Network Systems Science & Advanced Computing

Biocomplexity Institute & Initiative

University of Virginia

Estimation of COVID-19 Impact in Virginia

November 3rd, 2021

(data current to October 30th – Nov 2nd)

Biocomplexity Institute Technical report: TR 2021-115

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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

Key Takeaways

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

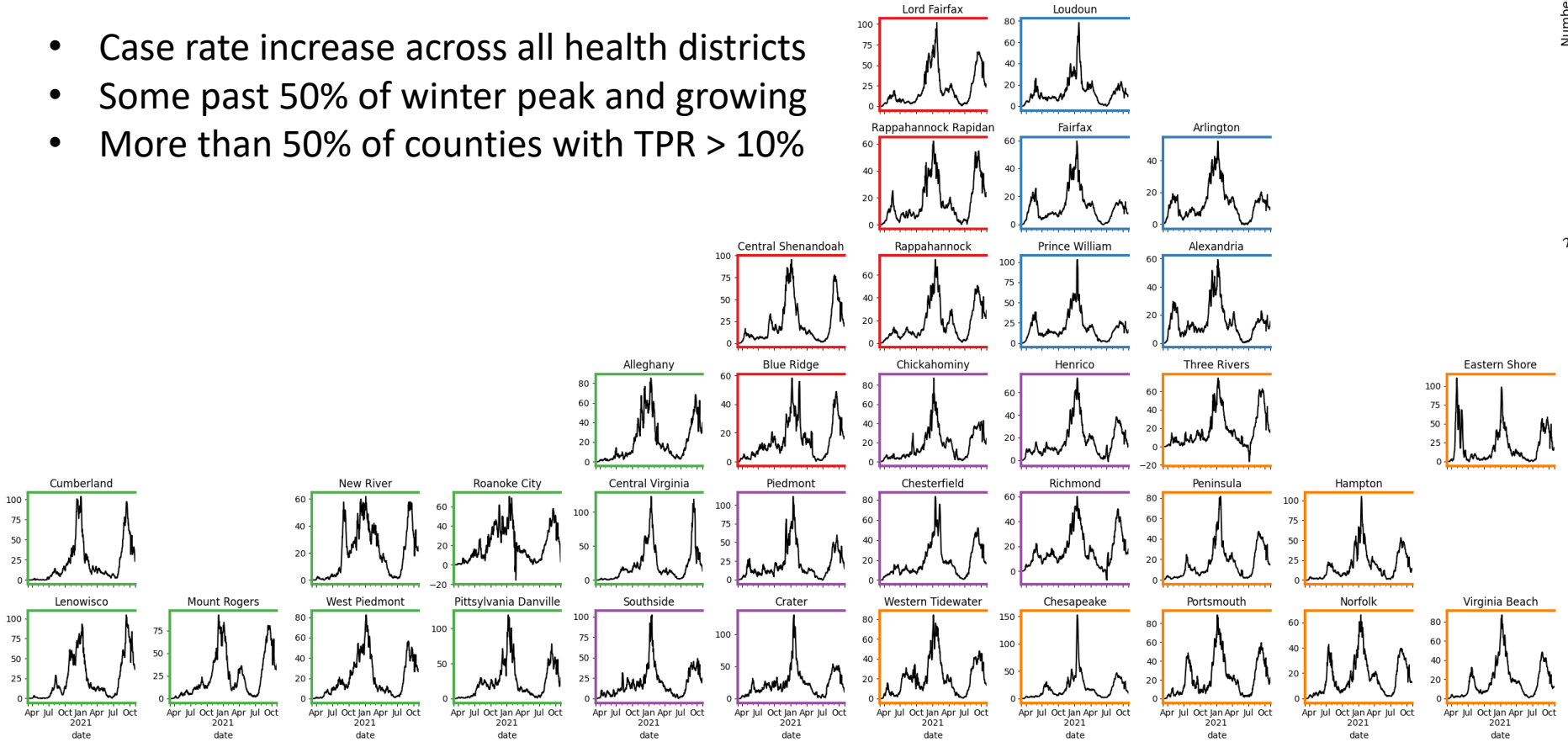
- **Case rates in Virginia continue to steadily decline across nearly all districts**
- VA 7-day mean daily incidence is slightly down to 15.5/100K from 18/100K; US is slightly up to 23/100K (from 21/100K)
- Projections show continued decline across the board
- Future case growth remains possible, however, when tested with transmission drivers from last year
- Recent updates:
  - Added 3rd doses to status quo vaccination schedule, with estimated coverage of 40%
  - Analysis to show potential impact of Influenza based on past seasons

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

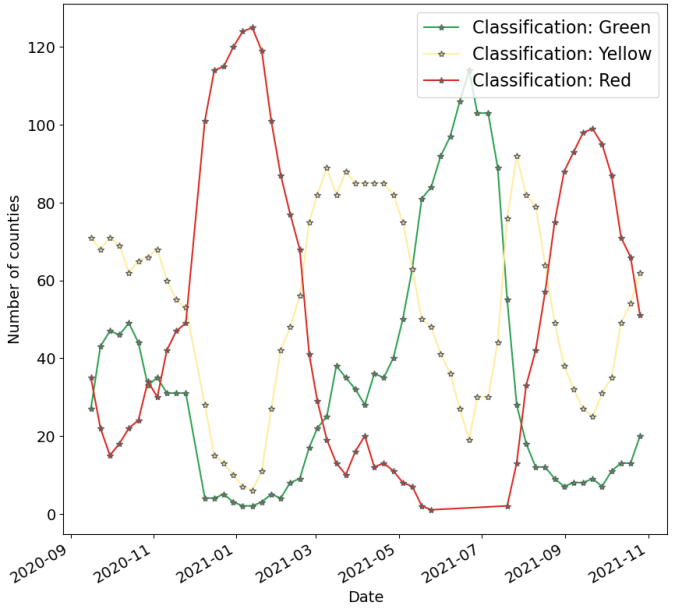
Situation Assessment

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)

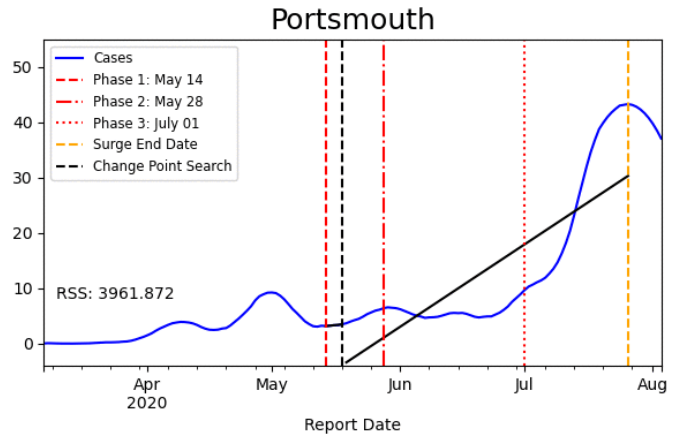
Red: >10.0% (and not "Green" or "Yellow")

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

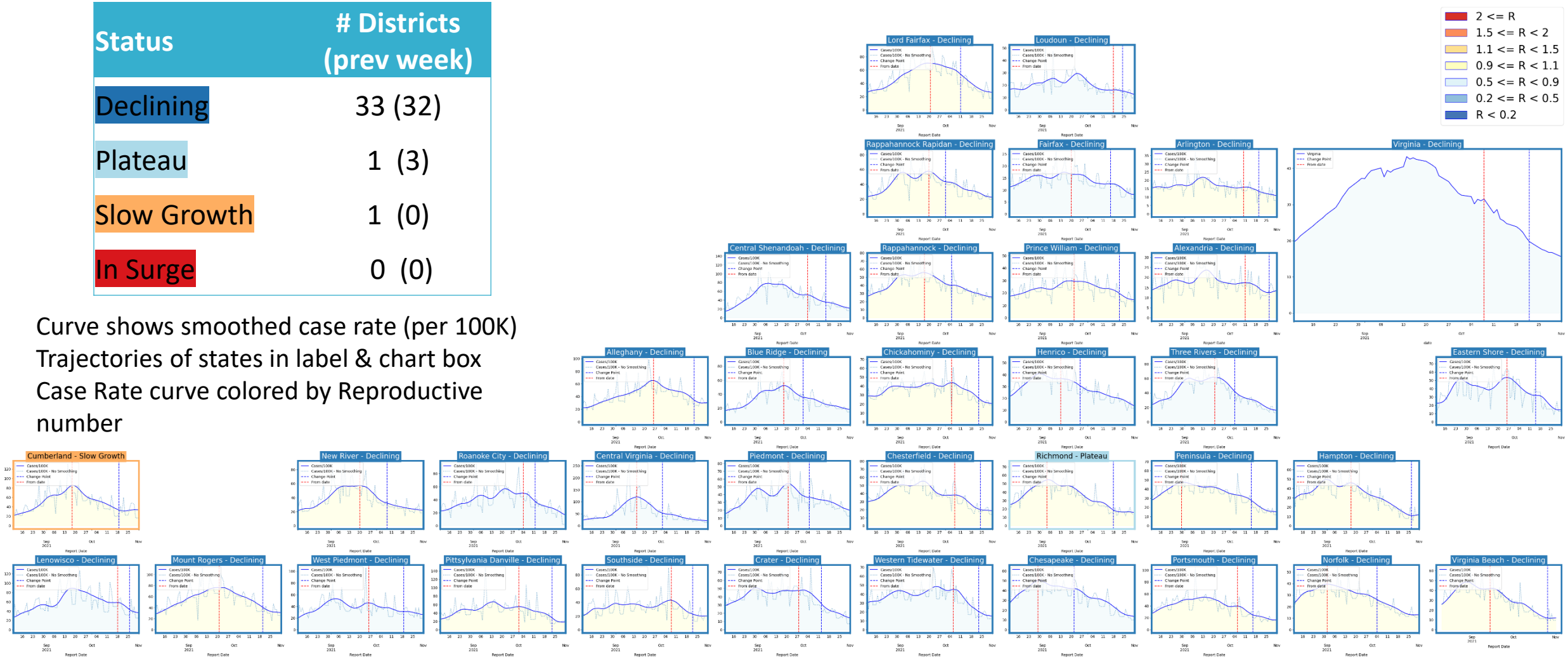


Trajectory	Description	Weekly Case Rate (per 100K) bounds	# Districts (prev week)
Declining	Sustained decreases following a recent peak	below -0.9	33 (32)
Plateau	Steady level with minimal trend up or down	above -0.9 and below 0.5	1 (3)
Slow Growth	Sustained growth not rapid enough to be considered a Surge	above 0.5 and below 2.5	1 (0)
In Surge	Currently experiencing sustained rapid and significant growth	2.5 or greater	0 (0)

District Trajectories – last 10 weeks

Status	# Districts (prev week)
Declining	33 (32)
Plateau	1 (3)
Slow Growth	1 (0)
In Surge	0 (0)

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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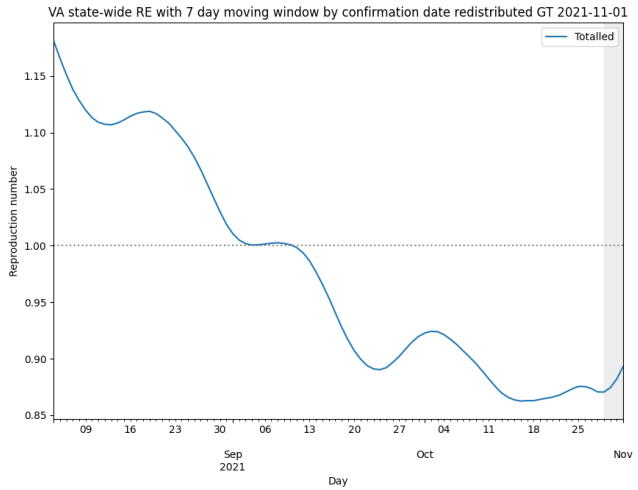
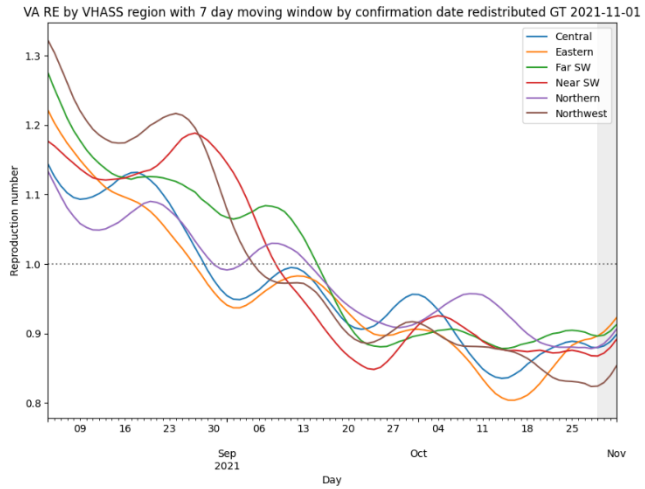
Estimating Daily Reproductive Number – Redistributed gap

Nov 1st Estimates

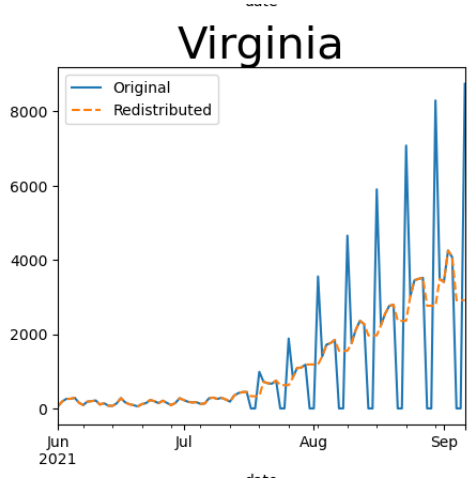
Region	Date Confirmed R_e	Date Confirmed Diff Last Week
State-wide	0.876	0.042
Central	0.897	0.025
Eastern	0.921	0.169
Far SW	0.912	0.066
Near SW	0.892	0.049
Northern	0.907	0.021
Northwest	0.848	0.009





Skipping Weekend Reports & holidays biases estimates

Redistributed "big" report day to fill in gaps, and then estimate R from "smoothed" time series



Methodology

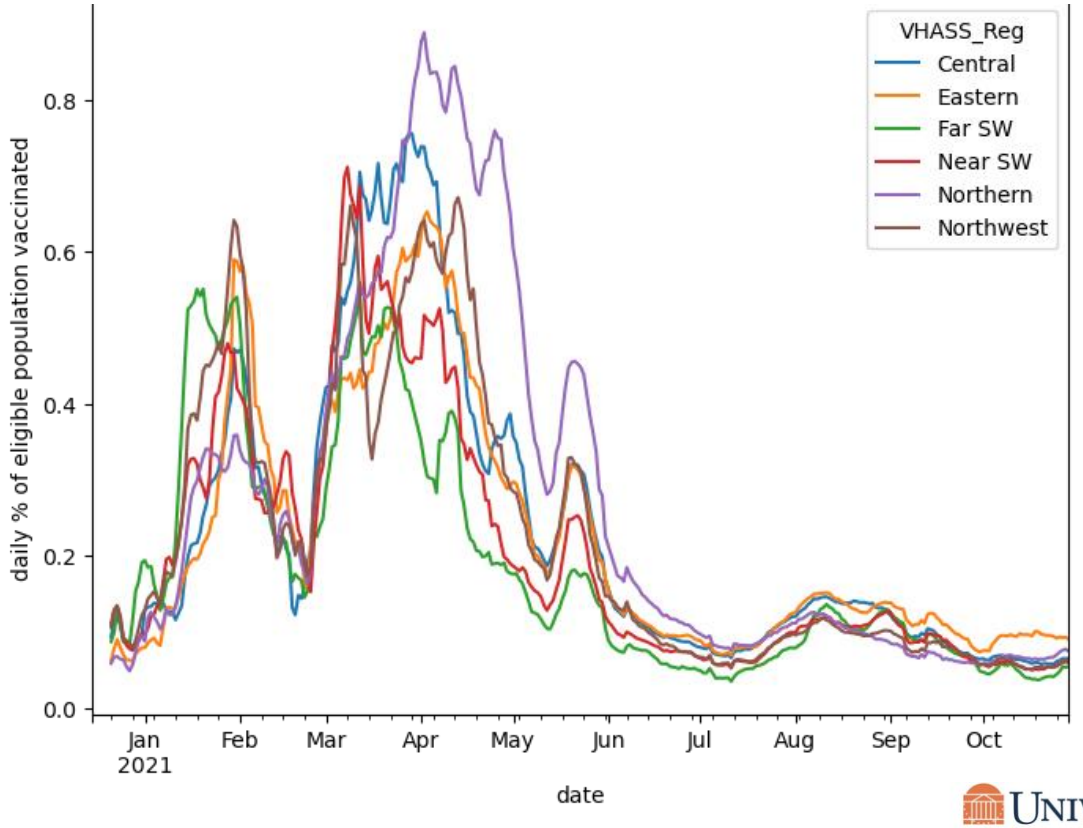
- Wallinga-Teunis method (EpiEstim[1]) for cases by **confirmation date**
- Serial interval: updated to discrete distribution from observations (mean=4.3, Flaxman et al, Nature 2020)
- Using Confirmation date since due to increasingly unstable estimates from onset date due to backfill

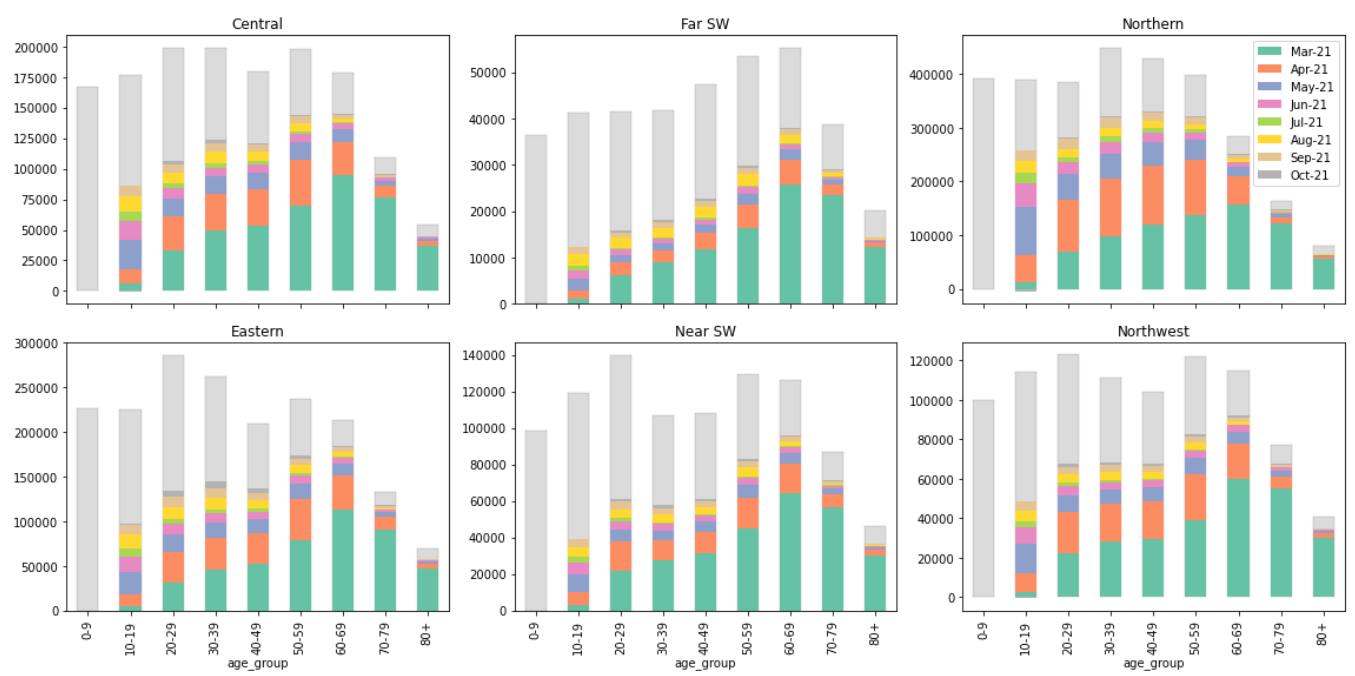
1. Anne Cori, Neil M. Ferguson, Christophe Fraser, Simon Cauchemez. A New Framework and Software to Estimate Time-Varying Reproduction Numbers During Epidemics. American Journal of Epidemiology, Volume 178, Issue 9, 1 November 2013, Pages 1505–1512, https://doi.org/10.1093/aje/kwt133

Vaccination Administration Slow

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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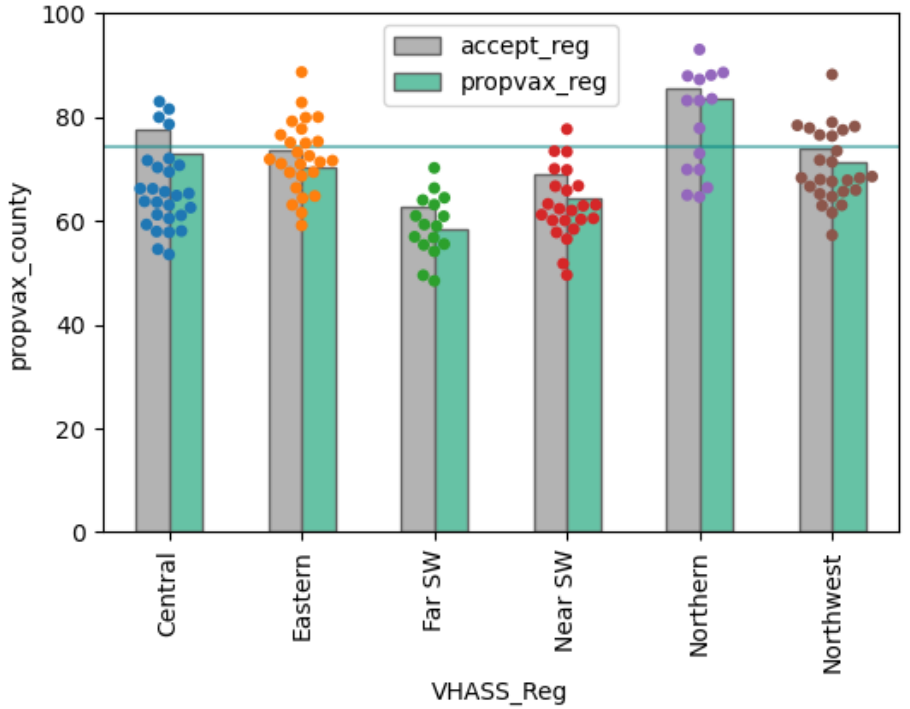
Vaccination Acceptance by Region

Corrections to surveys:

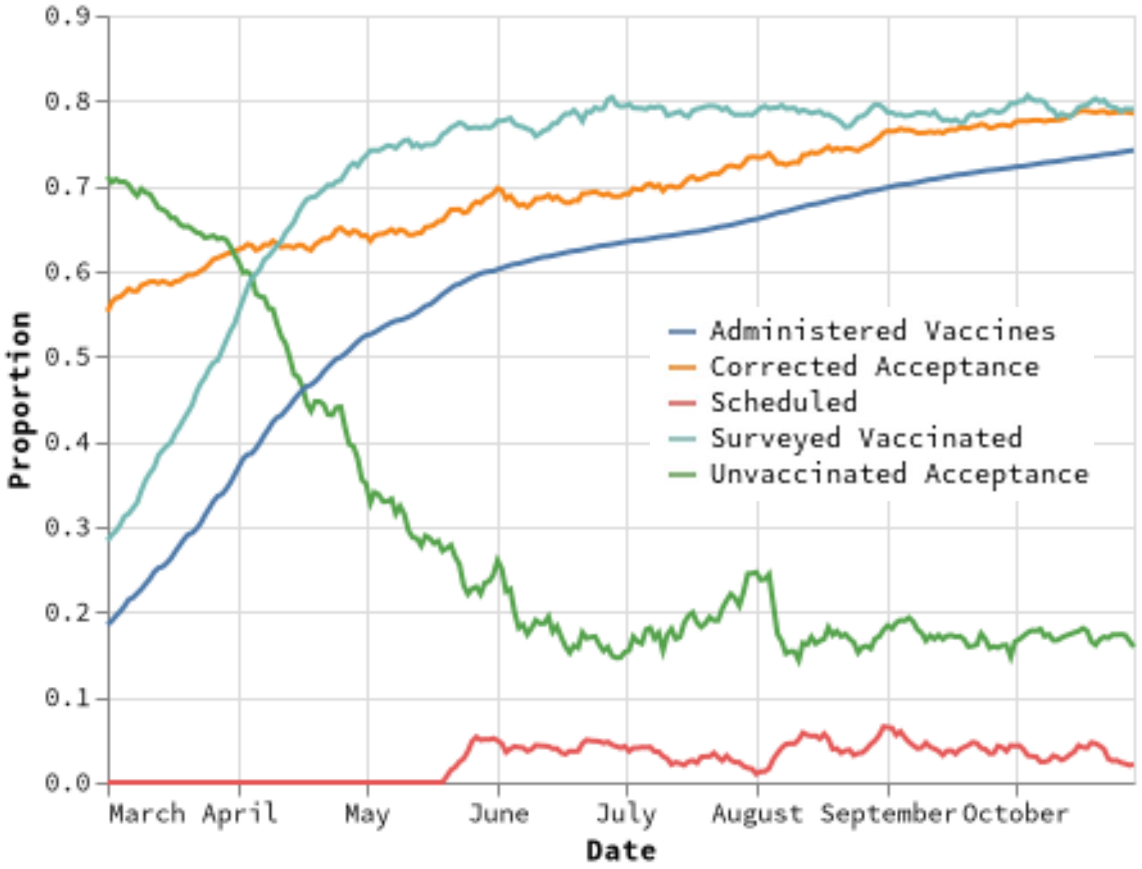
- Facebook administered survey is timely and broad, but biased by who accesses Facebook and answers the survey
- Correction approach:
  - Calculate an over-reporting fraction based on reported vaccinations compared to VDH administration data
  - Cross-validate coarse corrections against HPS survey at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

Region	COVIDcast accepting corrected	VDH proportion pop vaccinated
Central	77%	73%
Eastern	77%	70%
Far SW	61%	58%
Near SW	68%	64%
Northern	87%	84%
Northwest	76%	71%
Virginia	**79%**	**74%**



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

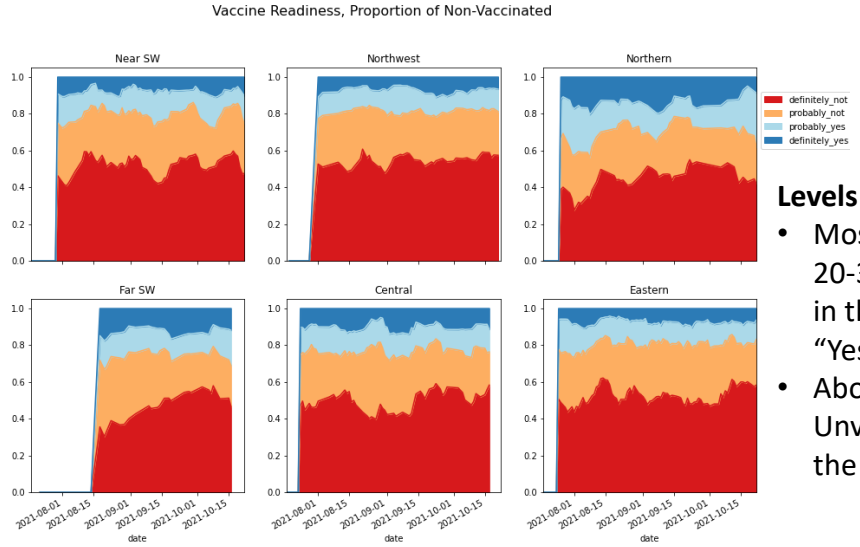
Vaccine Acceptance Components over Time



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

Levels of Vaccine Willingness



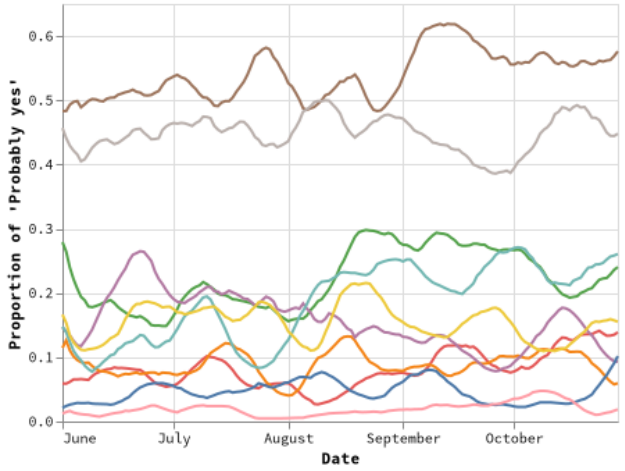
Levels of Acceptance in flux:

- Most regions are steady with 20-30% of unvaccinated still in the Definitely/Probably "Yes" categories.
- About 50% of the Unvaccinated seem to be in the "Definitely Not" category.

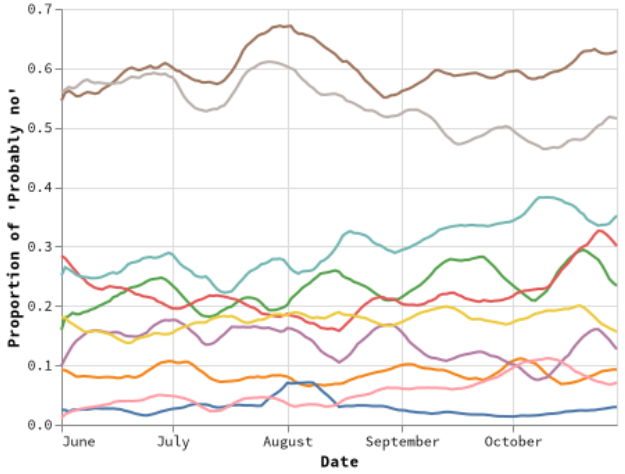
Data Source: https://covidcast.cmu.edu

Reasons for Hesitancy by Likeliness to Accept

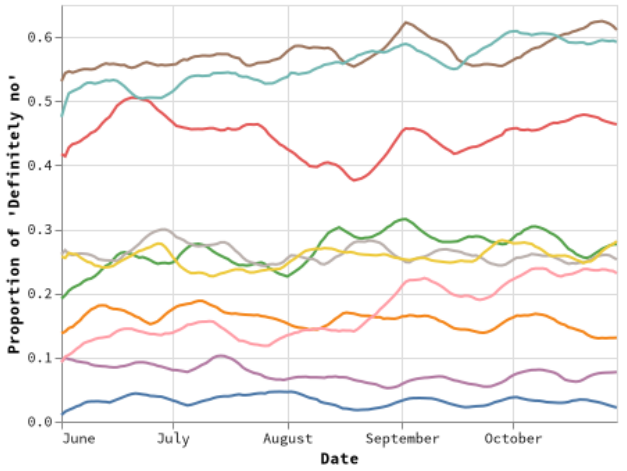
Probably Yes

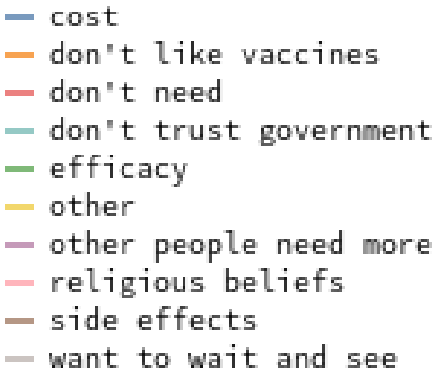


Probably No



Definitely No



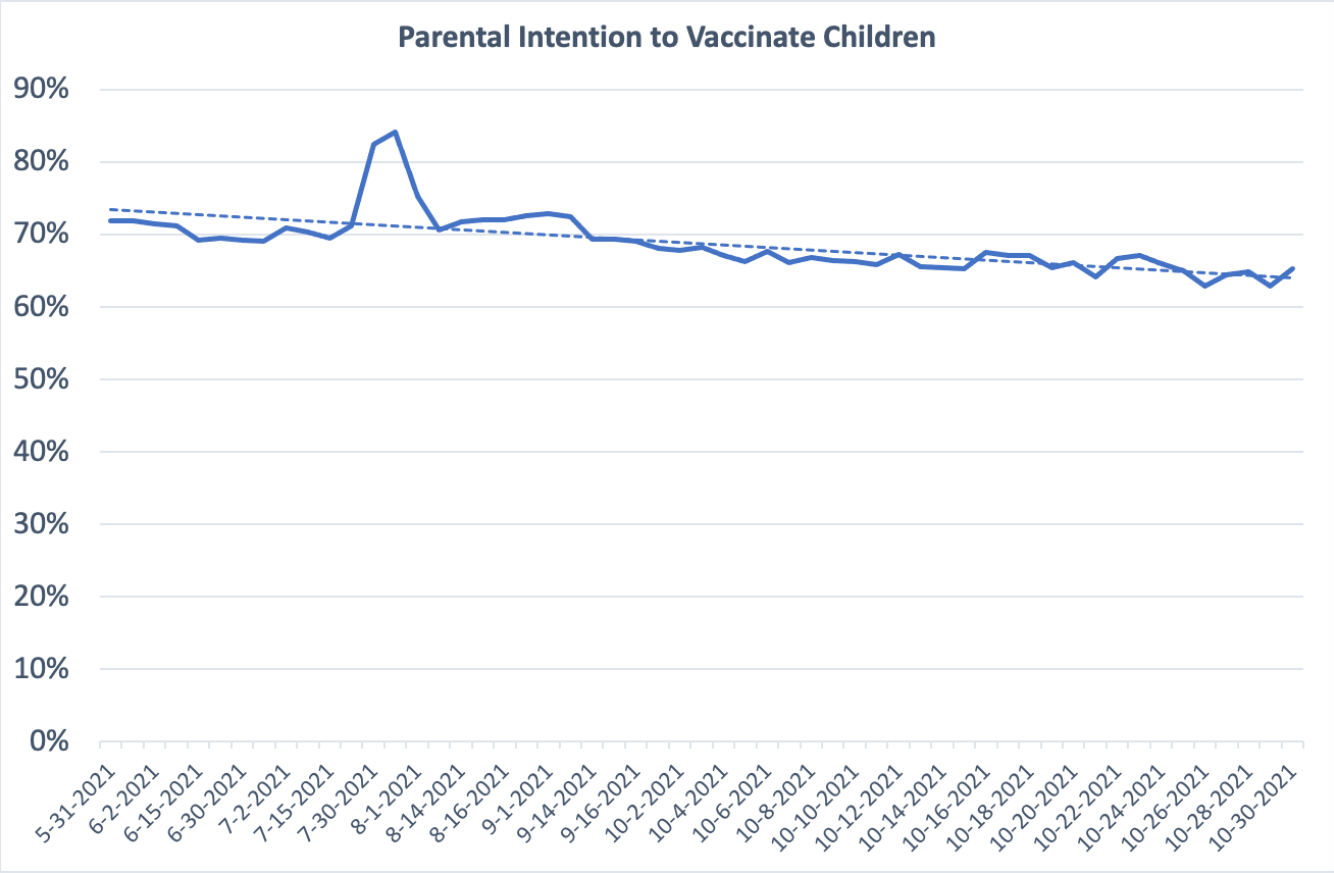


Reasons for Hesitancy vary across tiers of likeliness to accept the vaccine

- 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

Parental Intention to Vaccinate Children



Parental Intention to Vaccinate Children lower than overall Acceptance

- Steady decline from the beginning of the Summer to present, from ~72% to ~64%
- Response to question: “Will you choose to vaccinate your child / children when they are eligible?”
- Majority of responses are “Definitely Yes”
- Proportion unsure similar to ”Definitely No”

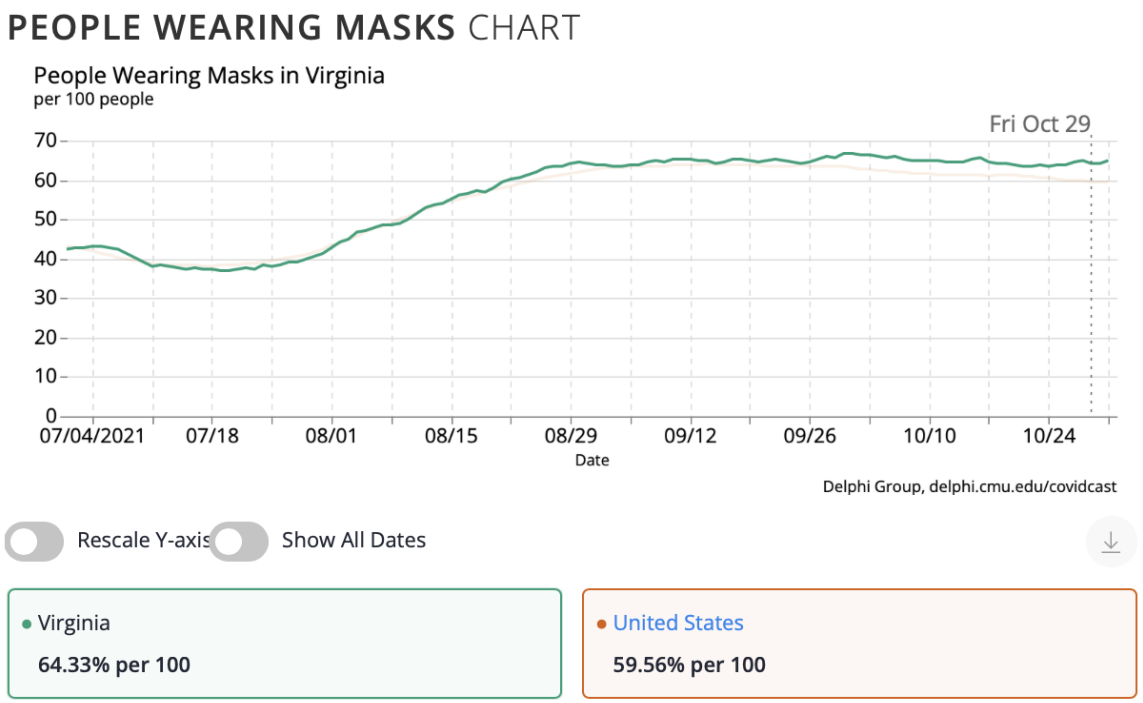
Definitely Yes	**54%**
Probably Yes	**13%**
Probably No	**9%**
Definitely No	**25%**

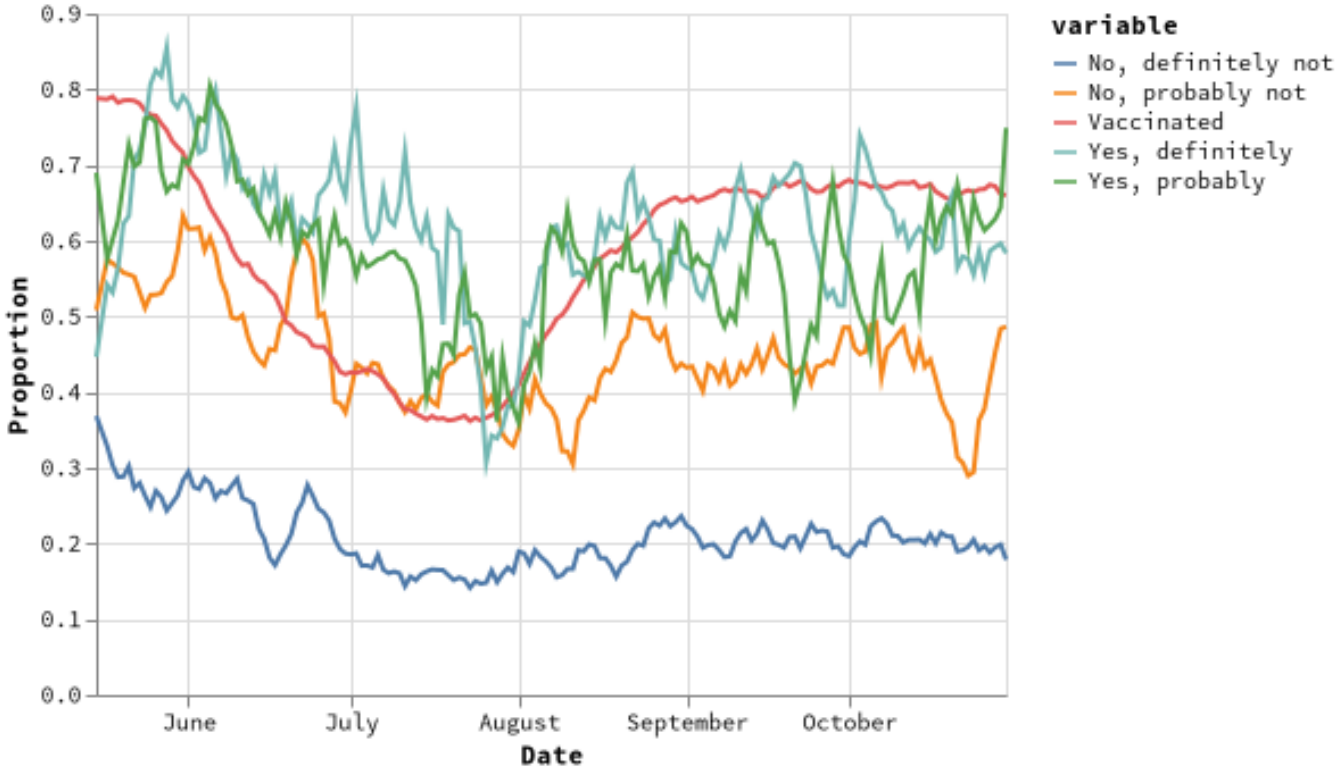
Data Source: https://covidcast.cmu.edu

Mask Usage Stalls

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

- US and VA similar, though US has slightly declined over past couple weeks
- Mask wearing remains lower amongst unvaccinated especially among least willing to be vaccinated





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

SARS-CoV2 Variants of Concern

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

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

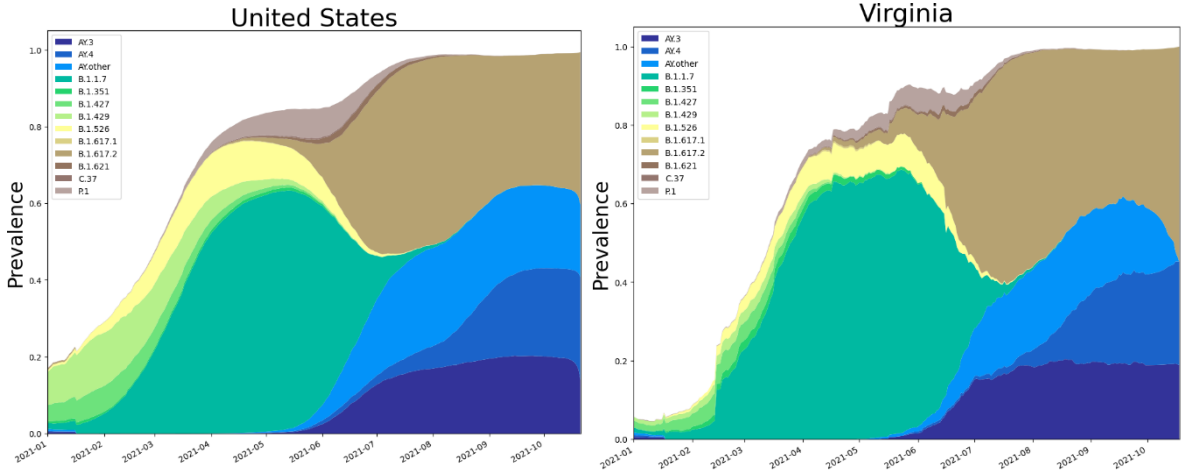
	New WHO Name	Transmissibility	Immune Evasiveness	Vaccine Effectiveness^
Ancestral		—	—	✓
D614G		+	—	✓
B.1.1.7	Alpha	+++	—	✓
B.1.351	Beta	+	++++	✓
P.1	Gamma	++	++	✓
B.1.429	Epsilon	+	+	✓
B.1.526	Iota	+	+	✓
B.1.617.2	Delta	++++*	++#	✓

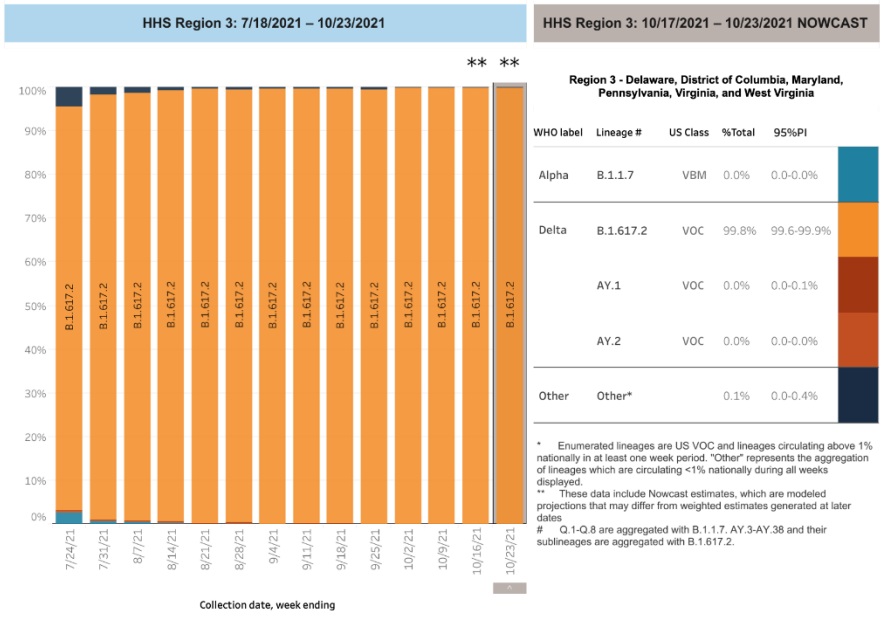
*Relative transmissibility to B.1.1.7 yet to be fully defined
^Effectiveness from real world evidence vs. severe illness, not all vaccines are effective vs all variants, and importance of 2-doses, especially for B.1.617.2 for which 1 dose of mRNA or AZ is only ~30% effective # May carry more immune escape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

World Health Organization

WHO and Eric Topol

GISAID outbreak.info



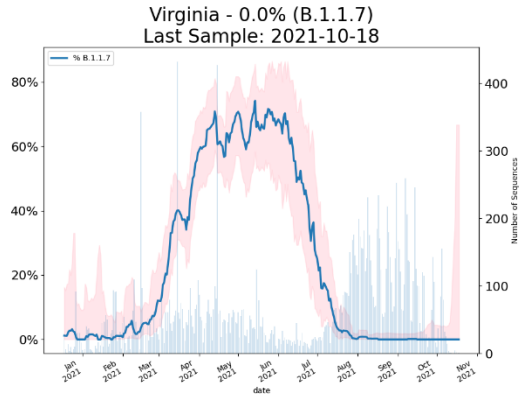


CDC Variant Tracking

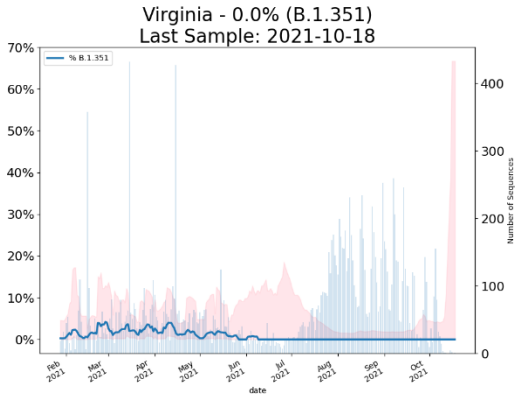
SARS-CoV2 Variants of Concern

Previous Variants

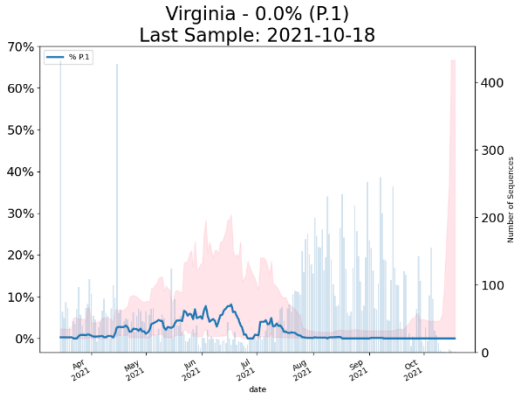
Alpha α - Lineage B.1.1.7



Beta β - Lineage B.1.351

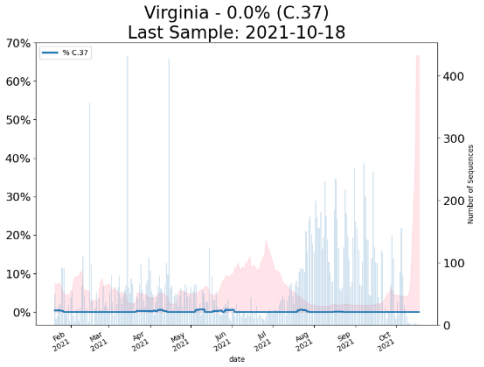


Gamma γ - Lineage P.1

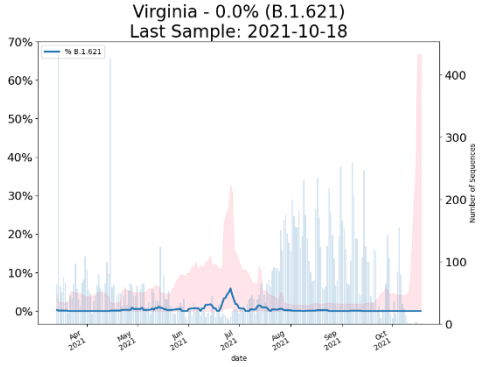


Emerging Variants

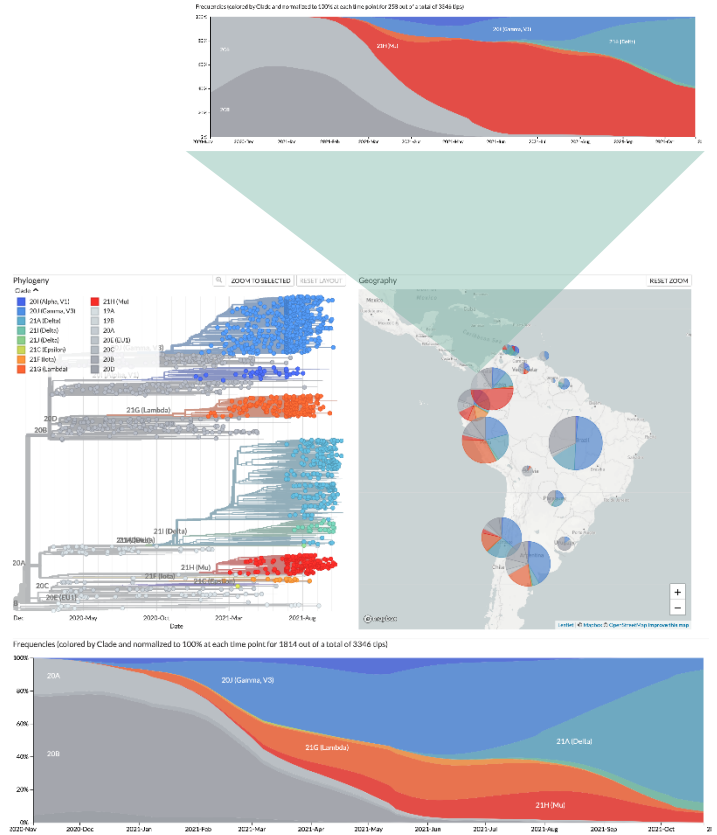
Lambda λ - Lineage C.37



Mu μ - Lineage B.1.621



Colombia has highest proportion Mu and it continues to lose ground to Delta



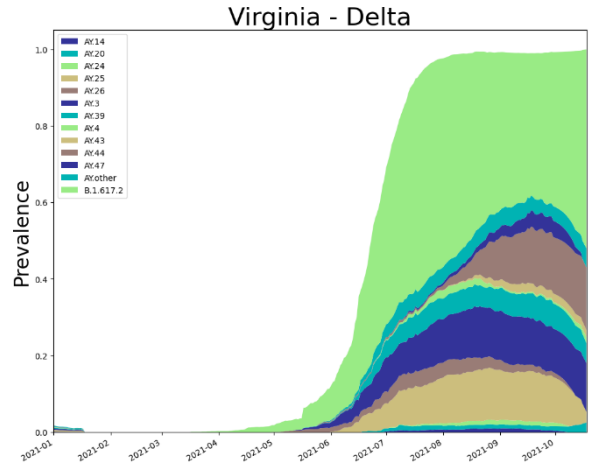
Delta continues to out compete Lambda and Mu in South America (over 80%, Lambda and Mu both below 10%)

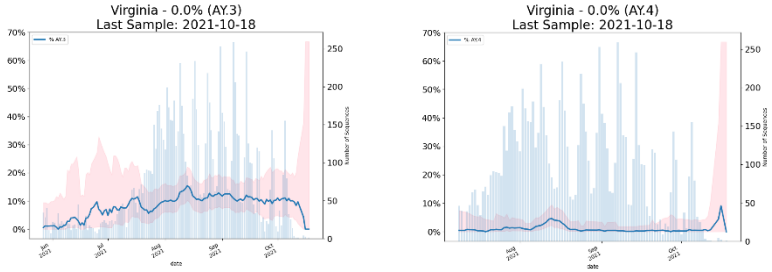
Trevor Bedford Tweet & Nextstrain Analysis

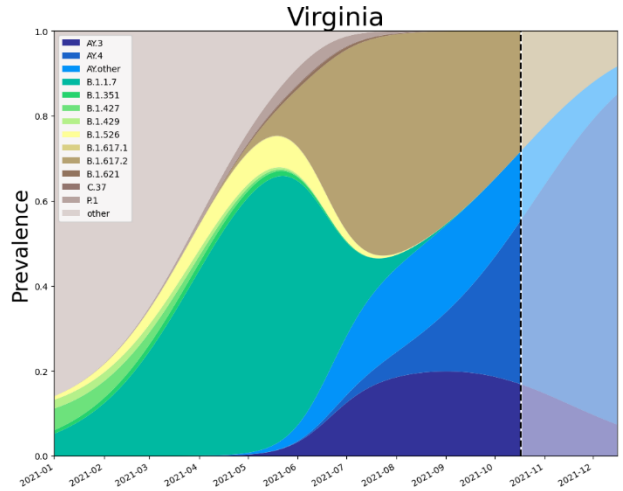
SARS-CoV2 Variants of Concern

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 and AY.4 with some significant variability while there are limited genomes submitted, these subvariants are mainly clustered in the US, others mainly outside of US







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

News, Variants & Vaccines

1. SARS-CoV-2 was detected in one-third of sampled White-tailed deer in Iowa between September 2020 and January of 2021 that likely resulted from multiple human-to-deer spillover events and deer-to-deer transmission.
2. NAb levels were higher after the extended dosing interval (6-14 weeks) compared to the conventional 3-4 week regimen, accompanied by enrichment of CD4+ T cells expressing IL2.
3. Findings suggest that a third dose of the BNT162b2 mRNA vaccine is effective in protecting individuals against severe COVID-19-related outcomes, compared with receiving only two doses at least 5 months ago
4. SARS-CoV-2 Vaccine Booster Clinical Trial using a mix and match booster strategy showed homologous boost increased neutralizing antibody titers **4.2-20-fold** whereas heterologous boost increased titers **6.2-76-fold. J&J priming demonstrated the largest improvement when paired with mRNA vaccine over all heterologous comparisons with a homologous baseline.**
https://www.medrxiv.org/content/10.1101/2021.10.10.21264827v2

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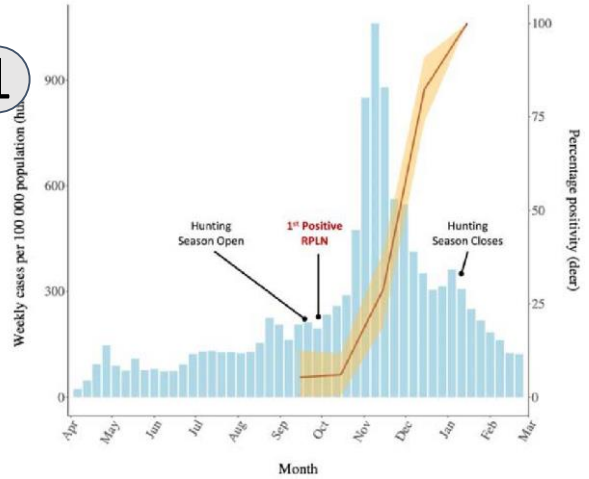

Researchers evaluated 283 retropharyngeal lymph node (RPLN) samples collected from 151 free-living and 132 captive deer in Iowa from April 2020 through December of 2020 for the presence of SARS-CoV-2 RNA. SARS-CoV-2 transmission in deer has important implications for the ecology and long-term persistence, as well as the potential for spillover to other animals and spillback into humans
https://www.biorxiv.org/content/10.1101/2021.10.31.466677v1

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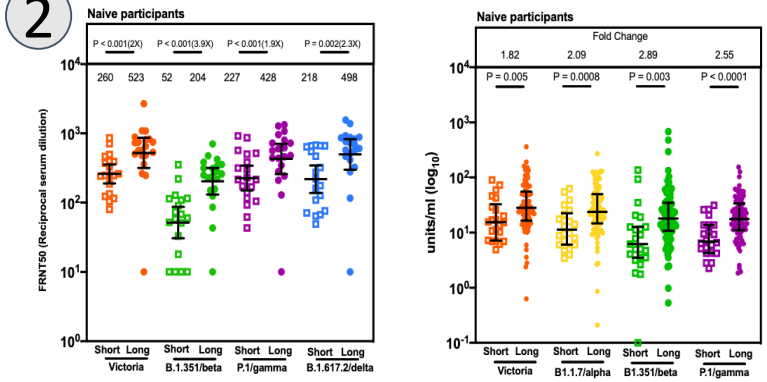

From the SIREN study in the UK: to demonstrate the impact of extended dosing intervals on vaccine effectiveness against infection, analysed data from the entire SIREN cohort. This study undertook clinical follow-up of healthcare workers (HCWs) between 7 December to 12 March 2021 with asymptomatic screening by PCR over a period of up to 95 days (13.6 weeks) from the first dose of BNT162b2 They found that .boosting (2nd dose) after a longer interval leads to maintained immunogenicity.
https://www.sciencedirect.com/science/article/pii/S0092867421012216?via%3Dihub

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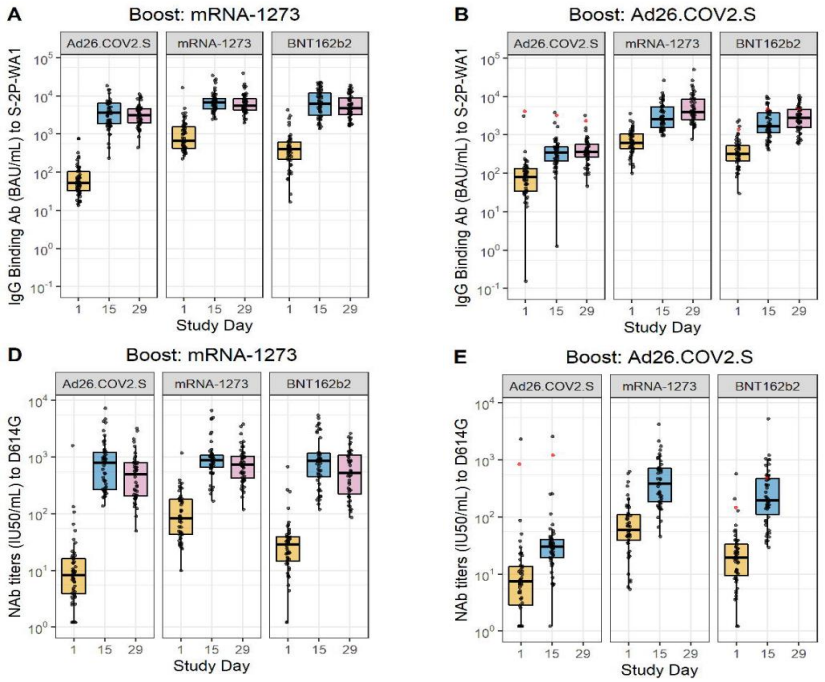

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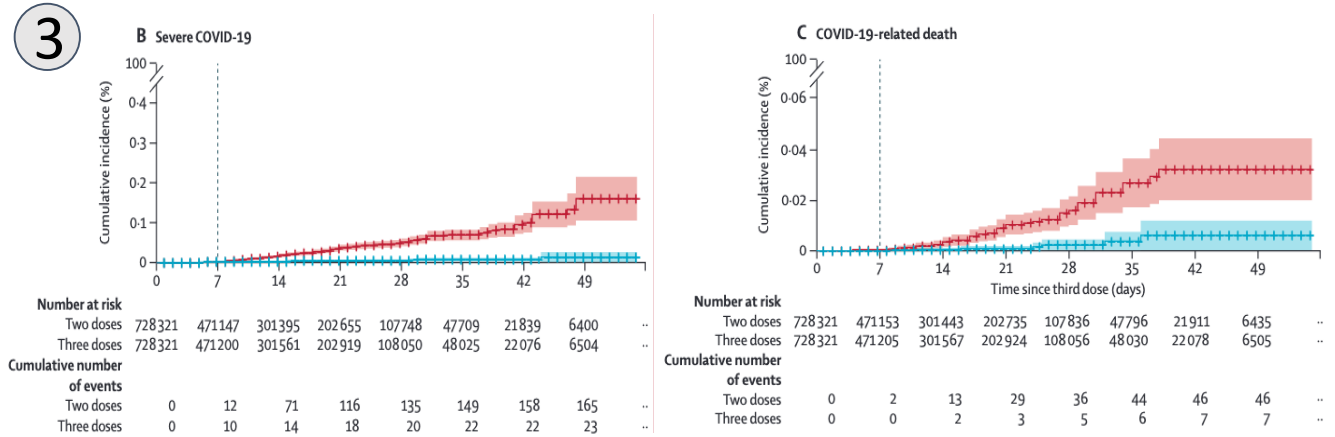
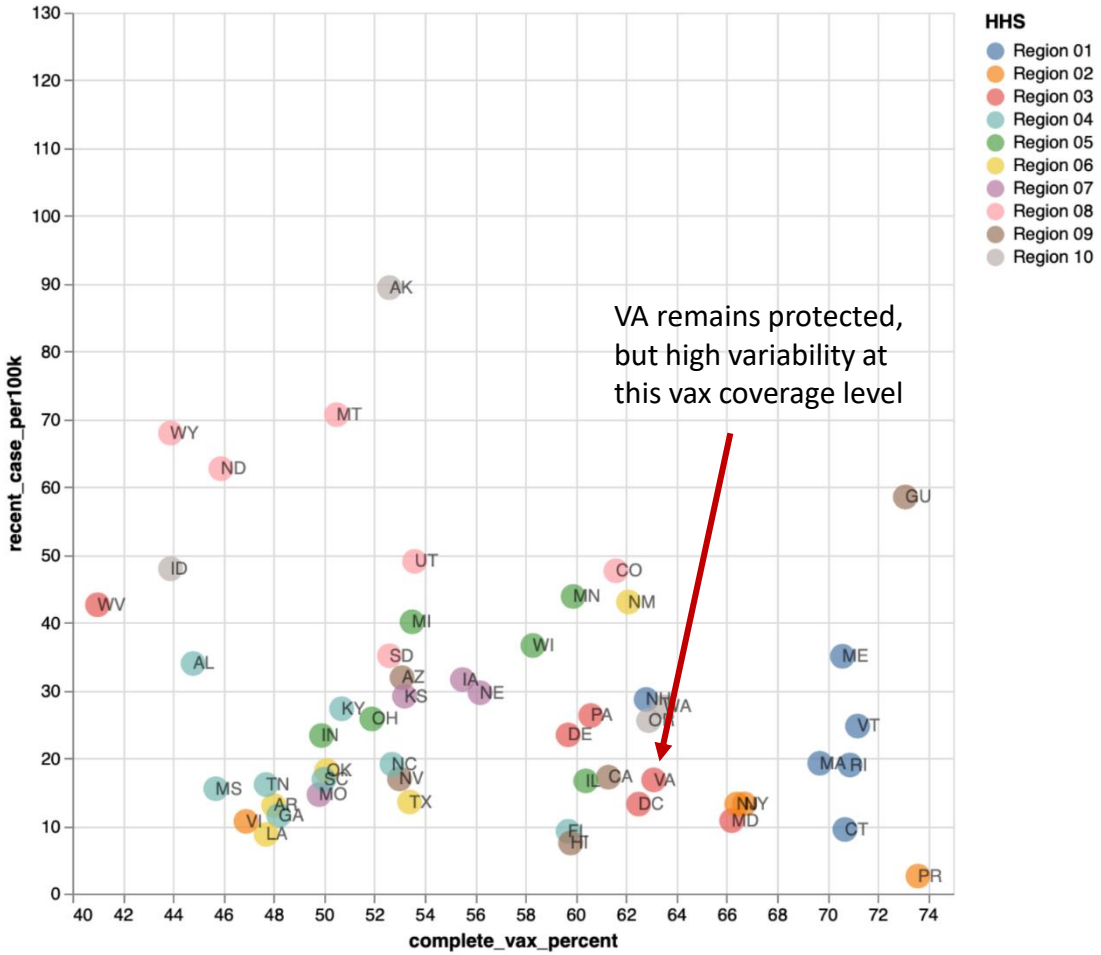


Using data from Clalit Health Services, which provides mandatory health-care coverage for over half of the Israeli population, individuals receiving a third vaccine dose between July 30, 2020, and Sept 23, 2021, were matched (1:1) to demographically and clinically similar controls who did not receive a third dose.Following matching, the third dose and control groups each included 728 321 individuals. Participants had a median age of 52 years (IQR 37–68) and 51% were female.
https://www.thelancet.com/action/showPdf?pii=S0140-6736%2821%2902249-2

Recent Cases Correlate with Vax Coverage

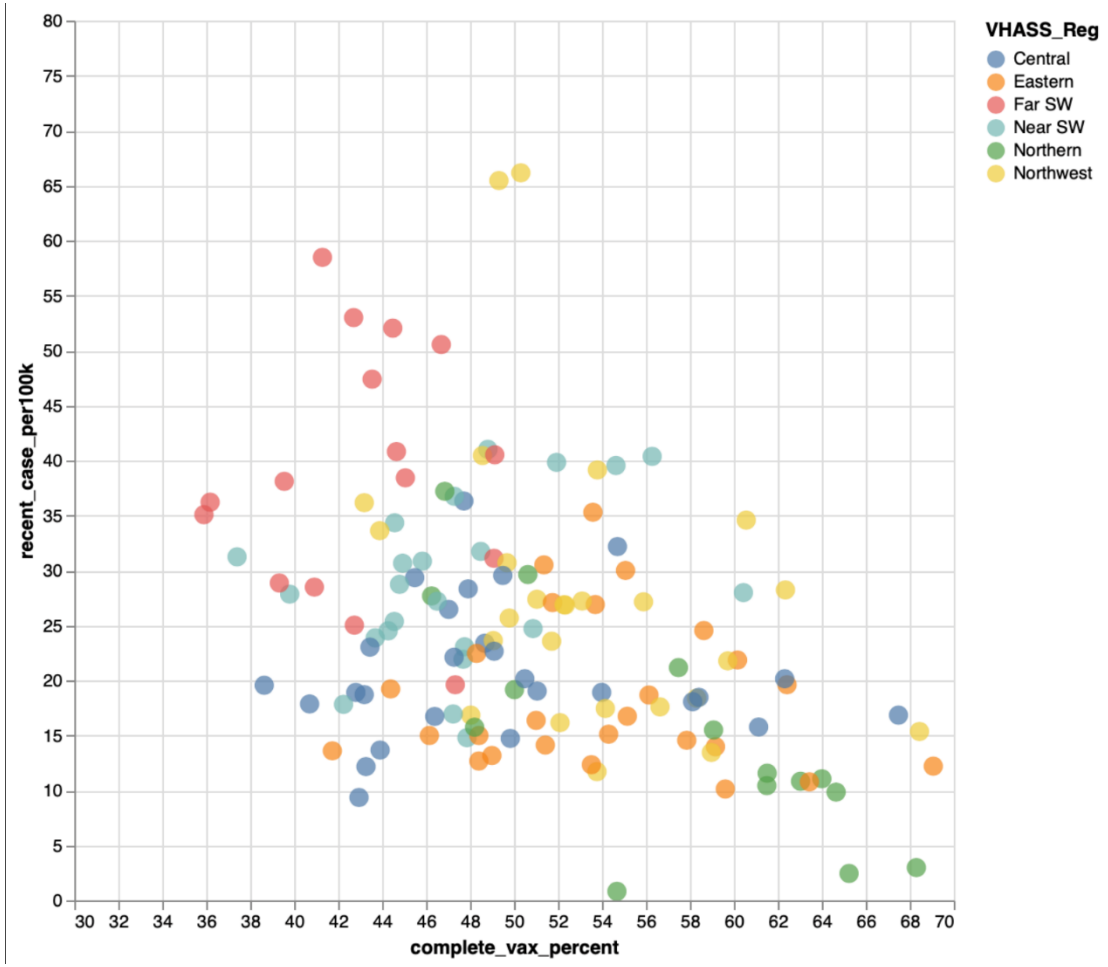
Mean cases per 100K vs. vaccine coverage

- States with lower vax coverage have had the worst case spikes



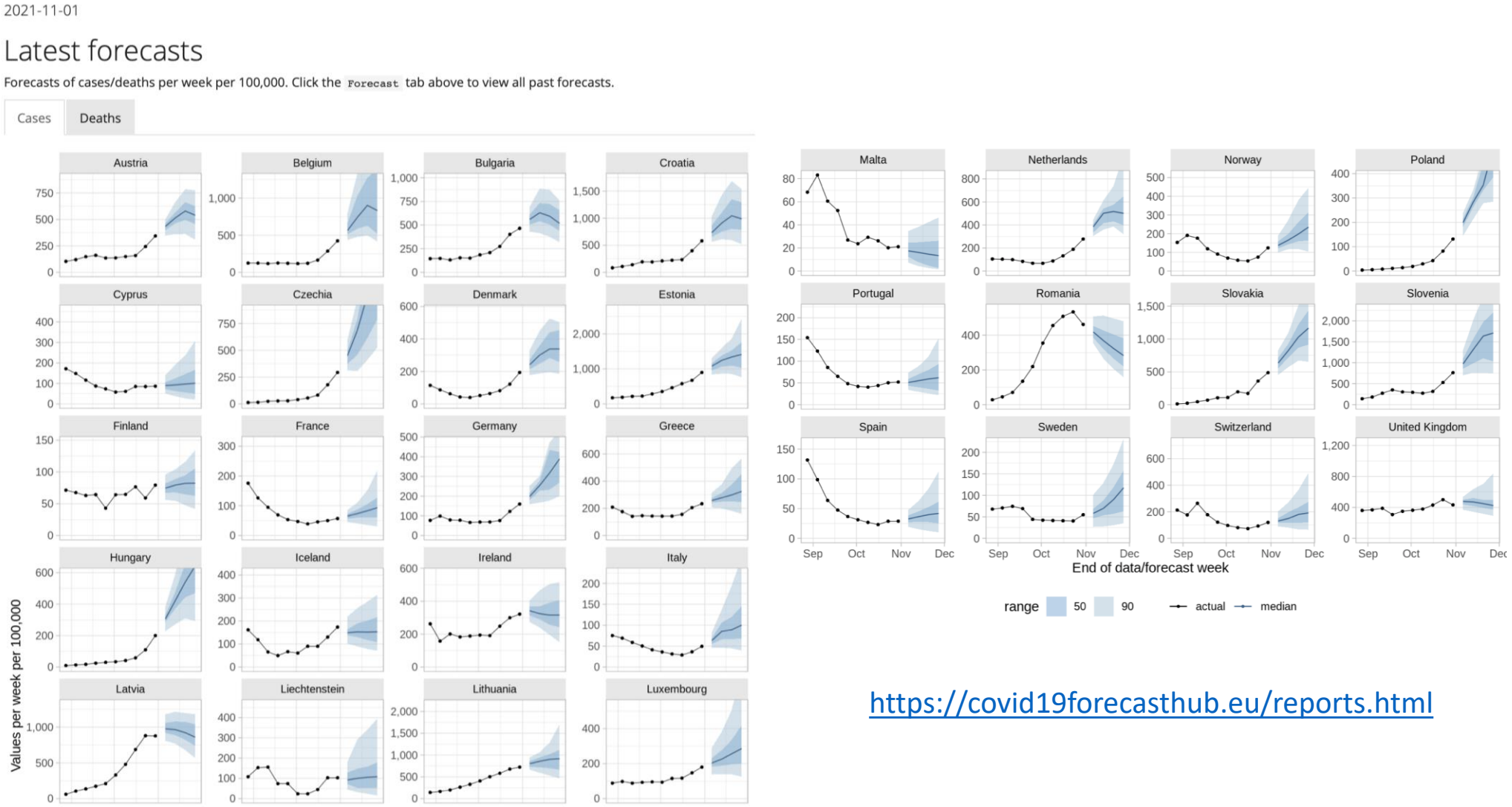
Virginia Counties

- Counties with higher vax coverage are maintaining lower case rates



European Nations

- Recent uptick in activity in many nations despite relatively high vaccine coverage
- Short term forecasts calling for increased cases or plateaus in most nations



https://covid19forecasthub.eu/reports.html

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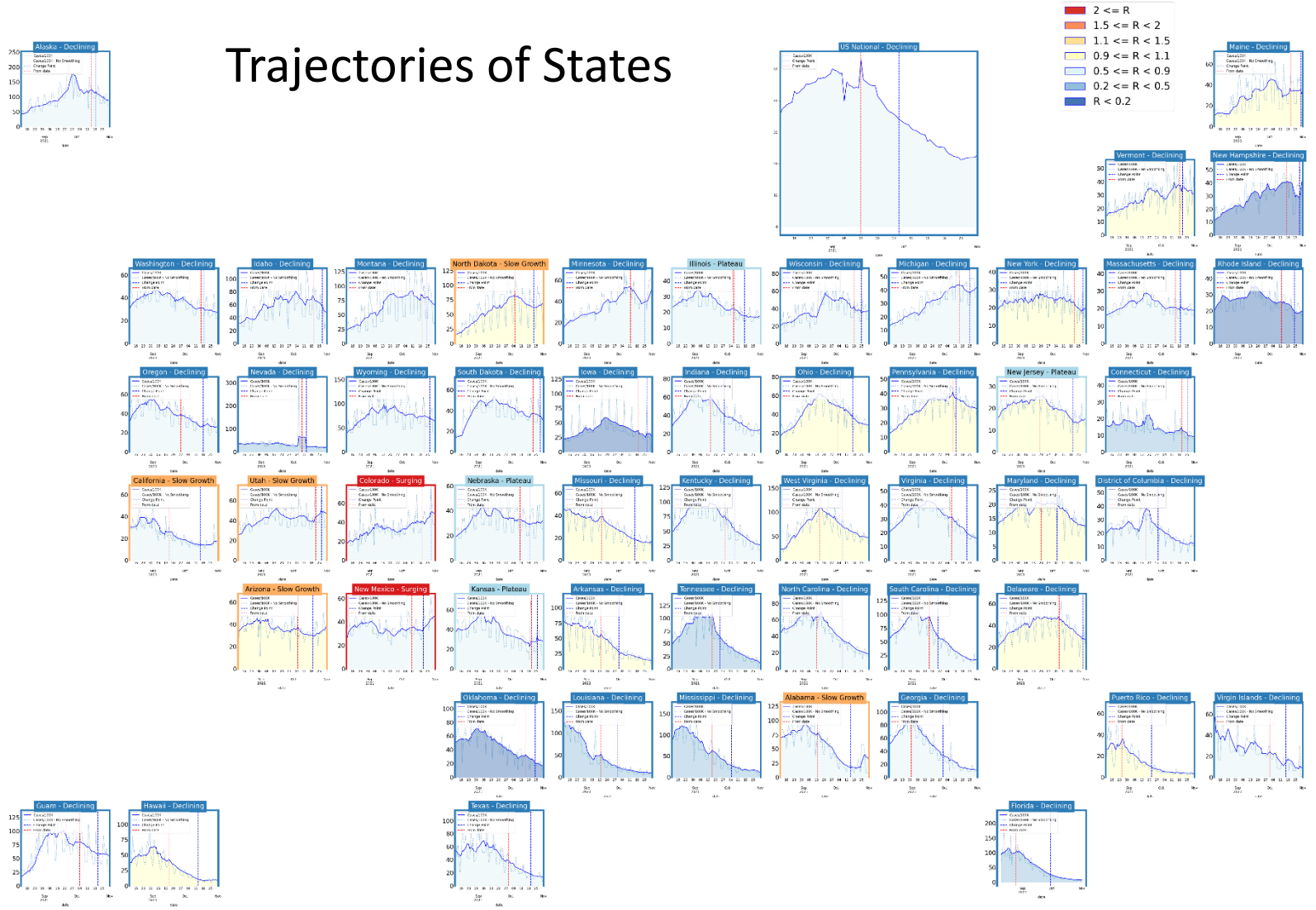
United States Overall

- Most states continue to decline (43) or plateau (5)
- However, more growth has emerged in some states, with 2 in surge, 5 in slow growth
- Case rates remain high, and nationally rates have flattened

Trajectories of States



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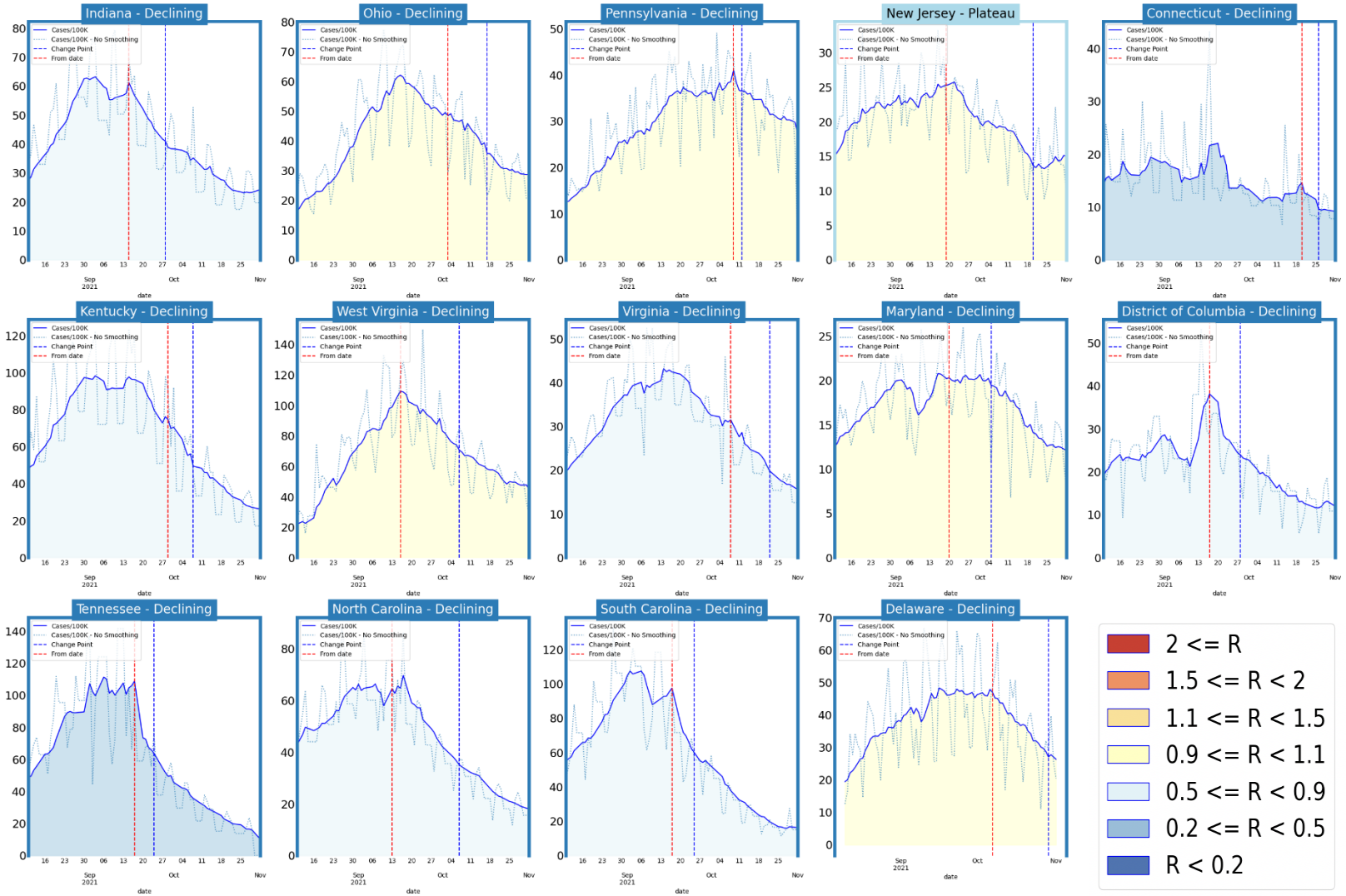
Virginia and Her Neighbors

- All neighbors remain in sustained decline
- Case rates have mostly moderated but some remain high
- Signs of slowing declines and plateaus emerging



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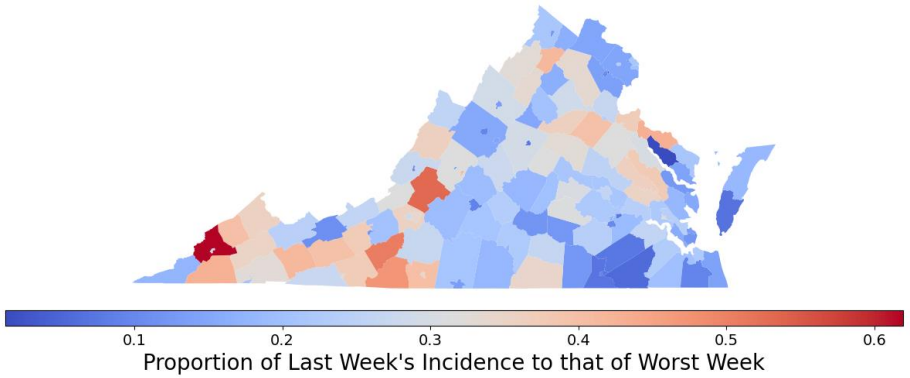
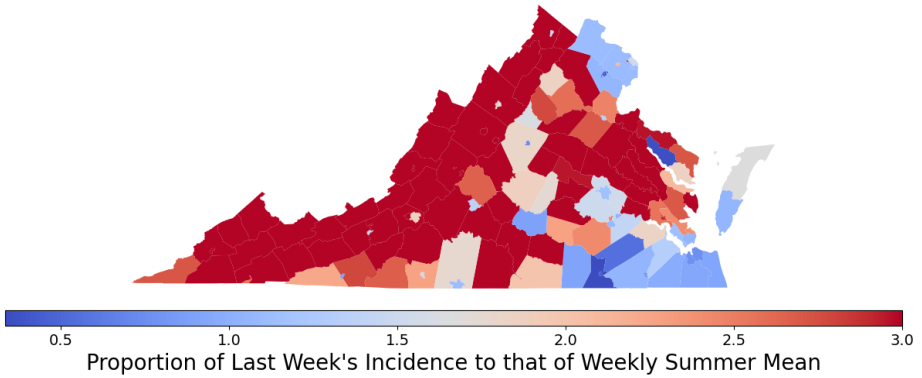
Last Week compared to the worst and the best

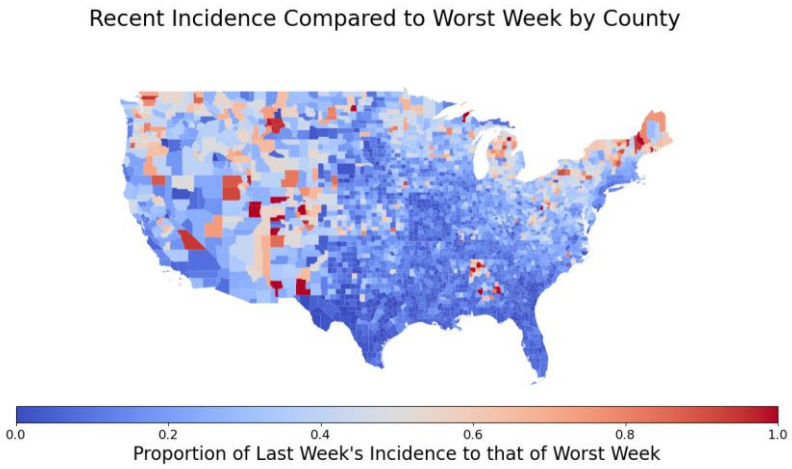
County level Case Rates (per 100K) proportion when comparing this most recent week to:

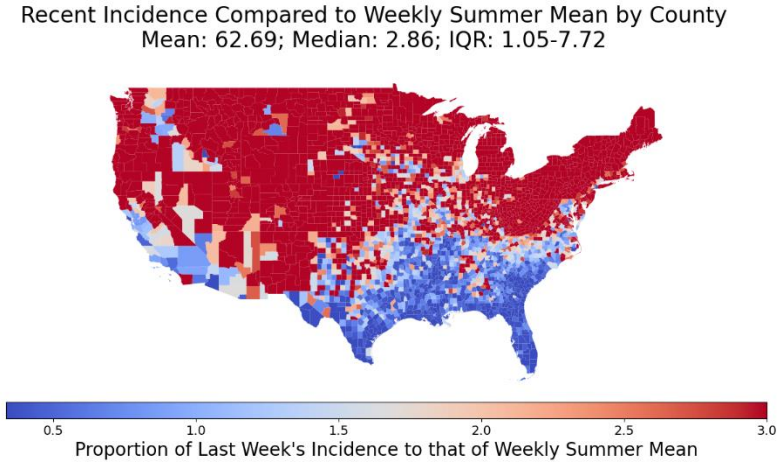
Worst Week of the Pandemic



Summer 2020 mean







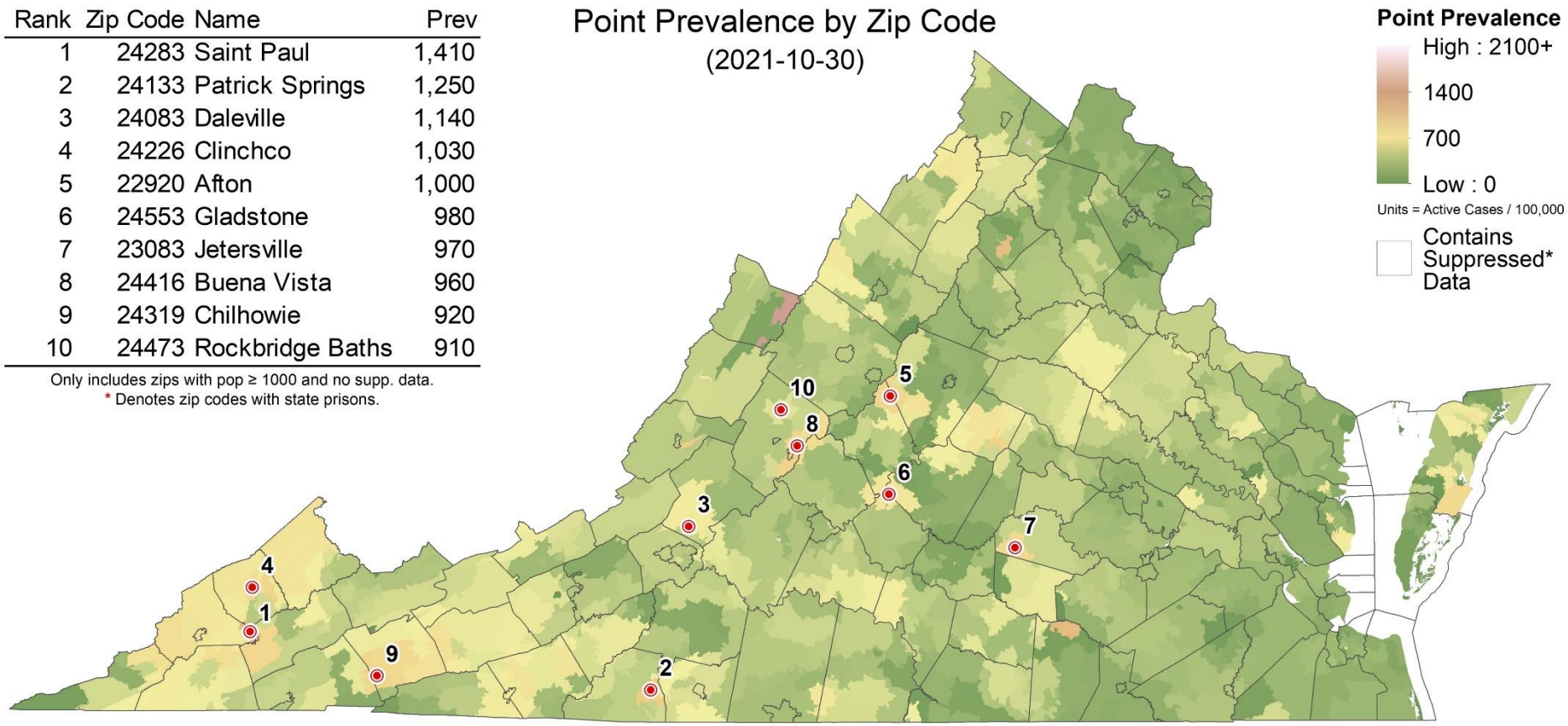
Zip code level weekly Case Rate (per 100K)

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

Rank	Zip Code	Name	Prev
1	24283	Saint Paul	1,410
2	24133	Patrick Springs	1,250
3	24083	Daleville	1,140
4	24226	Clinchco	1,030
5	22920	Afton	1,000
6	24553	Gladstone	980
7	23083	Jetersville	970
8	24416	Buena Vista	960
9	24319	Chilhowie	920
10	24473	Rockbridge Baths	910

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 2021-10-30.

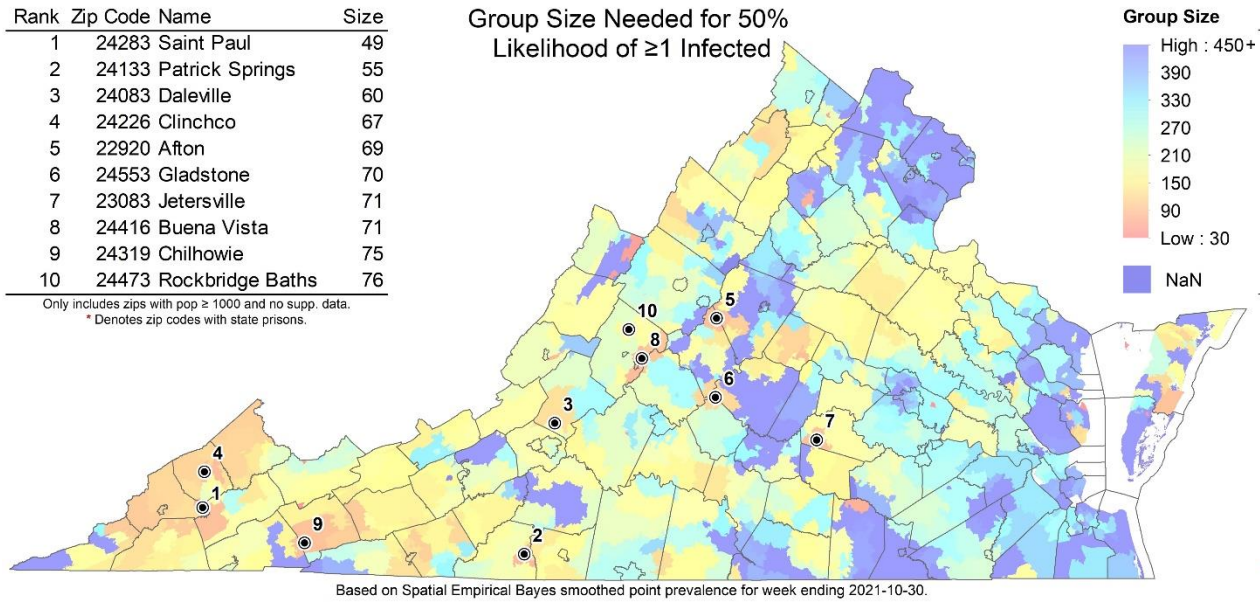
Risk of Exposure by Group Size and HCW prevalence

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 49 in Saint Paul, there is a 50% chance someone will be infected)
- **HCW ratio**: Case rate among health care workers (HCW) in the last week using patient facing health care workers as the denominator / general population's case prevalence

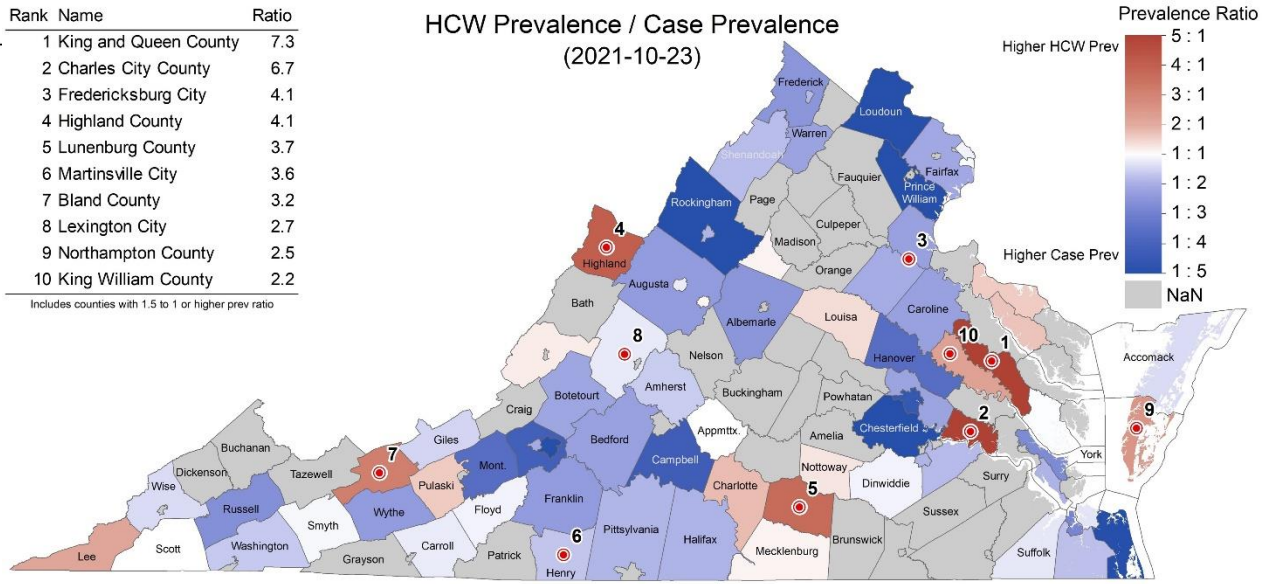
Rank	Zip Code	Name	Size
1	24283	Saint Paul	49
2	24133	Patrick Springs	55
3	24083	Daleville	60
4	24226	Clinchco	67
5	22920	Afton	69
6	24553	Gladstone	70
7	23083	Jetersville	71
8	24416	Buena Vista	71
9	24319	Chilhowie	75
10	24473	Rockbridge Baths	76

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



Rank	Name	Ratio
1	King and Queen County	7.3
2	Charles City County	6.7
3	Fredericksburg City	4.1
4	Highland County	4.1
5	Lunenburg County	3.7
6	Martinsville City	3.6
7	Bland County	3.2
8	Lexington City	2.7
9	Northampton County	2.5
10	King William County	2.2

Includes counties with 1.5 to 1 or higher prev ratio



Data from week ending Oct 23rd, No update due to Election Day

Current Hot-Spots

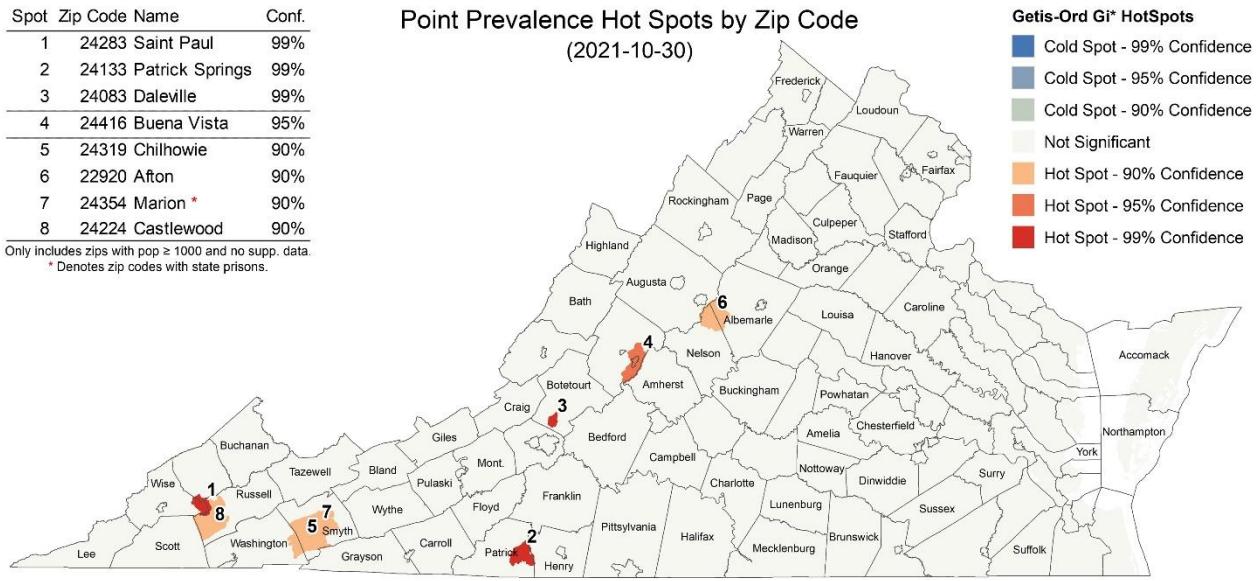
Case rates that are significantly different from neighboring areas or model projections

- **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

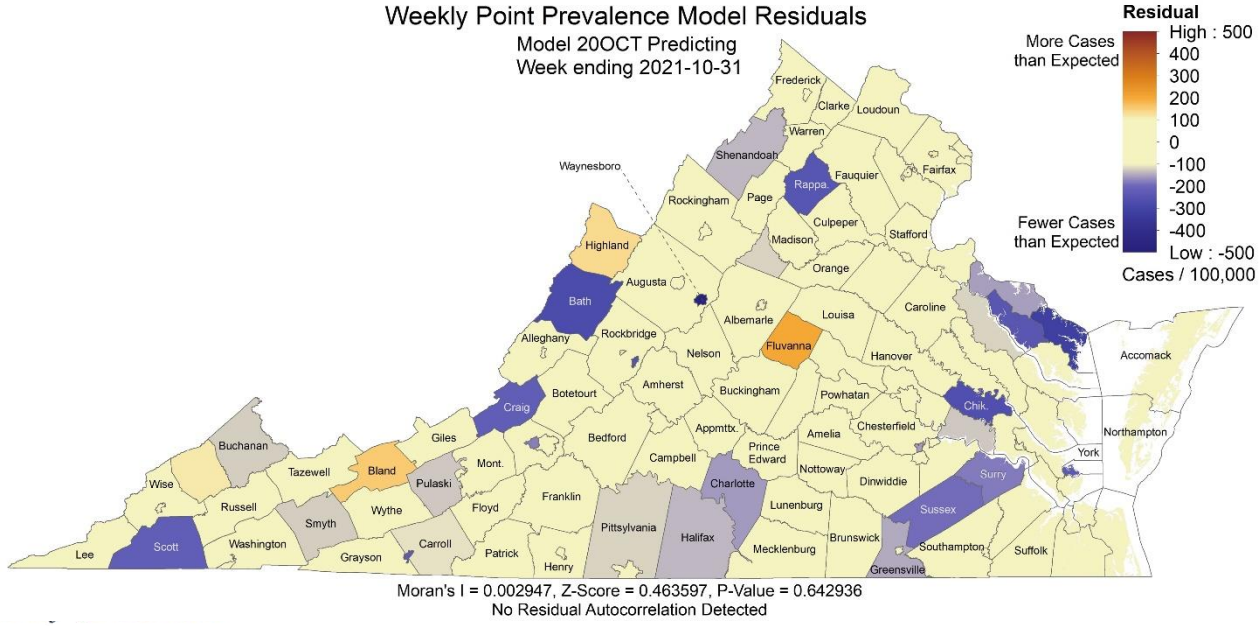
Spatial Hotspots

Spot	Zip Code	Name	Conf.
1	24283	Saint Paul	99%
2	24133	Patrick Springs	99%
3	24083	Daleville	99%
4	24416	Buena Vista	95%
5	24319	Chilhowie	90%
6	22920	Afton	90%
7	24354	Marion *	90%
8	24224	Castlewood	90%

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



Clustered Temporal Hotspots



Model Update – Adaptive Fitting

Adaptive Fitting Approach

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

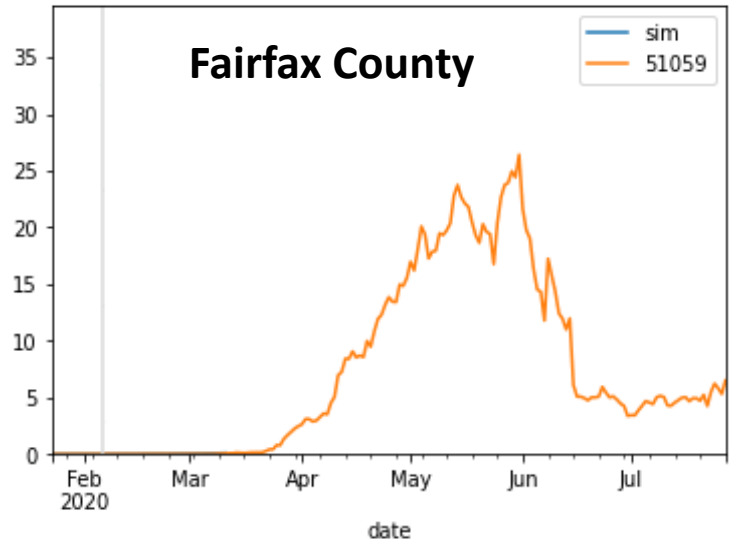
- Allows history to be precisely captured, and used to guide bounds on projections

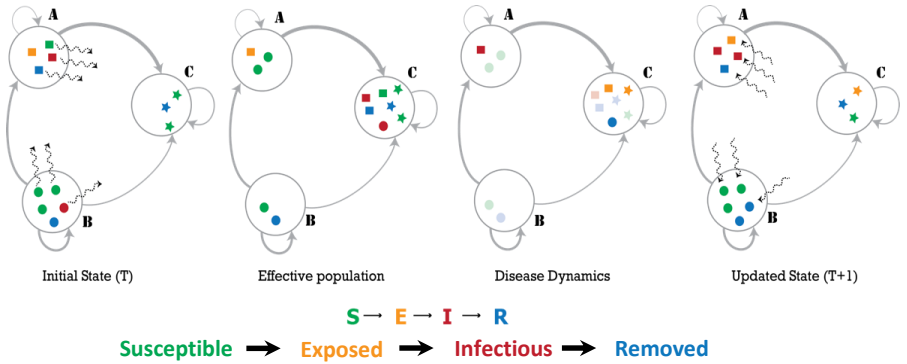
Model: An alternative use of the same meta-population model, PatchSim

- 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





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Using Ensemble Model to Guide Projections

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

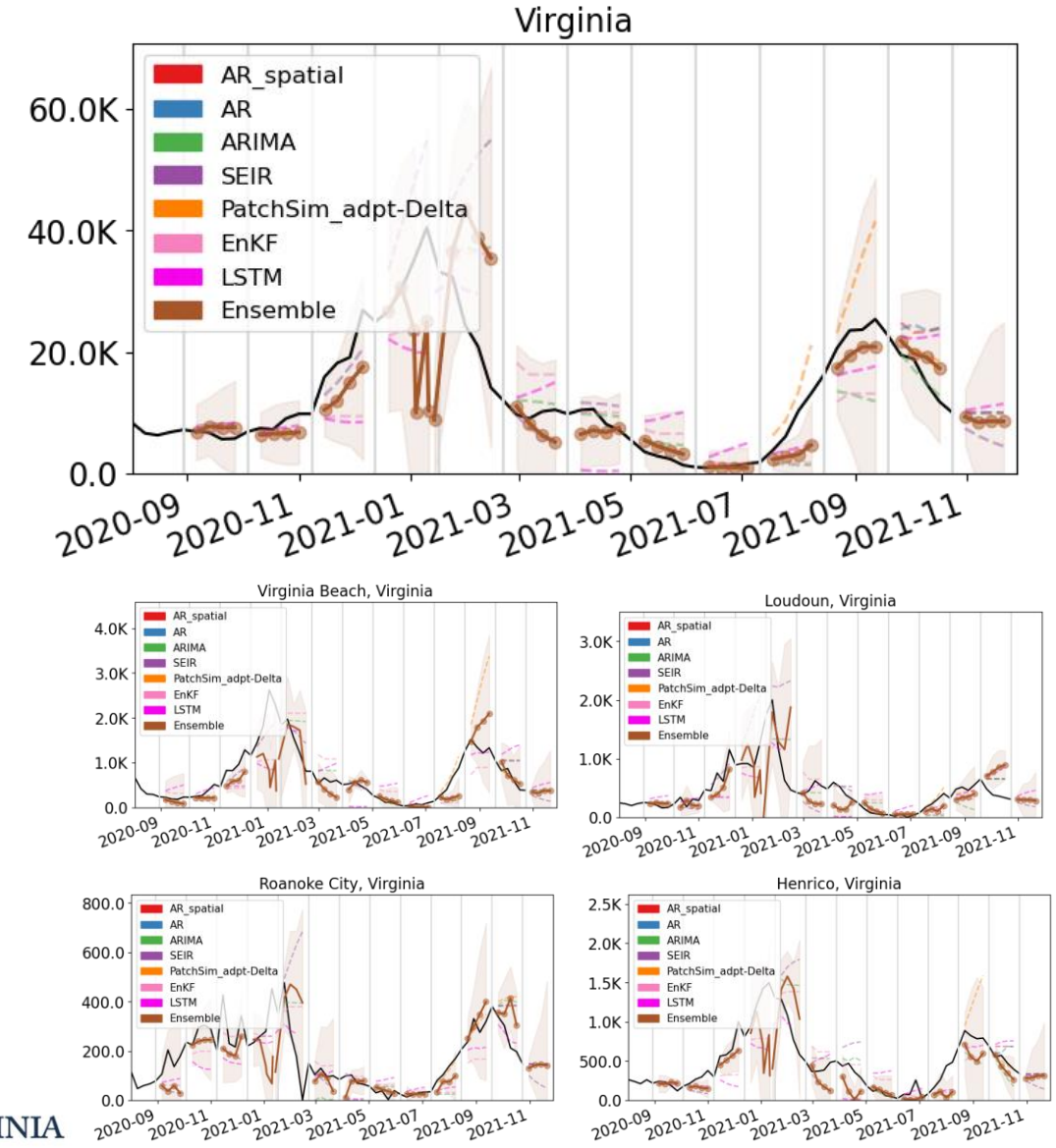
- Autoregressive (AR, ARIMA)
- Neural networks (LSTM)
- Kalman filtering (EnKF)

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

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

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

Also submitted to CDC Forecast Hub.



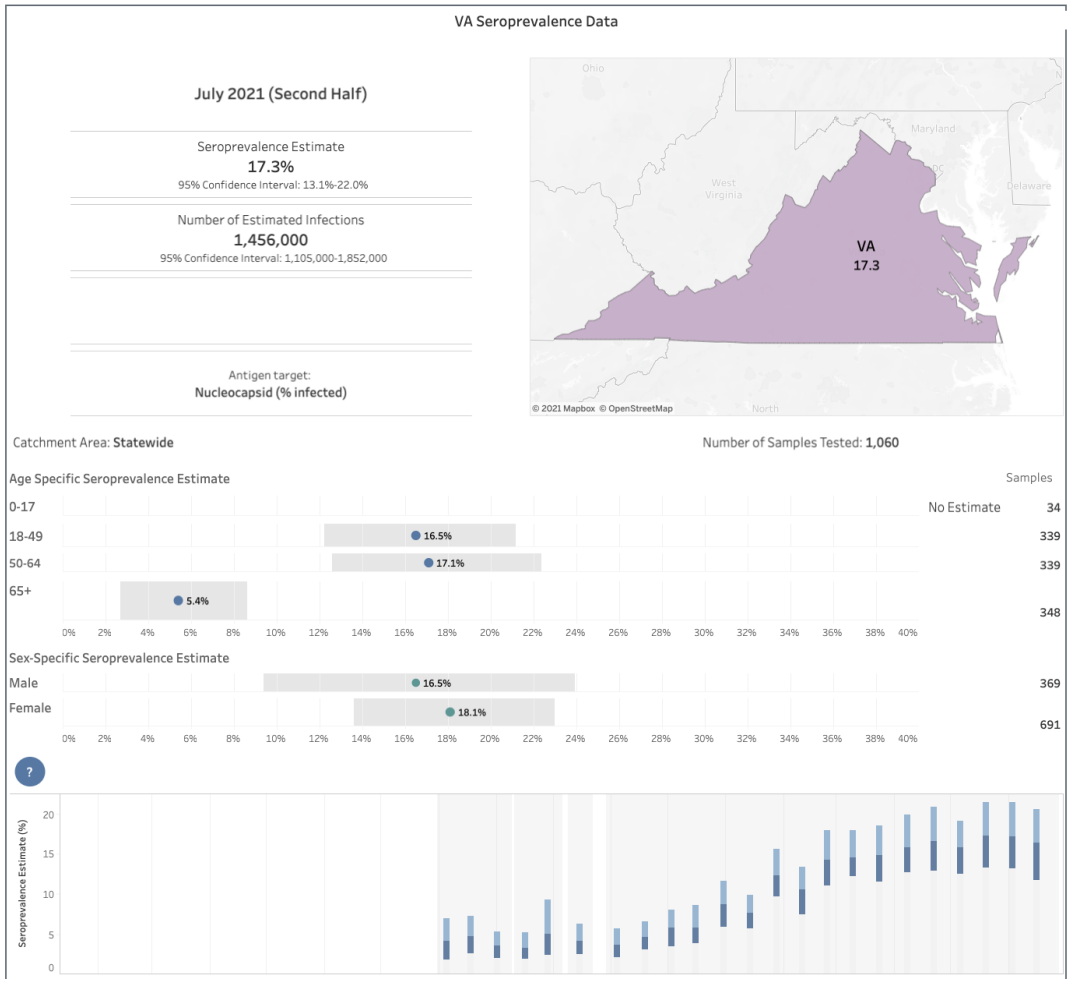
Seroprevalence updates to model design

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

- CDC Nationwide Commercial Laboratory Seroprevalence Survey

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

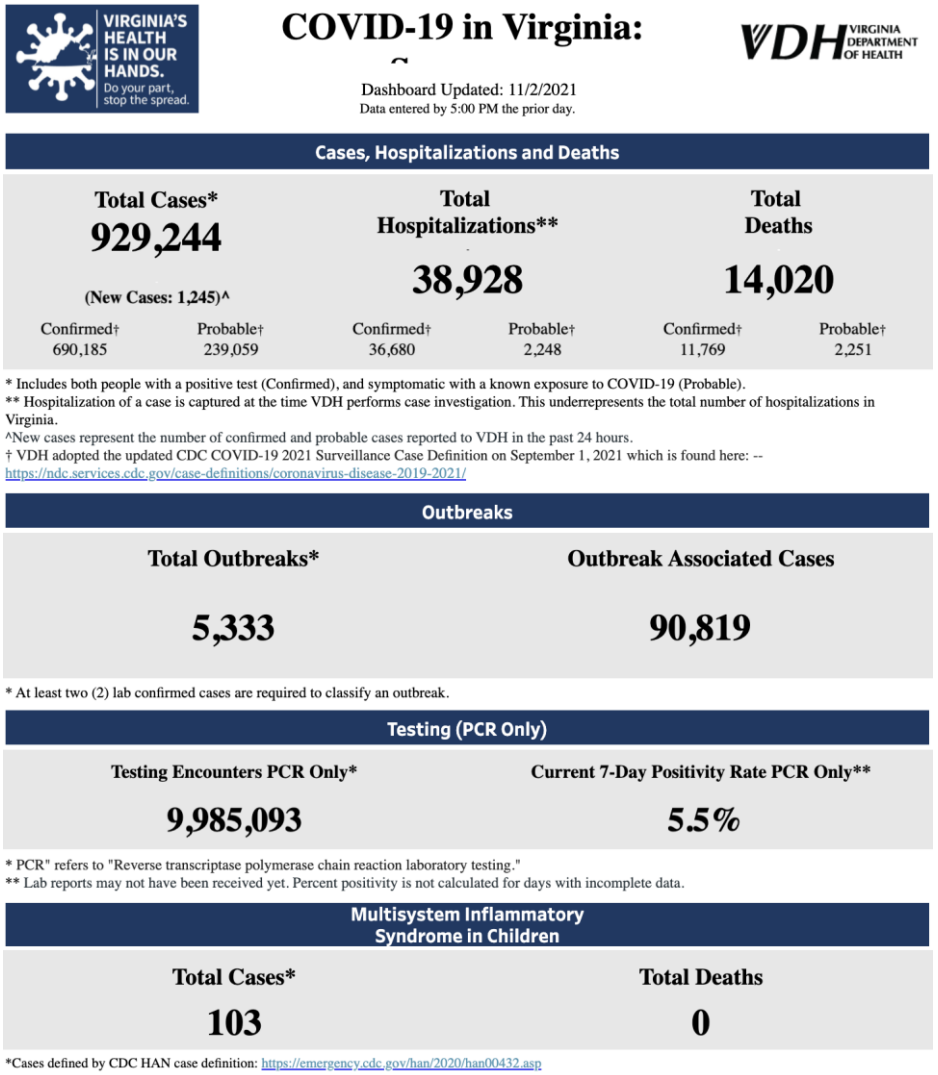
- Thus for 2x there are 2 total infections in the population for every confirmed case recently
- This measure now fully tracks the estimated ascertainment over time
- Uncertainty design has been shifted to these bounds (previously higher ascertainments as was consistent earlier in the pandemic were being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



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

Calibration Approach

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



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

COVID-19 in Virginia:

VDH VIRGINIA DEPARTMENT OF HEALTH

Dashboard Updated: 11/2/2021
Data entered by 5:00 PM the prior day.

Cases, Hospitalizations and Deaths

Total Cases*	Total Hospitalizations**	Total Deaths
929,244	38,928	14,020
(New Cases: 1,245)^		
Confirmed† 690,185 / Probable† 239,059	Confirmed† 36,680 / Probable† 2,248	Confirmed† 11,769 / Probable† 2,251

* 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
5,333	90,819

* 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**
9,985,093	5.5%

* 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
103	0

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

Accessed 8:30am November 3, 2021
https://www.vdh.virginia.gov/coronavirus/

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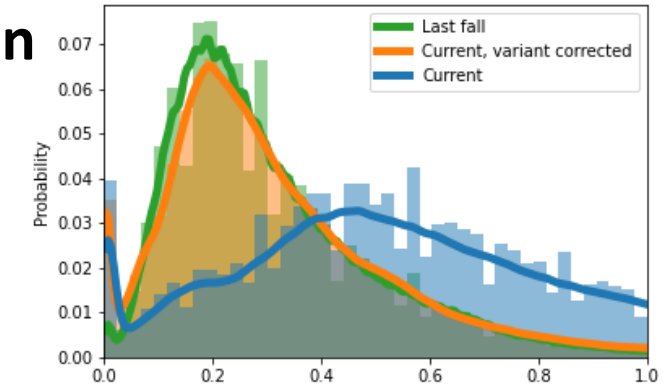
Scenarios – Transmission Conditions

- 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

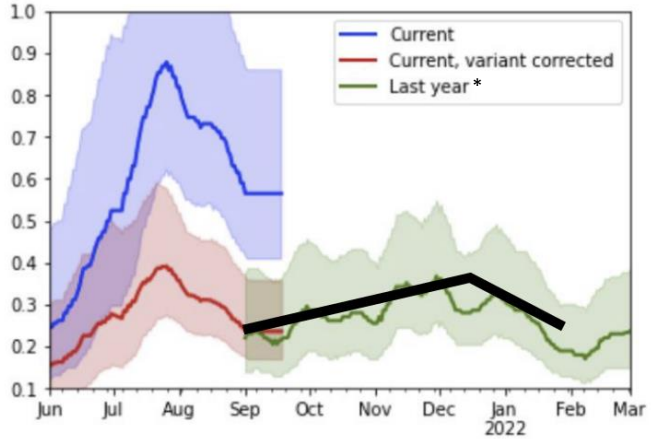
Scenarios – FallWinter2020 Description

September 2020 – February 2021 saw a strong wave of transmission

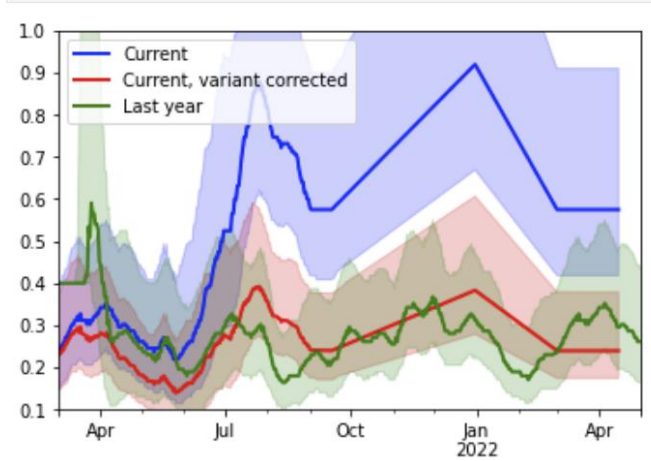


- We analyze previous Fall-Winter's wave vs. current Delta driven wave and observe surprising similarities
  - The distribution of fitted model transmissibility is nearly identical between these periods when corrected for Delta's increased transmissibility
- **FallWinter2020** tries to capture the "transmission 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

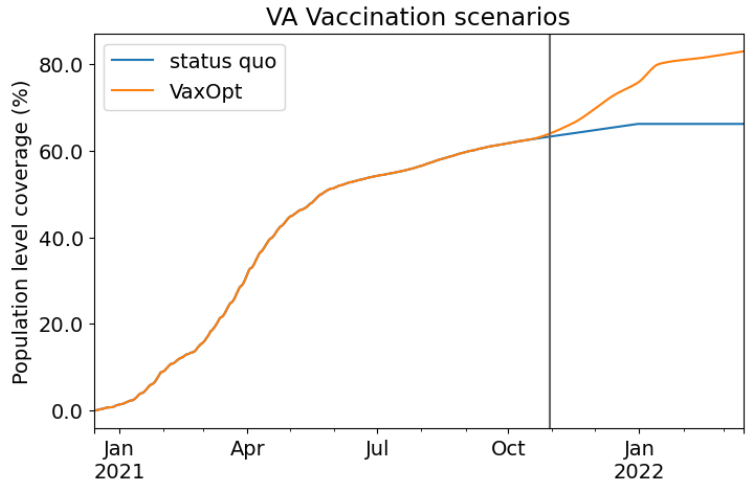
Scenarios – Vaccination Conditions

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. 3rd doses continue with total coverage of 40%
- **Optimistic (VaxOpt):** Expand VA mean acceptance to include "probably not" (~85% adults) with addition of childhood (5-11 yo) rollout starting in Nov 15th. 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 December. 3rd doses continue with total coverage of 60%
- Acceptance at county level = regional acceptance +/- relative current vax
- Front-loaded rollout (two-thirds of the remaining in half the time)



	Monthly		Cumulative	
Date	status quo	VaxOpt	status quo	VaxOpt
12/31/20	110.2K	110.2K	110.2K	110.2K
1/31/21	649.8K	649.8K	760.0K	760.0K
2/28/21	561.7K	561.7K	1.3M	1.3M
3/31/21	1.3M	1.3M	2.6M	2.6M
4/30/21	1.2M	1.2M	3.8M	3.8M
5/31/21	575.8K	575.8K	4.4M	4.4M
6/30/21	243.0K	243.0K	4.6M	4.6M
7/31/21	198.2K	198.2K	4.8M	4.8M
8/31/21	271.6K	271.6K	5.1M	5.1M
9/30/21	177.4K	177.4K	5.3M	5.3M
10/31/21	145.0K	249.9K	5.4M	5.5M
11/30/21	110.5K	432.3K	5.5M	6.0M
12/31/21	122.3K	507.6K	5.7M	6.5M
1/31/22	0	446.2K	5.7M	6.9M
2/28/22	0	103.2K	5.7M	7.0M
3/31/22	0	67.6K	5.7M	7.1M

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

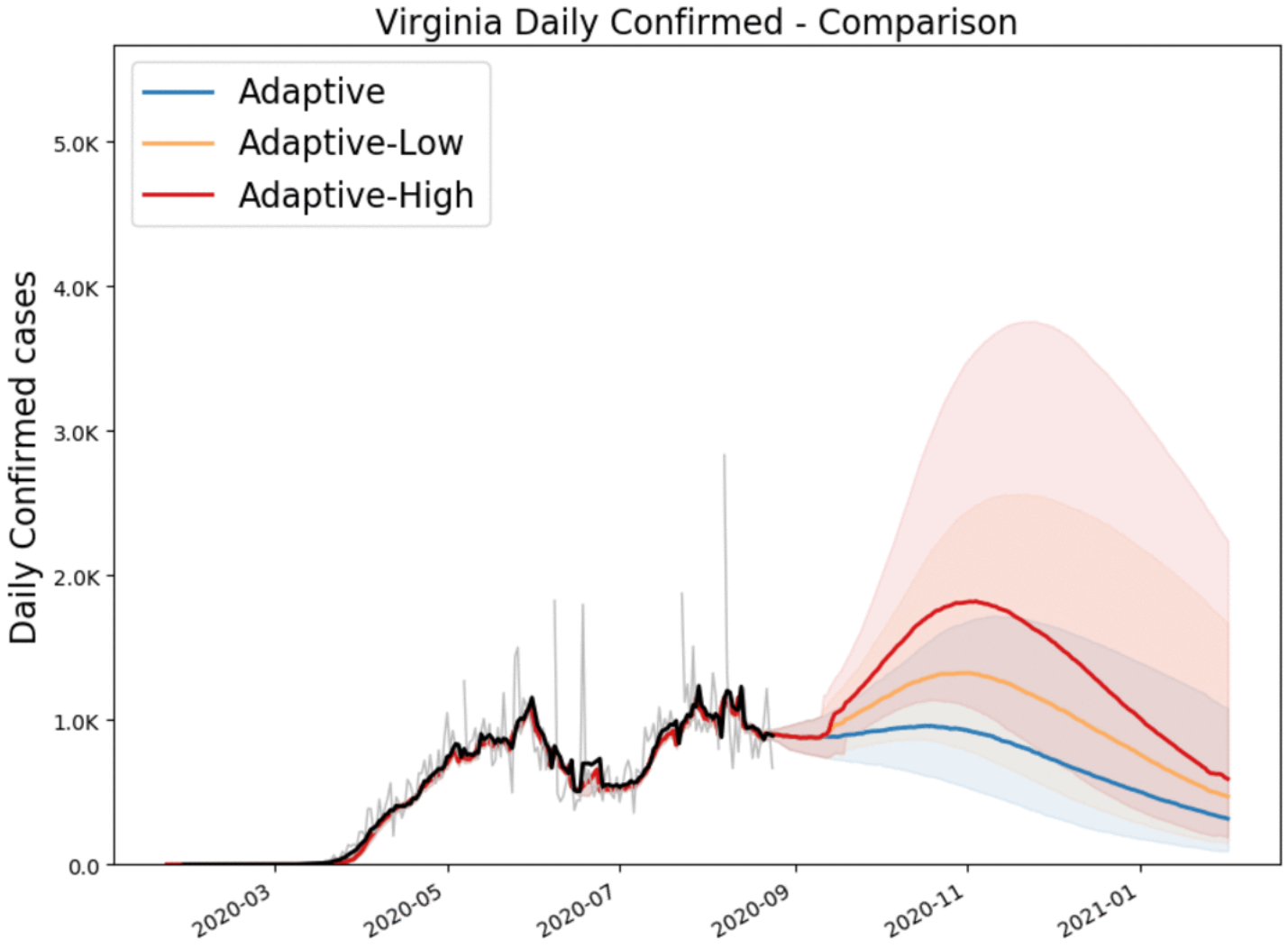
Transmission Controls:
C = Current levels persist into the future
25% = Transmission rates are reduced by 25% with a gradual introduction, concluding in 4 weeks
FallWinter2020 = Transmission rates from Sept 2020 – Feb 2021 are coarsely replayed but boosted by Delta's increased transmissibility

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

Review of “A Year of Projections”

Confirmed case Projections
Adaptive Approach with associated other projections

Sept 30th, 2020 to
Oct 20th, 2021



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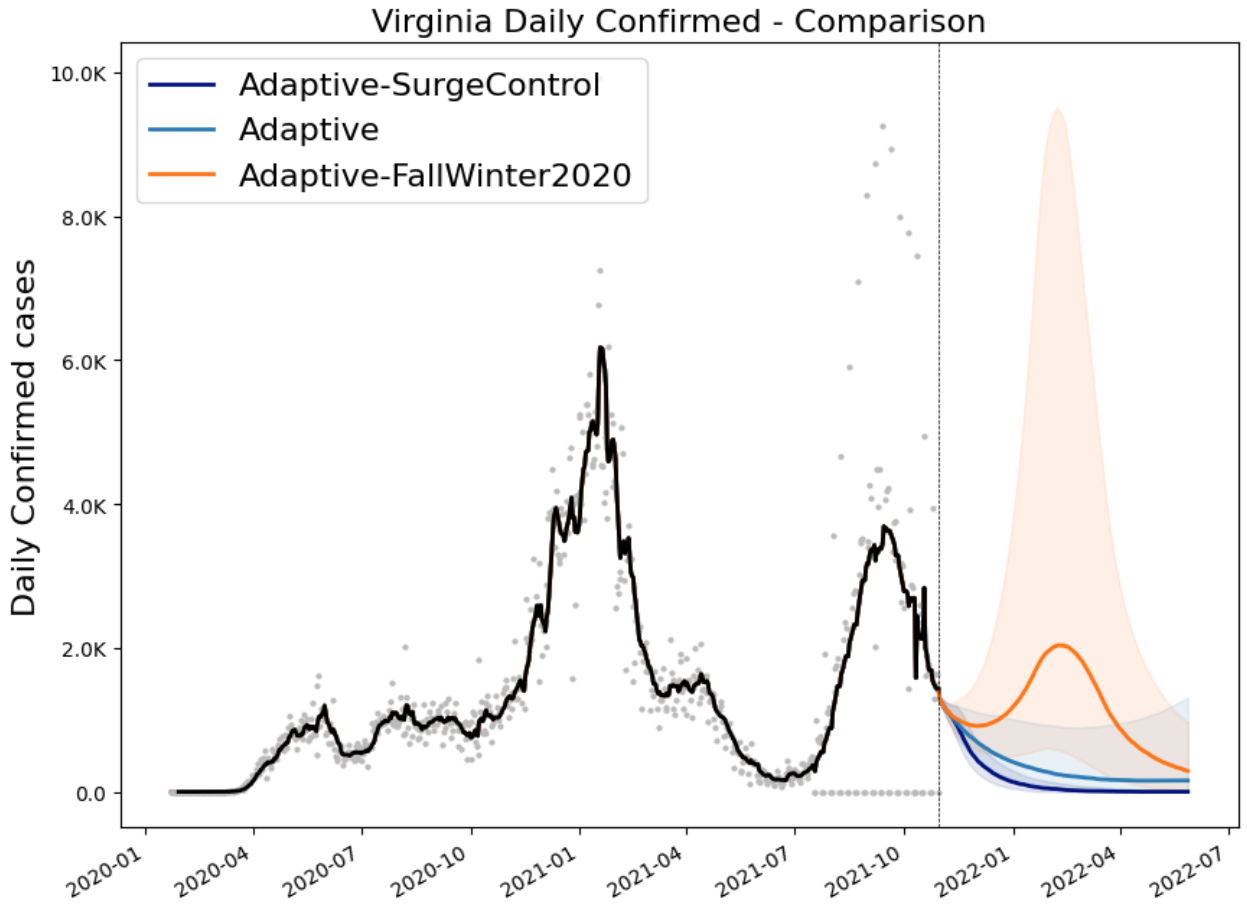
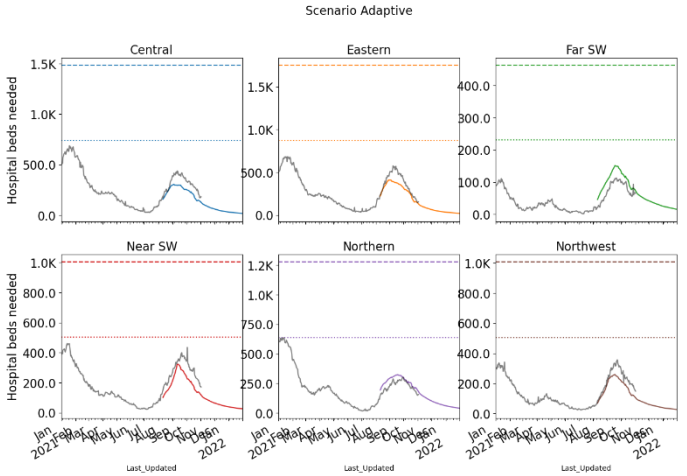
Model Results

Outcome Projections

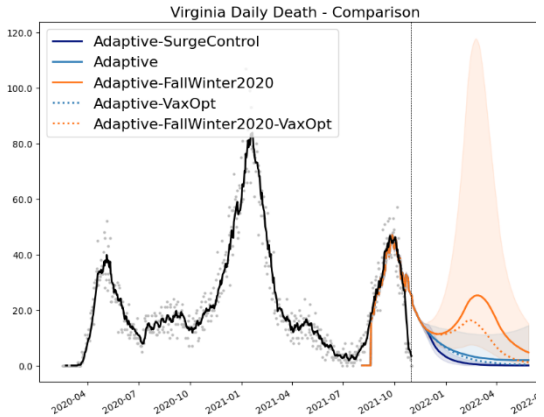
Confirmed cases



Estimated Hospital Occupancy

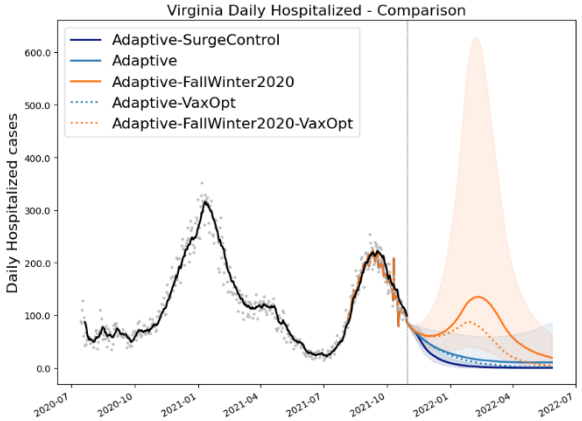


Daily Deaths



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

Daily Hospitalized



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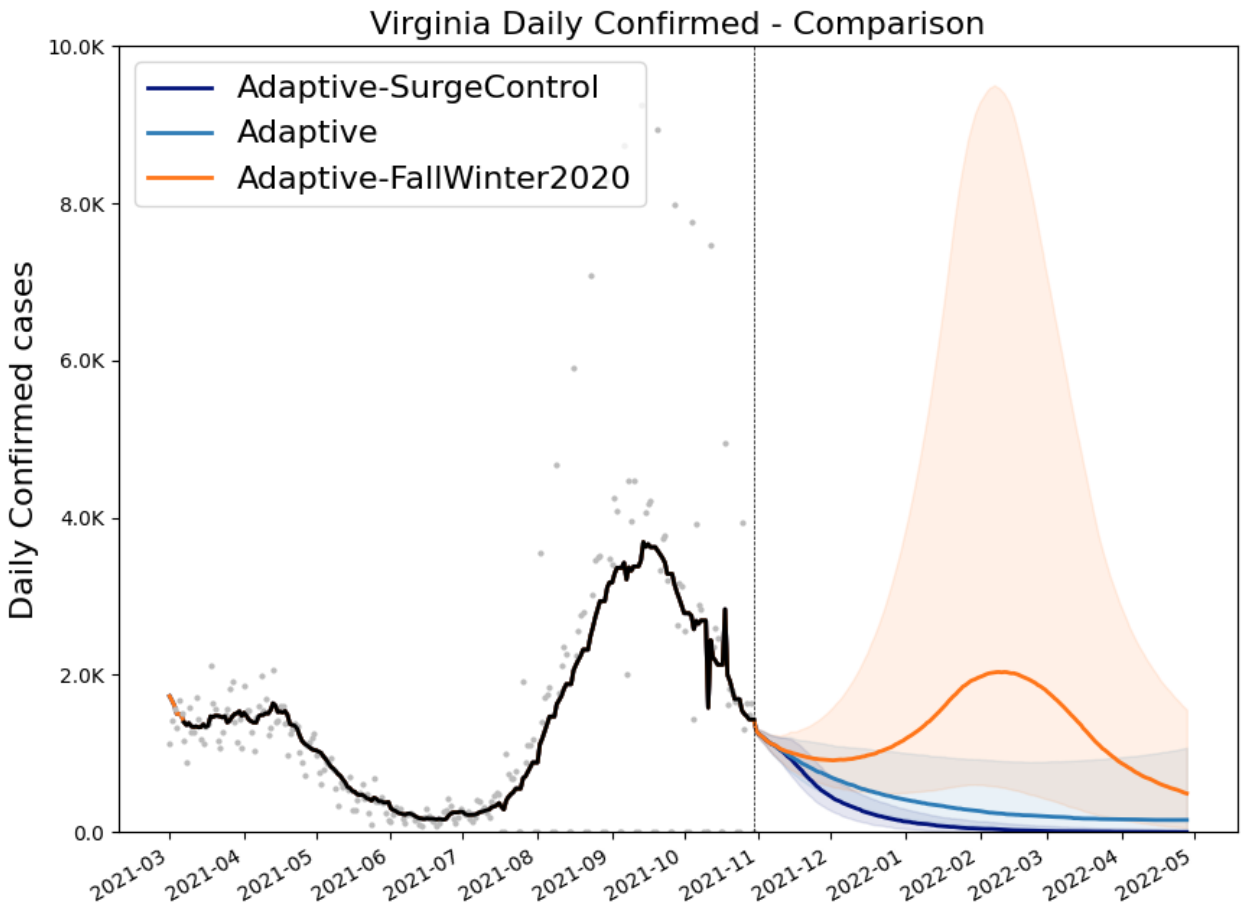
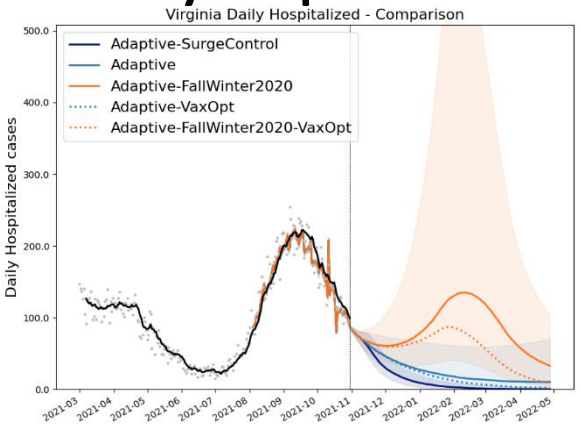
Outcome Projections – Closer Look

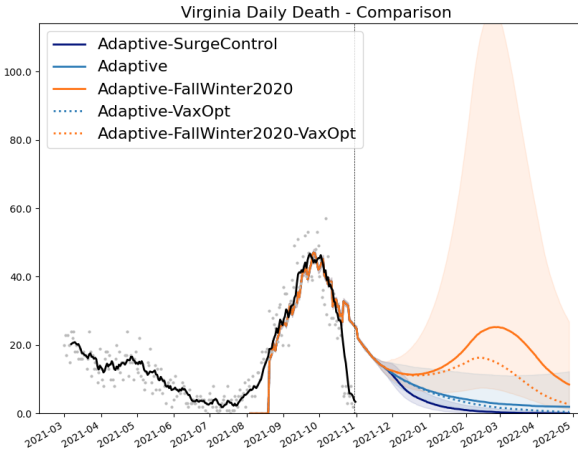
Confirmed cases



Daily Hospitalized



Daily Deaths



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

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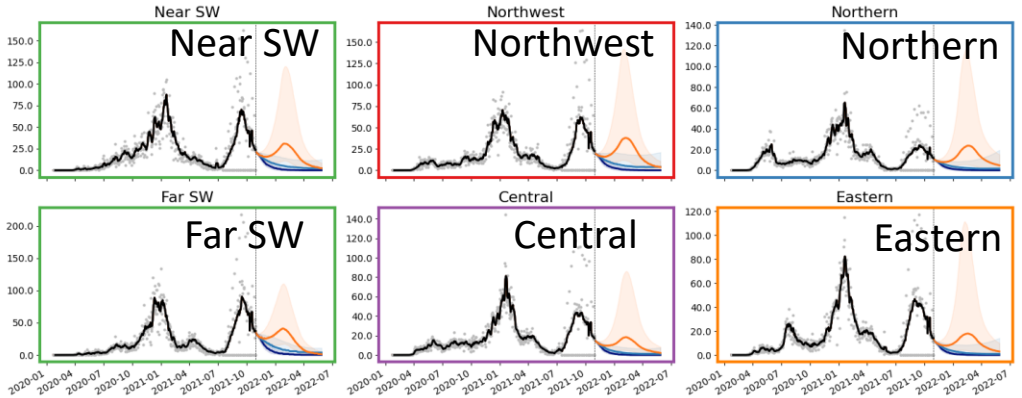
Detailed Projections: All Scenarios

Projections by Region

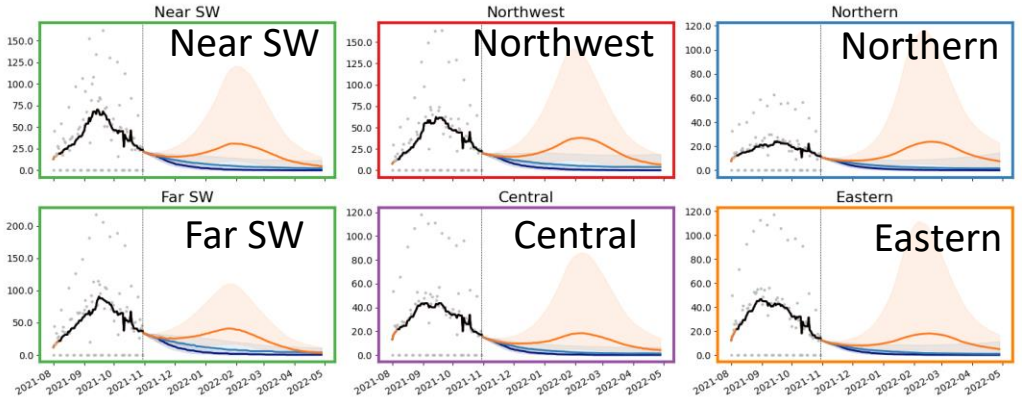


Projections by District

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

Detailed Projections: All Scenarios - Closer Look

Projections by Region



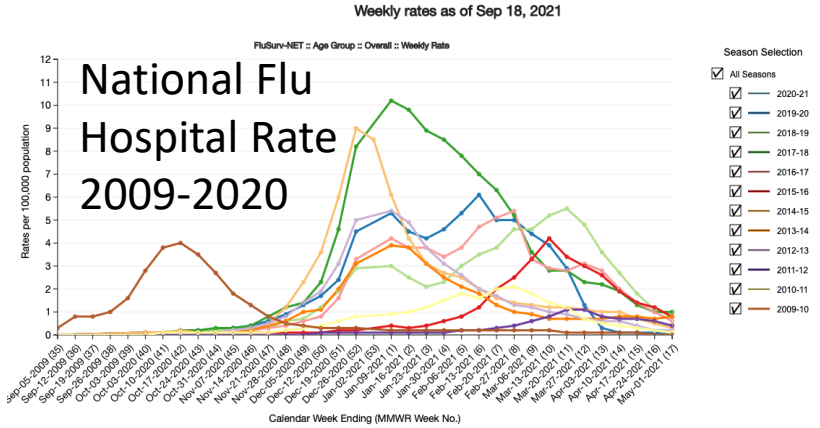
Projections by District

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

Impact of Influenza based on Previous Intense Flu Seasons

Augment COVID-19 daily hospitalizations with that of past Influenza seasons

- Include hybrid seasons that use timing of one season but are scaled by severity of another
- Due to limited historical data on Virginia flu hospitalizations currently using national rates applied to VA population



https://gis.cdc.gov/GRASP/Fluview/FluHospRates.html

2009-10 – Pandemic 2009 H1N1 season

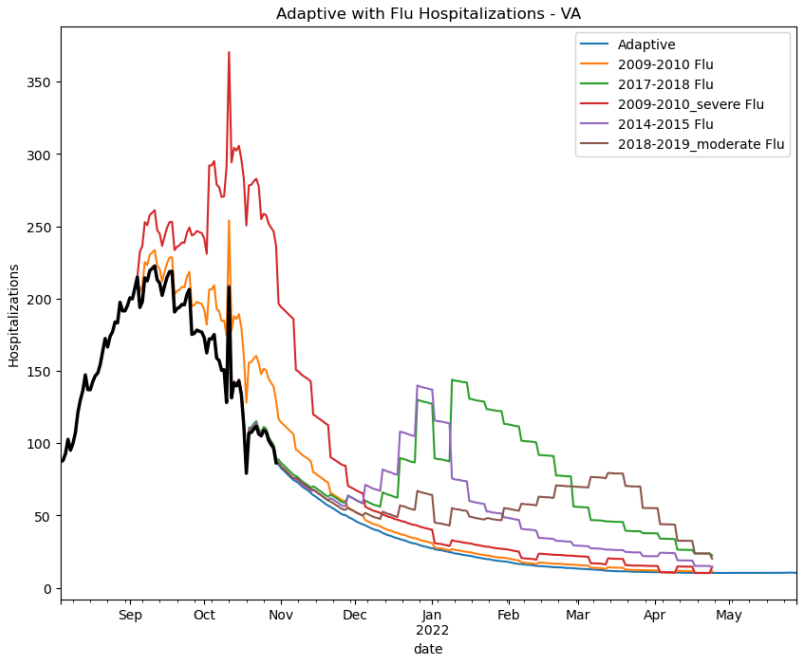
2017-18 – Timing and severity of 2017-18 season

2009-10_severe – Timing of 2009 pandemic (early) with the severity of the 2017-18 season

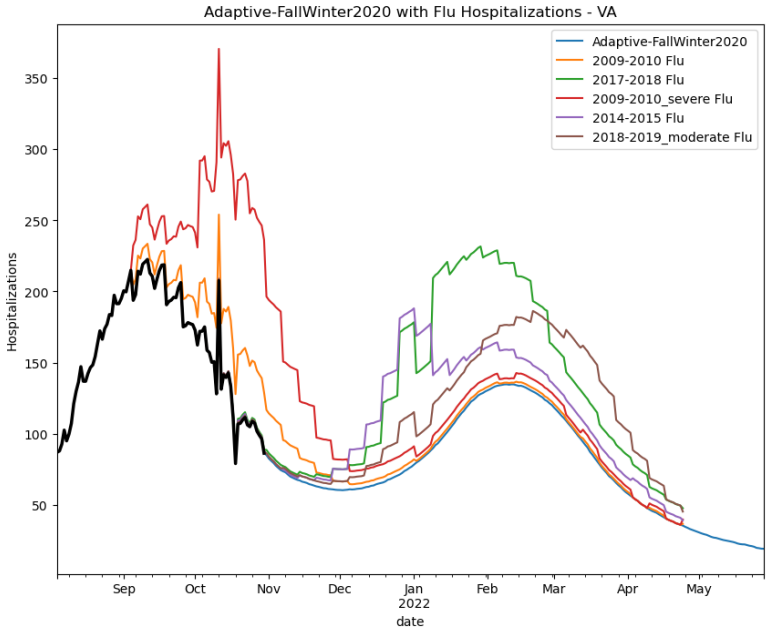
2014-15 – Timing and severity of 2014-15 season

2018-19_moderate – Timing of 2018-19 (late) season with severity of 2014-15

Adaptive



Adaptive – FallWinter2020



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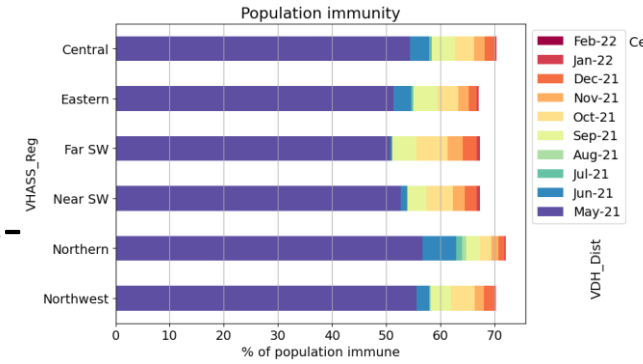
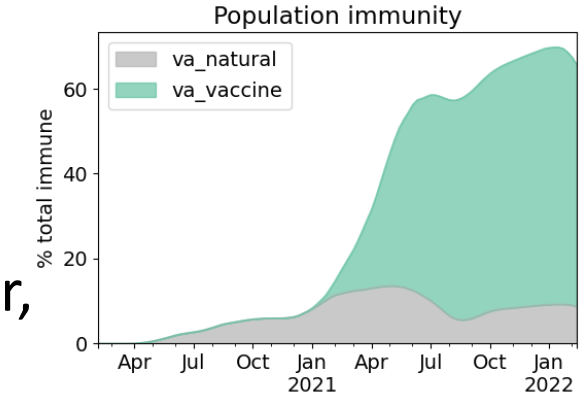
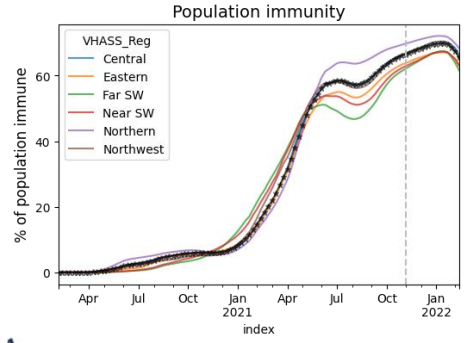
Virginia's Progress on Population Immunity

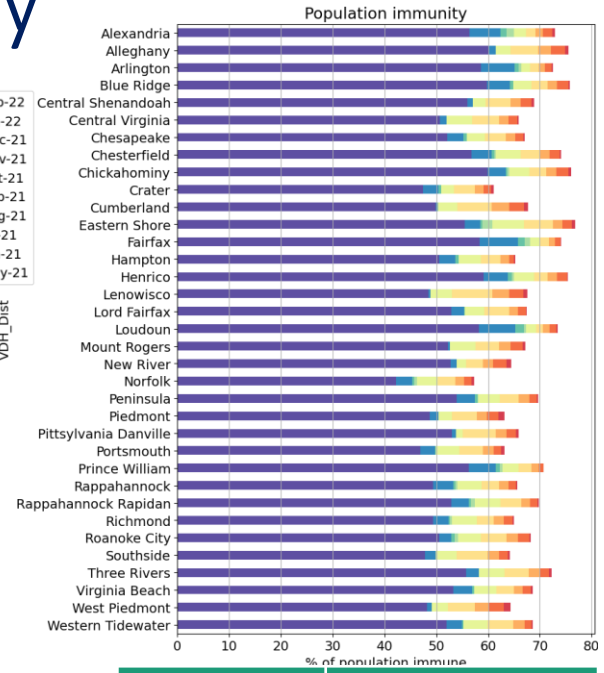
Natural Immunity and Vaccines combine to produce a population level of immunity

- 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









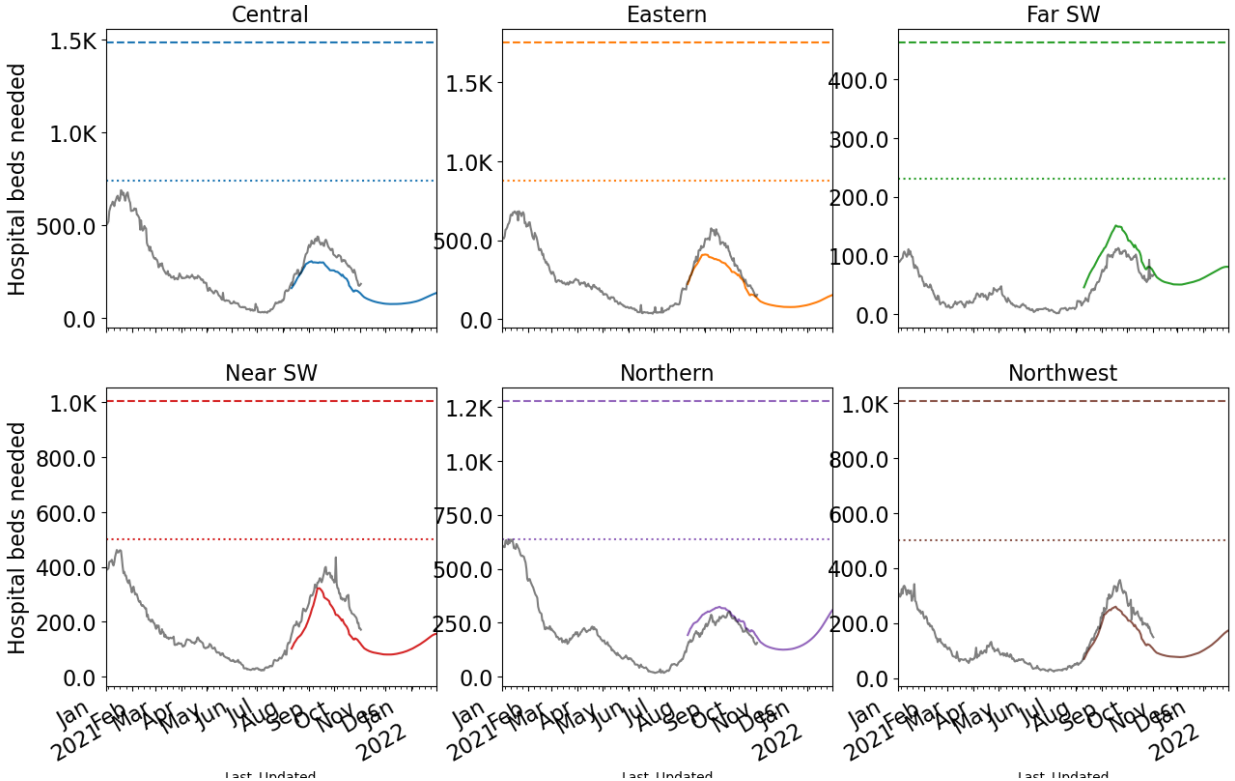
Region	% pop immune (est.)*
Central	66%
Eastern	64%
Far SW	61%
Near SW	62%
Northern	69%
Northwest	66%
Virginia	66%

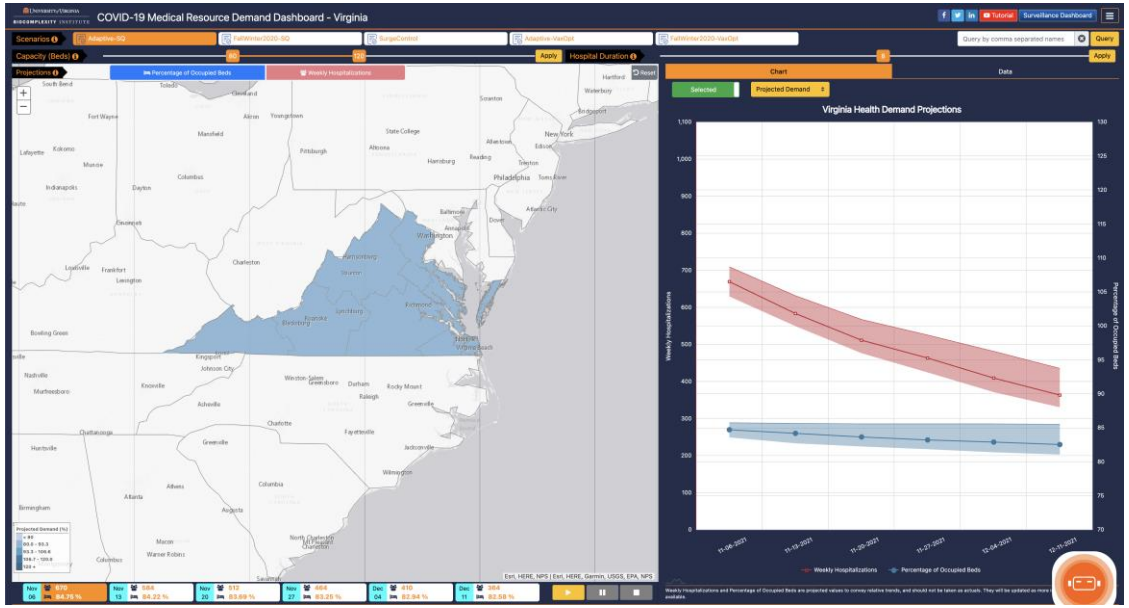
* As of Oct 31, 2021 for entire population

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 current capacities

* Assumes average length of stay of 8 days

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 steadily decline across nearly all districts**
- VA 7-day mean daily incidence is slightly down to 15.5/100K from 18/100K; US is slightly up to 23/100K (from 21/100K)
- Projections show continued decline across the board
- Future case growth remains possible, however, when tested with transmission drivers from last year
- Recent updates:
  - Added 3rd doses to status quo vaccination schedule, with estimated coverage
  - Analysis to show potential impact of Influenza based on past seasons

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

Additional Analyses

Weekly Cases and Hospitalizations

Weekly confirmed cases

Week Ending	Adaptive	Adaptive-VaxOpt	Adaptive-SurgeControl	Adaptive-FallWinter 2020	Adaptive-FallWinter 2020-VaxOpt
10/31/21	9621	9623	9622	9622	9623
11/7/21	8240	8239	8237	8240	8243
11/14/21	7216	7208	7130	7362	7357
11/21/21	6274	6252	5673	6858	6829
11/28/21	5478	5443	4148	6532	6475
12/5/21	4814	4741	3054	6420	6300
12/12/21	4244	4128	2330	6521	6308
12/19/21	3740	3565	1772	6817	6432
12/26/21	3336	3095	1342	7312	6682
1/2/2022	2972	2680	1028	8048	7051
1/9/2022	2684	2299	800	9022	7554
1/16/2022	2430	1957	626	10305	8148
1/23/2022	2198	1662	472	11870	8836
1/30/2022	1996	1416	360	13240	9193

Weekly Hospitalizations

Week Ending	Adaptive	Adaptive-VaxOpt	Adaptive-SurgeControl	Adaptive-FallWinter 2020	Adaptive-FallWinter 2020-VaxOpt
10/31/21	685	685	685	685	685
11/7/21	545	545	545	545	545
11/14/21	477	477	472	487	487
11/21/21	415	414	375	454	452
11/28/21	362	360	274	432	428
12/5/21	319	314	202	425	417
12/12/21	281	273	154	432	417
12/19/21	248	236	117	451	426
12/26/21	221	205	89	484	442
1/2/2022	197	177	68	533	467
1/9/2022	178	152	53	597	500
1/16/2022	161	129	41	682	539
1/23/2022	145	110	31	785	585
1/30/2022	132	94	24	876	608

Overview of relevant on-going studies

Other projects coordinated with CDC and VDH:

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

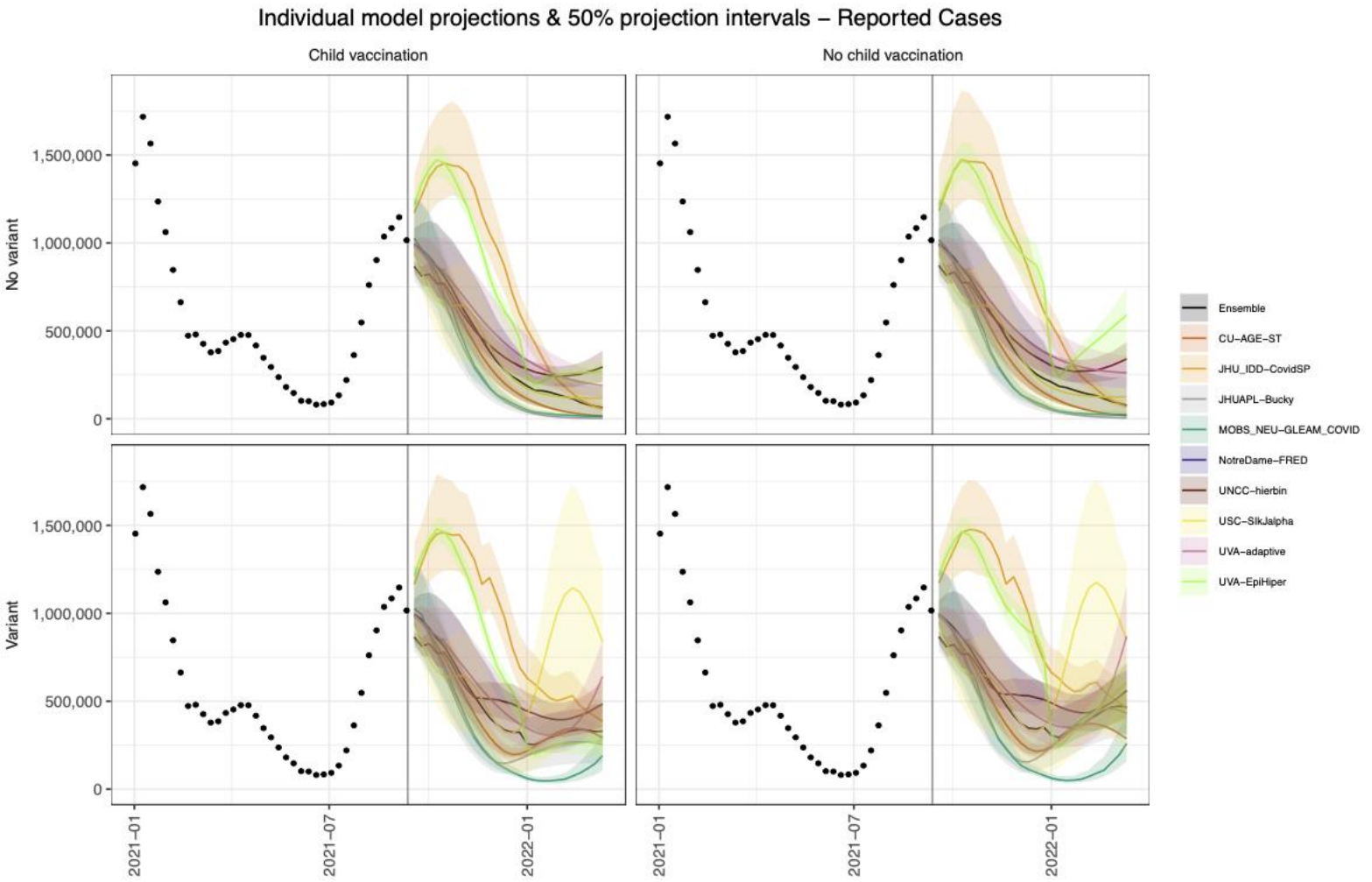
COVID-19 Scenario Modeling Hub

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



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)

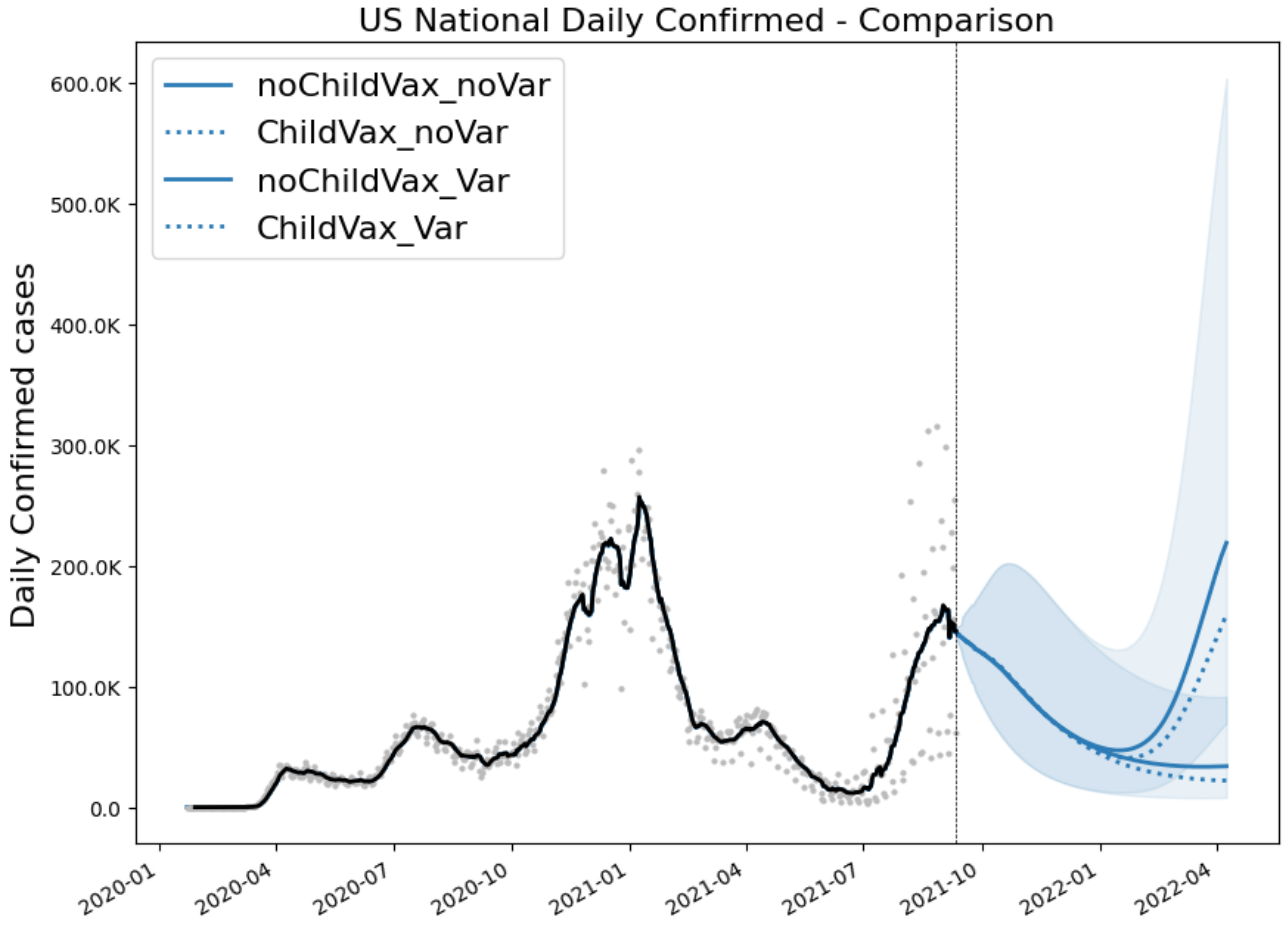
- 50% boost as it eventually predominates

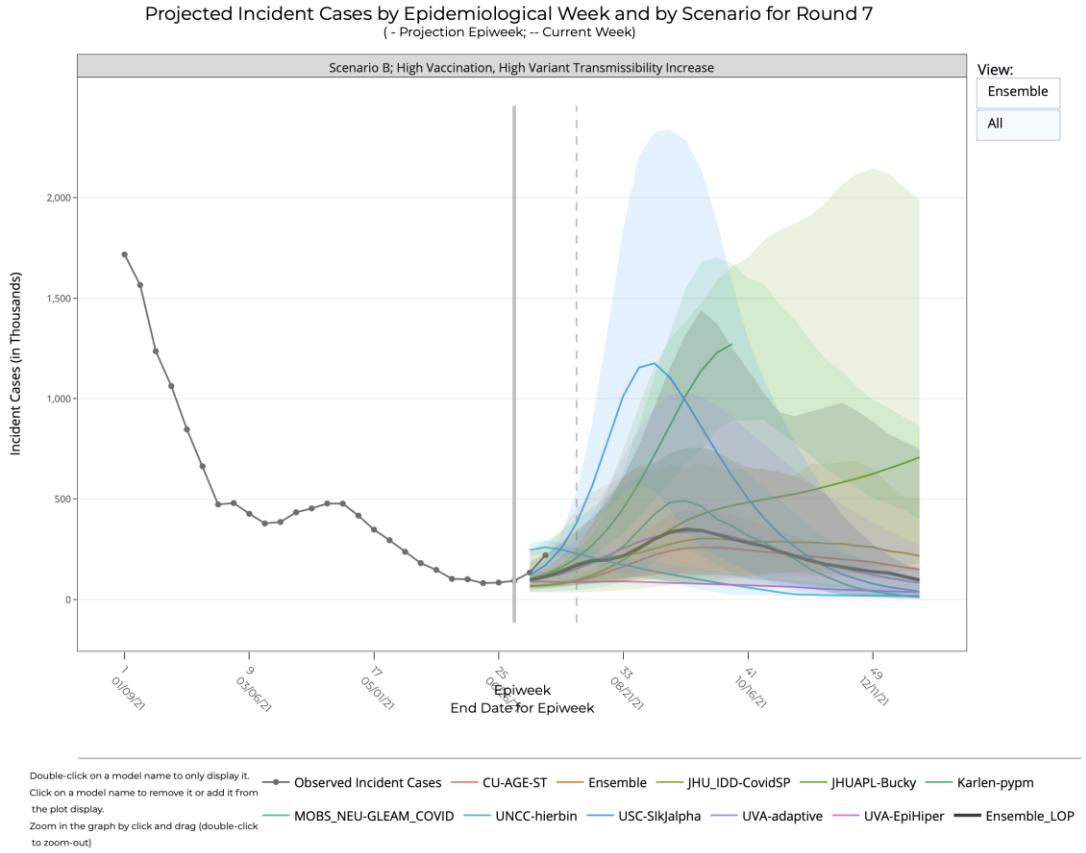
We consider a 2x2 scenario design, where childhood vaccination (5-11 years) is on the first axis, and a change in virus transmissibility is on the second axis. The second axis reflects a stress test, illustrating the potential impact of a new variant arising during the projection period:

	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

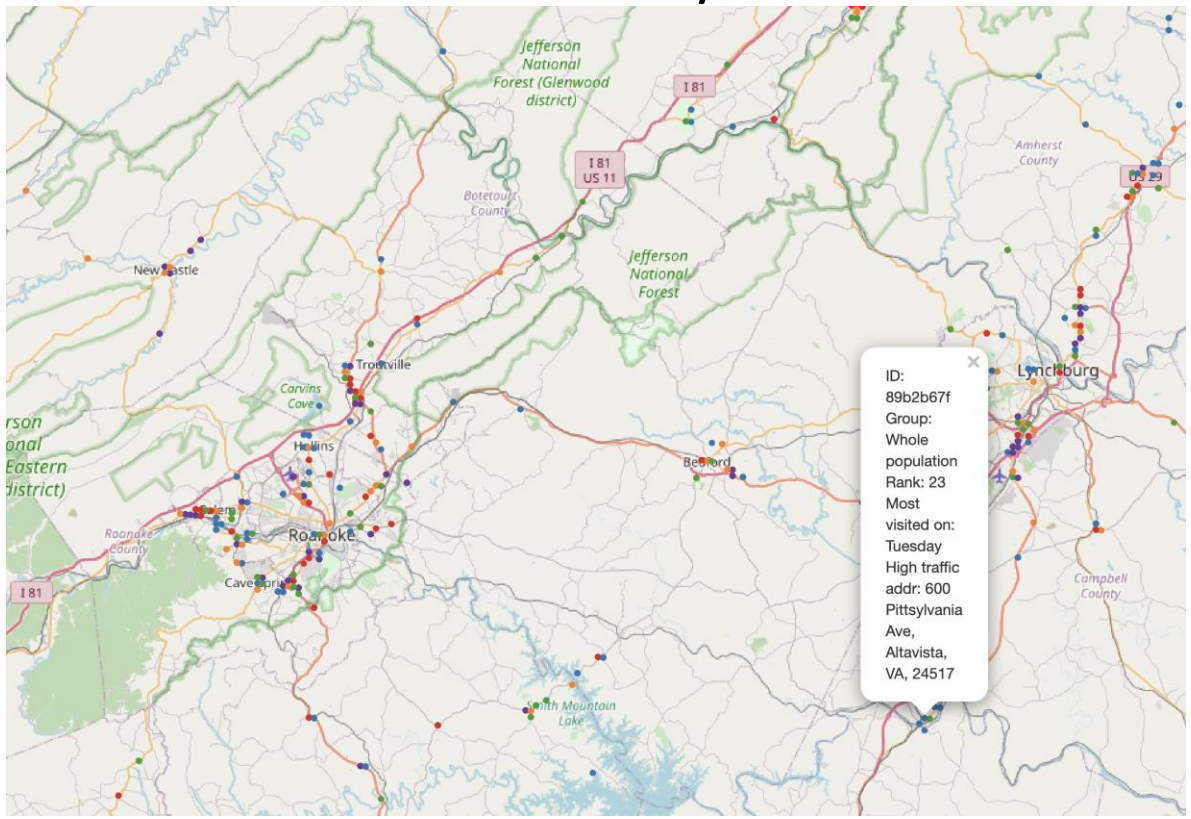




https://covid19scenariomodelinghub.org/viz.html

Data Recommended Mobile Vax Clinic Sites

Detailed and Timely Locations



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

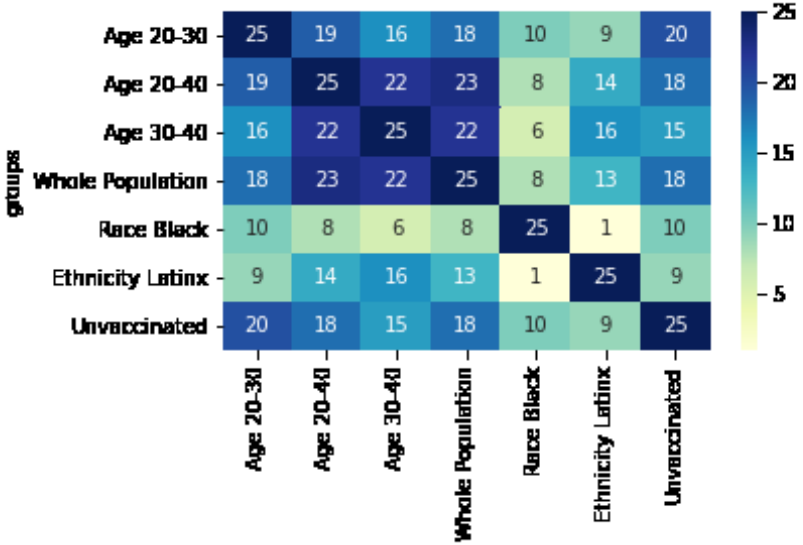
Goal: Provide frequently visited locations based on populations and vaccination levels one desires to reach

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

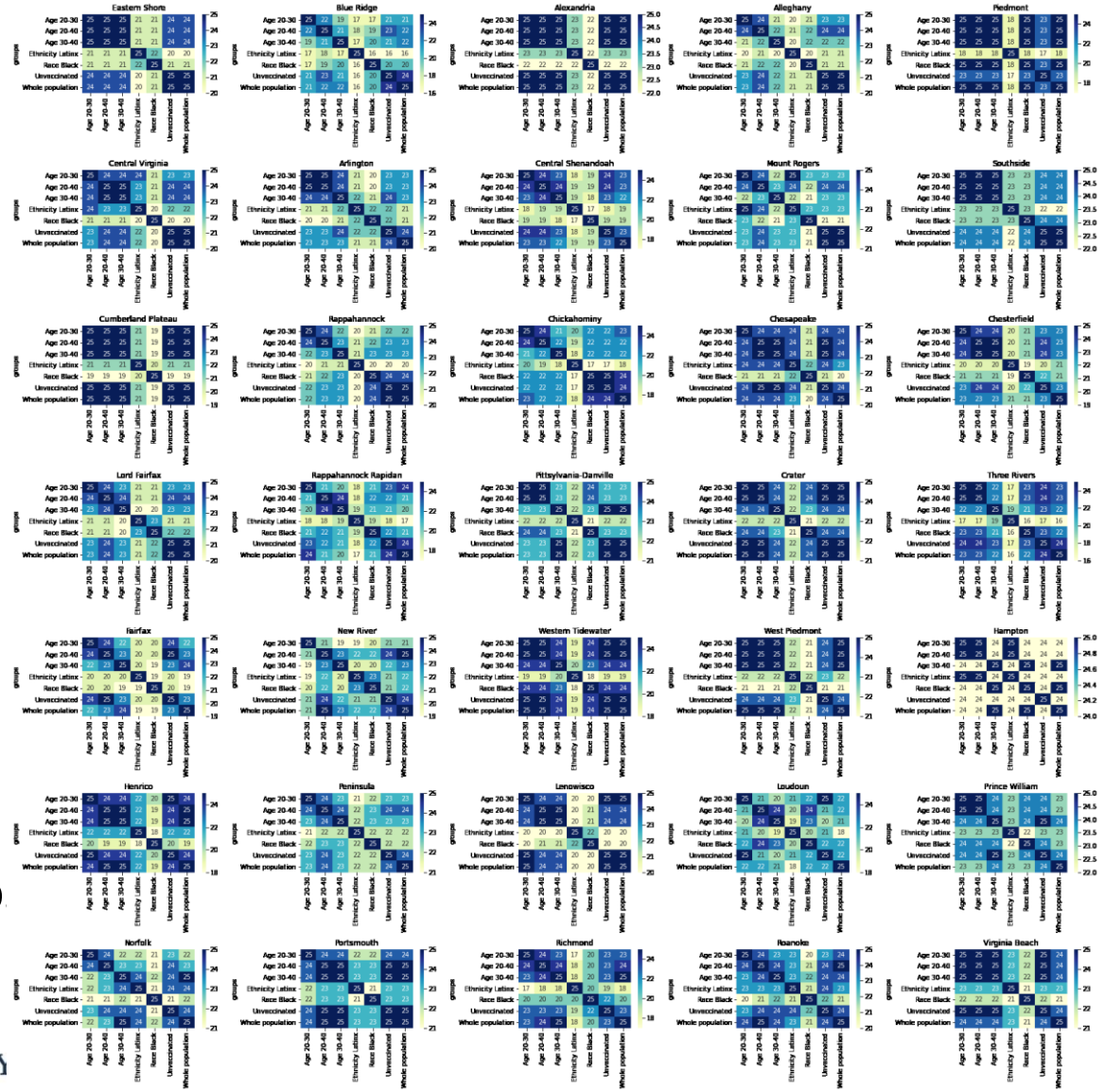
Data Recommended Mobile Vax Clinic Sites

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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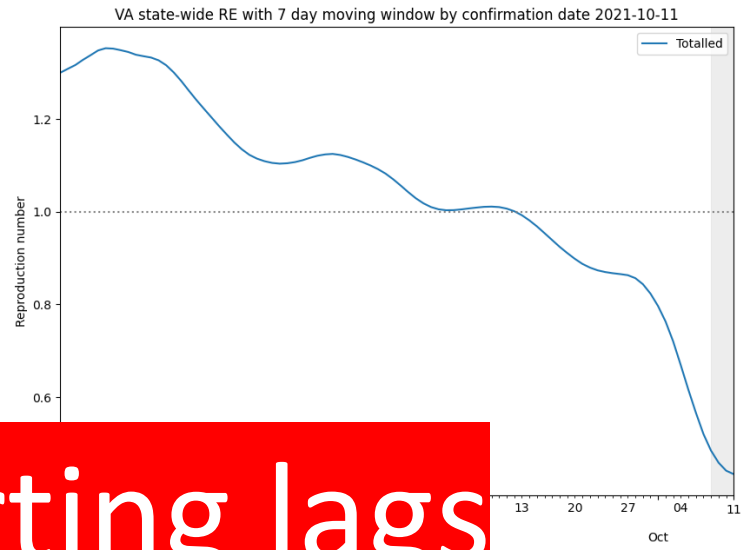
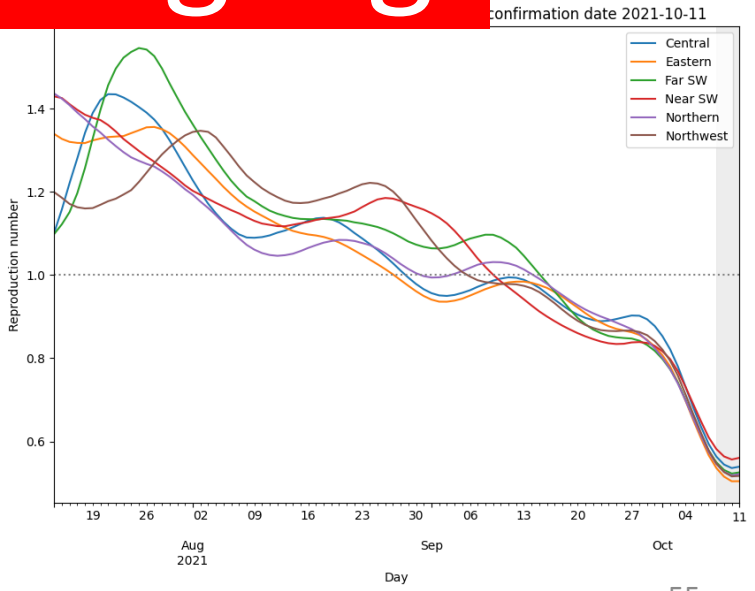
Estimating Daily Reproductive Number

October 11th Estimates

Region	Date Confirmed R_e	Date Confirmed Diff Last Week
State-wide	0.434	-0.581
Central	0.491	-0.550
Eastern		
Far SW		
Near SW	0.492	-0.491
Northern	0.462	-0.527
Northwest	0.456	-0.564

Erroneous due to reporting lags





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

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?

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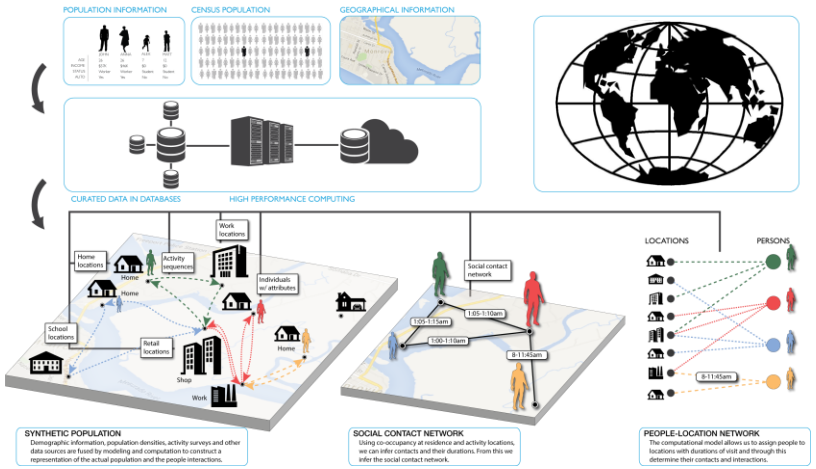
Supplemental Slides

Agent-based Model (ABM)

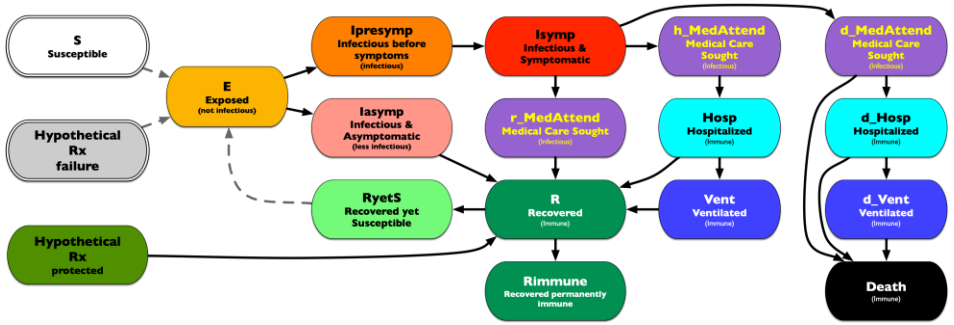
EpiHiper: Distributed network-based stochastic disease transmission simulations

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



Synthetic Population

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



Detailed Disease Course of COVID-19

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