Network Systems
Science & Advanced
Computing

Biocomplexity Institute
& Initiative

University of Virginia

Estimation of COVID-19 Impact in Virginia

May 5th, 2021

(data current to May 1st – May 4th)
Biocomplexity Institute Technical report: TR 2021-052

UNIVERSITY of VIRGINIA

BIOCOMPLEXITY INSTITUTE

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

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 with minimal growth in a few districts**
- VA mean weekly incidence down to 11/100K from 13/100K, US down (15 from 16 per 100K)
- Vaccination rates have slowed, but overall population immunity continues to rise over 50%
- Projections show declining rate overall across Commonwealth, only a few districts with short term growth
- Recent updates:
  - Updated estimates of regional vaccine hesitancy and folded into projections

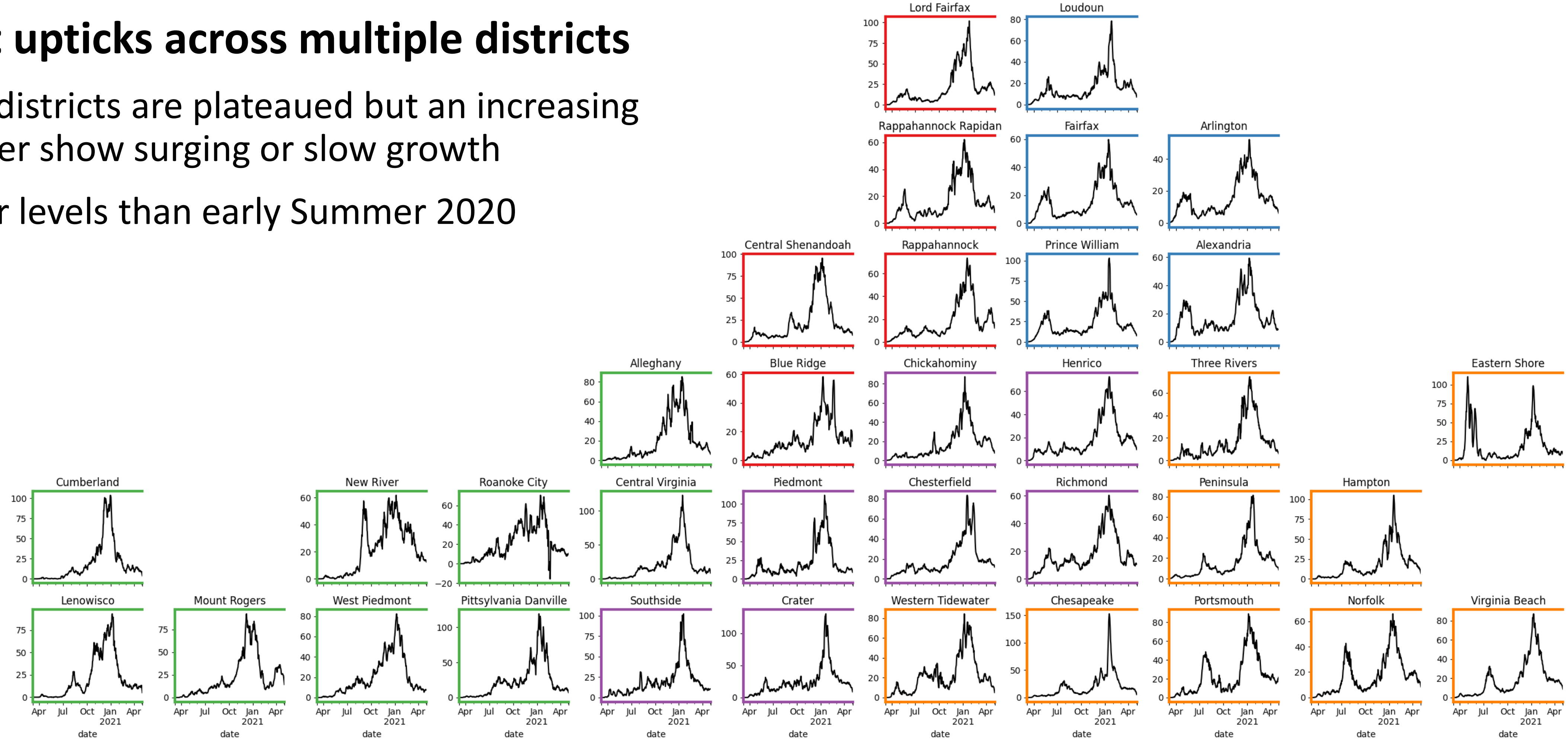
The situation continues to change. Models continue to be updated regularly.

Situation Assessment

Case Rate (per 100k) by VDH District

Recent upticks across multiple districts

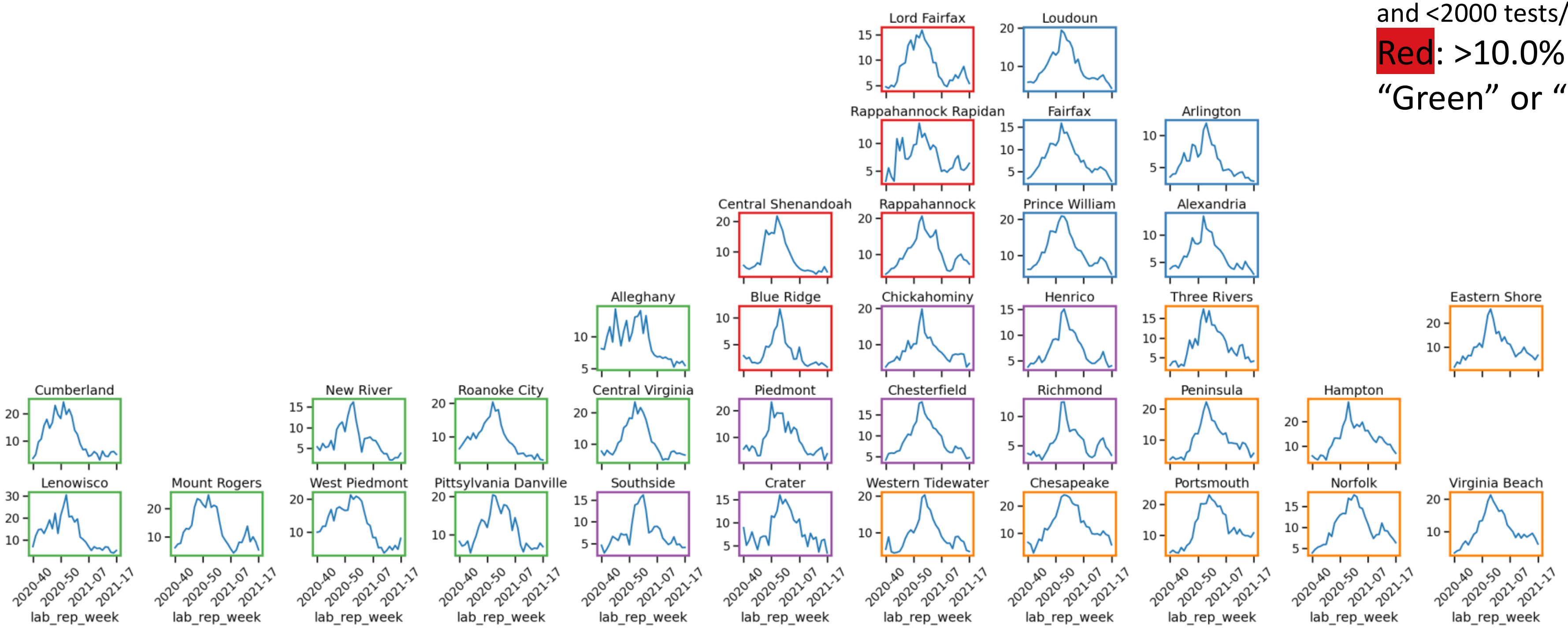
- Most districts are plateaued but an increasing number show surging or slow growth
- Higher levels than early Summer 2020



Test Positivity by VDH District

Weekly changes in test positivity by district

- Some upticks/flattening in the positivity rates
- Nearly 75% of counties still in Red or Yellow categories

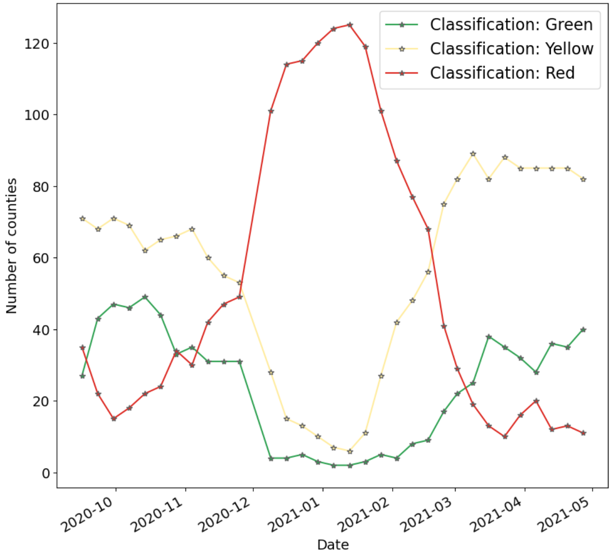


County level test positivity rates for RT-PCR tests.

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

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

Red: >10.0% and not meeting the criteria for "Green" or "Yellow"



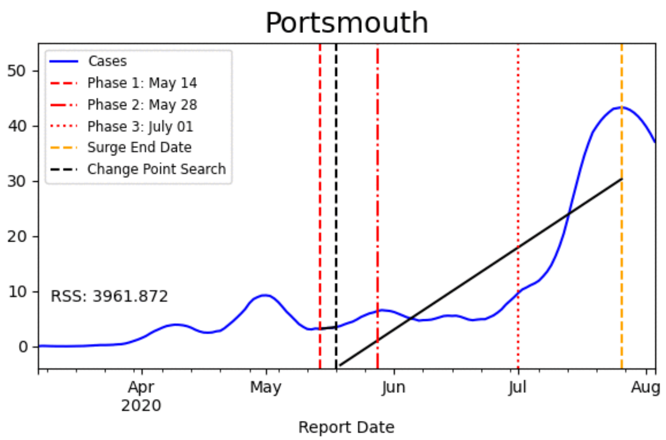
https://data.cms.gov/stories/s/q5r5-gjyu

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

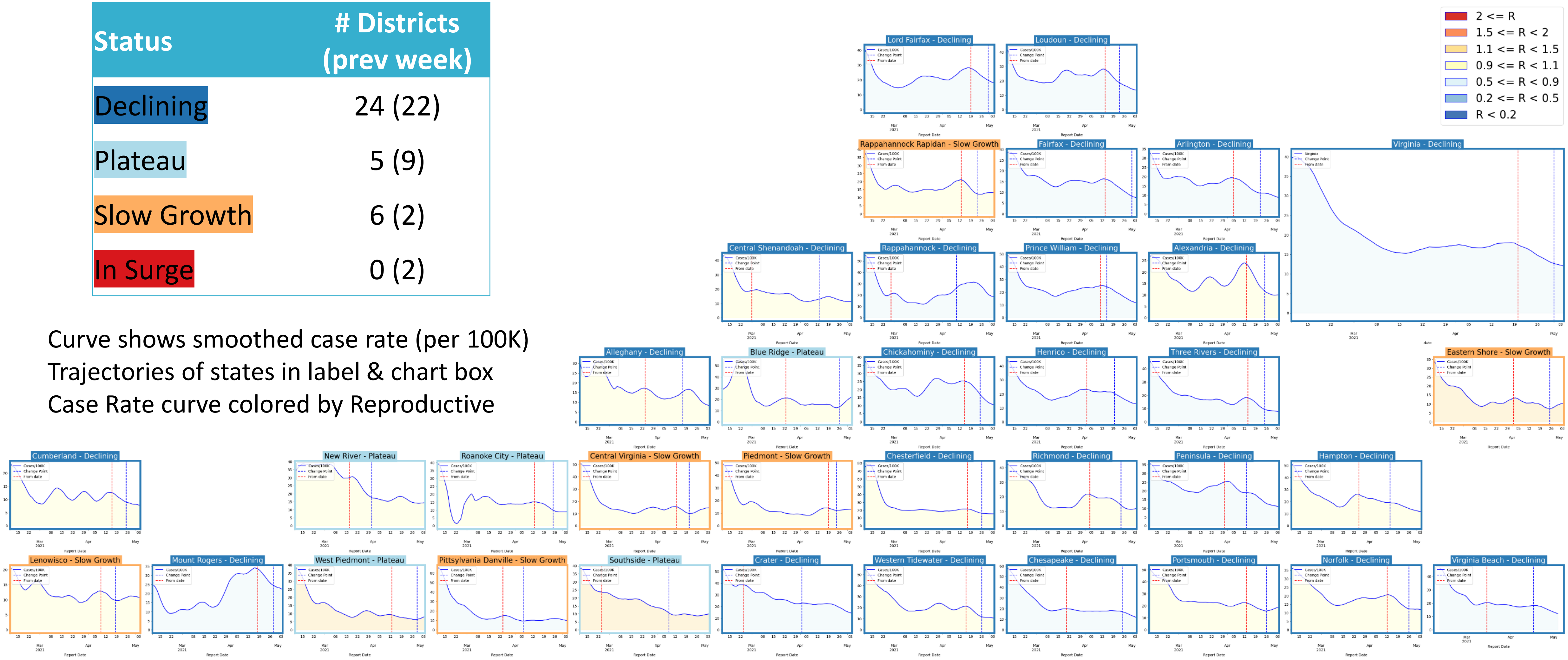


Trajectory	Description	Weekly Case Rate (per 100K) bounds	# Districts (prev week)
Declining	Sustained decreases following a recent peak	below -0.9	27 (22)
Plateau	Steady level with minimal trend up or down	above -0.9 and below 0.5	3 (9)
Slow Growth	Sustained growth not rapid enough to be considered a Surge	above 0.5 and below 2.5	5 (2)
In Surge	Currently experiencing sustained rapid and significant growth	2.5 or greater	0 (2)

District Trajectories – last 10 weeks

Status	# Districts (prev week)
Declining	24 (22)
Plateau	5 (9)
Slow Growth	6 (2)
In Surge	0 (2)

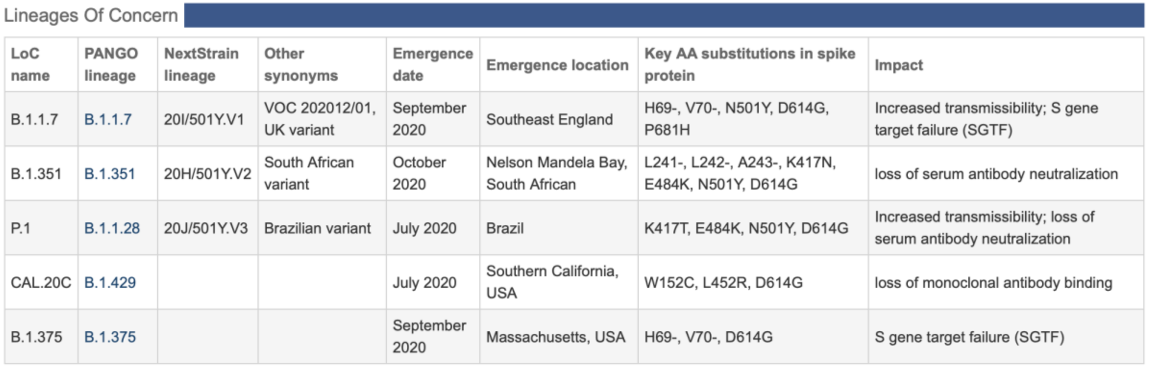
Curve shows smoothed case rate (per 100K)
Trajectories of states in label & chart box
Case Rate curve colored by Reproductive



SARS-CoV2 Variants of Concern

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

- Current evidence supports that new 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

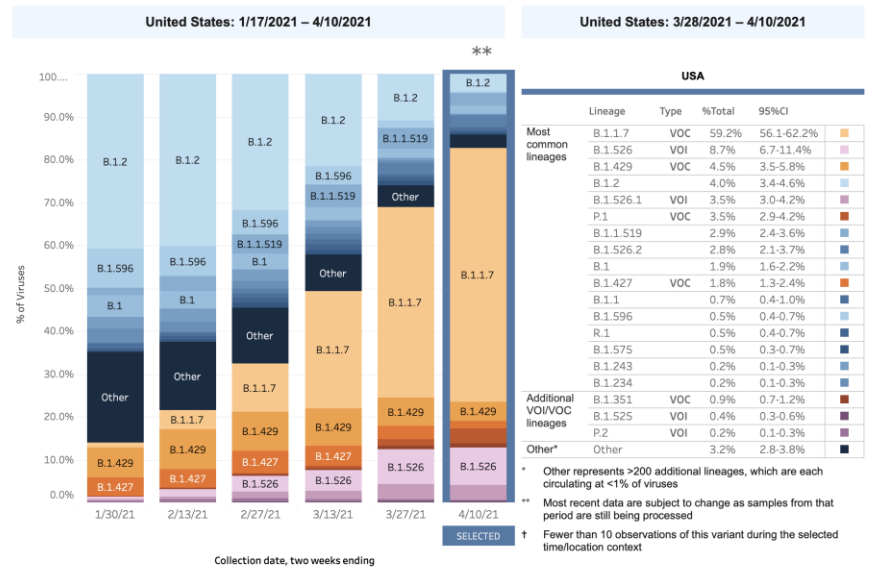


Lineages Of Concern

LoC name	PANGO lineage	NextStrain lineage	Other synonyms	Emergence date	Emergence location	Key AA substitutions in spike protein	Impact
B.1.1.7	B.1.1.7	20I/501Y.V1	VOC 202012/01, UK variant	September 2020	Southeast England	H69-, V70-, N501Y, D614G, P681H	Increased transmissibility; S gene target failure (SGTF)
B.1.351	B.1.351	20H/501Y.V2	South African variant	October 2020	Nelson Mandela Bay, South African	L241-, L242-, A243-, K417N, E484K, N501Y, D614G	loss of serum antibody neutralization
P.1	B.1.1.28	20J/501Y.V3	Brazilian variant	July 2020	Brazil	K417T, E484K, N501Y, D614G	Increased transmissibility; loss of serum antibody neutralization
CAL.20C	B.1.429			July 2020	Southern California, USA	W152C, L452R, D614G	loss of monoclonal antibody binding
B.1.375	B.1.375			September 2020	Massachusetts, USA	H69-, V70-, D614G	S gene target failure (SGTF)

[NIH-NIAID Bacterial-Viral Bioinformatics Resource Center]

Weighted Estimates of Proportions of SARS-CoV-2 Lineages



USA

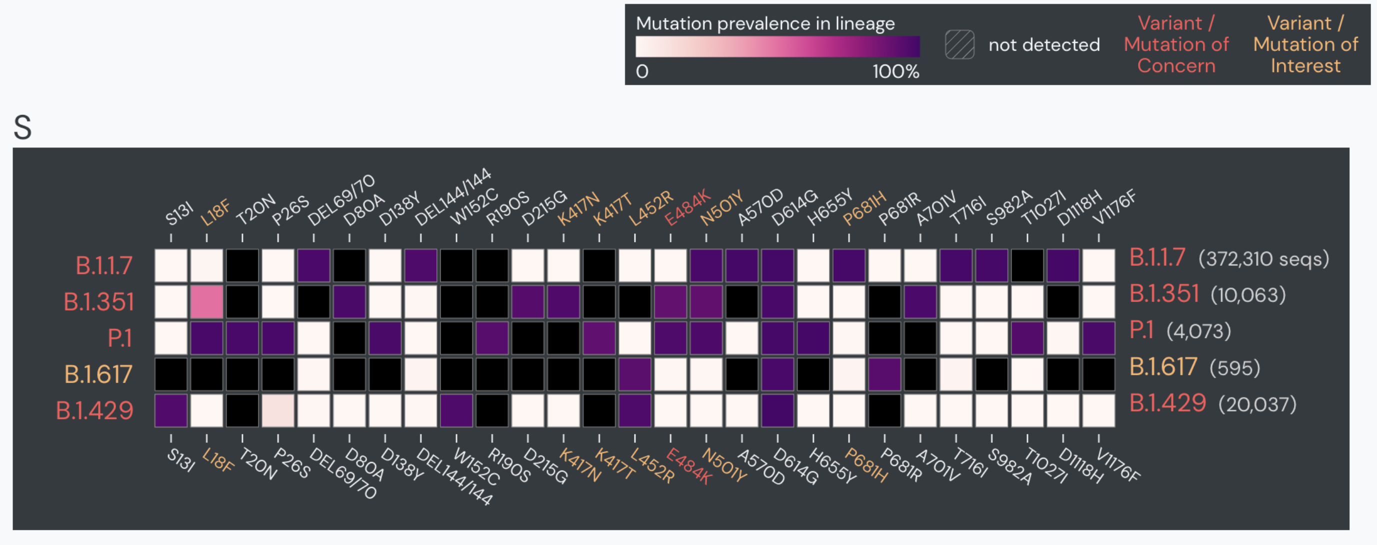
	Lineage	Type	%Total	95%CI	
Most common lineages	B.1.1.7	VOC	59.2%	56.1-62.2%	■
	B.1.526	VOI	8.7%	6.7-11.4%	■
	B.1.429	VOC	4.5%	3.5-5.8%	■
	B.1.2		4.0%	3.4-4.6%	■
	B.1.526.1	VOI	3.5%	3.0-4.2%	■
	P.1	VOC	3.5%	2.9-4.2%	■
	B.1.1.519		2.9%	2.4-3.6%	■
	B.1.526.2		2.8%	2.1-3.7%	■
	B.1		1.9%	1.6-2.2%	■
	B.1.427	VOC	1.8%	1.3-2.4%	■
	B.1.1		0.7%	0.4-1.0%	■
	B.1.596		0.5%	0.4-0.7%	■
	R.1		0.5%	0.4-0.7%	■
	B.1.575		0.5%	0.3-0.7%	■
	B.1.243		0.2%	0.1-0.3%	■
	B.1.234		0.2%	0.1-0.3%	■
Additional VOI/VOC lineages	B.1.351	VOC	0.9%	0.7-1.2%	■
	B.1.525	VOI	0.4%	0.3-0.6%	■
	P.2	VOI	0.2%	0.1-0.3%	■
Other*	Other		3.2%	2.8-3.8%	■

* Other represents >200 additional lineages, which are each circulating at <1% of viruses

** Most recent data are subject to change as samples from that period are still being processed

† Fewer than 10 observations of this variant during the selected time/location context

CDC [CDC Variant Tracking]

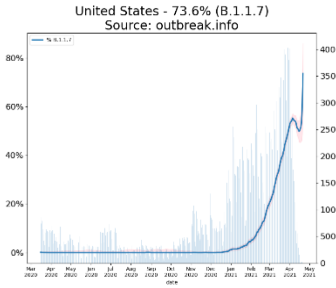


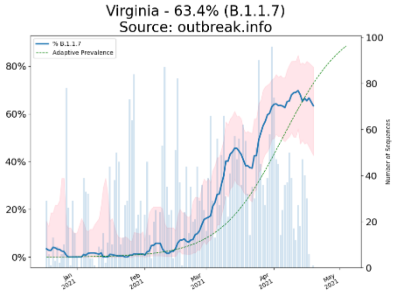
outbreak.info [Outbreak Info]

SARS-CoV2 Variants of Concern

Lineage B.1.1.7

- B.1.1.7 has been detected in Virginia and has continued to rapidly grow though has been hard to track. Currently estimated to account for over 2/3^{rds} of circulating virus in US and VA's volatile estimate is at 63%, likely higher

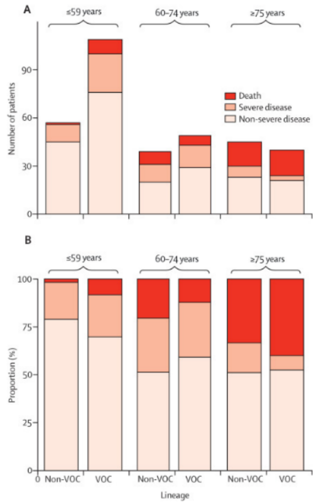

United States - 73.6% (B.1.1.7)
Source: outbreak.info


Virginia - 63.4% (B.1.1.7)
Source: outbreak.info

GISAID outbreak.info Outbreak Info

Transmissibility:

- Science study using two-strain model supports that increased transmissibility, duration of infectiousness, or increased transmission in children best fit the epi data observed in the UK across regions. Some combination of all also likely.
- Study from Public Health England shows contacts of B.1.1.7 cases are more likely (50%) to test positive than contacts of non-B.1.1.7 patients
- Study shows B.1.1.7 patients have longer periods of infection



Of 496 patients with samples positive for SARS-CoV-2 on PCR and who met inclusion criteria, 341 had samples that could be sequenced. 198 (58%) of 341 had B.1.1.7 infection and 143 (42%) had non-B.1.1.7 infection. We found no evidence of an association between severe disease and death and lineage (B.1.1.7 *vs* non-B.1.1.7) Lancet

Severity:

- Evidence continues to mount supporting increased risks of hospitalization and mortality for B.1.1.7 infected individuals
- 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 based on UK data estimates B.1.1.7 cases have 60% higher mortality
- Sequence based study of hospitalized patients in Lancet found no association with severity and death among hospitalized from B.1.1.7

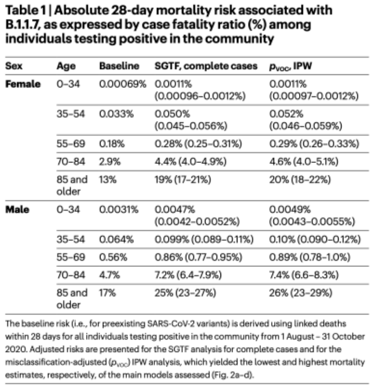
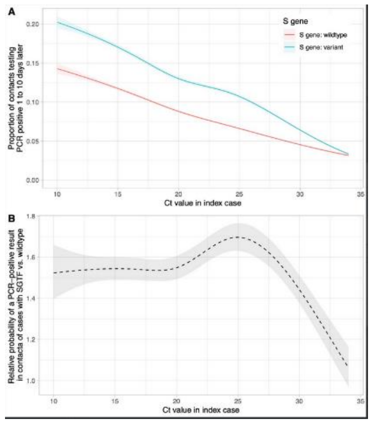


Table 1 | Absolute 28-day mortality risk associated with B.1.1.7, as expressed by case fatality ratio (%) among individuals testing positive in the community

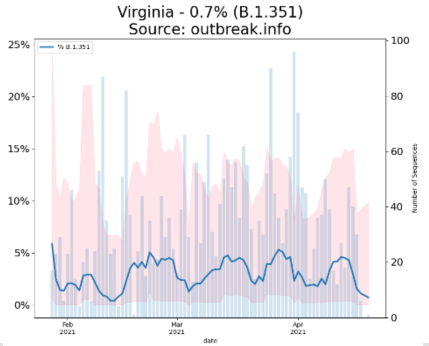
Sex	Age	Baseline	SGTF, complete cases	p_{VOC}, IPW
Female	0–34	0.00069%	0.0011% (0.00096–0.0012%)	0.0011% (0.00097–0.0012%)
	35–54	0.033%	0.050% (0.045–0.056%)	0.052% (0.046–0.059%)
	55–69	0.18%	0.28% (0.25–0.31%)	0.29% (0.26–0.33%)
	70–84	2.9%	4.4% (4.0–4.9%)	4.6% (4.0–5.1%)
	85 and older	13%	19% (17–21%)	20% (18–22%)
Male	0–34	0.0031%	0.0047% (0.0042–0.0052%)	0.0049% (0.0043–0.0055%)
	35–54	0.064%	0.099% (0.089–0.11%)	0.10% (0.090–0.12%)
	55–69	0.56%	0.86% (0.77–0.95%)	0.89% (0.78–1.0%)
	70–84	4.7%	7.2% (6.4–7.9%)	7.4% (6.6–8.3%)
	85 and older	17%	25% (23–27%)	26% (23–29%)

The baseline risk (i.e., for preexisting SARS-CoV-2 variants) is derived using linked deaths within 28 days for all individuals testing positive in the community from 1 August – 31 October 2020. Adjusted risks are presented for the SGTF analysis for complete cases and for the misclassification-adjusted (p_{VOC}) IPW analysis, which yielded the lowest and highest mortality estimates, respectively, of the main models assessed (Fig. 2a–d).



PCR testing in England from Sept 2020 – Feb 2021 combined with contact tracing data found B.1.1.7 cases to have higher viral loads (based on PCR cycle thresholds) and increased likelihood of causing infections among contacts. B.1.1.7 increased transmission by ~50%. Medrxiv

SARS-CoV2 Variants of Concern



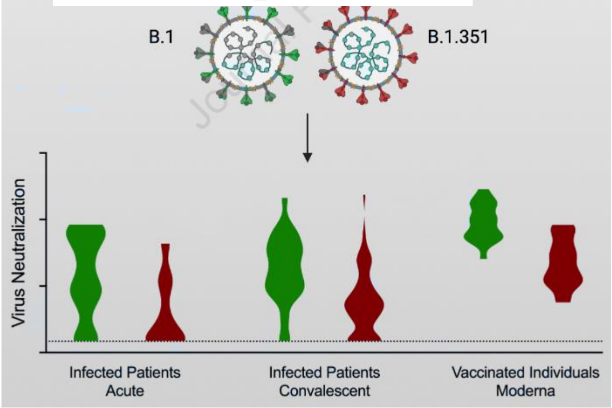
Outbreak Info

Lineage B.1.351

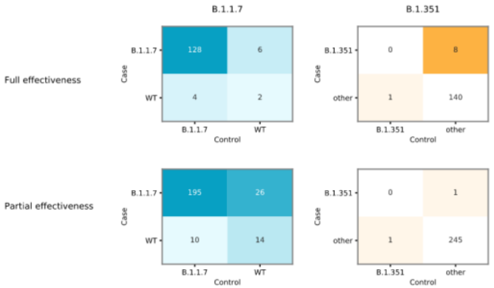
- Emerging strain initially identified in South Africa shows signs of vaccine escape, currently under 1% of circulating virus

Immune Escape:

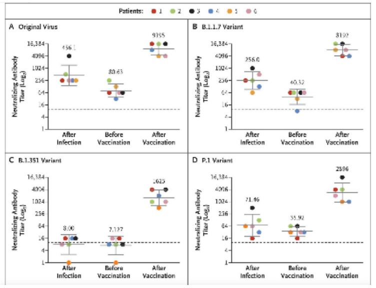
- Many studies show that convalescent sera from previously infected individuals does not neutralize B.1.351 virus well, however, vaccine induced immunity shows signs of effectiveness
- One study supports a previous study based on clinical trial data showing that convalescent serum neutralization is highly predictive of actual immune protection for infection
- Another study in Cell supports a previous report demonstrating that despite reduced antibody binding, the Moderna vaccinated individuals able to neutralize the B.1.351 variant
- New England Journal Study shows that for people with prior infections who are then vaccinated (one dose of Pfizer) the boosted immunity is effective against B.1.351
- Some evidence emerging that variants like B.1.351 may be more likely to cause secondary infections after vaccination. As more of the population is protected we may find B.1.351 and other immune evading variants becoming more prevalent.



Despite reduced antibody binding to the B.1.351 RBD, sera from infected (acute and convalescent) and Moderna (mRNA-1273) vaccinated individuals were still able to neutralize the SARS-CoV-2 B.1.351 variant. Cell



Small Case control study suggests that among those infected after their 1st and 2nd dose, they are more likely to be B.1.351 in the earlier infections, and B.1.1.7 in the later breakthrough infections. Medrxiv



Six patients previously infected with the original virus received the BNT162b2 vaccine. Before vaccination, they had neutralizing activity against the B.1.1.7 and P.1 variants but not B.1.351. After one dose, neutralizing activity against all variants increased greatly. NEJM

SARS-CoV2 Variants of Concern

Lineage P.1

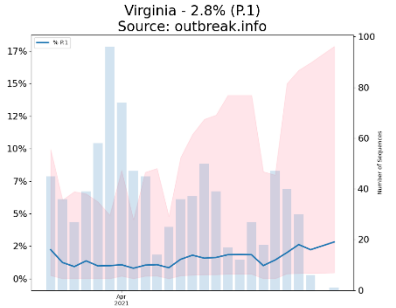
- At least 9.9% prevalence in US, thought a bit lower in VA (2.8%)
- [Data from Brazil]shows that P1 has maintained dominance in Rio despite B.1.1.7 being identified Jan 1st, and has remained at low levels

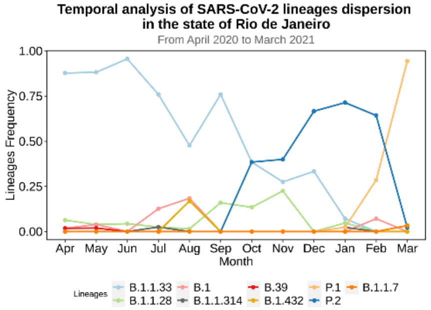
Lineage B.1.617

- Suspected of driving significant surge in India, and has mutations similar to other variants, appears more transmissible and able to evade immunity
- A few cases already identified in US, and [data show]rapidly increasing numbers in the UK (2.4% prevalence)
- [Preliminary study]from hard hit Maharashtra state shows vaccine induced and natural immunity convalescent sera can neutralize B.1.617 virus
- Initial analyses shows B.1.617 with E484Q mutation has a growth advantage over B.1.617 which in turn had advantage over B.1.1.7 and B.1.617 with E484Q mutation vs. B.1.

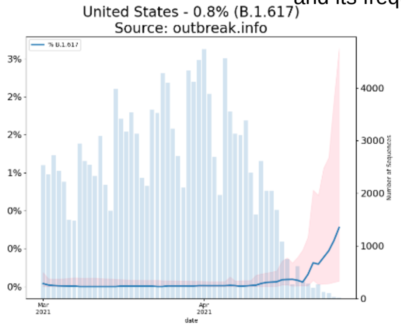
Lineage B.1.429/427 and B.1.526 and subvariants

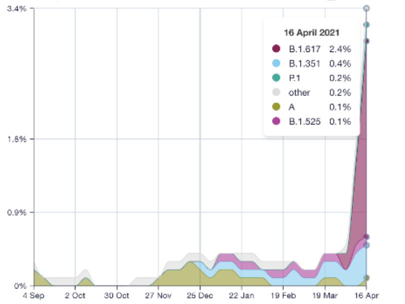
- Combined account for around 20% of circulating virus, share may be shrinking as B.1.1.7 outcompetes



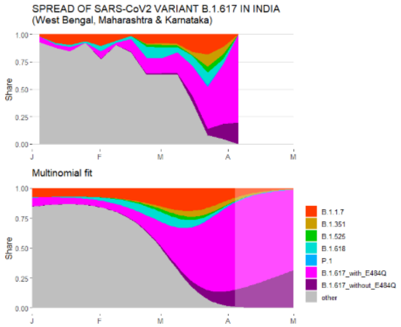


Currently, P.1 is the dominant lineage widespread across all regions in the State. B.1.1.7 lineage was first identified on January, 1st, 2021 and its frequency has remained low (total n=8) [virological.org]





Variants found in England through Sanger Institute sequences over time. Excludes traveller cases, surge testing and B.1.1.7. [Sanger]

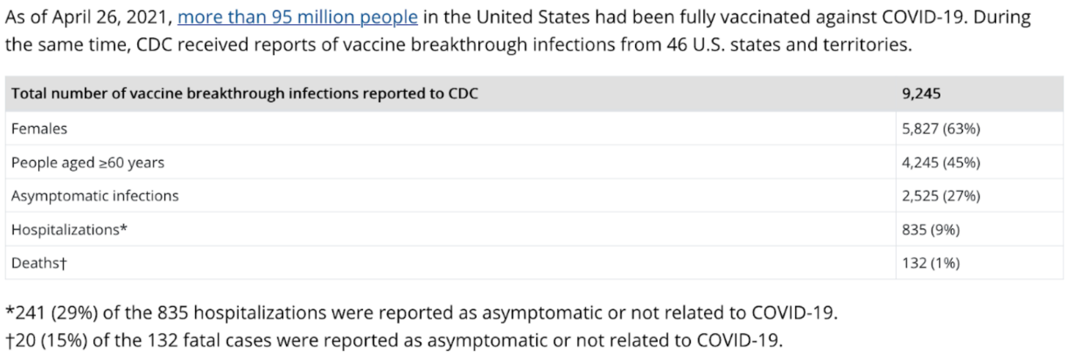


Growth advantage of B.1.617 rel to B.1.1.7 in Maharashtra, West Bengal & Karnataka similar to that of B.1.1.7 vs wild type in other countries. Based on multinomial fit to GISAID data: for B.1.617 with E484Q: 0.06 /d [0.03-0.09] 95% CLs, B.1.617 without E484Q: 0.11 /d [0.05-0.17].[https://twitter.com/twenseleers/status/1387409406753705985]

Vaccination Developments

Breakthroughs

- 9.2K reported infections among the 95M people fully vaccinated in the US
- 9% hospitalized, 1% mortality (some portion of these are due to non-COVID reasons)



As of April 26, 2021, more than 95 million people in the United States had been fully vaccinated against COVID-19. During the same time, CDC received reports of vaccine breakthrough infections from 46 U.S. states and territories.

Total number of vaccine breakthrough infections reported to CDC	9,245
Females	5,827 (63%)
People aged ≥60 years	4,245 (45%)
Asymptomatic infections	2,525 (27%)
Hospitalizations*	835 (9%)
Deaths†	132 (1%)

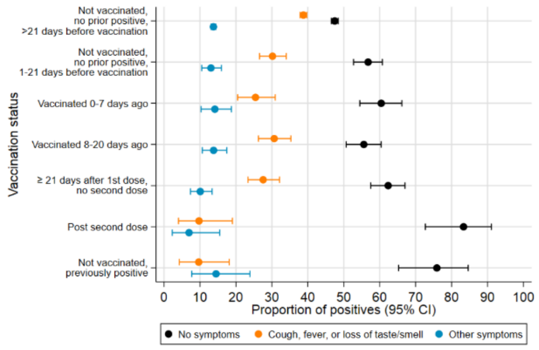
*241 (29%) of the 835 hospitalizations were reported as asymptomatic or not related to COVID-19.
†20 (15%) of the 132 fatal cases were reported as asymptomatic or not related to COVID-19.

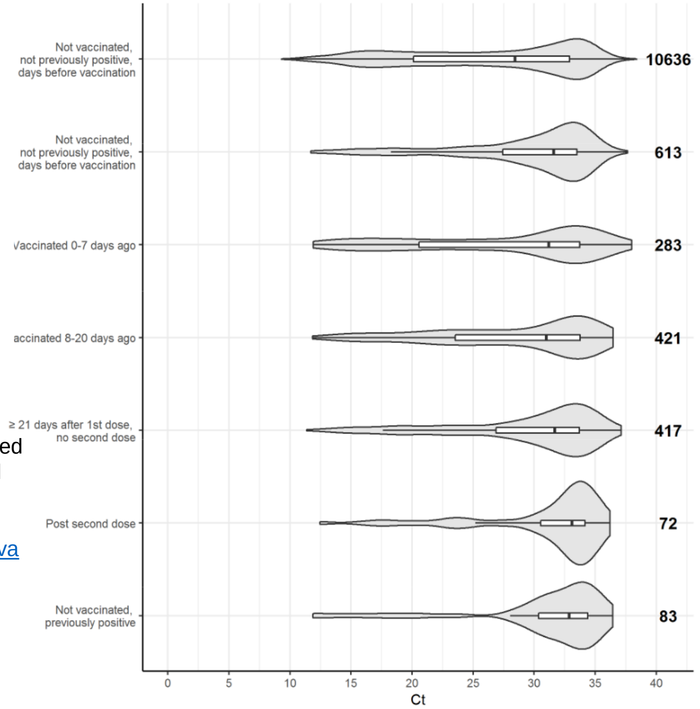
www.cdc.gov/vaccines/covid-19/health-departments/breakthrough-cases.html

Measured Reductions in Viral Load & Symptoms

- Recent study of breakthrough infections in the UK based on over 300K individuals providing PCR tests
- Full vaccination slightly stronger than natural immunity for eliminating symptoms and driving the lowest viral load
- Various combinations of timings after 1st dose are effective in reducing symptoms and limiting viral load, just not as effective as full vaccination or natural immunity
- Reduced viral loads in asymptomatic infections of vaccinated individuals suggest some effectiveness against on-going transmission

Figure 2: Percentage of symptoms in new positive episodes by vaccination status. Values given in **Supplementary Table 4**.





Greater reductions in symptomatic infections and/or infections with a higher viral burden are reflected in reduced rates of hospitalisations/deaths, but highlight the potential for limited ongoing transmission from asymptomatic infections in vaccinated individuals.
https://www.ndm.ox.ac.uk/files/coronavirus/ciscommunityvaccinationpaper20210417complete.pdf

Estimating Daily Reproductive Number

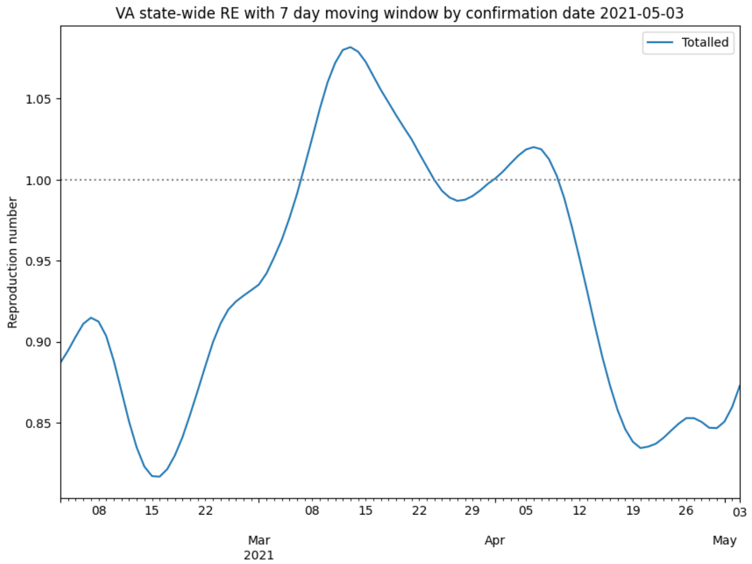
May 3rd Estimates

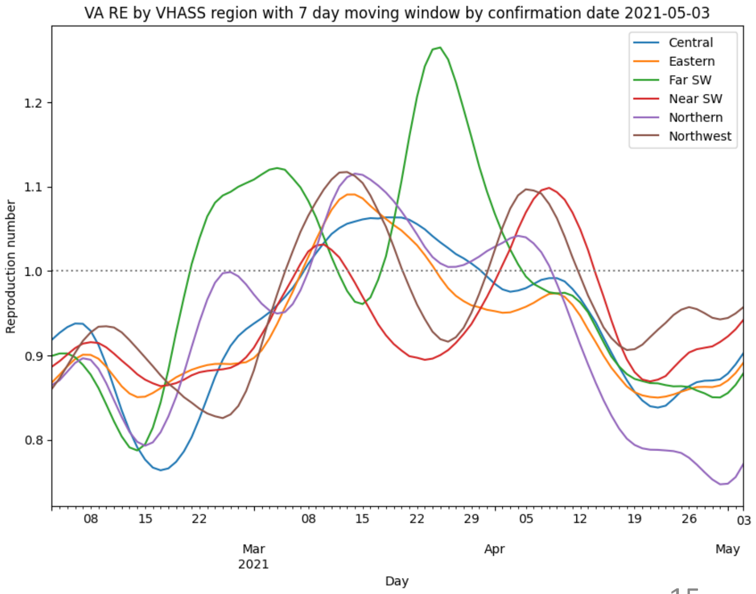
Region	Date Confirmed R_e	Date Confirmed Diff Last Week
State-wide	0.873	0.094
Central	0.903	0.115
Eastern	0.891	0.075
Far SW	0.879	0.063
Near SW	0.942	0.142
Northern	0.772	-0.008
Northwest	0.957	0.103

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

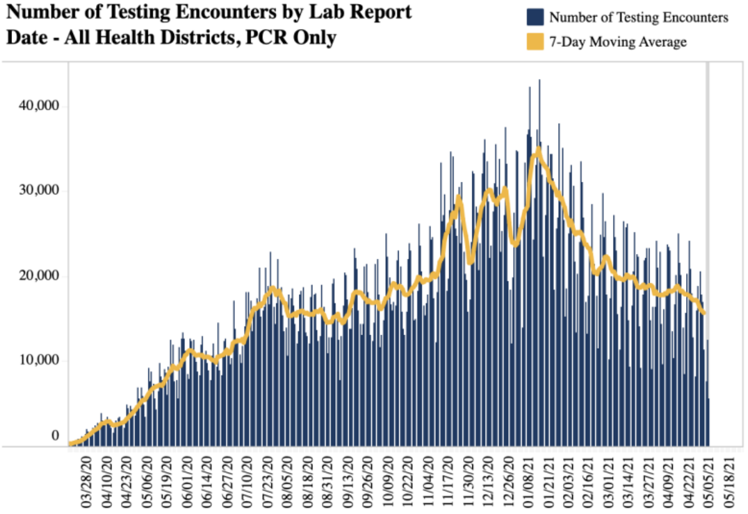
[1] Anne Cori, Neil M. Ferguson, Christophe Fraser, Simon Cauchemez. A New Framework and Software to Estimate Time-Varying Reproduction Numbers During Epidemics. American Journal of Epidemiology, Volume 178, Issue 9, 1 November 2013, Pages 1505–1512, https://doi.org/10.1093/aje/kwt133


VA state-wide RE with 7 day moving window by confirmation date 2021-05-03


VA RE by VHASS region with 7 day moving window by confirmation date 2021-05-03

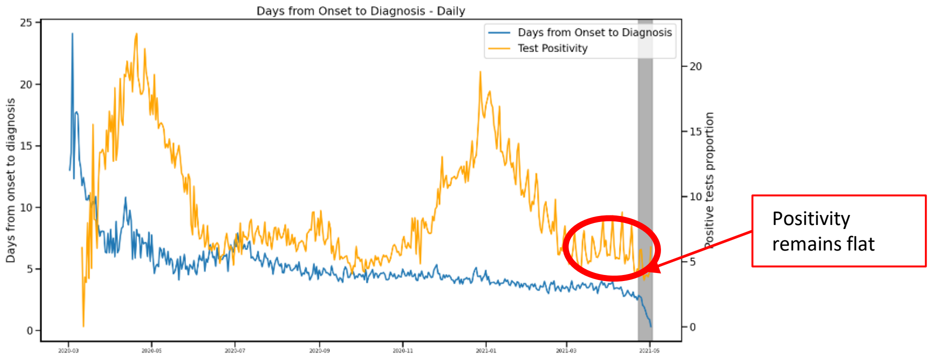
Changes in Case Detection

Timeframe (weeks)	Mean days	% difference from overall mean
July (26-30)	6.2	-3%
Aug (31-34)	4.9	-23%
Sept (35-38)	4.5	-28%
Oct (39-43)	4.5	-30%
Nov (44-47)	4.5	-29%
Dec (48-49)	4.2	-33%
Jan (00-04)	3.9	-38%
Feb (05-08)	3.5	-45%
Mar (09-13)	3.6	-44%
Apr (14-15)	3.2	-50%
Overall (13-12)	6.3	--

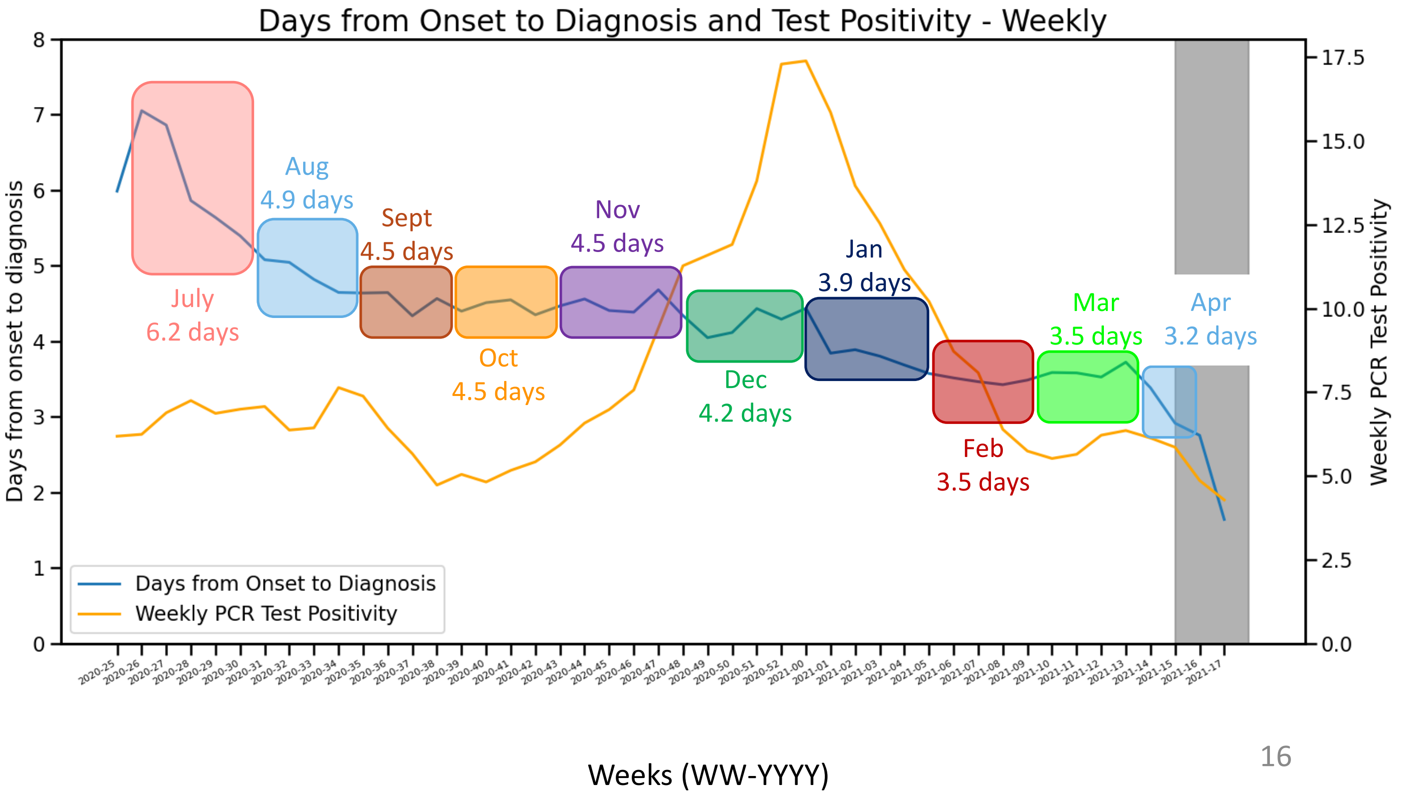


Accessed 9:30am May 5, 2021
https://www.vdh.virginia.gov/coronavirus/

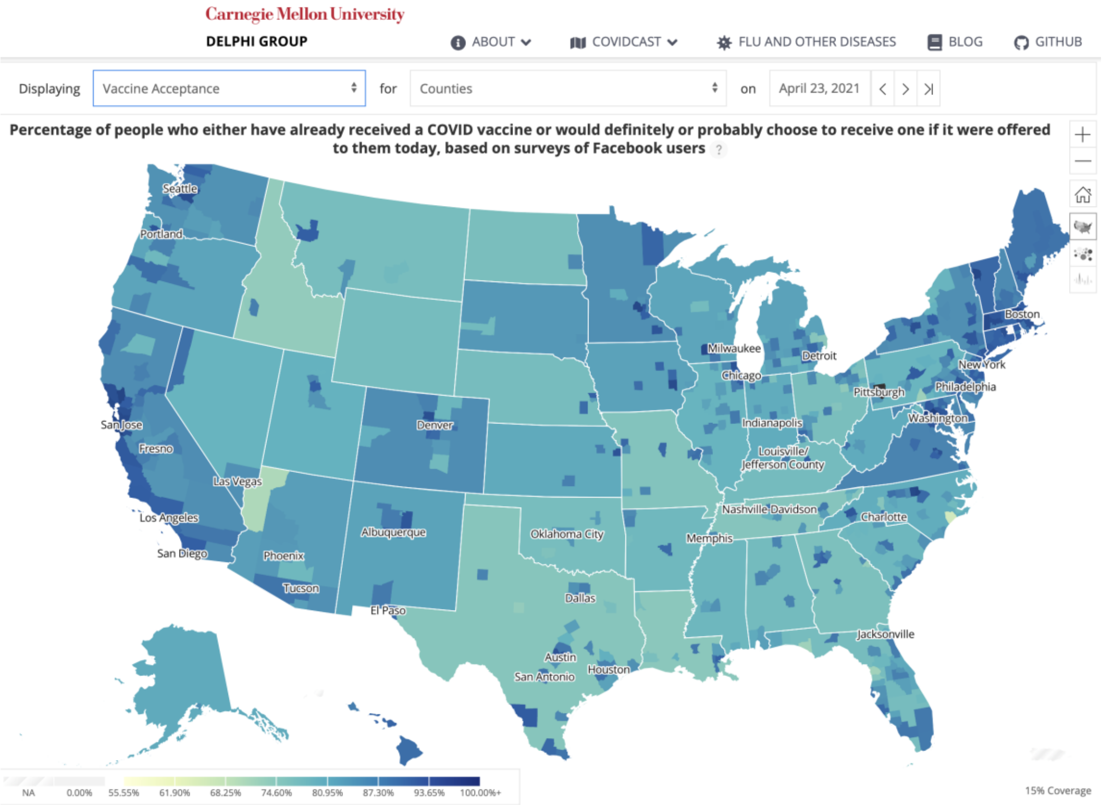
Test positivity vs. Onset to Diagnosis



Positivity remains flat

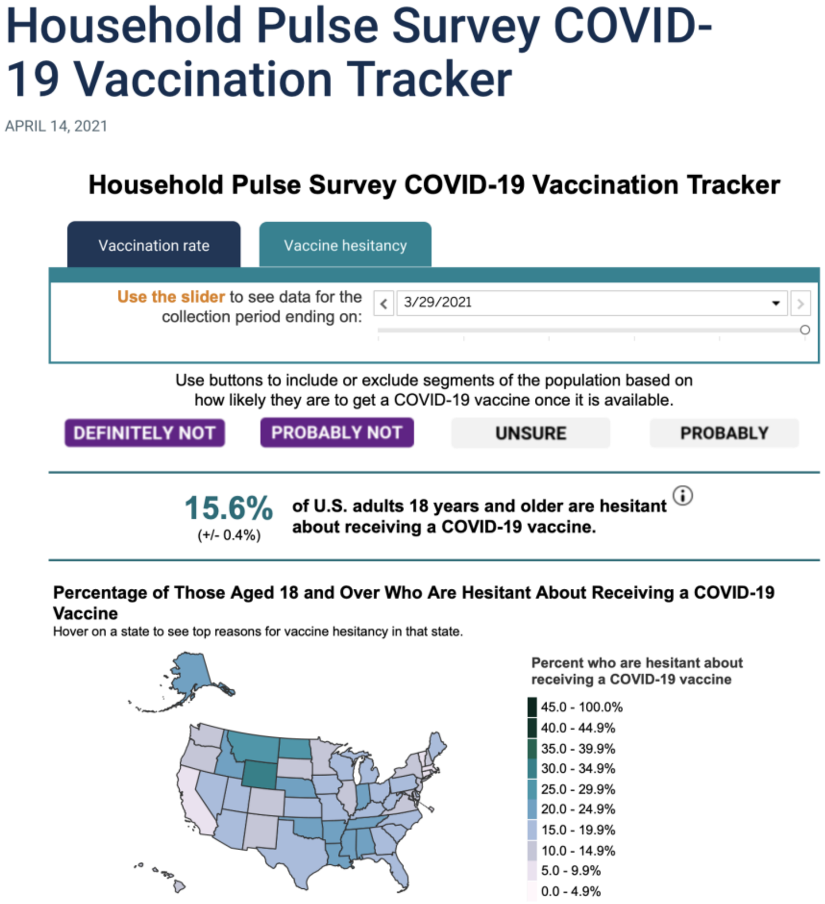


Vaccine Acceptance Data Sources



Displaying: Vaccine Acceptance for Counties on April 23, 2021

Percentage of people who either have already received a COVID vaccine or would definitely or probably choose to receive one if it were offered to them today, based on surveys of Facebook users



Household Pulse Survey COVID-19 Vaccination Tracker

APRIL 14, 2021

Household Pulse Survey COVID-19 Vaccination Tracker

Use the slider to see data for the collection period ending on: 3/29/2021

Use buttons to include or exclude segments of the population based on how likely they are to get a COVID-19 vaccine once it is available.

15.6% (+/- 0.4%) of U.S. adults 18 years and older are hesitant about receiving a COVID-19 vaccine.

Percentage of Those Aged 18 and Over Who Are Hesitant About Receiving a COVID-19 Vaccine

Hover on a state to see top reasons for vaccine hesitancy in that state.

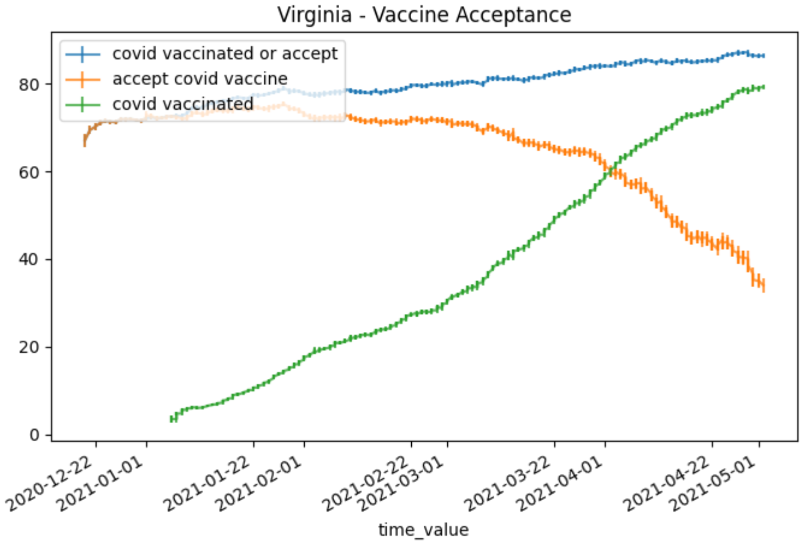
COVIDcast / Facebook Survey

https://covidcast.cmu.edu

Census Household Pulse Surveys (HPS)

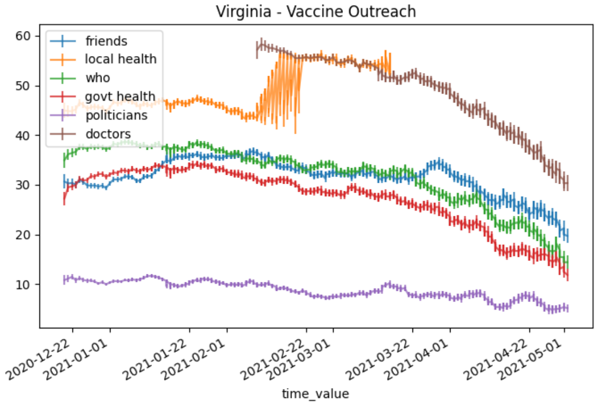
https://www.census.gov/library/visualizations/interactive/household-pulse-survey-covid-19-vaccination-tracker.html

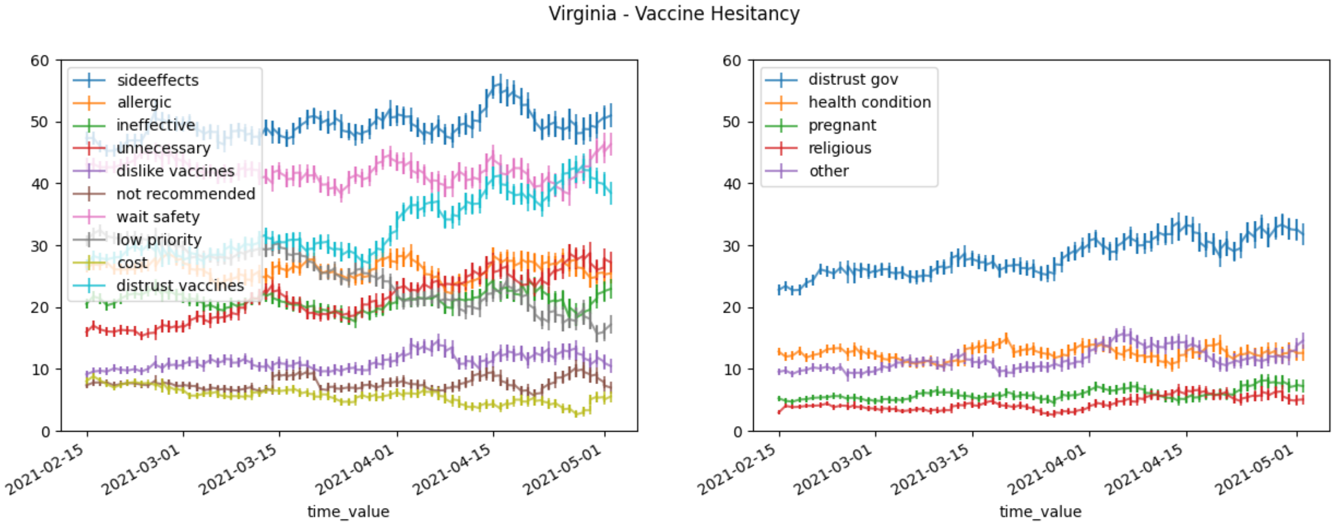
Vaccine Acceptance in Virginia - COVIDcast



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 ~70% reflecting some bias of the mechanism*
- Over 80% of Virginians have already or will choose to be vaccinated
- **Top reasons for hesitancy**: side effects, safety, distrust (increasing)
- **More likely to take if recommended by** doctors and friends





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

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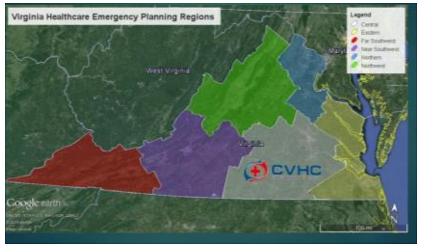
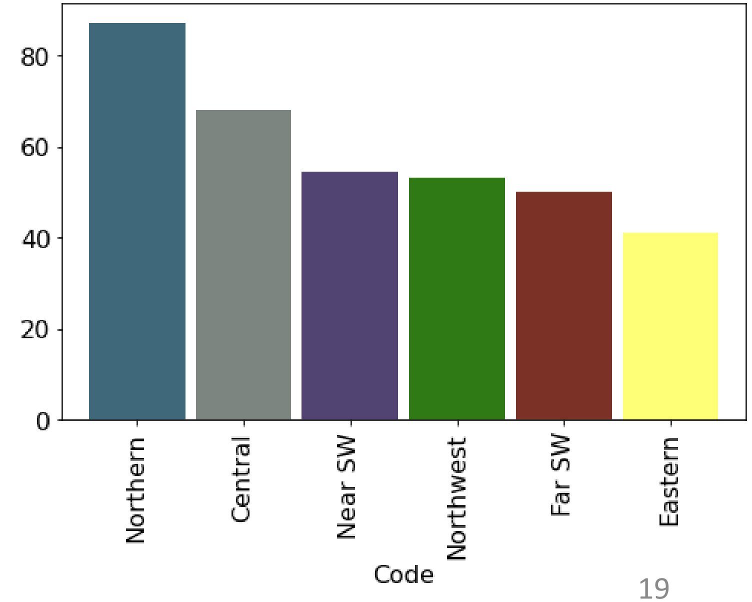
Vaccination Acceptance by Region

Combined Surveys:

- Facebook administered survey is timely and broad, but biased by who accesses Facebook and answers the survey
- Traditional phone-based survey administered several weeks ago for VDH vaccine messaging purposes is better sampled for true representativeness
- Correction approach:
  - Calculate an over-reporting fraction based on reported vaccinations (Apr 23-30) vs. VDH administration data
  - Cross-validate coarse corrections against traditional survey and found values were similar across regions, except in Eastern and Northwest which had more than 10% difference.
- Minor fluctuations compared to last week

Virginia Region	Vax Already or Accepting of Vaccine	Vax Already or Accepting of Vaccine (last week)
Northern	87%	88%
Central	68%	68%
Near Southwest	54%	47%
Northwest	53%	56%
Far Southwest	50%	53%
Eastern	41%	43%





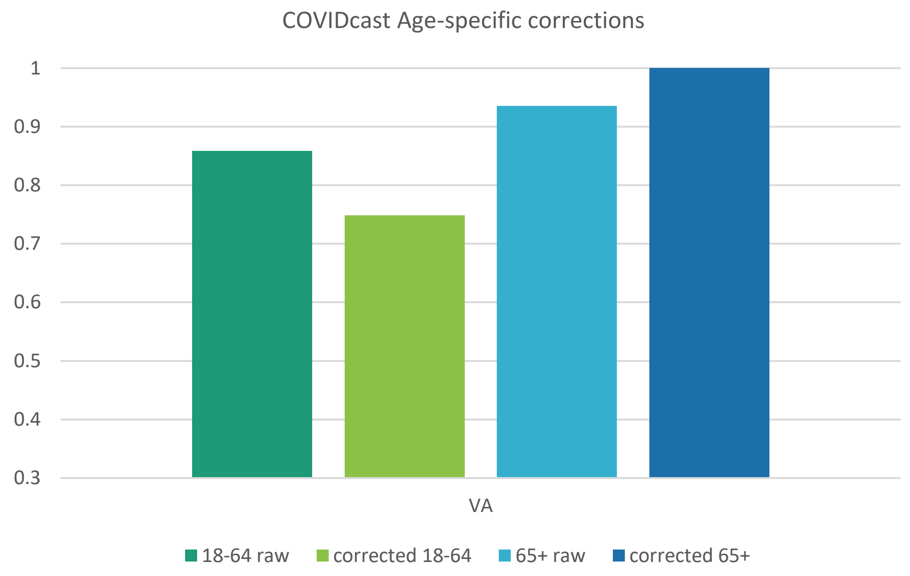
Data Source: https://covidcast.cmu.edu

Vaccination Acceptance - Age-Specific

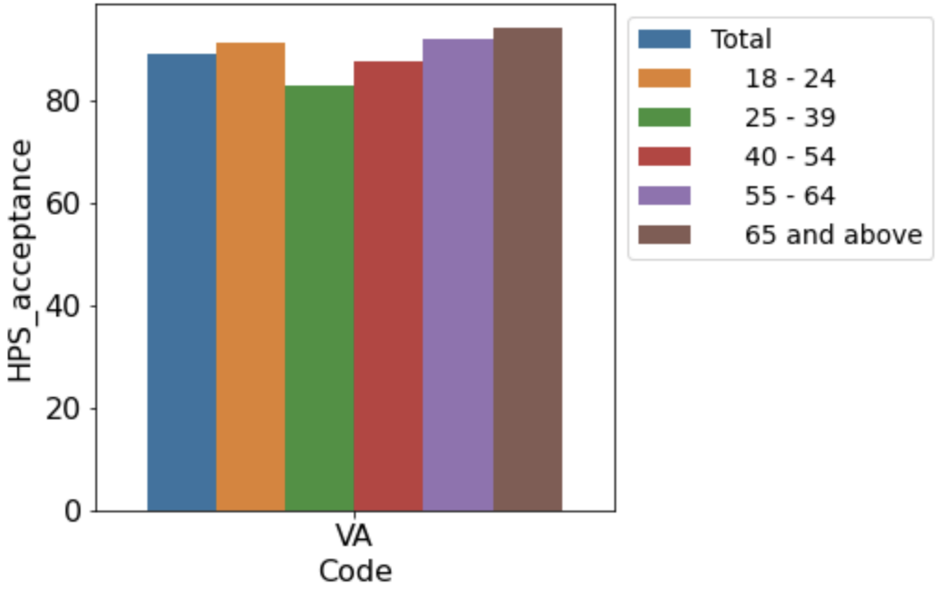
Acceptance levels across age-groups in Virginia:

- Oldest age-group the most accepting of vaccination, with the middle-aged the least
- COVIDcast represents results from last two weeks, can be adjusted to finer age ranges
- Household Pulse Survey last released for fortnight ending March 29th

COVIDcast with coarse age-breakdowns



HPS survey with finer grained age breakdown



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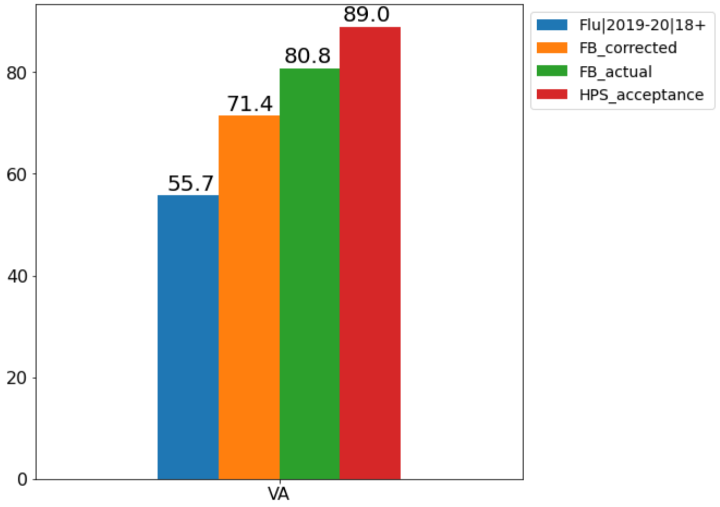
Vaccination Acceptance – Comparison of Sources

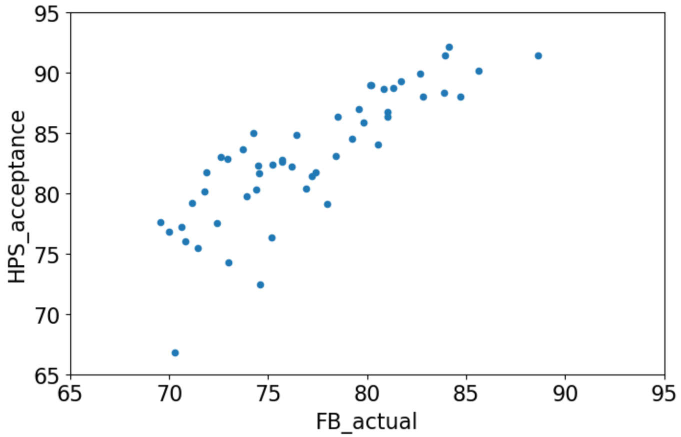
Measured acceptance varies across sources:

- **COVIDcast / Facebook (FB):** Both corrected and actual measurement
- **FluVax:** Acceptance levels in VA for influenza vaccine during 2019-20 flu season
- **Household Pulse (HPS):** Census administered survey, but with some time delay till release
- HPS has highest overall, while FluVax is expectedly the lowest
- Correlations between HPS and FB are reasonably high across states, with shifted values

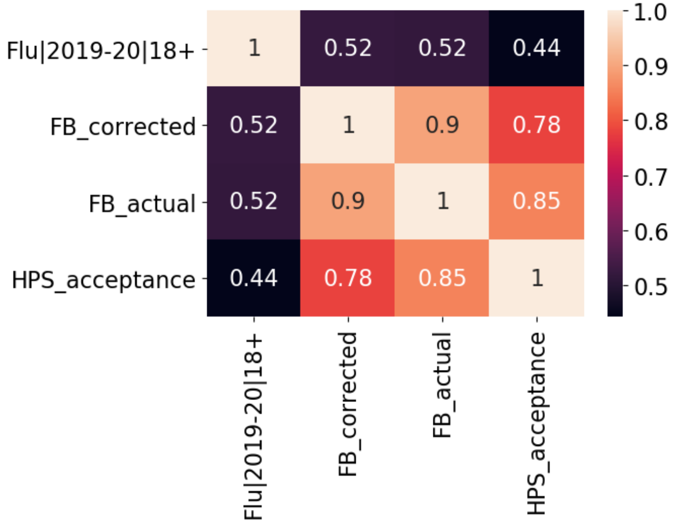
Virginia Vaccine Acceptance levels



State by State correlation COVIDcast and HPS



State level correlation between all four



	Flu|2019-20|18+	FB_corrected	FB_actual	HPS_acceptance
Flu|2019-20|18+	1	0.52	0.52	0.44
FB_corrected	0.52	1	0.9	0.78
FB_actual	0.52	0.9	1	0.85
HPS_acceptance	0.44	0.78	0.85	1

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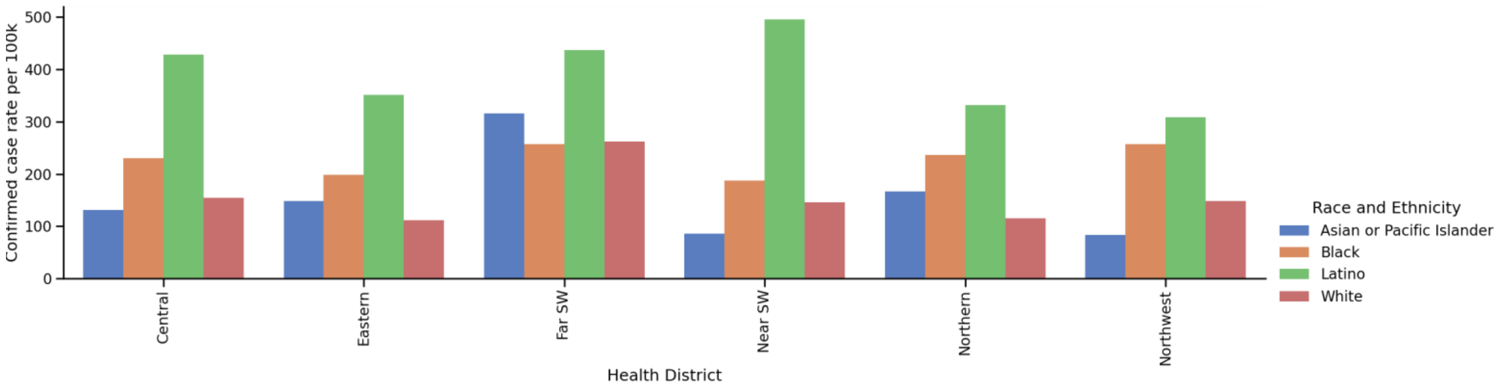
Race and Ethnicity – Recent Rate Changes (per 100K)

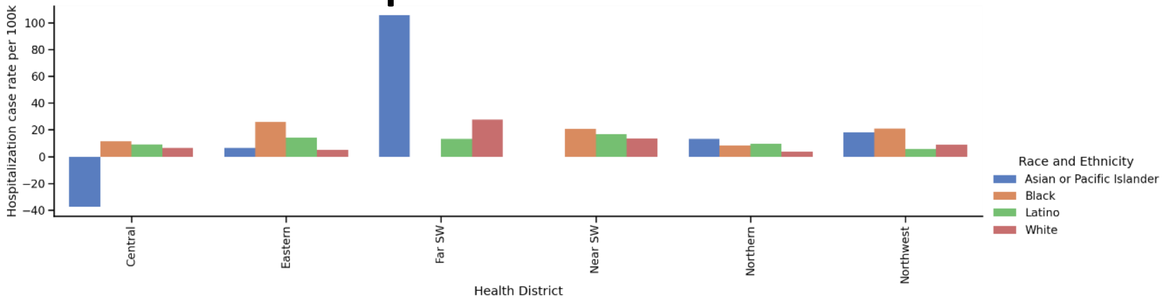
Changes in Race and Ethnicity Rates (per 100k) in past two weeks

- Two week change in population level rates
- Black, Latinx and 2 or more races populations have much higher changes in rates; disparity is more pronounced in some regions than others
- Based on 2019 census race-ethnicity data by county

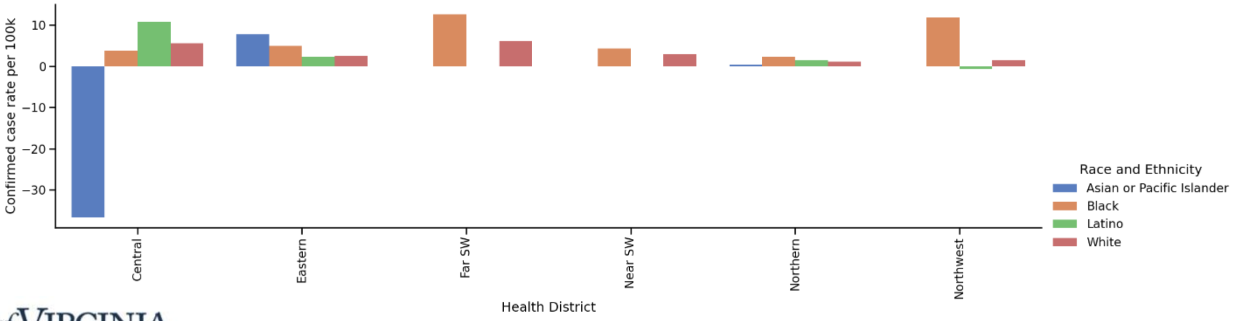
Case Rate



Hospitalization Rate



Death Rate



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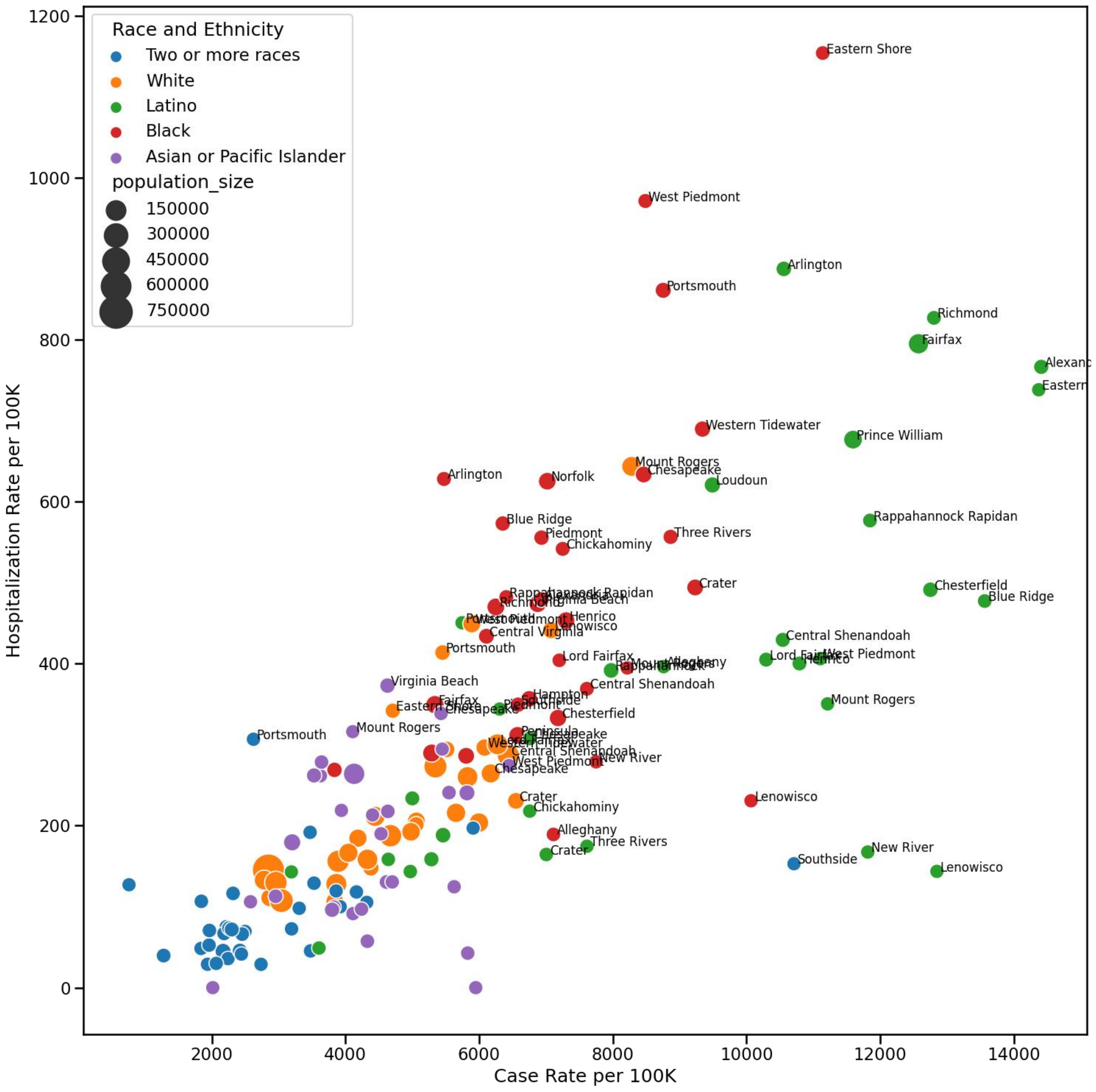
Race and Ethnicity cases per 100K

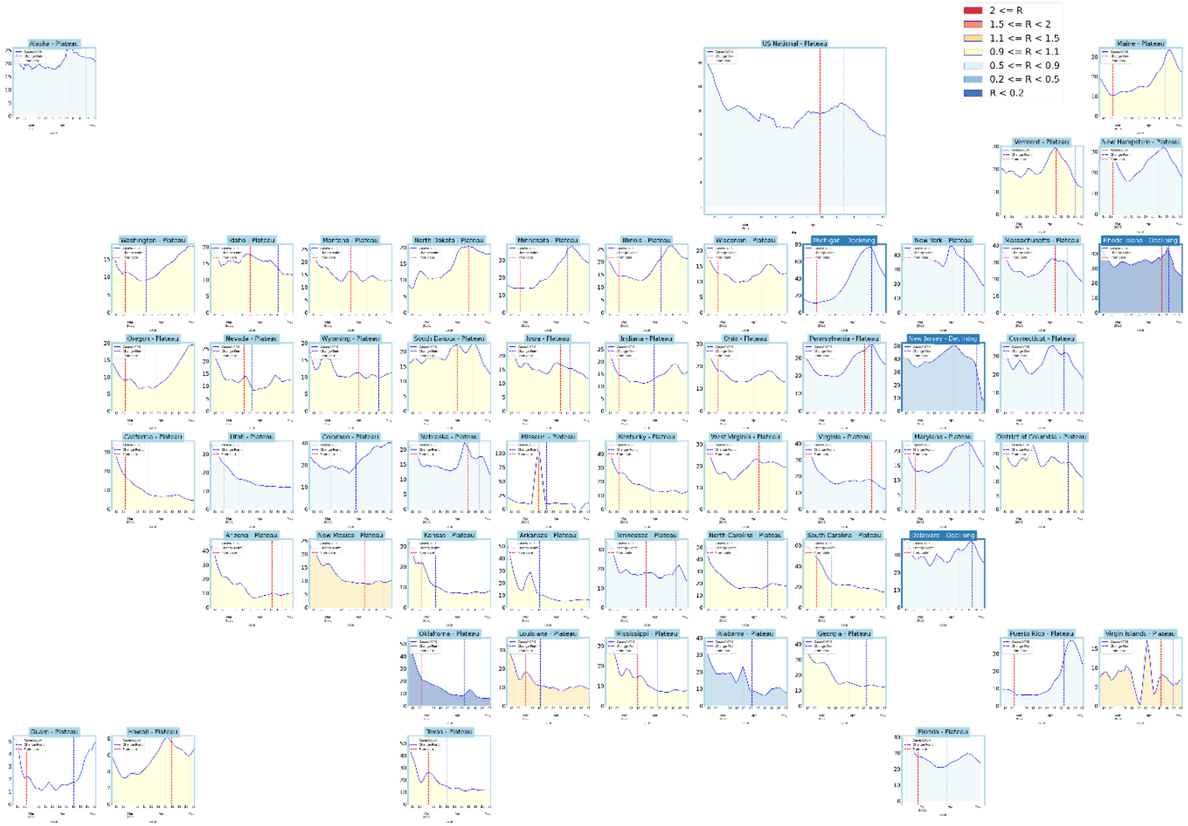


Rates per 100K of each Racial-Ethnic population by Health District

- 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)

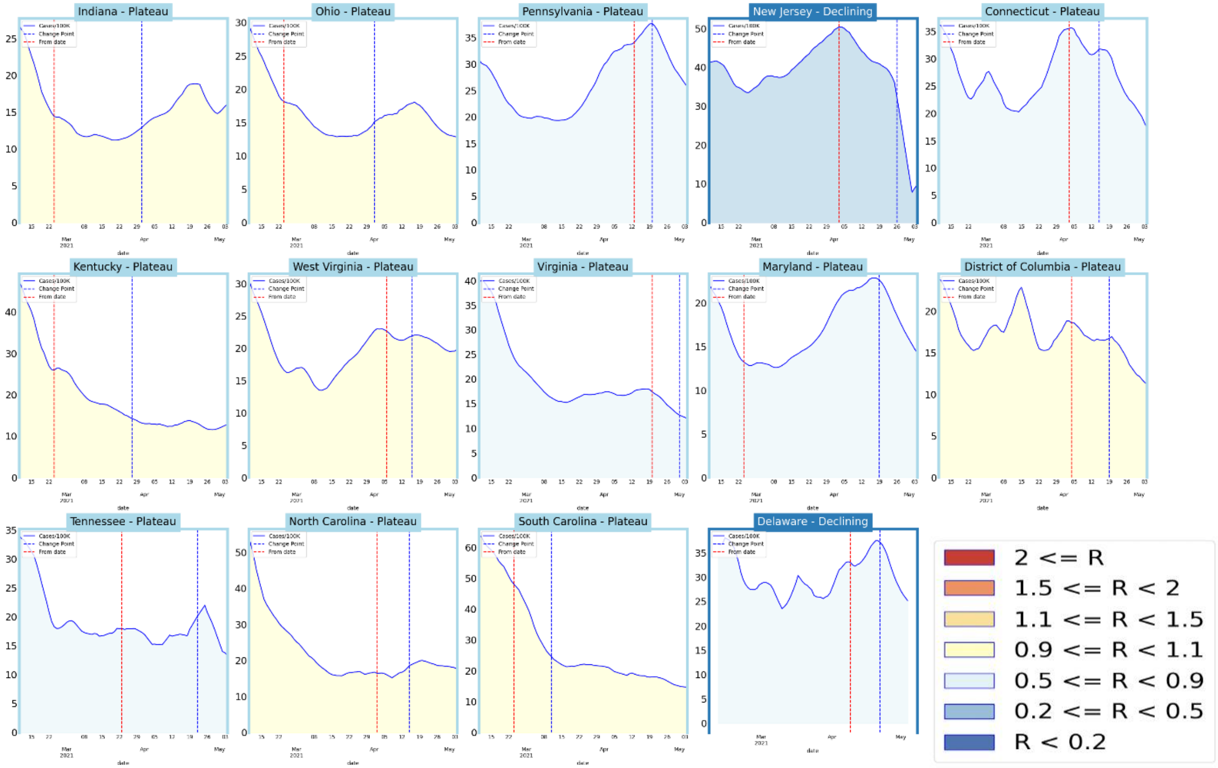
Other State Comparisons

Trajectories of States



- Nearly all states are plateaued, several now in significant decline
- Some states in West are growing but may be leveling off

Virginia and her neighbors



- VA and neighbors remain in plateau, with declines increasing their pace
- Levels remain high but are moderating

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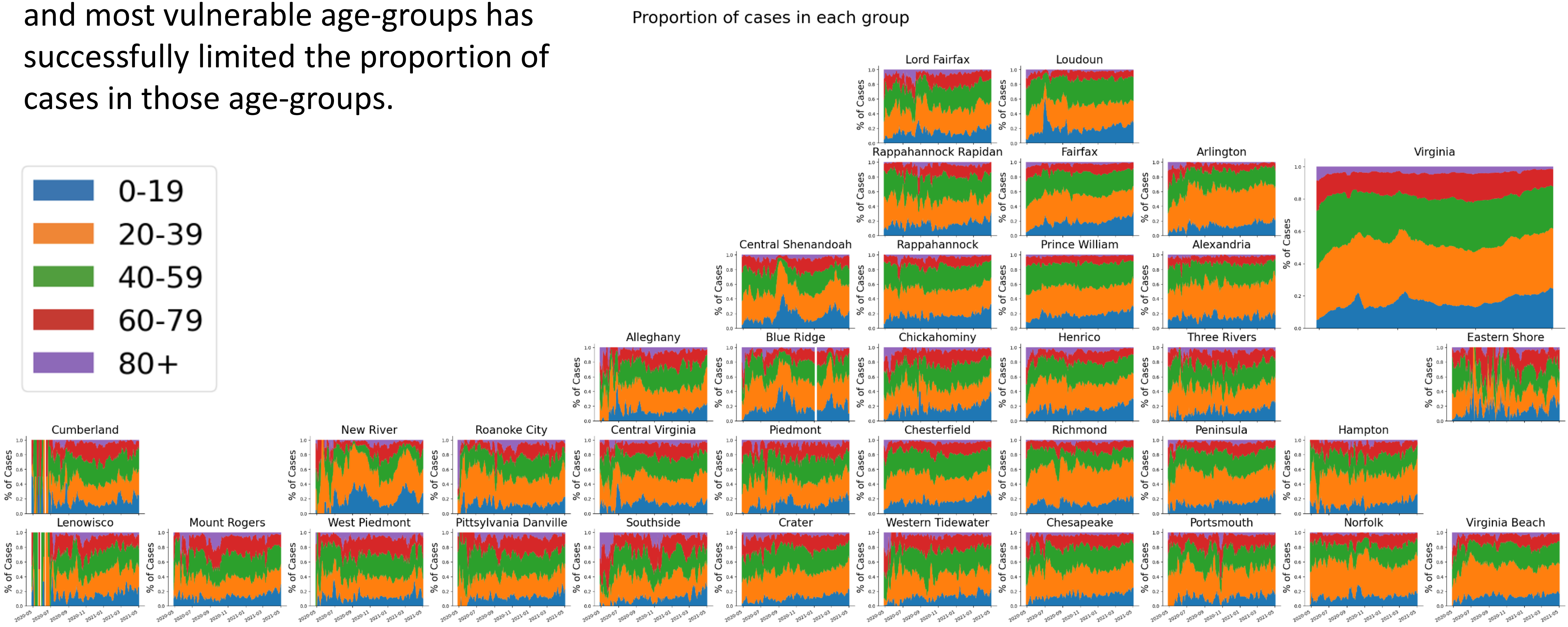
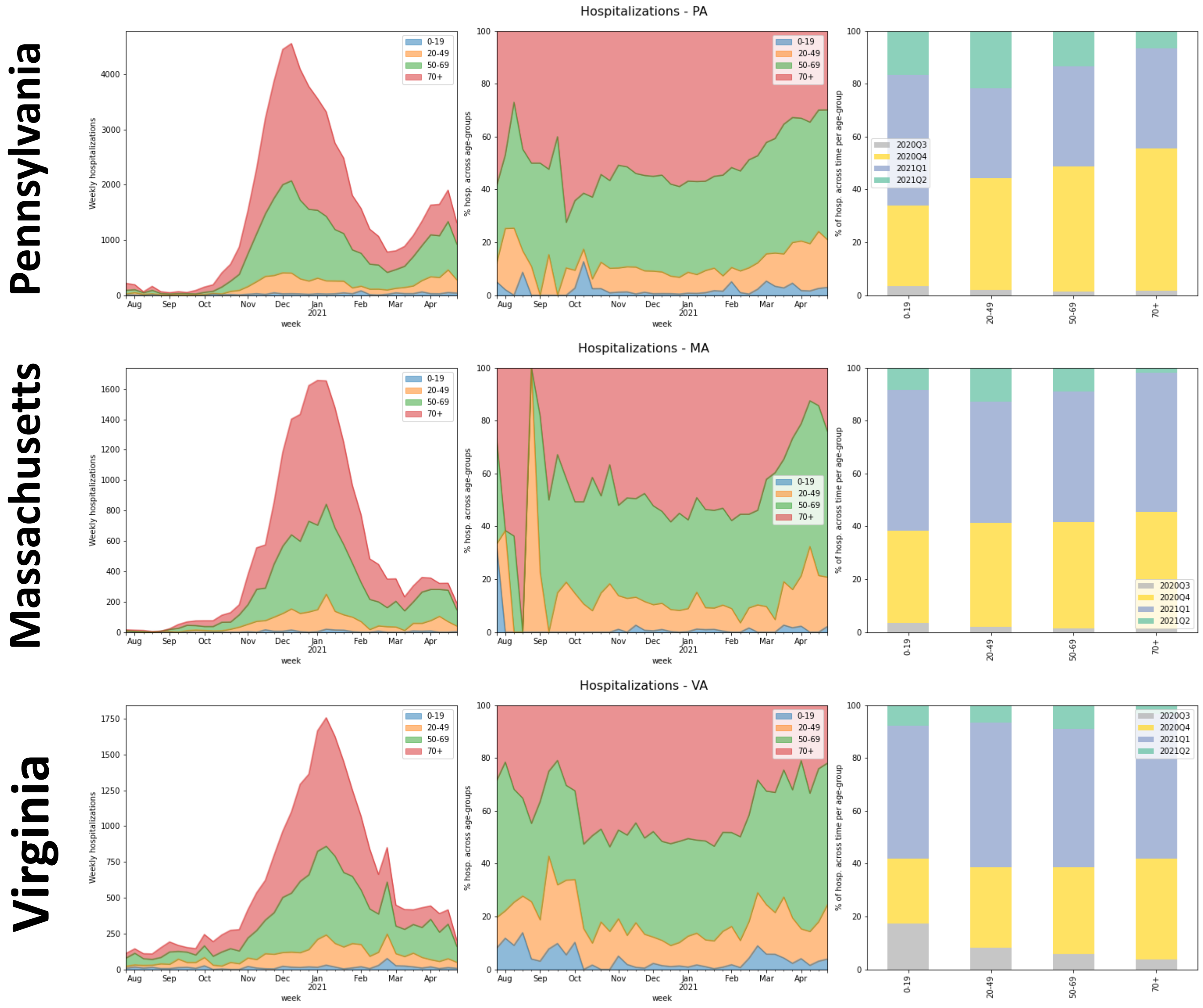
Shifting Age-Distribution – Cases within VA

Shifting Age Distribution of cases

- Vaccination prioritization to the older and most vulnerable age-groups has successfully limited the proportion of cases in those age-groups.



Shifting Age-Distributions - Hospitalizations



Shifting Age Distribution of cases being hospitalized

- Dual forces of vaccinations in older groups and severity of B.1.1.7 are shifting the age distribution of hospitalized patients
- Pennsylvania continues to make progress shrinking the share of 70+ hospitalized
- Massachusetts overall level has dropped significantly, though the share of 70+ has tipped up slightly
- Virginia has had a significant drop in hospitalizations as well, though the hospitalization proportions are relatively stable with a slowly shift younger

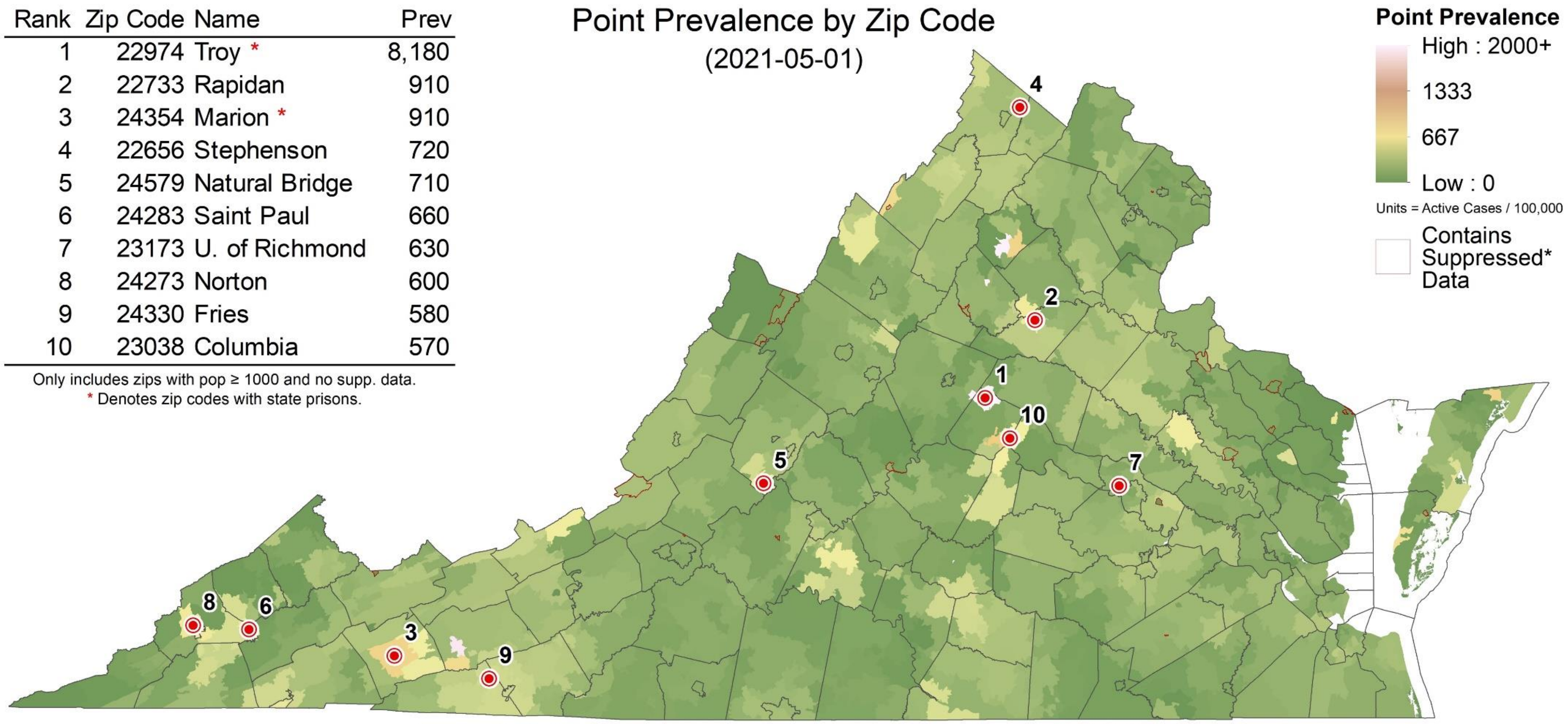
Zip code level weekly Case Rate (per 100K)

Case Rates in the last week by zip code

- Concentrations in Southwest, which was preceded by cluster of increased HCW rates last week
- Still some universities in top 10
- Some counts are low and suppressed to protect anonymity, those are shown in white

Rank	Zip Code	Name	Prev
1	22974	Troy *	8,180
2	22733	Rapidan	910
3	24354	Marion *	910
4	22656	Stephenson	720
5	24579	Natural Bridge	710
6	24283	Saint Paul	660
7	23173	U. of Richmond	630
8	24273	Norton	600
9	24330	Fries	580
10	23038	Columbia	570

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 2021-05-01.

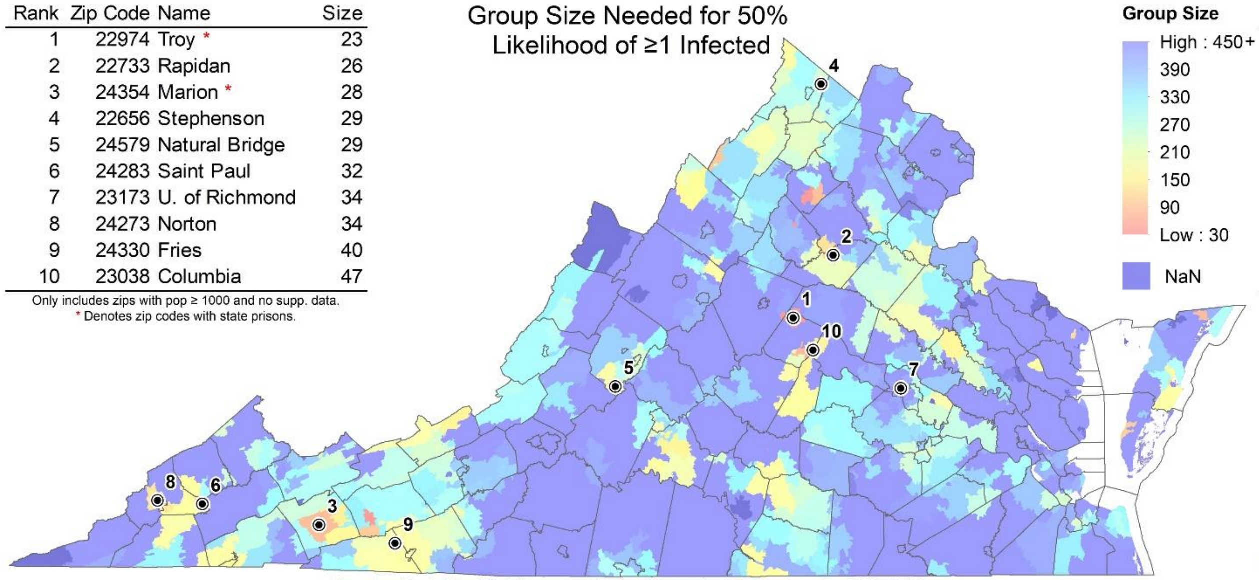
Risk of Exposure by Group Size and HCW prevalence

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 23 in Ruther Glen, 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

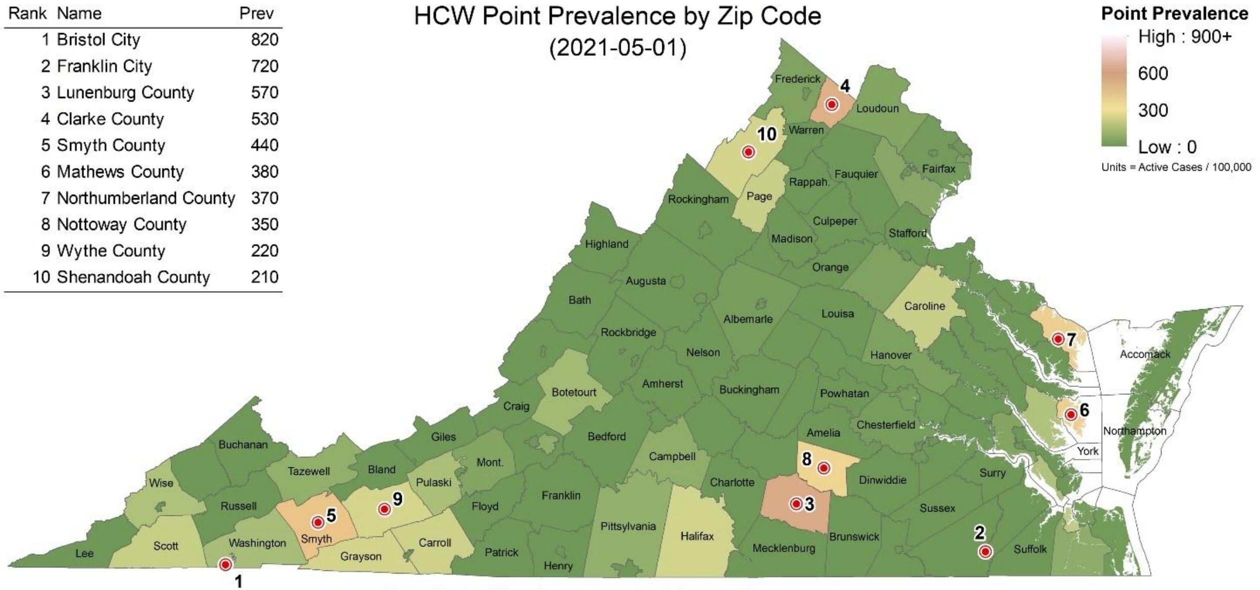
Rank	Zip Code	Name	Size
1	22974	Troy *	23
2	22733	Rapidan	26
3	24354	Marion *	28
4	22656	Stephenson	29
5	24579	Natural Bridge	29
6	24283	Saint Paul	32
7	23173	U. of Richmond	34
8	24273	Norton	34
9	24330	Fries	40
10	23038	Columbia	47

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 2021-05-01.

Rank	Name	Prev
1	Bristol City	820
2	Franklin City	720
3	Lunenburg County	570
4	Clarke County	530
5	Smyth County	440
6	Mathews County	380
7	Northumberland County	370
8	Nottoway County	350
9	Wythe County	220
10	Shenandoah County	210



Note: Scale differs from general public prevalence maps.

Current Hot-Spots

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

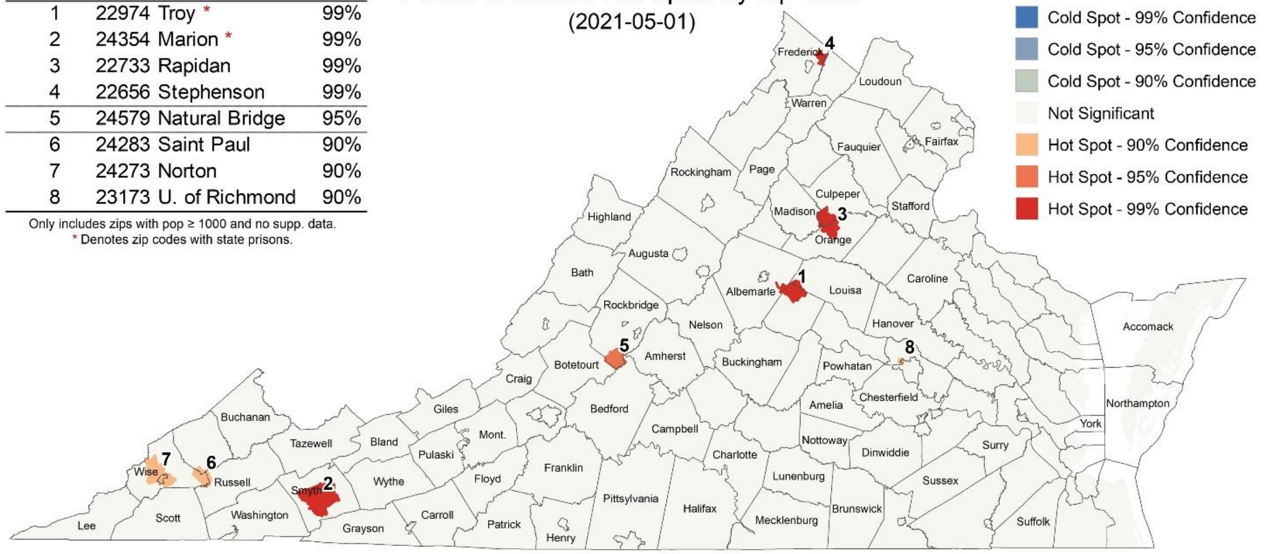
- **Spatial**: SaTScan based hot spots compare clusters of zip codes with weekly case prevalence higher than nearby zip codes to identify larger areas with statistically significant deviations
- **Temporal**: The weekly case rate (per 100K) projected last week compared to observed by county, which highlights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

Spatial Hotspots

Spot	Zip Code	Name	Conf.
1	22974	Troy *	99%
2	24354	Marion *	99%
3	22733	Rapidan	99%
4	22656	Stephenson	99%
5	24579	Natural Bridge	95%
6	24283	Saint Paul	90%
7	24273	Norton	90%
8	23173	U. of Richmond	90%

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

Point Prevalence Hot Spots by Zip Code
(2021-05-01)

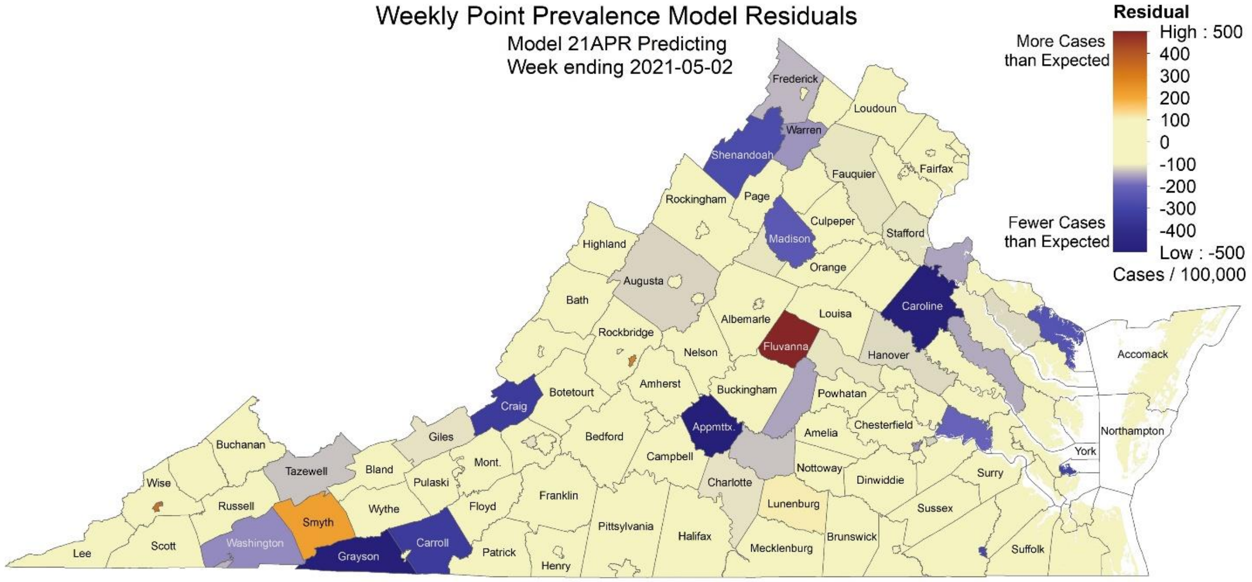


Based on Global Empirical Bayes smoothed point prevalence for week ending 2021-05-01.

Temporal Hotspots

Weekly Point Prevalence Model Residuals

Model 21APR Predicting
Week ending 2021-05-02

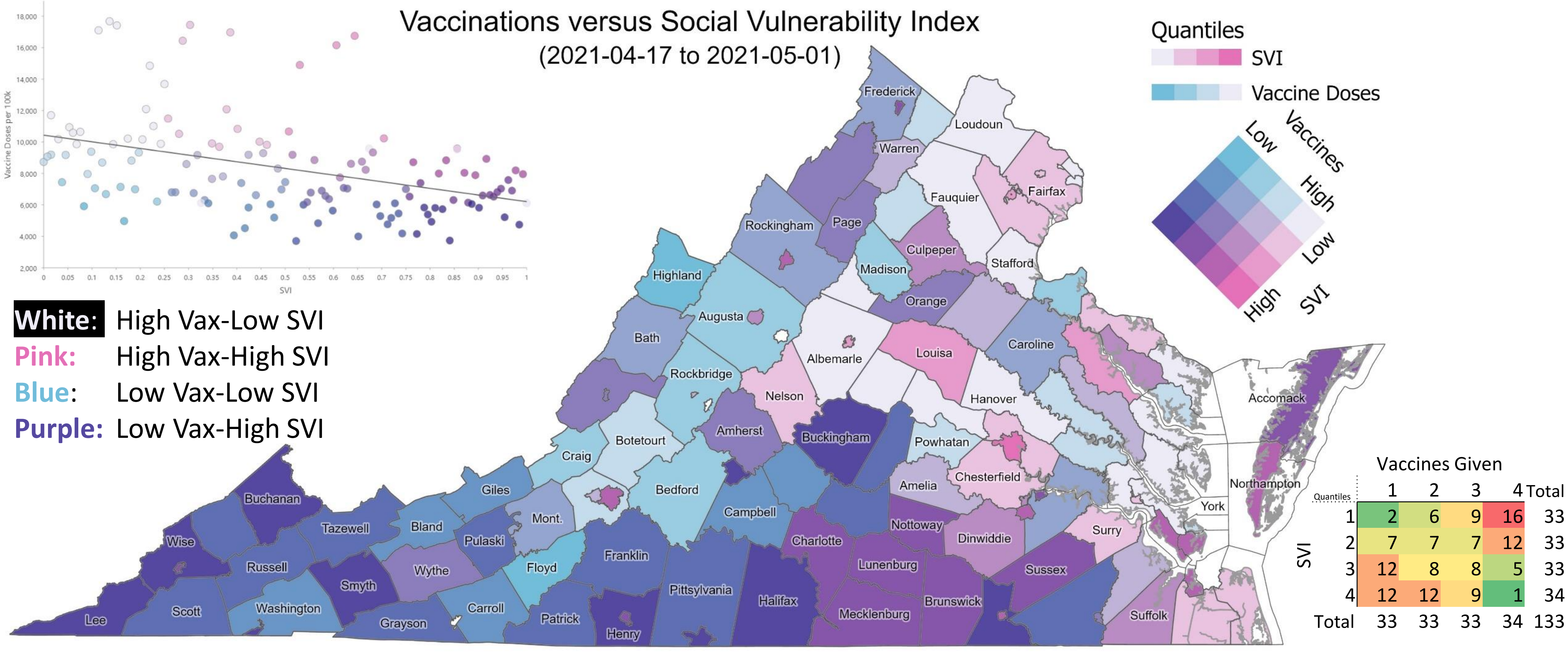


Moran's I = 0.034296, Z-Score = 0.587095, P-Value = 0.55714
No Residual Autocorrelation Detected

Social Vulnerability and Recent Vaccination Rates

Comparison of social vulnerability and vaccination rate in last 2 weeks by county

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



White: High Vax-Low SVI
Pink: High Vax-High SVI
Blue: Low Vax-Low SVI
Purple: Low Vax-High SVI

Vaccines Given

Quantiles		1	2	3	4	Total
SVI	1	2	6	9	16	33
	2	7	7	7	12	33
	3	12	8	8	5	33
	4	12	12	9	1	34
Total		33	33	33	34	133

Model Update – Adaptive Fitting

Adaptive Fitting Approach

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

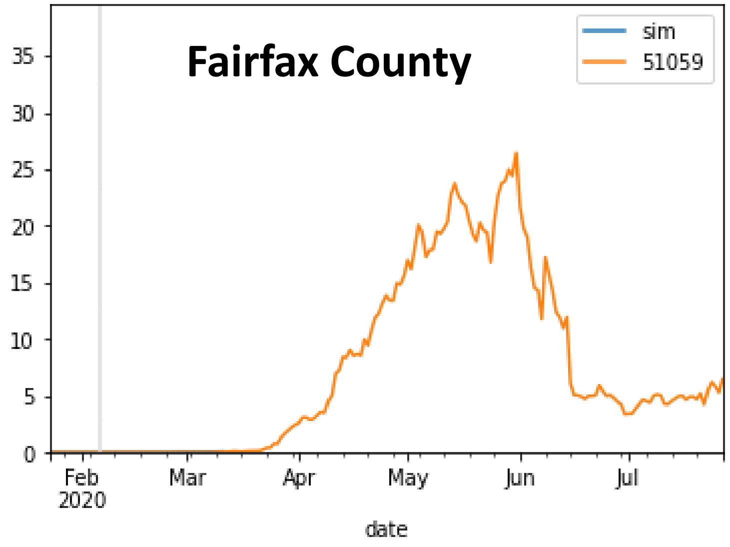
- Allows history to be precisely captured, and used to guide bounds on projections

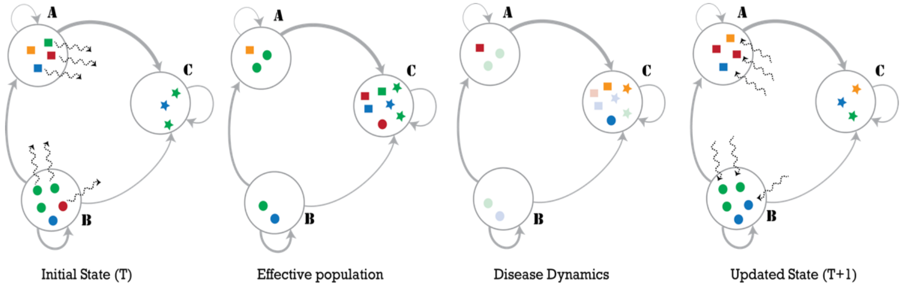
Model: An alternative use of the same meta-population model, PatchSim

  - 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





S → E → I → R

Susceptible → Exposed → Infectious → Removed

Using Ensemble Model to Guide Projections

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

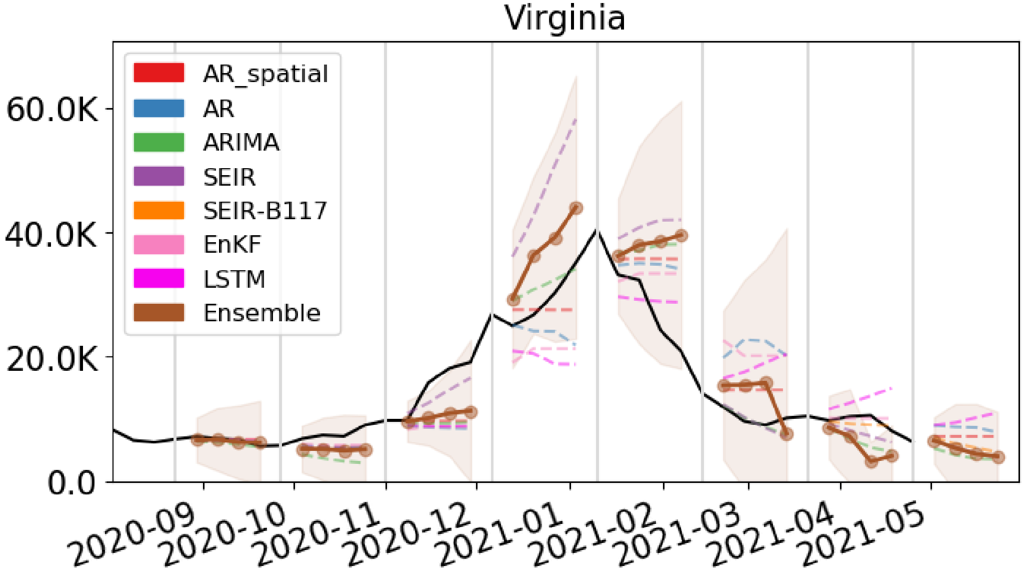
- Autoregressive (AR, ARIMA)
- Neural networks (LSTM)
- Kalman filtering (EnKF)

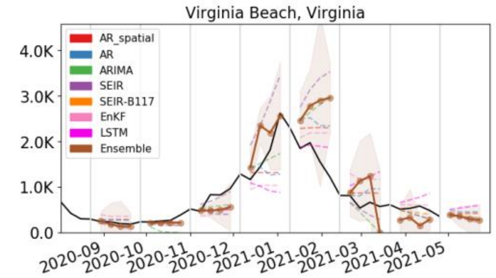
<ins>Weekly forecasts </ins>done at county level.

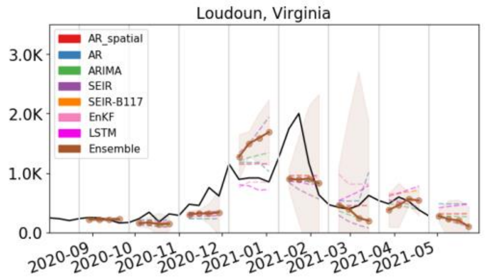
Models chosen because of their track record in disease forecasting and to increase diversity and robustness.

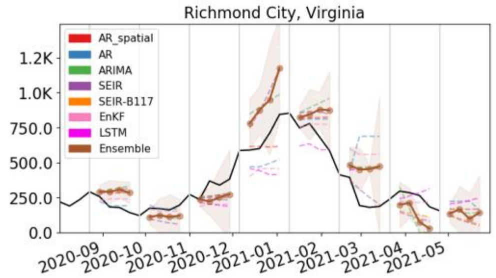
Ensemble forecast provides additional ‘surveillance’ for making scenario-based projections.

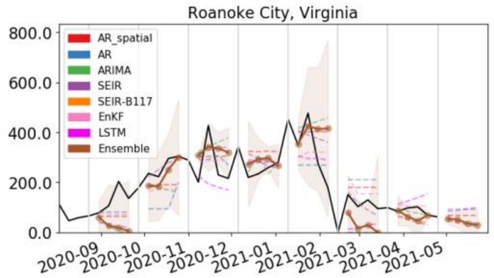
Also submitted to CDC Forecast Hub.











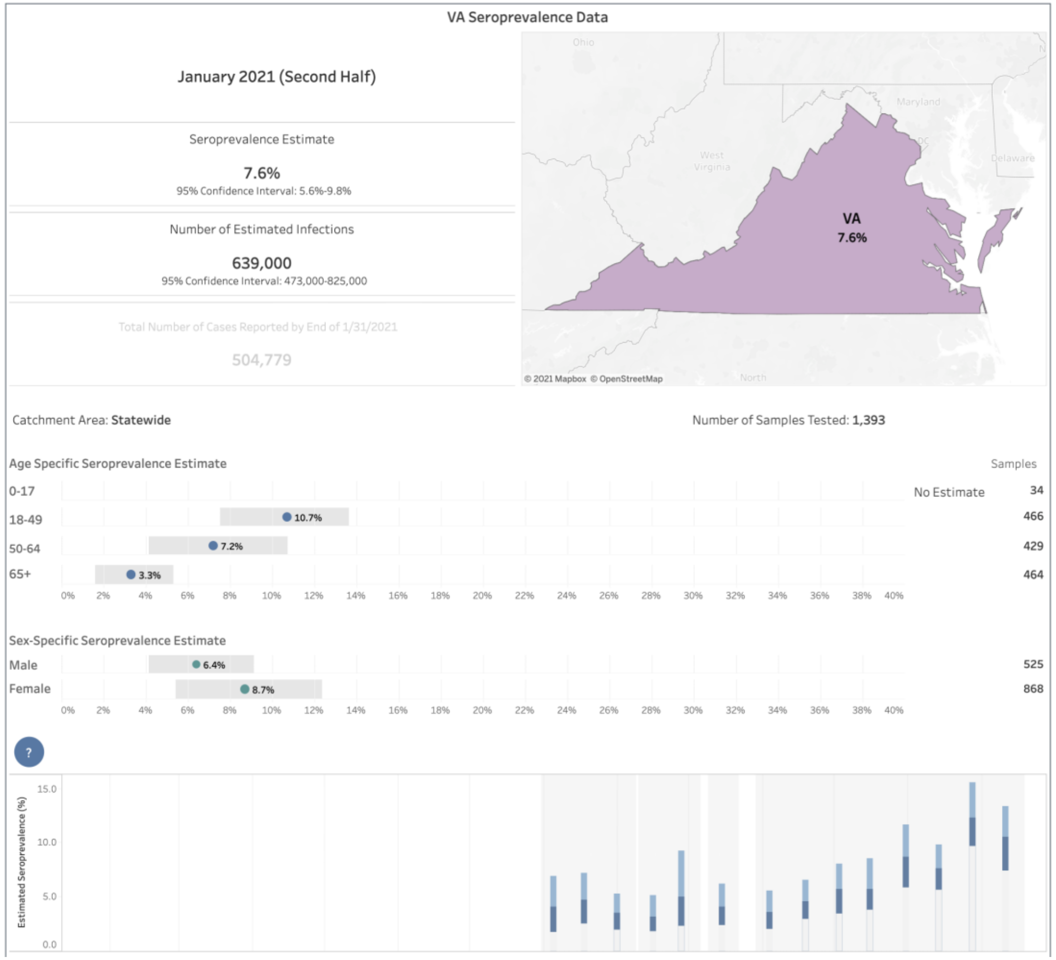
Seroprevalence updates to model design

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

- CDC Nationwide Commercial Laboratory Seroprevalence Survey estimated 7.6% [5.6% – 9.8%] seroprevalence as of Jan 7th – 21st up from 5.7% 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)



VA Seroprevalence Data

January 2021 (Second Half)

Seroprevalence Estimate

7.6%

95% Confidence Interval: 5.6%-9.8%

Number of Estimated Infections

639,000

95% Confidence Interval: 473,000-825,000

Total Number of Cases Reported by End of 1/31/2021

504,779

Catchment Area: **Statewide**

Number of Samples Tested: **1,393**

Age Specific Seroprevalence Estimate

		Samples
0-17	No Estimate	34
18-49	10.7%	466
50-64	7.2%	429
65+	3.3%	464

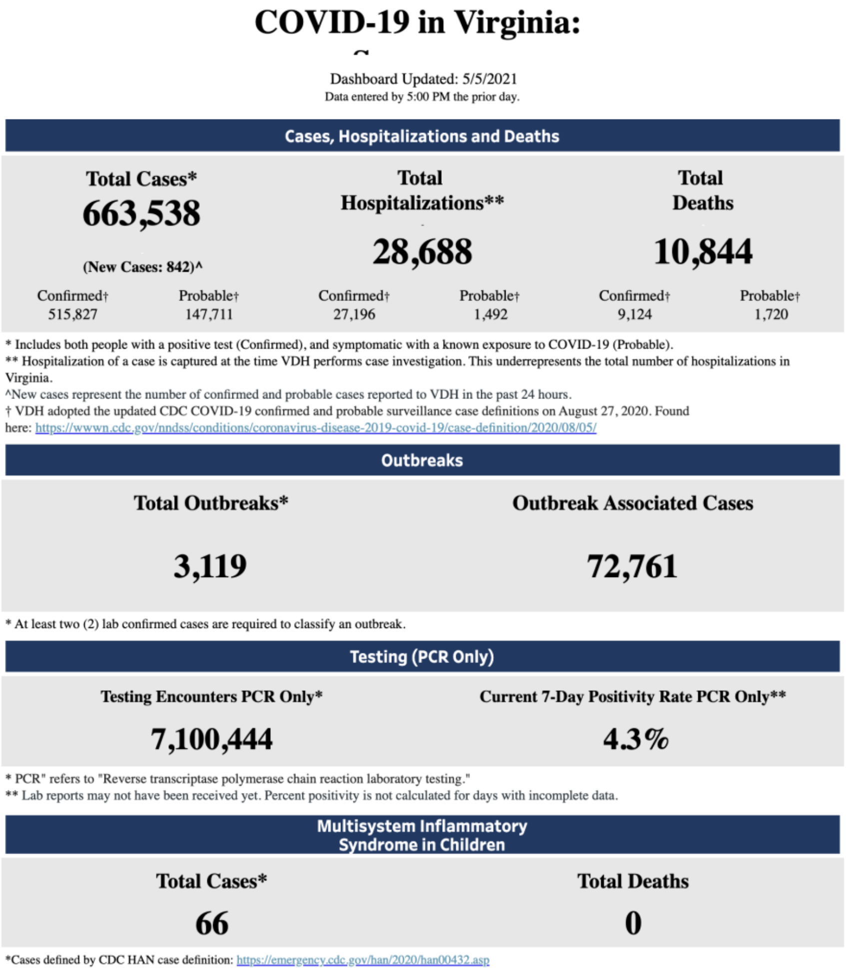
Sex-Specific Seroprevalence Estimate

Male	6.4%	525
Female	8.7%	868

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: 5/5/2021
Data entered by 5:00 PM the prior day.

Cases, Hospitalizations and Deaths

Total Cases*		**Total Hospitalizations****		**Total Deaths**	
663,538		**28,688**		**10,844**	
(New Cases: 842)^					
Confirmed†	Probable†	Confirmed†	Probable†	Confirmed†	Probable†
515,827	147,711	27,196	1,492	9,124	1,720

* 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**
3,119	**72,761**

* 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****
7,100,444	**4.3%**

* 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**
66	**0**

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

Accessed 9:30am May 5, 2021

https://www.vdh.virginia.gov/coronavirus/

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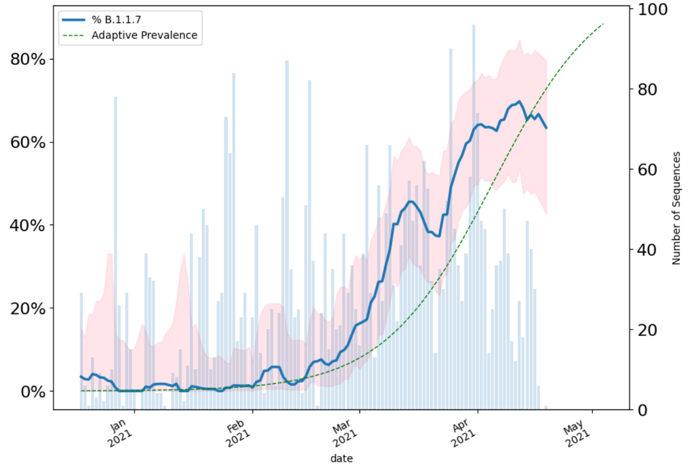
Scenarios – Transmission Control

- 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. BestPast from May 1, 2020 – present; FatigueControl from May 1, 2020 – Sept 1, 2020 or current whichever is highest.
  - Use the highest and lowest levels experienced (excluding outliers) as plausible bounds for levels of control achievable
  - Transition from current levels of projection to the new levels over 2 months
  - BestPast Control starts with 3 week delay to account for transition to higher levels of control
- Projection Scenario:
  - **BestPast Control:** Lowest level of transmission (5th percentile)
  - **Fatigued Control**: Highest level of transmission (95th percentile) increased by additional 5%

Scenarios – Variant B.1.17

- New Variant B.1.1.7 is best understood and is in Virginia
  - **Transmission increase**: 50% increase from the current baseline projection based on estimated prevalence in past and future
  - **Increased Severity**: 60% increase in likelihood of hospitalization and a 60% increase in mortality Nature
  - **Emergence timing:** Gradual frequency increase reaching 50% frequency on April 5th, a couple weeks after the national estimate in MMWR report from CDC and refined by Andersen et al.
- Variant planning Scenario:
  - **DominantB117**: Current projected transmissibility continues to increase through June to a level 50% more transmissible

Virginia - 63.4% (B.1.1.7)
Source: outbreak.info

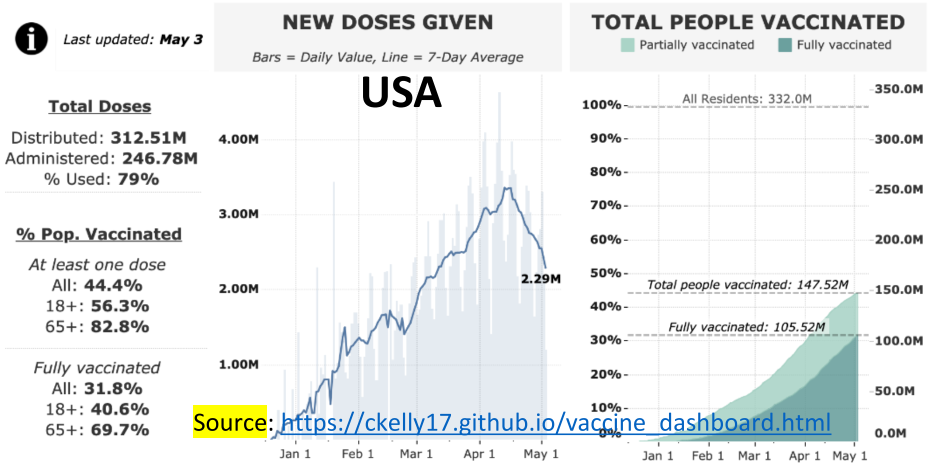


Estimated frequency from public genome repository with added analysis: 63%
Current frequency used in model: 86%

Outbreak Info

Scenarios – Vaccines

- Projected vaccine schedules constructed using current administration rates by dose and manufacturer for VA counties.
- Assumed vaccine efficacies
  - **Pfizer/Moderna**: 50% after first dose, 95% after second dose (3.5 week gap between doses)
  - **J &J** : 67% efficacy after first (and only) dose
  - Delay to efficacy from dose assumed to be 14 days
  - Immunity assumed to last duration of simulation ([NEJM study](#) shows long lasting, at least 7 months)
- J&J administration has resumed, till data available, assuming it will resume previous levels
- Administration Rate:
  - Pfizer: 52K courses initiated per week
  - Moderna: 30K courses initiated per week
  - J &J: 3K courses initiated per week



Last updated: **May 3**

Total Doses

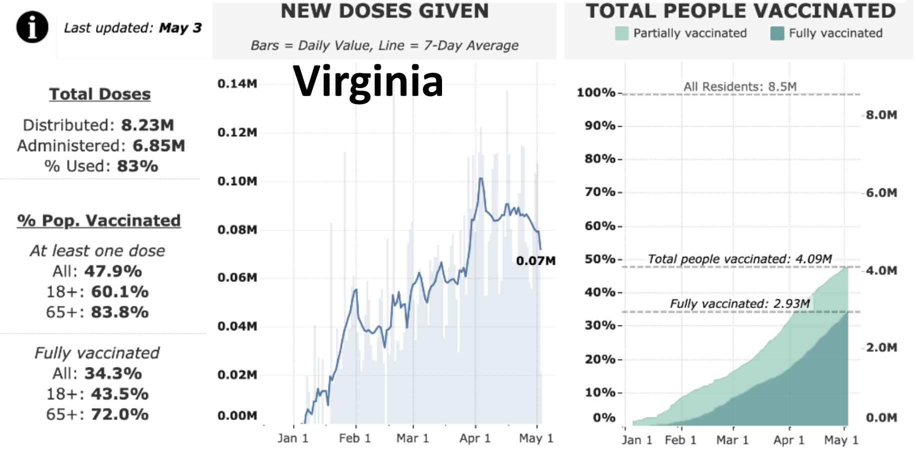
Distributed: **312.51M**
Administered: **246.78M**
% Used: **79%**

% Pop. Vaccinated

At least one dose
All: **44.4%**
18+: **56.3%**
65+: **82.8%**

Fully vaccinated
All: **31.8%**
18+: **40.6%**
65+: **69.7%**

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



Last updated: **May 3**

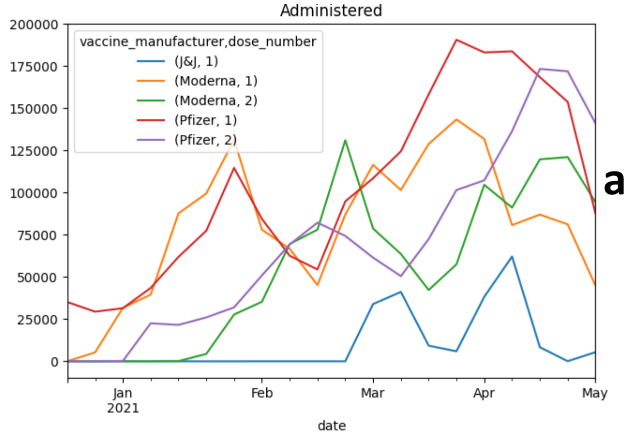
Total Doses

Distributed: **8.23M**
Administered: **6.85M**
% Used: **83%**

% Pop. Vaccinated

At least one dose
All: **47.9%**
18+: **60.1%**
65+: **83.8%**

Fully vaccinated
All: **34.3%**
18+: **43.5%**
65+: **72.0%**

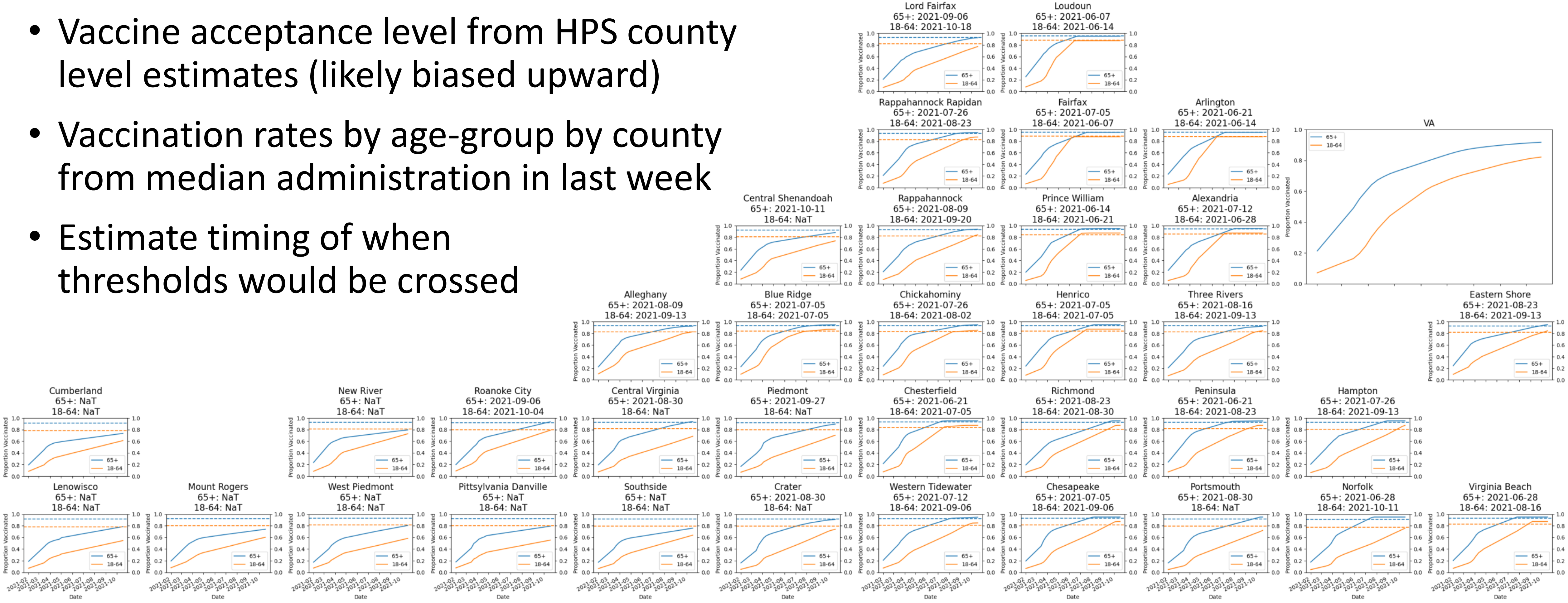


VA doses administered by manufacturer

Scenarios – Vaccines and Age-specific Acceptance

- Vaccine acceptance level from HPS county level estimates (likely biased upward)
- Vaccination rates by age-group by county from median administration in last week
- Estimate timing of when thresholds would be crossed

Acceptance levels from Household Pulse Survey ending 3-15-2021



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Scenarios – Seasonal Effects and Vaccines

Three scenarios combine these control effects and use the current vaccine schedule

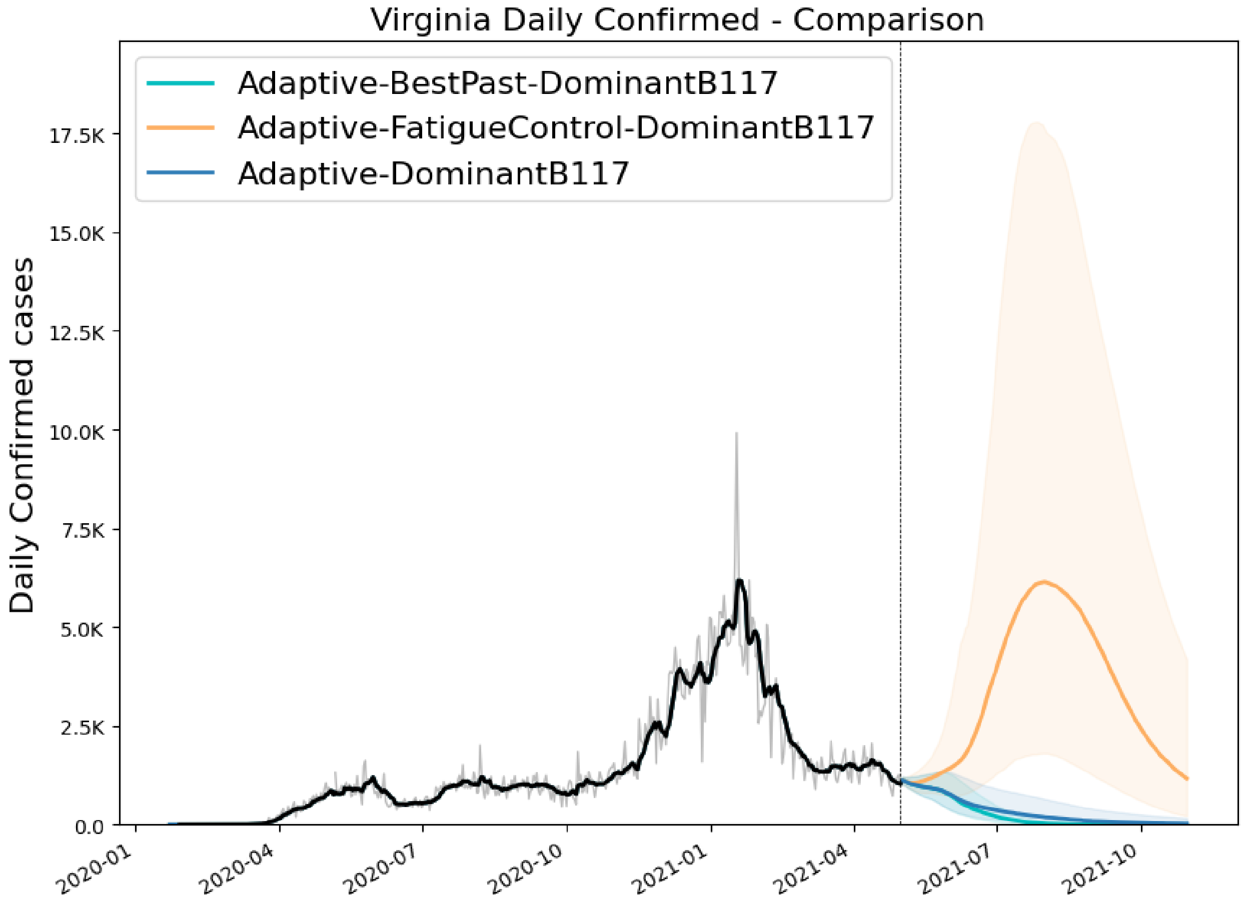
- **Adaptive-DominantB117**: Boosting of transmissibility from the emergence and likely dominance of B.1.1.7
- **Adaptive-BestPast-DominantB117:** Best Past controls with transmission boost from B.1.1.7
- **Adaptive-FatigueControl-DominantB117:** Fatigued controls and transmission boost from B.1.1.7

Counterfactuals with no vaccine ("NoVax") are provided for comparison purposes

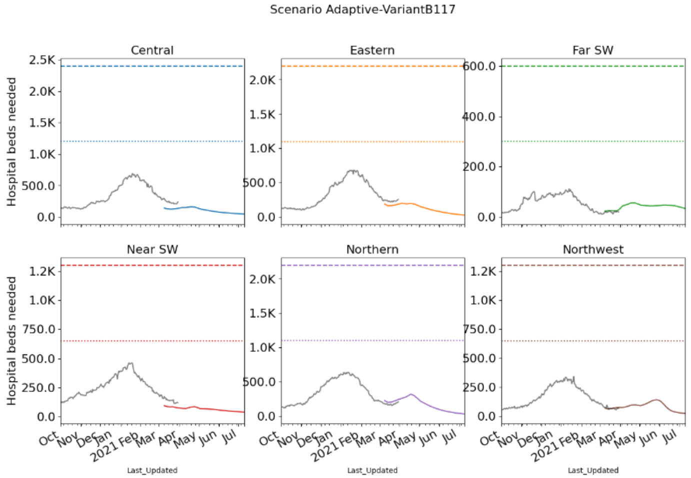
Model Results

Outcome Projections

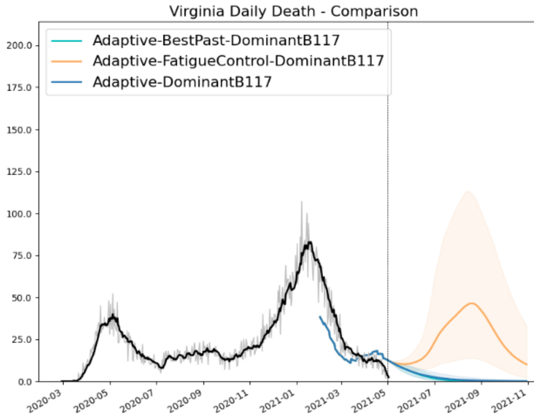
Confirmed cases



Estimated Hospital Occupancy

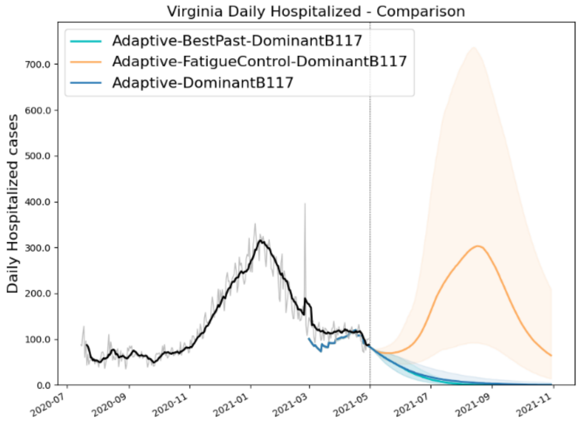


Daily Deaths



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

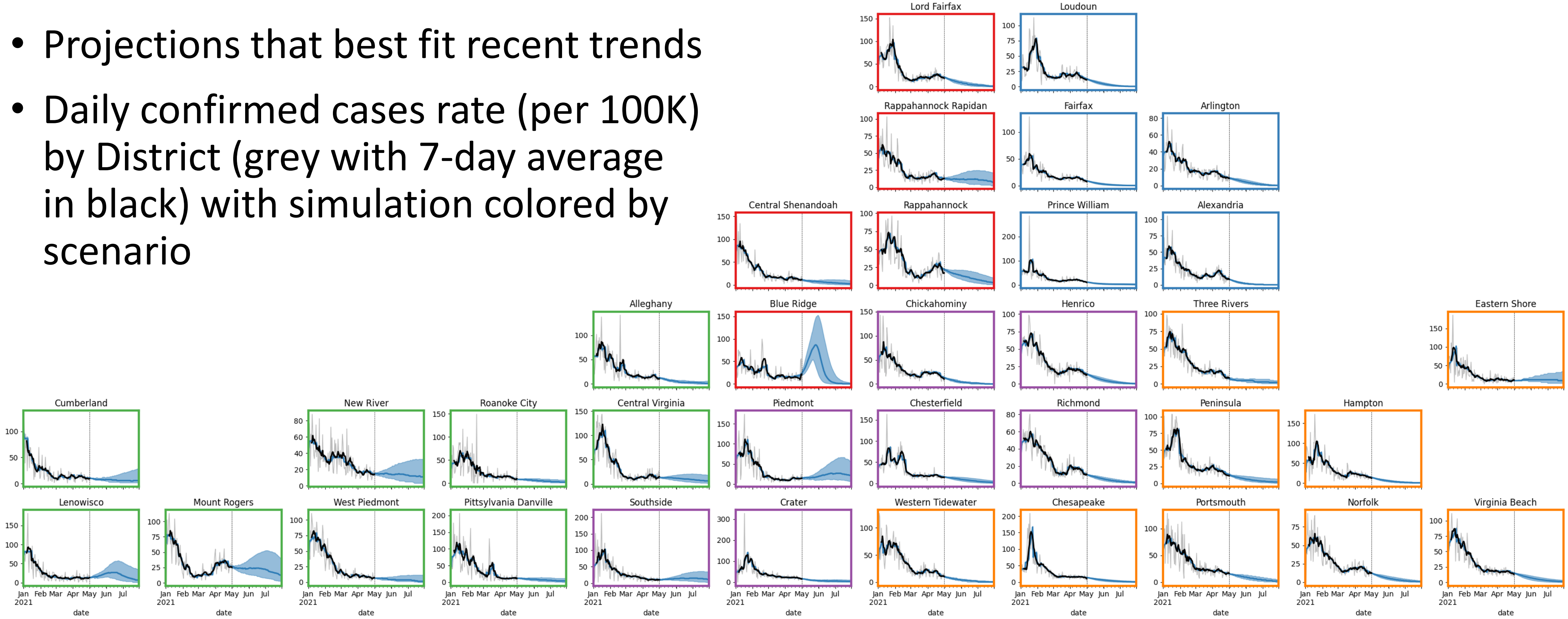
Daily Hospitalized



District Level Projections: Adaptive-DominantB117

Adaptive projections by District

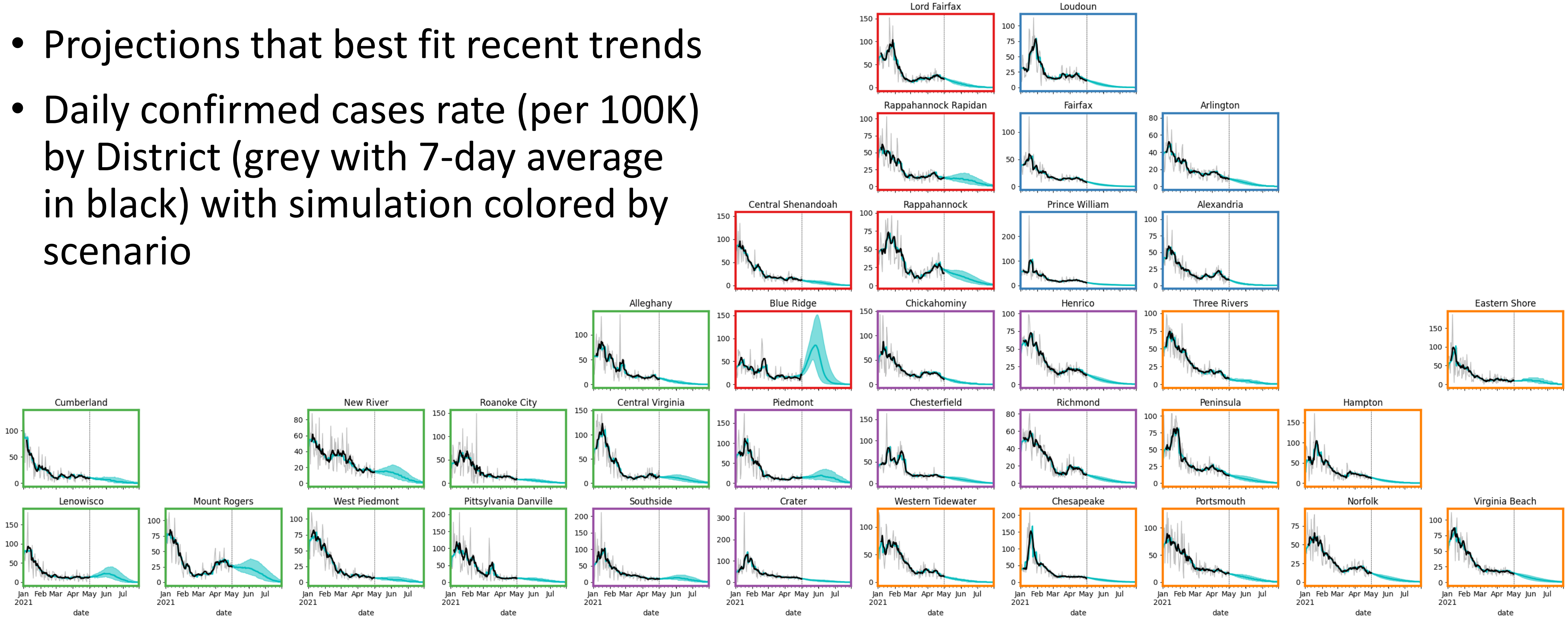
- Projections that best fit recent trends
- Daily confirmed cases rate (per 100K) by District (grey with 7-day average in black) with simulation colored by scenario



District Level Projections: Adaptive-BestPast-DominantB117

Adaptive projections by District

- Projections that best fit recent trends
- Daily confirmed cases rate (per 100K) by District (grey with 7-day average in black) with simulation colored by scenario



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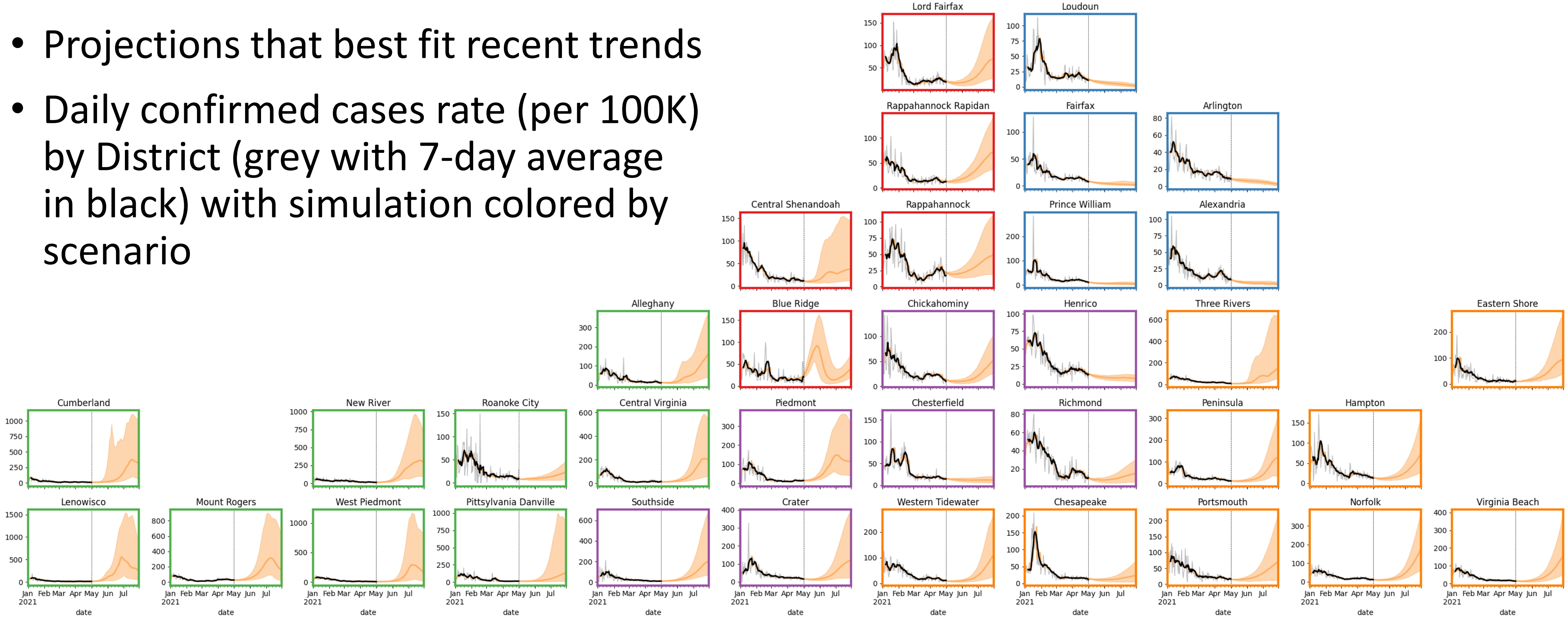
District Level Projections: Adaptive-FatigueControl-DominantB117

Adaptive projections by District

- Projections that best fit recent trends
- Daily confirmed cases rate (per 100K) by District (grey with 7-day average in black) with simulation colored by scenario



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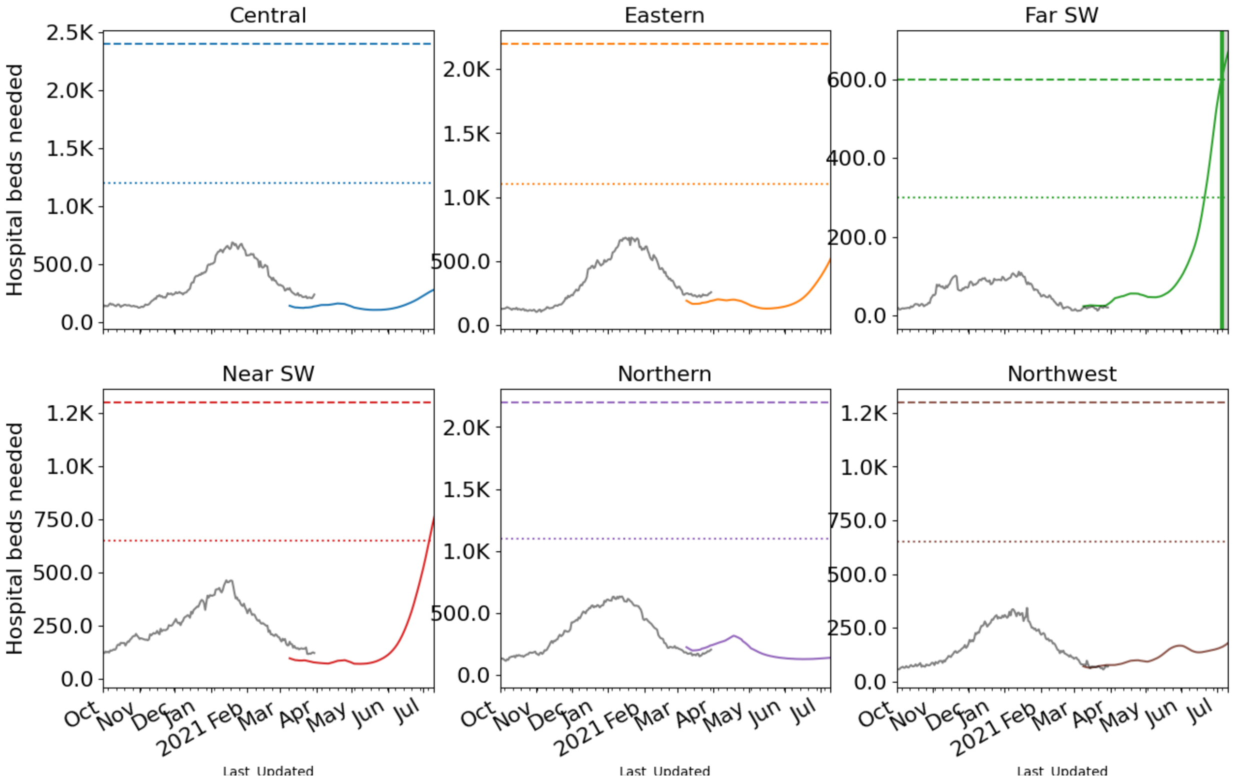
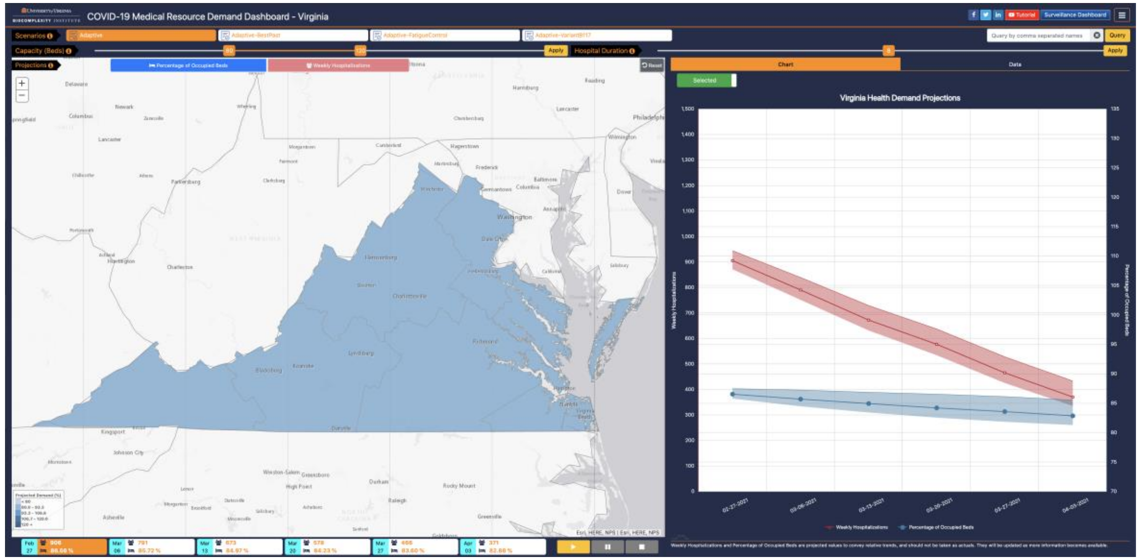
Hospital Demand and Bed Capacity by Region

Capacities* by Region – Adaptive-FatigueControl-DominantB117

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





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

If Adaptive-FatigueControl-DominantB117 scenario persists:

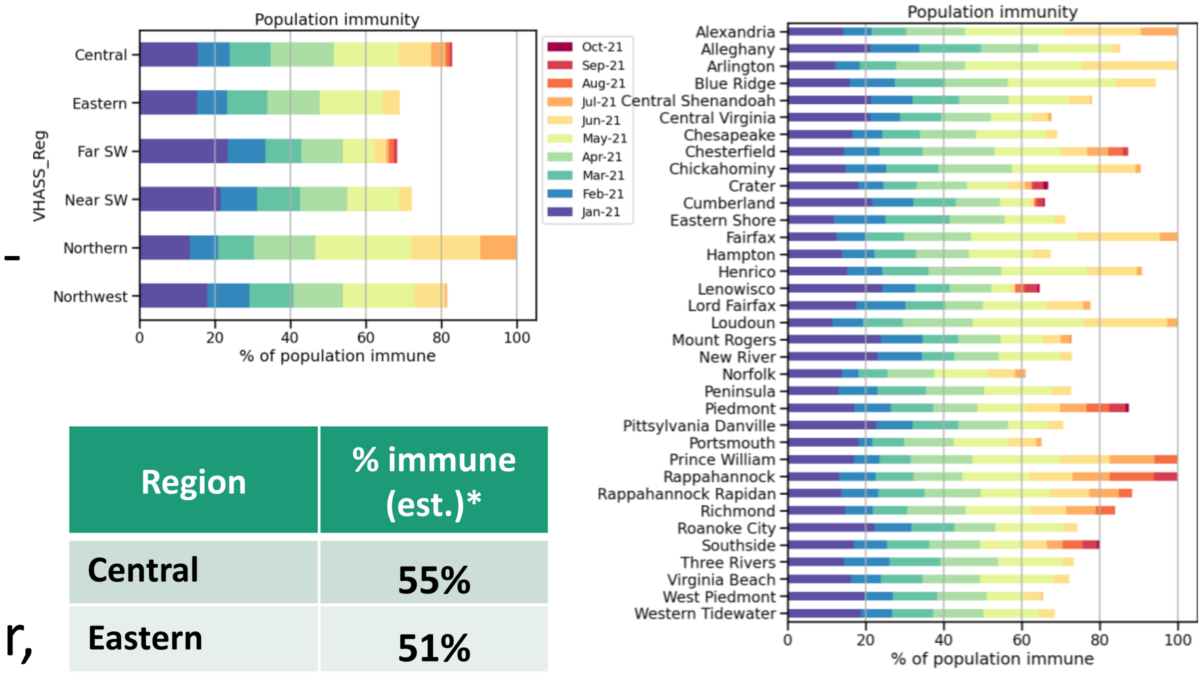
- Far SW approaches surge capacity in mid-July and Near SW approach initial capacity also in mid-July

* Assumes average length of stay of 8 days

Virginia’s Progress on Population Immunity

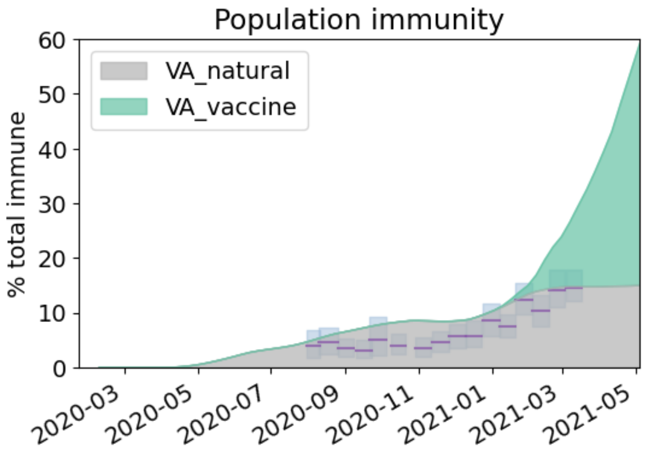
Natural Immunity and Vaccines combine to produce a population level of immunity

- 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	**55%**
Eastern	**51%**
Far SW	**56%**
Near SW	**58%**
Northern	**52%**
Northwest	**58%**
Virginia	**54%**

* As of April 25th 2021



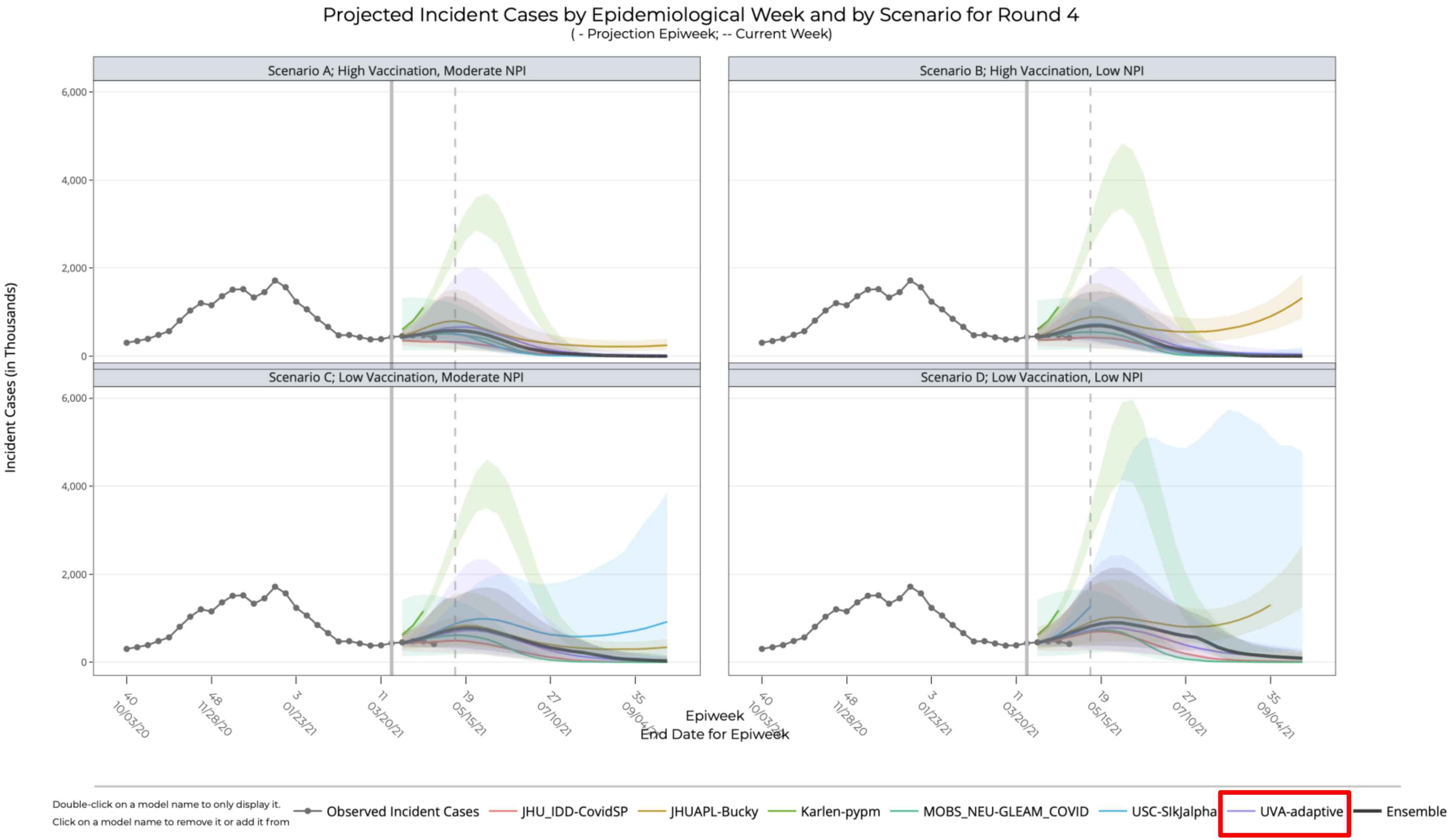
COVID-19 Scenario Modeling Hub

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)

  - Similar to our current scenarios with regular updates, round 5 should be done in 1st week in May

Published May 5th, 2021 in [MMWR]()

https://covid19scenariomodelinghub.org/viz.html



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 with minimal growth in a few districts**
- VA mean weekly incidence down to 11/100K from 13/100K, US down (15 from 16 per 100K)
- Vaccination rates have slowed, but overall population immunity continues to rise over 50%
- Projections show declining rate overall across Commonwealth, only a few districts with short term growth
- Recent updates:
  - Updated estimates of regional vaccine hesitancy and folded into projections
- 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?

Biocomplexity COVID-19 Response Team

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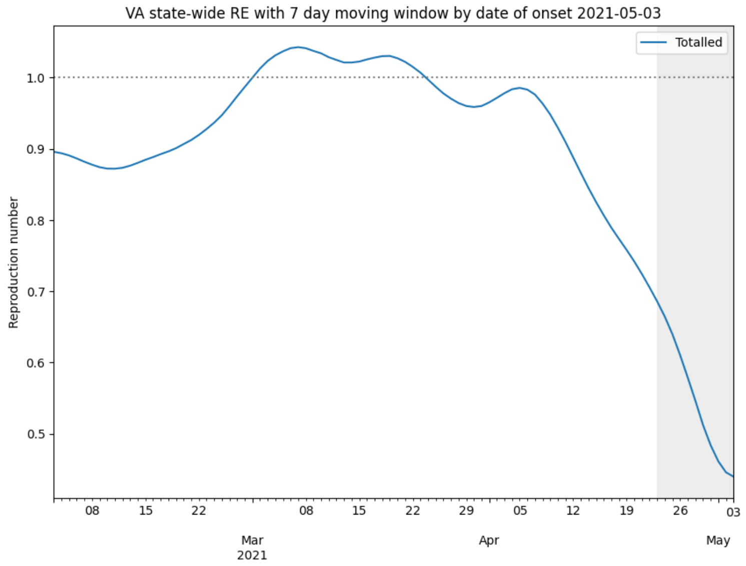
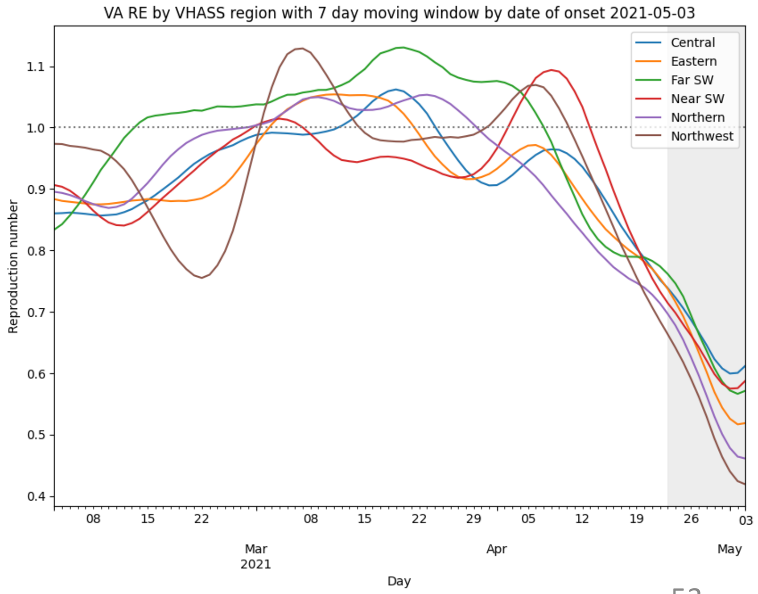
Supplemental Slides

Estimating Daily Reproductive Number

April 24th Estimates

Region	Date of Onset R_e	Date Onset Diff Last Week
State-wide	0.662	0.019
Central	0.722	-0.031
Eastern	0.718	0.018
Far SW	0.749	0.087
Near SW	0.690	-0.065
Northern	0.678	0.062
Northwest	0.647	-0.039





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

Weekly Cases and Hospitalizations

Weekly confirmed cases

Week Ending	Adaptive-DominantB117	Adaptive-BestPast-Dominant B117	Adaptive-Fatigued Control -DominantB117
4/25/21	9,598	9,599	9,597
5/2/21	9,747	9,767	9,850
5/9/21	8,858	8,894	9,683
5/16/21	8,048	8,086	10,150
5/23/21	7,392	7,428	11,250
5/30/21	6,713	6,561	13,152
6/6/21	5,994	5,553	16,388
6/13/21	5,365	4,521	21,163
6/20/21	4,746	3,508	27,038
6/27/21	4,201	2,575	32,380
7/4/21	3,647	1,808	38,477
7/11/21	3,131	1,204	42,721

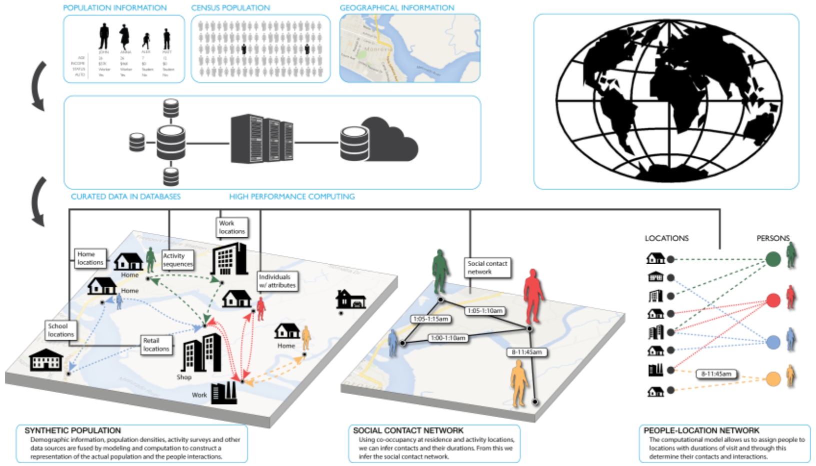
Weekly Hospitalizations

Week Ending	Adaptive-DominantB117	Adaptive-BestPast-Dominant B117	Adaptive-Fatigued Control -DominantB117
4/25/21	750	750	750
5/2/21	659	659	666
5/9/21	548	548	601
5/16/21	451	452	575
5/23/21	373	372	580
5/30/21	302	292	609
6/6/21	241	219	654
6/13/21	196	159	707
6/20/21	161	112	771
6/27/21	131	74	784
7/4/21	103	48	748
7/11/21	81	29	659

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



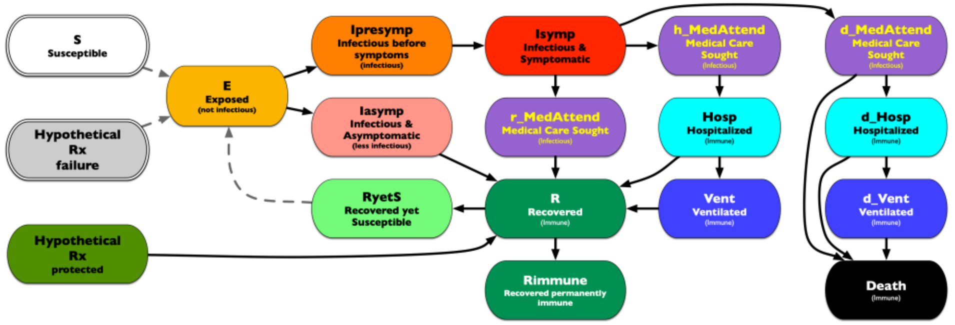
SYNTHETIC POPULATION
Demographic information, population densities, activity surveys and other data sources are fused by modeling and computation to construct a representation of the actual population and the people interactions.

SOCIAL CONTACT NETWORK
Using co-occupancy at residence and activity locations, we can infer contacts and their durations. From this we infer the social contact network.

PEOPLE-LOCATION NETWORK
The computational model allows us to assign people to locations with durations of visit and through this determine their contacts and interactions.

Synthetic Population

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



S
Susceptible

Hypothetical
Rx
failure

Hypothetical
Rx
protected

E
Exposed
(not infectious)

Ipresymp
Infectious before symptoms
(infectious)

Iasymp
Infectious & Asymptomatic
(less infectious)

RyetS
Recovered yet Susceptible

Isymp
Infectious & Symptomatic

r_MedAttend
Medical Care Sought
(Infectious)

R
Recovered
(Immune)

Rimmune
Recovered permanently immune

h_MedAttend
Medical Care Sought
(Infectious)

Hosp
Hospitalized
(Immune)

Vent
Ventilated
(Immune)

d_MedAttend
Medical Care Sought
(Infectious)

d_Hosp
Hospitalized
(Immune)

d_Vent
Ventilated
(Immune)

Death
(Immune)

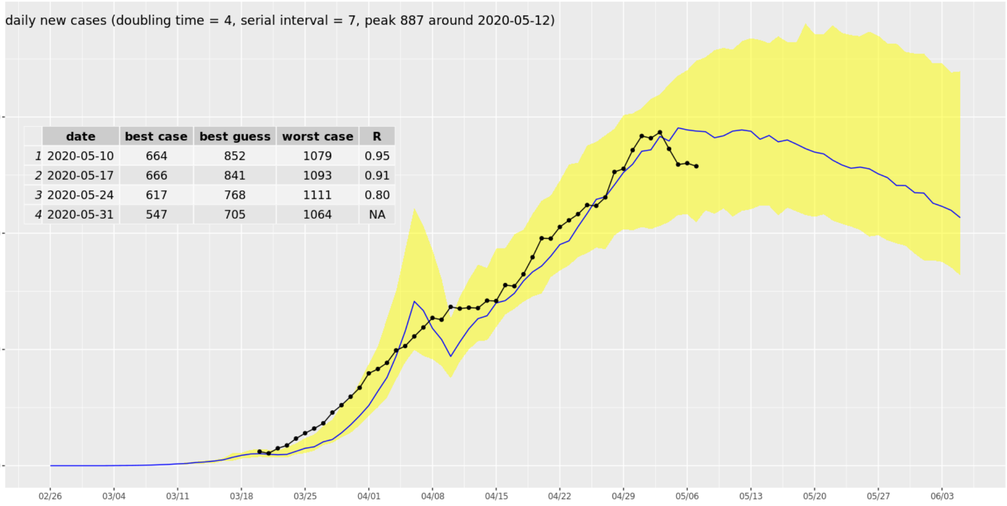
Detailed Disease Course of COVID-19

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

ABM Social Distancing Rebound Study Design

Study of ”Stay Home” policy adherence

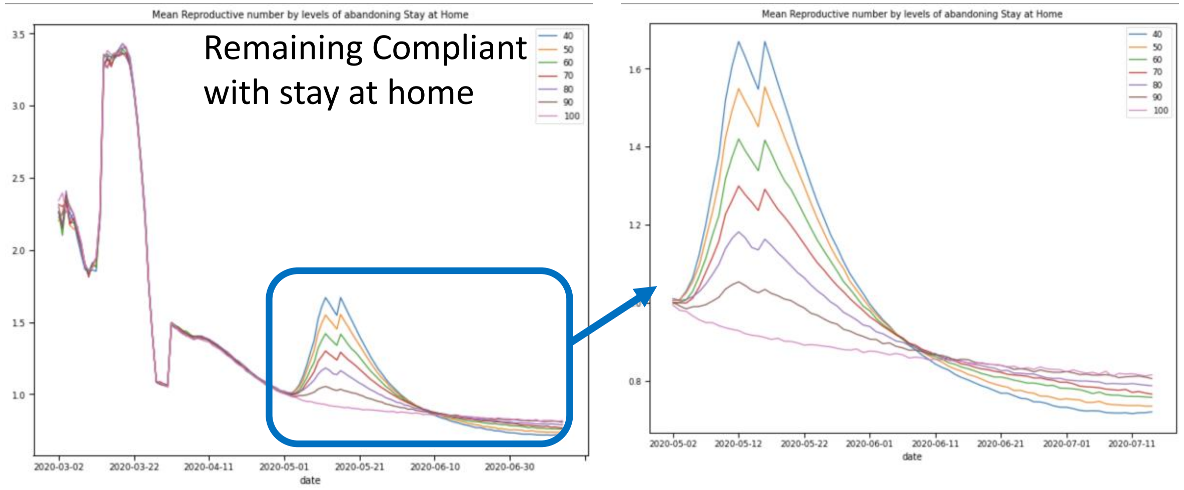
- Calibration to current state in epidemic
- Implement “release” of different proportions of people from ”staying at home”


daily new cases (doubling time = 4, serial interval = 7, peak 887 around 2020-05-12)

	date	best case	best guess	worst case	R
1	2020-05-10	664	852	1079	0.95
2	2020-05-17	666	841	1093	0.91
3	2020-05-24	617	768	1111	0.80
4	2020-05-31	547	705	1064	NA

Calibration to Current State

- Adjust transmission and adherence to current policies to current observations
- For Virginia, with same seeding approach as PatchSim


Mean Reproductive number by levels of abandoning Stay at Home

Remaining Compliant with stay at home

Impacts on Reproductive number with release

- After release, spike in transmission driven by additional interactions at work, retail, and other
- At 25% release (70-80% remain compliant)
- Translates to 15% increase in transmission, which represents a 1/6th return to pre-pandemic levels