4/ 5, the escape fraction cannot be estimated

The approach of using population level data to estimate population immunity yields similar results for different jurisdictions.

Using this method, data from jurisdictions first experiencing new waves can be used to forecast the eventual waves elsewhere, even with highly immunized populations.

Key messages

The third Omicron wave, driven by BA.5, has peaked.

- BA.5 is the predominant variant across Canada, representing >80% of cases.
- BA.5 consists of several sub-lineages, with some sub-lineages (e.g., BA.5.2, BE.# & BF.#) showing signs of a slight growth advantage.
- No strain is showing such a strong selective advantage that it would drive another wave in the near future, until immune protection from infection further wanes.

Underreporting the impacts of COVID make it challenging for the public to have a full understanding of current risks. Deaths due to COVID may be ~2-fold underreported based on excess mortality. Current infection rates may be ~100-fold underreported based on serology data.

Population immunity can be estimated based on the shape of the pandemic curves, providing a way to estimate immune evasion.

- BA.5 was estimated to have a 5-25% larger fraction of susceptible individuals in the population, providing a substantial advantage from immune evasion.
- Nevertheless, immunity levels have been high enough to turn the BA.5 wave down across most of Canada.

Key messages

The third Omicron wave, driven by BA.5, has peaked.

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The BC COVID-19 Modelling group will continue to monitor the available data and provide analyses when new Variants of Concern arise, but reports are likely to be intermittent as our teaching duties resume.

We thank you for reading our reports and adjusting behaviours appropriately in light of what data is available in BC to understand the pandemic.

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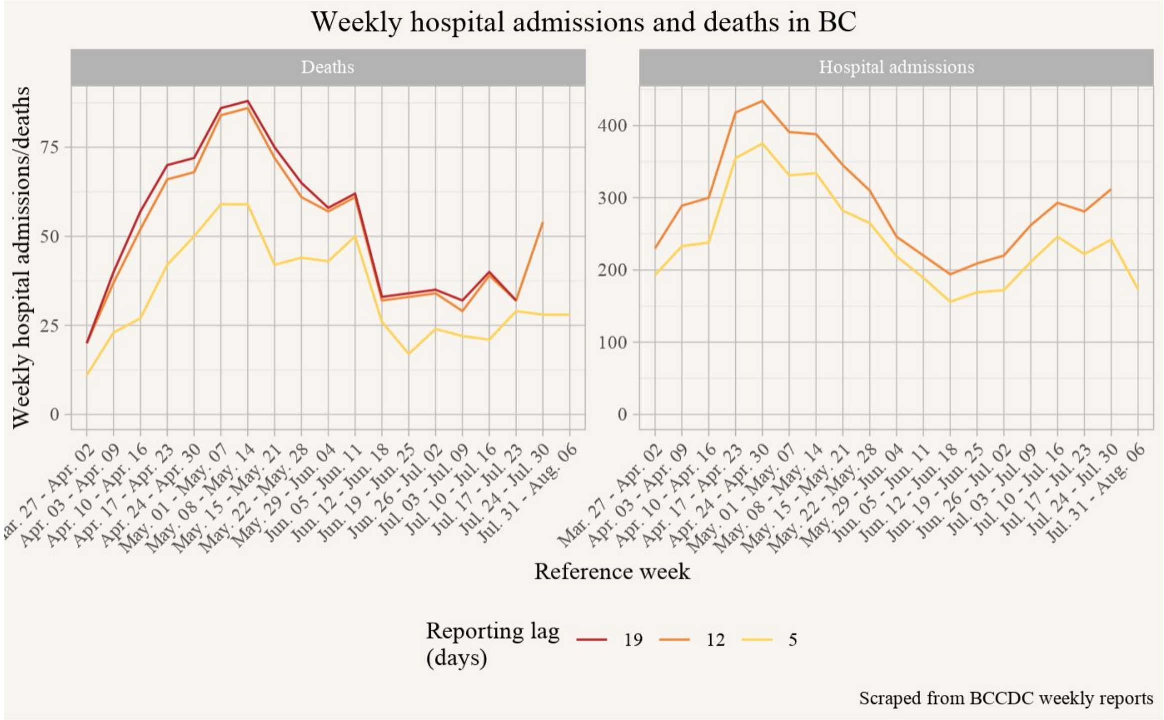
- Nevertheless, immunity levels have been high enough to turn the BA.5 wave down across most of Canada.

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.