Network Systems Science & Advanced Computing

Biocomplexity Institute & Initiative

University of Virginia

Estimation of COVID-19 Impact in Virginia

June 16th, 2021

(data current to June 12th – 15th)

Biocomplexity Institute Technical report: TR 2021-071

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biocomplexity.virginia.edu

About Us

- Biocomplexity Institute at the University of Virginia
  - Using big data and simulations to understand massively interactive systems and solve societal problems
- Over 20 years of crafting and analyzing infectious disease models
  - Pandemic response for Influenza, Ebola, Zika, and others

Points of Contact

Bryan Lewis
brylew@virginia.edu

Srini Venkatramanan
srini@virginia.edu

Madhav Marathe
marathe@virginia.edu

Chris Barrett
ChrisBarrett@virginia.edu

Model Development, Outbreak Analytics, and Delivery Team

Przemyslaw Porebski, Joseph Outten, Brian Klahn, Alex Telionis, Srinivasan Venkatramanan, Bryan Lewis, Aniruddha Adiga, Hannah Baek, Chris Barrett, Jiangzhuo Chen, Patrick Corbett, Stephen Eubank, Ben Hurt, Dustin Machi, Achla Marathe, Madhav Marathe, Mark Orr, Akhil Peddireddy, Asal Pilehvari, Erin Raymond, James Schlitt, Anil Vullikanti, Lijing Wang, James Walke, Andrew Warren, Amanda Wilson, Dawen Xie

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Overview

- **Goal**: Understand impact of COVID-19 mitigations in Virginia
- **Approach:**
  - Calibrate explanatory mechanistic model to observed cases
  - Project based on scenarios for next 4 months
  - Consider a range of possible mitigation effects in "what-if" scenarios
- **Outcomes:**
  - Ill, Confirmed, Hospitalized, ICU, Ventilated, Death
  - Geographic spread over time, case counts, healthcare burdens

Key Takeaways

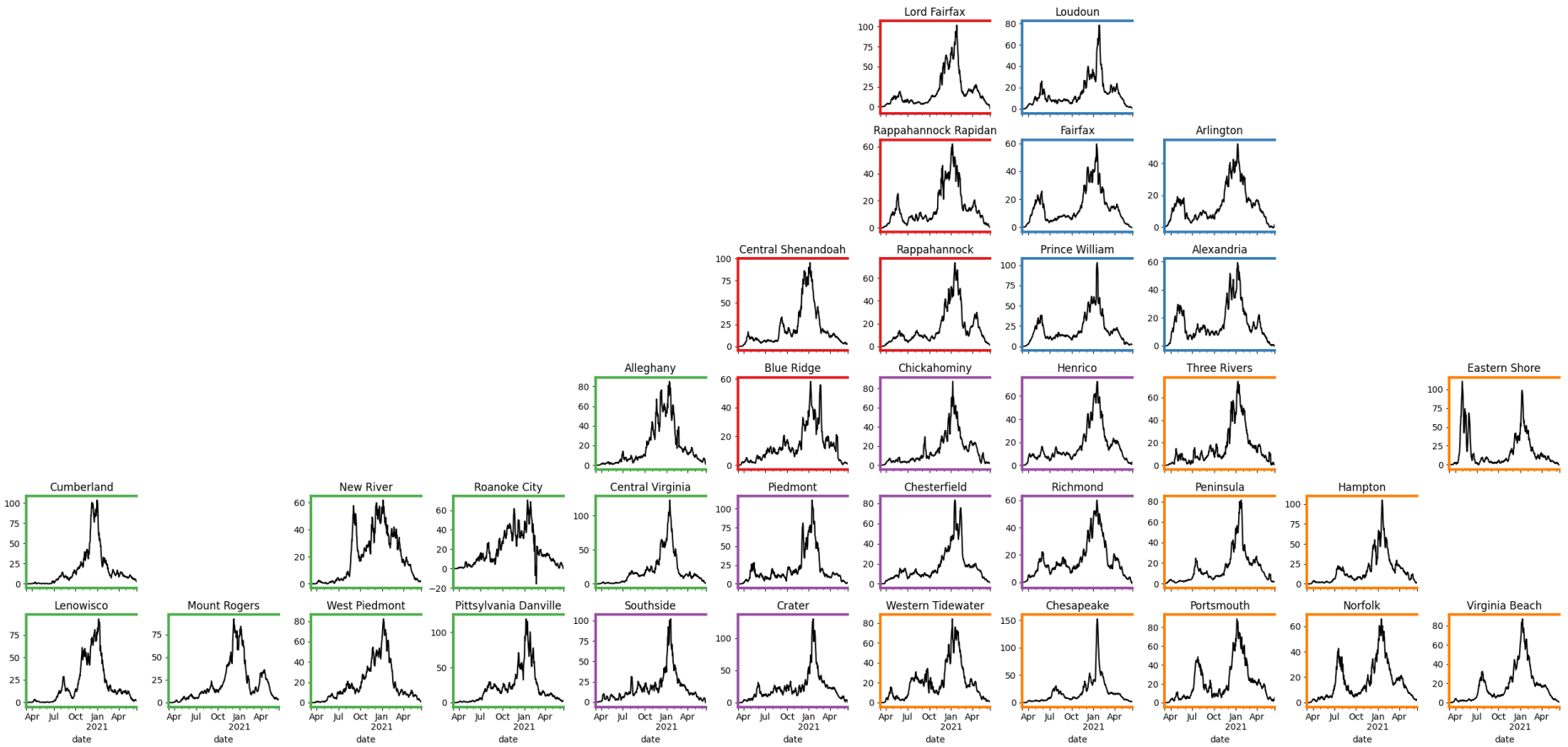
Projecting future cases precisely is impossible and unnecessary.
Even without perfect projections, we can confidently draw conclusions:

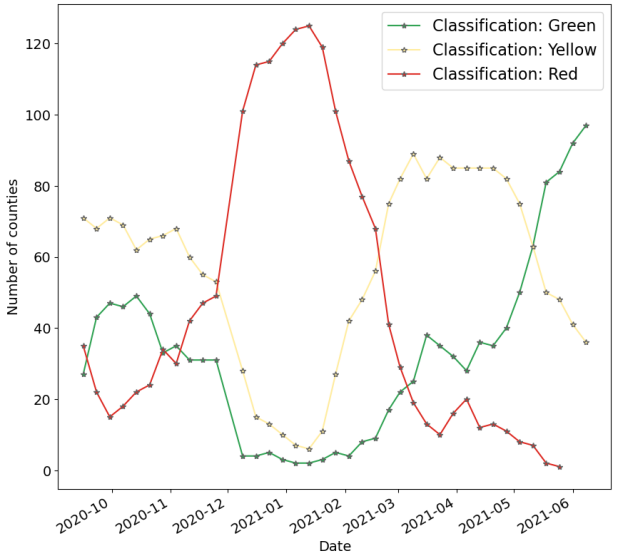
- **Case rates in Virginia continue to decline though some districts have small rebounds in rates**
- 60% of zip codes in Virginia (536 of 896 zips) had zero cases this past week; VA mean weekly incidence down at 1.6/100K from 2.4/100K, US flat at 4.2/100K
- Vaccination rates show signs of plateauing after steady decline
- Projections show declining rate overall across Commonwealth
- Recent updates:
  - Added Delta variant scenario as its growth becomes more predictable
  - Study scenarios: Fall resurgence and expanded vaccination
  - Limited waning of natural immunity included in fit and projections, also with seroprevalence update

The situation continues to change. Models continue to be updated regularly.

Situation Assessment

Case Rates (per 100k) and Test Positivity





https://data.cms.gov/stories/s/q5r5-gjyu

County level test positivity from RT-PCR tests.

Green: <5.0%
(or with <20 tests in past 14 days)

Yellow: 5.0%-10.0%
(or with <500 tests and <2000 tests/100k and >10% positivity over 14 days

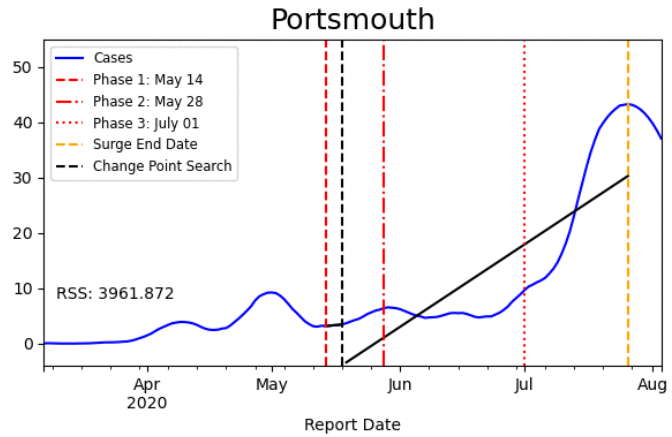
Red: >10.0%
(and not "Green" or "Yellow")

District Trajectories

Goal: Define epochs of a Health District's COVID-19 incidence to characterize the current trajectory

Method: Find recent peak and use hockey stick fit to find inflection point afterwards, then use this period's slope to define the trajectory

Hockey stick fit

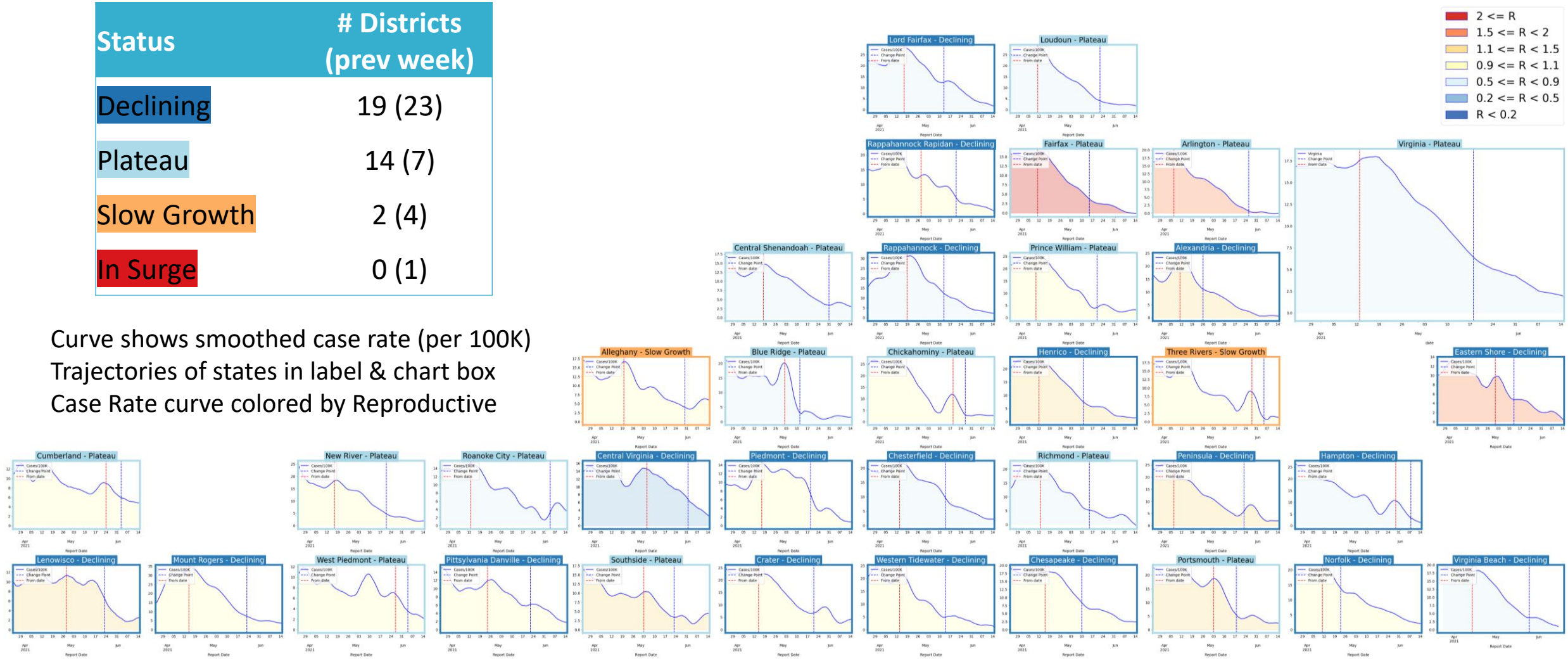


Trajectory	Description	Weekly Case Rate (per 100K) bounds	# Districts (prev week)
Declining	Sustained decreases following a recent peak	below -0.9	19 (23)
Plateau	Steady level with minimal trend up or down	above -0.9 and below 0.5	14 (7)
Slow Growth	Sustained growth not rapid enough to be considered a Surge	above 0.5 and below 2.5	2 (4)
In Surge	Currently experiencing sustained rapid and significant growth	2.5 or greater	0 (1)

District Trajectories – last 10 weeks

Status	# Districts (prev week)
Declining	19 (23)
Plateau	14 (7)
Slow Growth	2 (4)
In Surge	0 (1)

Curve shows smoothed case rate (per 100K)
Trajectories of states in label & chart box
Case Rate curve colored by Reproductive



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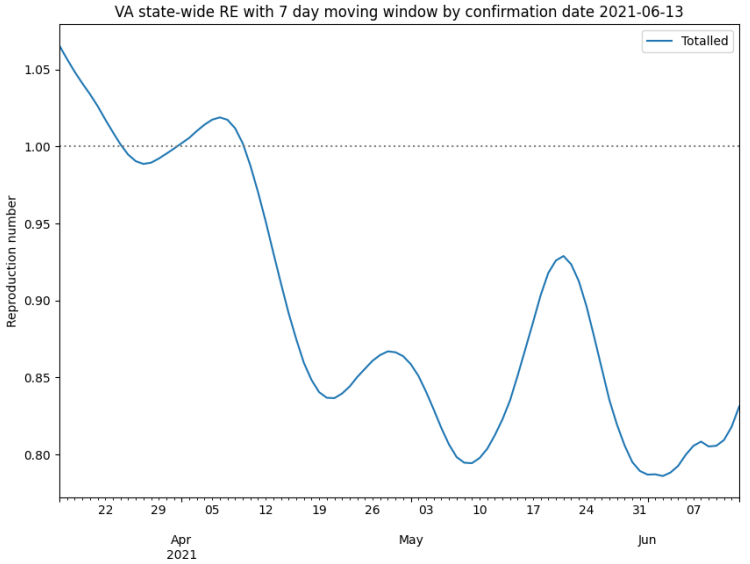
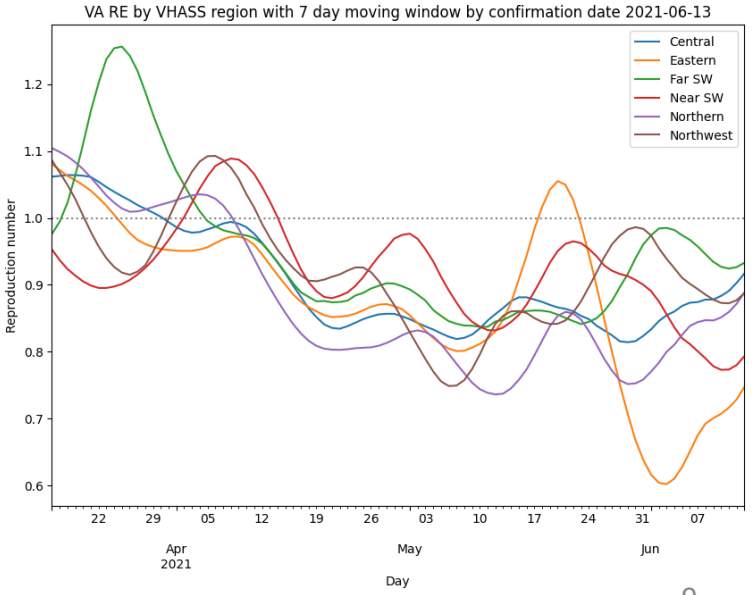
Estimating Daily Reproductive Number

June 15th Estimates

Region	Date Confirmed R_e	Date Confirmed Diff Last Week
State-wide	0.823	0.136
Central	0.909	0.186
Eastern	0.869	0.440
Far SW	0.925	0.003
Near SW	0.707	-0.179
Northern	0.870	0.209
Northwest	0.788	-0.135





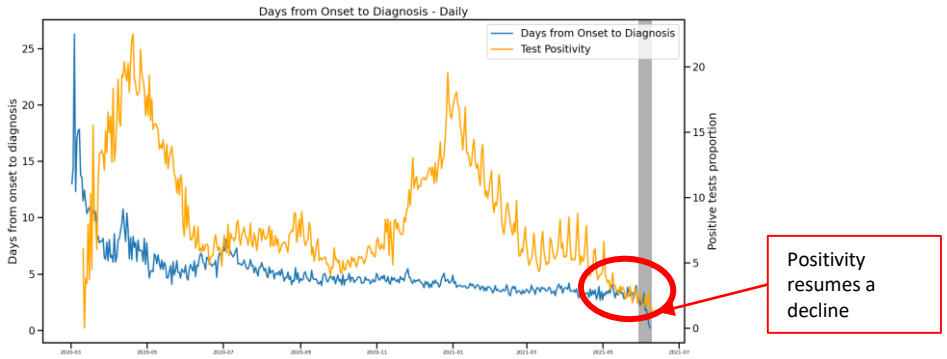
Methodology

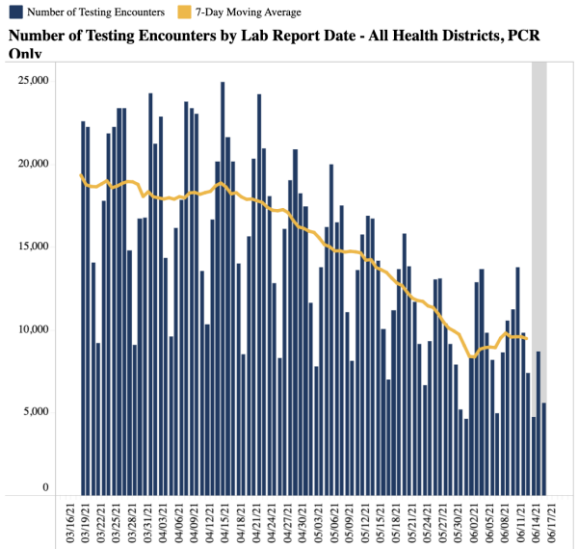
- Wallinga-Teunis method (EpiEstim[1]) for cases by **confirmation date**
- Serial interval: updated to discrete distribution from observations (mean=4.3, Flaxman et al, Nature 2020)
- Using Confirmation date since due to increasingly unstable estimates from onset date due to backfill

1. Anne Cori, Neil M. Ferguson, Christophe Fraser, Simon Cauchemez. A New Framework and Software to Estimate Time-Varying Reproduction Numbers During Epidemics. American Journal of Epidemiology, Volume 178, Issue 9, 1 November 2013, Pages 1505–1512, https://doi.org/10.1093/aje/kwt133

Changes in Case Detection

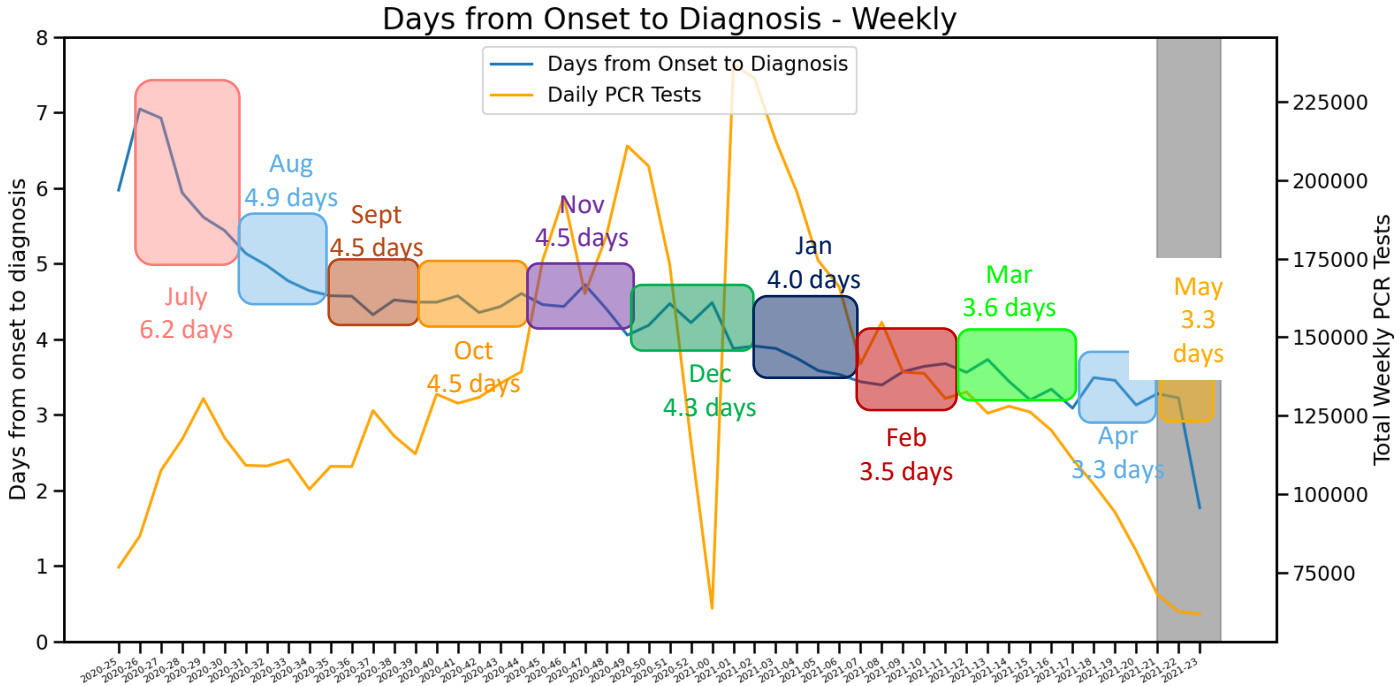
Test positivity vs. Onset to Diagnosis



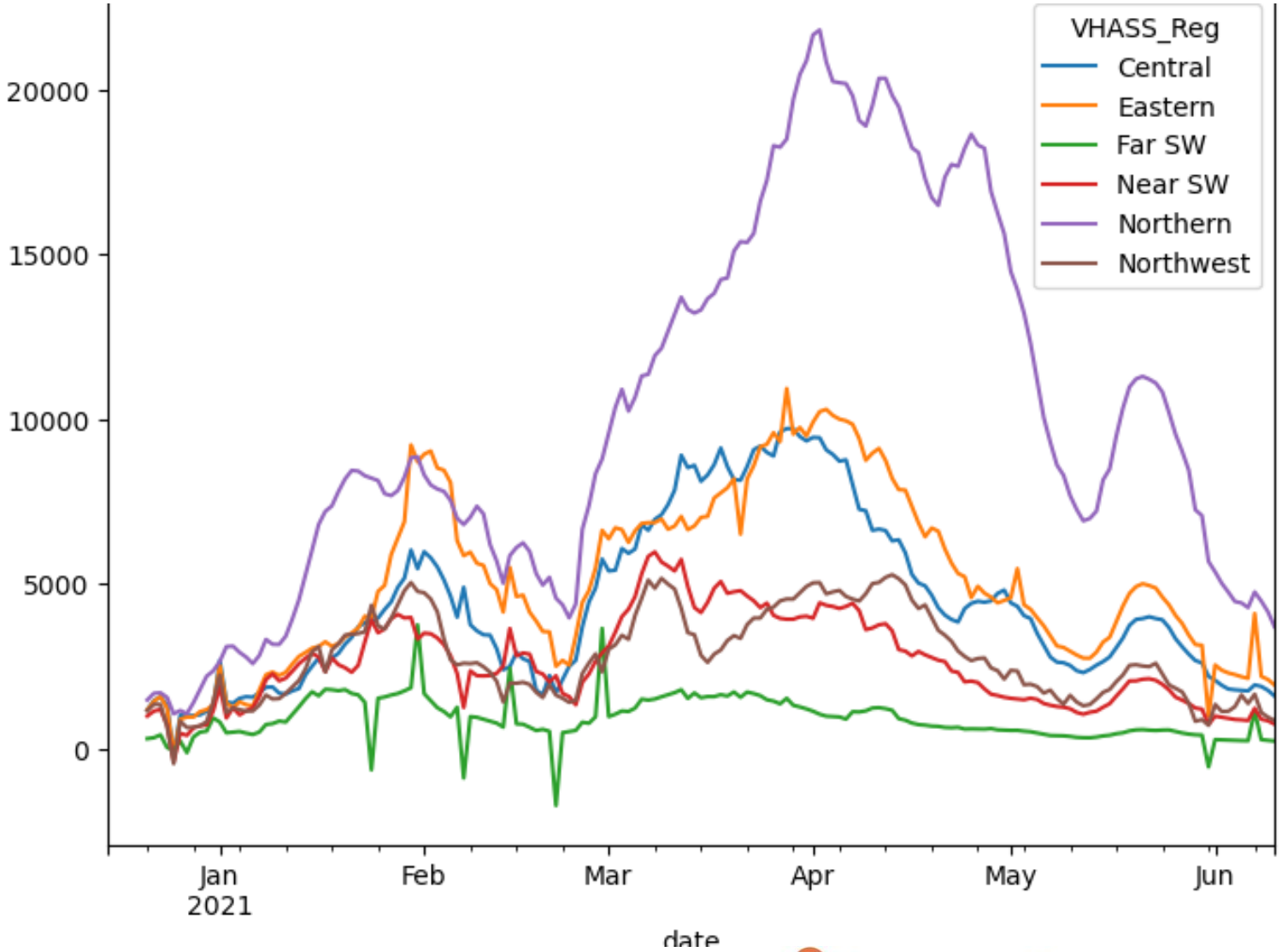


Accessed 9:00am June 16, 2021
https://www.vdh.virginia.gov/coronavirus/

Timeframe (weeks)	Mean days	% difference from overall mean
July (26-30)	6.2	-2%
Aug (31-34)	4.9	-22%
Sept (35-38)	4.5	-28%
Oct (39-43)	4.5	-28%
Nov (44-47)	4.5	-27%
Dec (48-49)	4.3	-30%
Jan (00-04)	4.0	-35%
Feb (05-08)	3.5	-43%
Mar (09-13)	3.6	-41%
Apr (14-17)	3.3	-47%
May (18-21)	3.3	-46%
Overall (13 - 11)	6.3	--

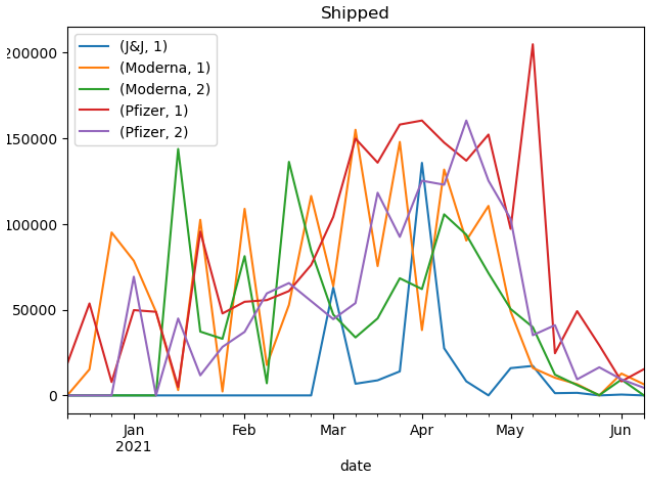


Vaccination Administration Slows



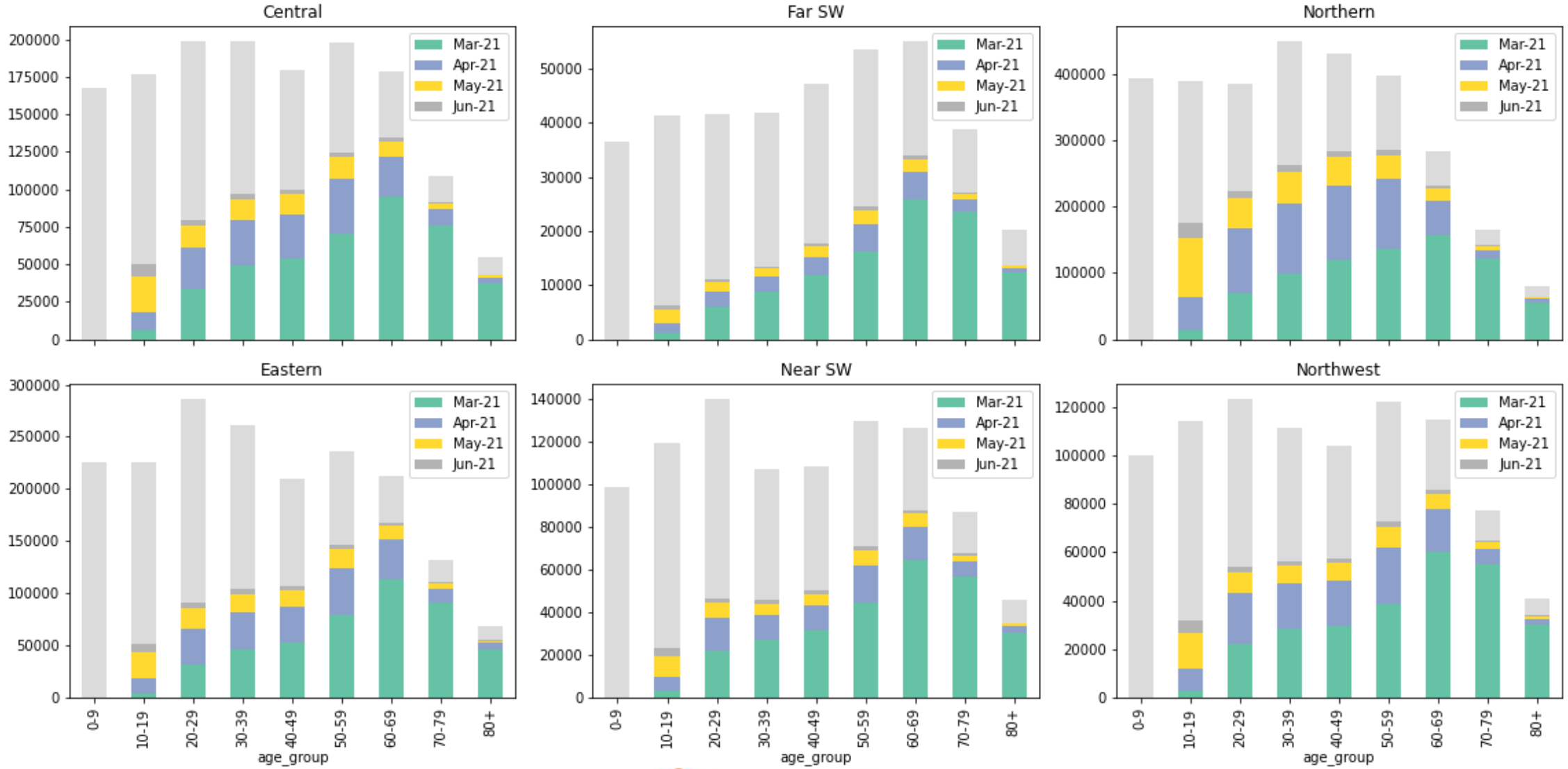
Regional Vaccine courses initiated per day:

- Total counts of first dose of vaccines across regions
- Recent rise due to opening of vaccinations to 12-16 year olds



Shipments have slowed with decreased demand

Vaccinations Shift to Younger Populations



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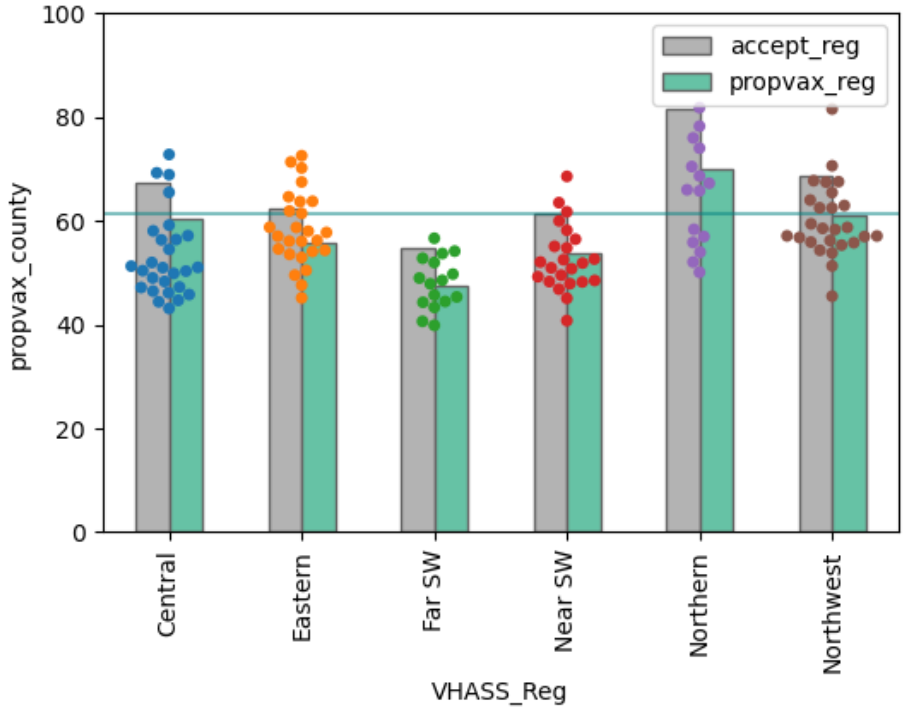
Vaccination Acceptance by Region

Corrections to surveys:

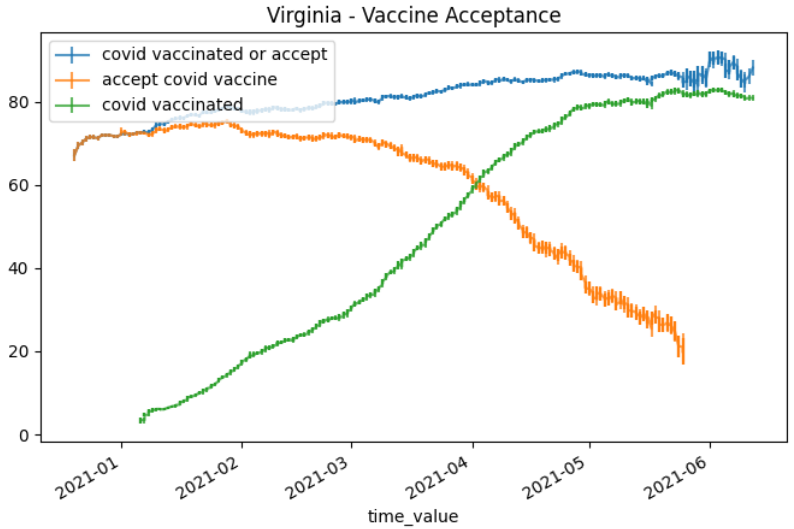
- Facebook administered survey is timely and broad, but biased by who accesses Facebook and answers the survey
- Correction approach:
  - Calculate an over-reporting fraction based on reported vaccinations compared to VDH administration data
  - Cross-validate coarse corrections against HPS survey at the state level and corrected in same manner

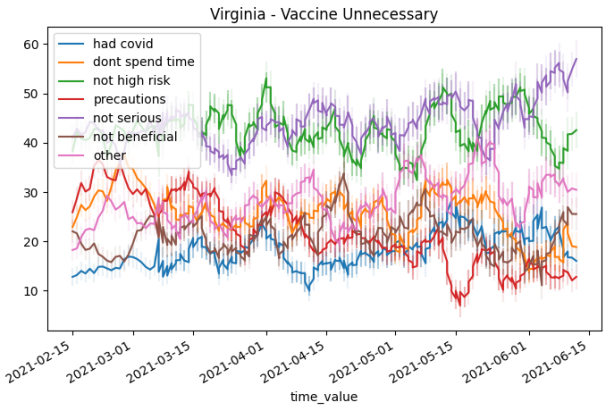
Region	COVIDcast accepting corrected	VDH proportion vaccinated	COVIDcast reported vaccinated
Central	68%	60%	81%
Eastern	63%	56%	79%
Far SW	53%	48%	72%
Near SW	61%	54%	76%
Northern	79%	70%	89%
Northwest	65%	61%	79%



Grey Bar: Survey measured and corrected acceptance
Green Bar: Proportion of eligible population administered a vaccine
Dots: Proportion administered at least one dose for each county

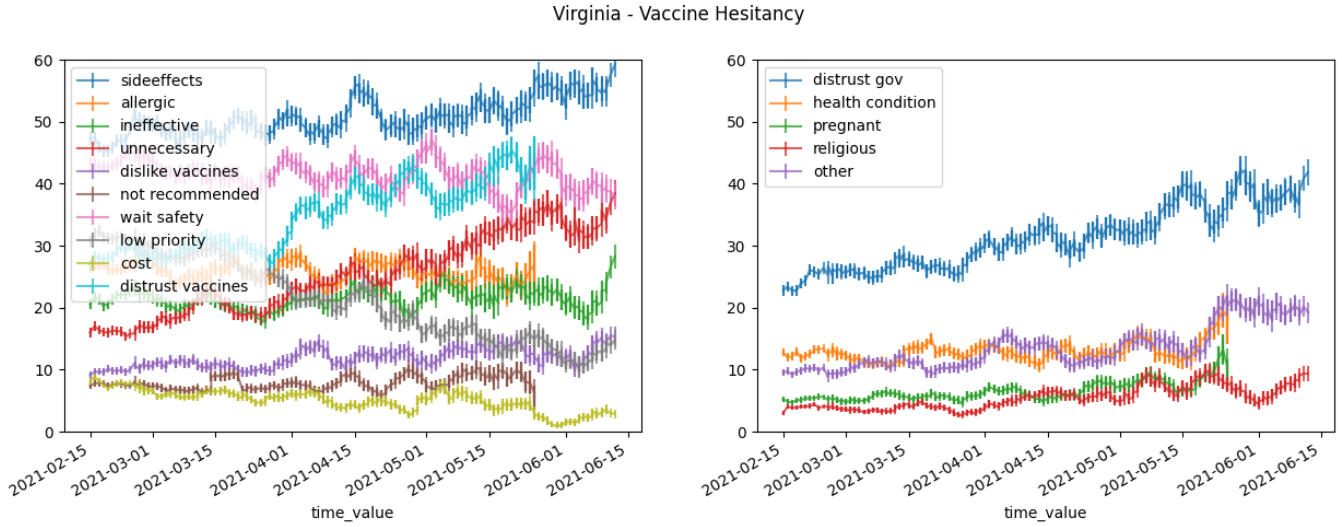
Vaccine Acceptance in Virginia - COVIDcast





Acceptance remains high:

- Proportion of Virginians that have already or would definitely or probably accept vaccination if offered today
- *Survey respondents are reporting high levels of vaccination of ~80% reflecting bias of the mechanism*
- **Top reasons for hesitancy**: side effects, distrust (increasing), unnecessary (increasing)
- **More likely to take if recommended by:** doctors and friends
- **Reasons unnecessary**: Not serious, not high risk, or other



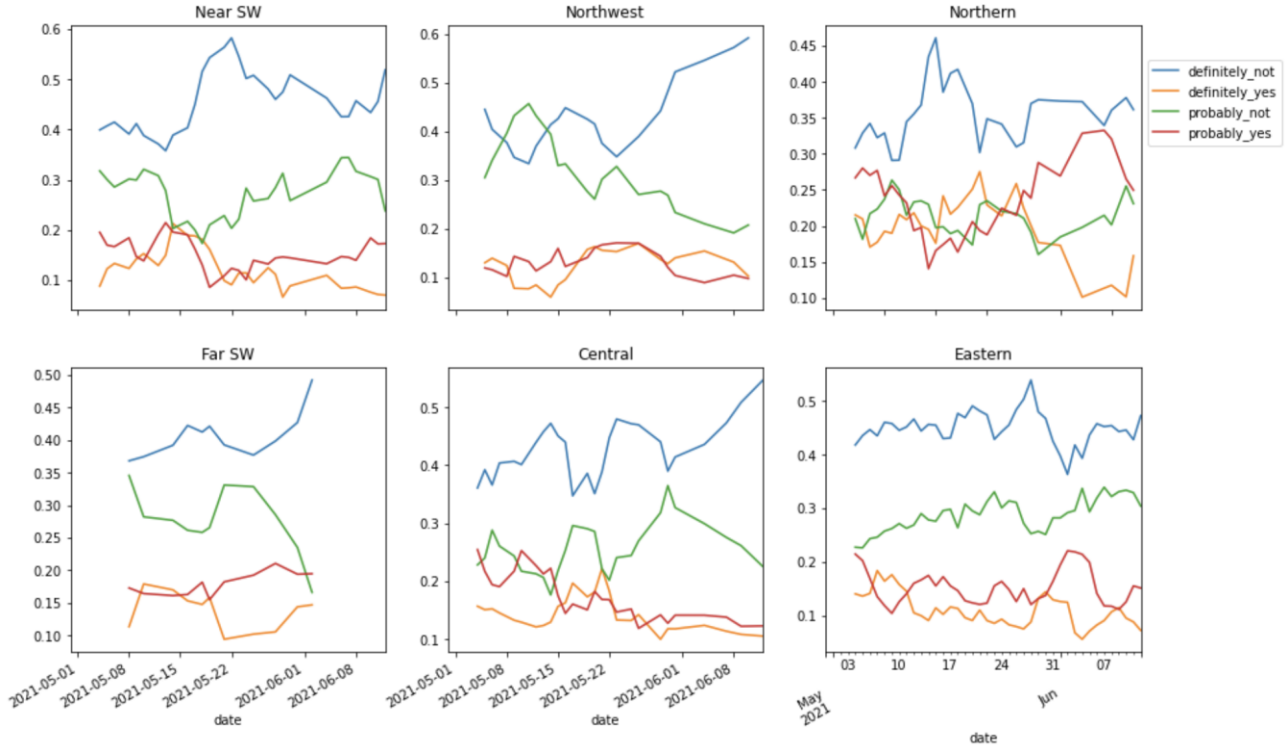
Data Source: https://covidcast.cmu.edu

Vaccine Acceptance by Region- COVIDcast

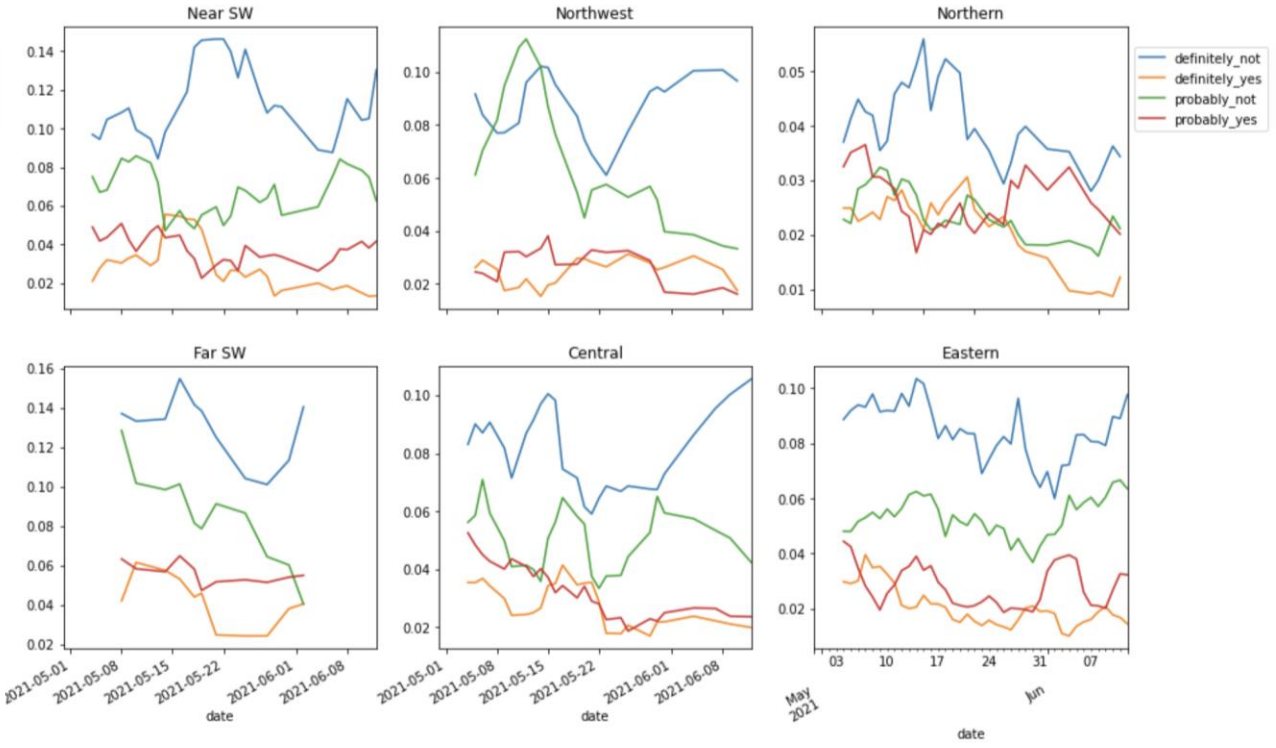
Levels of Acceptance and potential acceptance in flux:

- Nearly all the “Definitely Yes” have been vaccinated, yet there are 10-15% remaining across the regions
- Northwest and Southwest (to lesser degree) see growth in “probably not”, seemingly from “definitely not”

Unvaccinated Only



All Respondents



Data Source: https://covidcast.cmu.edu

SARS-CoV2 Variants of Concern

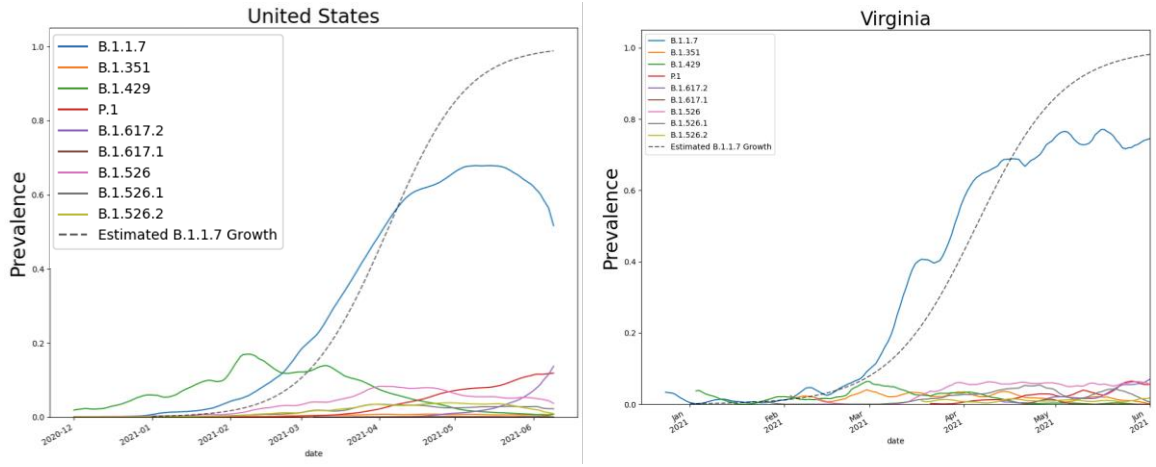
Emerging new variants will alter the future trajectories of pandemic and have implications for future control

- Emerging variants can:
  - Increase transmissibility
  - Increase severity (more hospitalizations and/or deaths)
  - Limit immunity provided by prior infection and vaccinations
- Genomic surveillance remains very limited
  - Challenges ability to estimate impact in US to date and estimation of arrival and potential impact in future

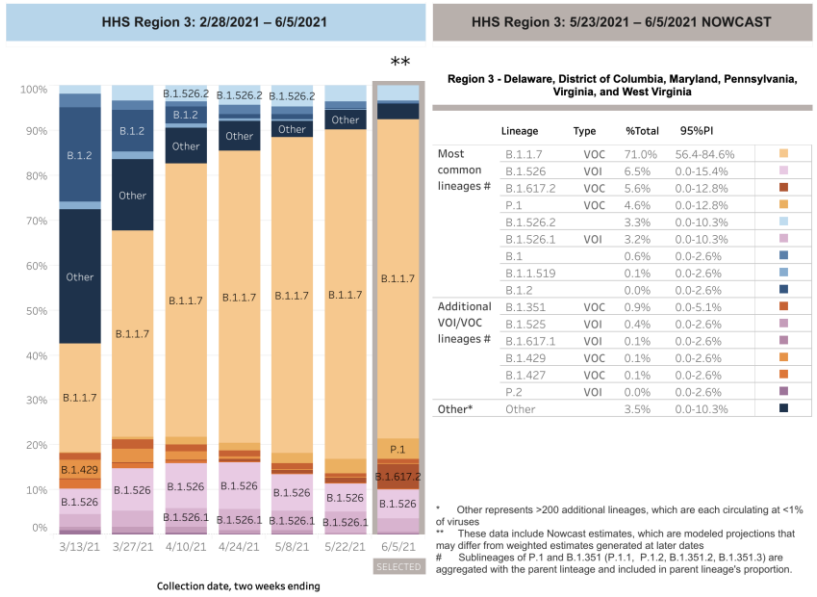
	New WHO Name	Transmissibility	Immune Evasiveness	Vaccine Effectiveness^
Ancestral		—	—	✓
D614G		+	—	✓
B.1.1.7	Alpha	+++	—	✓
B.1.351	Beta	+	++++	✓
P.1	Gamma	++	++	✓
B.1.429	Epsilon	+	+	✓
B.1.526	Iota	+	+	✓
B.1.617.2	Delta	++++*	++#	✓

*Relative transmissibility to B.1.1.7 yet to be fully defined
^Effectiveness from real world evidence vs. severe illness, not all vaccines are effective vs all variants, and importance of 2-doses, especially for B.1.617.2 for which 1 dose of mRNA or AZ is only ~30% effective # May carry more immune escape than P.1, to be determined

World Health Organization [WHO](#) and [Eric Topol](#)



GISAID outbreak.info [Outbreak Info](#)



CDC [CDC Variant Tracking](#)

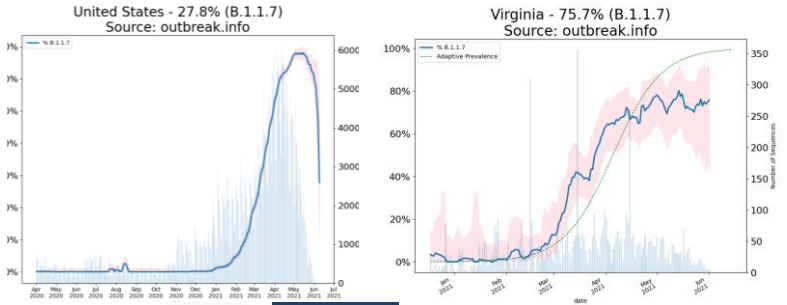
SARS-CoV2 Variants of Concern

Alpha α - Lineage B.1.1.7

Prevalence: Levels have stalled and are now dropping in most states; flat in VA

Transmissibility: Estimated increase of 50% compared to previous variants. B.1.1.7's mutations boost its overall levels of viremia; study from Public Health England shows contacts of B.1.1.7 cases are more likely (50%) to test positive

Severity: Increased risk of hospitalization (60%) and mortality (60%). Danish study shows B.1.1.7 to have a 64% higher risk of hospitalization, while Public Health Scotland studies showed a range of 40% to 60%; Study in Nature estimates 60% higher mortality

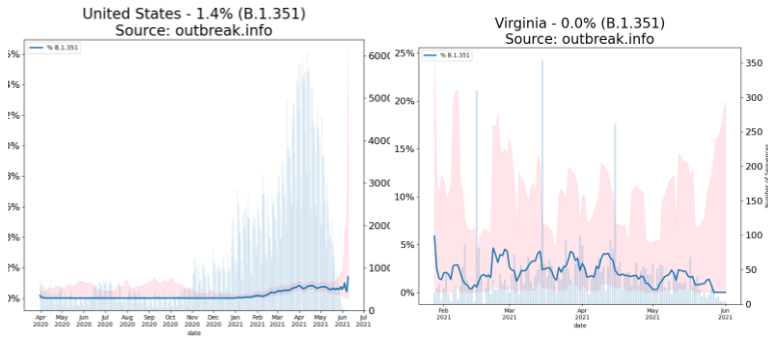


GISAID outbreak.info Outbreak Info

Beta β - Lineage B.1.351

Prevalence: Levels have remained low, as this variant's transmissibility can't compete with B.1.1.7, however, as more of the population becomes immune it may gain an advantage

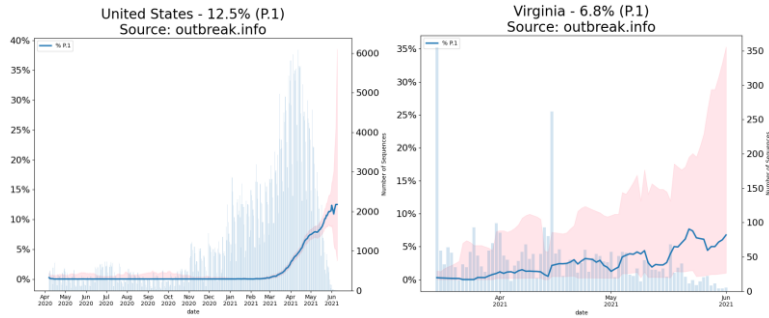
Immune Escape: Many studies show that convalescent sera from previously infected individuals does not neutralize B.1.351 virus well which is predictive of protection, however, vaccine induced immunity shows signs of effectiveness



Gamma γ - Lineage P.1

Prevalence: Nationally at 13.4%, slow increase in VA at 6.8%

Study estimates 17-32% of all infections in Manaus in 2021 were reinfections, which helps explain data from Brazil demonstrating P.1's continued dominance in Rio despite presence of B.1.1.7



SARS-CoV2 Variants of Concern

Delta δ - Lineage B.1.617.2 and related subvariants

- Continues to drive outbreak in India and neighbors, with immeasurable numbers of cases surpassing healthcare capacities in many regions
- CDC finally declares it is a **Variant of Concern** following Public Health England and WHO
- Now accounts for 75% of cases in the last 2 weeks in the UK
- Strain shows continued growth in Europe and in US
- Several studies estimate B.1.617.2 to have 100% faster growth than B.1.1.7, and a UK study suggests a 13% advantage over B.1.1.7; we are roughly tracking what seems to be a ~60% growth rate advantage in VA
- More studies show limited immune escape similar to B.1.351, however, many studies still suggest protection remains for vaccinated, especially 2 doses and mRNA vaccines
- PHE study shows limited efficacy of Astra-Zeneca with only one dose, efficacy returns following 2nd dose
- Public Health Scotland study in Lancet suggests Delta is 2x more likely to cause hospitalization than Alpha

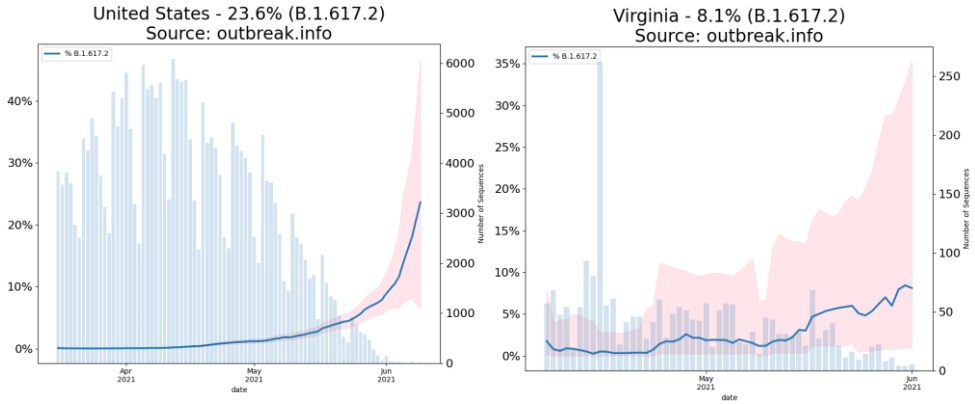
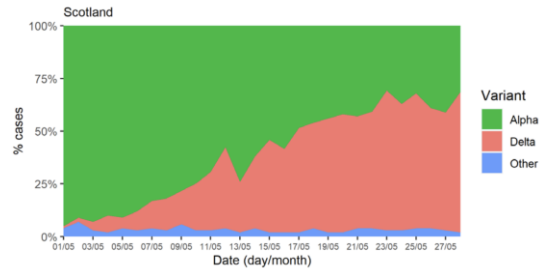


Table 1: Estimated vaccine effectiveness against hospitalisation

		Alpha			Delta		
Vaccination status		OR vs symptomatic disease	HR vs hospitalisation	VE vs hospitalisation	OR vs symptomatic disease	HR vs hospitalisation	VE vs hospitalisation
Any vaccine							
	Dose 1	0.51 (0.48-0.55)	0.44 (0.28-0.70)	78% (65-86)	0.69 (0.64-0.75)	0.37 (0.22-0.63)	75% (57-85)
	Dose 2	0.13 (0.1-0.15)	0.64 (0.24-1.72)	92% (78-97)	0.20 (0.18-0.23)	0.29 (0.11-0.72)	94% (85-98)
Pfizer							
	Dose 1	0.53 (0.47-0.58)	0.32 (0.14-0.73)	83% (62-93)	0.64 (0.54-0.77)	0.10 (0.01-0.76)	94% (46-99)
	Dose 2	0.06 (0.05-0.08)	0.88 (0.21-3.77)	95% (78-99)	0.12 (0.1-0.15)	0.34 (0.10-1.18)	96% (86-99)
Astrazeneca							
	Dose 1	0.51 (0.48-0.55)	0.48 (0.30-0.77)	76% (61-85)	0.70 (0.65-0.76)	0.41 (0.24-0.70)	71% (51-83)
	Dose 2	0.26 (0.21-0.32)	0.53 (0.15-1.80)	86% (53-96)	0.33 (0.28-0.39)	0.25 (0.08-0.78)	92% (75-97)

Public Health Englad study shows vaccines are effective against hospitalization with Delta variant infections (94-96% for Pfizer). Also shows that one dose AZ has much lower efficacy (71%) PHE

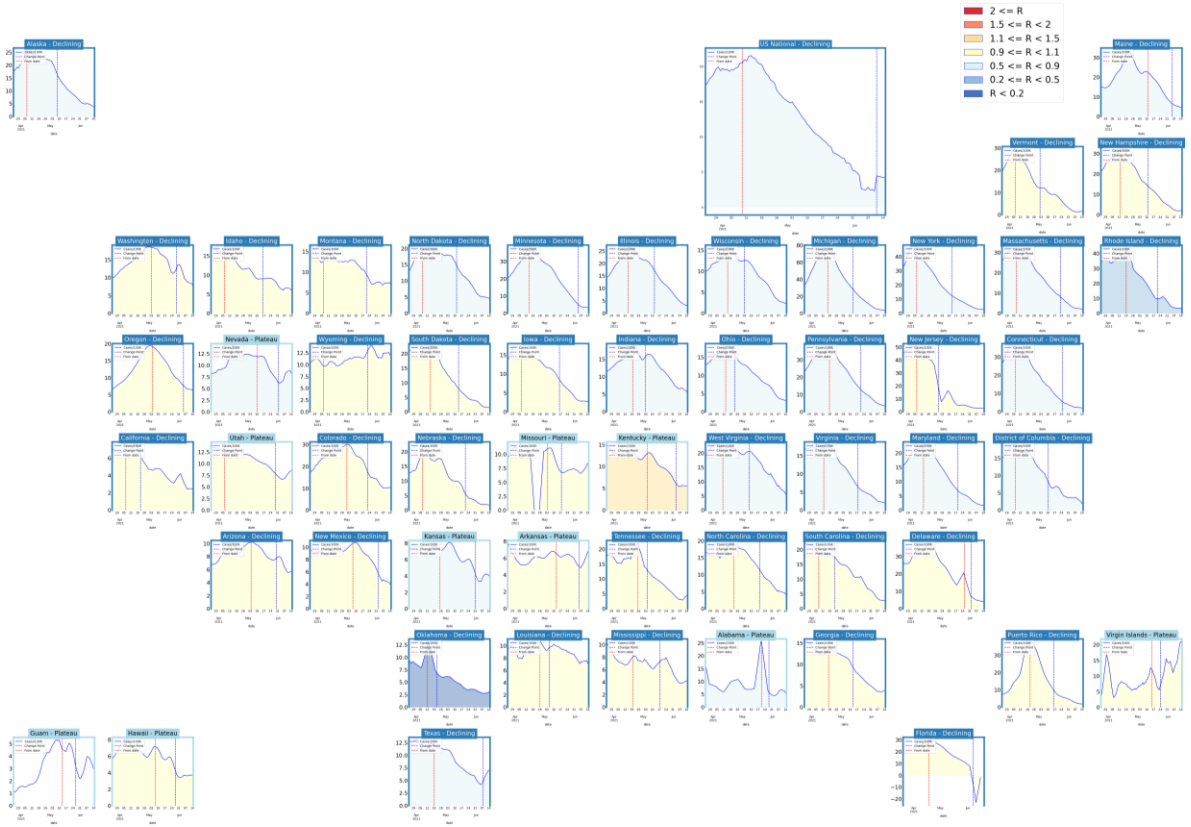
Figure S1: Changing proportion of infections due to Alpha and Delta VOCs in Scotland over time



Scotland has experienced explosive growth of Delta in the month of May. Their experience found that infections with Delta variant were 2x more likely to be hospitalized than infections with Alpha variant Lancet

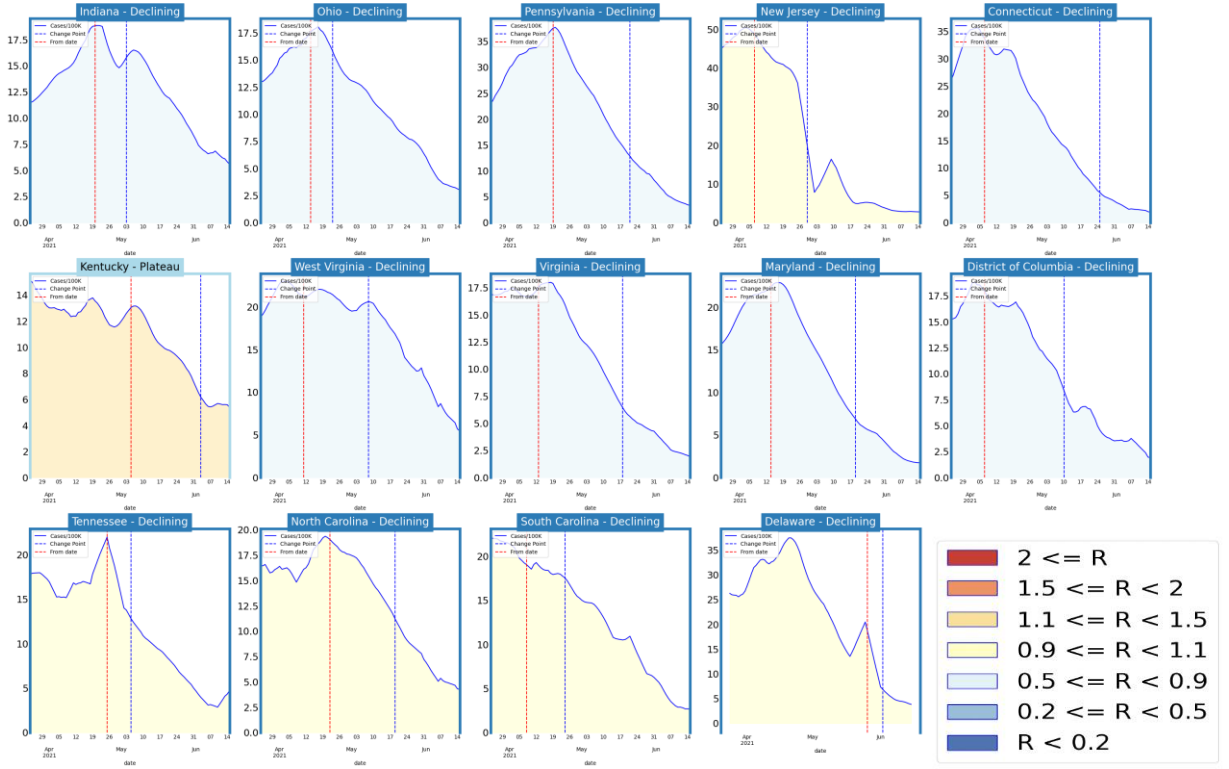
Other State Comparisons

Trajectories of States



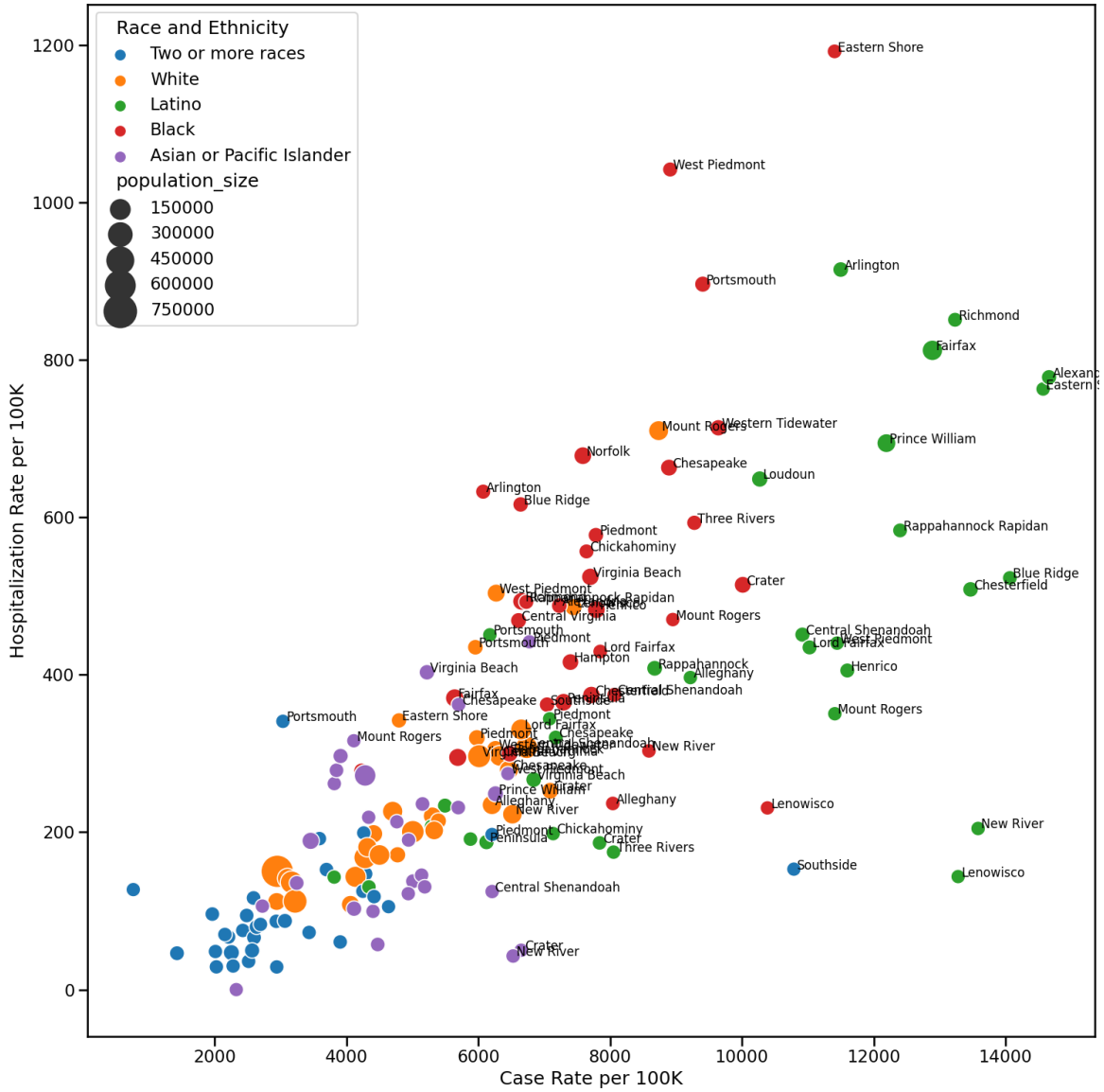
- Nearly all states are declining
- Some states, most with low vaccination rates or high Delta show some rebounds

Virginia and her neighbors



- VA and neighbors are all declining with steady pace
- All neighbors are now well below 10/100K level

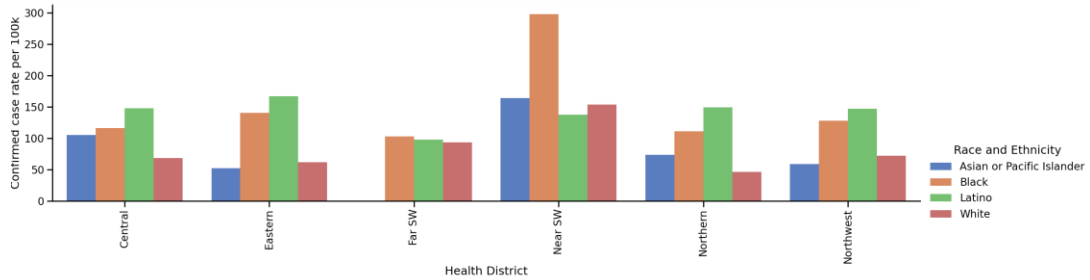
Race and Ethnicity cases per 100K



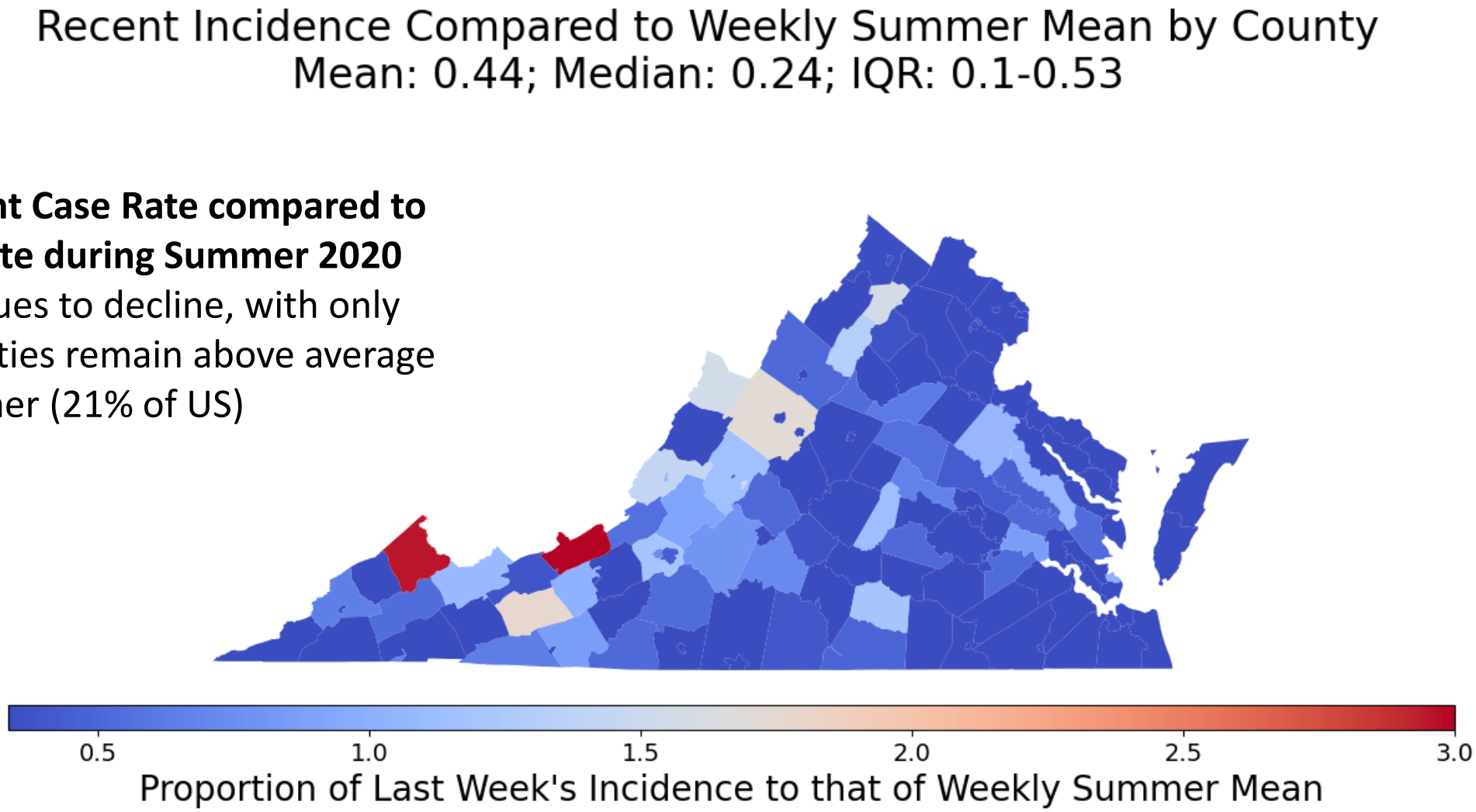
Rates per 100K of each Racial-Ethnic population by Health District

- Each Health District's Racial-Ethnic population is plotted by their Hospitalization and Case Rate
- Points are sized based on their overall population size (overlapping labels removed)
- Change in rates over the last 2 weeks

Case Rate Change in last 14 days



Recent Incidence Compared to Summer 2020



Ratio of Recent Case Rate compared to mean Case Rate during Summer 2020

- Ratio continues to decline, with only 13% of counties remain above average of last summer (21% of US)

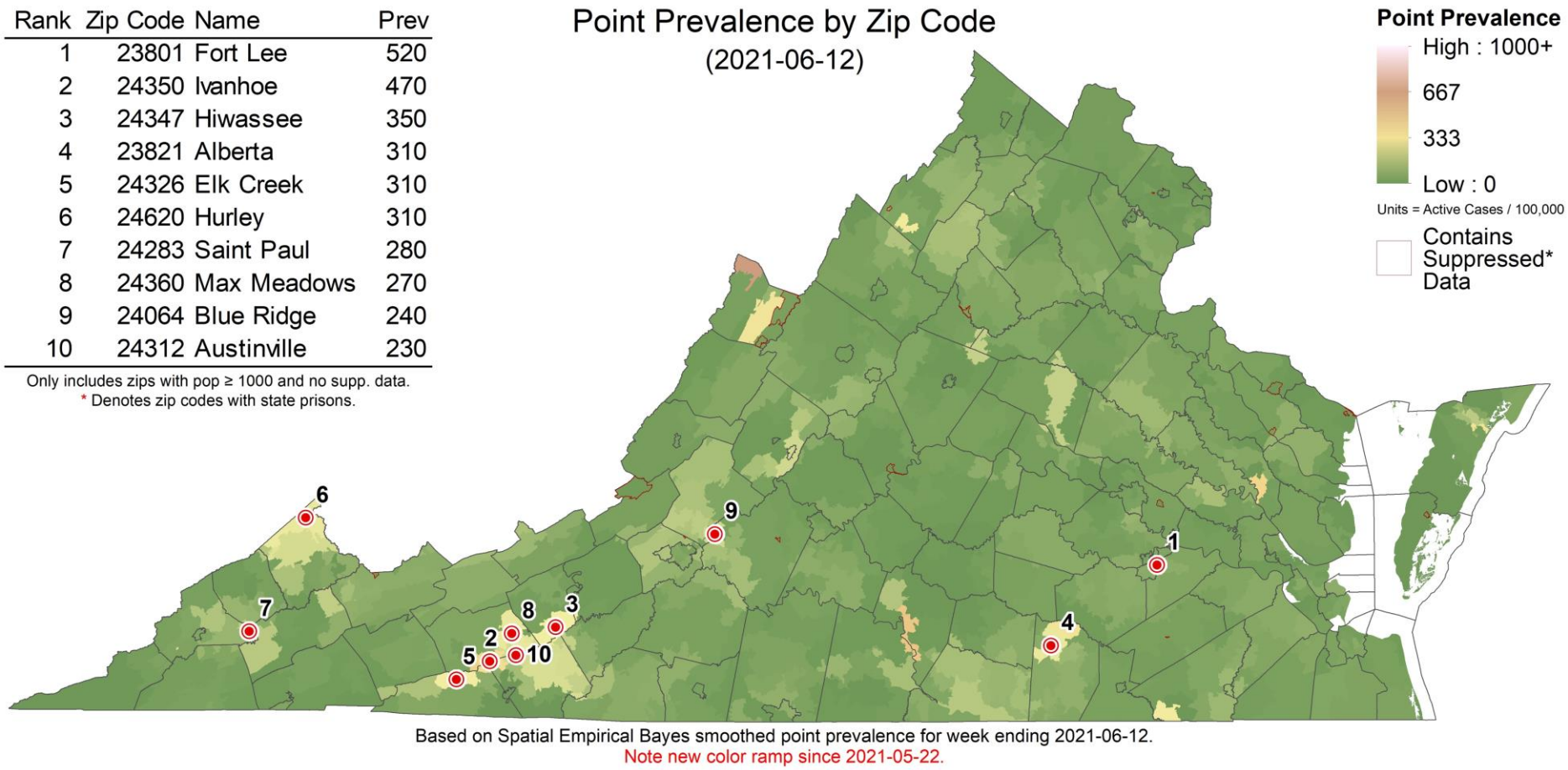
Zip code level weekly Case Rate (per 100K)

Case Rates in the last week by zip code

- Adjusted Color gradient to lower rates, thus red is a lower prevalence
- Some counts are low and suppressed to protect anonymity, those are shown in white

Rank	Zip Code	Name	Prev
1	23801	Fort Lee	520
2	24350	Ivanhoe	470
3	24347	Hiwassee	350
4	23821	Alberta	310
5	24326	Elk Creek	310
6	24620	Hurley	310
7	24283	Saint Paul	280
8	24360	Max Meadows	270
9	24064	Blue Ridge	240
10	24312	Austinville	230

Only includes zips with pop ≥ 1000 and no supp. data.
* Denotes zip codes with state prisons.



Based on Spatial Empirical Bayes smoothed point prevalence for week ending 2021-06-12.
Note new color ramp since 2021-05-22.

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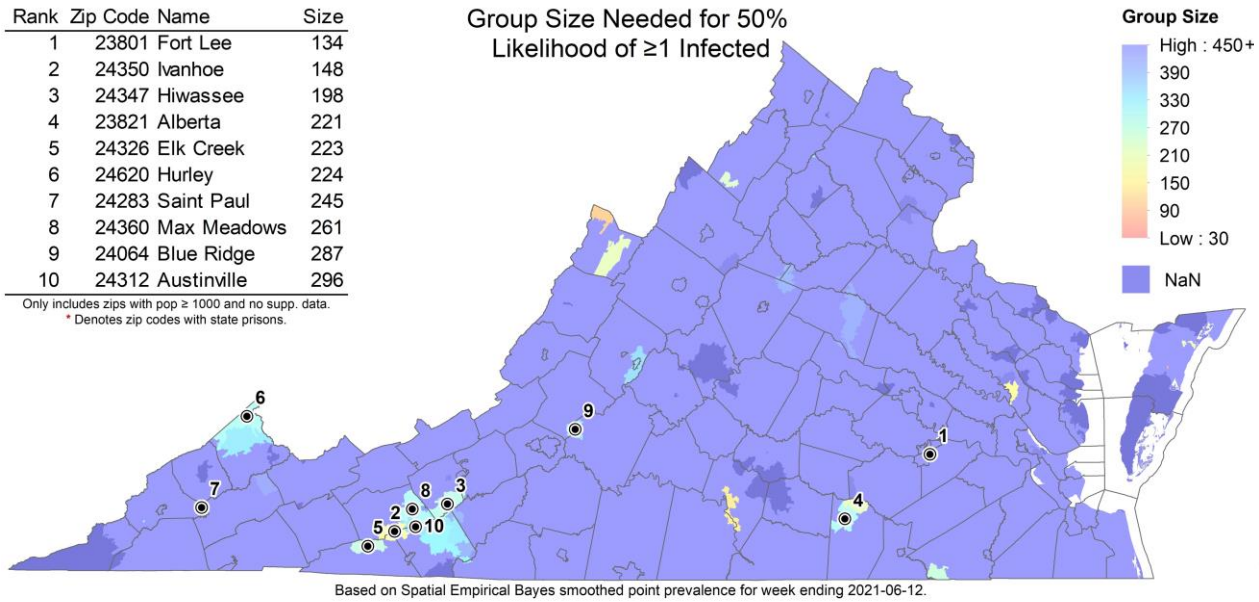
Risk of Exposure by Group Size and HCW prevalence

Case Prevalence in the last week by zip code used to calculate risk of encountering someone infected in a gathering of randomly selected people (group size 25)

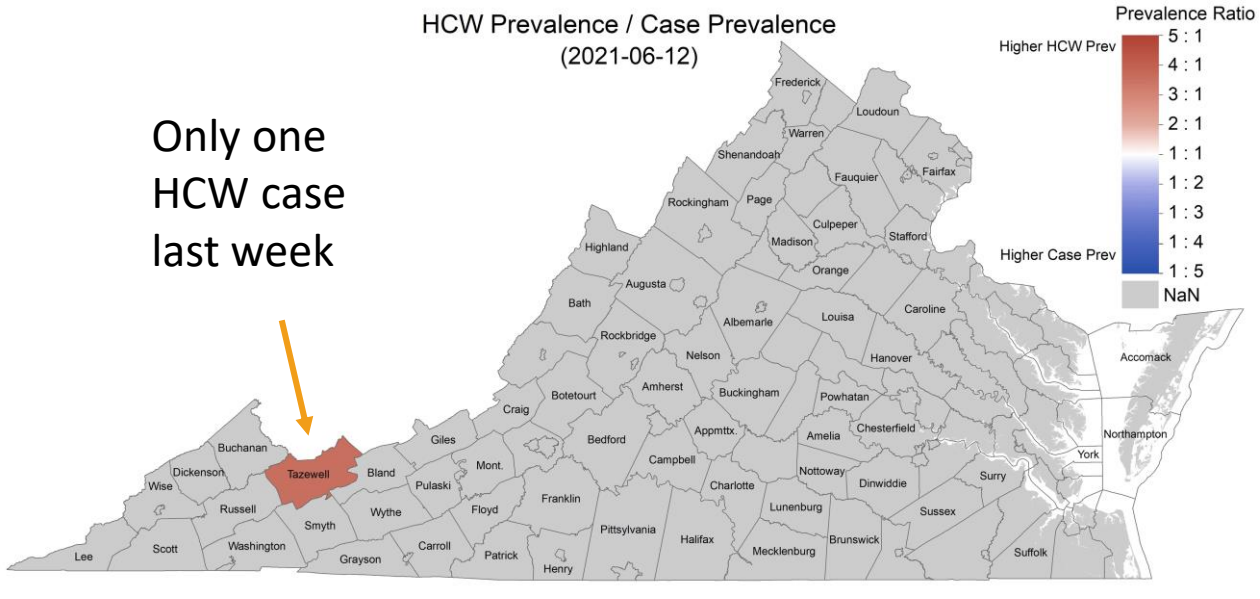
- **Group Size**: Assumes 2 undetected infections per confirmed case (ascertainment rate from recent seroprevalence survey), and shows minimum size of a group with a 50% chance an individual is infected by zip code (eg in a group of 134 in Fort Lee, there is a 50% chance someone will be infected)
- **HCW prevalence**: Case rate among health care workers (HCW) in the last week using patient facing health care workers as the denominator

Rank	Zip Code	Name	Size
1	23801	Fort Lee	134
2	24350	Ivanhoe	148
3	24347	Hiwassee	198
4	23821	Alberta	221
5	24326	Elk Creek	223
6	24620	Hurley	224
7	24283	Saint Paul	245
8	24360	Max Meadows	261
9	24064	Blue Ridge	287
10	24312	Austinville	296

Only includes zips with pop ≥ 1000 and no supp. data.
* Denotes zip codes with state prisons.



Based on Spatial Empirical Bayes smoothed point prevalence for week ending 2021-06-12.



Current Hot-Spots

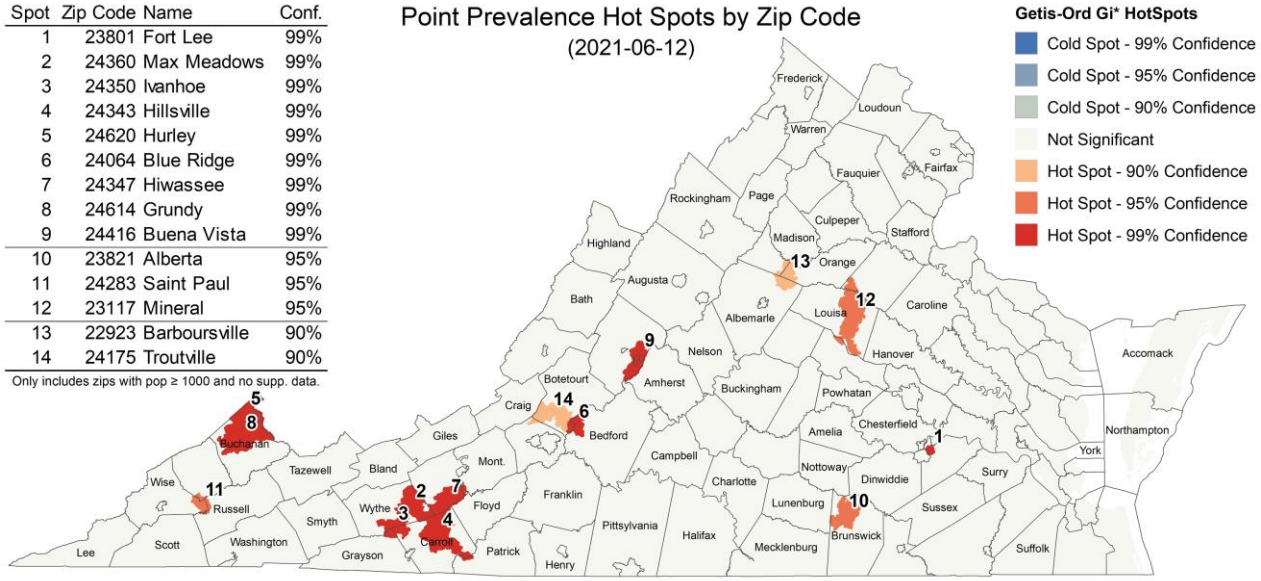
Case rates that are significantly different from neighboring areas or model projections

- **Spatial**: SaTScan based hot spots compare clusters of zip codes with weekly case prevalence higher than nearby zip codes to identify larger areas with statistically significant deviations
- **Temporal**: The weekly case rate (per 100K) projected last week compared to observed by county, which highlights temporal fluctuations that differ from the model's projections

Spatial Hotspots

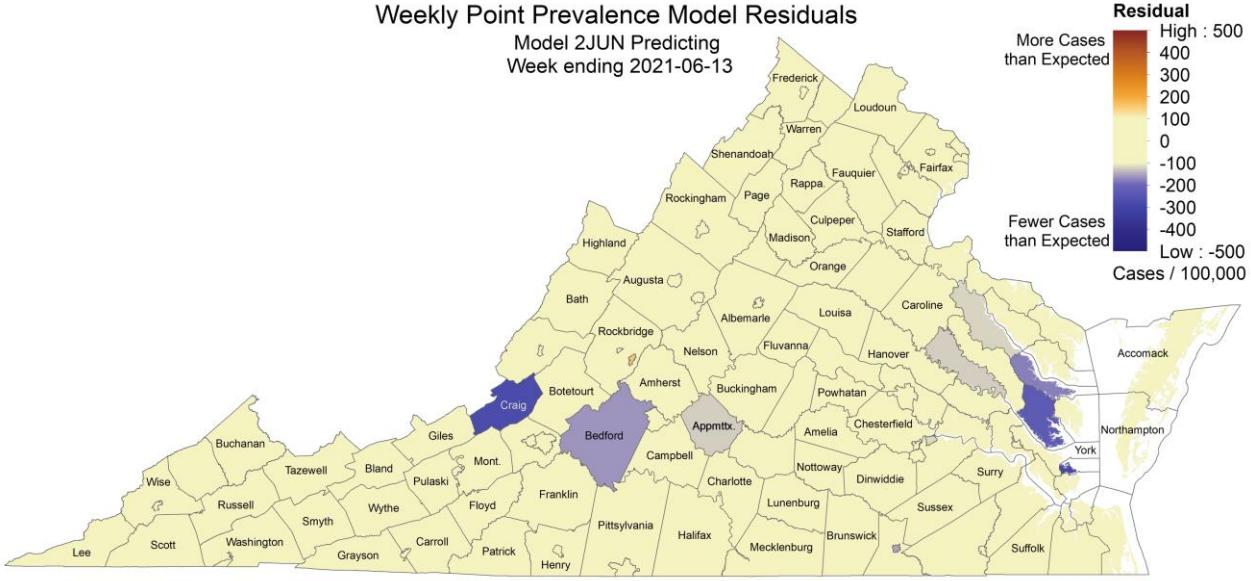
Spot	Zip Code	Name	Conf.
1	23801	Fort Lee	99%
2	24360	Max Meadows	99%
3	24350	Ivanhoe	99%
4	24343	Hillsville	99%
5	24620	Hurley	99%
6	24064	Blue Ridge	99%
7	24347	Hiwassee	99%
8	24614	Grundy	99%
9	24416	Buena Vista	99%
10	23821	Alberta	95%
11	24283	Saint Paul	95%
12	23117	Mineral	95%
13	22923	Barboursville	90%
14	24175	Troutville	90%

Only includes zips with pop ≥ 1000 and no supp. data.



Based on Global Empirical Bayes smoothed point prevalence for week ending 2021-06-12.

Clustered Temporal Hotspots

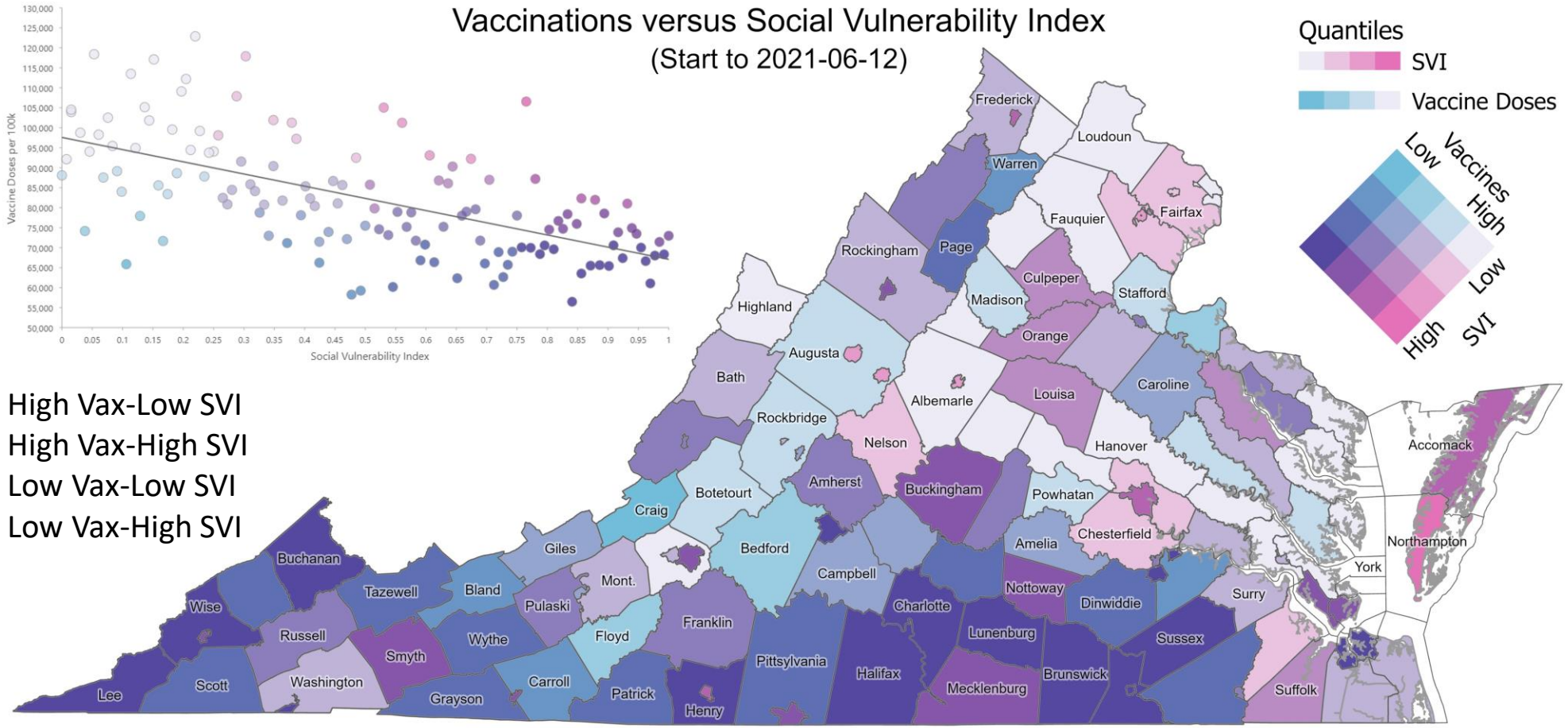


Moran's I = 0.092863, Z-Score = 1.30074, P-Value = 0.193348
No Residual Autocorrelation Detected

Social Vulnerability and Total Vaccination Rates

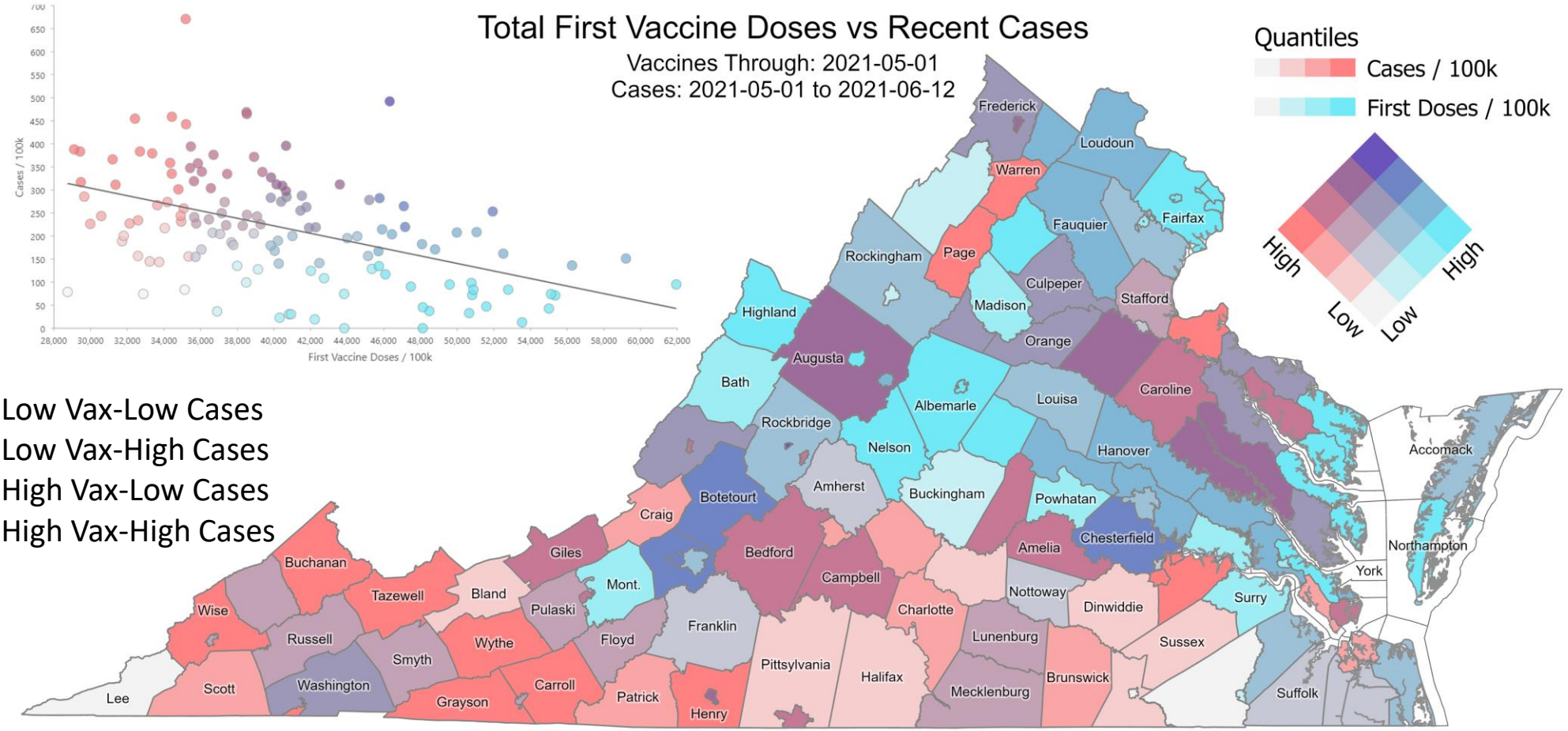
Comparison of social vulnerability and total vaccination rate since the start of vaccination

- **Social Vulnerability:** Each county's Social Vulnerability Index (CDC) compared with the level of vaccination



Vaccination and and Recent Case Rates

Comparison of total vaccination rate and case prevalence in the last month



White: Low Vax-Low Cases
Salmon: Low Vax-High Cases
Blue: High Vax-Low Cases
Purple: High Vax-High Cases

Model Update – Adaptive Fitting

Adaptive Fitting Approach

Each county fit precisely, with recent trends used for future projection

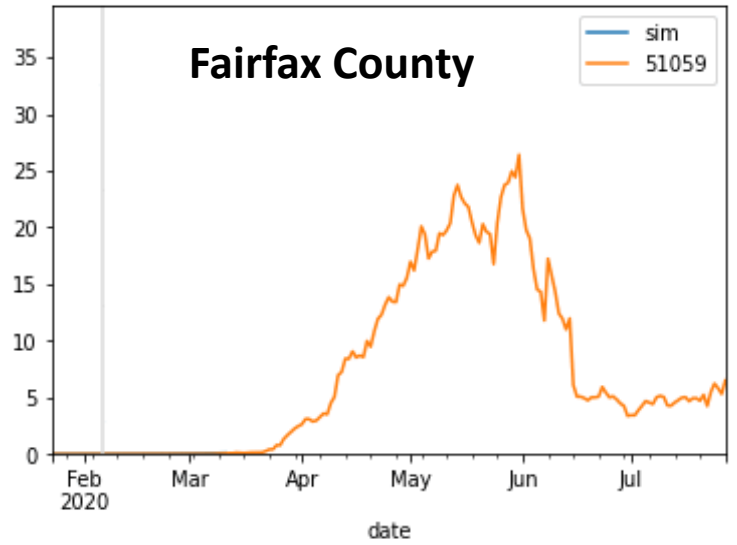
- Allows history to be precisely captured, and used to guide bounds on projections

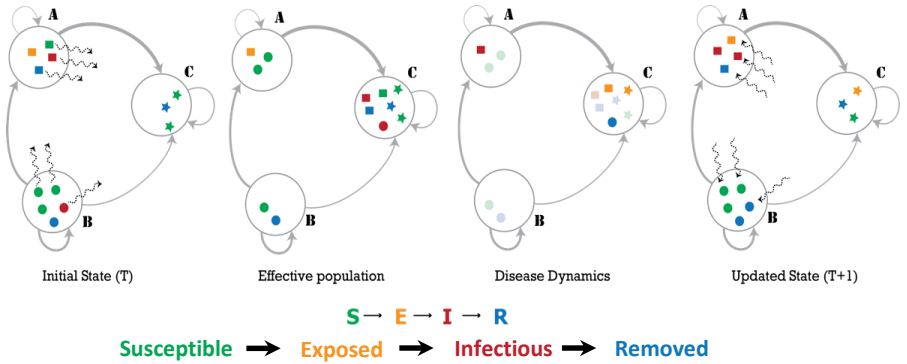
Model: An alternative use of the same meta-population model, PatchSim

- Allows for future "what-if" Scenarios to be layered on top of calibrated model
- Eliminates connectivity between patches, to allow calibration to capture the increasingly unsynchronized epidemic

External Seeding: Steady low-level importation

- Widespread pandemic eliminates sensitivity to initial conditions
- Uses steady 1 case per 10M population per day external seeding





Using Ensemble Model to Guide Projections

Ensemble methodology that combines the Adaptive with machine learning and statistical models such as:

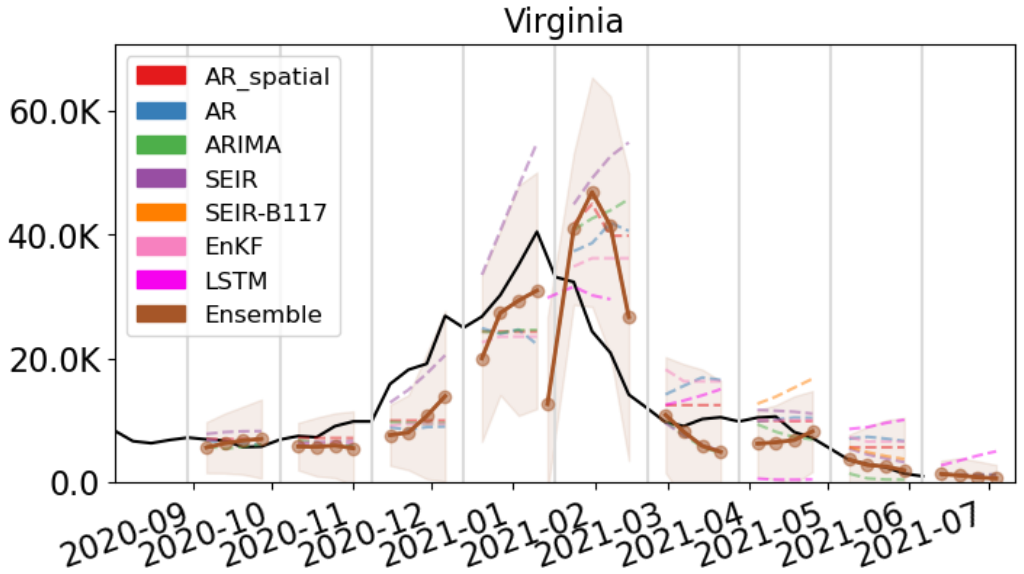
- Autoregressive (AR, ARIMA)
- Neural networks (LSTM)
- Kalman filtering (EnKF)

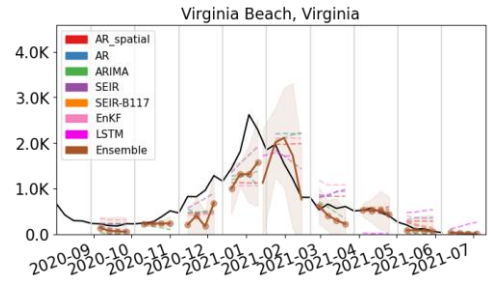
<u>Weekly forecasts</u> done at county level.

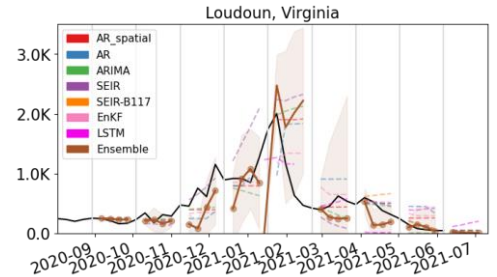
Models chosen because of their track record in disease forecasting and to increase diversity and robustness.

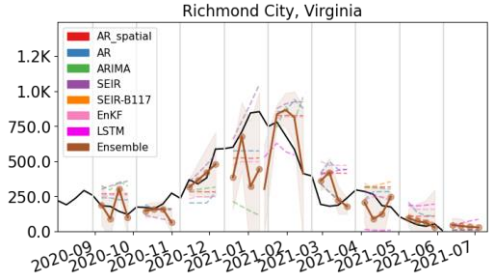
Ensemble forecast provides additional ‘surveillance’ for making scenario-based projections.

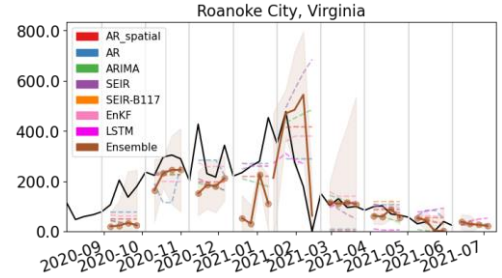
Also submitted to CDC Forecast Hub.











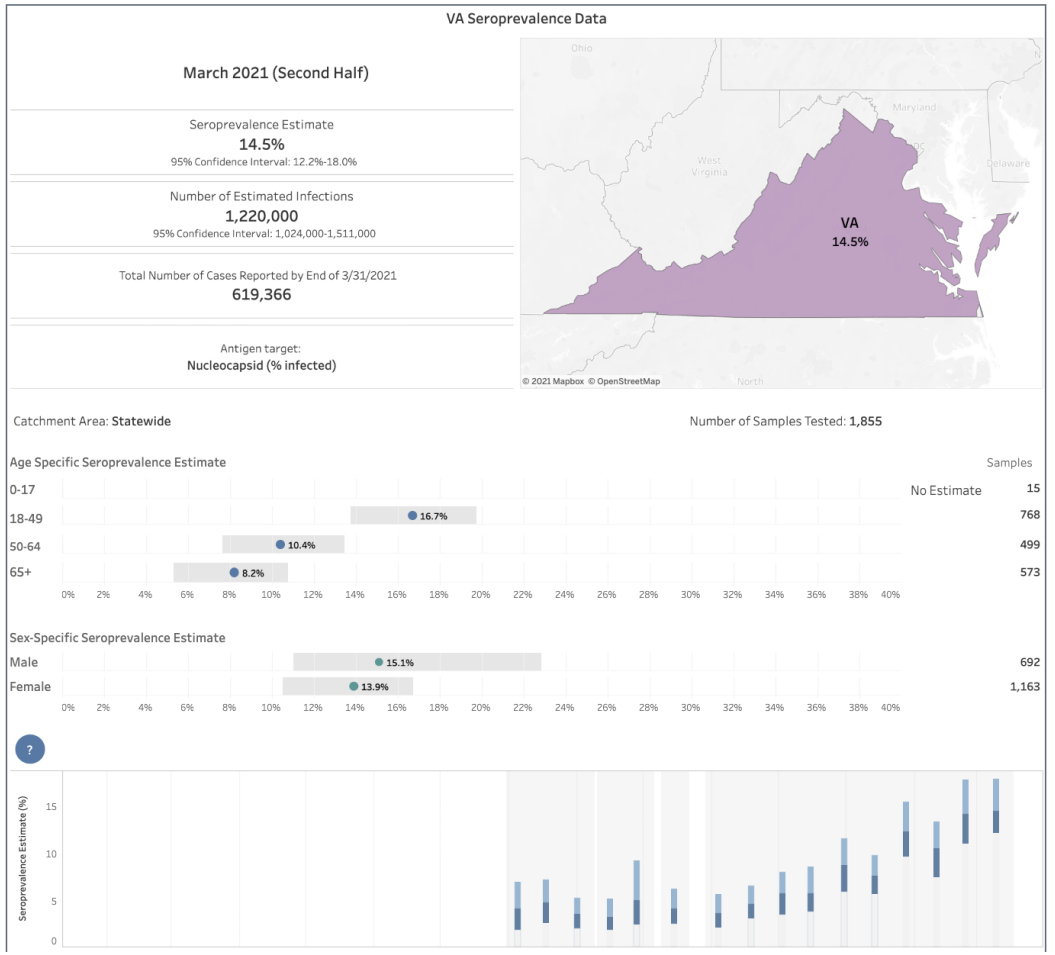
Seroprevalence updates to model design

Several seroprevalence studies provide better picture of how many actual infections have occurred

- CDC Nationwide Commercial Laboratory Seroprevalence Survey estimated 14.5% [12% – 18%] seroprevalence as of March 4th – 17th up from 10.5% a month earlier

These findings are equivalent to an ascertainment ratio of ~2x in the future, with bounds of (1.3x to 3x)

- Thus for 2x there are 2 total infections in the population for every confirmed case recently
- This measure now fully tracks the estimated ascertainment over time
- Uncertainty design has been shifted to these bounds (previously higher ascertainments as was consistent earlier in the pandemic were being used)



https://covid.cdc.gov/covid-data-tracker/#national-lab

Calibration Approach

- **Data:**
  - County level case counts by date of onset (from VDH)
  - Confirmed cases for model fitting
- **Calibration:** fit model to observed data and ensemble's forecast
  - Tune transmissibility across ranges of:
    - Duration of incubation (5-9 days), infectiousness (3-7 days)
    - Undocumented case rate (1x to 7x) guided by seroprevalence studies
    - Detection delay: exposure to confirmation (4-12 days)
  - Approach captures uncertainty, but allows model to precisely track the full trajectory of the outbreak
- **Project:** future cases and outcomes generated using the collection of fit models run into the future
  - **Mean trend from last 7 days of observed cases and first week of ensemble's forecast used**
  - Outliers removed based on variances in the previous 3 weeks
  - 2 week interpolation to smooth transitions in rapidly changing trajectories

COVID-19 in Virginia:

Dashboard Updated: 6/16/2021
Data entered by 5:00 PM the prior day.

Cases, Hospitalizations and Deaths

Total Cases*	Total Hospitalizations**	Total Deaths
678,226	30,241	11,330
(New Cases: 277)^		
Confirmed† 527,938 / Probable† 150,288	Confirmed† 28,697 / Probable† 1,544	Confirmed† 9,565 / Probable† 1,765

* Includes both people with a positive test (Confirmed), and symptomatic with a known exposure to COVID-19 (Probable).
** Hospitalization of a case is captured at the time VDH performs case investigation. This underrepresents the total number of hospitalizations in Virginia.
^New cases represent the number of confirmed and probable cases reported to VDH in the past 24 hours.
† VDH adopted the updated CDC COVID-19 confirmed and probable surveillance case definitions on August 27, 2020. Found here: https://wwwn.cdc.gov/nndss/conditions/coronavirus-disease-2019-covid-19/case-definition/2020/08/05/

Outbreaks

Total Outbreaks*	Outbreak Associated Cases
3,656	77,105

* At least two (2) lab confirmed cases are required to classify an outbreak.

Testing (PCR Only)

Testing Encounters PCR Only*	Current 7-Day Positivity Rate PCR Only**
7,578,332	1.6%

* PCR" refers to "Reverse transcriptase polymerase chain reaction laboratory testing."
** Lab reports may not have been received yet. Percent positivity is not calculated for days with incomplete data.

Multisystem Inflammatory Syndrome in Children

Total Cases*	Total Deaths
75	0

*Cases defined by CDC HAN case definition: https://emergency.cdc.gov/han/2020/han00432.asp

Accessed 9:00am June 16, 2021
https://www.vdh.virginia.gov/coronavirus/

Scenarios – Transmission Conditions

- Variety of factors continue to drive transmission rates
  - Seasonal impact of weather patterns, travel and gatherings, fatigue and premature relaxation of infection control practices
- Plausible levels of transmission can be bounded by past experience
  - Assess transmission levels at the county level from May 1, 2020 – Sept 1, 2020 or current, whichever is highest
- Projection Scenario:
  - **Adaptive:** Control remains as is currently experienced into the future
  - **Fatigued Control**:
    - Highest level of transmission (95th percentile) increased by additional 5%
    - Transition to this level over 4 weeks, remain at this level for the summer, then return to Adaptive
- Additional study scenarios with Fall Resurgence:
  - **Fall:** Resurgence to worst of Fall 2020 starting in September and ramping up quickly

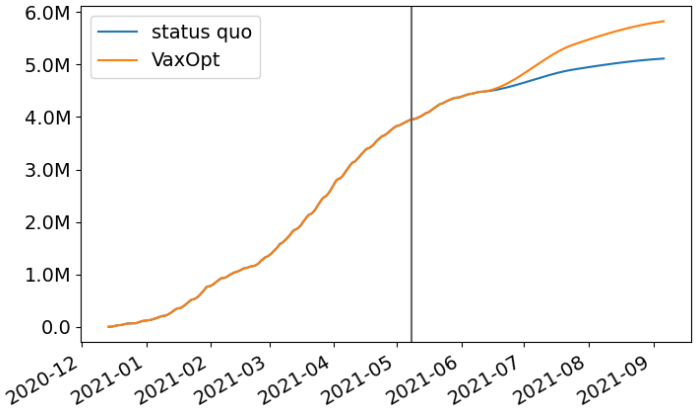
Scenarios – Vaccination Conditions

Vaccine Characteristics

- **Pfizer/Moderna**: 50% after first dose, 95% after second dose (3.5 week gap)
- **J & J** : 67% efficacy after first (and only) dose
- Delay to efficacy from doses is 14 days, immunity lasts at least 7m (NEJM study)

Vaccine Administration Study Scenarios

- **Status quo (no label):** COVIDcast corrected acceptance estimates (statewide mean is ~73%) reached by Labor Day.
- **Optimistic (VaxOpt):** Expand VA mean acceptance to ~85% (with all counties reaching a minimum of 65%, max of 95%).
- Acceptance at county level = regional acceptance +/- relative current vax
- Front-loaded rollout (two-thirds of the remaining in half the time)

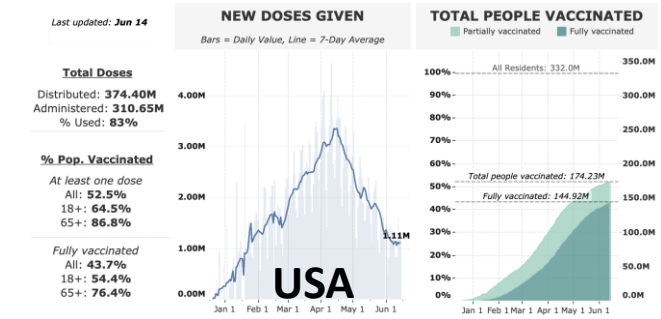


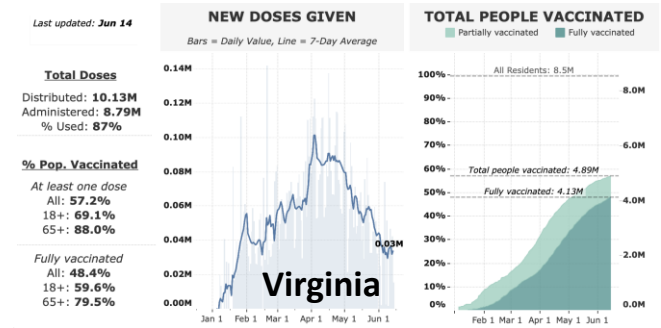
Monthly first doses

Date	status quo	VaxOpt
2020-12-31	114.4K	114.4K
2021-01-31	655.1K	655.1K
2021-02-28	568.9K	568.9K
2021-03-31	1.3M	1.3M
2021-04-30	1.2M	1.2M
2021-05-31	567.9K	567.9K
2021-06-30	269.3K	431.0K
2021-07-31	302.0K	660.5K
2021-08-31	152.6K	324.2K
2021-09-30	17.3K	36.5K

Cumulative

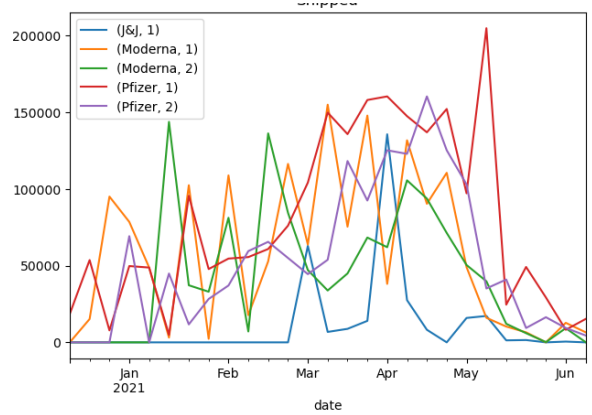
Date	status quo	VaxOpt
2020-12-31	114.4K	114.4K
2021-01-31	769.5K	769.5K
2021-02-28	1.3M	1.3M
2021-03-31	2.7M	2.7M
2021-04-30	3.8M	3.8M
2021-05-31	4.4M	4.4M
2021-06-30	4.6M	4.8M
2021-07-31	4.9M	5.5M
2021-08-31	5.1M	5.8M
2021-09-30	5.1M	5.8M





Source: https://ckelly17.github.io/vaccine_dashboard.html

Weekly VA doses administered by manufacturer



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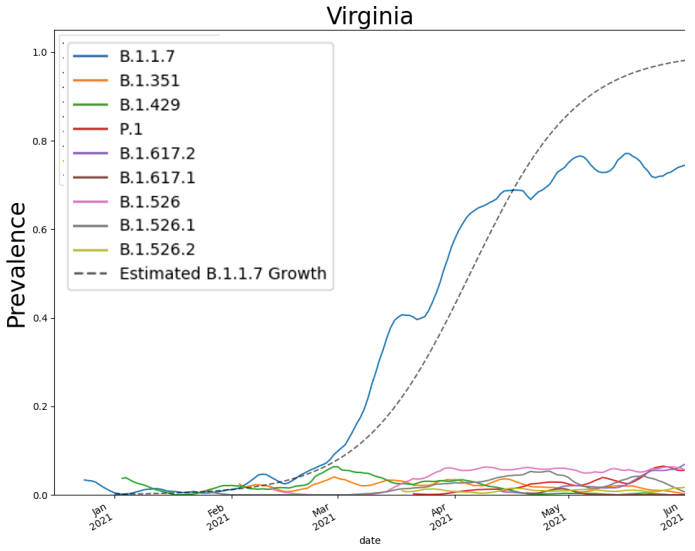
Scenarios – Mixed Variants Condition

- Variant Delta δ has exhibited ability to outcompete other variants and has started steady growth in other countries and states, and now VA
  - Delta reached 5% prevalence in VA on May 23rd, current fit with 60% transmissibility estimates dominance (50% prevalence) on July 4th
- Variant Alpha α (B.1.1.7) has reached dominance in Virginia but no longer is growing at a predictable pace as other variants compete
- **Transmissibility:** Delta's relative transmissibility compared to Alpha is better understood (60% more transmissible) and its growth can be estimated
- **Immune Escape:** Delta has been observed to evade immunity, both natural and vaccine-induced, however, uncertainty remains high thus this is **NOT** factored into the model
- **Severity**: Delta, similar to alpha, appears to cause more severe illness with estimates ranging from 50% to 200%, at the moment assume 60%

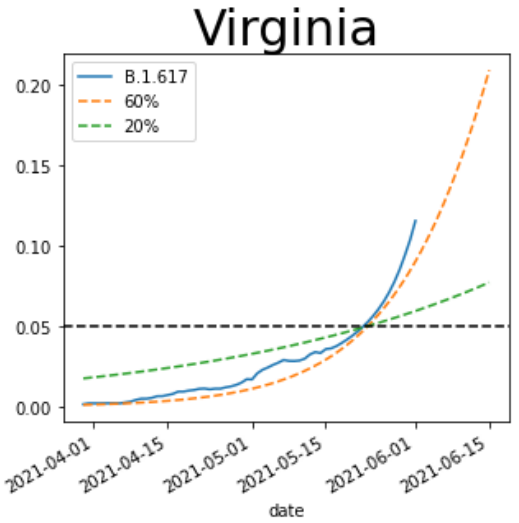
Scenario

- Delta reached 5% prevalence in VA on May 23rd, current fit with 60% transmissibility estimates dominance (50% prevalence) on July 4th



outbreak.info GISAID

Outbreak Info



Projection Scenarios – Combined Conditions

Name	Txm Controls	Variant Boosting	Vax	Description
Adaptive	C	None	SQ	Likely trajectory based on conditions remaining similar to how they are now
Adaptive-FatigueControl	F	None	SQ	Worst case trajectory if control conditions deteriorate to highest transmission rates of the past
Adaptive-Delta	C	60%	SQ	Likely trajectory based on conditions remaining similar to now, but with increasing prevalence of Delta variant
Adaptive-FatigueControl-Delta	F	60%	SQ	Worst case trajectory if control conditions deteriorate to worst of the past, with increasing prevalence of Delta variant

Transmission Controls: C = Current levels persist into the future
F = Fatiguing controls drift to worst levels of last summer and persist

Variant Boosting: None = Variety of variants, no future txm boosting, but with severity impacts from current levels
60% = Prevalence of Delta ramps up according to logistic growth and is 60% more transmissible

Vaccinations: SQ = Status quo acceptance leads to low rates of vaccination through the summer
VO = Vaccination acceptance optimistically expands with increased rates through the summer

Study Scenarios – Additional Conditions

Name	Abbv	Description
Fall Surge	Fall	Shift to worst transmission from Fall 2020 starting on Labor day and continue for 4 weeks to replicate increased transmission from seasonal effects and changes in human activities
Expanded vaccination to optimistic levels	VaxOpt	Apply vaccination from now to Labor days at rates that reach an optimistically high level of expanded coverage for eligible population (85%)

Added to existing conditions:

Transmission Controls: C = Current levels persist into the future
F = Fatiguing controls drift to worst levels of last summer and persist

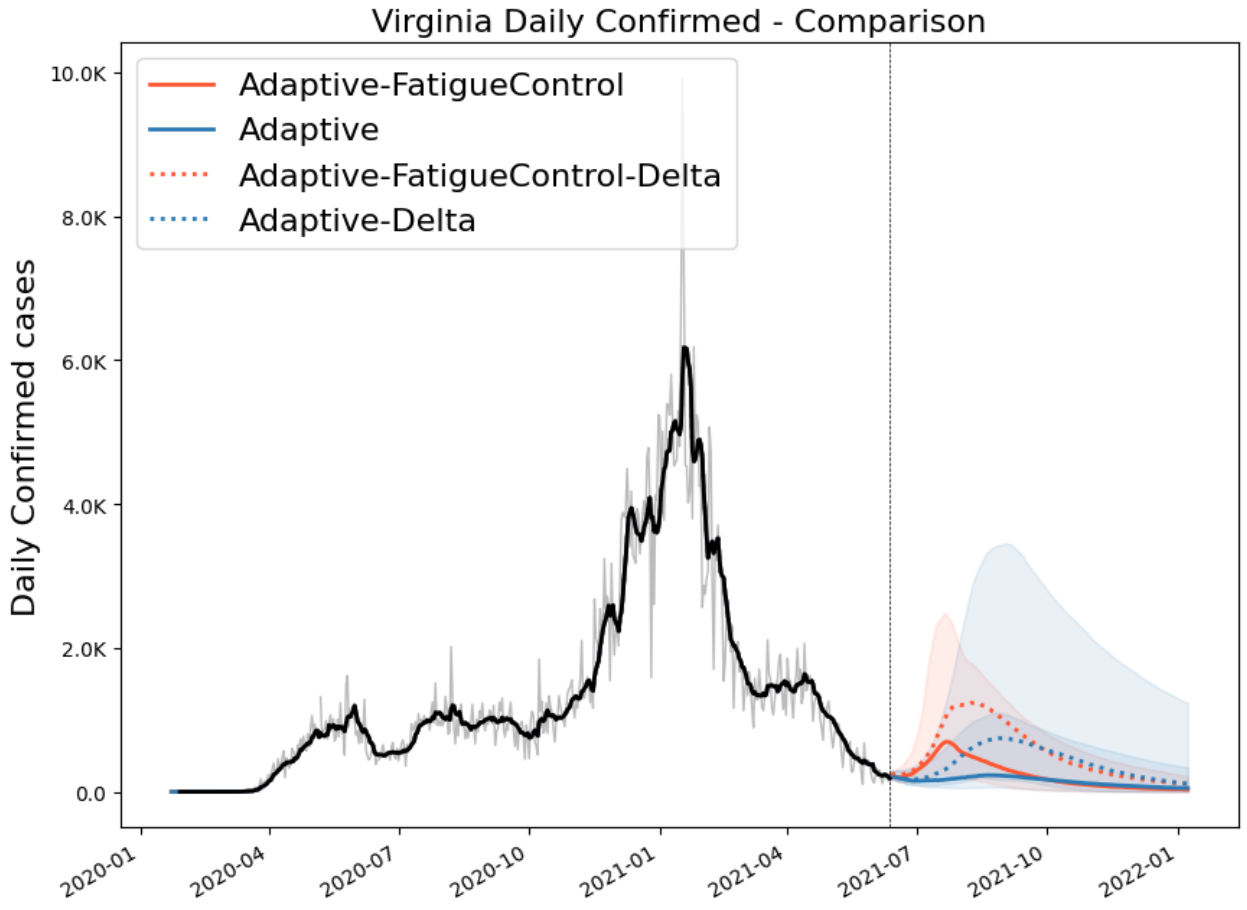
Variant Boosting: None = Variety of variants, no future txm boosting, but with severity impacts from current levels
60% = Prevalence of Delta ramps up according to logistic growth and is 60% more transmissible

Vaccinations: SQ = Status quo acceptance leads to low rates of vaccination through the summer

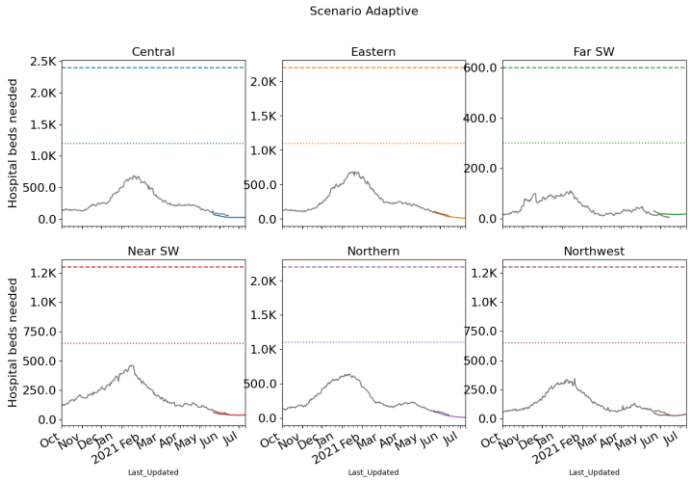
Model Results

Outcome Projections

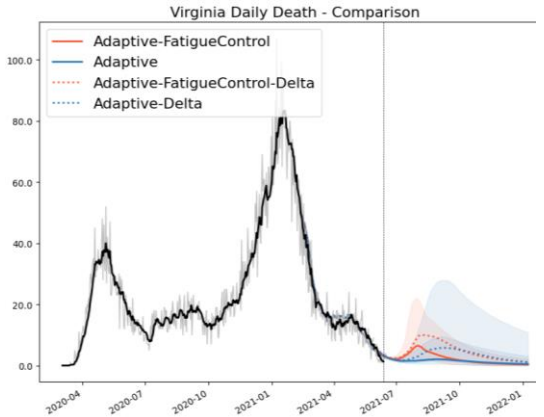
Confirmed cases



Estimated Hospital Occupancy

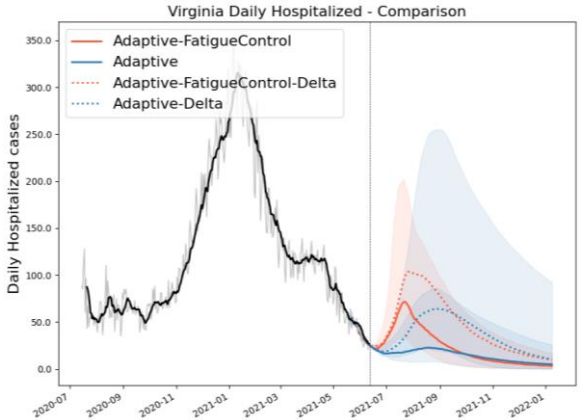


Daily Deaths



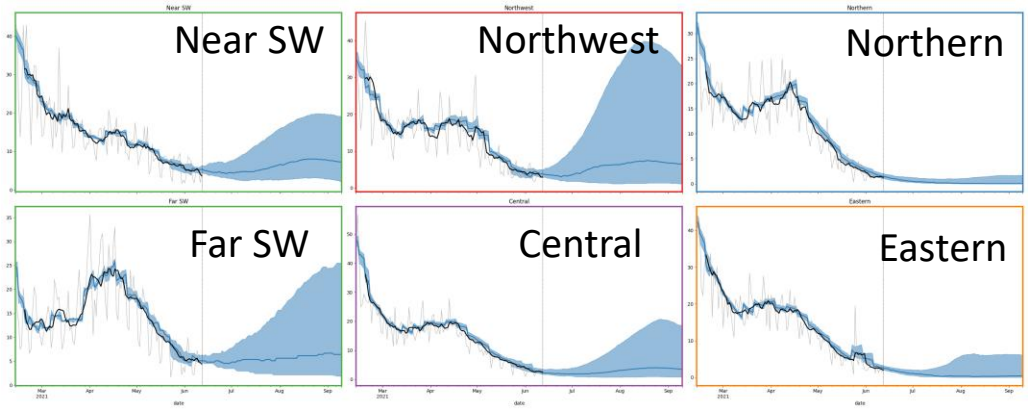
Death ground truth from VDH "Event Date" data, most recent dates are not complete

Daily Hospitalized



District Level Projections: Adaptive

Projections by Region



Projections by District

Daily confirmed cases rate (per 100K) by District (grey with 7-day average in black) with simulation colored by scenario

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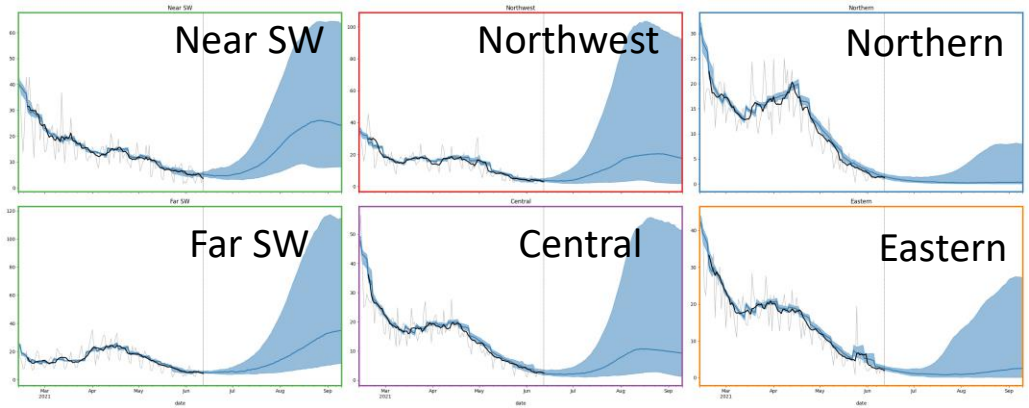
District Level Projections: Adaptive-Delta

Projections by Region



Projections by District

Daily confirmed cases rate (per 100K) by District (grey with 7-day average in black) with simulation colored by scenario

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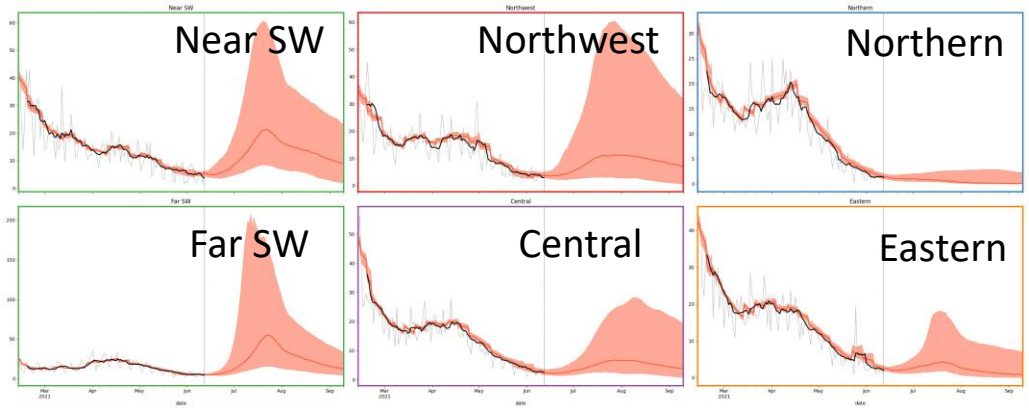
District Level Projections: Adaptive-FatigueControl

Projections by Region

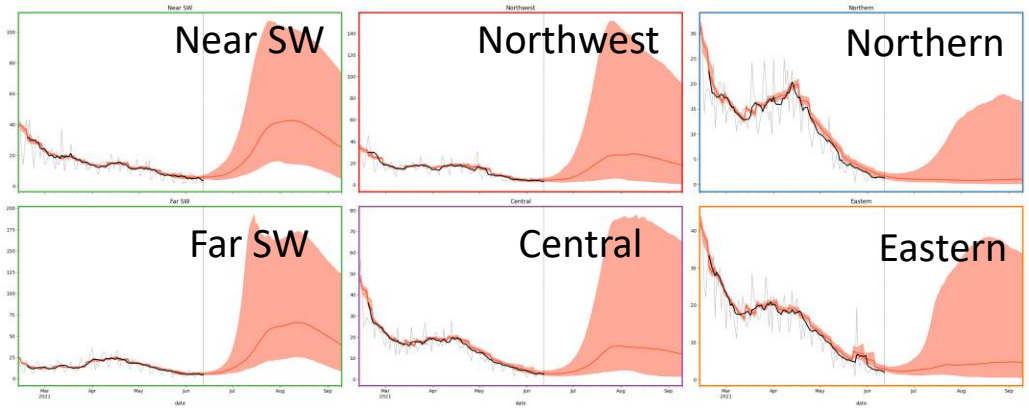


Projections by District

Daily confirmed cases rate (per 100K) by District (grey with 7-day average in black) with simulation colored by scenario

District Level Projections: Adaptive-FatigueControl-Delta

Projections by Region



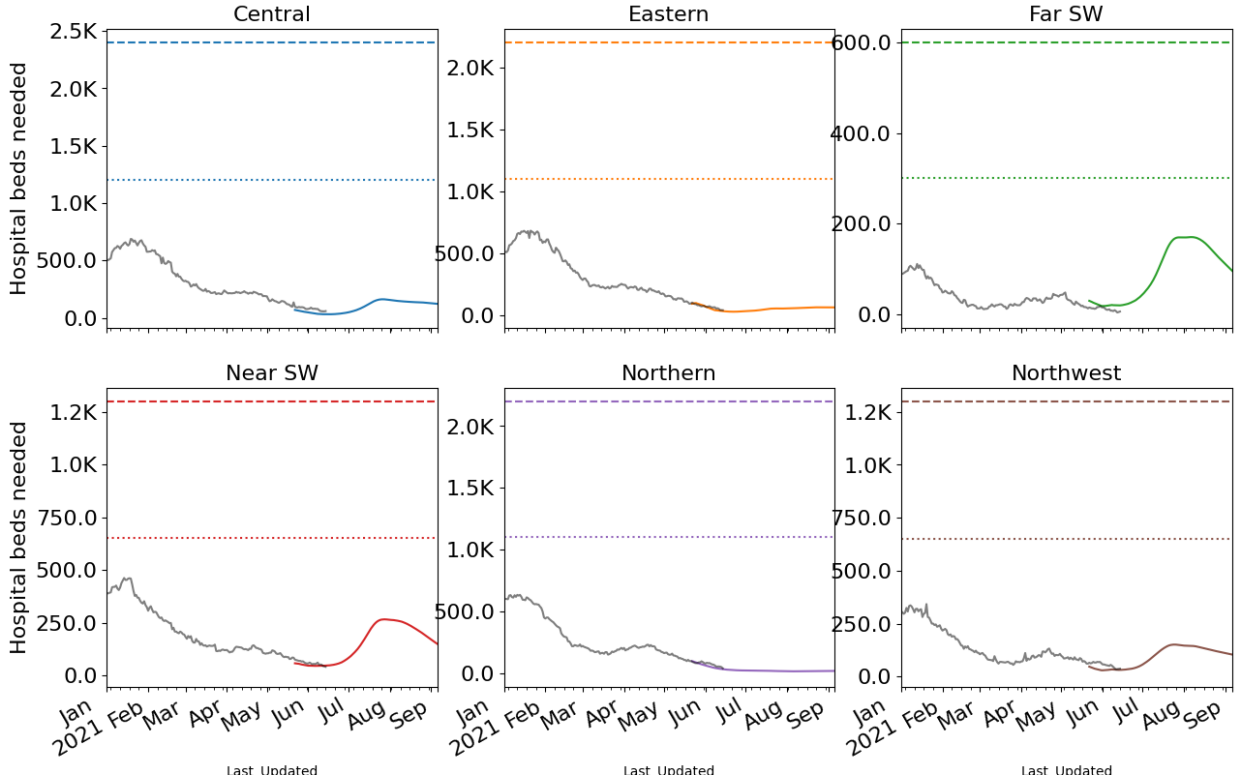
Projections by District

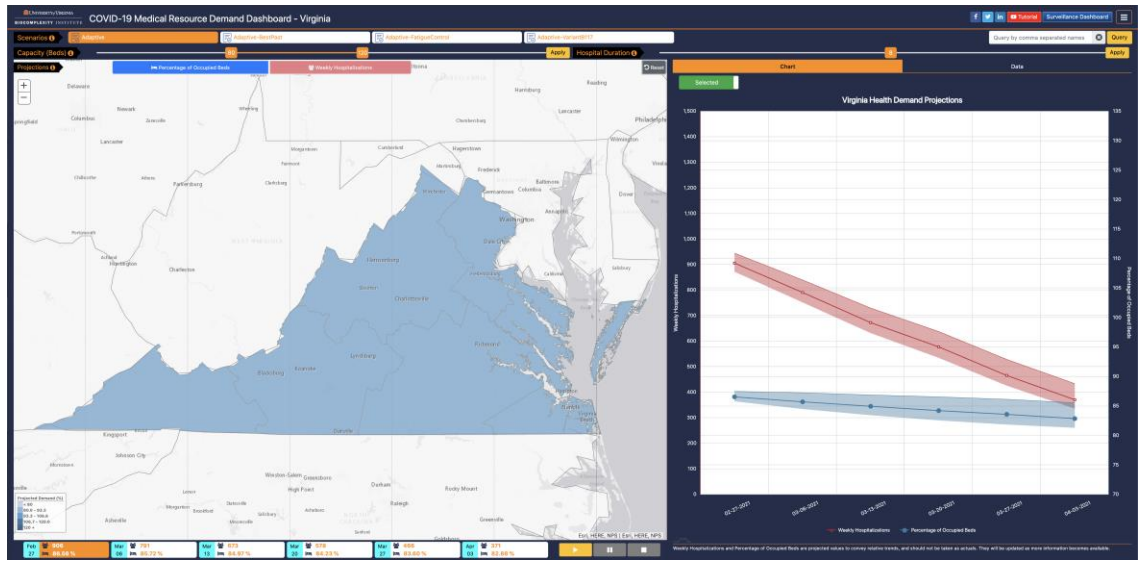
Daily confirmed cases rate (per 100K) by District (grey with 7-day average in black) with simulation colored by scenario

Hospital Demand and Bed Capacity by Region

Capacities* by Region – Adaptive-FatigueControl-Delta

COVID-19 capacity ranges from 80% (dots) to 120% (dash) of total beds





https://nssac.bii.virginia.edu/covid-19/vmrddash/

Adaptive-FatigueControl-Delta scenario shows it remains possible to generate more hospitalizations:

- Far Southwest and Near Southwest have highest potential

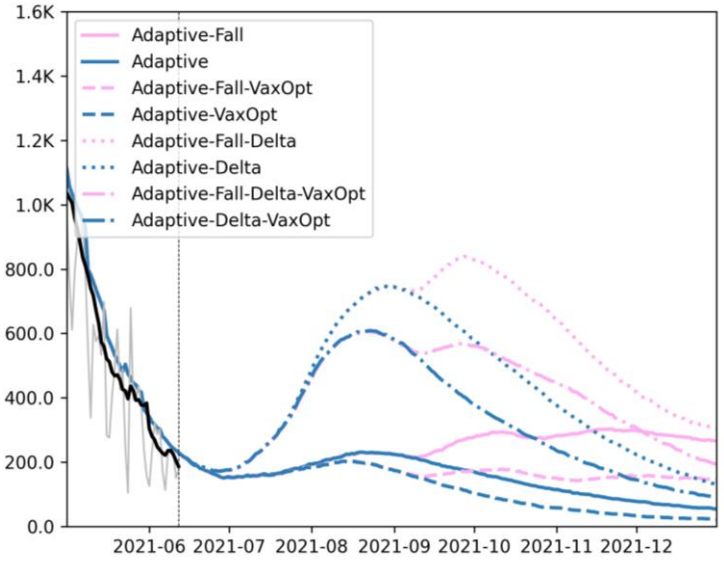
* Assumes average length of stay of 8 days

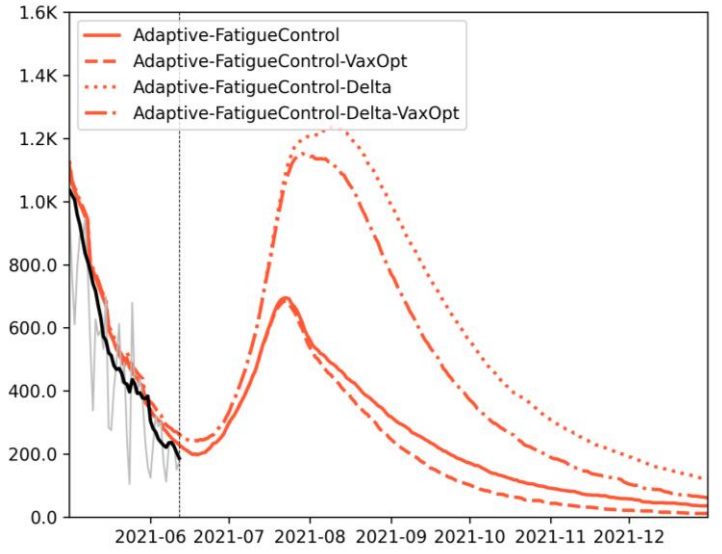
All Scenarios – Fall Surge and Optimistic Vaccination

Impact of expanded vaccine acceptance against a Fall Surge

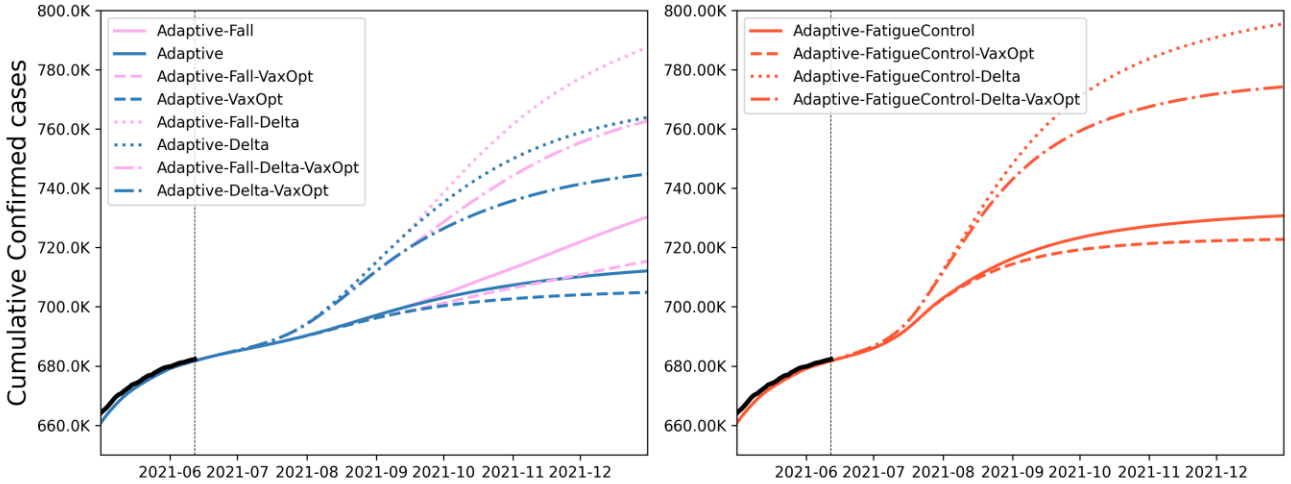
- Fall Surge on top of more prevalent Delta can create a sizeable spike in cases though it remains below 1000 cases/day
- Expanded vaccination coverage to optimistic levels curtails the impact of a Fall Surge as well as Delta (20K-40K cases)
- Despite range of plausible bad cases for the summer and fall, case rates are relatively moderate compared early 2021

Daily Infections





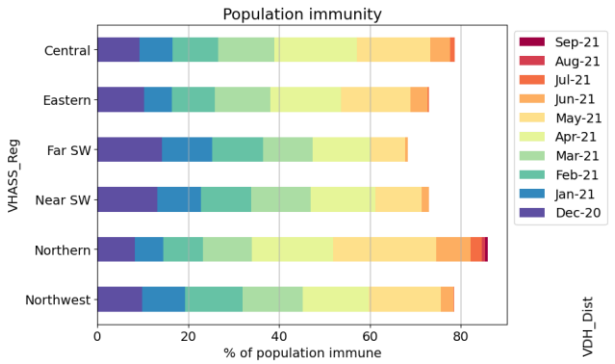
Cumulative Infections

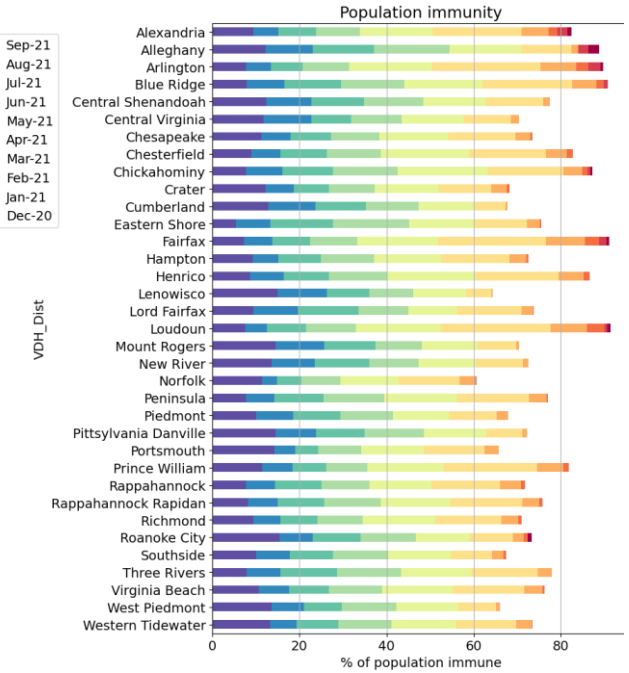


Virginia's Progress on Population Immunity

Natural Immunity and Vaccines combine to produce a population level of immunity

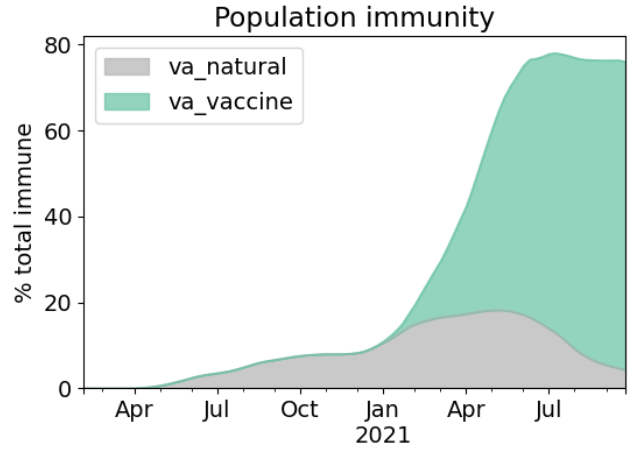
- Duration of immunity from infection with SARS-CoV2 still not well understood
  - We assume a conservative 6 month period of protection for these calculations
  - Natural immunity is well calibrated to recent seroprevalence surveys
- Vaccine induced immunity is likely to last longer, we assume indefinite protection
  - This also assumes that all administered vaccines remain protective against current and future novel variants
- Population immunity depends on a very high proportion of the population getting vaccinated
  - Using regional vaccine acceptance





Region	% immune (est.)*
Central	79%
Eastern	72%
Far SW	68%
Near SW	73%
Northern	81%
Northwest	78%
Virginia	76%

* As of May 30, 2021



Additional Analyses

Overview of relevant on-going studies

Other projects coordinated with CDC and VDH:

- **Scenario Modeling Hub:** Consortium of academic teams coordinated via MIDAS / CDC to that provides regular national projections based on timely scenarios
- **Genomic Surveillance:** Analyses of genomic sequencing data, VA surveillance data, and collaboration with VA DCLS to identify sample sizes needed to detect and track outbreaks driven by introduction of new variants etc.
- **Mobility Data driven Mobile Vaccine Clinic Site Selection:** Collaboration with VDH state and local, Stanford, and SafeGraph to leverage anonymized cell data to help identify

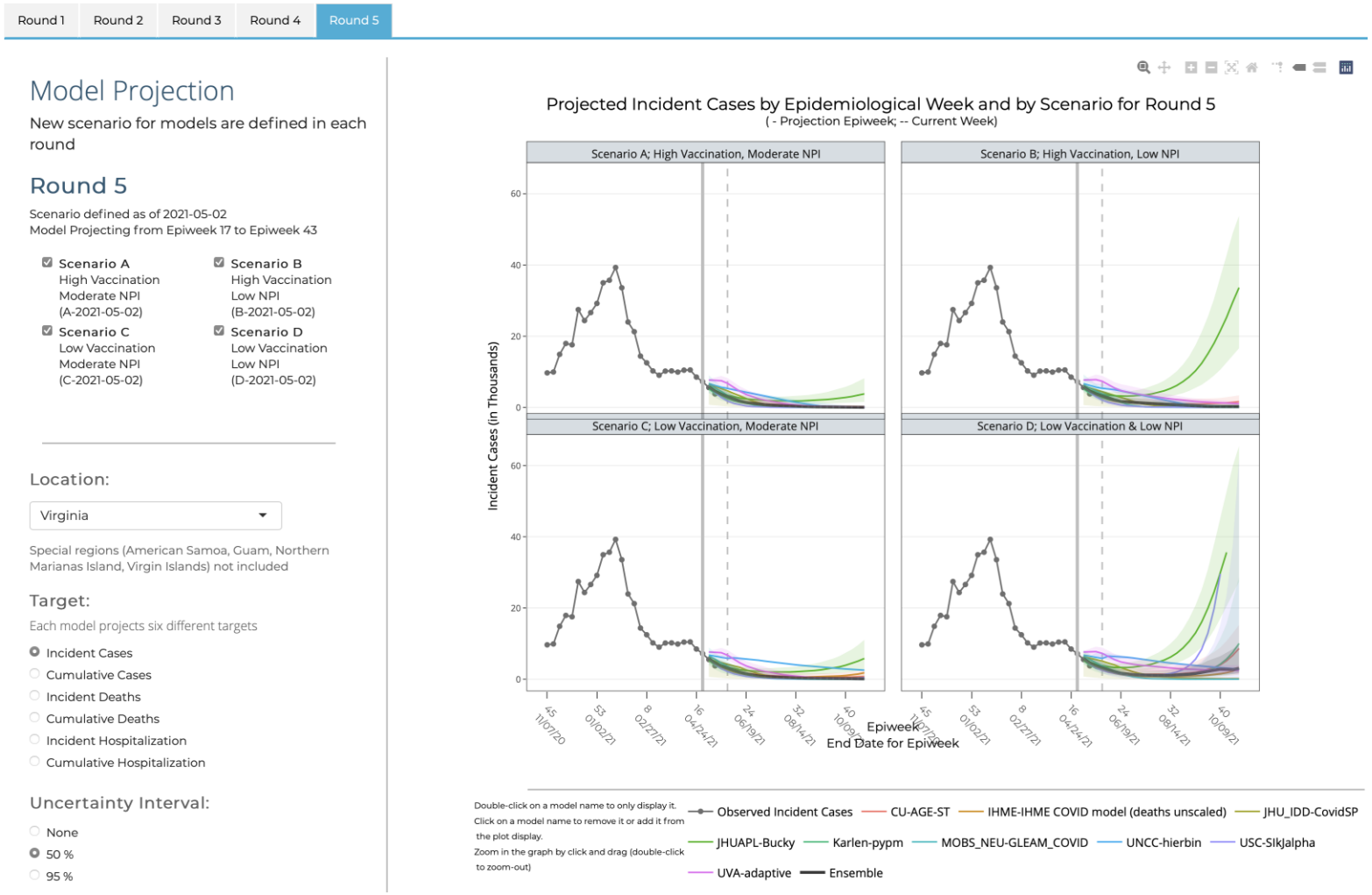
COVID-19 Scenario Modeling Hub

Collaboration of multiple academic teams to provide national and state-by-state level projections for 4 aligned scenarios that vary vaccine rates (high – low) and levels of control (moderate and low)

- Round 6 concluded and will be available next week
- Round 5 updates now available

Round 4 Results were published May 5th, 2021 in MMWR

https://covid19scenariomodelinghub.org/viz.html



COVID-19 Scenario Modeling Hub – Round 6

Round 6 scenarios explore the effects of a variant similar to the Delta (B.1.617.2) against different backgrounds of vaccination.

Vaccinations by Nov 30

- LowVacc – 68% overall coverage
- HighVacc – 86% overall coverage

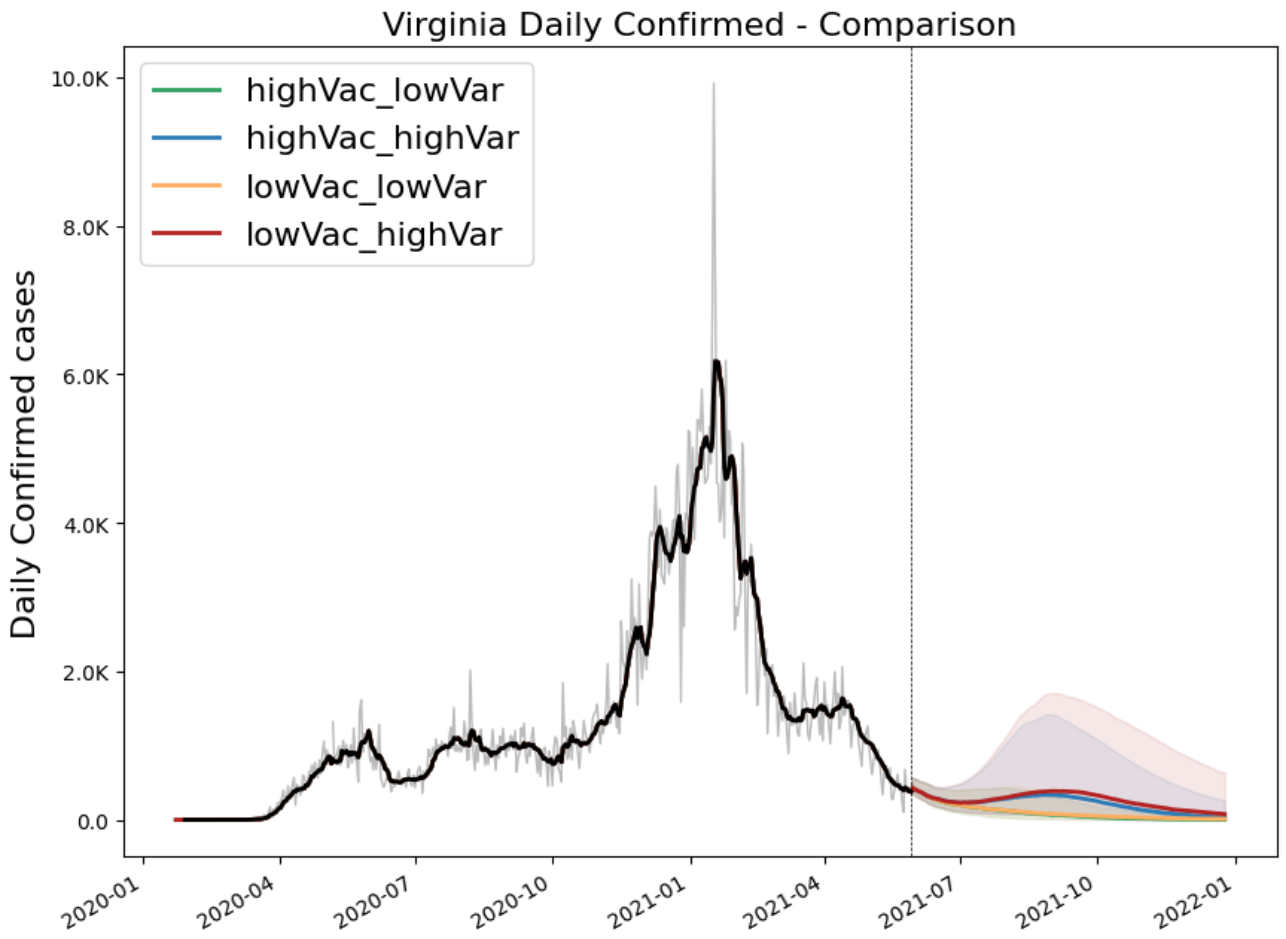
Emerging Variant Impact (5% prevalence on May 29th)

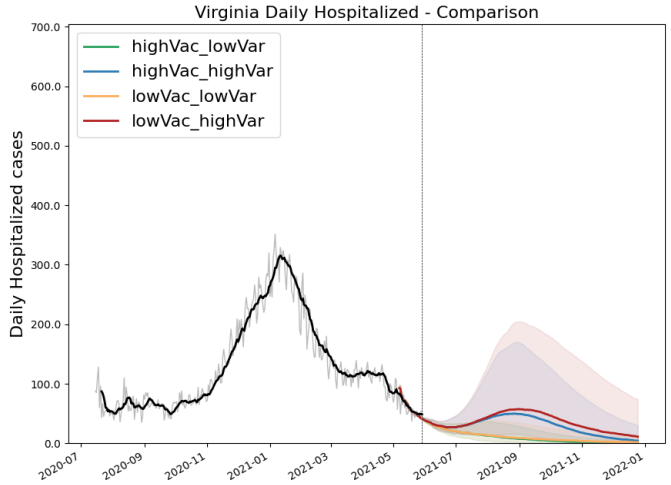
- LowVar – 20% more transmissible
- HighVar – 60% more transmissible

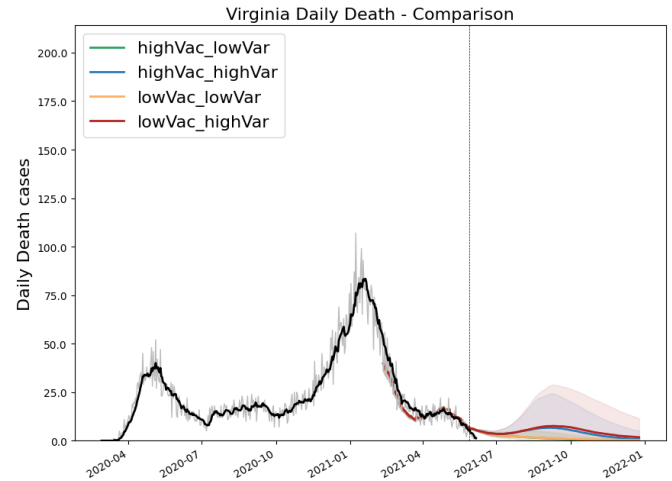
	LowVar	**HighVar**
See more detailed notes for each scenario below	**Low Impact Variant** *(low transmissibility increase, no immune escape)*	**High Impact Variant** *(high transmissibility increase, no immune escape)*
High Vaccination *(Low hesitancy)* **HighVacc**	***Scenario A*** Vaccination: - Coverage saturates at **86% nationally** among the vaccine-eligible population* by November 30, 2021** - VE is **50%/90%** for Pfizer/Moderna against currently circulating variants (1st /2nd dose) - J&J no longer used Variant: - **20% increased transmissibility** as compared with B.1.1.7 for B.1.617+ variant. **5%** prevalence of B.1.617+ nationally on May 29.	***Scenario B*** Vaccination: - Coverage saturates at **86% nationally** among the vaccine-eligible population* by November 30, 2021** - VE is **50%/90%** for Pfizer/Moderna against currently circulating variants (1st /2nd dose) - J&J no longer used Variant: **60% increased transmissibility** as compared with B.1.1.7 for B.1.617+ variant. **5%** prevalence of B.1.617+ nationally on May 29.
Low Vaccination *(High hesitancy)* **LowVacc**	***Scenario C*** Vaccination: - Coverage saturates at **75% nationally** among the vaccine-eligible population* by November 30, 2021** - VE is **50%/90%** for Pfizer/Moderna against currently circulating variants (1st /2nd dose) and 60% for JJ (1 dose) - J&J no longer used Variant: - **20% increased transmissibility** as compared with B.1.1.7 for B.1.617+ variant. **5%** prevalence of B.1.617+ nationally on May 29.	***Scenario D*** Vaccination: - Coverage saturates at **75% nationally** among the vaccine-eligible population* by November 30, 2021** - VE is **50%/90%** for Pfizer/Moderna against currently circulating variants (1st /2nd dose) and 60% for JJ (1 dose) - J&J no longer used Variant: **60% increased transmissibility** as compared with B.1.1.7 for B.1.617+ variant. **5%** prevalence of B.1.617+ nationally on May 29.

https://covid19scenariomodelinghub.org/viz.html

Modeling Hub – Round 6 Prelim Results







https://covid19scenariomodelinghub.org/viz.html

Genomic Sequencing: What size effort is needed?

Focused Questions: What number of sequences do we need to detect a variant of concern/interest in the population?

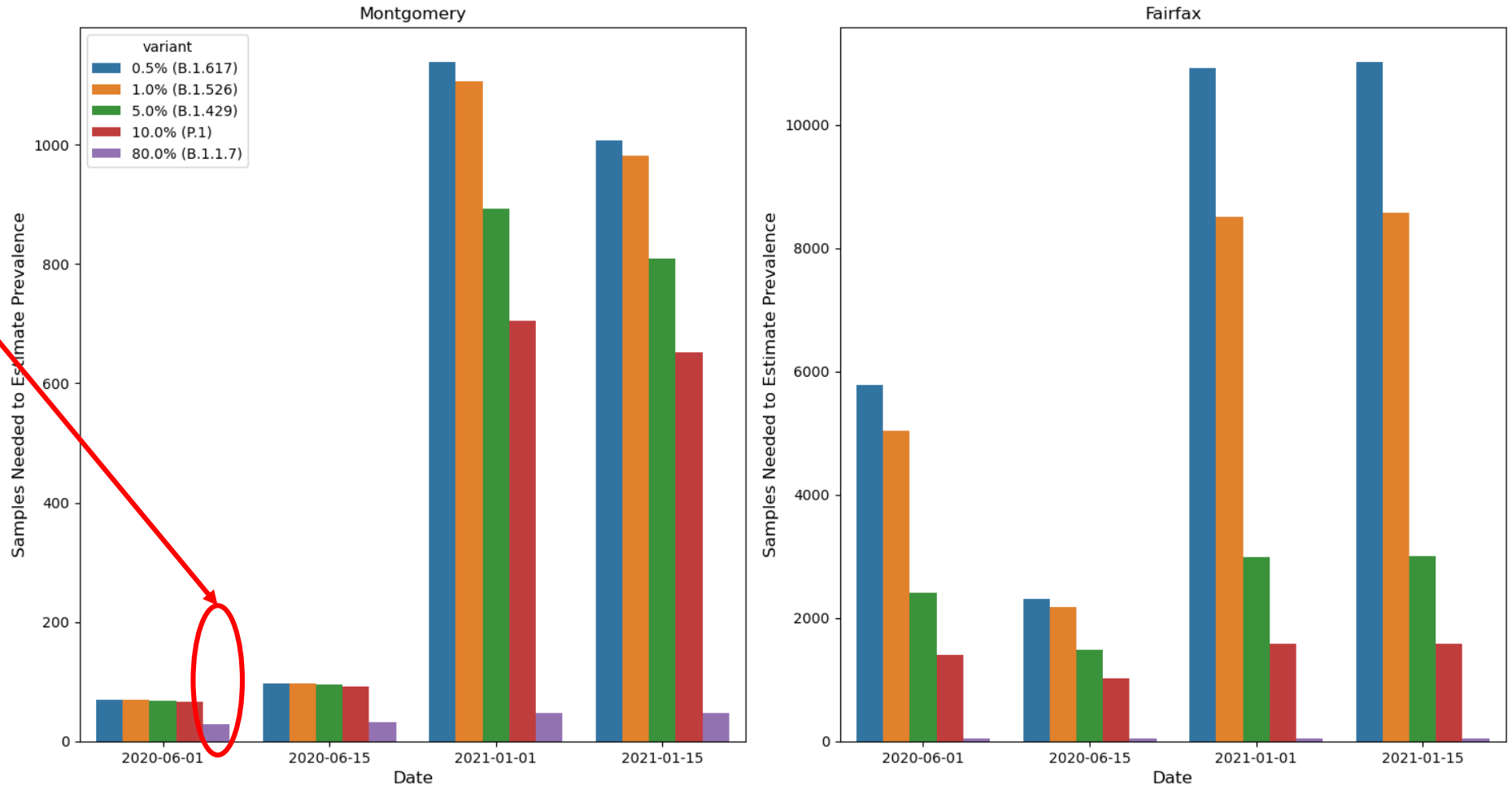
$$\hat{p} \pm z_{\alpha/2}\sqrt{\frac{\hat{p}(1-\hat{p})}{n} \cdot \frac{N-n}{N-1}}$$

Experiment Details:

- Consider two periods of COVID prevalence high and low (Jan 2021 and June 2020)
- Total infections taken from adaptive
- Confirmed cases from historical data
- Two counties: Fairfax, Montgomery
- 95% Confidence Interval
- +/- 20% of true prevalence

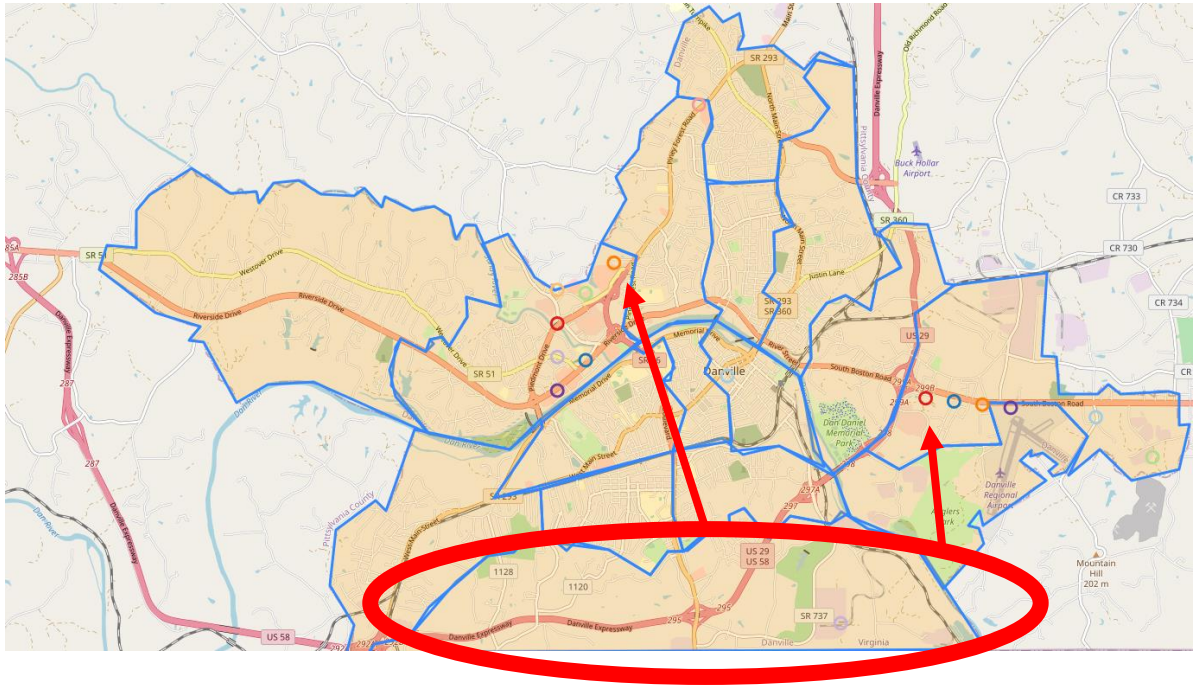
Window size: 14 days
Assumptions:
Test pool is representative
Sequences are of sufficient quality and timeliness to be representative of the window.
45% asymptomatic

To determine a confidence interval with a 95% chance of containing the true variant proportion (+/-10% of the prevalence), you need ~35 samples



Mobility Data Recommended Mobile Vax Clinic Sites

Census Block Groups in Danville



Work in Progress

1. Use census data to characterize the populations of the different census block groups
2. Identify most frequently visited POIs for each CBG
3. Cluster most visited POIs
4. Provide potential sites and the demographic groups they likely serve

Goal: Provide frequently visited locations based on populations and vaccination levels one desires to reach

Example: List of location in the Southside frequented by 30-49 year old Black Virginians

Key Takeaways

Projecting future cases precisely is impossible and unnecessary.
Even without perfect projections, we can confidently draw conclusions:

- **Case rates in Virginia continue to decline though some districts have small rebounds in rates**
- 60% of zip codes in Virginia (536 of 896 zips) had zero cases this past week; VA mean weekly incidence down at 1.6/100K from 2.4/100K, US flat at 4.2/100K
- Vaccination rates show signs of plateauing after steady decline
- Projections show declining rate overall across Commonwealth
- Recent updates:
  - Added Delta variant scenario as its growth becomes more predictable
  - Study scenarios: Fall resurgence and expanded vaccination
  - Limited waning of natural immunity included in fit and projections, also with seroprevalence update
- The situation continues to change. Models continue to be updated regularly.

References

Venkatramanan, S., et al. "Optimizing spatial allocation of seasonal influenza vaccine under temporal constraints." *PLoS Computational Biology* 15.9 (2019): e1007111.

Arindam Fadikar, Dave Higdon, Jiangzhuo Chen, Bryan Lewis, Srinivasan Venkatramanan, and Madhav Marathe. Calibrating a stochastic, agent-based model using quantile-based emulation. SIAM/ASA Journal on Uncertainty Quantification, 6(4):1685–1706, 2018.

Adiga, Aniruddha, Srinivasan Venkatramanan, Akhil Peddireddy, et al. "Evaluating the impact of international airline suspensions on COVID-19 direct importation risk." *medRxiv* (2020)

NSSAC. PatchSim: Code for simulating the metapopulation SEIR model. https://github.com/NSSAC/PatchSim

Virginia Department of Health. COVID-19 in Virginia. http://www.vdh.virginia.gov/coronavirus/

Biocomplexity Institute. COVID-19 Surveillance Dashboard. https://nssac.bii.virginia.edu/covid-19/dashboard/

Google. COVID-19 community mobility reports. https://www.google.com/covid19/mobility/

Biocomplexity page for data and other resources related to COVID-19: https://covid19.biocomplexity.virginia.edu/

Questions?

Points of Contact

Bryan Lewis
brylew@virginia.edu

Srini Venkatramanan
srini@virginia.edu

Madhav Marathe
marathe@virginia.edu

Chris Barrett
ChrisBarrett@virginia.edu

Biocomplexity COVID-19 Response Team

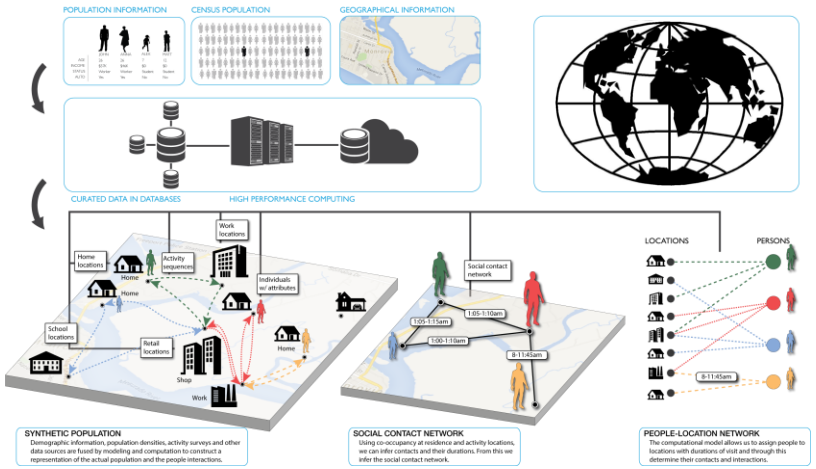
Aniruddha Adiga, Abhijin Adiga, Hannah Baek, Chris Barrett, Golda Barrow, Richard Beckman, Parantapa Bhattacharya, Jiangzhuo Chen, Clark Cucinell, Patrick Corbett, Allan Dickerman, Stephen Eubank, Stefan Hoops, Ben Hurt, Ron Kenyon, Brian Klahn, Bryan Lewis, Dustin Machi, Chunhong Mao, Achla Marathe, Madhav Marathe, Henning Mortveit, Mark Orr, Joseph Outten, Akhil Peddireddy, Przemyslaw Porebski, Erin Raymond, Jose Bayoan Santiago Calderon, James Schlitt, Samarth Swarup, Alex Telionis, Srinivasan Venkatramanan, Anil Vullikanti, James Walke, Andrew Warren, Amanda Wilson, Dawen Xie

Supplemental Slides

Agent-based Model (ABM)

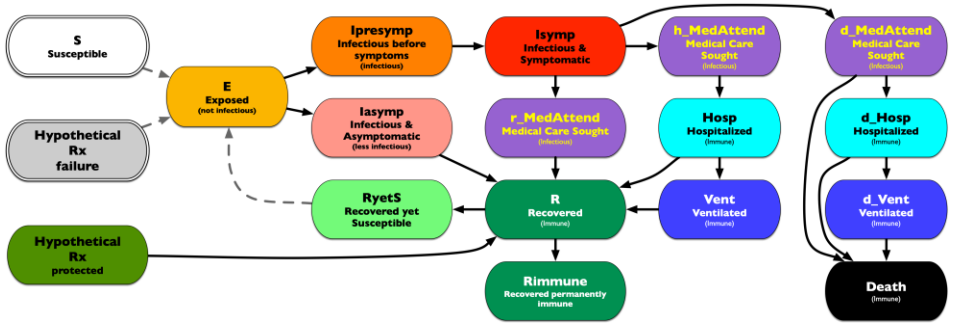
EpiHiper: Distributed network-based stochastic disease transmission simulations

- Assess the impact on transmission under different conditions
- Assess the impacts of contact tracing



Synthetic Population

- Census derived age and household structure
- Time-Use survey driven activities at appropriate locations



Detailed Disease Course of COVID-19

- Literature based probabilities of outcomes with appropriate delays
- Varying levels of infectiousness
- Hypothetical treatments for future developments