Network Systems Science & Advanced Computing

Biocomplexity Institute & Initiative

University of Virginia

Estimation of COVID-19 Impact in Virginia

September 29th, 2021

(data current to September 25th – 28th)

Biocomplexity Institute Technical report: TR 2021-107

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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

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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

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Key Takeaways

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

- **Case rate growth in Virginia has started decline, though growth remains in many districts; case rates remain high as we may begin to decline from the peak of the Delta wave**

- VA 7-day mean daily incidence is slightly down to 35/100K from 42/100K; US is also slightly down to 43/100K (from 48/100K)

- Projections show continued decline, though some districts have some growth potential, and a scenario based on last year's transmission drivers show that significant future case growth remains possible

- Recent updates:
  - Added FallWinter2020 scenario which replays the transmission drivers of last Fall-Winter season
  - Prelim analysis of impact of expanded immunity through 3rd doses
 - Adjustment to higher levels of assumed immunity waning (natural and vaccine)

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

Situation Assessment

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Case Rates (per 100k) and Test Positivity

- Case rate increase across all health districts
- Some past 50% of winter peak and growing
- More than 50% of counties with TPR > 10%

Data source: https://data.cms.gov/covid-19/covid-19-nursing-home-data
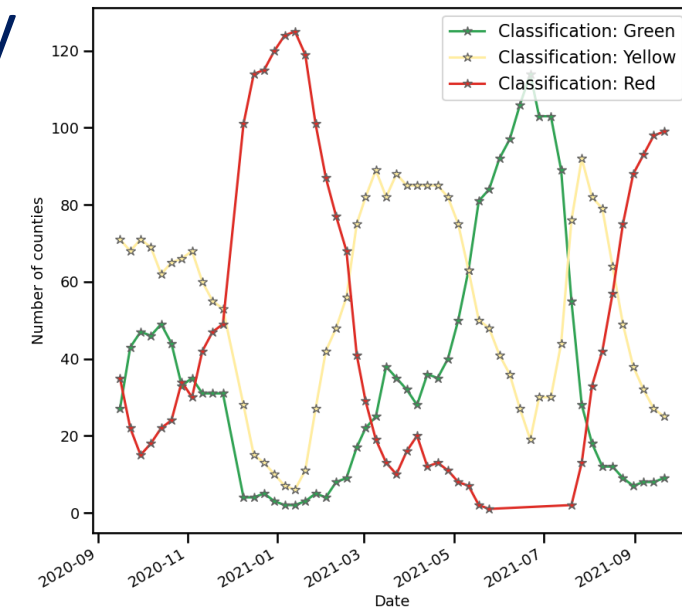
**County level RT-PCR test positivity**
Green: <5.0% (or <20 tests in past 14 days)
Yellow: 5.0%-10.0% (or <500 tests and <2000 tests/100k and >10% positivity over 14 days)
Red: >10.0% (and not "Green" or "Yellow")

Classification	Green	Yellow	Red
date			
2021-06-28	103.0	30.0	0.0
2021-07-06	103.0	30.0	0.0
2021-07-13	89.0	44.0	0.0
2021-07-20	55.0	76.0	2.0
2021-07-27	28.0	92.0	13.0
2021-08-03	18.0	82.0	33.0
2021-08-10	12.0	79.0	42.0
2021-08-17	12.0	64.0	57.0
2021-08-24	9.0	49.0	75.0
2021-08-31	7.0	38.0	88.0

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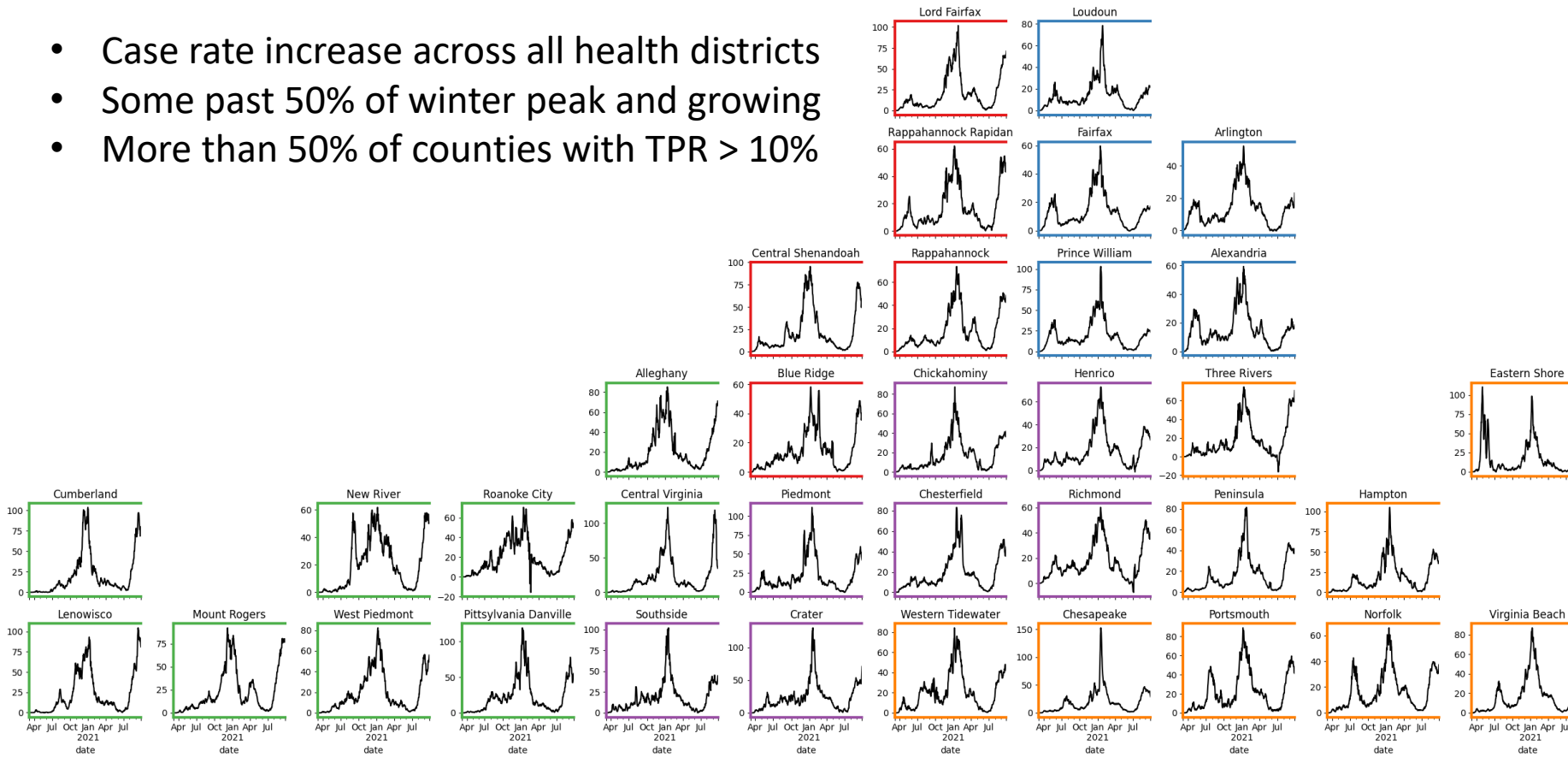
District Trajectories

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
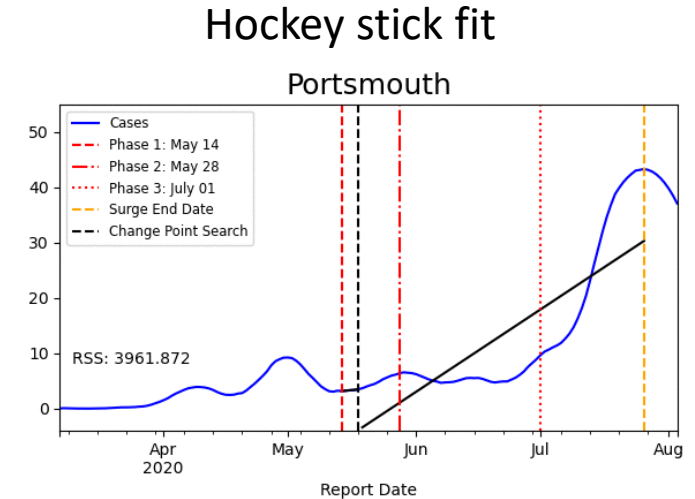
Trajectory	Description	Weekly Case Rate (per 100K) bounds	# Districts (prev week)
Declining	Sustained decreases following a recent peak	below -0.9	20 (8)
Plateau	Steady level with minimal trend up or down	above -0.9 and below 0.5	5 (4)
Slow Growth	Sustained growth not rapid enough to be considered a Surge	above 0.5 and below 2.5	8 (15)
In Surge	Currently experiencing sustained rapid and significant growth	2.5 or greater	2 (8)

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District Trajectories – last 10 weeks

Status	# Districts (prev week)
Declining	20 (8)
Plateau	5 (4)
Slow Growth	8 (15)
In Surge	2 (8)

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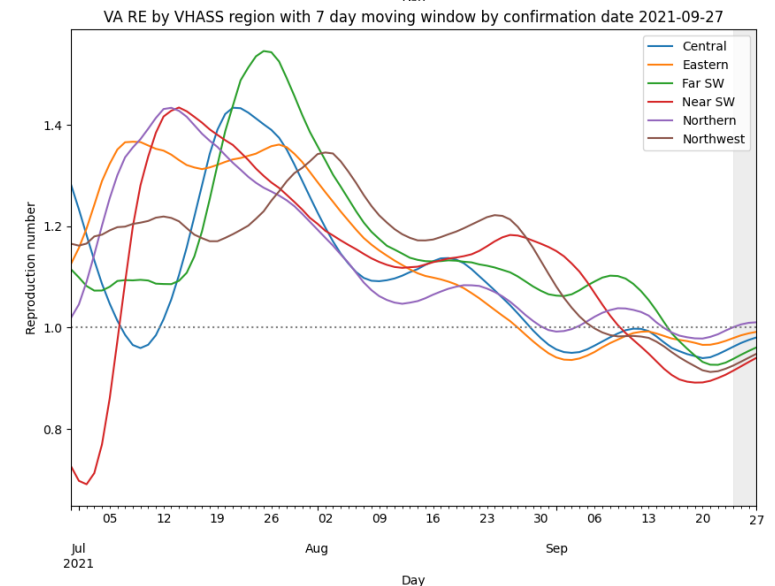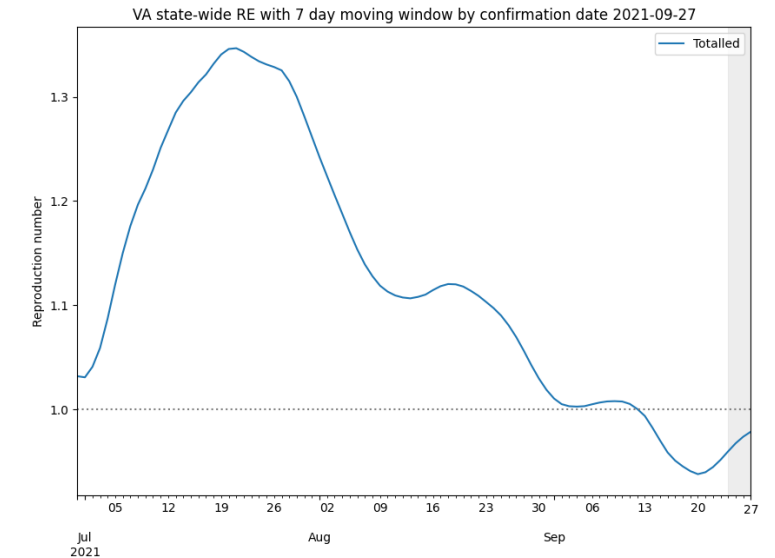Case Rate curve colored by Reproductive number

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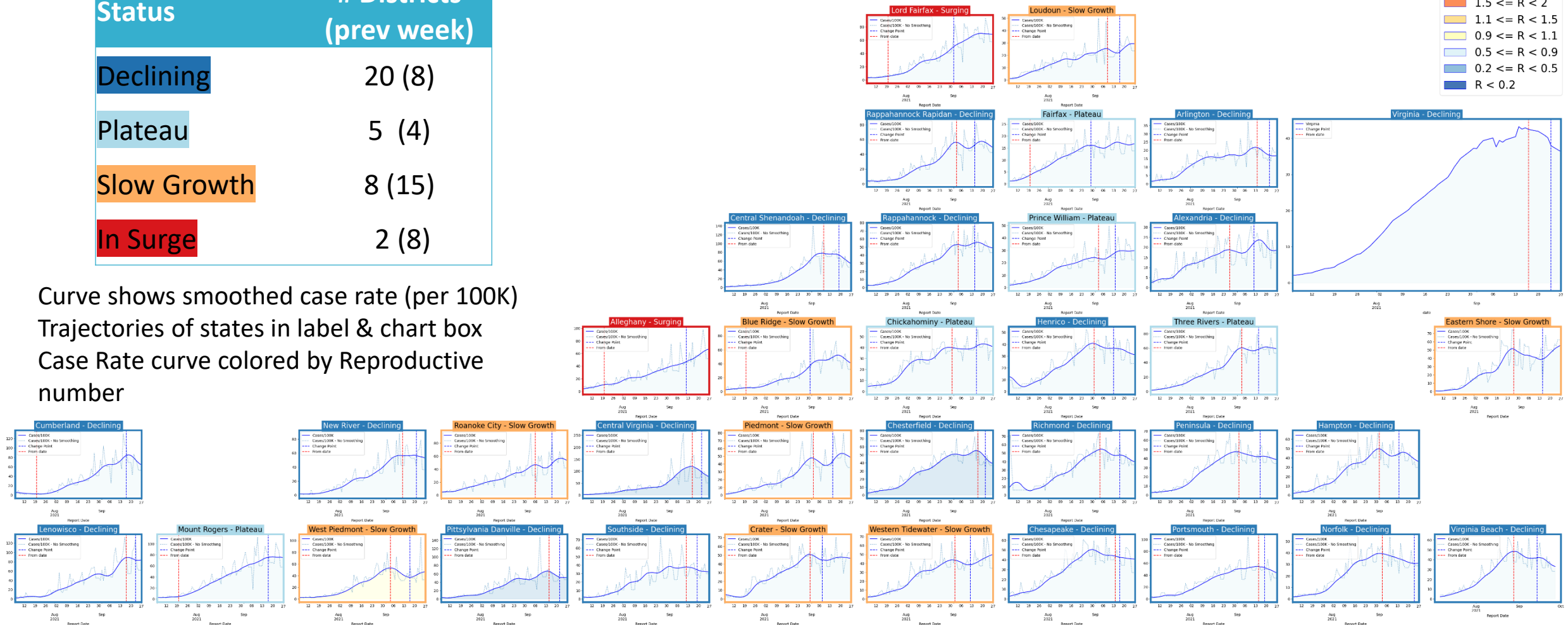
Estimating Daily Reproductive Number

Sept 27th Estimates

Region	Date Confirmed R_e	Date Confirmed Diff Last Week
State-wide	0.978	-0.069
Central	0.978	-0.071
Eastern	0.994	-0.049
Far SW	0.965	-0.094
Near SW	0.941	-0.072
Northern	1.012	-0.024
Northwest	0.951	-0.120

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

VA state-wide RE with 7 day moving window by confirmation date 2021-09-27

VA RE by VHASS region with 7 day moving window by confirmation date 2021-09-27

Vaccination Administration Slows

Regional Vaccine courses initiated per day (% eligible):

- Proportion eligible for first dose of vaccines across regions (in the ~0.1% or 100 per 100K a day)
- Age-specific proportions of population vaccinated show recent progress in younger ages

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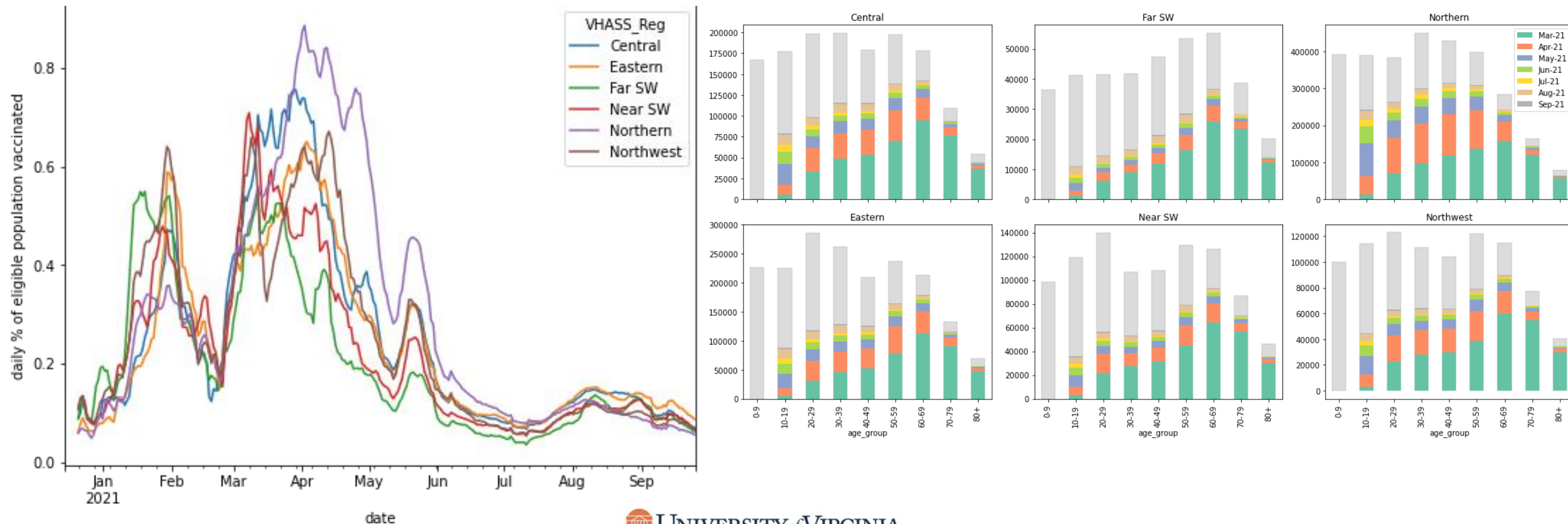
# Vaccination Acceptance by Region

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 pop vaccinated
Central	75%	71%
Eastern	73%	67%
Far SW	63%	57%
Near SW	68%	62%
Northern	86%	81%
Northwest	74%	69%
Virginia	**77%**	**72%**
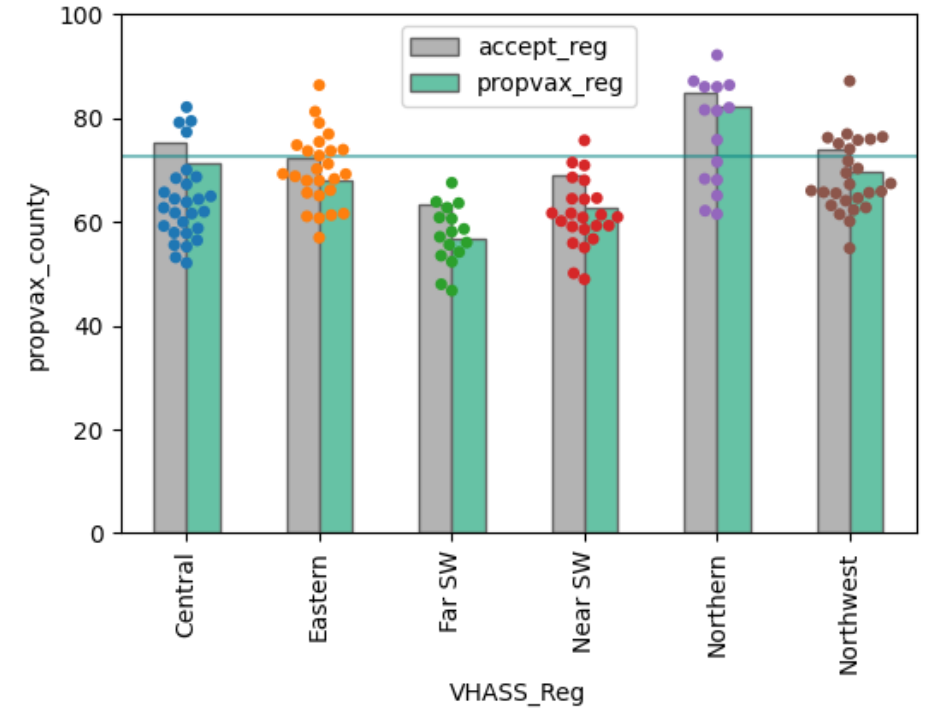
Grey Bar: Survey measured and corrected acceptance
Green Bar: Proportion of eligible population administered a vaccine
Dots: Proportion administered at least one dose for each county

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Vaccine Acceptance Components over Time
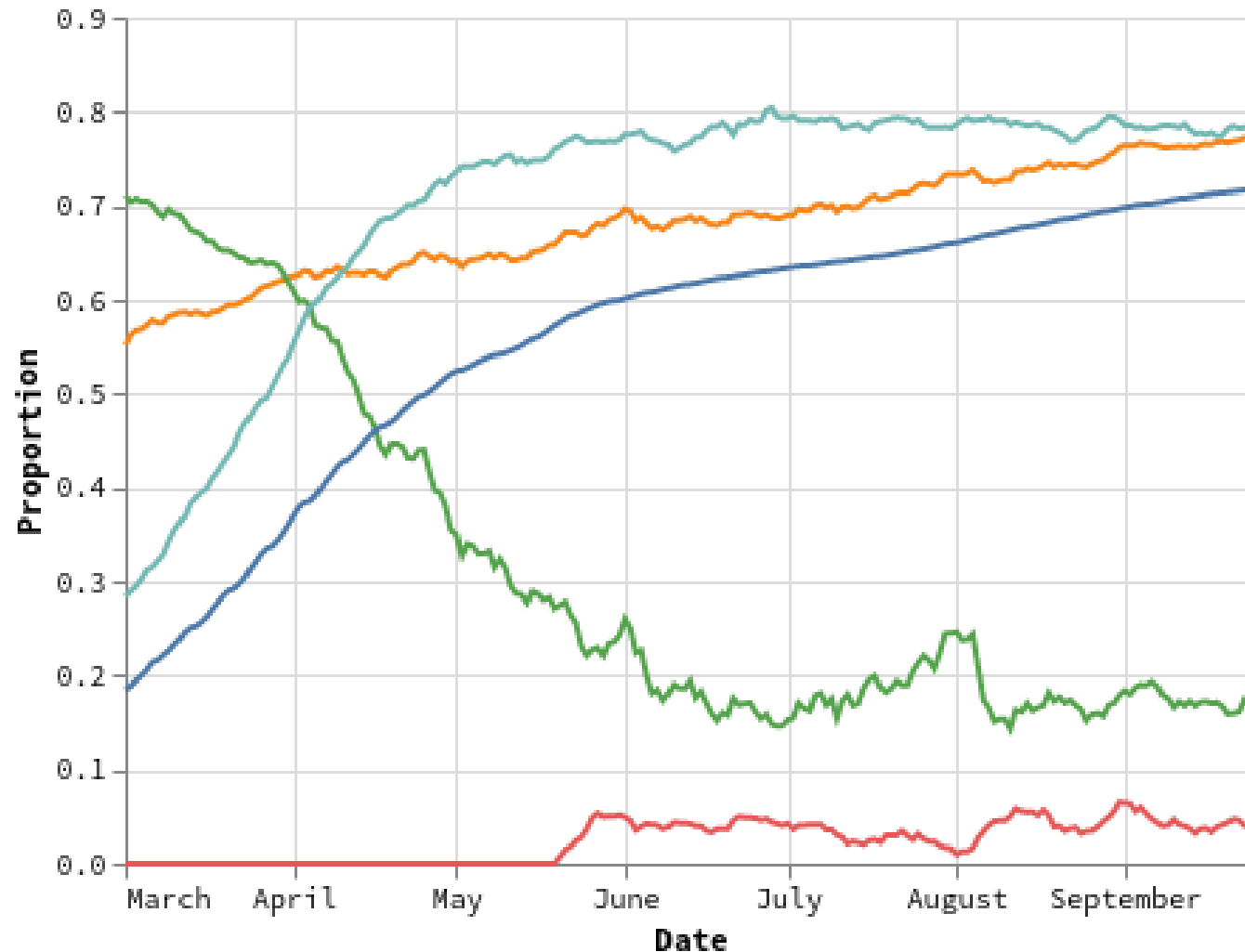
Vaccine Willingness
- Administered Vaccines
- Corrected Acceptance
- Scheduled
- Surveyed Vaccinated
- Unvaccinated Acceptance

Vaccine Acceptance adjusted to include scheduled appointments
- Steady rise in acceptance over the past couple months
- Unvaccinated Acceptance shows ~20% of those who are unvaccinated are definitely or probably willing to be vaccinated
- Scheduled appointments for vaccination have increased through August but seem to be leveling off
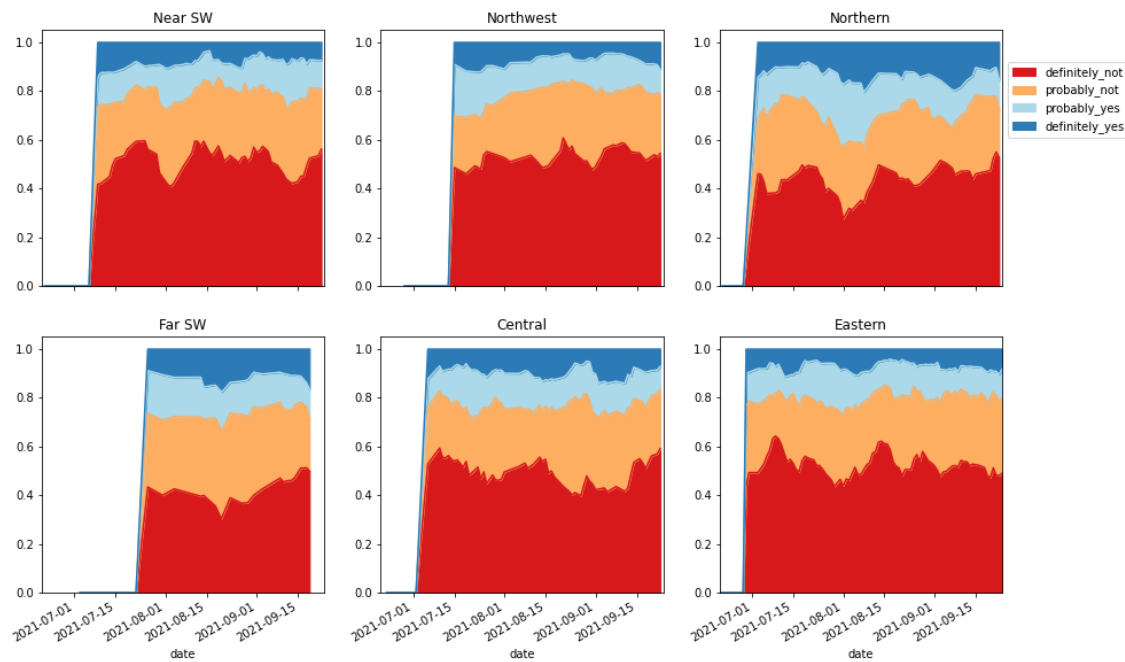
Data Source: https://covidcast.cmu.edu

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# Vaccine Acceptance by Region- COVIDcast

Levels of Acceptance and potential acceptance in flux:

- Most regions (except Central and Far SW) see vaccine uptake in the "Definitely Yes".
- Among the unvaccinated, about 20-30% remain in the Definitely/Probably "Yes" categories.
- About 50% of the Unvaccinated seem to be in the "Definitely Not" category.
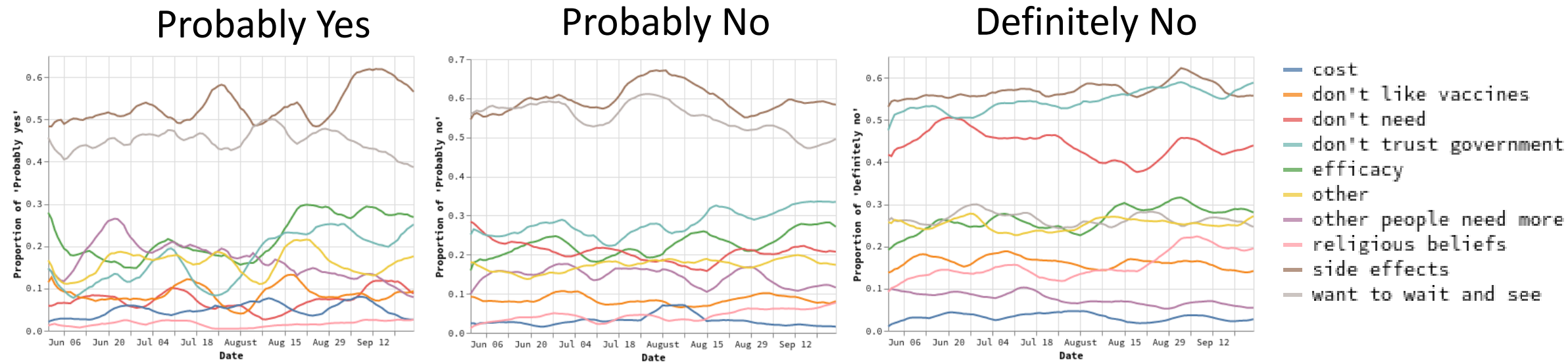
Unvaccinated Only

All Respondents

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

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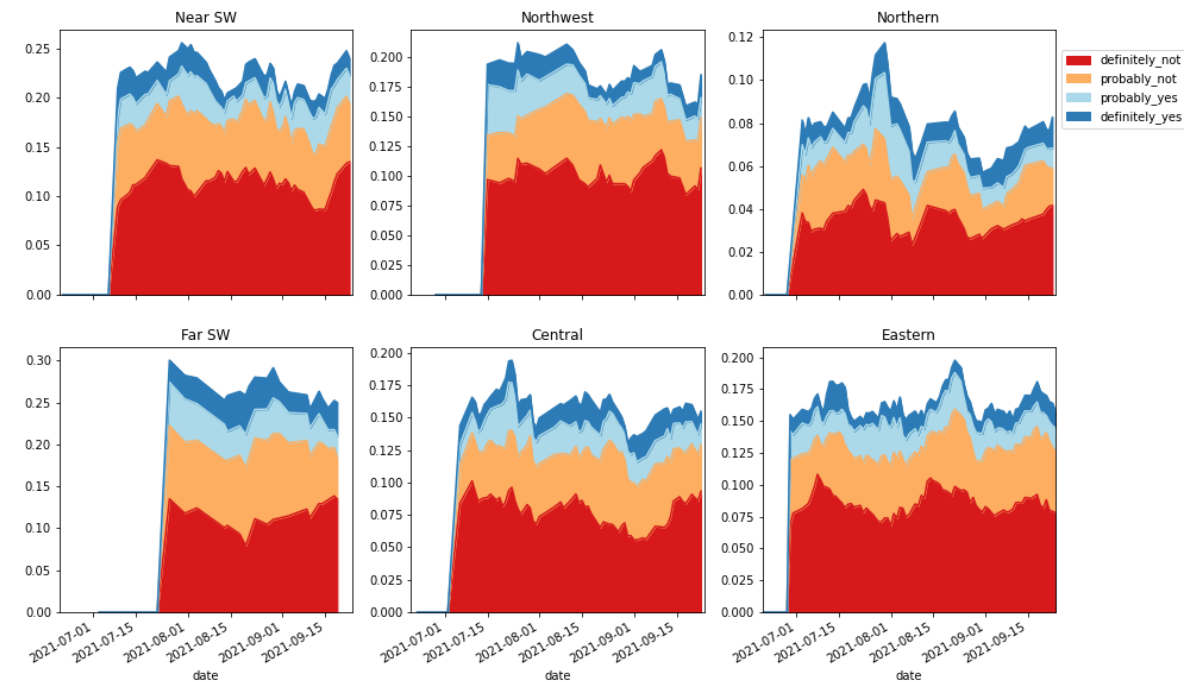
Reasons for Hesitancy by Likeliness to Accept

**Reasons for Hesitancy vary across tiers of likeliness to accept the vaccine**

- Probably Yes and Probably No most concerned about side effects & are waiting to see
- Definitely No are concerned about side effects but also don't think they need the vaccine and don't trust the government, though don't need is declining
- Most other reasons are below 30% within these tiers of likeliness

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

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Mask Usage Stalls

Self-reported mask usage has plateaued out to ~65%

- US and VA similar, though with considerable variation across counties and states
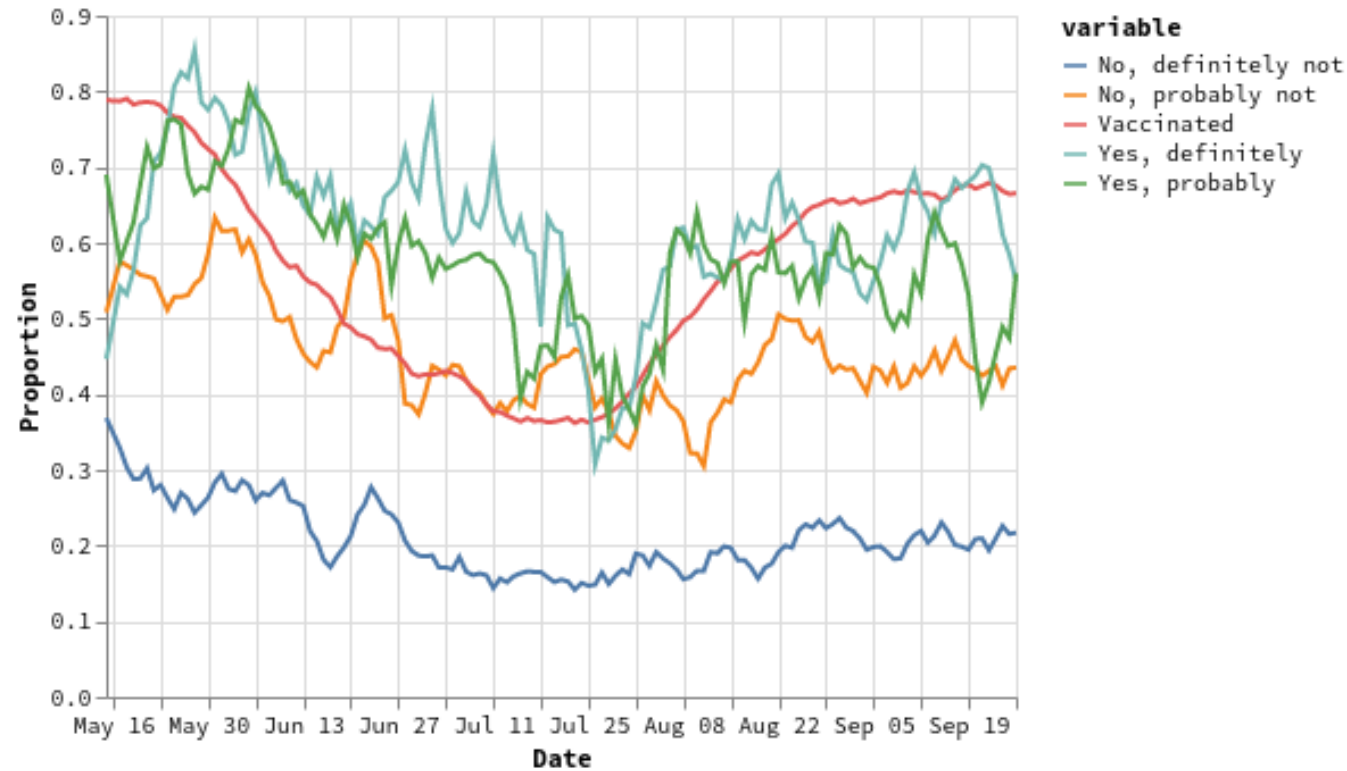- Mask wearing remains lower amongst unvaccinated especially among least willing to be vaccinated
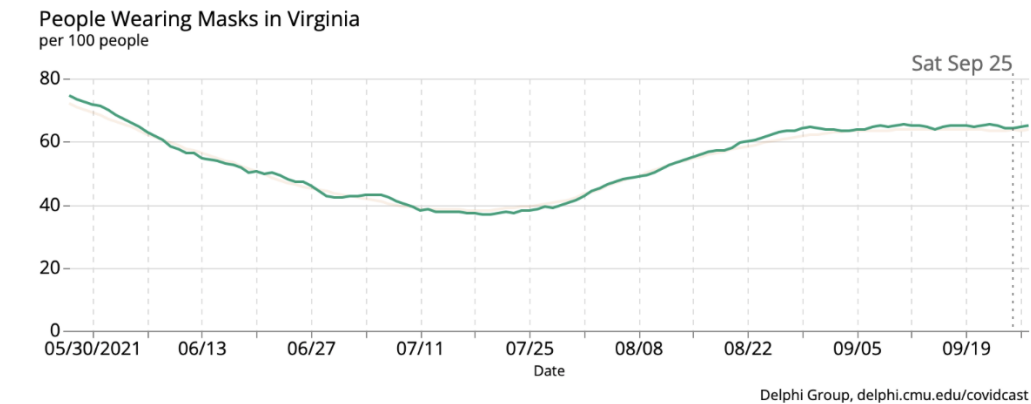
Data Source: https://covidcast.cmu.edu

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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

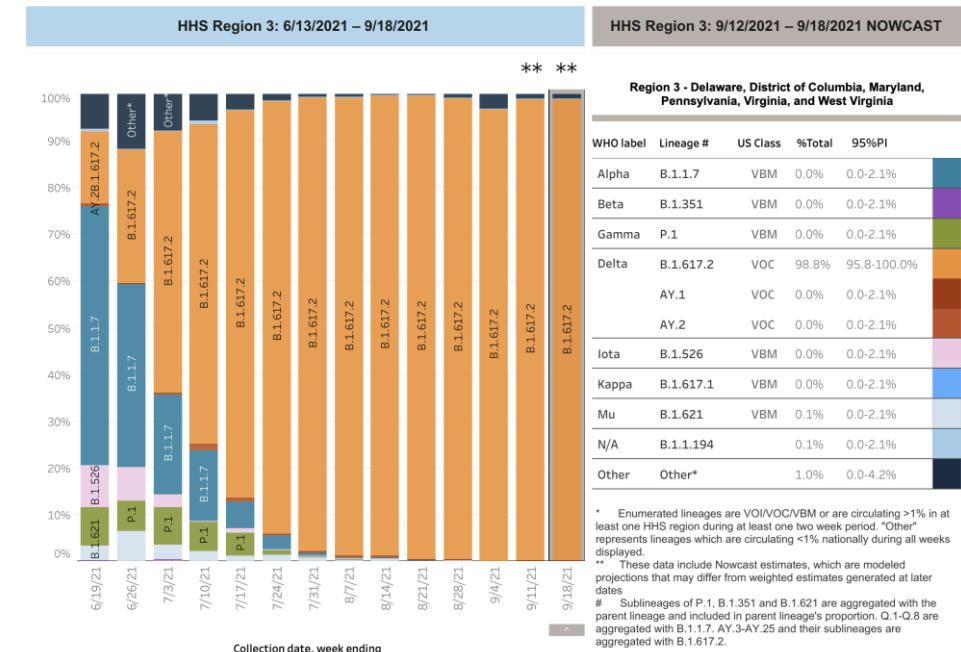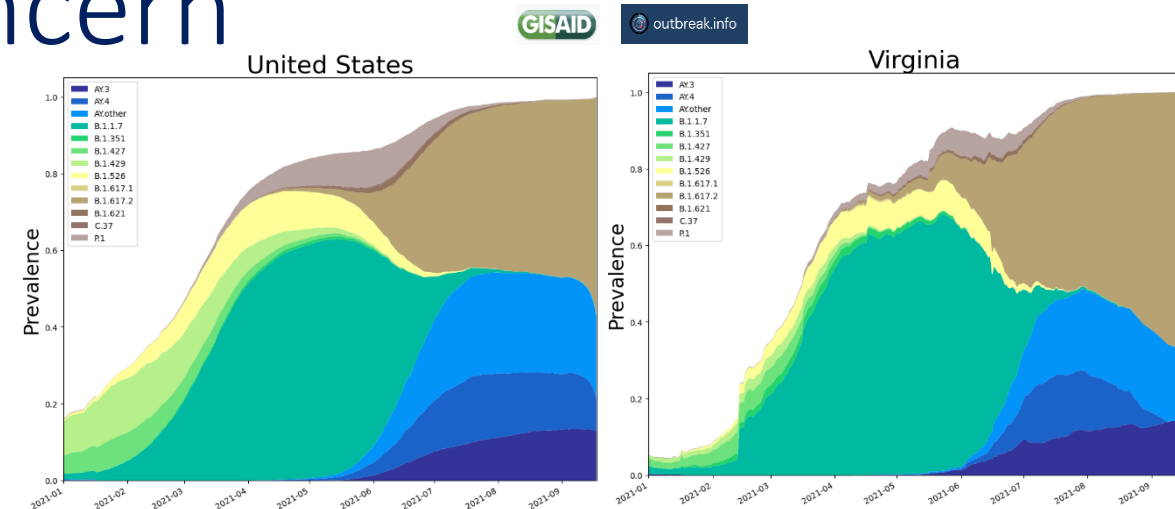|	New WHO Name	Transmissibility	Immune Evasiveness	Vaccine Effectiveness^
Ancestral		—	—	✓
D614G		+	—	✓
B.1.1.7	Alpha	+++	—	✓
B.1.351	Beta	+	++++	✓
P.1	Gamma	++	++	✓
B.1.429	Epsilon	+	+	✓
B.1.526	Iota	+	+	✓
B.1.617.2	Delta	++++*	++#	✓

*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
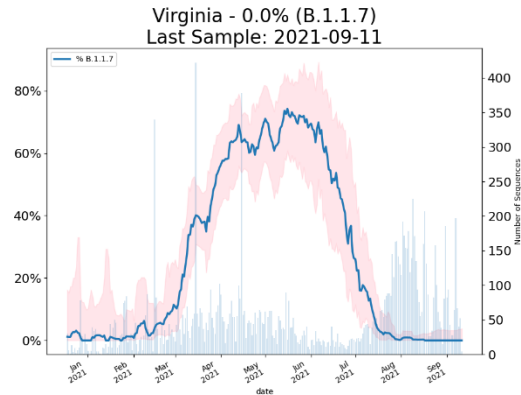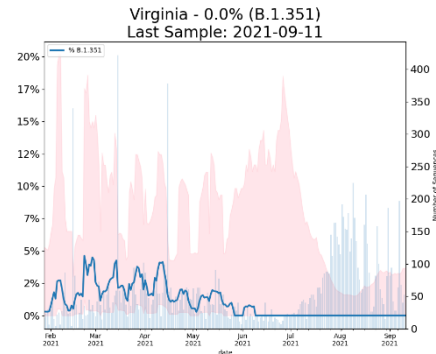
World Health Organization

WHO and Eric Topol

United States

Virginia

HHS Region 3: 6/13/2021 – 9/18/2021

HHS Region 3: 9/12/2021 – 9/18/2021 NOWCAST

Region 3 - Delaware, District of Columbia, Maryland, Pennsylvania, Virginia, and West Virginia

WHO label	Lineage #	US Class	%Total	95%PI
Alpha	B.1.1.7	VBM	0.0%	0.0-2.1%
Beta	B.1.351	VBM	0.0%	0.0-2.1%
Gamma	P.1	VBM	0.0%	0.0-2.1%
Delta	B.1.617.2	VOC	98.8%	95.8-100.0%
	AY.1	VOC	0.0%	0.0-2.1%
	AY.2	VOC	0.0%	0.0-2.1%
Iota	B.1.526	VBM	0.0%	0.0-2.1%
Kappa	B.1.617.1	VBM	0.0%	0.0-2.1%
Mu	B.1.621	VBM	0.1%	0.0-2.1%
N/A	B.1.1.194		0.1%	0.0-2.1%
Other	Other*		1.0%	0.0-4.2%

* Enumerated lineages are VOI/VOC/VBM or are circulating >1% in at least one HHS region during at least one two week period. "Other" represents lineages which are circulating <1% nationally during all weeks displayed.
** These data include Nowcast estimates, which are modeled projections that may differ from weighted estimates generated at later dates
\# Sublineages of P.1, B.1.351 and B.1.621 are aggregated with the parent lineage and included in parent lineage's proportion. Q.1-Q.8 are aggregated with B.1.1.7. AY.3-AY.25 and their sublineages are aggregated with B.1.617.2.

Collection date, week ending

CDC Variant Tracking
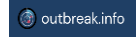
SARS-CoV2 Variants of Concern
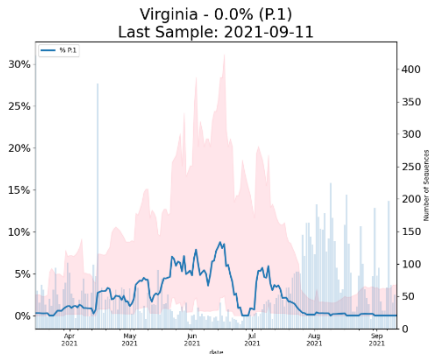
Previous Variants

Alpha α - Lineage B.1.1.7
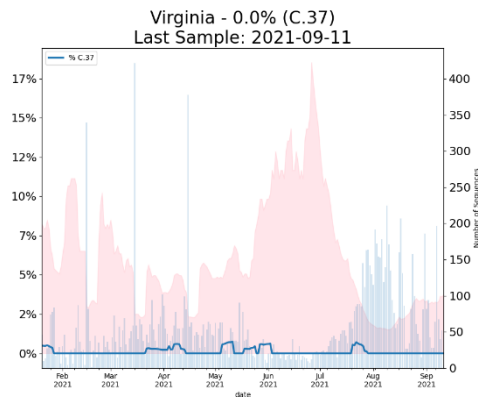

Beta β - Lineage B.1.351
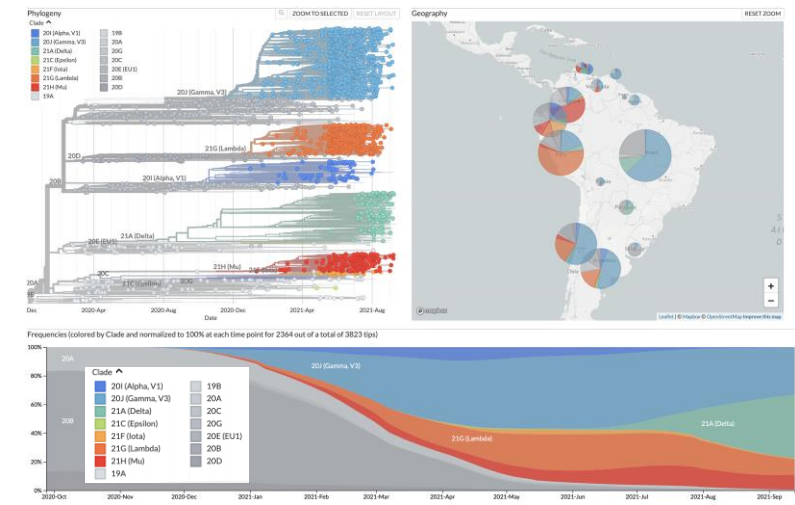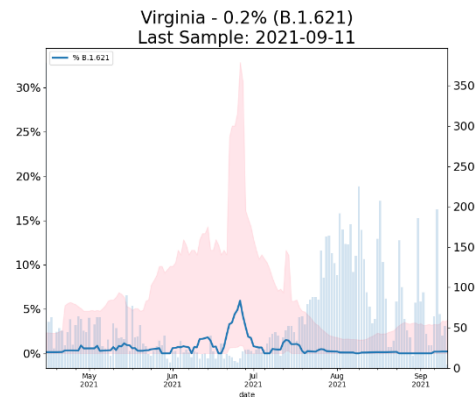

Gamma γ - Lineage P.1

Emerging Variants

Lambda λ - Lineage C.37

Mu μ - Lineage B.1.621


Delta continues to out compete Lambda and Mu in South America
Trevor Bedford Tweet & Nextstrain Analysis

SARS-CoV2 Variants of Concern

Delta δ - Lineage B.1.617.2 and related subvariants

- Delta plus δ+ lineage which contains the K417N mutation is emerging as a sub-variant that is even more transmissible; declared a VoC in India

- Delta variant now dominates most of Europe and US

- CDC recommends resumption of mask wearing indoors due to reports of breakthrough infections of the vaccinated possibly being transmissible

- Recent study from Mayo clinic shows Delta reducing the efficacy of mRNA vaccines (Pfizer more so than Moderna) along with other reports. Israeli study showed 64% efficacy against infection, however, a 3rd dose may counteract this reduction

- Public Health Scotland study in Lancet suggests Delta is 2x more likely to cause hospitalization than Alpha

- Subvariants AY.3 remains in the 10-15% range and is barely detectable under 2% prevalence, these subvariants are mainly clustered in the US, others mainly outside of US
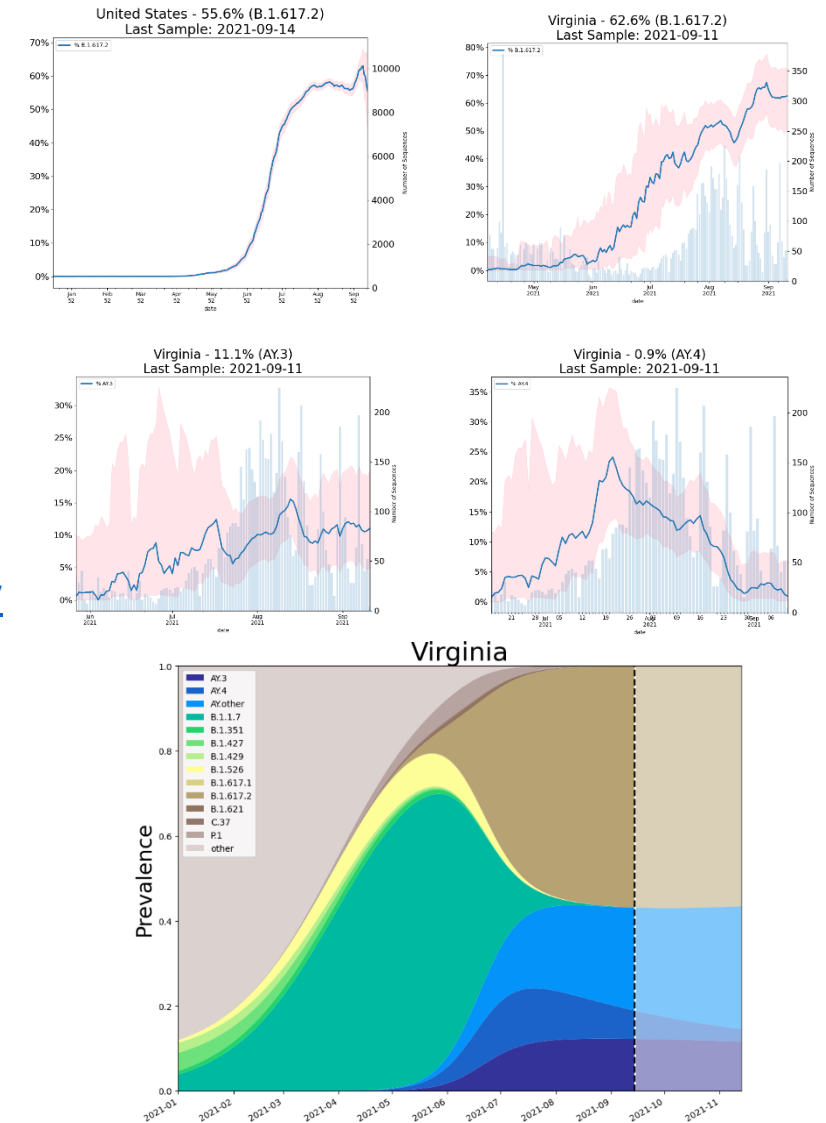

Current fits suggest stable mix of Delta & subvariants into the future

Variants & Vaccines

1. mRNA vaccines continue to show superior neutralization and binding profiles to that of adenovirus vector-based vaccines.
   a. **The proportion of individuals who did not show detectable VOC neutralization was substantial in the AZD1222 (AstraZeneca) and Ad26.COV2.S (J&J) recipients.**
   b. VOC neutralization was reduced in all vaccine groups,
2. Lancet study found second dose of mRNA after an Adenovirus (Pfizer with AZ) vaccine had higher efficacy than AZ alone (specifically AZ followed by Pfizer). Also saw higher immunogenicity of ChAd/BNT compared with ChAD/ChAd.
3. Science: Anti-viral defenses outside the human immune system shown to govern the severity of disease, illustrating a source of the highly variable severity of disease experienced. Based on a single SNP, OAS1 based defense is important to monitor for immune escape going forward (not based on spike protein sequence)
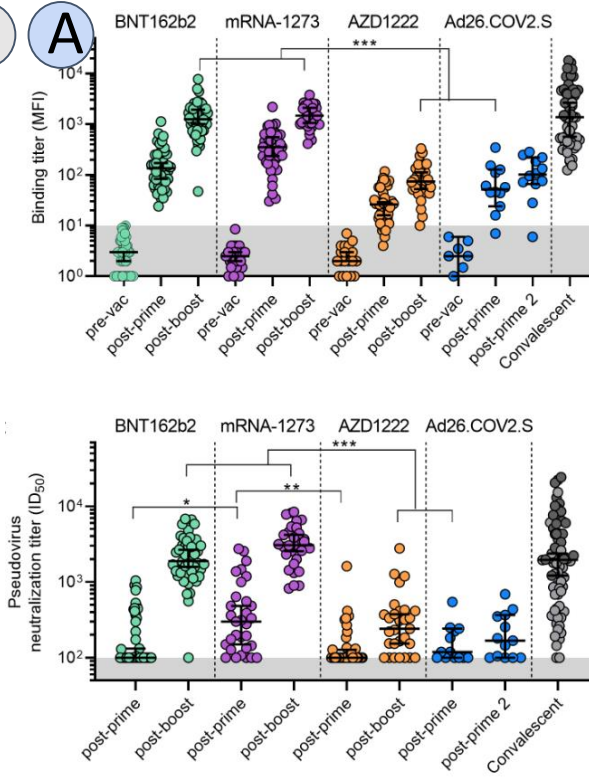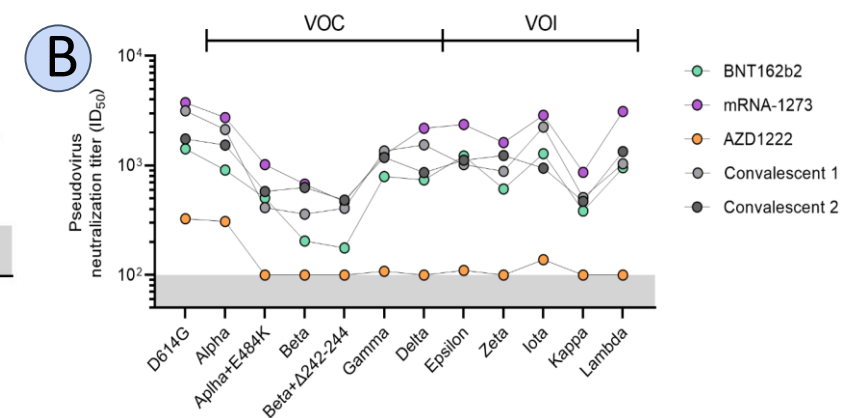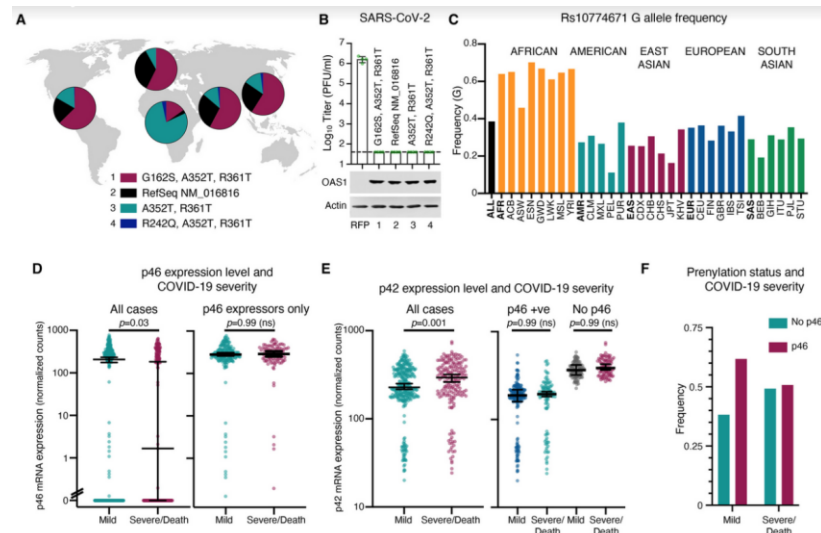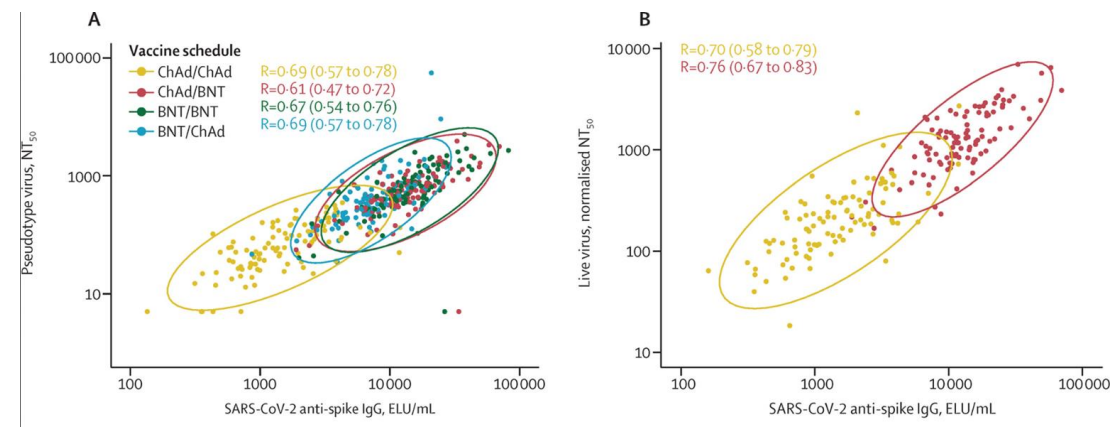

In a recent preprint researchers from Amsterdam showed results from a head-to-head comparison of the binding and neutralizing activity against all four VOCs in the serum of individuals who received the BNT162b2 (n=50), mRNA-1273 (n=40), AZD1222 (n=41) or Ad26.COV2.S vaccination (n=13). The largest (5.8-fold) reduction in neutralization being observed against the Beta variant. Introducing the E484K variant into Alpha resulted in a 2.8 fold reduced neutralization. This positional spike mutation seems to have a complementary impact only with certain other spike with configurations as observed in ID50 for Beta, Gamma, Iota, Zeta, Kappa (E484Q).
https://www.medrxiv.org/content/10.1101/2021.09.27.21264163v1.article-info

Lancet study provides evidence for benefit of heterologous vaccine schedule. Between Feb 11 and Feb 26, 2021, 830 participants were enrolled and randomised in a study by the Oxford vaccine group.
https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)01694-9/fulltext#%20

SNP (Rs10774671) governs whether people express either (A) prenylated OAS1 isoforms that are membrane-associated and sense specific regions of SARS-CoV-2 RNAs, or (B) only express cytosolic, nonprenylated OAS1 that does not efficiently detect SARS-CoV-2. (A) has been associated with protection from severe COVID-19.
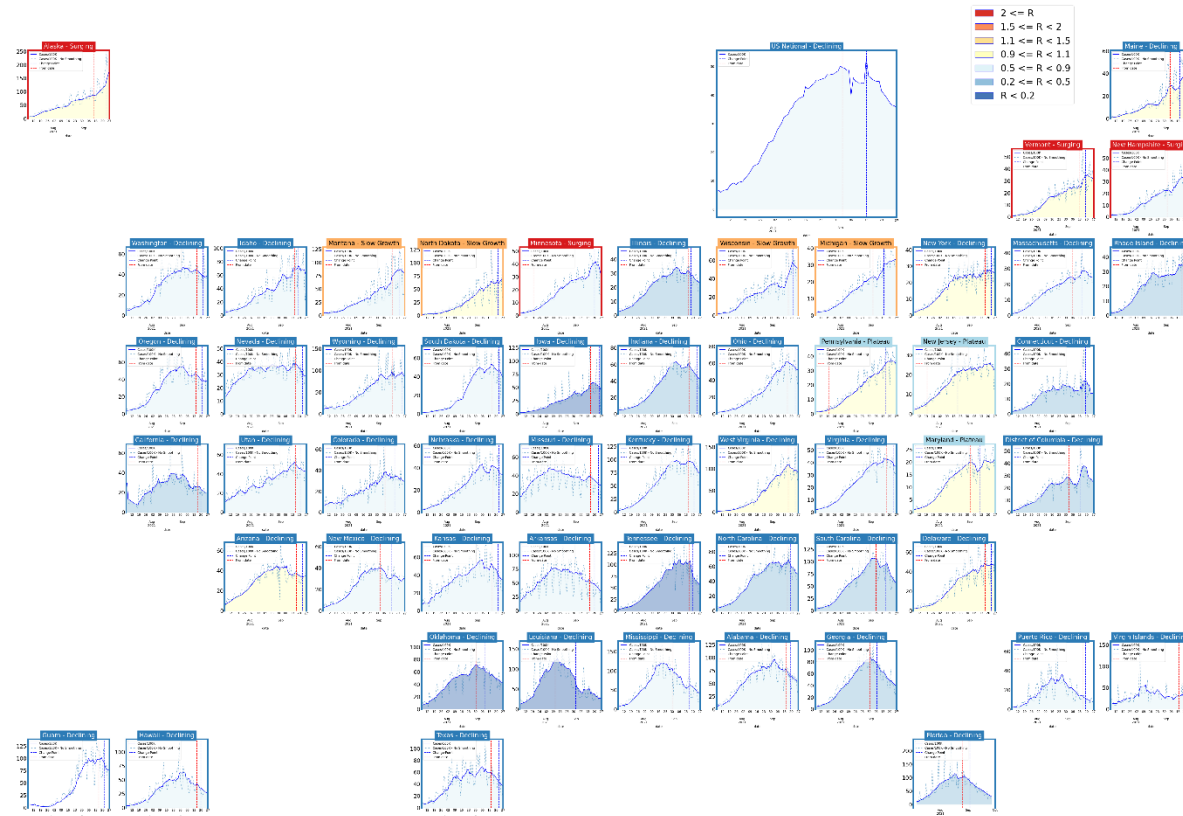https://www.science.org/doi/10.1126/science.abj3624

Other State Comparisons

Trajectories of States

Virginia and her neighbors

- More of the country has plateaued and started to decline
- Many states remain in surge, but show signs of slowing
- Case rates remain very high, but nationally rates are starting to come down
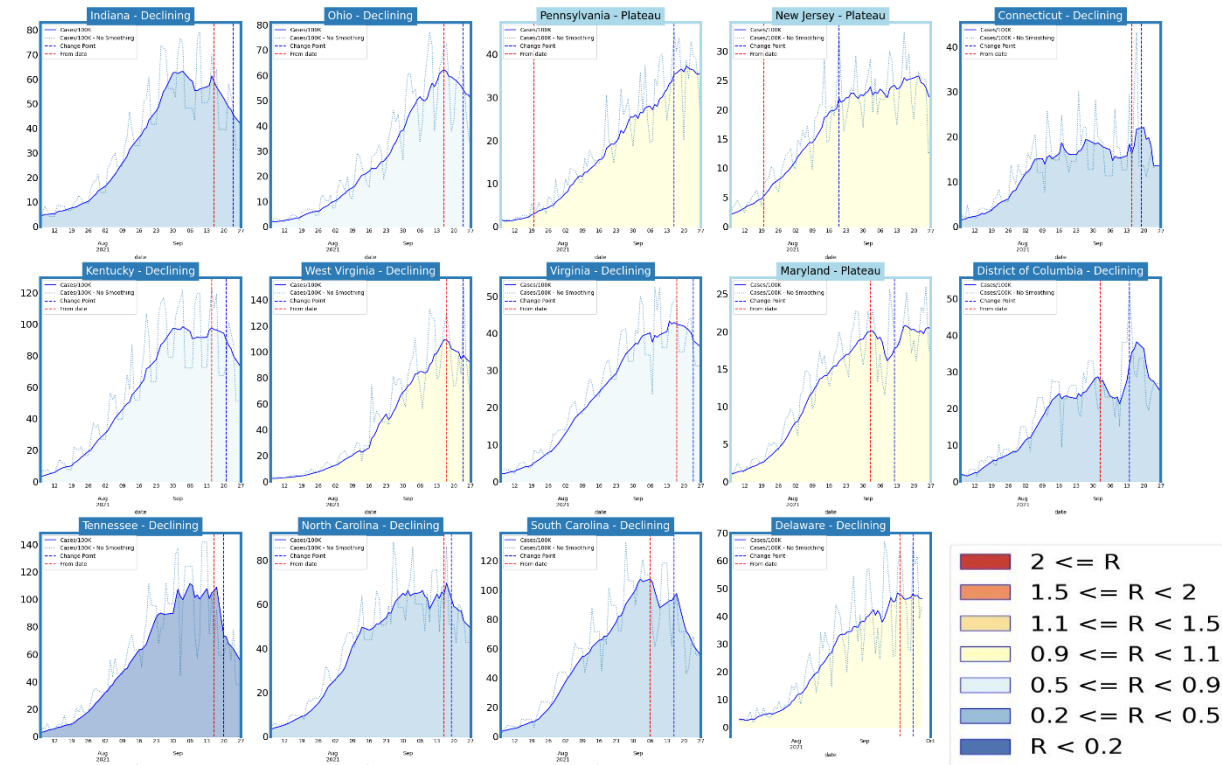
- Nearly all states show signs of plateau or slowing growth, with several declining in the past week
- Case rates remain high

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Last Week compared to worst week of Pandemic

County level Case Rates (per 100K) from this week compared to worst week of the entire pandemic

- Many counties exceed or have similar rates to the worst week

- Ratios have reduced this week with about half at 50% or more of the worst week in the pandemic

Recent Incidence Compared to Worst Week by County

Proportion of Last Week's Incidence to that of Worst Week

Proportion of Last Week's Incidence to that of Worst Week
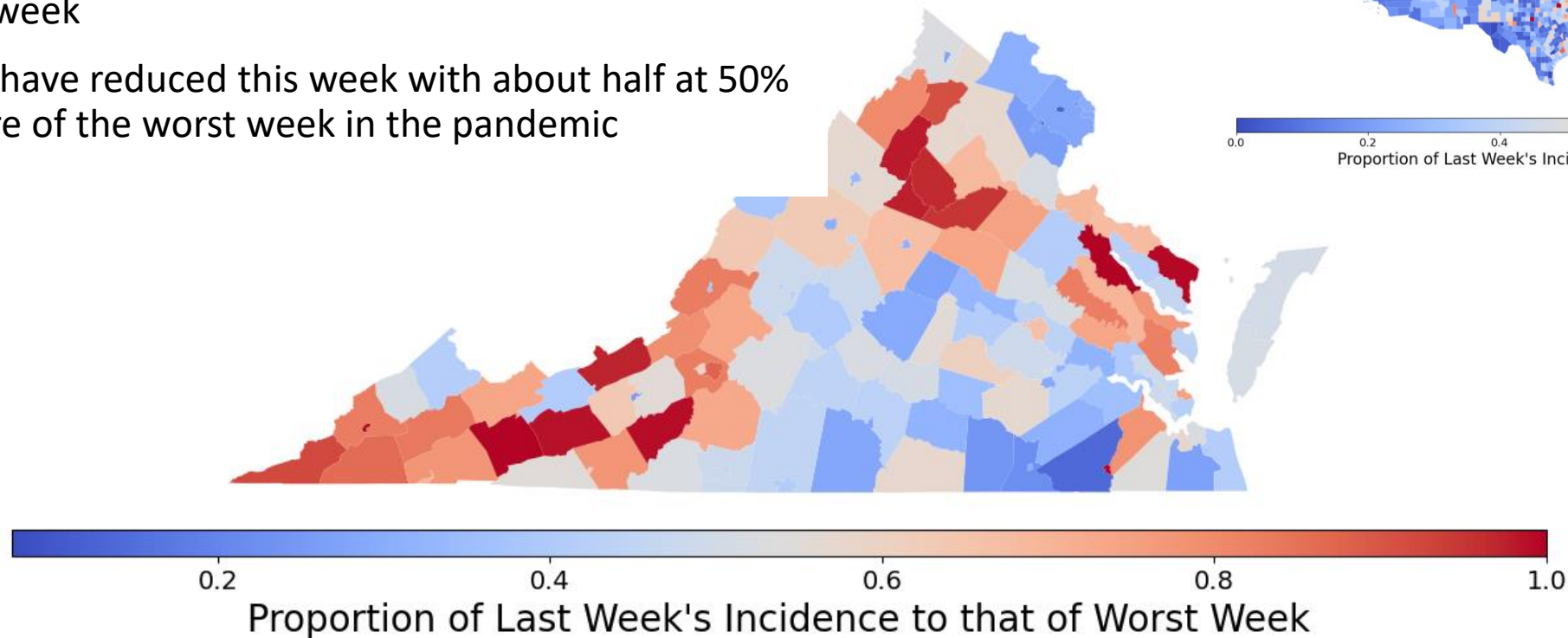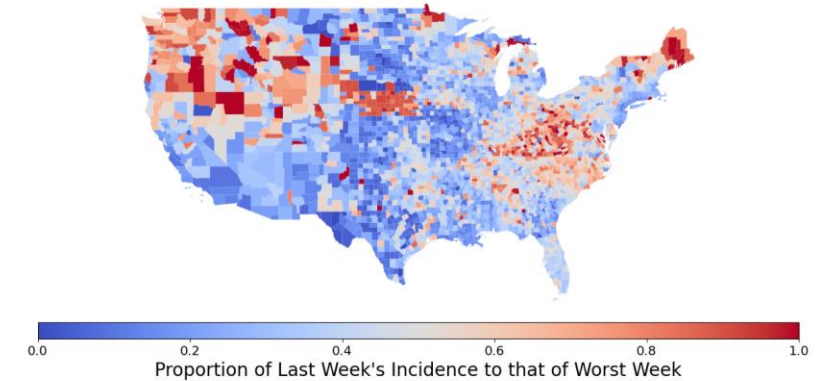
Delta Wave compared to Last Fall – Winter wave

Total cases in Delta wave compared to cases in Fall wave and progress

- Virginia's Delta wave has caused 40% of the total cases experienced in the Fall-Winter wave

- Total for this wave to date is similar to what had been experienced by Dec 24th in Fall-Winter wave

- Progress against the winter wave varies by district, ranging from ~25% to over 50%

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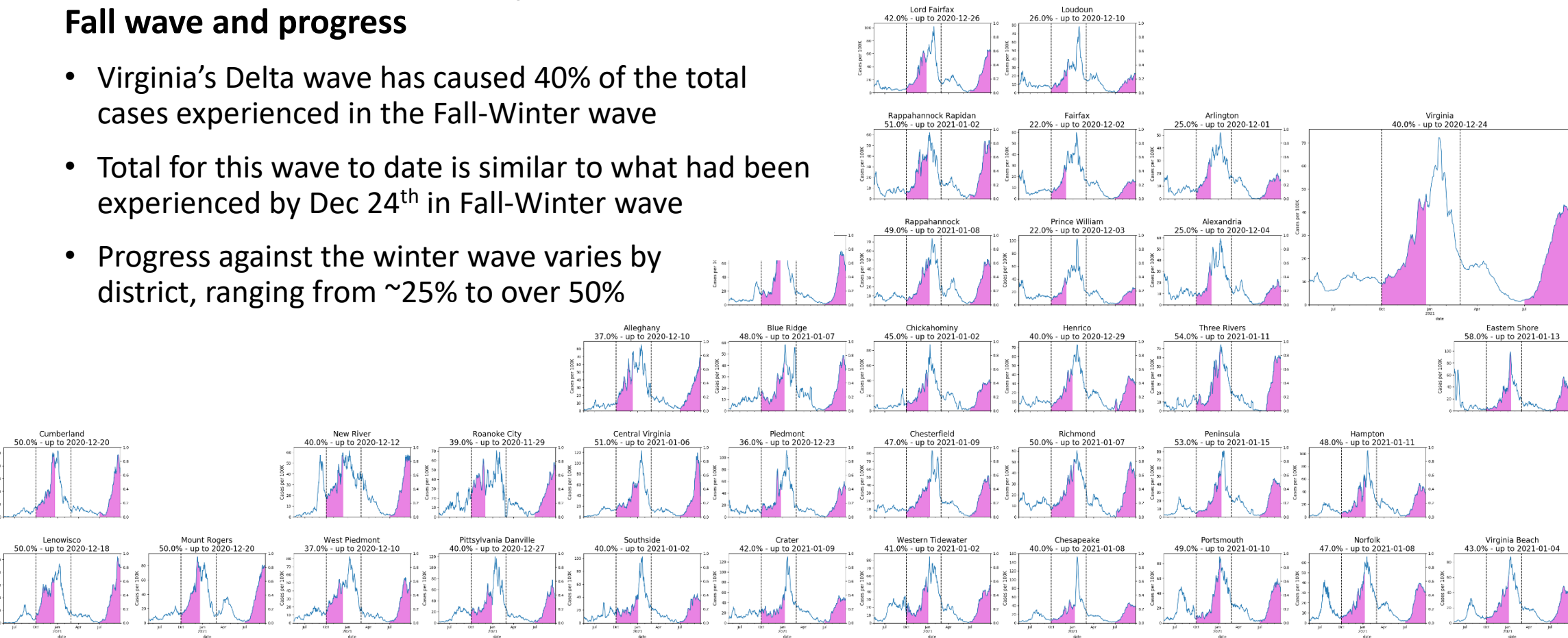
Recent Cases Correlate with Vax Coverage

Mean cases per 100K vs. vaccine coverage
- States with lower vax coverage have had the worst case spikes

Virginia Counties
- Counties with higher vax coverage are maintaining lower case rates

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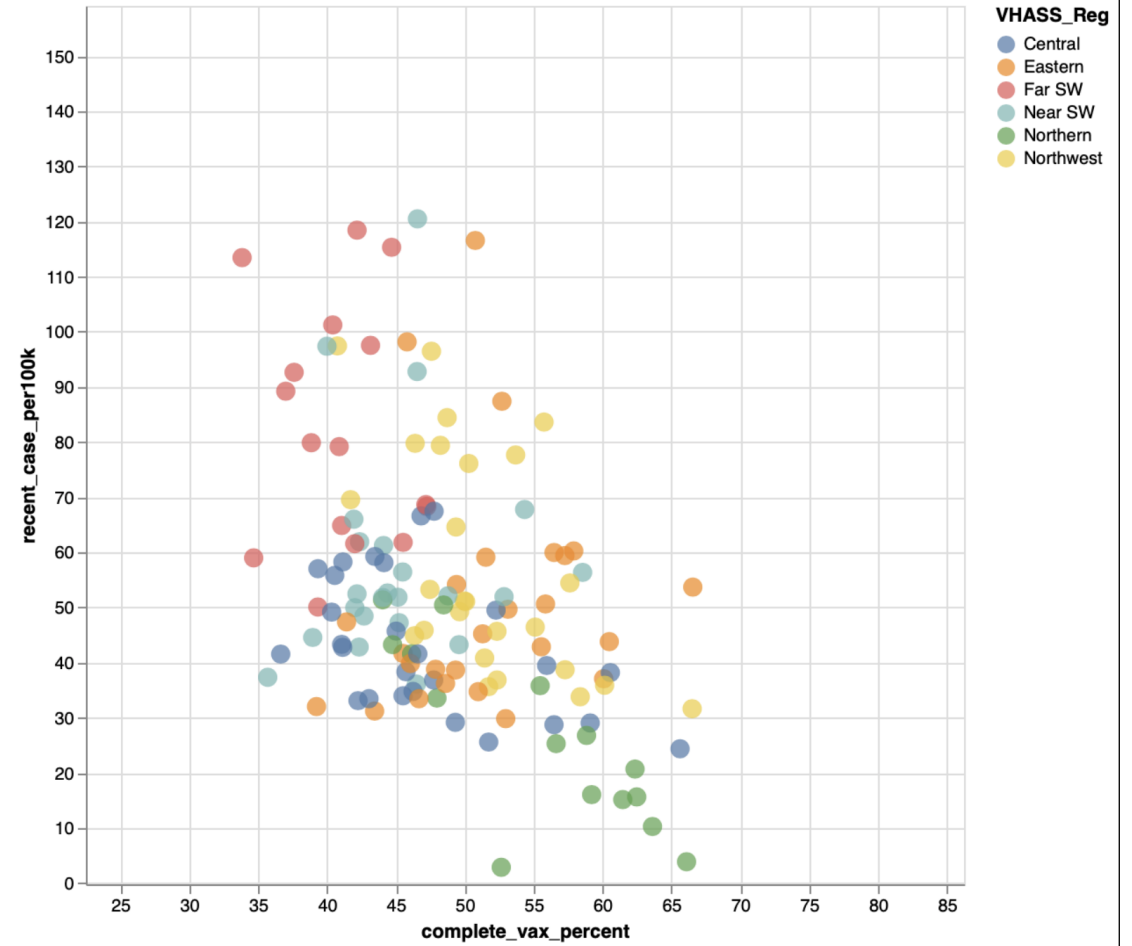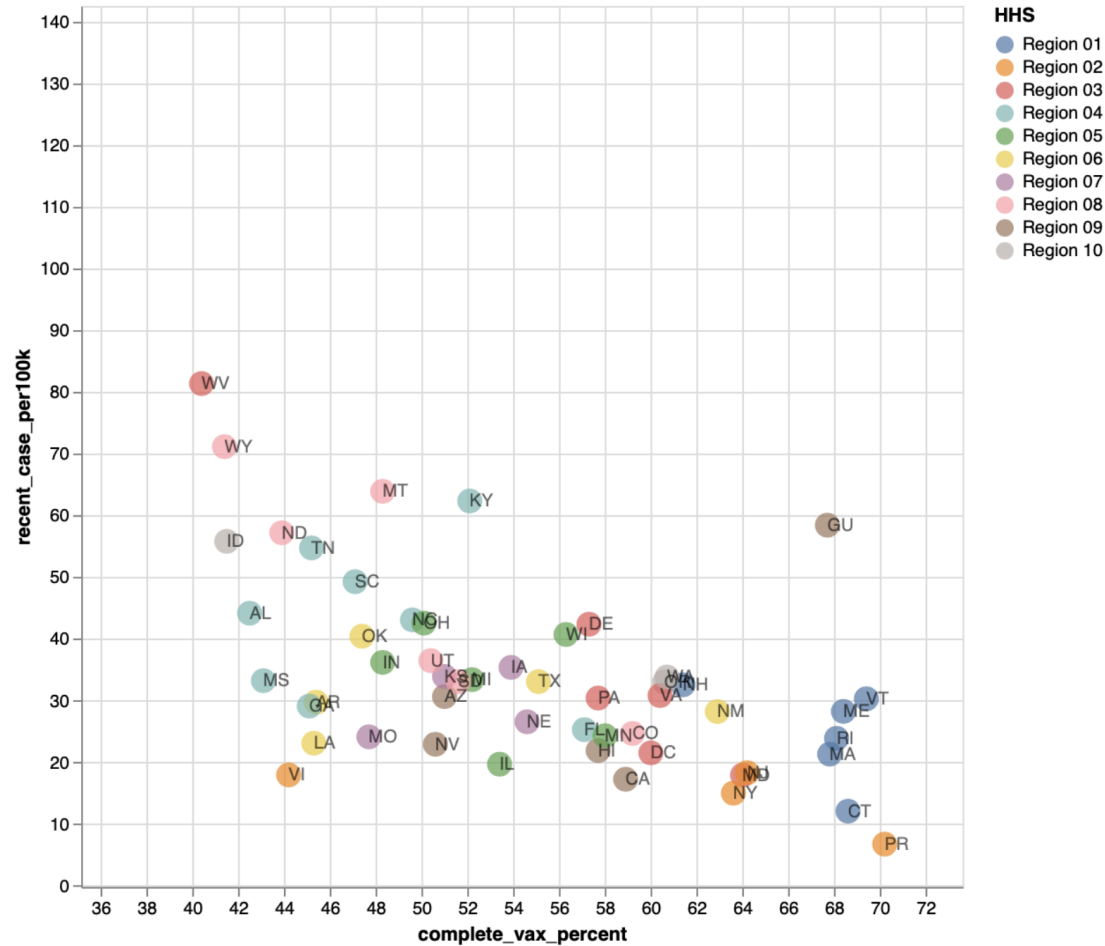# Zip code level weekly Case Rate (per 100K)

Case Rates in the last week by zip code

- Color scaled adjusted to accommodate the very high prevalence levels this week

- Clusters of high prevalence in Southwest and Eastern

- Some counts are low and suppressed to protect anonymity, those are shown in white

Rank	Zip Code	Name	Prev	
1	23410	Melfa	2,660	
2	24431	Crimora	2,460	Beyond Scale
3	24124	Narrows	2,360	
4	24277	Pennington Gap	2,130	
5	24122	Montvale	2,090	
6	24248	Ewing	2,080	
7	24134	Pearisburg	2,080	
8	24439	Goshen	1,990	
9	24370	Saltville	1,960	
10	24281	Rose Hill	1,840	

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

Point Prevalence by Zip Code
(2021-09-25)

Point Prevalence
High : 2100+
1400
700
Low : 0
Units = Active Cases / 100,000

Contains Suppressed* Data
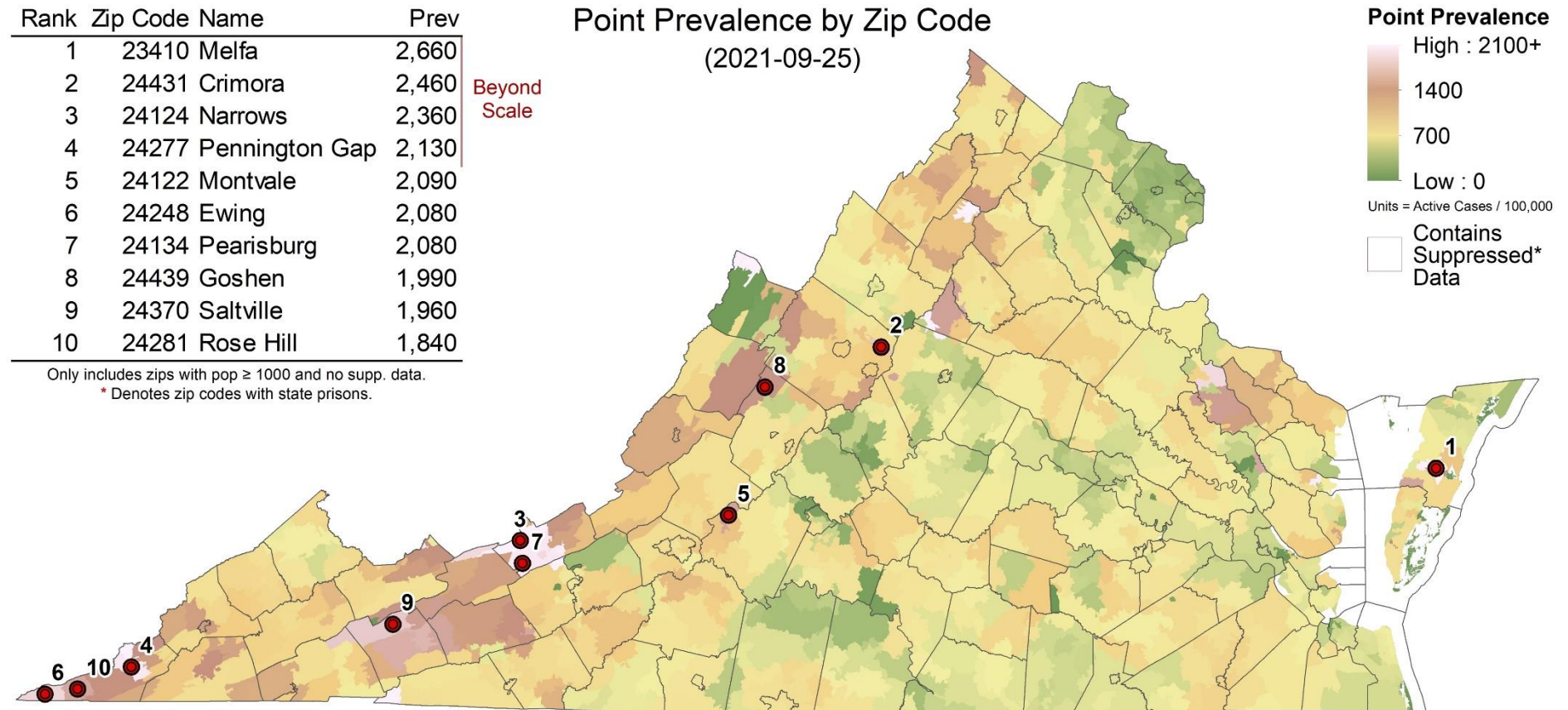
Based on Spatial Empirical Bayes smoothed point prevalence for week ending 2021-09-25.

HCW Prevalence

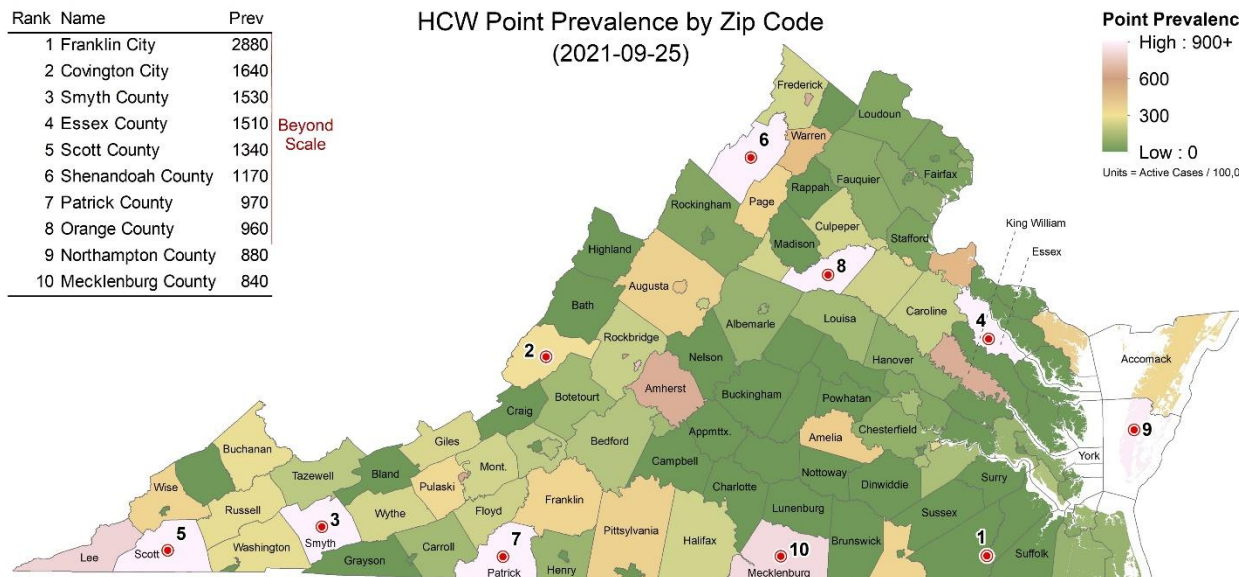- **HCW prevalence**: Case rate among health care workers (HCW) in the last week using patient facing health care workers as the denominator
  - Clusters of high HCW point prevalence in Franklin City, along the southern border, and far southwest

- **HCW Ratio**: HCW Prevalence / Total Case Prevalence
  - (blue = higher case rate among public, red = higher case rate among HCW)

HCW Prevalence

HCW Point Prevalence by Zip Code
(2021-09-25)

Rank	Name	Prev
1	Franklin City	2880
2	Covington City	1640
3	Smyth County	1530
4	Essex County	1510
5	Scott County	1340
6	Shenandoah County	1170
7	Patrick County	970
8	Orange County	960
9	Northampton County	880
10	Mecklenburg County	840

Note: Scale differs from general public prevalence maps.

HCW to Public Prevalence Ratio

HCW Prevalence / Case Prevalence
(2021-09-25)

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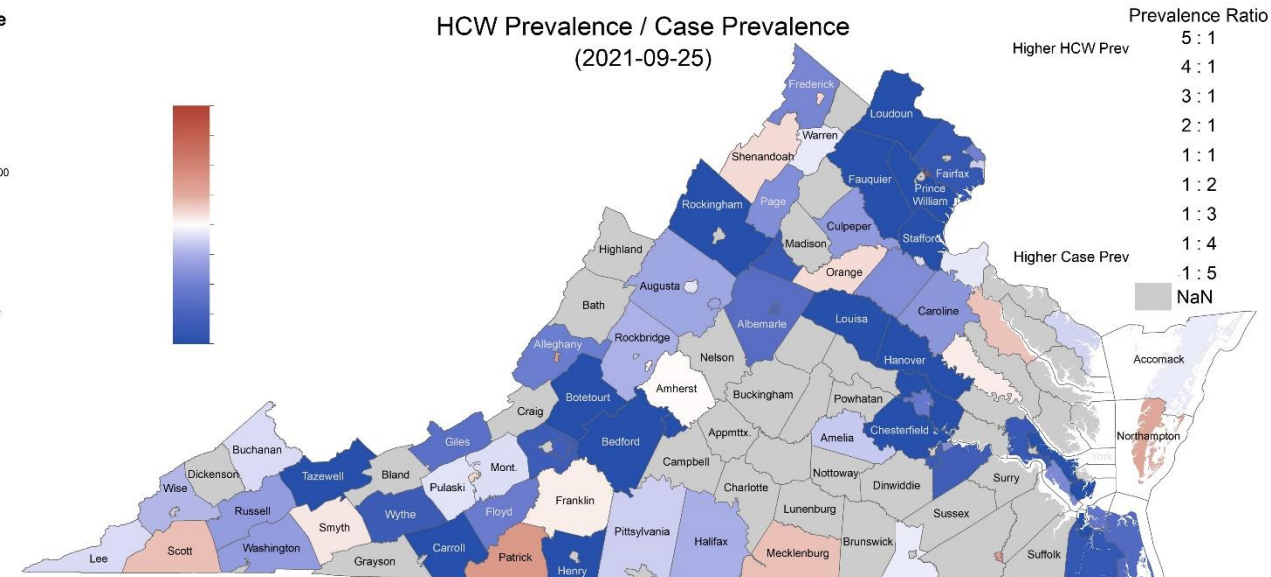
Current Hot-Spots

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

- **Spatial**: Getis-Ord Gi* 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	24124	Narrows	99%
2	23410	Melfa	99%
3	24431	Crimora	99%
4	24277	Pennington Gap	95%
5	24134	Pearisburg	95%
6	24370	Saltville	90%

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

Point Prevalence Hot Spots by Zip Code
(2021-09-25)

Getis-Ord Gi* HotSpots
- Cold Spot - 99% Confidence
- Cold Spot - 95% Confidence
- Cold Spot - 90% Confidence
- Not Significant
- Hot Spot - 90% Confidence
- Hot Spot - 95% Confidence
- Hot Spot - 99% Confidence

Based on Global Empirical Bayes smoothed point prevalence for week ending 2021-09-25.

Clustered Temporal Hotspots

Weekly Point Prevalence Model Residuals
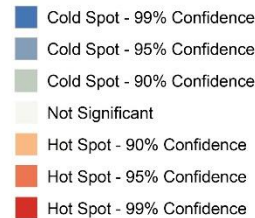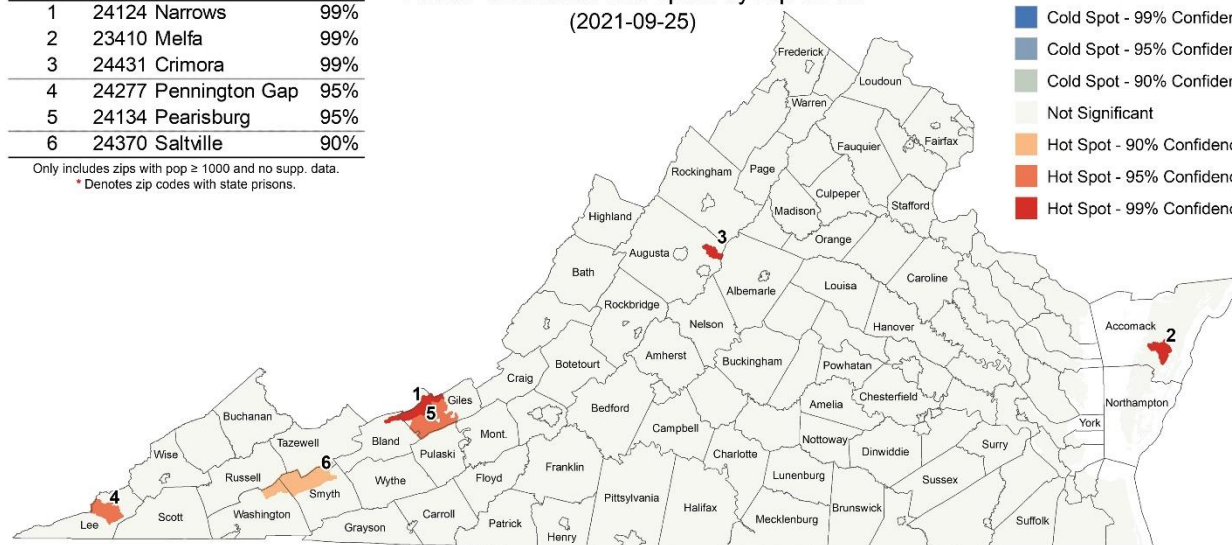Model 15SEP Predicting
Week ending 2021-09-26

Residual
More Cases than Expected
High : 500
400
300
200
100
0
-100
-200
-300
-400
Fewer Cases than Expected
Low : -500
Cases / 100,000
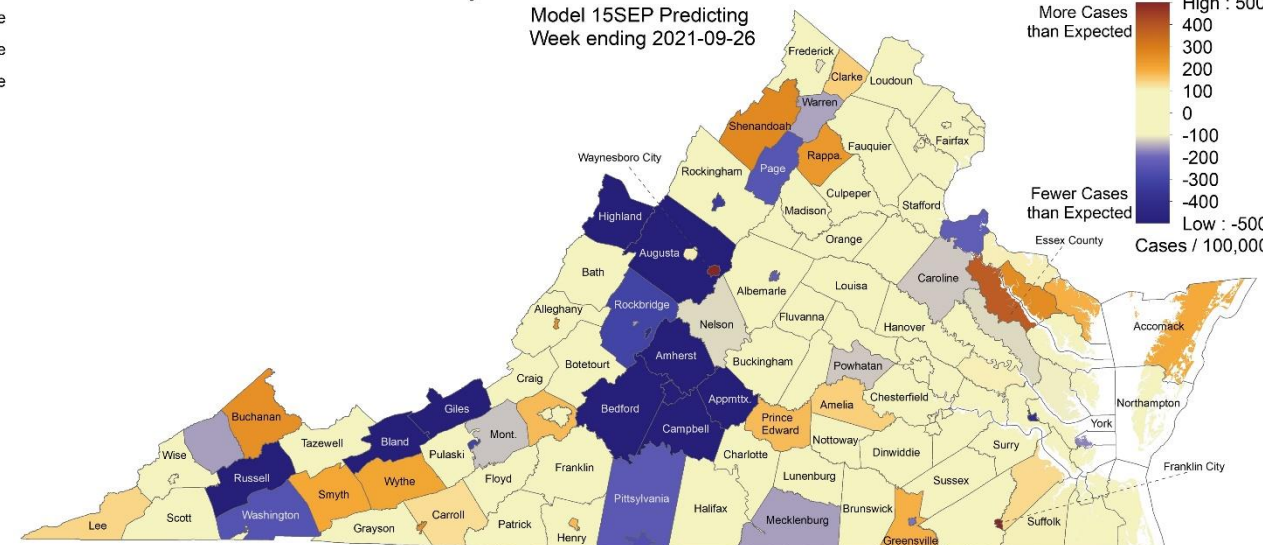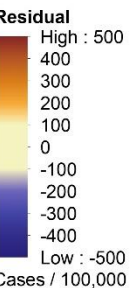
Moran's I = 0.046927, Z-Score = 2.627622, P-Value = 0.008598
Residual Autocorrelation DETECTED

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Model Update – Adaptive Fitting

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Adaptive Fitting Approach

Each county fit precisely, with recent trends used for future projection
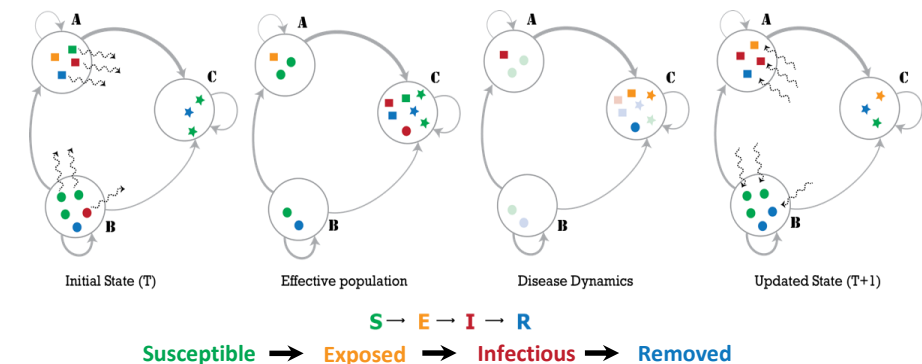
- Allows history to be precisely captured, and used to guide bounds on projections

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

S → E → I → R
Susceptible ➡ Exposed ➡ Infectious ➡ Removed

Initial State (T)   Effective population   Disease Dynamics   Updated State (T+1)

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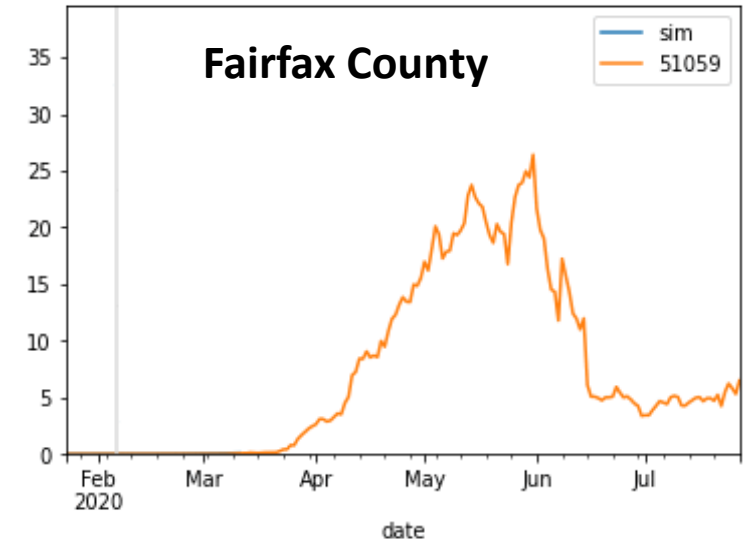
Using Ensemble Model to Guide Projections

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

- Autoregressive (AR, ARIMA)

- Neural networks (LSTM)

- Kalman filtering (EnKF)

Weekly forecasts 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.

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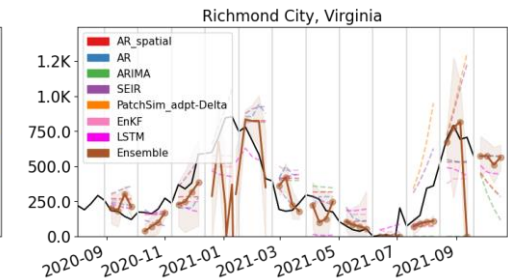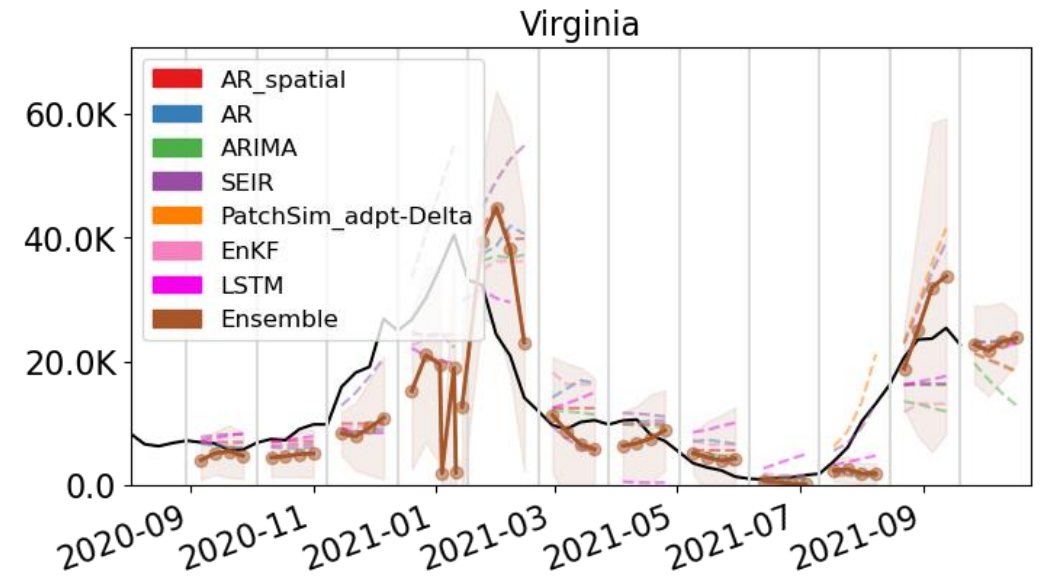
Seroprevalence updates to model design

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

- CDC Nationwide Commercial Laboratory Seroprevalence Survey

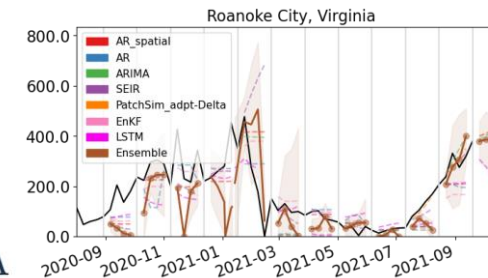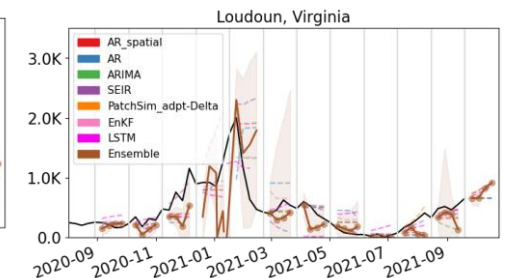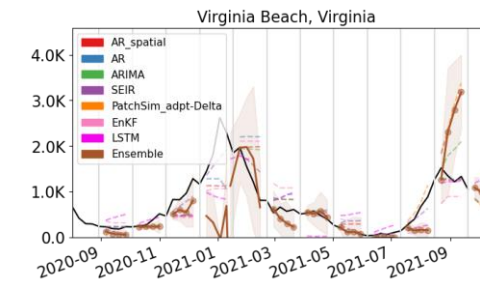**These findings are equivalent to an ascertainment ratio of ~2x in the future, with bounds of (1.3x to 3x)**

- 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

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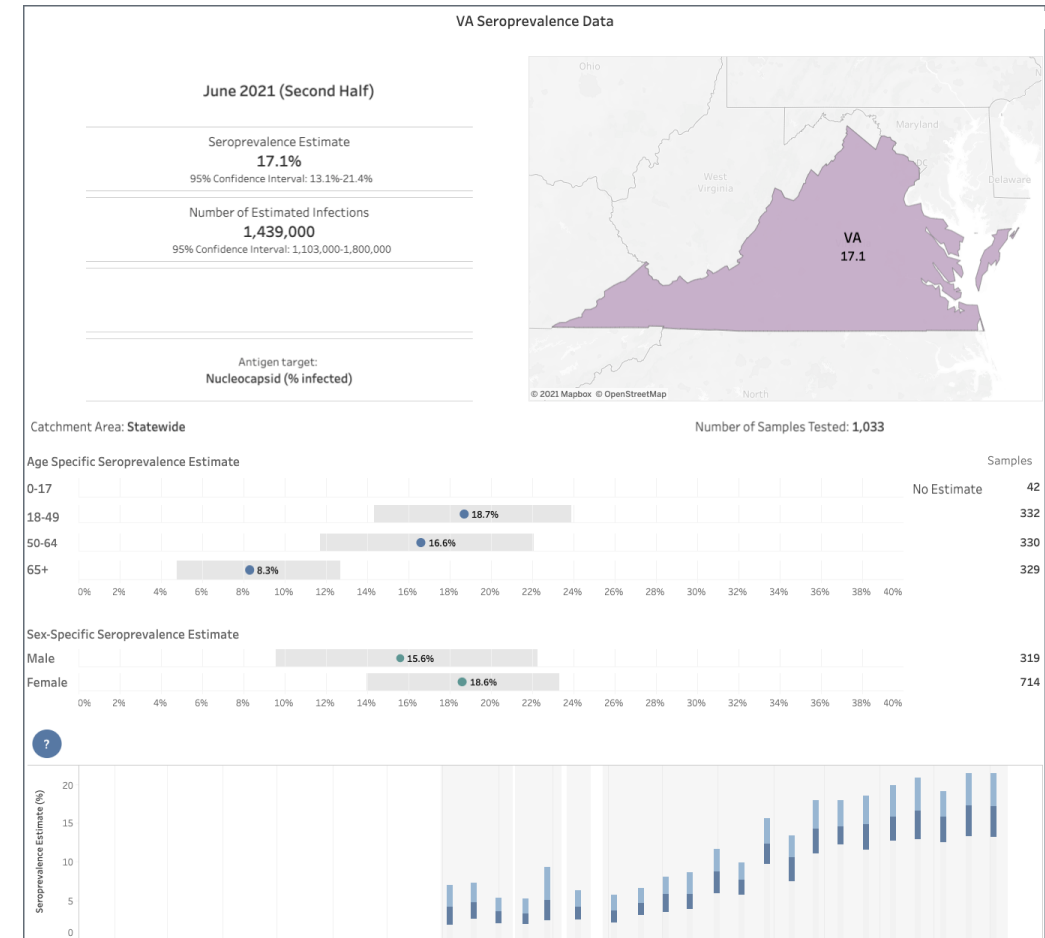
Calibration Approach

- **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
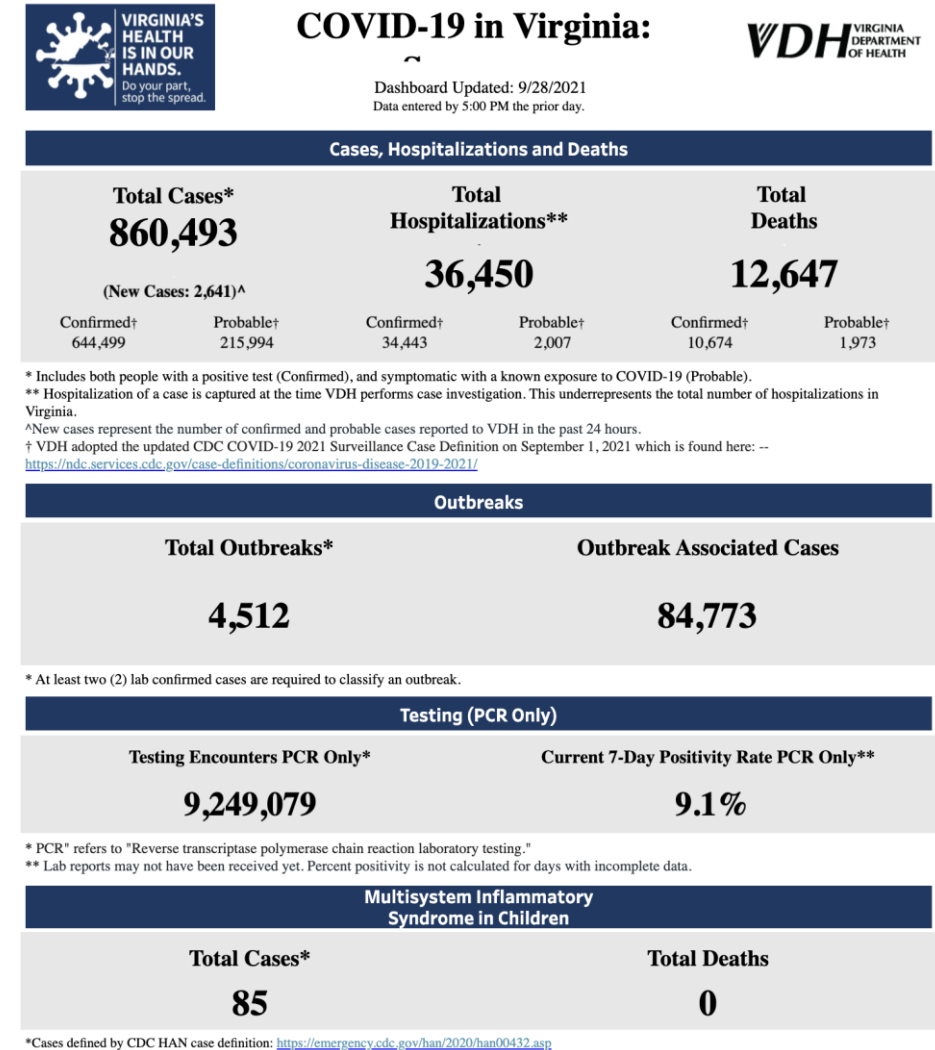- **Project:** future cases and outcomes generated using the collection of fit models run into the future
  - **Mean trend from last 14 days of observed cases and first week of ensemble's forecast used**
  - Outliers removed based on variances in the previous 3 weeks
  - 2 week interpolation to smooth transitions in rapidly changing trajectories
- **Outcomes:** Data driven by shift and ratio that has least error in last month of observations
  - Hospitalizations: 3 days from confirmation, 6.8% of cases hospitalized
  - Deaths: 11 days from confirmation, 1.45% of cases die

COVID-19 in Virginia:

VIRGINIA'S HEALTH IS IN OUR HANDS. Do your part, stop the spread.

VDH VIRGINIA DEPARTMENT OF HEALTH

Dashboard Updated: 9/28/2021
Data entered by 5:00 PM the prior day.

Cases, Hospitalizations and Deaths

Total Cases*	Total Hospitalizations**	Total Deaths
860,493	**36,450**	**12,647**
(New Cases: 2,641)^		

Confirmed† 644,499	Probable† 215,994	Confirmed† 34,443	Probable† 2,007	Confirmed† 10,674	Probable† 1,973

* 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 2021 Surveillance Case Definition on September 1, 2021 which is found here: --
https://ndc.services.cdc.gov/case-definitions/coronavirus-disease-2019-2021/

Outbreaks

Total Outbreaks*	Outbreak Associated Cases
4,512	**84,773**

* 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**
9,249,079	**9.1%**

* 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
85	**0**

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

Accessed 8:30am September 29, 2021
https://www.vdh.virginia.gov/coronavirus/

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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
- **Waning Immunity**:   Mean of one year protection (rate of 0.0027) similar to [Pfizer study](#)
- **Projection Scenarios**:
  - **Adaptive:** Control remains as is currently experienced into the future with assumption that Delta remains as the majority strain
  - **Adaptive-FallWinter2020:** Starting this week the core drivers of transmission from Sept 2020 – Feb 2021 are coarsely replayed but boosted to account for Delta's increased transmissibility
  - **Adaptive-Surge Control:** Starting in one week behaviors and mitigation efforts ramp up over a 2-week period culminating in a 25% reduction in transmission

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Scenarios – FallWinter2020 Description

September 2020 – February 2021 saw a strong wave of transmission

- We analyze previous Fall-Winter's wave vs. current Delta driven wave and observe surprising similarities
  - The distribution of fitted model transmissibility is nearly identical between these periods when corrected for Delta's increased transmissibility

- **FallWinter2020** tries to capture the "transmission drivers" from the past and use them as if they were to occur again this season but with Delta variant (compared to ancestral)
  - Use the above analysis of fitted model transmissibilities from Sept 2020 – Feb 2021 to guide the future transmissibility from Sept 2021 through Feb 2022, but add the enhanced transmissibility of Delta back in
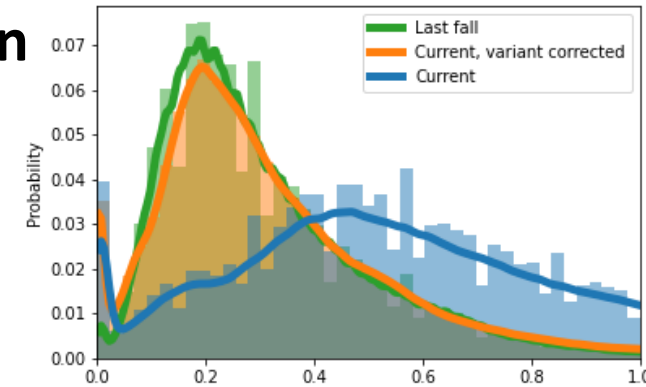
Fitting:
Black line represents the coarsely fitted base transmissibility
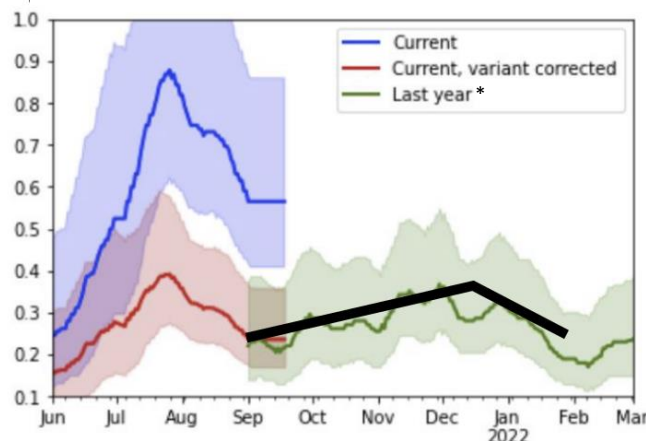
* "Last year" is transplanted into 2021-22
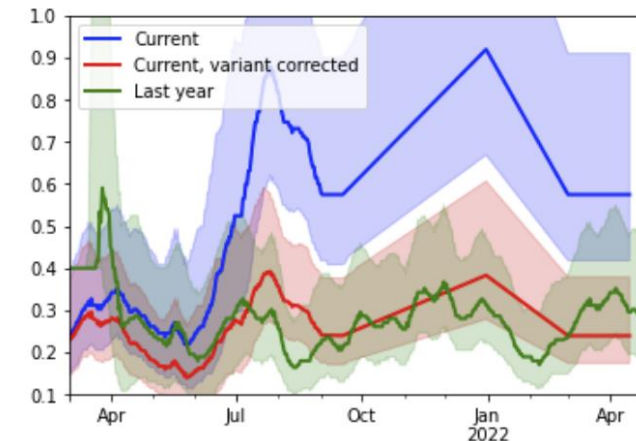
Delta enhanced:
Blue trajectory represents current fitted and then projected transmissibility in FallWinter2020

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 dose
- Delay to efficacy from doses is 14 days, immunity lasts at least 7m ([NEJM study](#))

Vaccine Administration Scenarios

- **Status quo (no label):** COVIDcast corrected acceptance estimates (statewide mean is ~80% adults, 65% of population) reached by end of October.
- **Optimistic (VaxOpt):** Expand VA mean acceptance to include "probably not" (~85% adults) with addition of childhood (5-11 yo) rollout starting in Nov 1st. This follows the same rates as observed of adolescents and results in a net increase of ~10% of population by end of February. Additionally, all counties guaranteed to reach a minimum of 65%, max of 95% by end of October
- Acceptance at county level = regional acceptance +/- relative current vax
- Front-loaded rollout (two-thirds of the remaining in half the time)

VA Vaccination scenarios
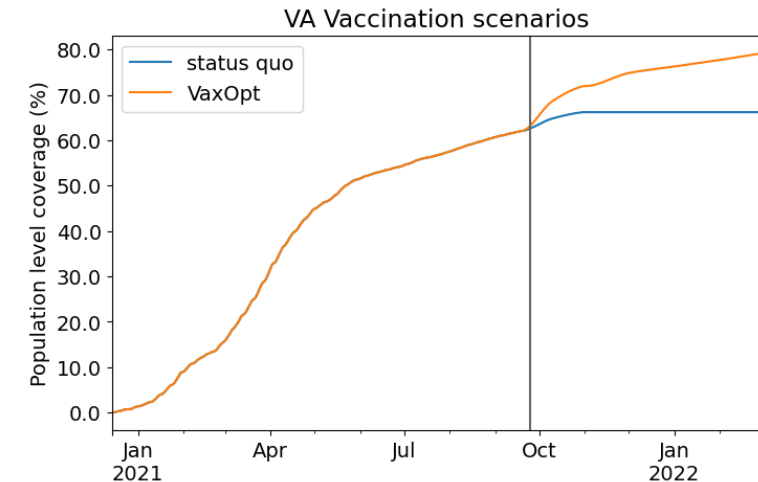
Date	status quo	VaxOpt	Date	status quo	VaxOpt
12/31/20	110.1K	110.1K	12/31/20	110.1K	110.1K
1/31/21	648.9K	648.9K	1/31/21	759.0K	759.0K
2/28/21	560.9K	560.9K	2/28/21	1.3M	1.3M
3/31/21	1.3M	1.3M	3/31/21	2.6M	2.6M
4/30/21	1.2M	1.2M	4/30/21	3.8M	3.8M
5/31/21	575.3K	575.3K	5/31/21	4.4M	4.4M
6/30/21	242.6K	242.6K	6/30/21	4.6M	4.6M
7/31/21	197.8K	197.8K	7/31/21	4.8M	4.8M
8/31/21	271.0K	271.0K	8/31/21	5.1M	5.1M
9/30/21	195.3K	236.4K	9/30/21	5.3M	5.3M
10/31/21	306.1K	821.4K	10/31/21	5.6M	6.1M
11/30/21	0	240.6K	11/30/21	5.6M	6.4M
12/31/21	0	125.1K	12/31/21	5.6M	6.5M
1/31/22	0	123.0K	1/31/22	5.6M	6.6M
2/28/22	0	122.8K	2/28/22	5.6M	6.8M
3/31/22	0	4.7K	3/31/22	5.6M	6.8M

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Projection Scenarios – Combined Conditions

Name	Txm Controls	Vax	Description
Adaptive	C	SQ	Likely trajectory based on conditions remaining similar to the current experience
Adaptive-VaxOpt	C	VO	Vaccination through October reaches an optimistically high level of expanded coverage (85%)
Adaptive-SurgeControl	25%	SQ	Transmission rates in the next month reduced through increased control from non-pharmaceutical interventions, with status quo vax and Delta
Adaptive-FallWinter2020	FallWinter 2020	SQ	Transmission rates coarsely follow the rates from last September through this February but are boosted by Delta's enhanced transmissibility
Adaptive-FallWinter2020-VaxOpt	FallWinter 2020	VO	Transmission rates coarsely follow the rates from last September through this February but are boosted by Delta's enhanced transmissibility, with optimistic vax

Transmission Controls: C = Current levels persist into the future

25% = Transmission rates are reduced by 25% with a gradual introduction, concluding in 4 weeks

FallWinter2020 = Transmission rates from Sept 2020 – Feb 2021 are coarsely replayed but boosted by Delta's increased transmissibility
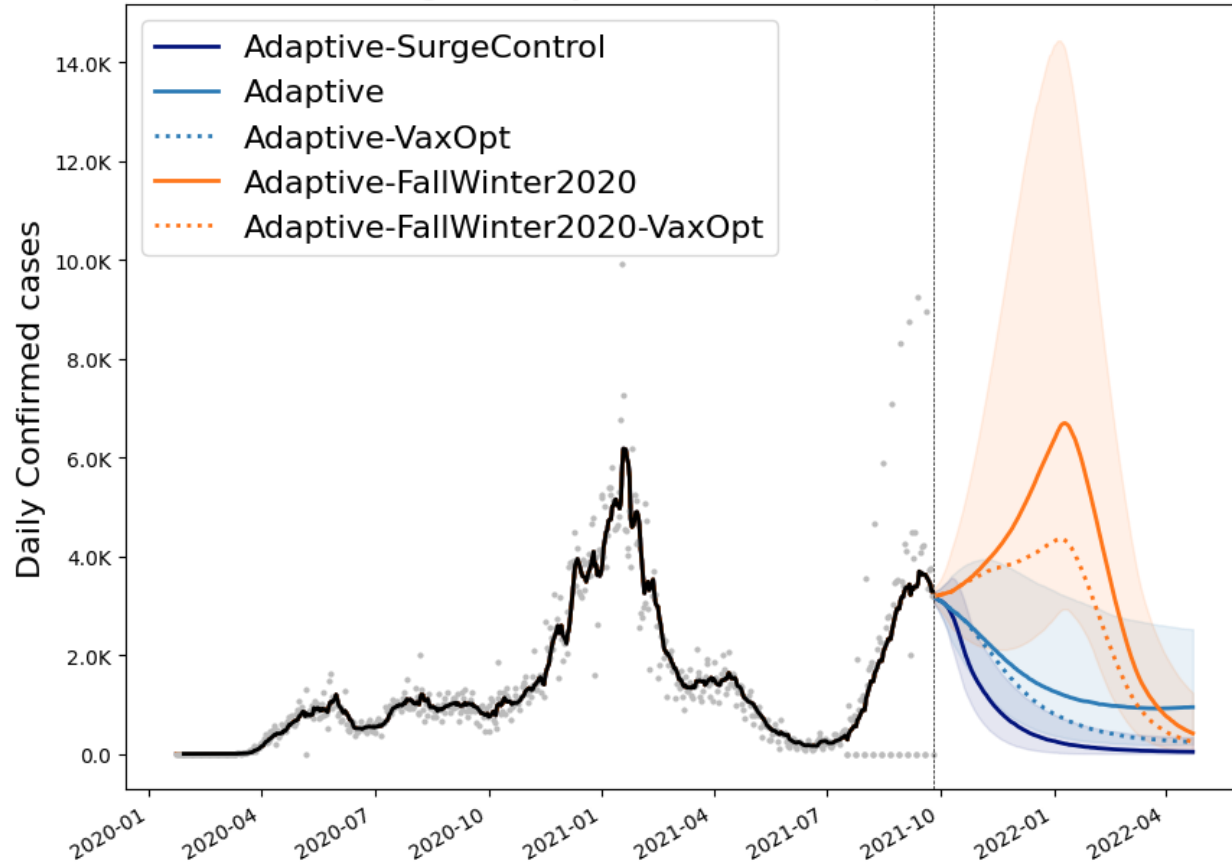
Vaccinations: SQ = Status quo acceptance leads to low rates of vaccination through the summer

VO = Vaccination acceptance optimistically expands with increased rates through the summer
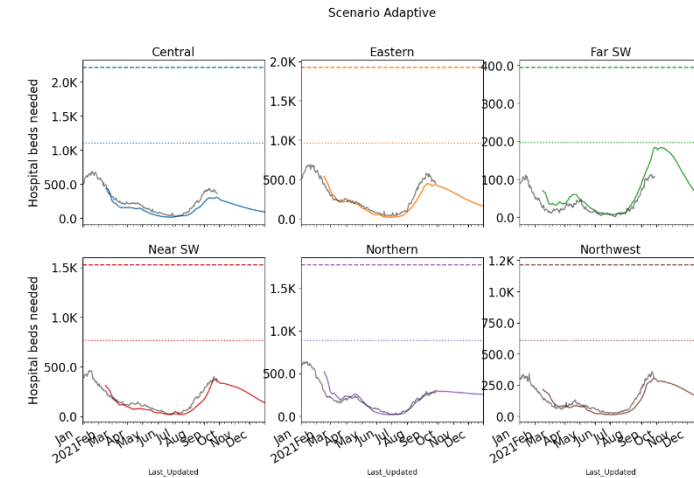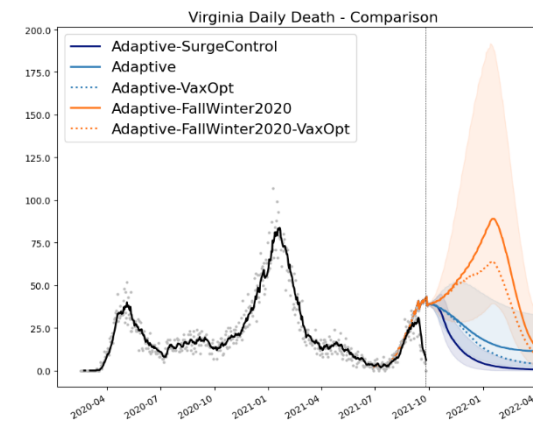
Model Results

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Outcome Projections

Confirmed cases

Daily Deaths

Daily Hospitalized

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

30-Sep-21

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Outcome Projections – Closer Look

Confirmed cases

Virginia Daily Confirmed - Comparison

Legend:
- Adaptive-SurgeControl
- Adaptive
- Adaptive-VaxOpt
- Adaptive-FallWinter2020
- Adaptive-FallWinter2020-VaxOpt

Daily Hospitalized

Virginia Daily Hospitalized - Comparison

Daily Deaths

Virginia Daily Death - Comparison

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

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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
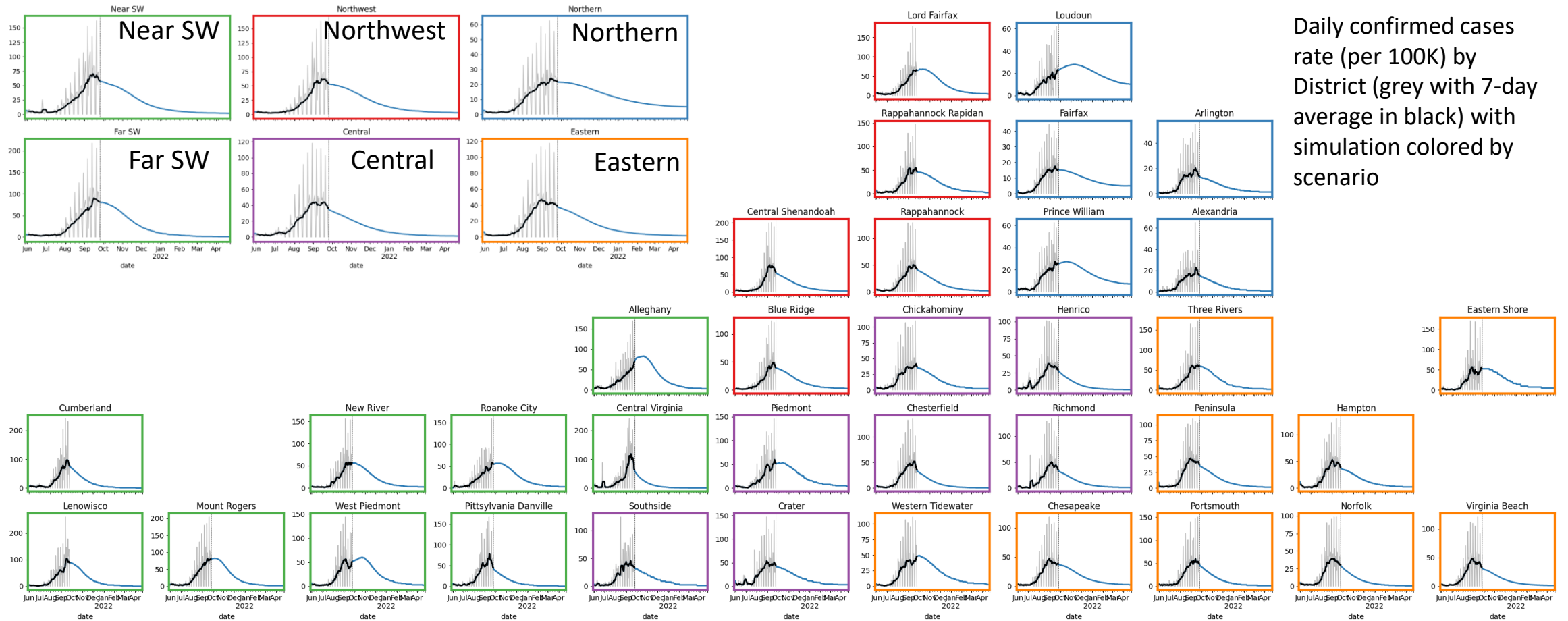
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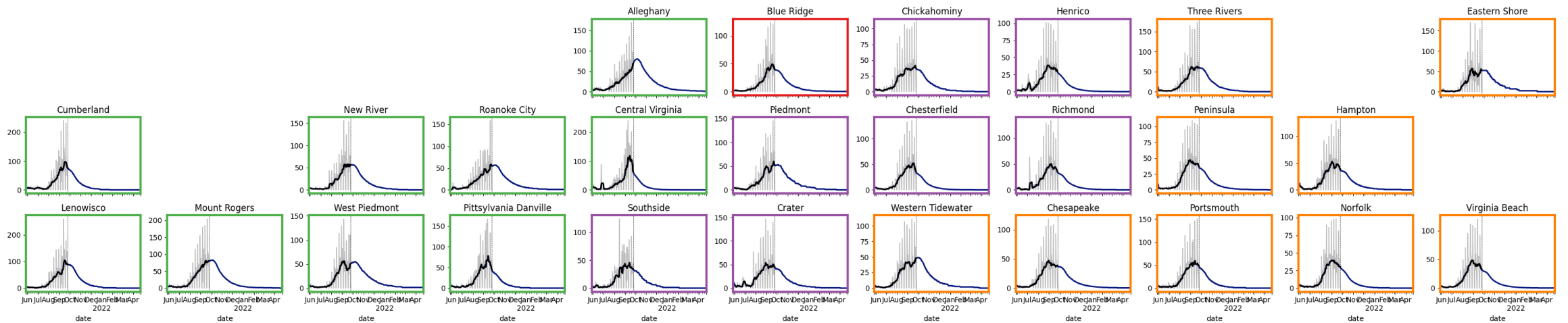# District Level Projections: Adaptive-VaxOpt

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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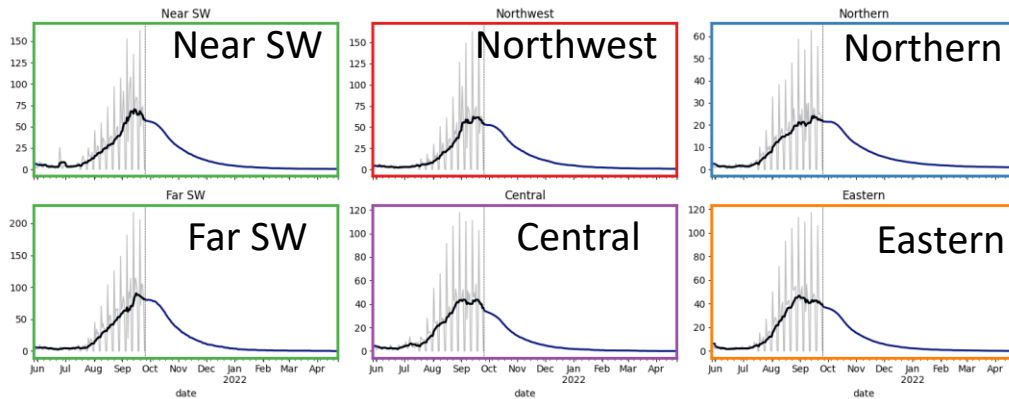# District Level Projections: Adaptive-SurgeControl

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-FallWinter2020

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
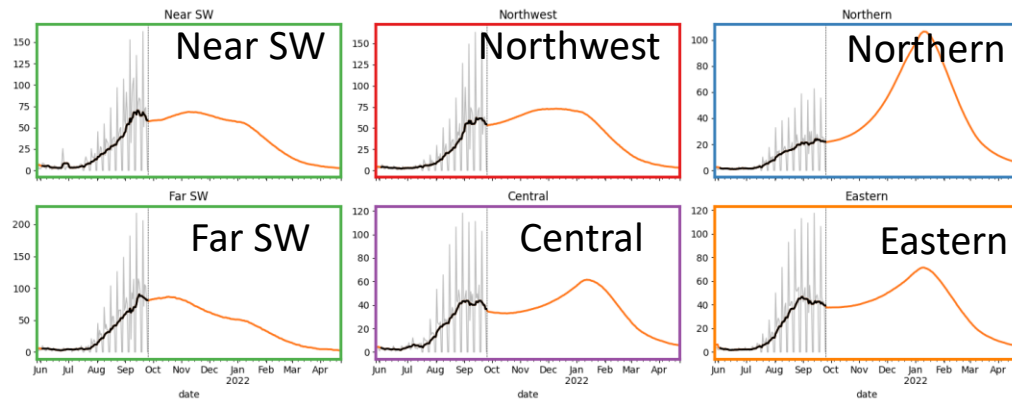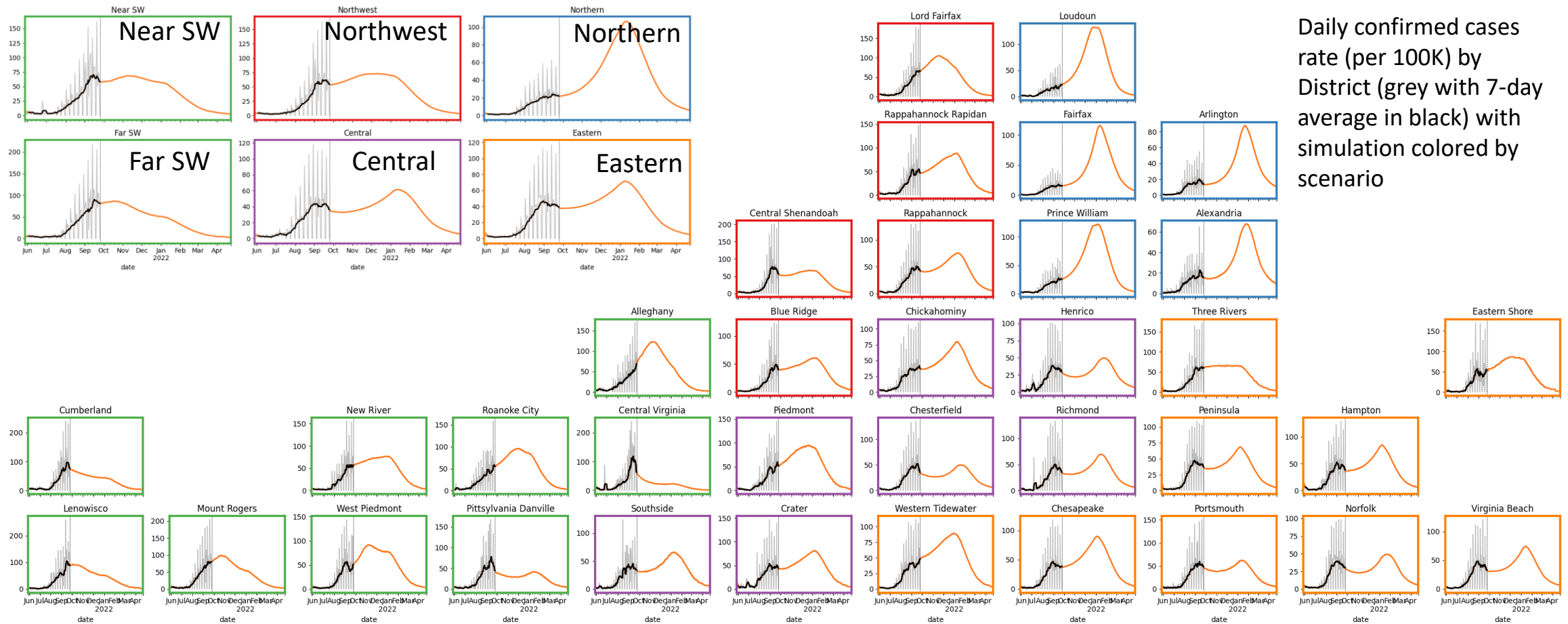
District Level Projections: Adaptive-FallWinter2020-VaxOpt
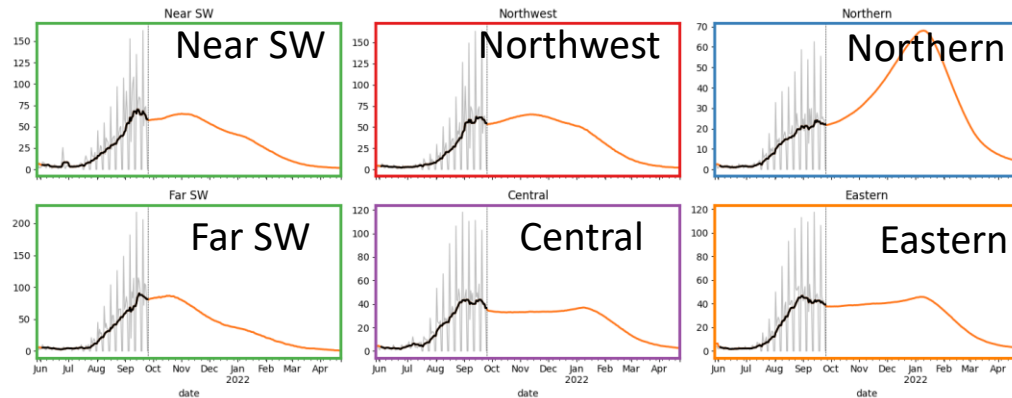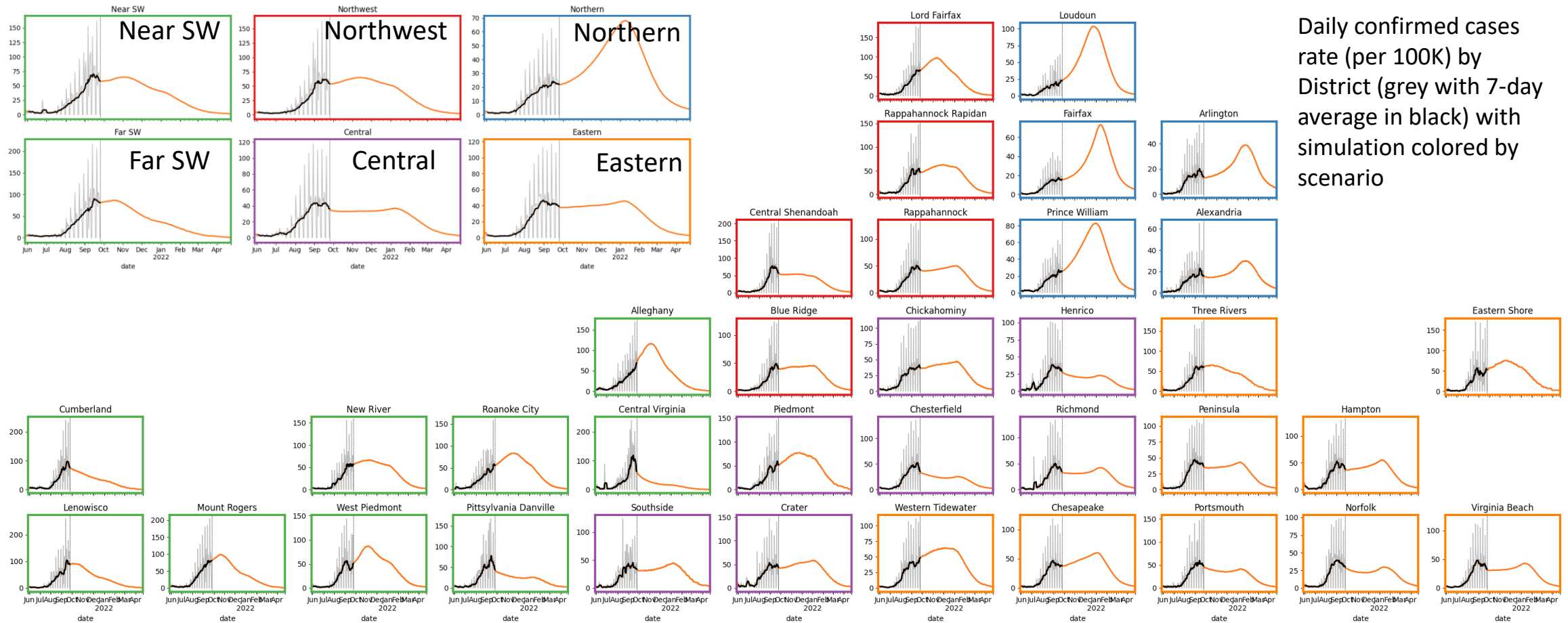
## Projections by Region

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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Impact of Expanded Vaccine Coverage & Boosted Immunity

Immunity from Vaccine is expanding, with 3rd doses as well as potential for higher adult coverage & 5-11 year olds potentially becoming eligible soon.

- Model boosters with 50% uptake after 6 months of initial vax, returning waned immunity back to 95% and 5-11 yo becoming eligible Nov 1st

- Third doses may reduce case counts by ~50K, VaxOpt alone by ~80K, and combined ~100K

- When challenged with another FallWinter wave like 2020, the 3rd dose may reduce cases by ~100K, VaxOpt alone by ~180K, and combined by ~260K

- Distribution and uptake of 3rd dose and its full impact on transmission dynamics are not well understood, these estimates are preliminary

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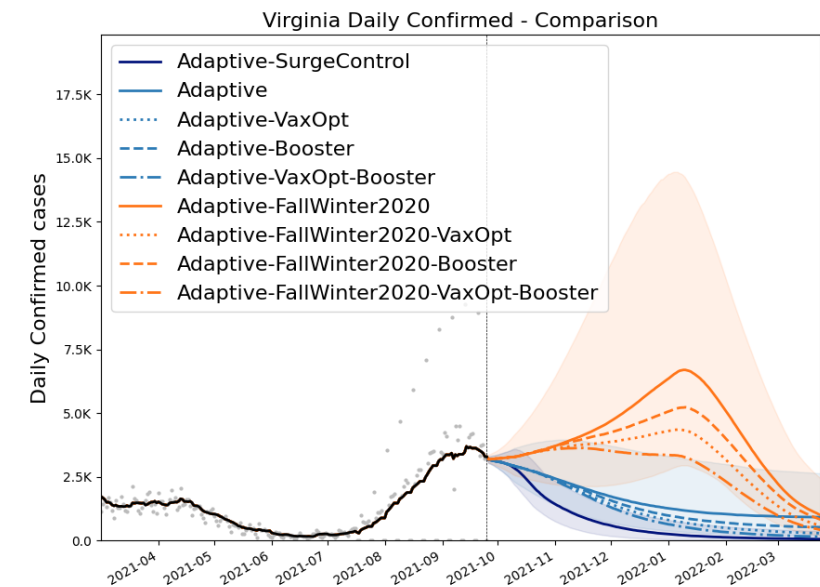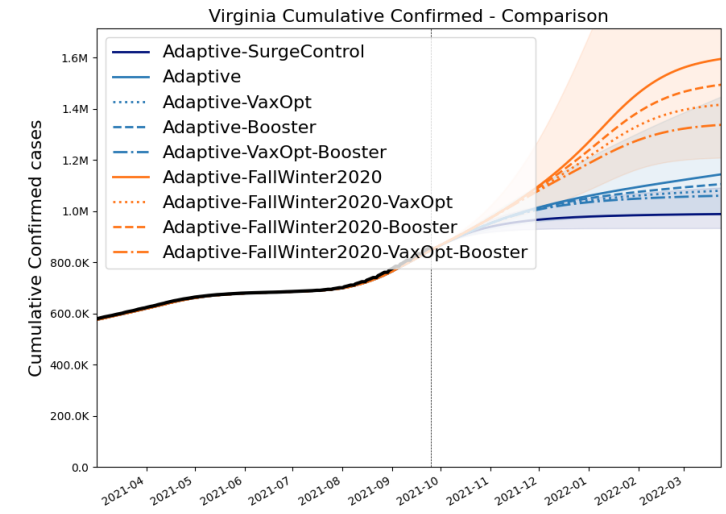
Virginia's Progress on Population Immunity

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
  - Do **not** factor in variant immune escape
  - 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 variants

- Population immunity depends on a very high proportion of the population getting vaccinated
  - Current models track measured seroprevalence
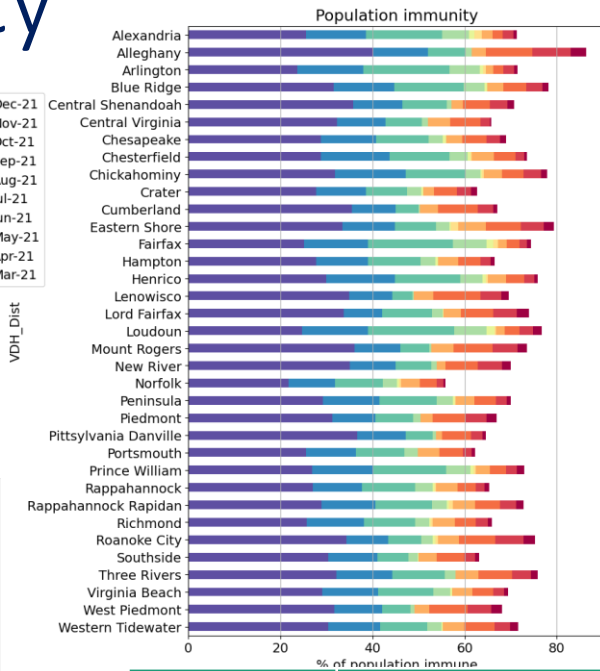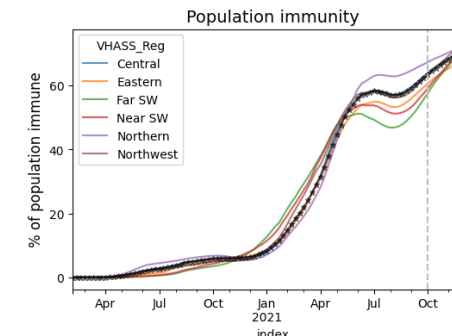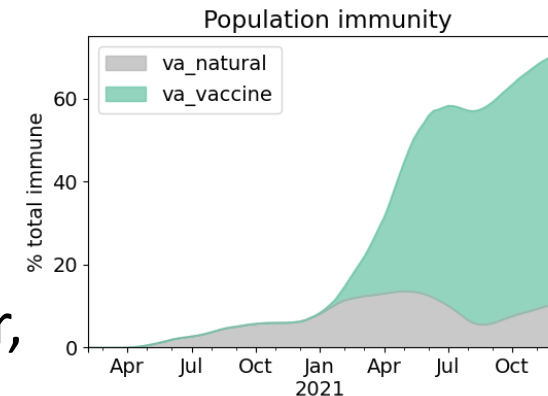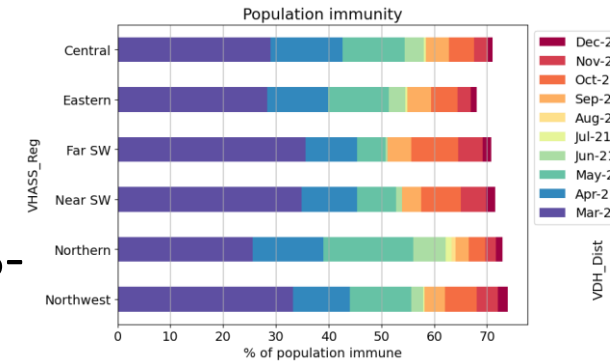
Region	% pop immune (est.)*
Central	63%
Eastern	59%
Far SW	56%
Near SW	57%
Northern	67%
Northwest	62%
Virginia	62%

* As of Sept 26, 2021 (updated to account for entire population)

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Hospital Demand and Bed Capacity by Region

Capacities* by Region – Adaptive FallWinter2020

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

https://nssac.bii.virginia.edu/covid-19/vmrddash/
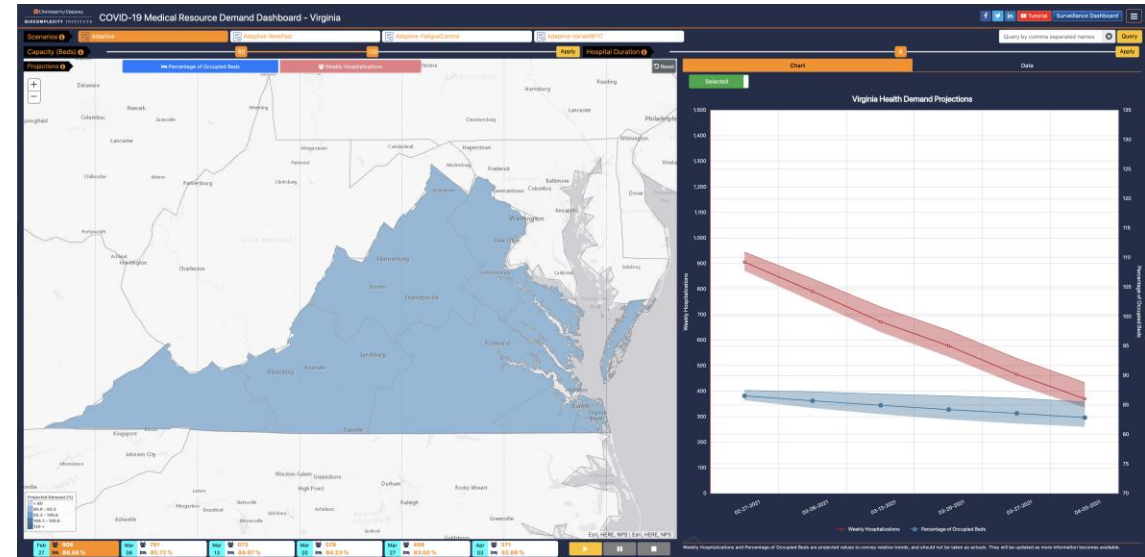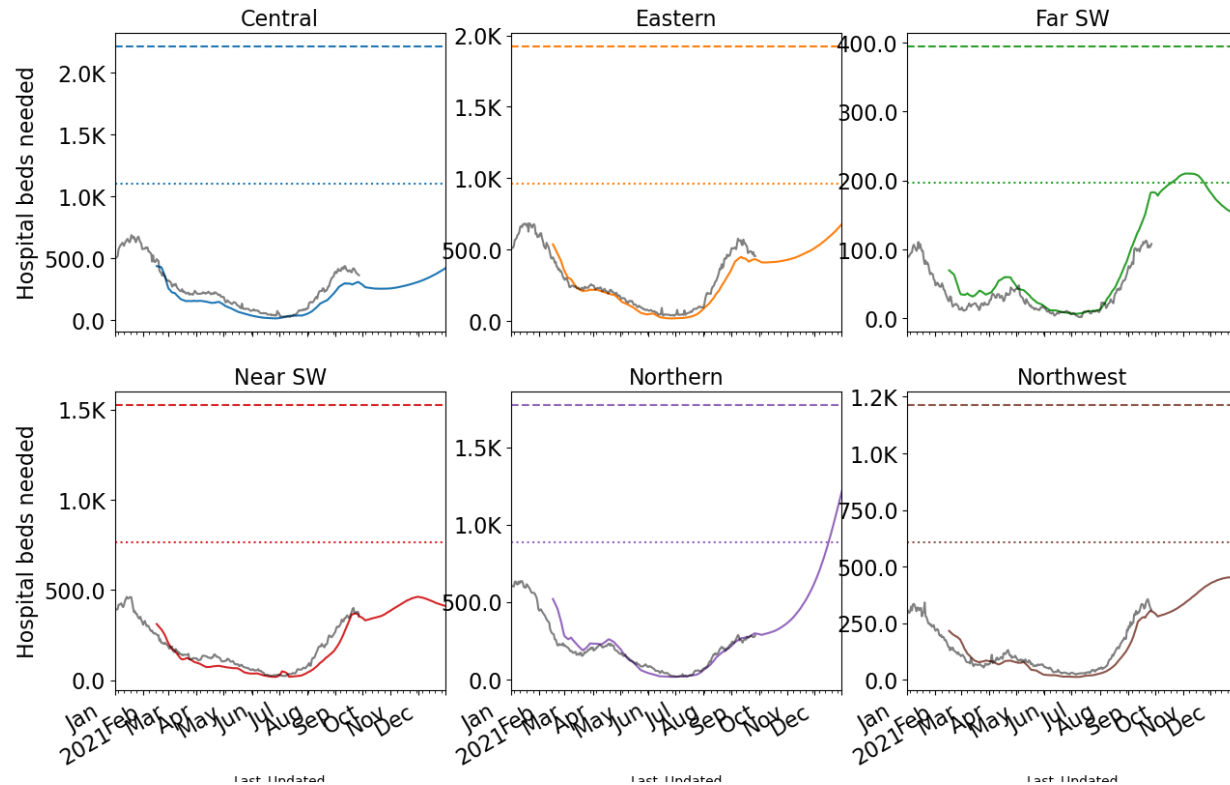
Adaptive FallWinter2020 scenario shows that even with Delta enhanced severity:

- No regions should exceed their surge capacities
- Some regions may exceed initial capacities

* Assumes average length of stay of 8 days

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Key Takeaways

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

- **Case rate growth in Virginia has started decline, though growth remains in many districts; case rates remain high as we may begin to decline from the peak of the Delta wave**

- VA 7-day mean daily incidence is slightly down to 35/100K from 42/100K; US is also slightly down to 43/100K (from 48/100K)

- Projections show continued decline, though some districts have some growth potential, and a scenario based on last year's transmission drivers show that significant future case growth remains possible

- Recent updates:
  - Added FallWinter2020 scenario which replays the transmission drivers of last Fall-Winter season
  - Prelim analysis of impact of expanded immunity through 3rd doses
  - Adjustment to higher levels of assumed immunity waning (natural and vaccine)

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

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Additional Analyses

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Estimating Daily Reproductive Number –
Redistributed weekend gap

Sept 20th Estimates

Region	Date Confirmed R_e	Date Confirmed Diff Last Week
State-wide	0.893	-0.093
Central	0.897	-0.096
Eastern	0.925	-0.051
Far SW	0.903	-0.137
Near SW	0.848	-0.111
Northern	0.943	-0.050
Northwest	0.876	-0.117

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

VA state-wide RE with 7 day moving window by confirmation date redistributed GT 2021-09-13

VA RE by VHASS region with 7 day moving window by confirmation date redistributed GT 2021-09-13
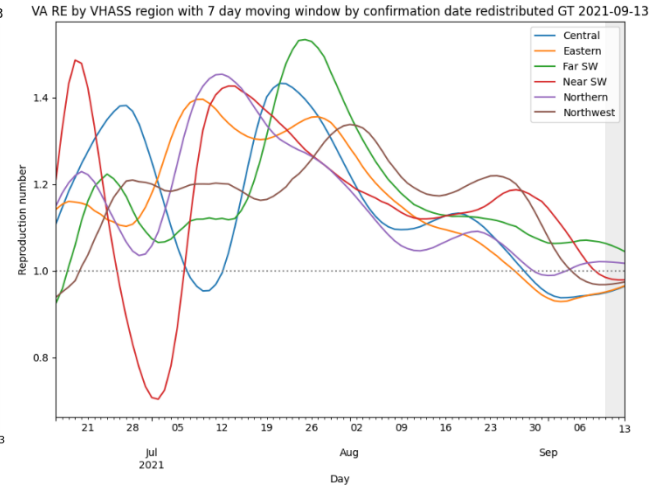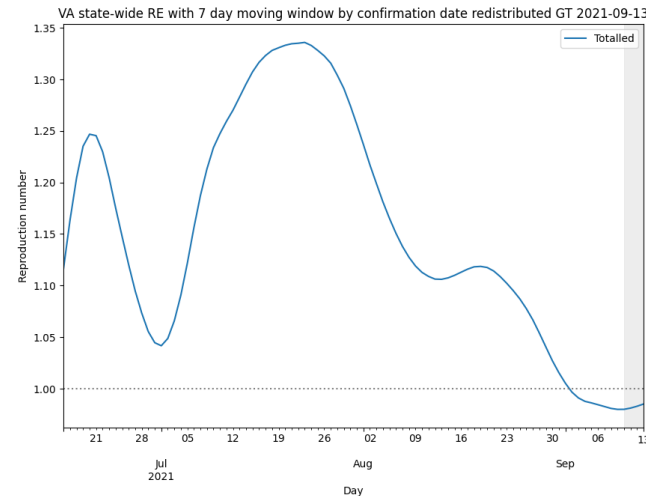
Skipping Weekend Reports biases estimates

Redistributed Monday to fill in weekend, and then estimate R from "smoothed" time series

Virginia
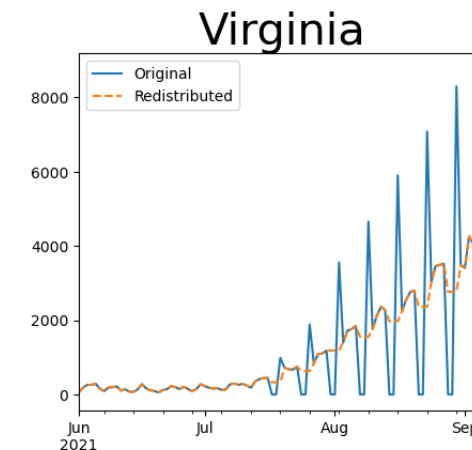
Weekly Cases and Hospitalizations

Weekly confirmed cases

Week Ending	Adaptive	Adaptive-VaxOpt	Adaptive-SurgeControl	Adaptive-FallWinter 2020	Adaptive-FallWinter 2020-VaxOpt
9/26/21	23767	23769	23768	23792	23791
10/3/21	21764	21748	21782	22487	22478
10/10/21	20862	20866	20684	22820	22822
10/17/21	19876	19896	18068	23422	23458
10/24/21	18837	18762	14304	24292	24235
10/31/21	17674	17340	11258	25334	24853
11/7/21	16475	15802	9141	26559	25455
11/14/21	15272	14278	7404	27916	26052
11/21/21	14086	12668	6000	29390	26429
11/28/21	12958	11148	4862	31112	26756
12/5/21	11924	9786	3995	33180	27196
12/12/21	11028	8586	3257	35587	27749
12/19/21	10220	7526	2678	38268	28364
12/26/21	9556	6624	2221	41088	29138

Weekly Hospitalizations

Week Ending	Adaptive	Adaptive-VaxOpt	Adaptive-SurgeControl	Adaptive-FallWinter 2020	Adaptive-FallWinter 2020-VaxOpt
9/26/21	1534	1534	1534	1539	1539
10/3/21	1515	1514	1516	1566	1565
10/10/21	1463	1463	1450	1601	1602
10/17/21	1406	1405	1278	1658	1659
10/24/21	1344	1336	1020	1736	1729
10/31/21	1272	1251	809	1827	1795
11/7/21	1196	1158	662	1934	1873
11/14/21	1116	1060	540	2049	1944
11/21/21	1035	952	439	2167	1992
11/28/21	958	847	357	2293	2034
12/5/21	882	750	295	2440	2079
12/12/21	815	661	241	2607	2127
12/19/21	753	579	198	2792	2179
12/26/21	700	510	163	2992	2242

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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

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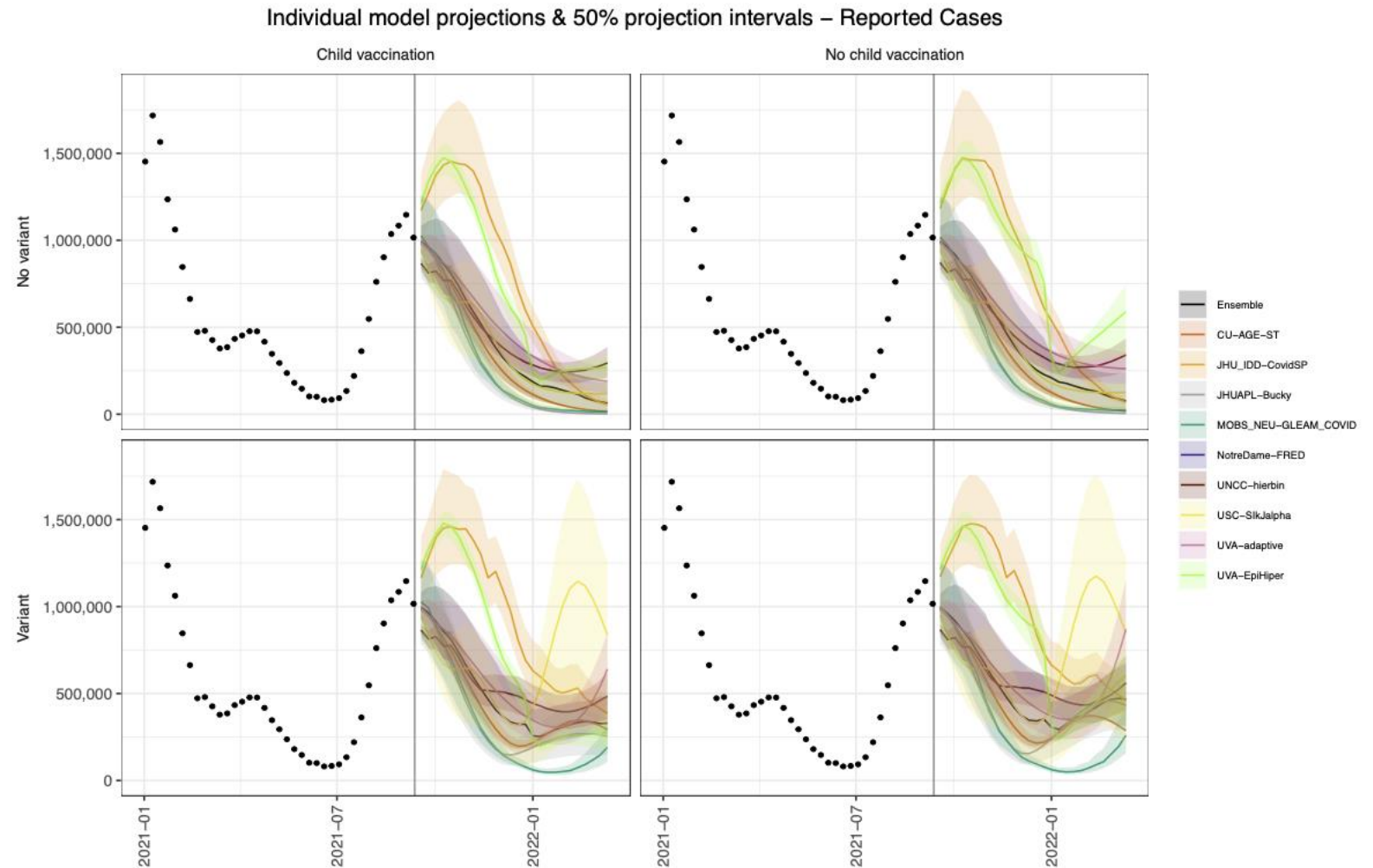
COVID-19 Scenario Modeling Hub

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 impact of the Delta variant (high and low)

- Round 9 released to assist in support of 5-11 vax consideration (ACIP meeting Sept 22-23)

- Rounds 4-8 now available

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

https://covid19scenariomodelinghub.org/viz.html

Individual model projections & 50% projection intervals – Reported Cases

COVID-19 Scenario Modeling Hub – Round 7

Round 7 scenarios explore the effects of a variant similar to Delta (B.1.617.2) against different backgrounds of vaccination. Includes some vax escape

Vaccinations in 5-11 start in Nov

- Follows same rates as adolescents

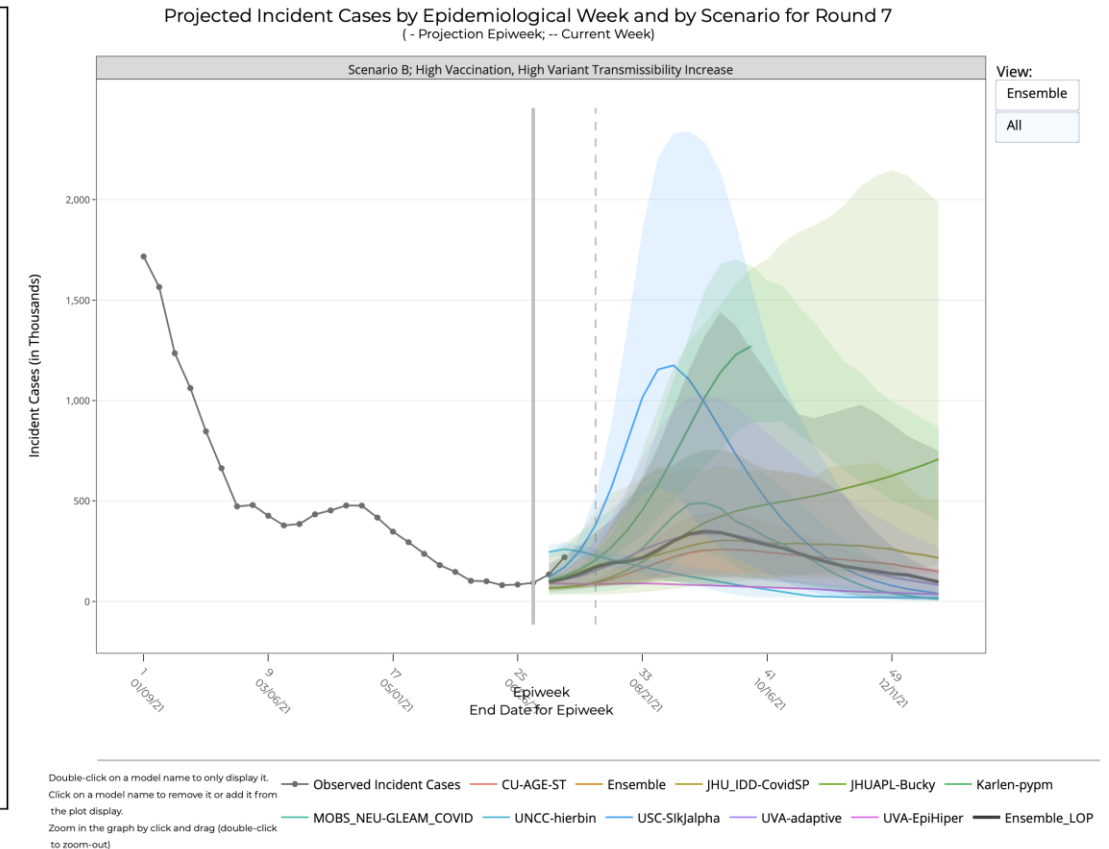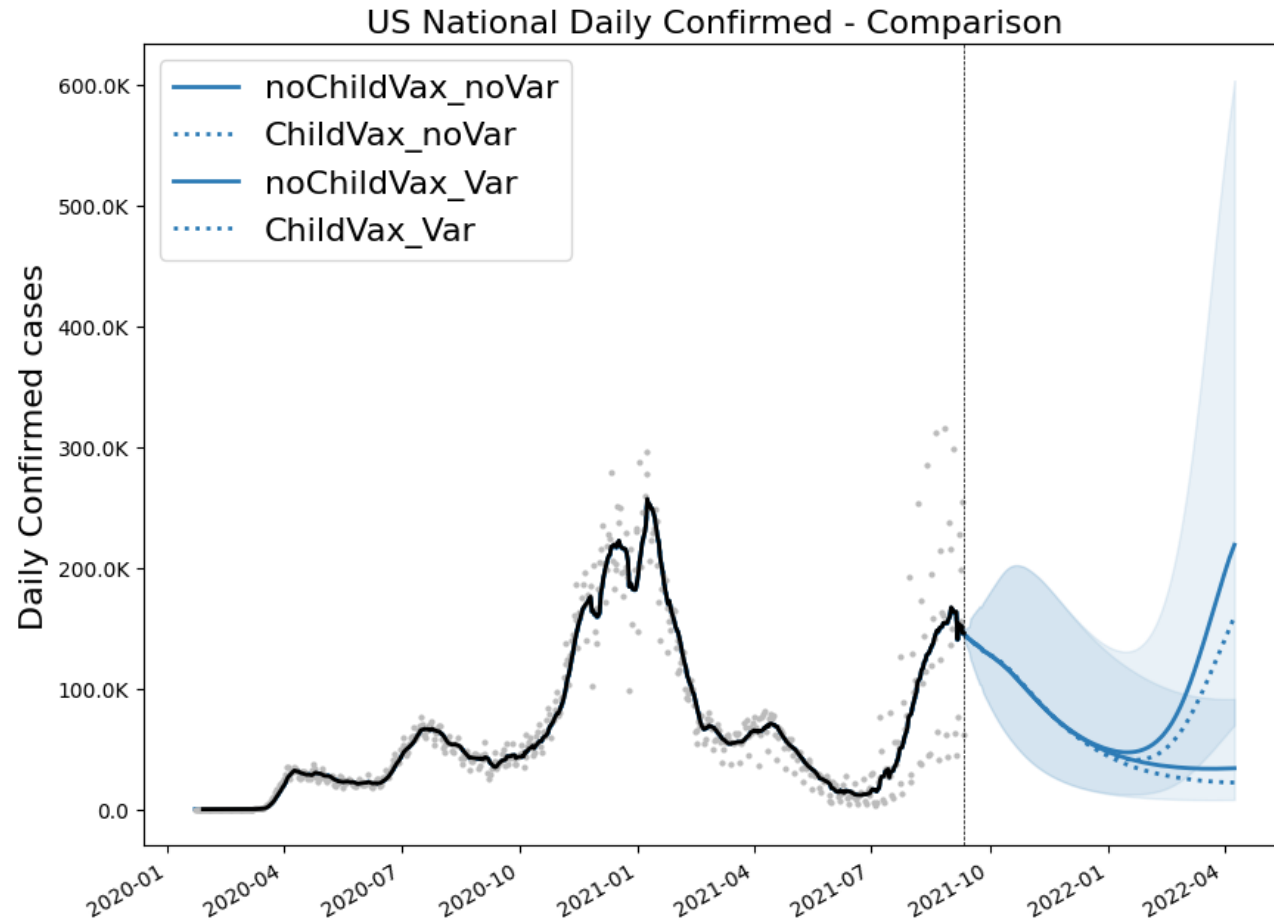**Emerging Variant Impact** (5% prevalence on Nov 15)

- 50% boost as it eventually predominates

We consider a 2x2 scenario design, where childhood vaccination (5-11 years) is on the first axis, and a change in virus transmissibility is on the second axis. The second axis reflects a stress test, illustrating the potential impact of a new variant arising during the projection period:

	The same mix of variants circulate throughout the projection period. No change in virus transmissibility.	A more transmissible variant emerges, comprising 1% of circulating viruses on **Nov 15**. The new variant is **1.5X** as transmissible as viruses circulating at the beginning of the projection period.
Vaccination among 5-11yrs is approved and immunization begins on Nov 1. Each state's uptake rate reflects the percent coverage increases observed for 12-17-year-olds since distribution began on May 13.	A	C
No vaccination for children under 12	B	D

https://covid19scenariomodelinghub.org/viz.html

Modeling Hub – Round 9 Prelim Results

US National Daily Confirmed - Comparison

Projected Incident Cases by Epidemiological Week and by Scenario for Round 7
(- Projection Epiweek; -- Current Week)

https://covid19scenariomodelinghub.org/viz.html

Data Recommended Mobile Vax Clinic Sites

Detailed and Timely Locations

ID: 89b2b67f
Group: Whole population
Rank: 23
Most visited on: Tuesday
High traffic addr: 600 Pittsylvania Ave, Altavista, VA, 24517
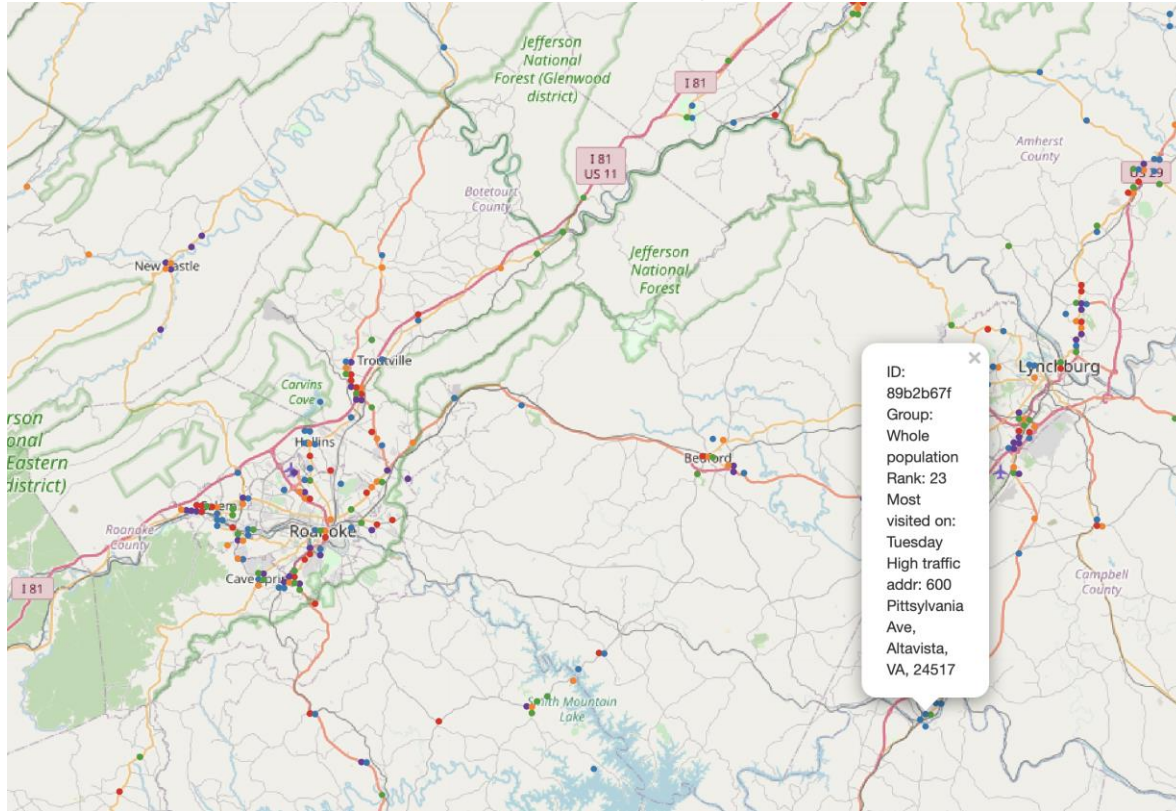
Data Delivered and Disseminated to Locals

Provides a list of areas most visited by a given demographic group based on SafeGraph mobility data that links visits to specific sites and the home Census Block Group of the anonymized visitors

Demographic Groups: Black, Lantinx, Young Adults (20-40), Unvaccinated, and Whole Population

Data Included: Rank, Weight, most visited Day of Week, Highly Visited Address, and Lat-Long of area

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

Example: List of location in the Southside frequented by 20-40 year olds

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Data Recommended Mobile Vax Clinic Sites

Overlap of locations between groups

State Level

Within VDH Health Districts

Different groups visit different areas

- Least overlap between Black and Latinx
- Overlap in ages highest, but drops with large gap
- Districts have different overlap patterns

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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/

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Questions?

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Supplemental Slides

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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
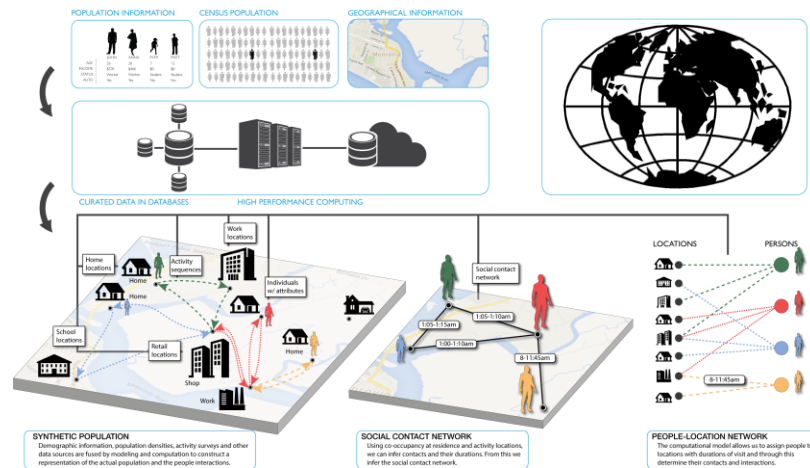
Synthetic Population
- Census derived age and household structure
- Time-Use survey driven activities at appropriate locations
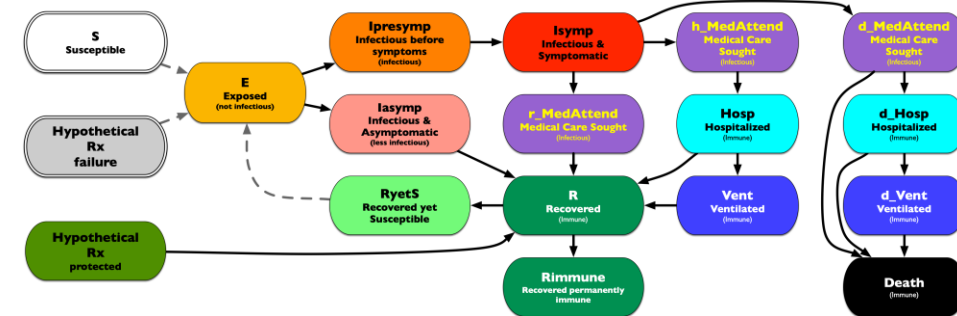
Detailed Disease Course of COVID-19
- Literature based probabilities of outcomes with appropriate delays
- Varying levels of infectiousness
- Hypothetical treatments for future developments