COVID Model Projections

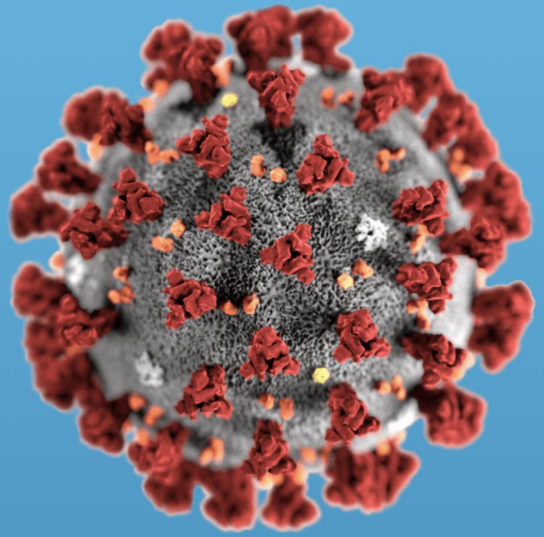
June 16, 2021

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 was convened by Caroline Colijn (SFU) and Dan Coombs (UBC) 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.

BC: Facing old and new variants of concern

Key messages (currently “what we plan to include”)

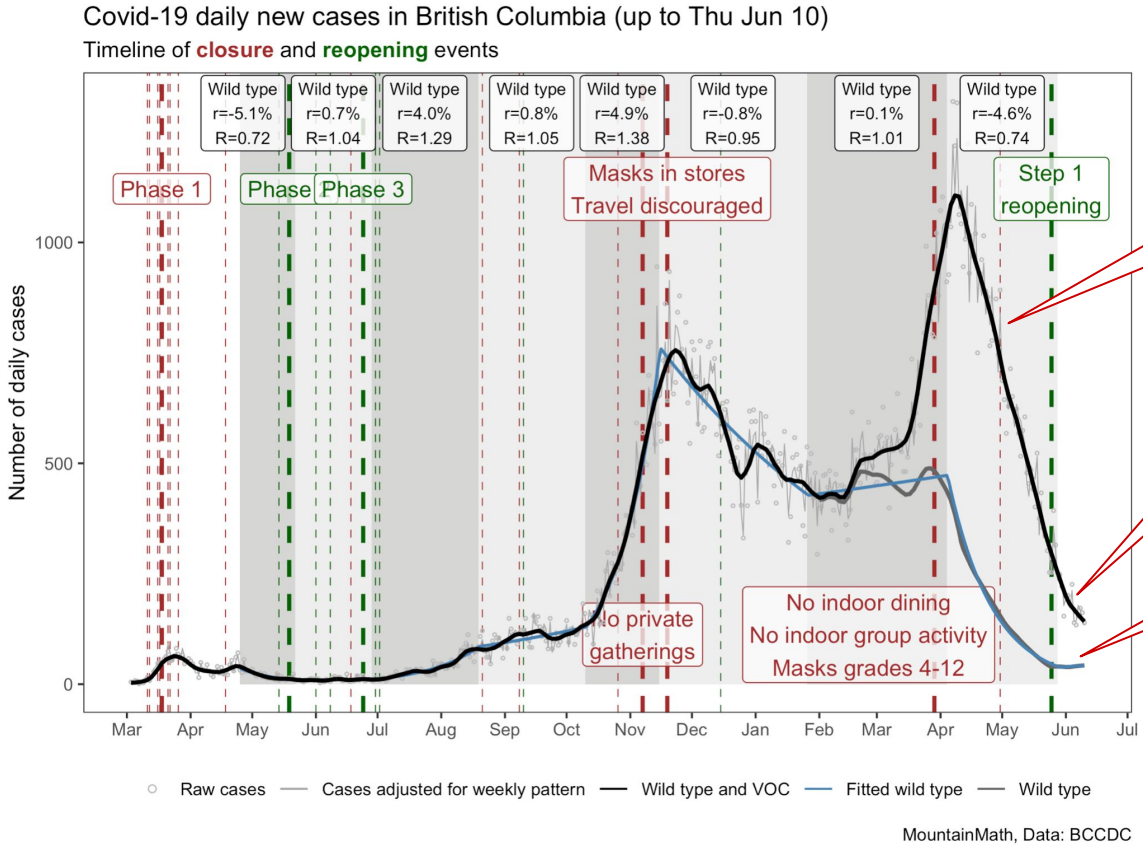
- Effect of the May 25 lifting of measures
- Delta update
- Revisit early Feb B.1.1.7 predictions of third wave (Jens’ cartoon idea)
- Impact of 1-dose/2-dose on growth rate
- Vaccination progress update
- Why we don’t project months ahead.

Key messages

OLD SLIDE

- Cases in BC are currently dominated by B.1.1.7 and P.1 (>80% frequency).
- With these currently dominant strains, cases are projected to increase briefly and then turn around later in June, as vaccination levels rise.
- With these currently dominant strains, hospital and ICU occupancy are projected to continue to decline.
- The new variant of concern B.1.617.2 appears to be increasing in number in many

State of the COVID-19 Pandemic in BC



April 2021: BC bent down the COVID-19 curve following March 30 “circuit breaker”

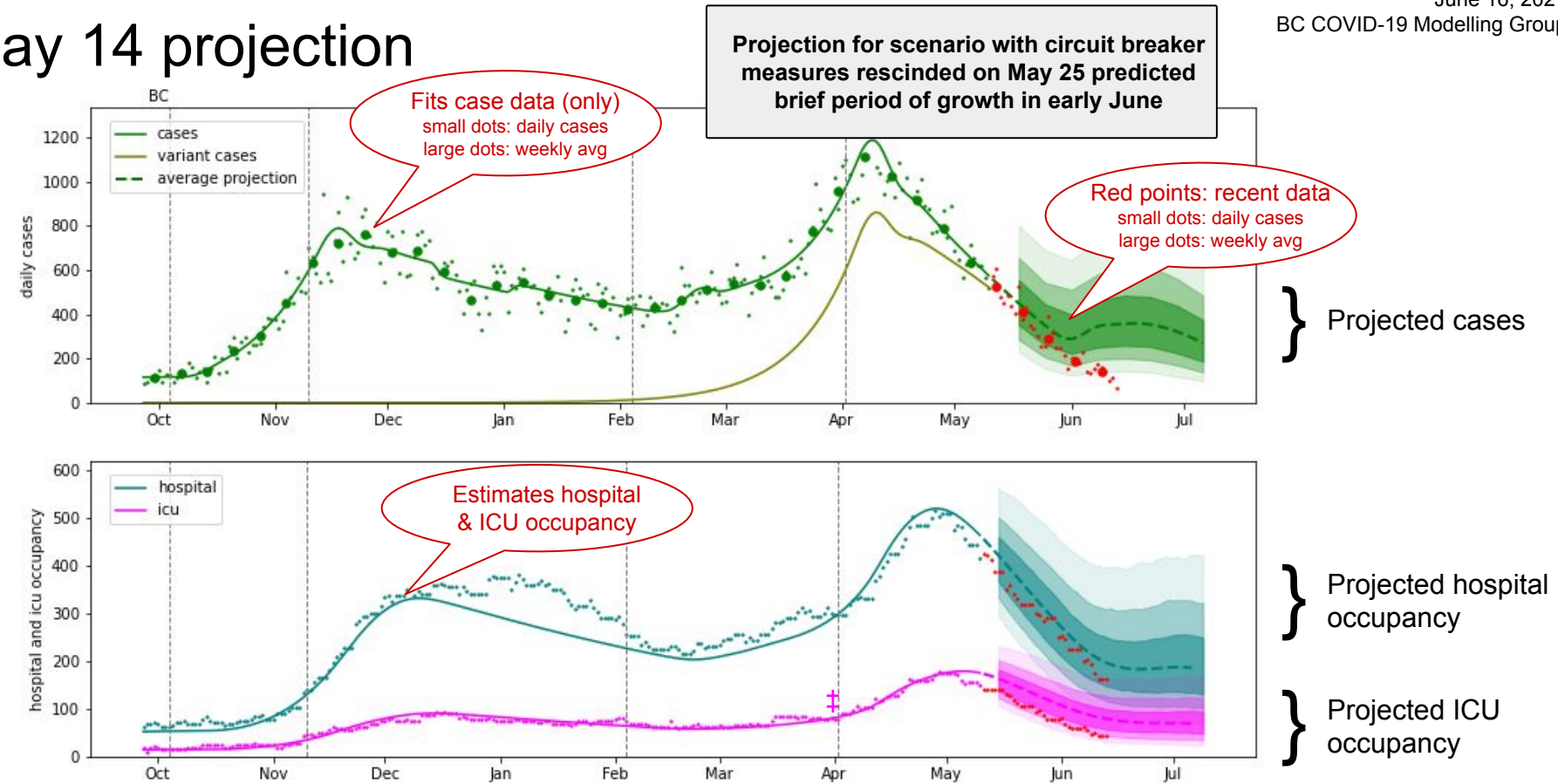
June 2021: Change in growth rate after Step 1 reopening

Sudden upswing in non-VOC cases indicates unknown variants or poor variant data quality

Poor data on delta VOC makes it hard to interpret current trends (VOC data likely of poor quality).

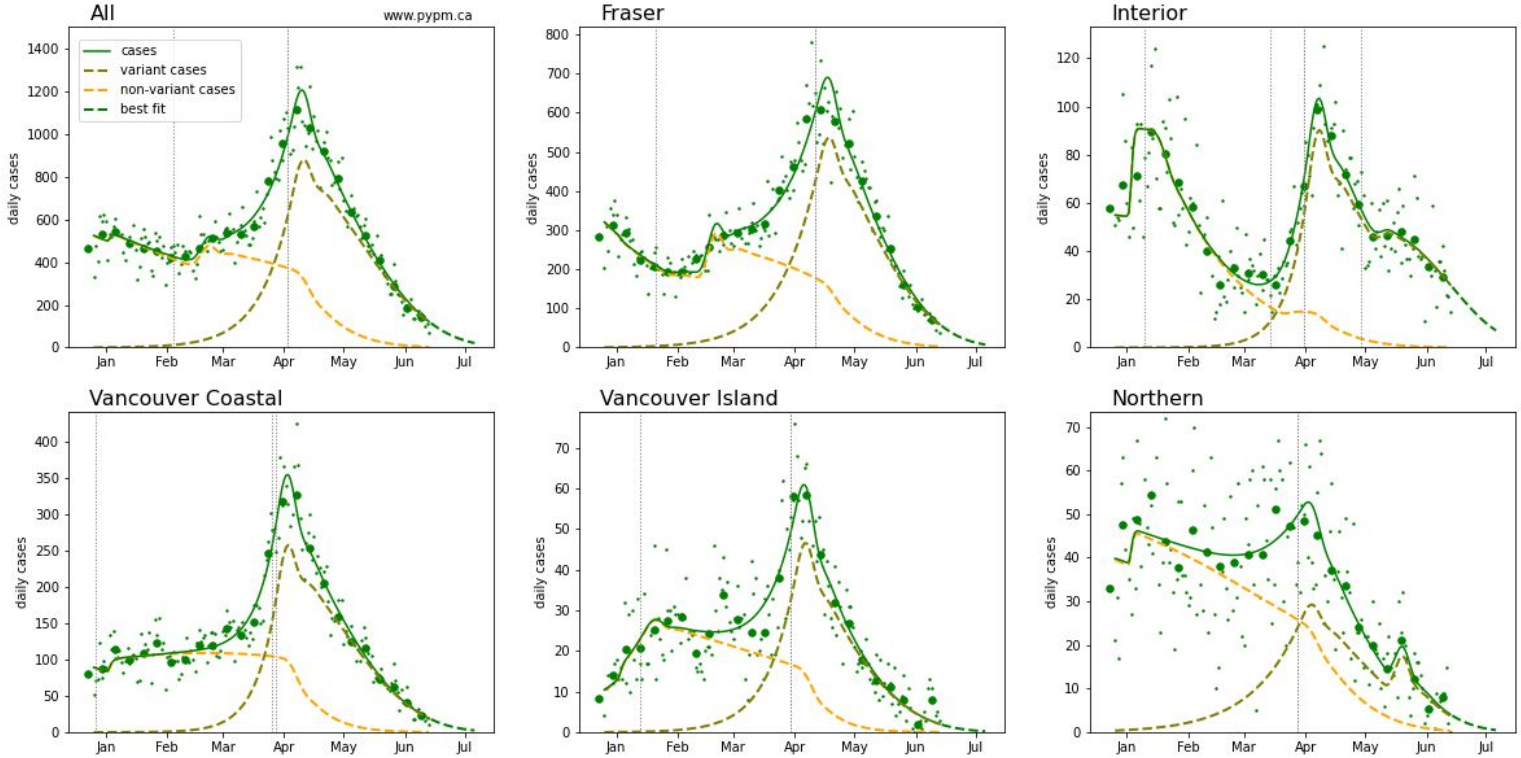
Source (J. von Bergmann) Case data from BC COVID-19 Database (http://www.bccdc.ca/health-info/diseases-conditions/covid-19/data). Vertical lines give dates of public health measures (major as thick lines, minor as thin lines). Grey dots are raw case counts, grey lines is cases abused for weekly pattern, black STL trend line and blue fitted periods of constant exponential growth.

May 14 projection



Source (D. Karlen). See www.pypm.ca. Homogeneous mixing (no age structure). Vaccination rate assumptions: 45,000/day up until 75% vs 65% vaccinated, with 90% asymptotic effectiveness of first dose (see Appendix of May 14 report for comparison to real-world effectiveness). Projection is for a scenario rescinding the March 30 measures (the "circuit breaker") on May 25, returning BC to activity levels in early 2021. ‡To match ICU data, the fraction of cases leading to ICU admission is increased by 60% ± 20% in early April. Bands show approximate 50%, 80%, and 95% intervals.

Updated model fit to case data by Health Authority



Continued decline in all HA except:

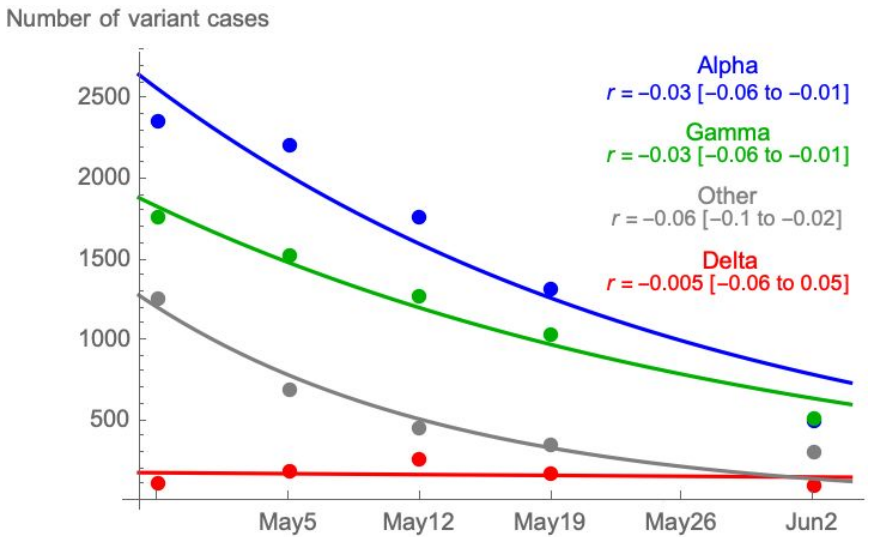
Interior: transmission rate increased (late April)

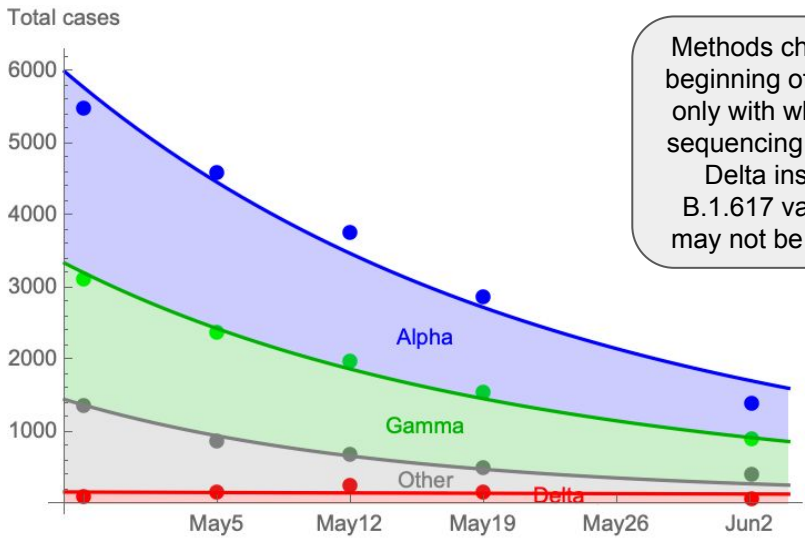
Northern: Burst of infections in May (outbreak?)

Source (D. Karlen). See www.pypm.ca. These models have no age structure. Assumes future vaccination rate of 1st doses of 45,000/day (given to all ages and in proportion to HA populations until 75% of the population is vaccinated), ultimate 1st dose effectiveness is 90%. Vaccination model benchmarked with data from Israel: see Appendix and link. Assumes current public health measures remain in place in June.

Spread of Delta in BC

Typing of cases reported by the BCCDC from April 25 to June 5 indicates that all variants are declining, except Delta, which remains steady.

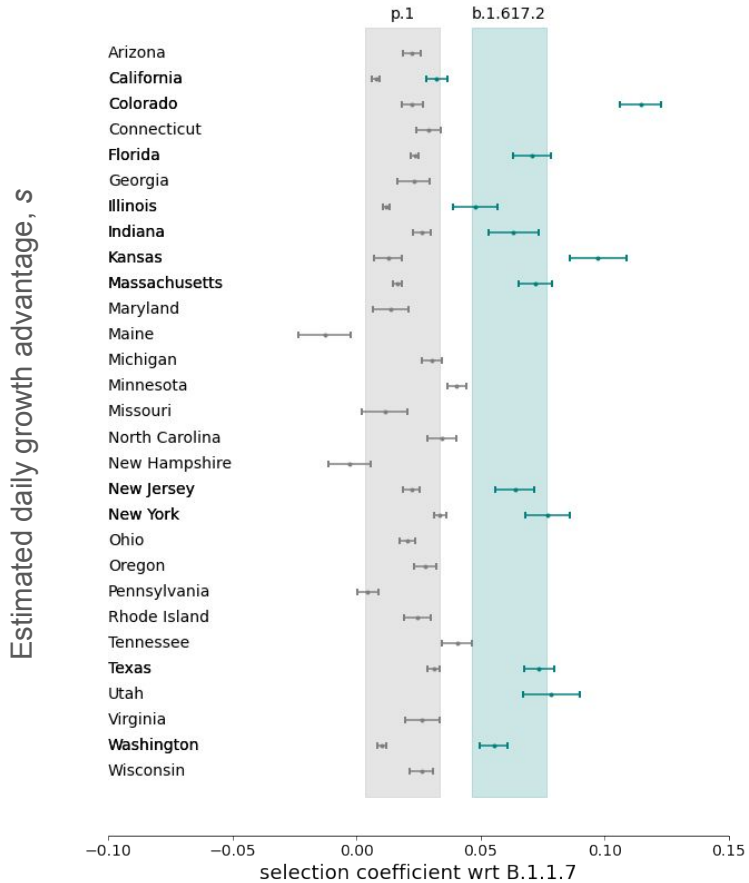


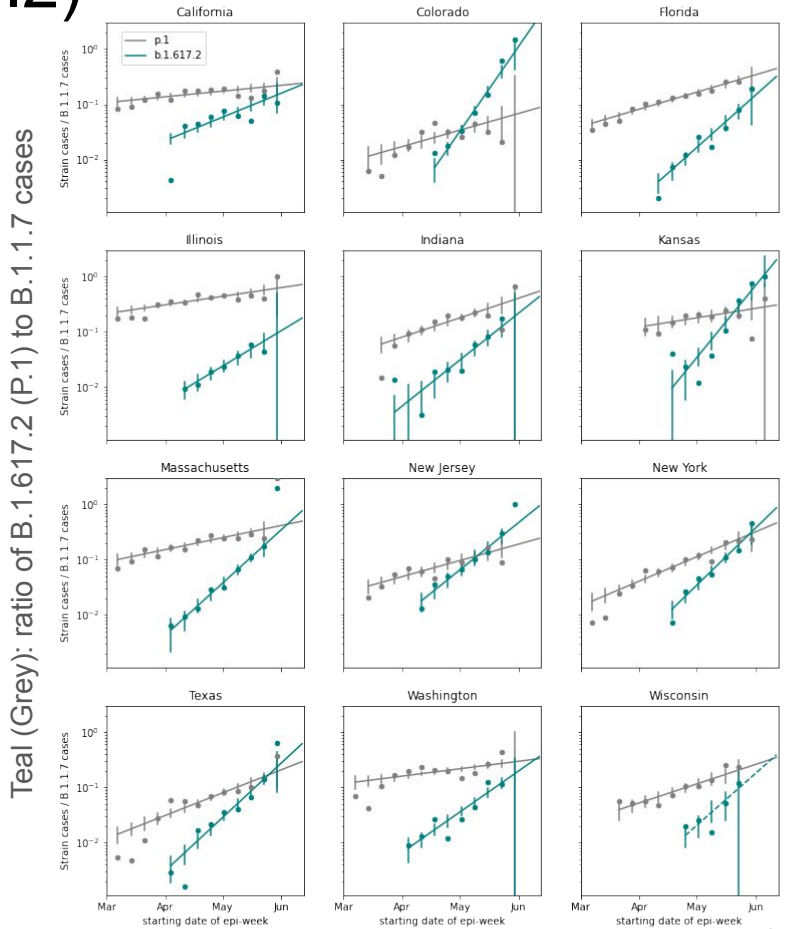


Methods changed at the beginning of June to type only with whole genome sequencing and to report Delta instead of all B.1.617 variants. Data may not be comparable.

Source (S. Otto). Fit to weekly Variant report from BCCDC (subtypes of B.1.617 not distinguished). Uses weekly cumulative case numbers for each epiweek (mid-date of epiweek shown on the x axis) and multiplies by the "Sample prevalence VOCs" to estimate the number of each variant in each week. Exponential model fit is used to estimate daily growth rate, *r*. Note that *r* estimates are highly uncertain with only three data points [95% CI in square brackets]. The selective advantage for B.1.617 relative to B.1.1.7 is $s = 0.08$ per day (the difference in their daily growth rates, consistent with other jurisdictions, next slide)

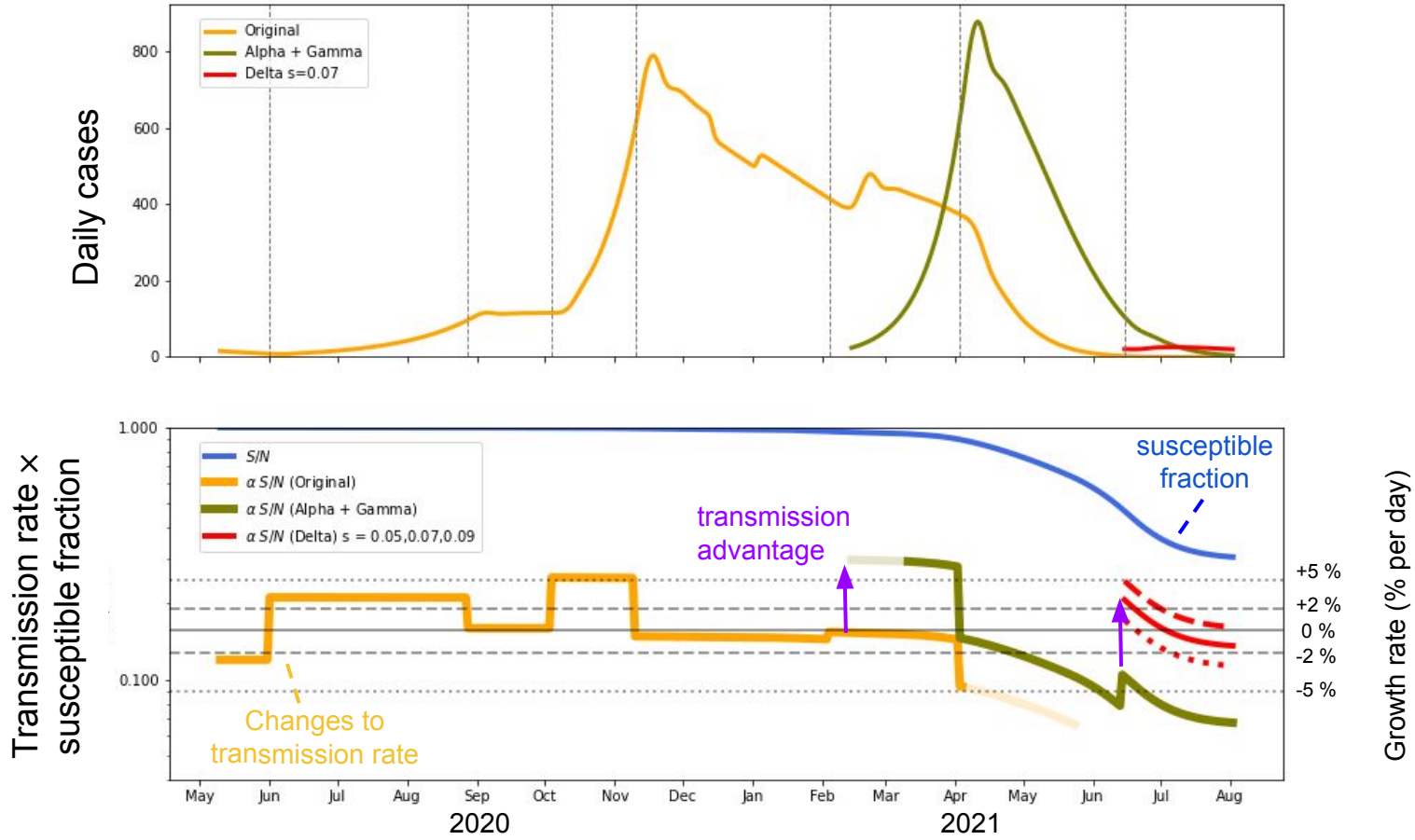
Growth advantage of Delta (B.1.617.2)





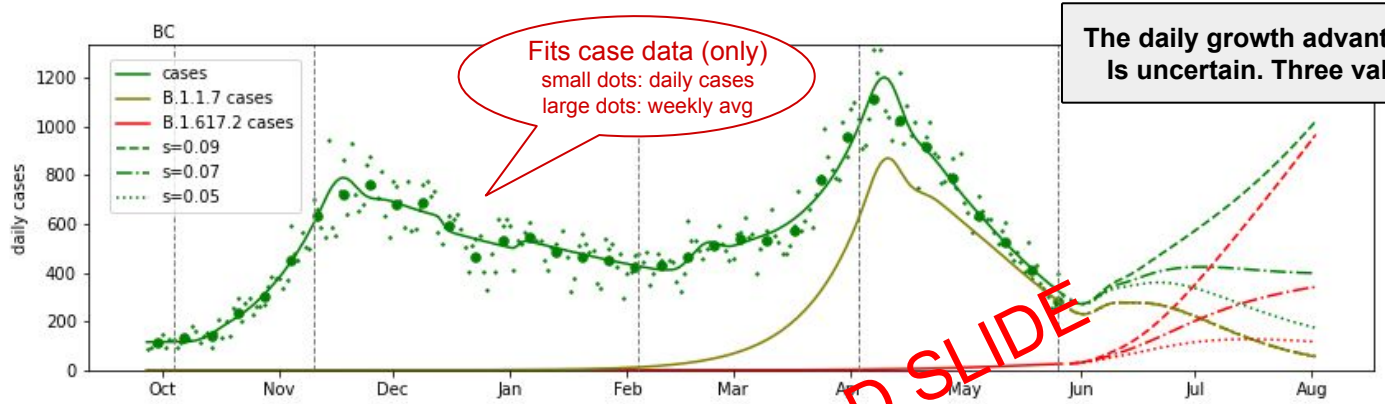
Source (D. Karlen). Fit to GISAID data as compiled by outbreak.info for USA. Growth advantage ("selection coefficient", *s*) measures the daily rise in the frequency of a variant, either Delta(B.1.617.2) or Gamma (P.1), relative to the frequency of Alpha (B.1.1.7).

Past and future growth



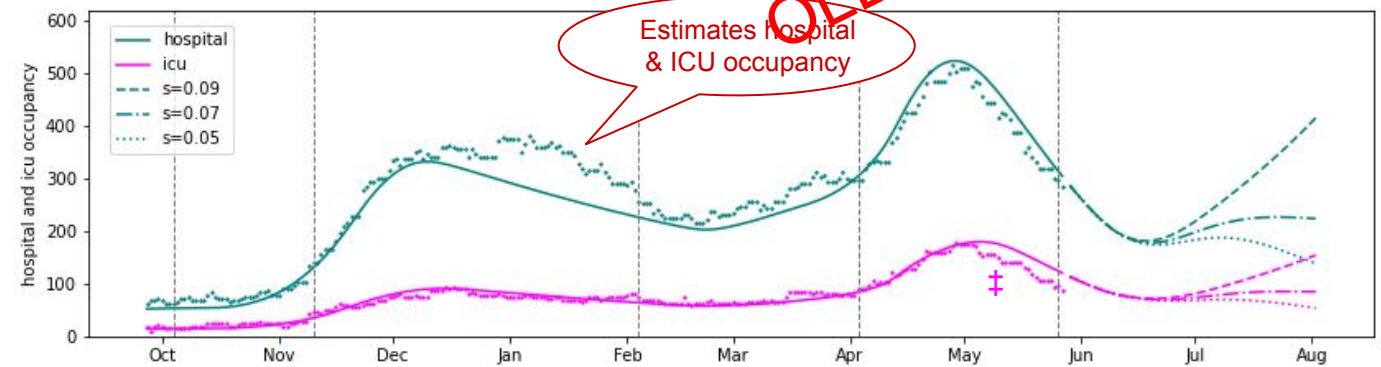
Source (D. Karlen). See www.pypm.ca. These plots illustrate how transmission rate and susceptible fraction combine to determine the growth rate.

Model projections with B.1.617.2 variant



The daily growth advantage of B.1.617 (compared to B.1.1.7) is uncertain. Three values are shown*: *s* = 0.09, 0.07, 0.05

} Projected cases



} Projected hospital occupancy

} Projected ICU occupancy

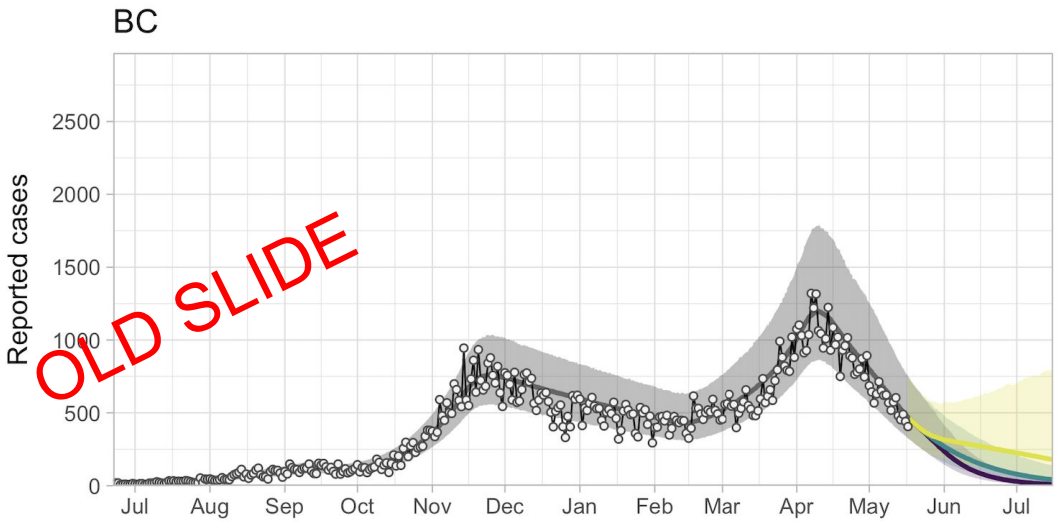
Source (D. Karlen). See www.pypm.ca. Homogeneous mixing (no age structure). Vaccination rate assumption: 52,000/day until 75% vaccinated, with 90% asymptotic effectiveness (see Appendix from May 14 report for comparison to real-world effectiveness). ‡To better match ICU data, the fraction of cases leading to ICU admission is increased by 60% in early April. Assumes current public health measures remain in place. *Range of growth advantage (selection coefficient, *s*) for B.1.617.2 with respect to B.1.1.7 is based on genomic data from other jurisdictions (see previous slide).

BC incidence projections: contact and slight reopening

Incidence continues to decline, with vaccinations§ contributing to that decline.

This decline is robust to a slight increase in contact rates* among those distancing (+30% in yellow, -30% in purple).

It is too early to determine impact of Step 1 of BC's reopening plan relative to these projections.

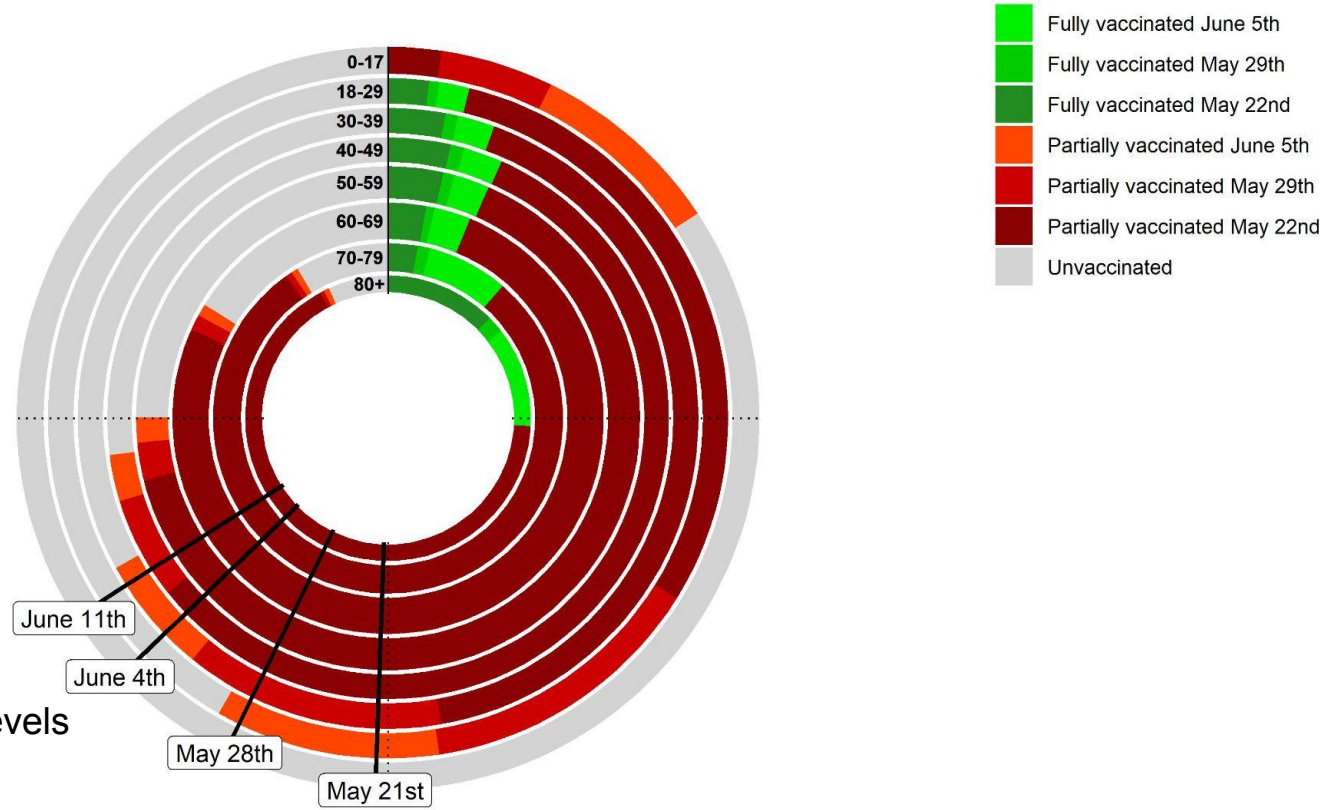


Yellow: 30% increase in contact*. Green: as now. Purple: 30% decrease in contact.

Source (E. Are, C. Colijn). Daily case numbers projected forward, accounting for B.1.1.7 and P.1 data from BCCDC variant reports. These data provide % of cases that were VOC by week (see appendix slide 23). These data were fit by a logistic function to estimate percent VOC by day (see Appendix of April 14 report). Assuming a 40% increase in transmissibility (consistent with the estimated selection *s* in the Appendix of April 14 report), the percent VOC is used to create an overall reproduction number *R* for the virus population. *R* changes in time as the VOC rises in frequency. The social distancing parameter (among others) is estimated to fit the data using the 'covidseir' R package (M. Irvine, S. Anderson). §Vaccination is incorporated by removing susceptibles at a rate accounting for contact by age, vaccination by age and susceptibility of contacts. * Measured as *f*, the relative contact rate among those willing and able to distance.

Closing the circle: Vaccination status by age

June 12th update includes data through June 4th, 2021



Making progress:
Average vaccination levels by date in BC

Source (B. Wiley). Design by Blake Shaffer (https://blakeshaffer.shinyapps.io/app_vaccines/) BC Vaccination data from https://health-infobase.canada.ca/covid-19/vaccination-coverage/, with the area of each circle segment proportional to BC's population in that age class.

Closing the circle: Vaccination status by age

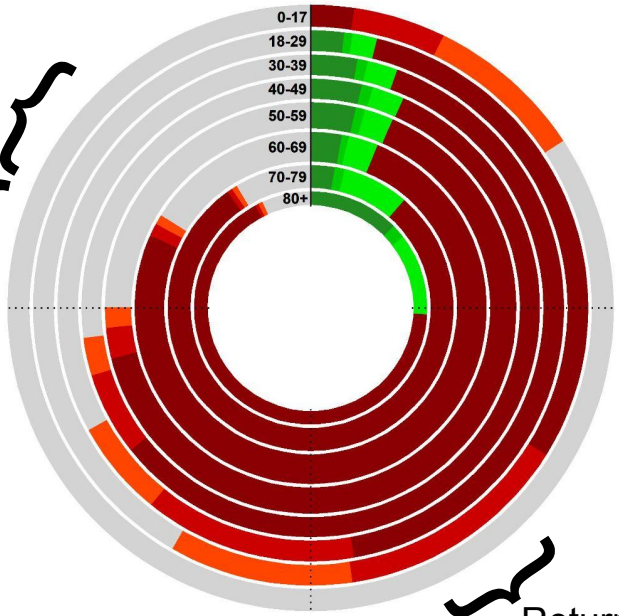
June 12th update includes data through June 4th, 2021

If vaccines were 100% effective:

Herd immunity if R_0~5-6

Herd immunity if R_0~4-5

R_0 for B.1.617.2 unknown but may be ~4 to 7 given an R_0 for B.1.1.7 of ~2.8 to 5.4* without control measures



Fully vaccinated June 5th
Fully vaccinated May 29th
Fully vaccinated May 22nd
Partially vaccinated June 5th
Partially vaccinated May 29th
Partially vaccinated May 22nd
Unvaccinated

Herd immunity: the level of immunity in a population at which a disease starts to decline*

→ (1-*f*) $R < 1$ where *f* is level of immunity

Reproductive number (*R*): number of new cases per case, called R_0 in the absence of any control measures.

Return to Feb/March 2021 activities when R~1.7 for B.1.1.7 & P.1 in BC†

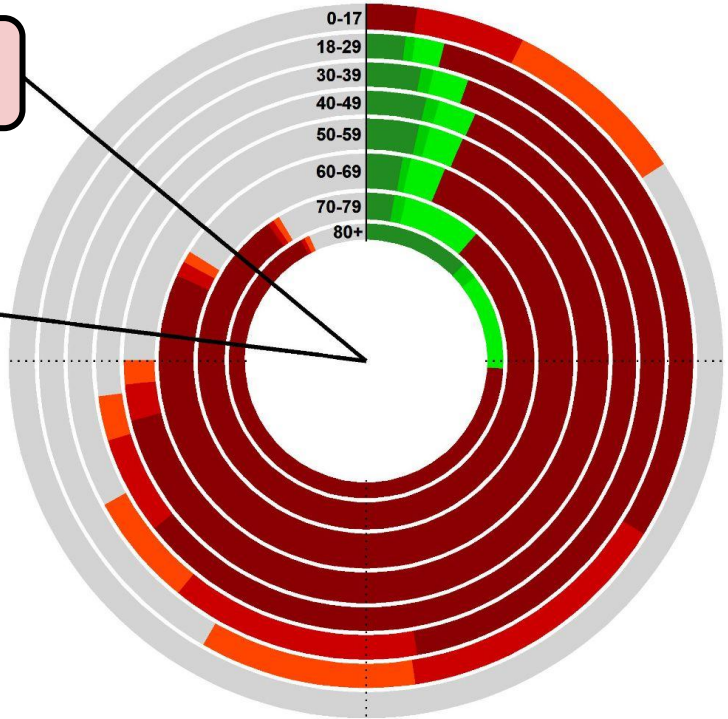
Source (B. Wiley). Design by Blake Shaffer (https://blakeshaffer.shinyapps.io/app_vaccines/) †https://bccovid-19group.ca/post/april-2021-report/
*Public Health Ontario: https://www.publichealthontario.ca/-/media/documents/ncov/covid-wwksf/2021/02/wwksf-herd-immunity.pdf, assuming B.1.617.2 has a selective advantage of *s*=0.05 and using a 6.5 day generation time to translate to reproductive numbers (as in Volz et al.). *Typically assumes no or minimal control measures.

Closing the circle: Vaccination status by age

June 12th update includes data through June 4th, 2021

Only 86% of BC willing to get vaccinated*

Only 90% of those are eligible (≥12)†



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Source (B. Wiley). Design by Blake Shaffer. *Angus Reid (April 26, 2021): https://angusreid.org/vaccine-astrazeneca-johnson/. †BCCDC (April 24, 2021) Epi-week 16 Situation Report. ‡NACI "Recommendations on the use of COVID-19 vaccines" (May 3, 2021), Efficacy against symptoms >14 days after one dose (>21 days for Astrazeneca) but before two doses; Pfizer: 92.3% [95%CI: 69-98%]; Moderna: 92.1% [95%CI: 68.8-91.1%]; AstraZeneca: 71.3% [95%CI: 49.0-83.8%].

Closing the circle: Vaccination status by age

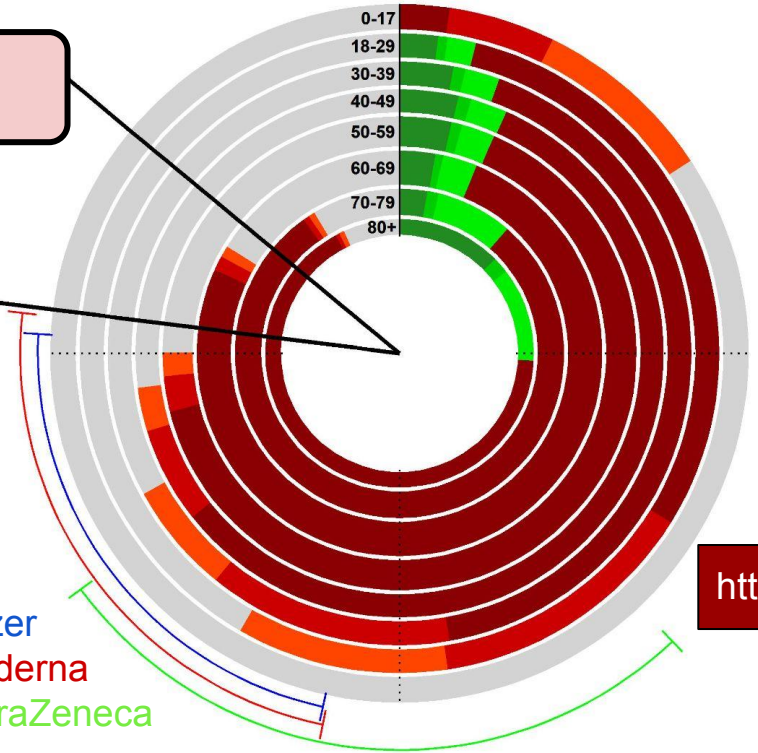
June 12th update includes data through June 4th, 2021

Only 86% of BC willing to get vaccinated*

Only 90% of those are eligible (≥12)†

&

First dose only partially effective against symptomatic infection‡



Fully vaccinated June 5th
Fully vaccinated May 29th
Fully vaccinated May 22nd
Partially vaccinated June 5th
Partially vaccinated May 29th
Partially vaccinated May 22nd
Unvaccinated

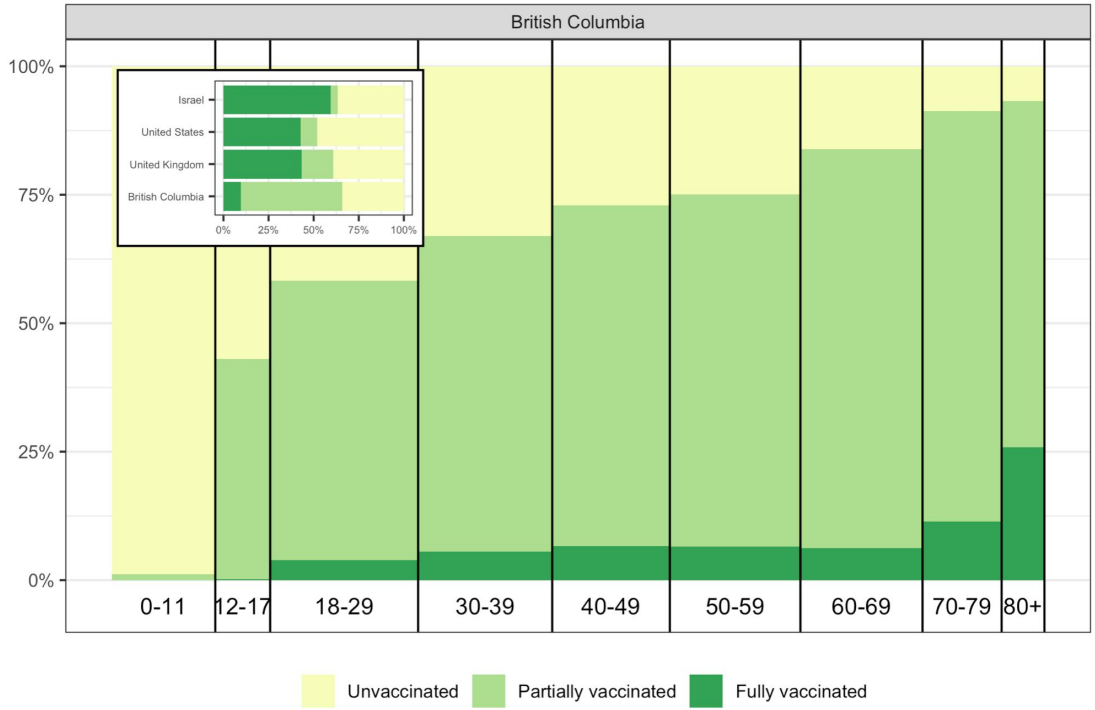
Herd immunity with no control measures will not be achieved until more of BC is fully vaccinated.

http://www.getvaccinated.gov.bc.ca

Source (B. Wiley). Design by Blake Shaffer. *Angus Reid (April 26, 2021): https://angusreid.org/vaccine-astrazeneca-johnson/. †BCCDC (April 24, 2021) Epi-week 16 Situation Report. ‡NACI "Recommendations on the use of COVID-19 vaccines" (May 3, 2021), Efficacy against symptoms >14 days after one dose (>21 days for Astrazeneca) but before two doses; Pfizer: 92.3% [95%CI: 69-98%]; Moderna: 92.1% [95%CI: 68.8-99.1%]; AstraZeneca: 71.3% [95%CI: 49.0-83.8%].

Vaccination status by age group

Last age-based BC data update June 05



Data: PHAC, StatCan Table 17-10-0005, Our World in Data

Israel: 63.3% vaccinated (at least one dose, 59.4% fully vaccinated). Schools fully reopened on Apr 26 with no restrictions; no restrictions on travel; immunity passports being used for indoor dining, gyms and sports; no restrictions on indoor/outdoor socialization in groups of 50 or less

UK: 60.1% vaccinated (at least one dose, 43.4% fully vaccinated). Schools fully open with optional rapid testing available and masks for secondary students; travel is discouraged; indoor dining remains closed; outdoor socializing only, in groups of up to 6. Further reopening starting May 17.

Countries with high vaccination levels are reopening slowly

Source (J. von Bergmann). Vaccination data https://health-infobase.canada.ca/covid-19/vaccination-coverage/
Benchmarks from Israel and UK: https://ourworldindata.org

Data gap: Where are the genomes?

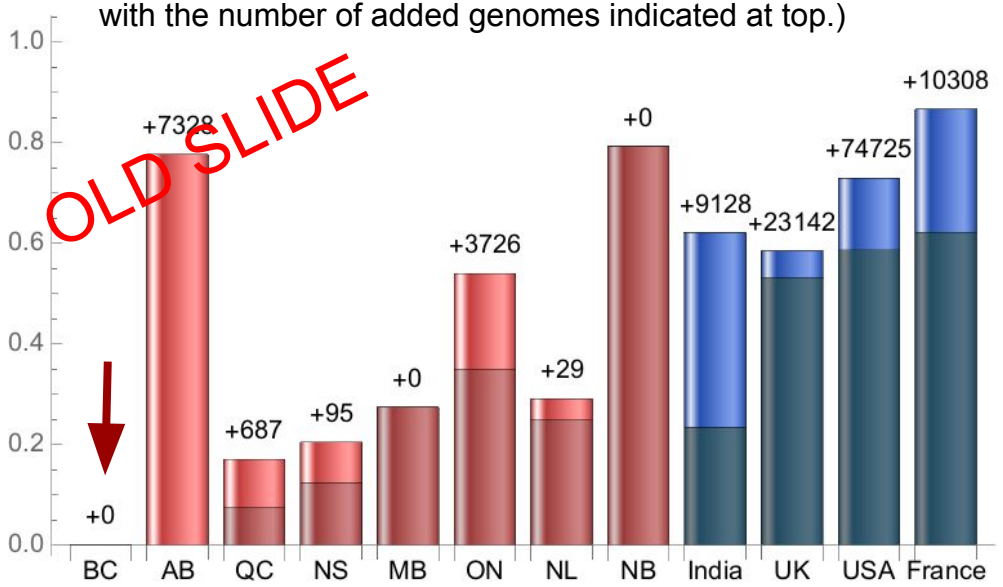
BC is a global leader in genomics, yet BC has not publicly shared the thousands of SARS-CoV-2 genomes sequenced in 2021.

These sequences are needed for global analyses to:

- Identify new variants
- Estimate rates of spread
- Assess efficacy of restrictions
- Detect importations

Alberta has recently submitted over 7000 viral sequences from 2021!

Fraction of SARS-CoV-2 genomes in GISAID from samples collected in 2021
(Light bars indicate newly added 2021 sequences since May 14, with the number of added genomes indicated at top.)



	BC	AB	QC	NS	MB	ON	NL	NB	India	UK	USA	France
2021 samples:	11	7328	1217	242	369	10 605	199	303	14 671	251 922	382 240	36 585
All samples:	5876	9431	7112	1181	1344	19 626	683	382	23 608	430 477	523 800	42 197

Source (S. Otto). http://gisaid.org (May 31, 2021)

Further messages

If B.1.617.2 remains contained, the Step 1 reopening* on May 25 is expected to lead to only a moderate increase in cases, which will decline as more people are vaccinated.

We should aim for more than 70% vaccination of 18+ (~60% of all ages) in order to allow more reopening safely, especially in light of newly emerging VOC, like B.1.617.2.

OLD SLIDE

Spread of B.1.617.2 is consistent with it growing 5-10% faster *per day* relative to B.1.1.7.

Although data is limited to three weekly variant reports from BC's whole genome sequencing, these data indicate that B.1.617 was increasing in absolute numbers even before the May 25 reopening.

Data gaps identified in last report remain.

*Including restaurant reopenings, small indoor gatherings, allowance for low impact gym activities.

Interpreting “vaccine efficacy”

What does 80% effective mean?

- You and your friend do everything together.
- Only you are fully vaccinated.
- Your friend is 5x more likely to get COVID19 than you

How to understand 80%

- 80% describes your RELATIVE risk.
- This is what clinical trials are designed to measure.
- In the real world, given that you have been vaccinated, you are 1/5 as likely to get COVID19 as if you had been unvaccinated.

It’s like having an umbrella that opens up and works, but only 80% of the time.
You are going hiking. Do you get wet?
Well, *if it rains,* you get wet with probability 20%.

Interpreting “vaccine efficacy”

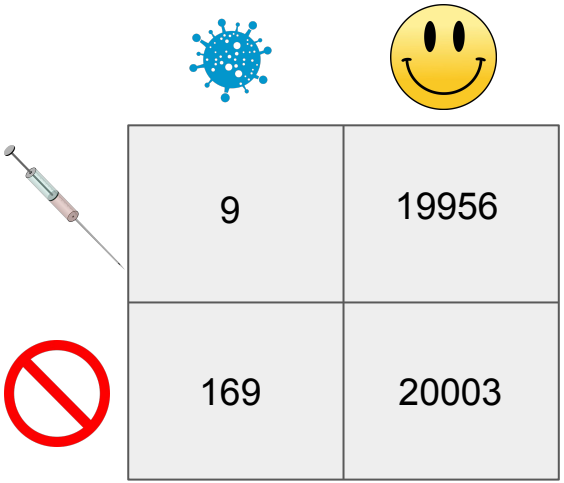
Common interpretations of “80% effective” that are WRONG

1. X You are 80% protected.
2. X You have a 20% chance of getting COVID19.
3. X Each time you get exposed to someone with COVID19, you have a 1/5 chance of getting infected.
4. X Out of 100 vaccinated people like you, 20% will get COVID19.
5. X If you get COVID, your symptoms will be only 20% as severe.
6. X 80% of the time I encounter someone with COVID, I’m protected. I’m at risk 20% of the time.
7. I got vaccinated, so I can safely behave as normal with little risk of infection

Points 1-6 are wrong.
Point 3 is close: “you have 1/5 the chance of being infected as if you were unvaccinated” is correct
Point 7 is reasonably accurate, with the caveat that risk depends on behavioral, personal and environmental factors. But “80%” does not describe your individual risk of infection.

People want to say “if I go to a bar my chance of getting COVID19 is z%”.
Unfortunately, this probability depends on unique circumstances, and cannot be accurately estimated.
What we CAN say is that “if I go to a bar, my risk is only 1/5 as much as it would be if I weren’t vaccinated.”

Interpreting vaccine efficacy



	9	19956
	169	20003

$$\text{Estimated effectiveness rate} = 1 - \frac{\widehat{P}(\text{COVID} \mid \text{Vaccinated},\ B)}{\widehat{P}(\text{COVID} \mid \text{Unvaccinated},\ B)}$$
$$= 1 - \frac{9/19965}{169/20172}$$
$$\approx 95\%$$

Important caveats

- The rate is estimated based on data in the table. Another trial would lead to slightly different estimates
- “Real world” efficacy for “vaccines” is closer to 80%, which is still extremely good.
- The event B means “enrolled in the clinical trial”
- B is important. It incorporates many features of interest that occurred during the trial. Among these are:
  - Prevailing infectiousness (variants, number of surrounding infectious,...)
  - Behavior (lockdowns, how much individuals interact)
  - Environmental factors (weather)
  - Duration of the study (longer time means more exposure)
  - All of these are “as they occurred during the trial”
- Randomization means that B is the same in both arms. It can be cancelled from the numerator and denominator, allowing the estimate to be extrapolated to others scenarios, independent of B.
- This is the magic of randomization and well constructed clinical trials. They allow for extrapolation outside of the trial setting.
- The same data can be used to estimate

$$\widehat{P}(\text{COVID} \mid \text{Vaccinated},\ B) \approx 0.045\%$$

- But the dependence on B can no longer be removed
- Understanding “your susceptibility in your current environment” requires knowing how your current environment relates to that during the trial
- So this estimate is not useful for your decision making. We don’t know your probability of infection if you go out to eat on a specific day. We only know that it is lower (80% lower) if you’re vaccinated.

Data in the above table comes from the second row of Table 2 in the article Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine. These are the reported positives and negatives 7 days after the second dose in Phase 2 / 3 trials of the Pfizer/BioNtech vaccine.

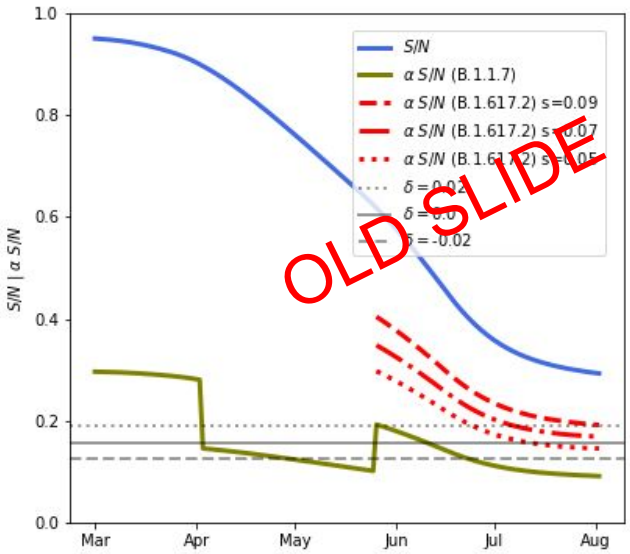
Appendix: Looking under the hood

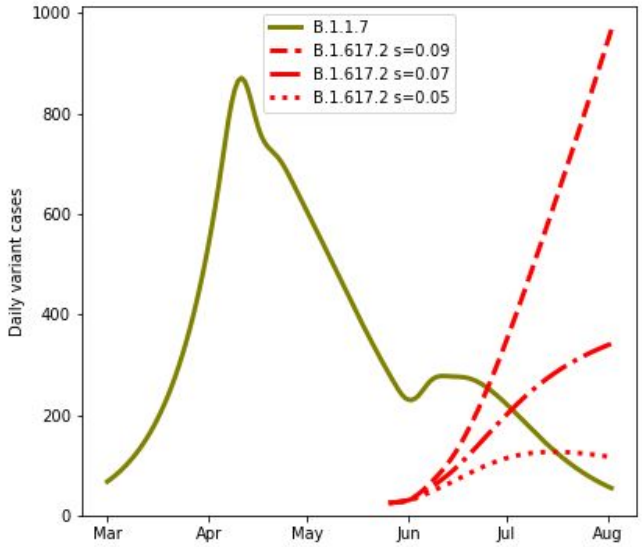
The decline in the number of susceptible individuals (blue) due to vaccination leads to a reduction in the growth rates of B.1.1.7 (olive) and B.1.617.2 (red) in pypm model (slide 11)

The daily growth rate (δ) depends on the product of the transmission rate (α) and the susceptible fraction (S/N in blue). This product is shown for B.1.1.7 (olive) and B.1.617.2* (red).

The values for the product (α S/N) that produce growth rates of δ = -0.02, 0, and 0.02 are shown as grey horizontal lines.

The decline in the susceptible fraction stalls due to the incomplete vaccination of the population.





Source (D. Karlen). Vaccination 1st dose rate assumption: 52,000/day until 75% vaccinated, with 90% asymptotic effectiveness (see Appendix from May 14 report for comparison to real-world effectiveness). *Range of growth advantage, *s*, for B.1.617.2 wrt B.1.1.7 is based on case data from other jurisdictions (slide 10).

Appendix: Measuring growth of an epidemic

New cases/day and **New cases/day/100K population** are two common ways to think about epidemics but there are other measures:

- ***R*(*t*) [Called the "reproduction number"]** estimates, at time *t*, how many new infections are generated from one case over the course of their infection. An $R(t) < 1$ implies the epidemic is shrinking; an $R(t) > 1$ implies it is growing. While conceptually useful, it is hard to measure $R(t)$ directly unless all cases can be tracked.

OLD SLIDE

- ***r* [Called "little r"]** is the daily growth rate in new cases (comparable to a daily interest rate, compounding over time), which can be more easily measured. The relationship between daily growth ("little r") and $R(t)$ depends on the model (e.g., see Figure for one example).

- ***s* [Called the "selection coefficient"]** is a measure of the daily growth rate advantage of one variant over another. So, if the growth rate for type A is 0.05 and for type B is -0.04, then $s = 0.09$ and the ratio of A to B (A/B) grows at 9% per day.

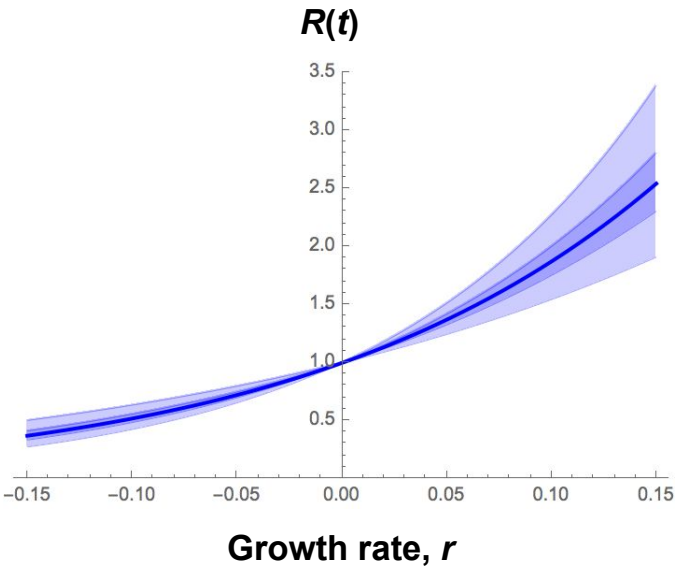


Figure translates between *r* and $R(t)$ using the renewal equation below, as used by Volz et al. to estimate $R(t)$ for B.1.1.7. Assumes infections last for an average of 6.4 ± 1 days, with infectivity rising and falling according to a gamma distribution, $g()$, with a coefficient of variation of 0.6. The bands describe 50% and 95% CI given the uncertainty in the length of the infectious period. Assumes no age structure or heterogeneity.

$$1 = R \int_{a=0}^{\infty} \exp(-r\,a)\, g(a)\, da$$

Appendix: SARS-CoV-2 evolution

- As COVID-19 spreads from person to person, the virus SARS-CoV-2 replicates, mutations occur, and the mutated virus can be passed along.
- The virus has an RNA genome with ~30,000 positions. Most mutations have little to no effect on the functioning of the virus, others harm the virus and are rapidly eliminated. Rare mutations, however, can change the virus in a way that is suspected ("variant of interest") or demonstrated ("variant of concern") to make the disease worse.
- Because strains can have more than one mutation, strains are given designations that indicate their ancestry, e.g. **B.1.1** and **B.1.1.7** arise from the earlier strain **B.1** (see figure).
- Some mutations change the amino acid structure of proteins. These mutations can be identified by the amino acid that was expected, the amino acid that was observed, and the position, e.g. S:N501Y refers to a mutation in the 501st position of spike ("S") that changes an "N" amino acid to a "Y".
- There are **1273** amino acids that make up the SARS-CoV-2 spike protein.
- Mutations in the spike protein are tracked closely because this protein is essential for the virus to get into our cells and is encoded by many vaccines.
- It is thought that many mutations in the virus are needed before vaccines will stop working, but partial vaccine "escape" mutations have been observed and are being closely monitored.

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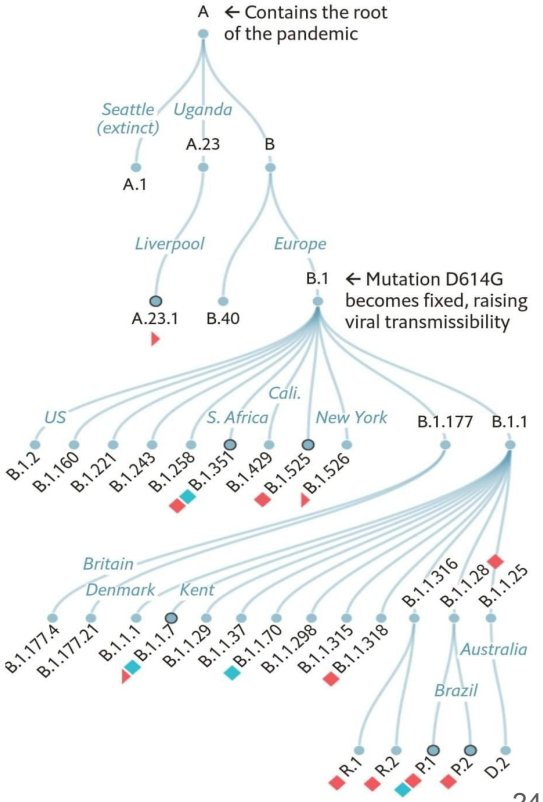


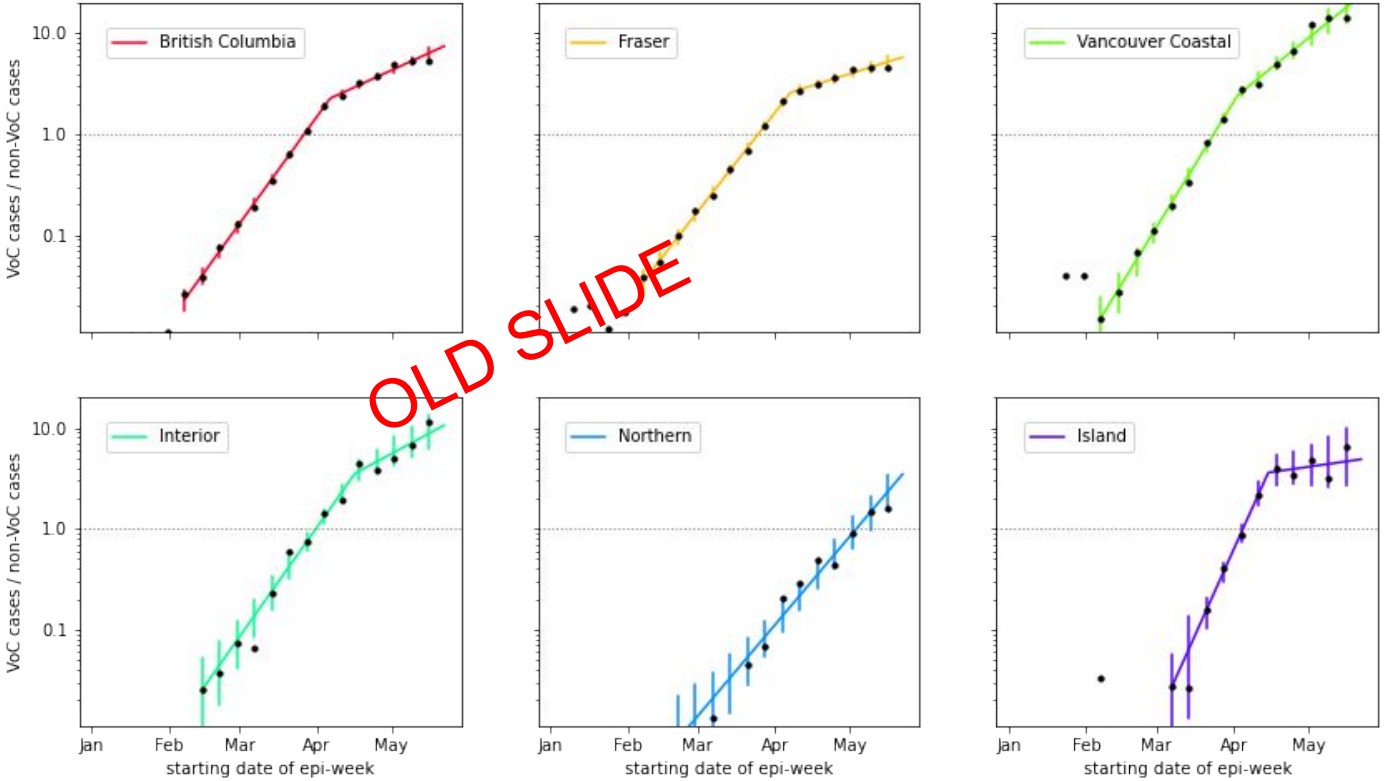
Figure source: The Economist

Appendix: Growth advantage of B.1.1.7 and P.1 in BC

B.1.1.7 and P.1 initially grew 8%/day faster than original strains (*s*)

The majority of BC's virus population now consists of these two VOC (>50% above horizontal line)

With "circuit breaker", advantage reduced to 4%/day faster than original strains: measures had greater effect on B.1.1.7 and P.1 than on the original strains



Source (D. Karlen). Fit to weekly VoC and non-VoC case data from BCCDC. Except for Northern HA, a change to the daily growth advantage (selection coefficient, *s*) is apparent in early April, and fit estimates the change to occur near April 10. There are insufficient data in Northern and Island regions to accurately estimate the change.