Network Systems Science & Advanced Computing

Biocomplexity Institute & Initiative

University of Virginia

Estimation of COVID-19 Impact in Virginia

December 1st, 2021

(data current to November 27th – 30th)

Biocomplexity Institute Technical report: TR 2021-123

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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:

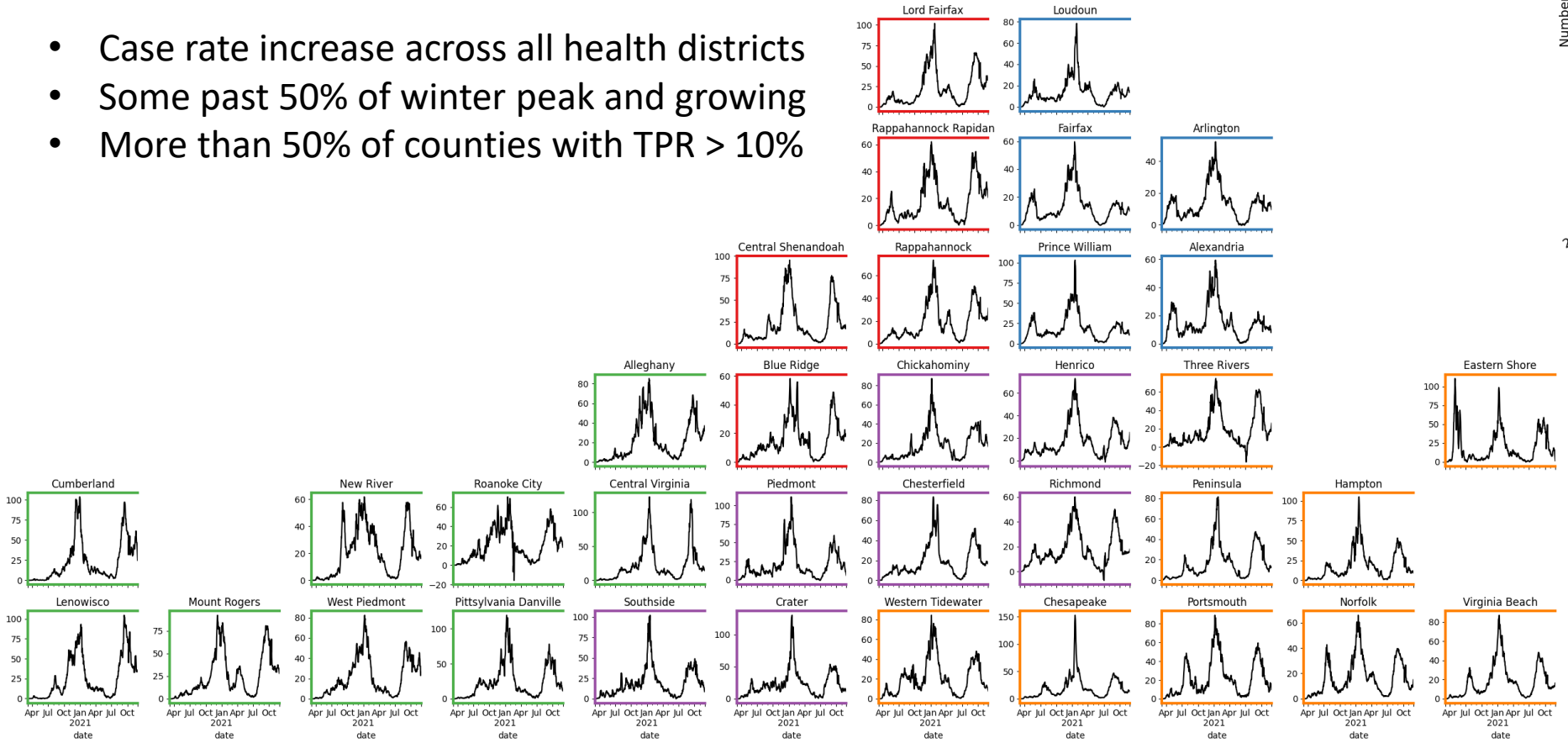
- **Case rates after holiday break decline after brief rise with a mix of activity across the commonwealth; holiday effects caused brief dips in activity last year**
- VA 7-day mean daily case rate receded to 16.7/100K from 20/100K; US is down to 25/100K (from 29/100K)
- Projections show a flattening with eventual rise should current low transmission drivers persist
- As seasonal factors mount trajectories may shift towards the FallWinter2020 scenario with more rapid near-term growth; this scenario shows considerable growth is still possible.
- Recent updates:
  - Overhauled model structure to better capture different tiers of immunity and the effects of waning
  - Analysis of the effects of increasing 3rd dose coverage

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

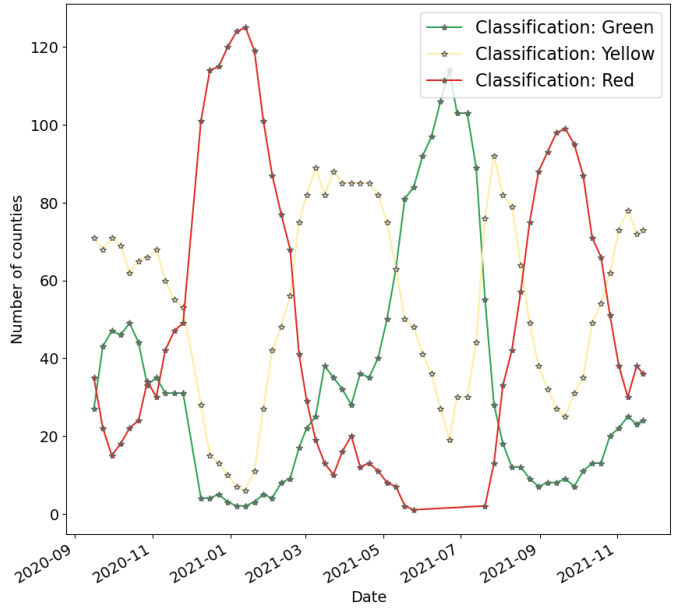
Situation Assessment

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)

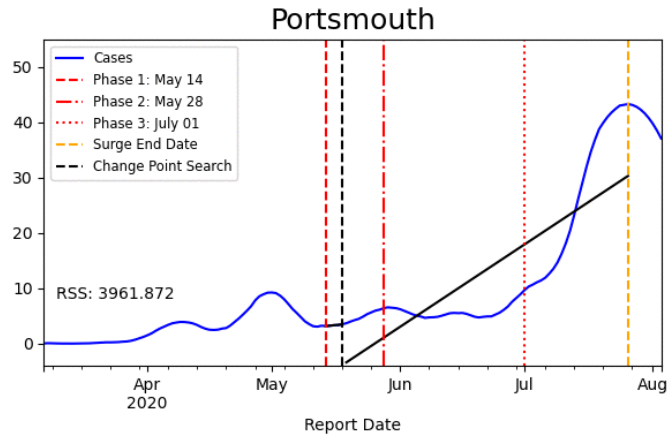
Red: >10.0% (and not "Green" or "Yellow")

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

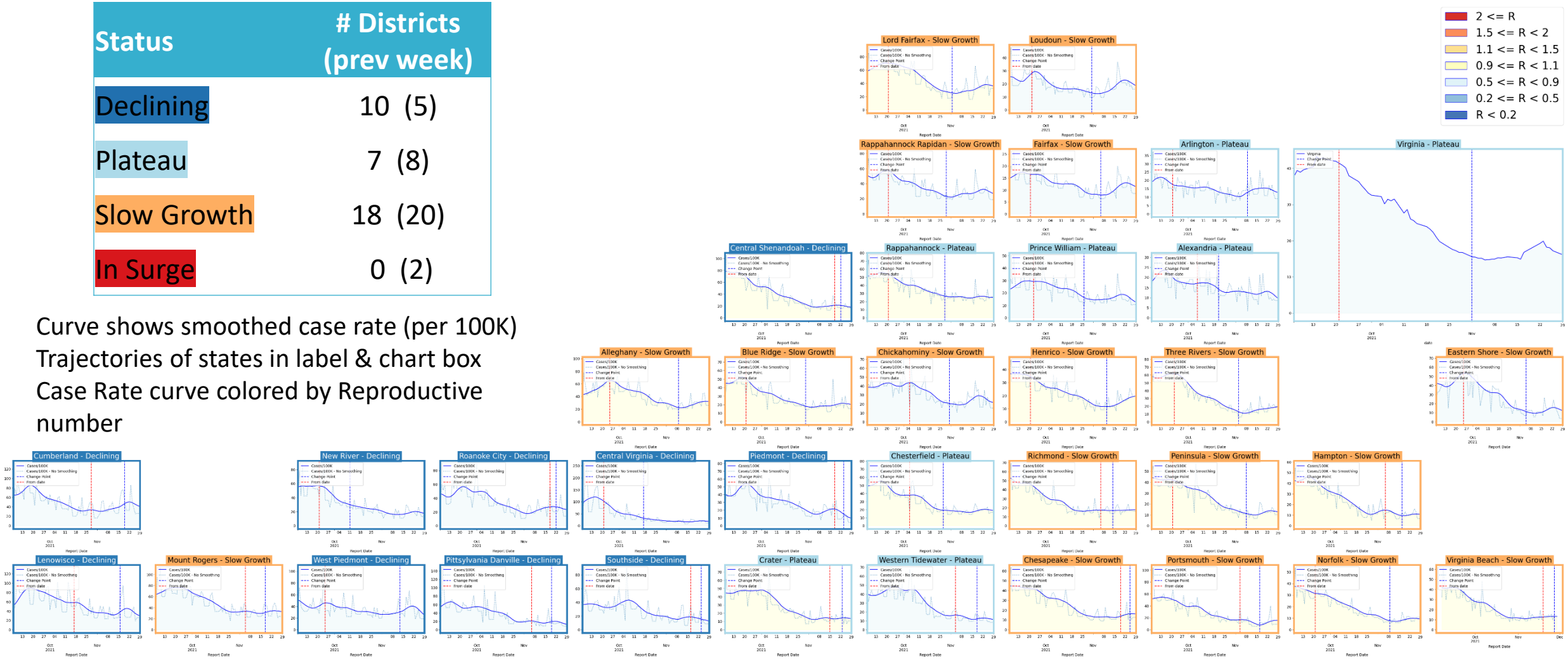


Trajectory	Description	Weekly Case Rate (per 100K) bounds	# Districts (prev week)
Declining	Sustained decreases following a recent peak	below -0.9	10 (5)
Plateau	Steady level with minimal trend up or down	above -0.9 and below 0.5	7 (8)
Slow Growth	Sustained growth not rapid enough to be considered a Surge	above 0.5 and below 2.5	18 (20)
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	10 (5)
Plateau	7 (8)
Slow Growth	18 (20)
In Surge	0 (2)

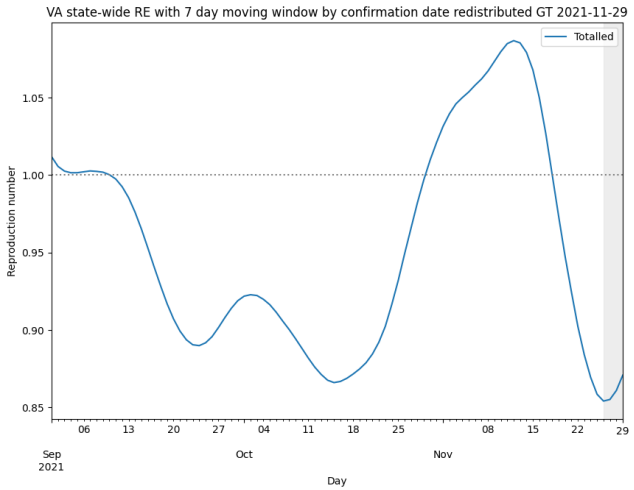
Curve shows smoothed case rate (per 100K)
Trajectories of states in label & chart box
Case Rate curve colored by Reproductive number

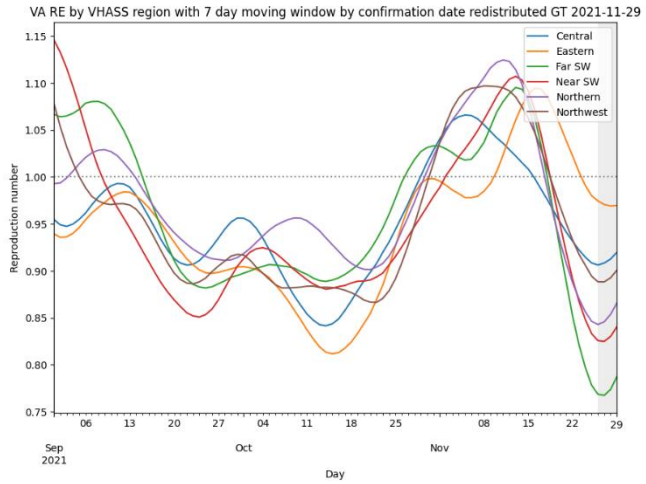


Estimating Daily Reproductive Number –
Redistributed gap

Nov 29th Estimates

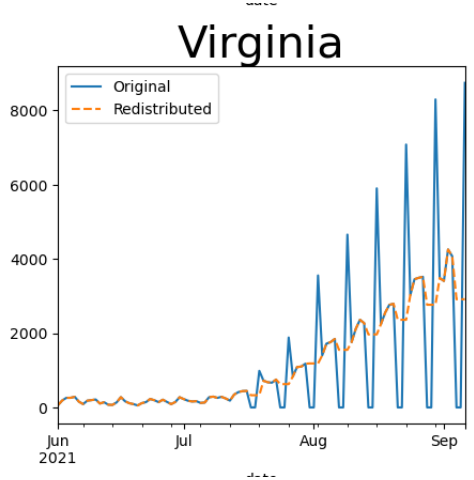
Region	Date Confirmed R_e	Date Confirmed Diff Last Week
State-wide	0.904	0.000
Central	0.924	-0.011
Eastern	0.972	-0.053
Far SW	0.790	-0.063
Near SW	0.844	-0.052
Northern	0.869	-0.020
Northwest	0.899	-0.030





Skipping Weekend Reports & holidays biases estimates

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



Methodology

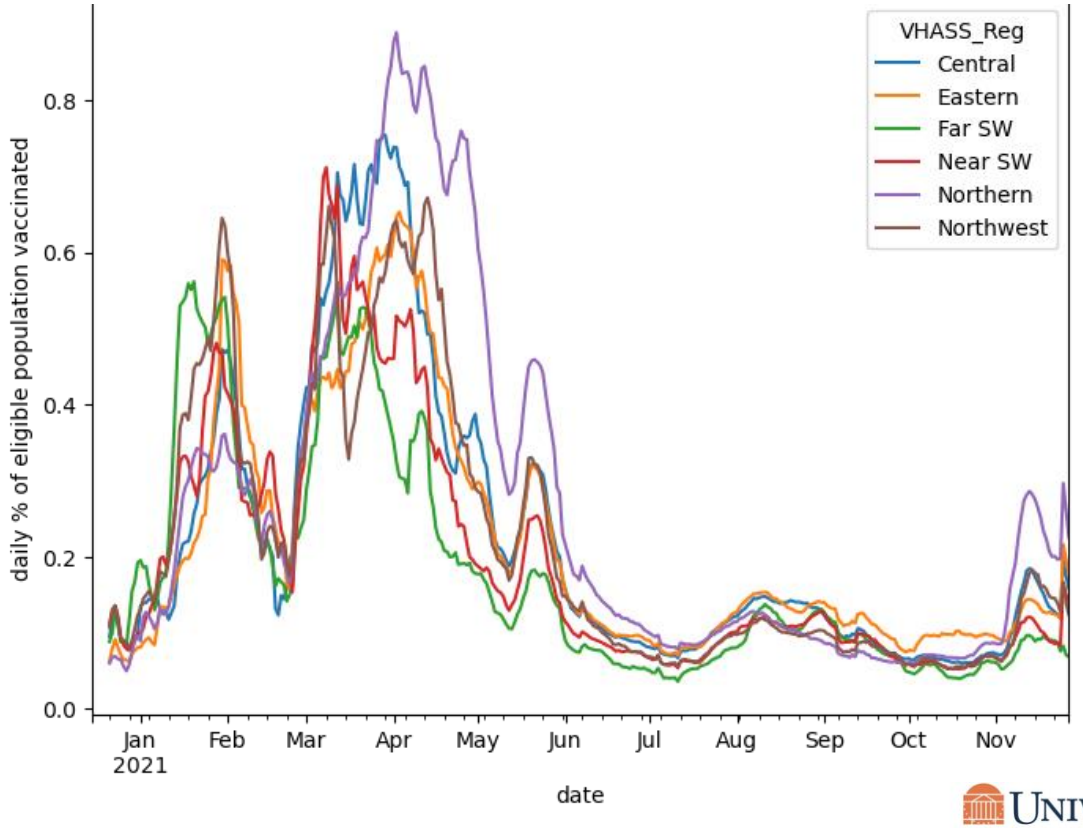
- Wallinga-Teunis method (EpiEstim[1]) for cases by **confirmation date**
- Serial interval: updated to discrete distribution from observations (mean=4.3, Flaxman et al, Nature 2020)
- Using Confirmation date since due to increasingly unstable estimates from onset date due to backfill

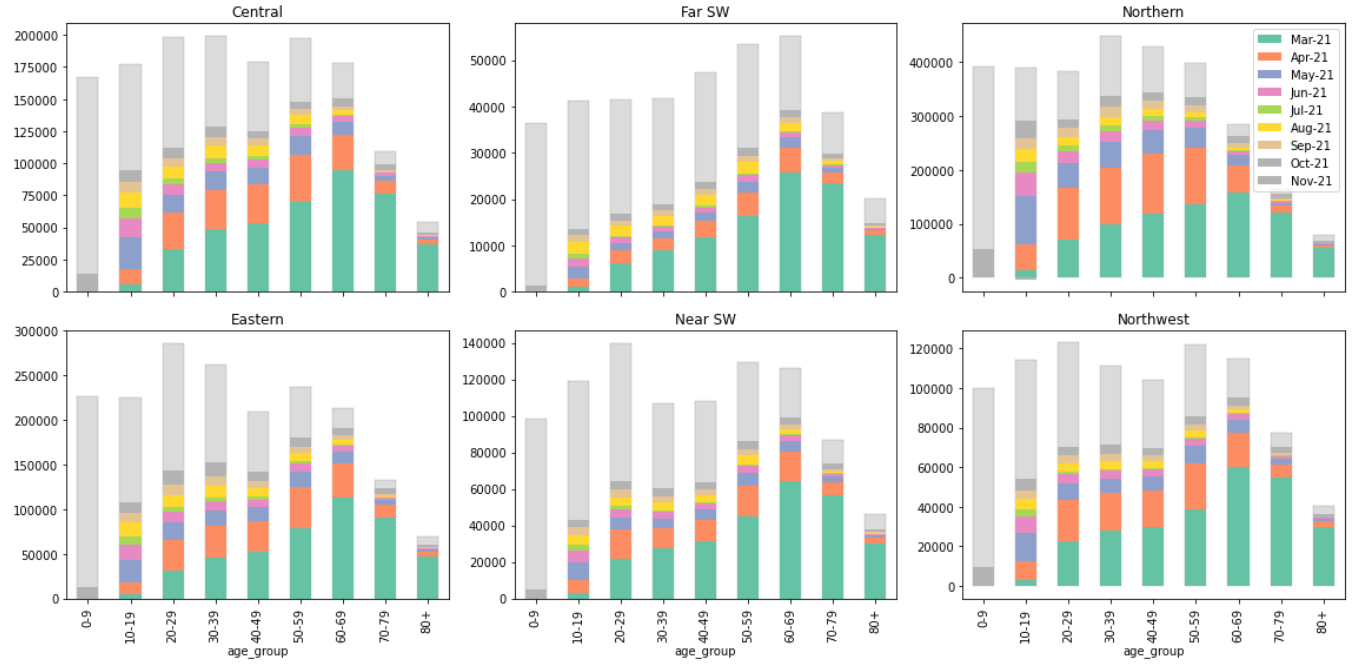
1. Anne Cori, Neil M. Ferguson, Christophe Fraser, Simon Cauchemez. A New Framework and Software to Estimate Time-Varying Reproduction Numbers During Epidemics. American Journal of Epidemiology, Volume 178, Issue 9, 1 November 2013, Pages 1505–1512, https://doi.org/10.1093/aje/kwt133

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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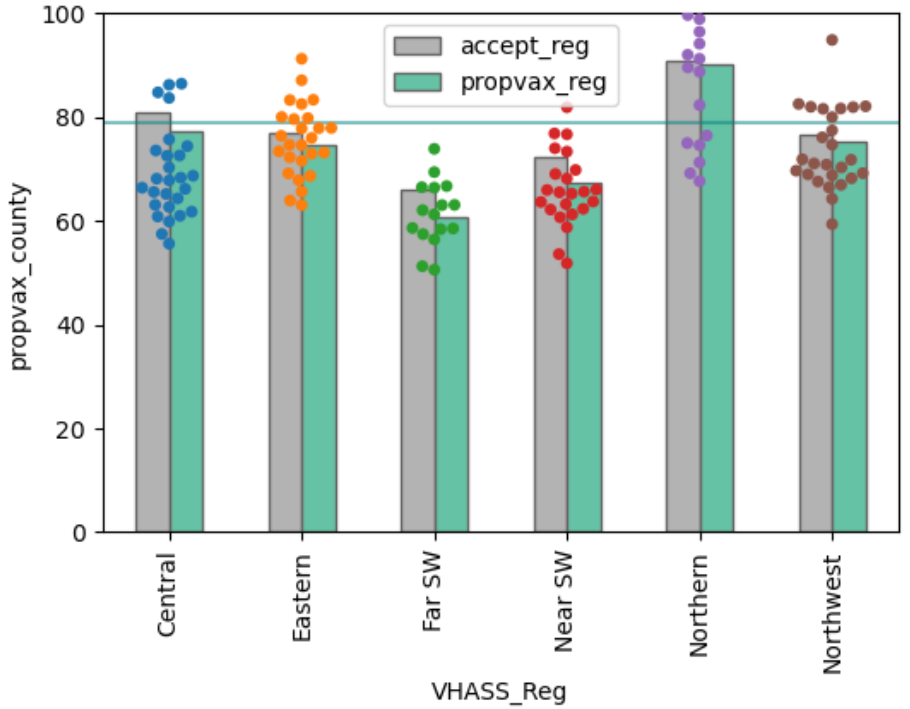
Vaccination Acceptance by Region

Corrections to surveys:

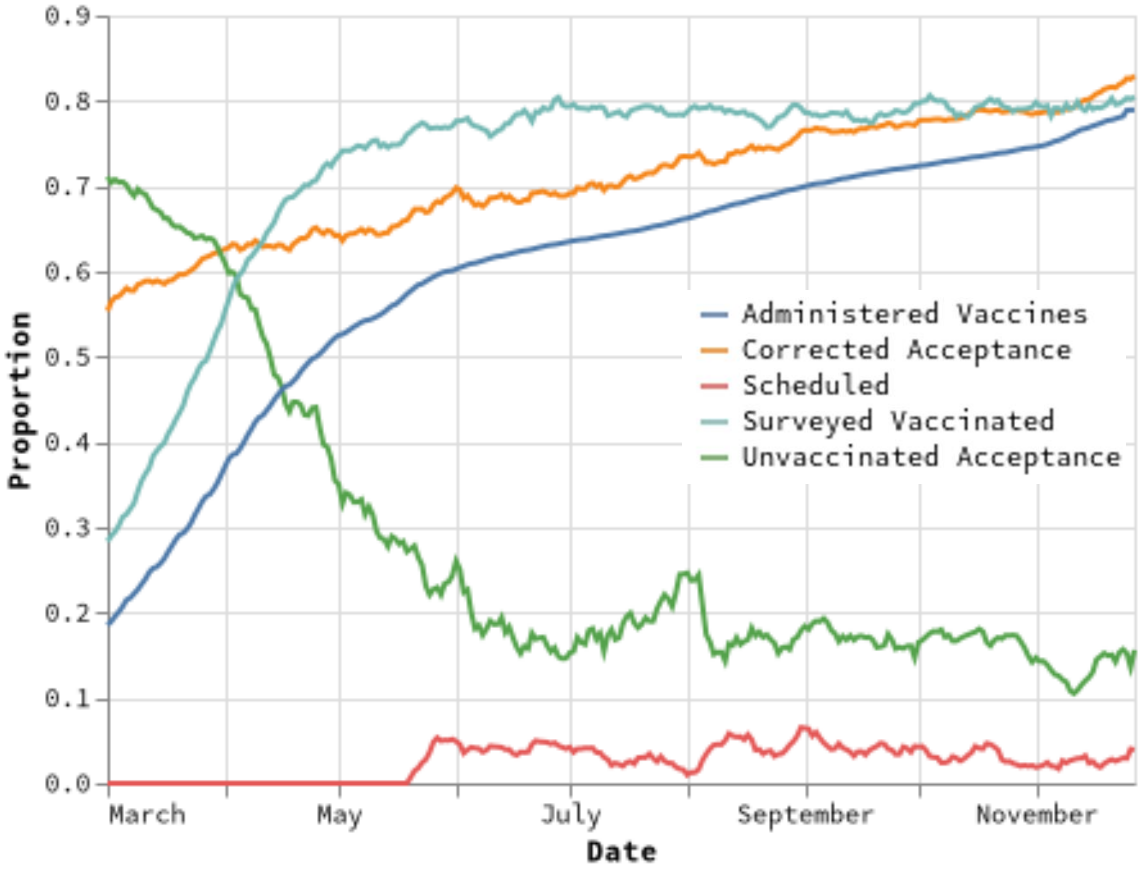
- Facebook administered survey is timely and broad, but biased by who accesses Facebook and answers the survey
- Correction approach:
  - Calculate an over-reporting fraction based on reported vaccinations compared to VDH administration data
  - Cross-validate coarse corrections against HPS survey at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

Region	COVIDcast accepting corrected	VDH proportion pop vaccinated
Central	81%	77%
Eastern	79%	74%
Far SW	66%	61%
Near SW	73%	67%
Northern	94%	90%
Northwest	78%	75%
Virginia	**83%**	**79%**



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

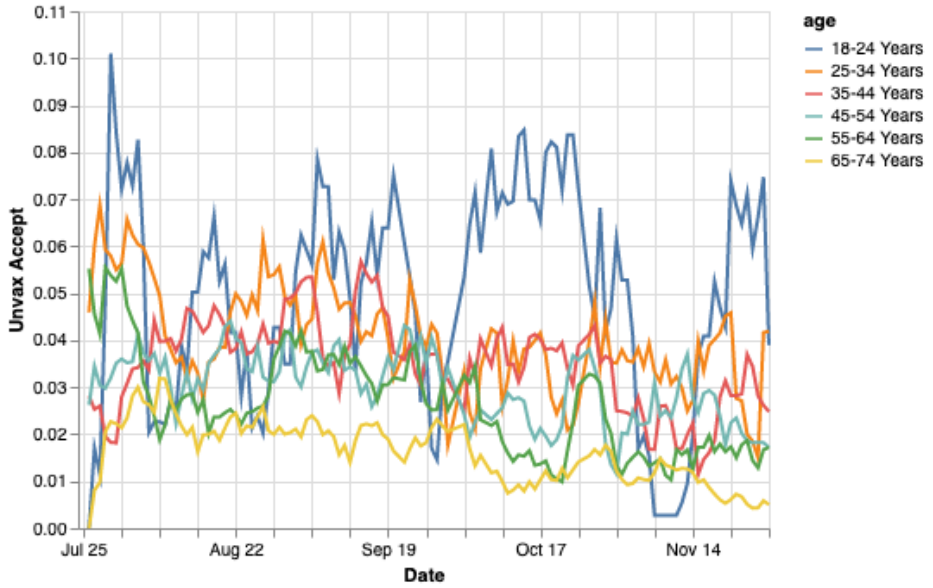
Vaccine Acceptance Components over Time



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

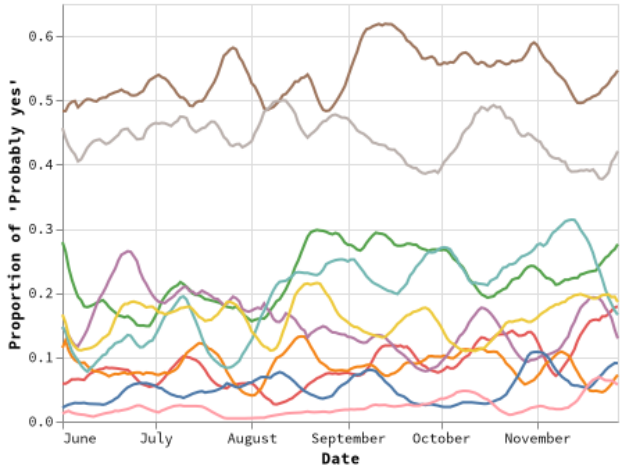
Acceptance Across Age groups among Unvaccinated



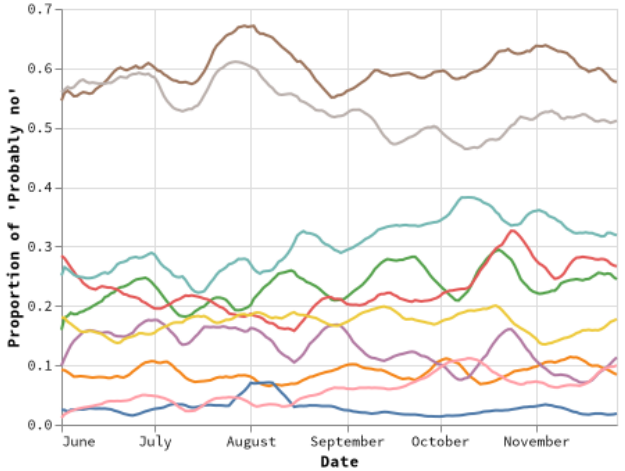
Data Source: https://covidcast.cmu.edu

Reasons for Hesitancy by Likeliness to Accept

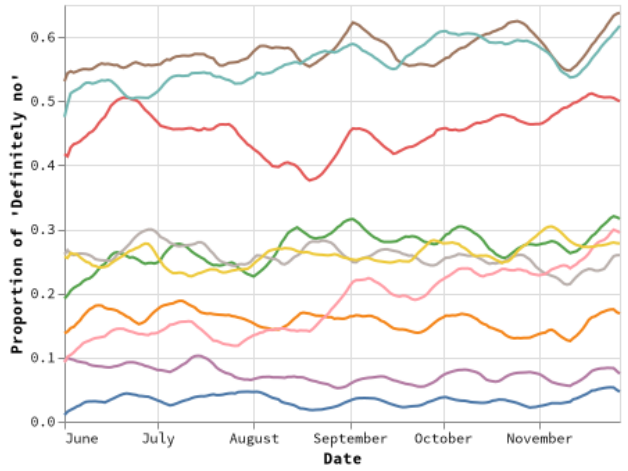
Probably Yes

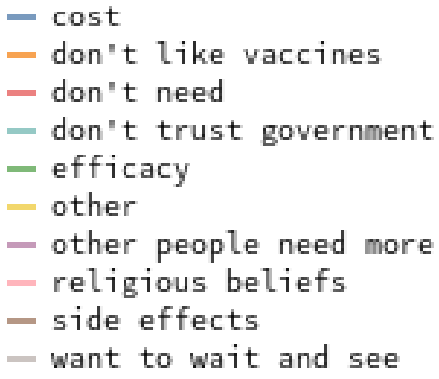


Probably No



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

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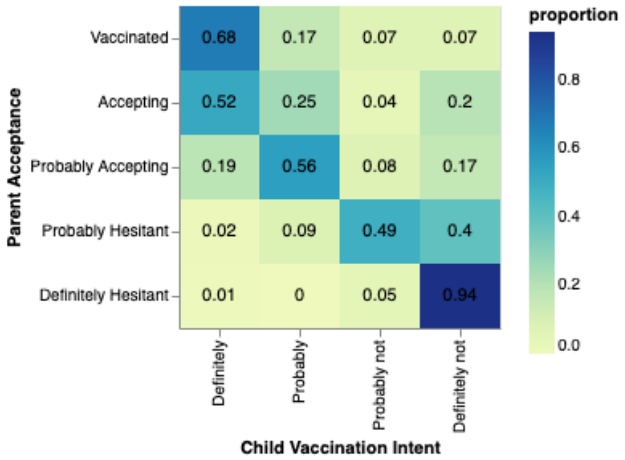
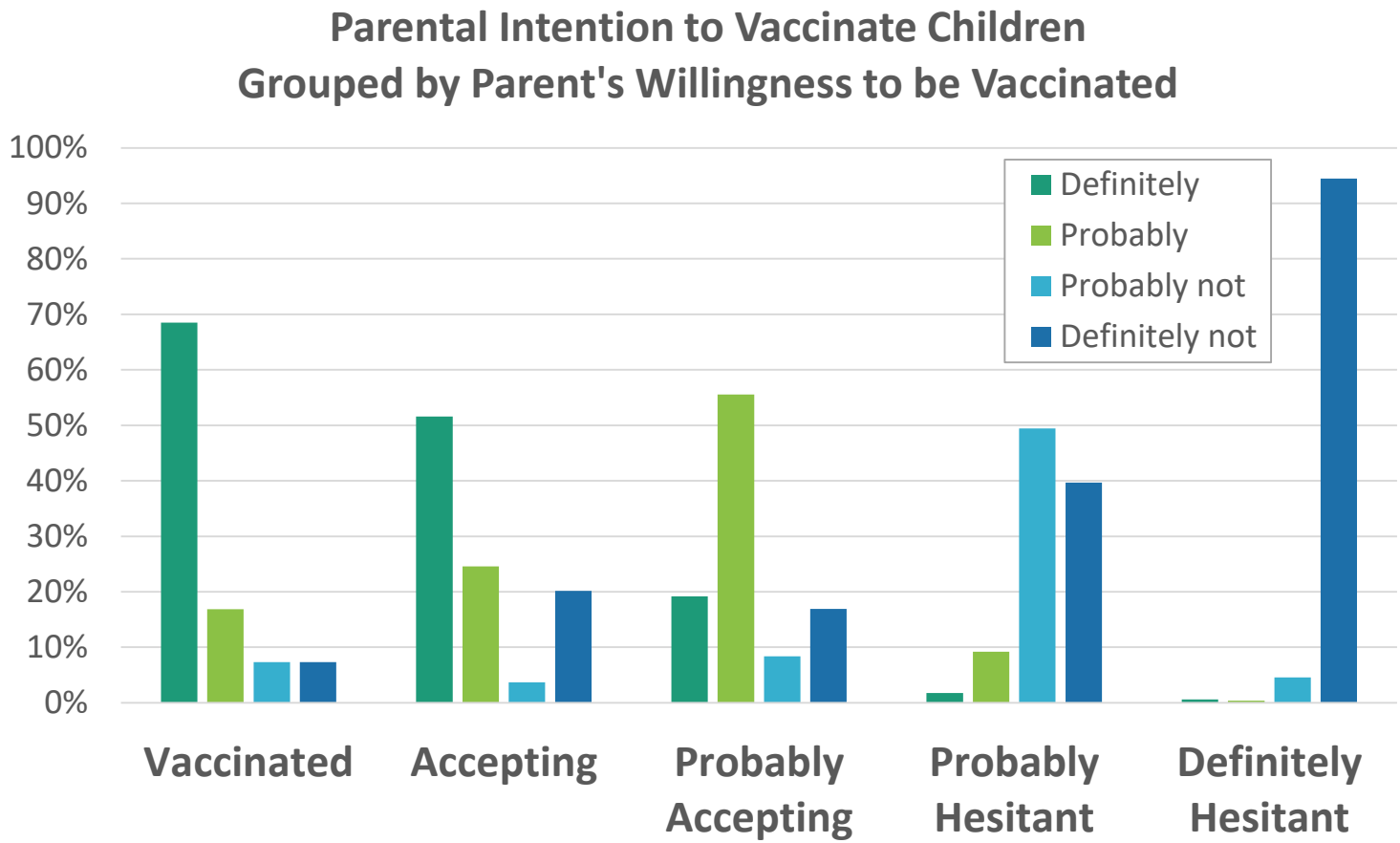
Data Source: https://covidcast.cmu.edu

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%
- Intention strongly biased by the willingness of the parent, and skews towards unwillingness to vaccinate



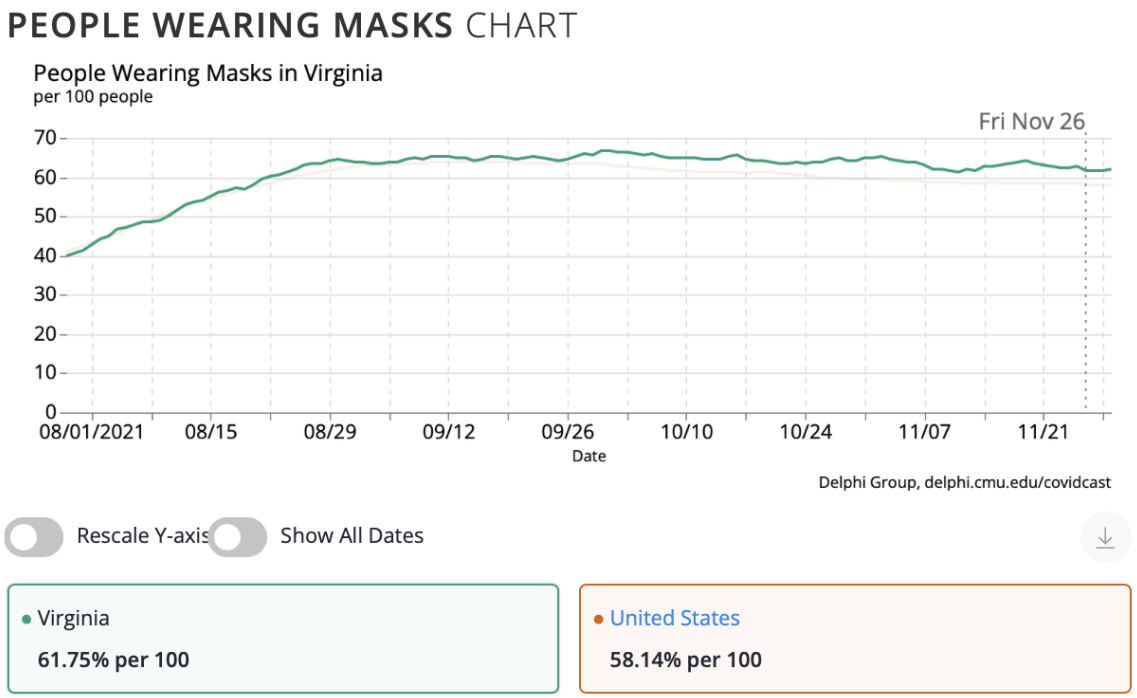


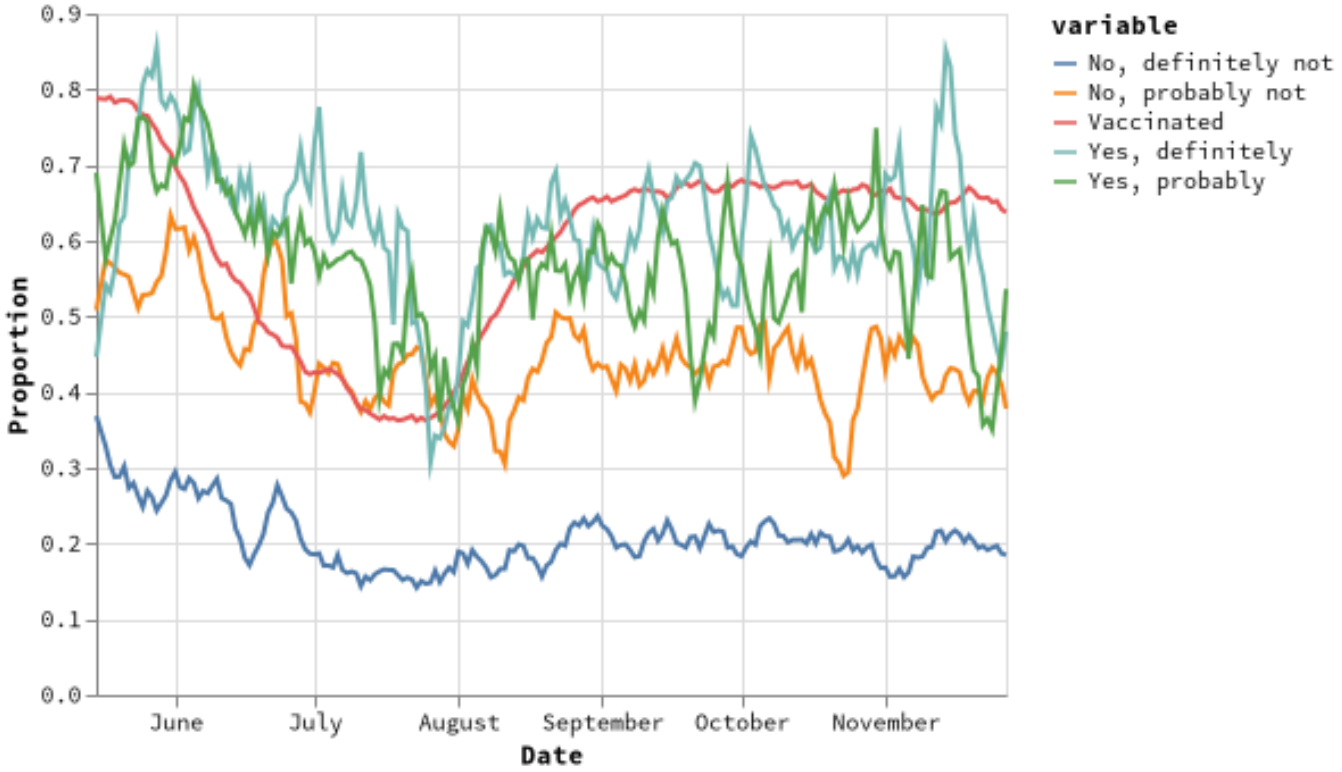
Data Source: https://covidcast.cmu.edu

Mask Usage Stalls

Self-reported mask usage has declined slightly to ~62% (mid 60s in previous months)

- US and VA similar, though US is down a little more in past month
- 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

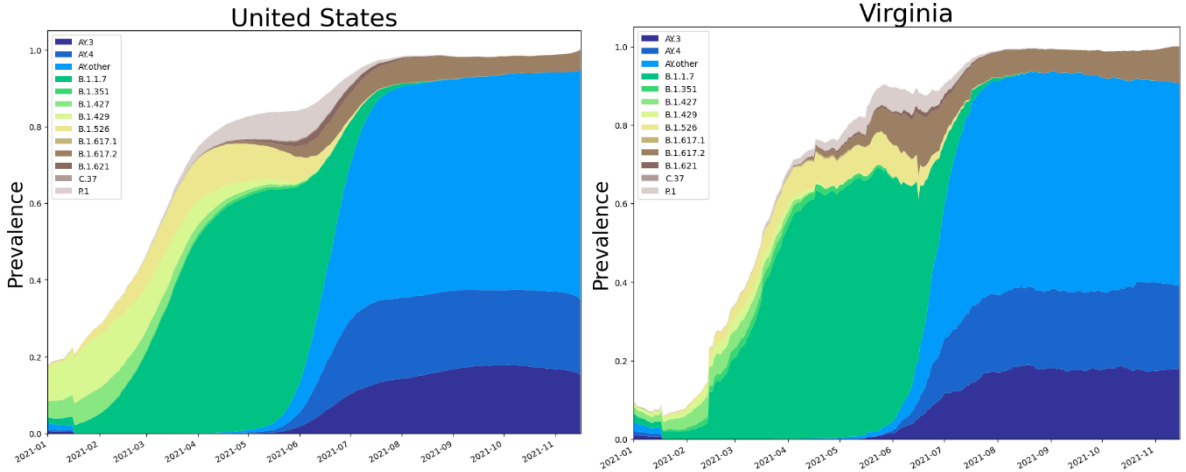
	New WHO Name	Transmissibility	Immune Evasiveness	Vaccine Effectiveness^
Ancestral		—	—	✓
D614G		+	—	✓
B.1.1.7	Alpha	+++	—	✓
B.1.351	Beta	+	++++	✓
P.1	Gamma	++	++	✓
B.1.429	Epsilon	+	+	✓
B.1.526	Iota	+	+	✓
B.1.617.2	Delta	++++*	++#	✓

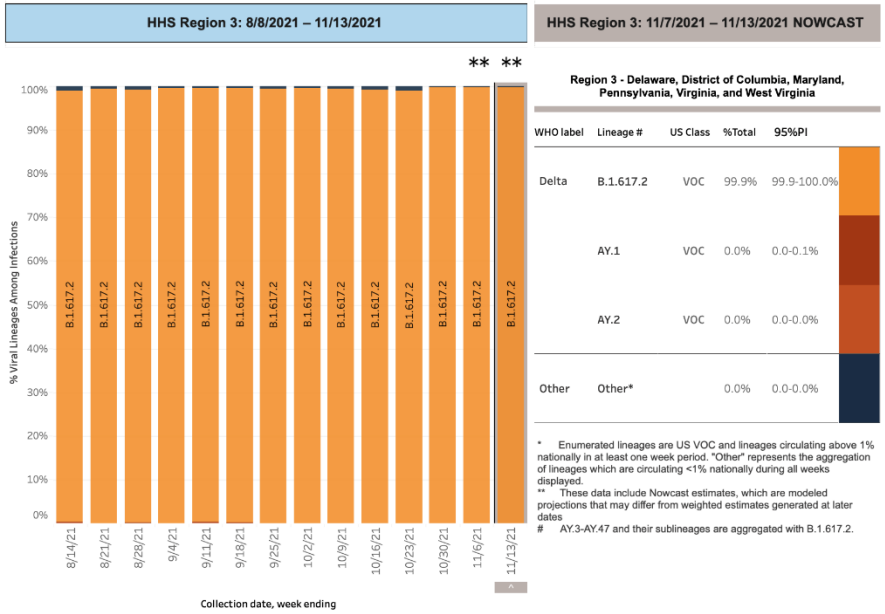
*Relative transmissibility to B.1.1.7 yet to be fully defined
^Effectiveness from real world evidence vs. severe illness, not all vaccines are effective vs all variants, and importance of 2-doses, especially for B.1.617.2 for which 1 dose of mRNA or AZ is only ~30% effective # May carry more immune escape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

World Health Organization

WHO and Eric Topol

GISAID outbreak.info



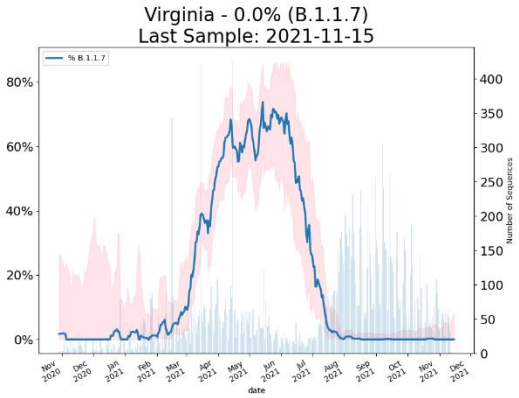


CDC

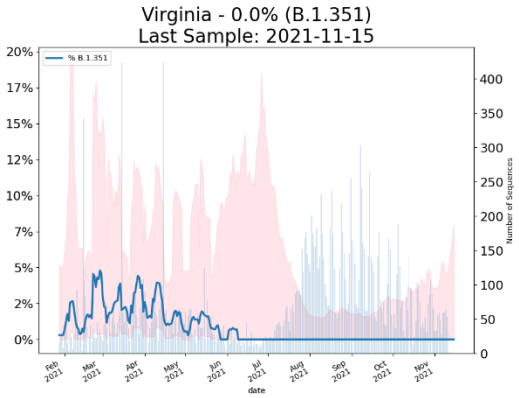
CDC Variant Tracking

SARS-CoV2 Variants of Concern

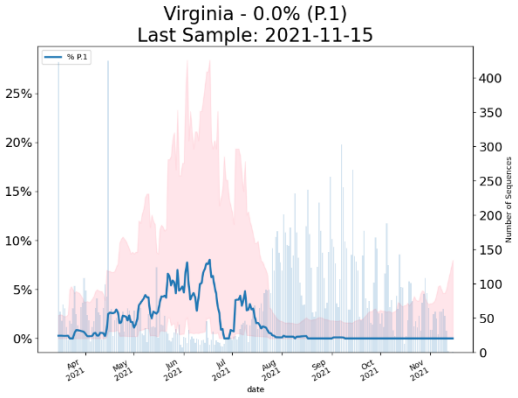
Alpha α - Lineage B.1.1.7



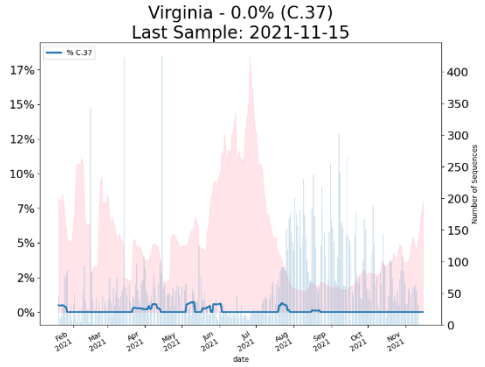
Beta β - Lineage B.1.351



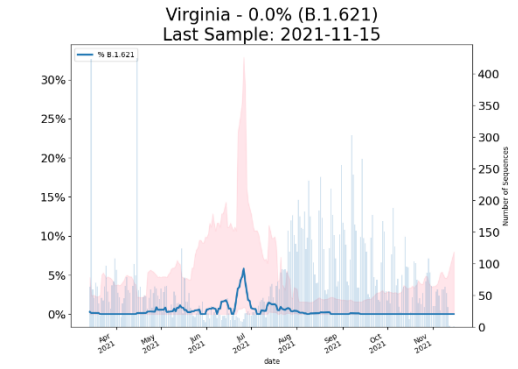
Gamma γ - Lineage P.1



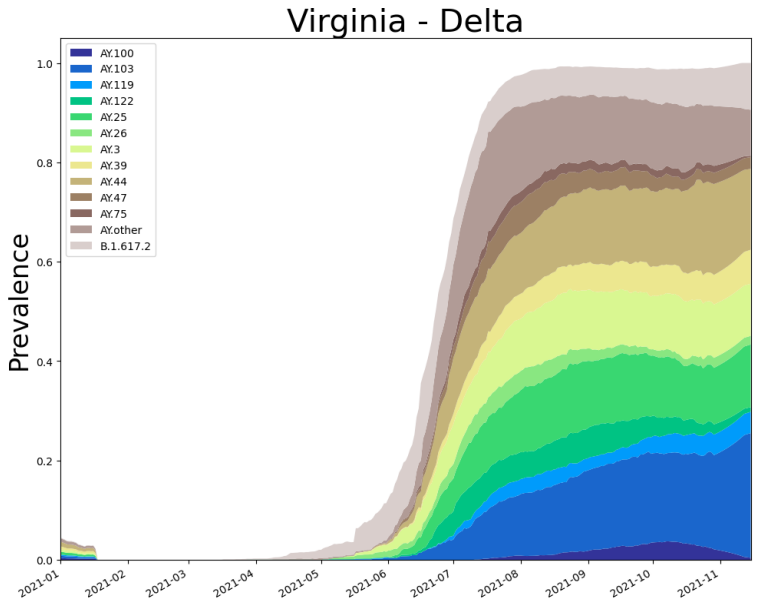
Lambda λ - Lineage C.37

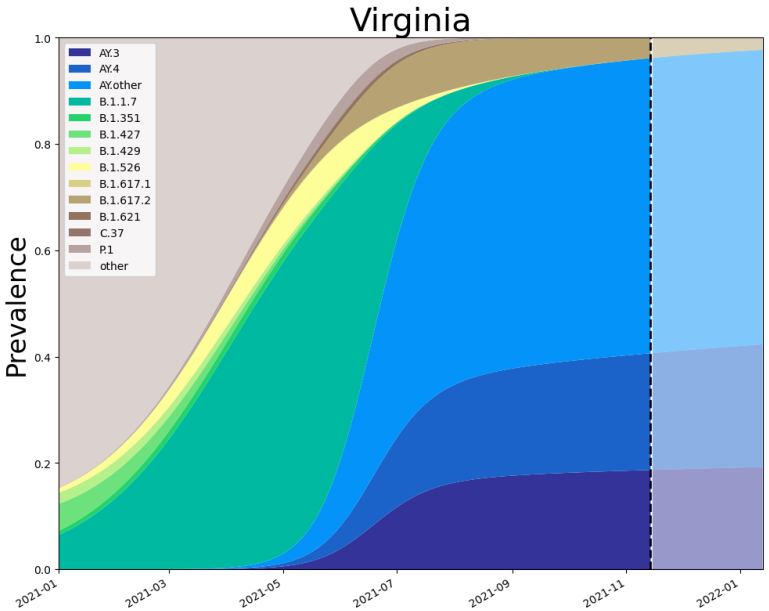


Mu μ - Lineage B.1.621



Delta δ - Lineage B.1.617.2



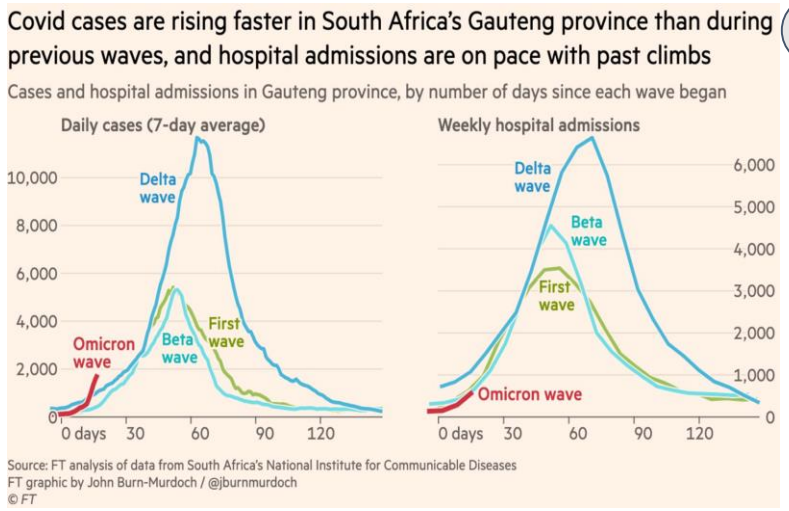


Delta Subvariant Activity
Current fits suggest slow shifts among subvariants in the future, no major movement

Vaccines and Variants, Omicron

1. South Africa's case count has shown a steep increase since the detection of the Omicron variant. Details are still forthcoming on the number of breakthrough cases, Omicron prevalence, severity of infection.
2. Within RSA the recent increase in cases is centered around Gauteng which has the lowest vaccination levels in the country.
3. Omicron has a high number of mutations in the spike protein. Many associated with immune escape.
4. Among those, three of the mutations in combination have demonstrated complete neutralization escape in some sera. In this study mRNA-1273 demonstrates better neutralization than convalescent sera.
5. Previous VoC's with high immune escape ability have demonstrated lower intrinsic transmissibility. Even if this is the case immune escape ability could allow Omicron to spread more effectively.
6. The S69/70 deletion may enable detection of Omicron via PCR based on SGTF dropout on certain platforms. Mutational prevalence among circulating infections in VA currently appears low, potentially boosting precision for this early detection method.

1



https://twitter.com/jburnmurdoch/status/1465659957546782725

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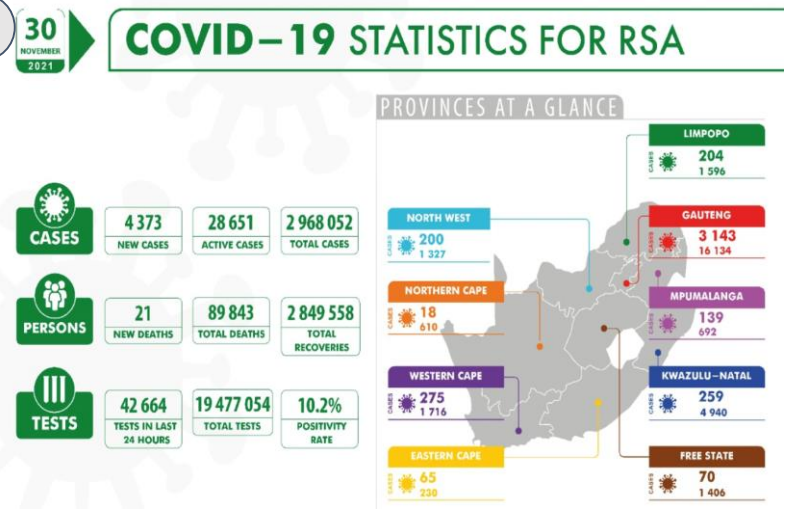

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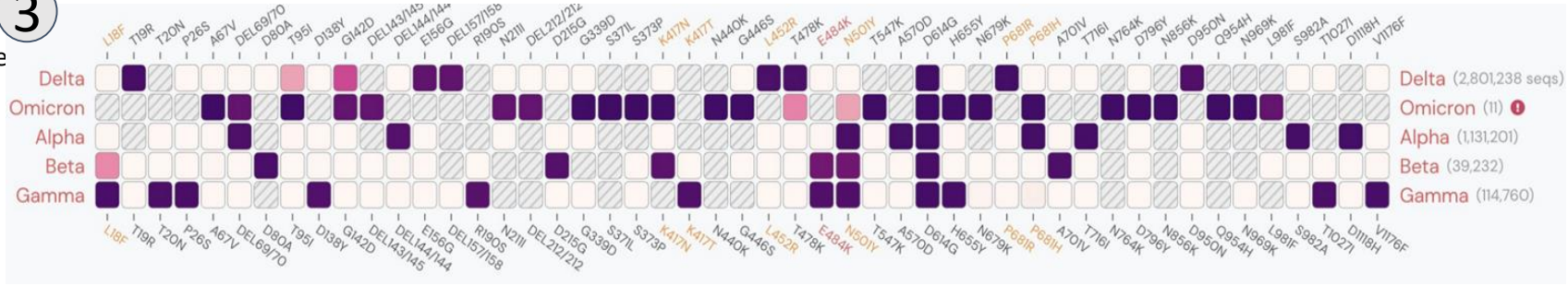

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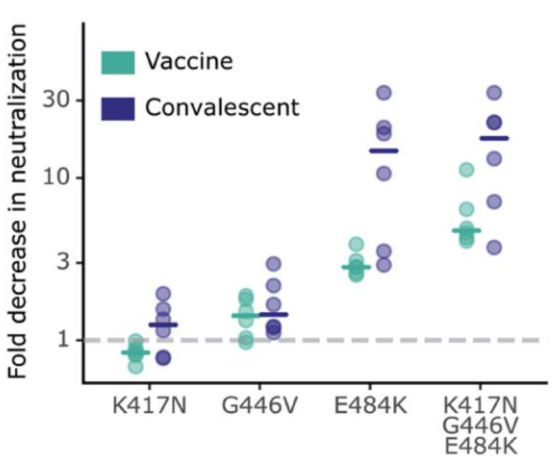

https://www.science.org/doi/10.1126/scitranslmed.abi9915#F5

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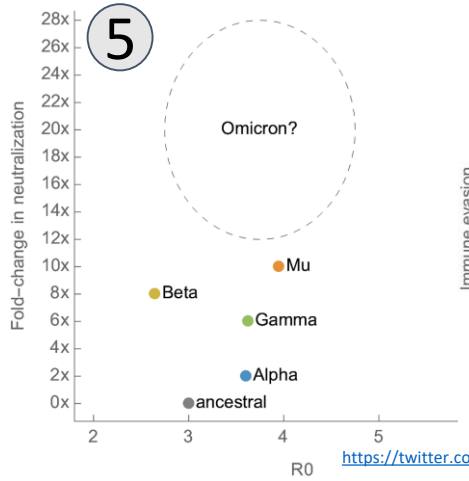

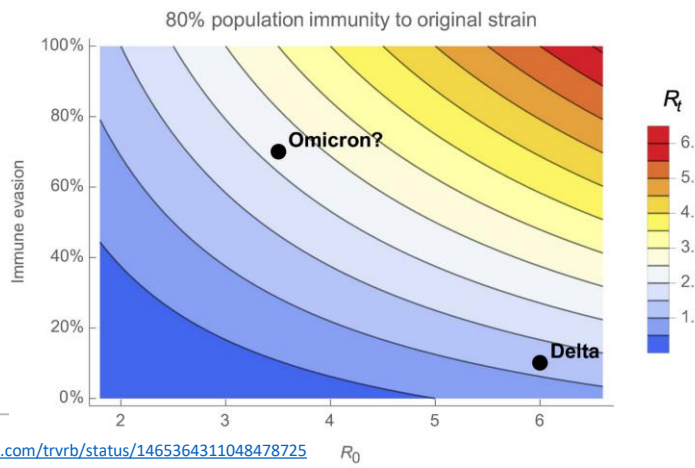

https://twitter.com/trvrb/status/1465364311048478725

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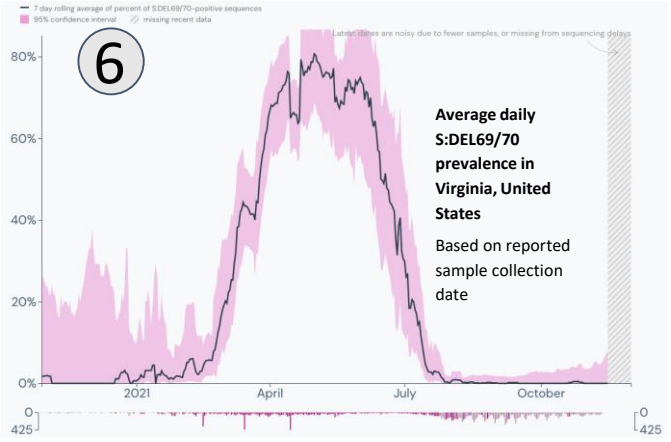
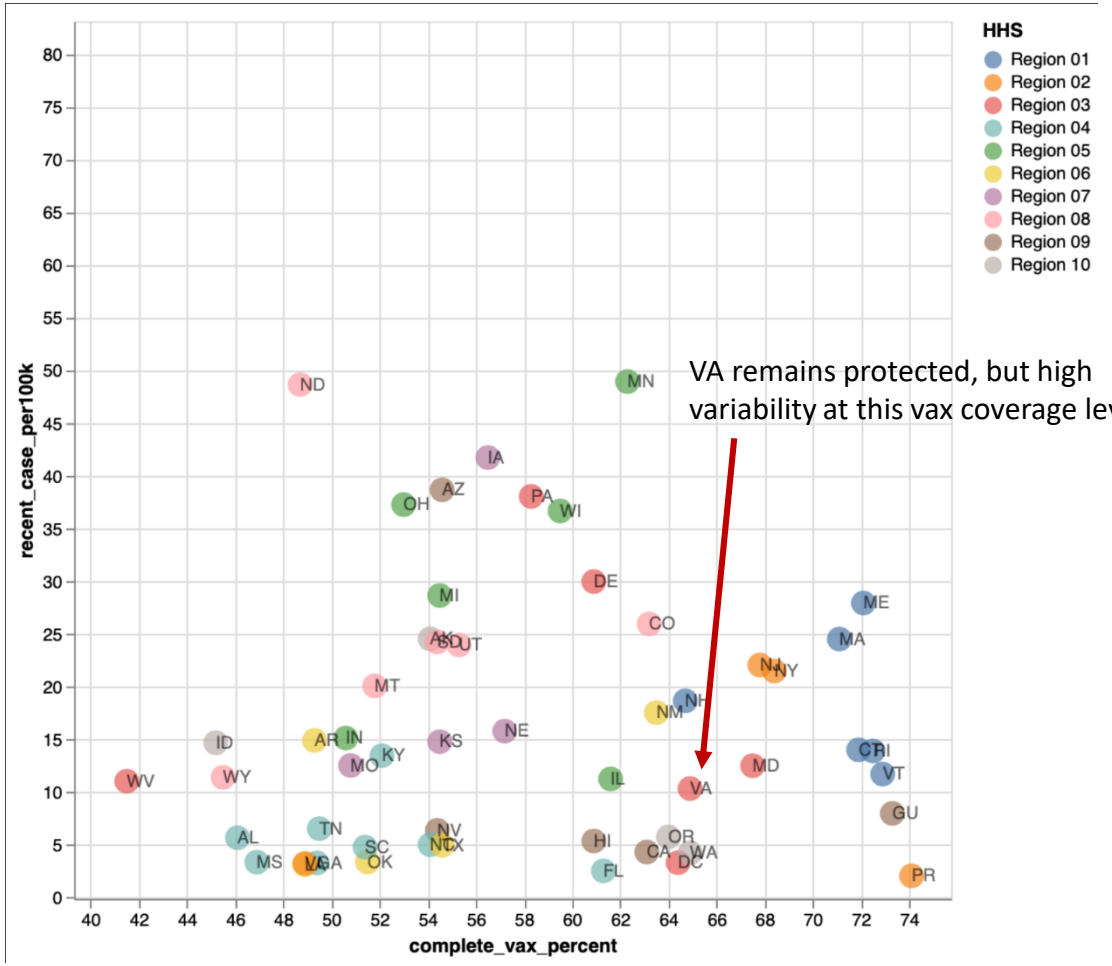


https://outbreak.info/situation-reports?muts=S%3ADEL69%2F70&loc=USA&loc=USA_US-VA&selected=USA_US-VA&overlay=false

Recent Cases Correlate with Vax Coverage

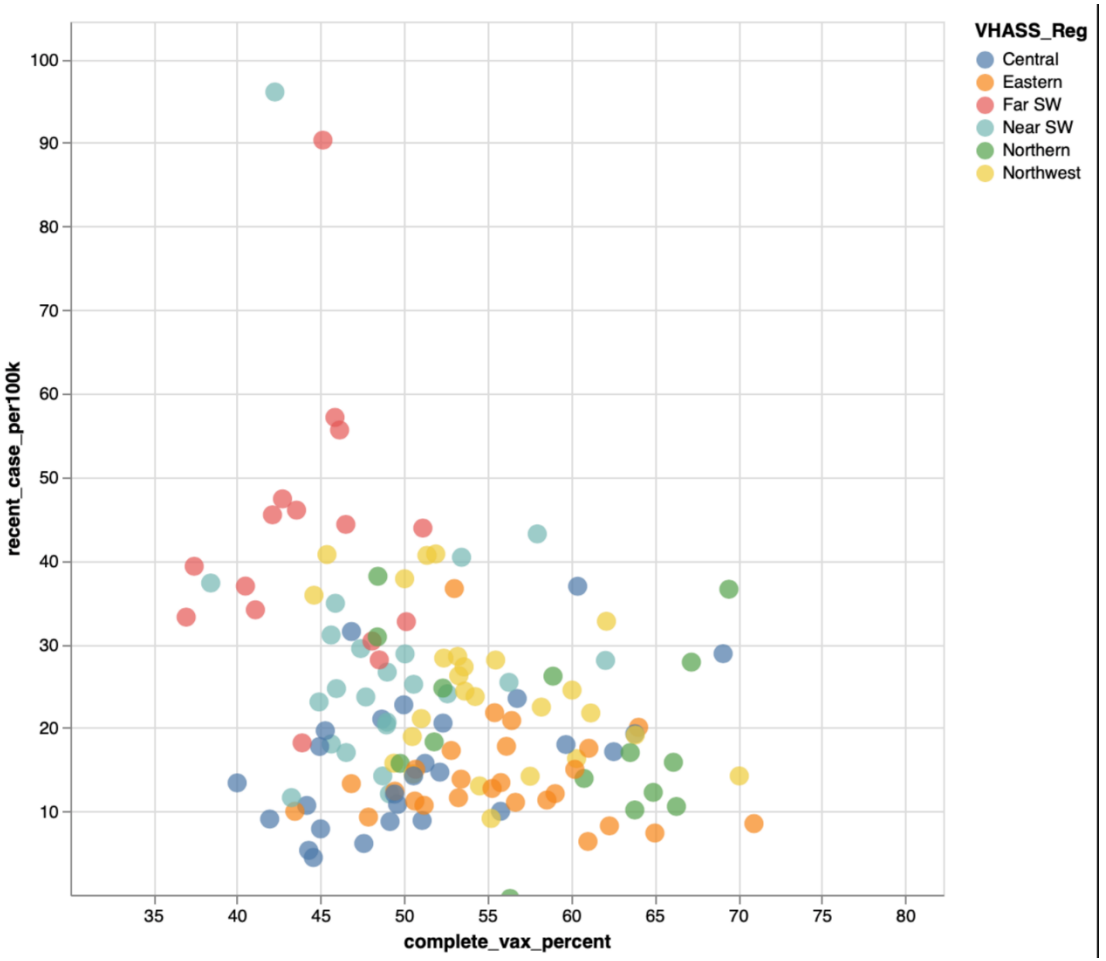
Mean cases per 100K vs. vaccine coverage

- Correlations between vax coverage and



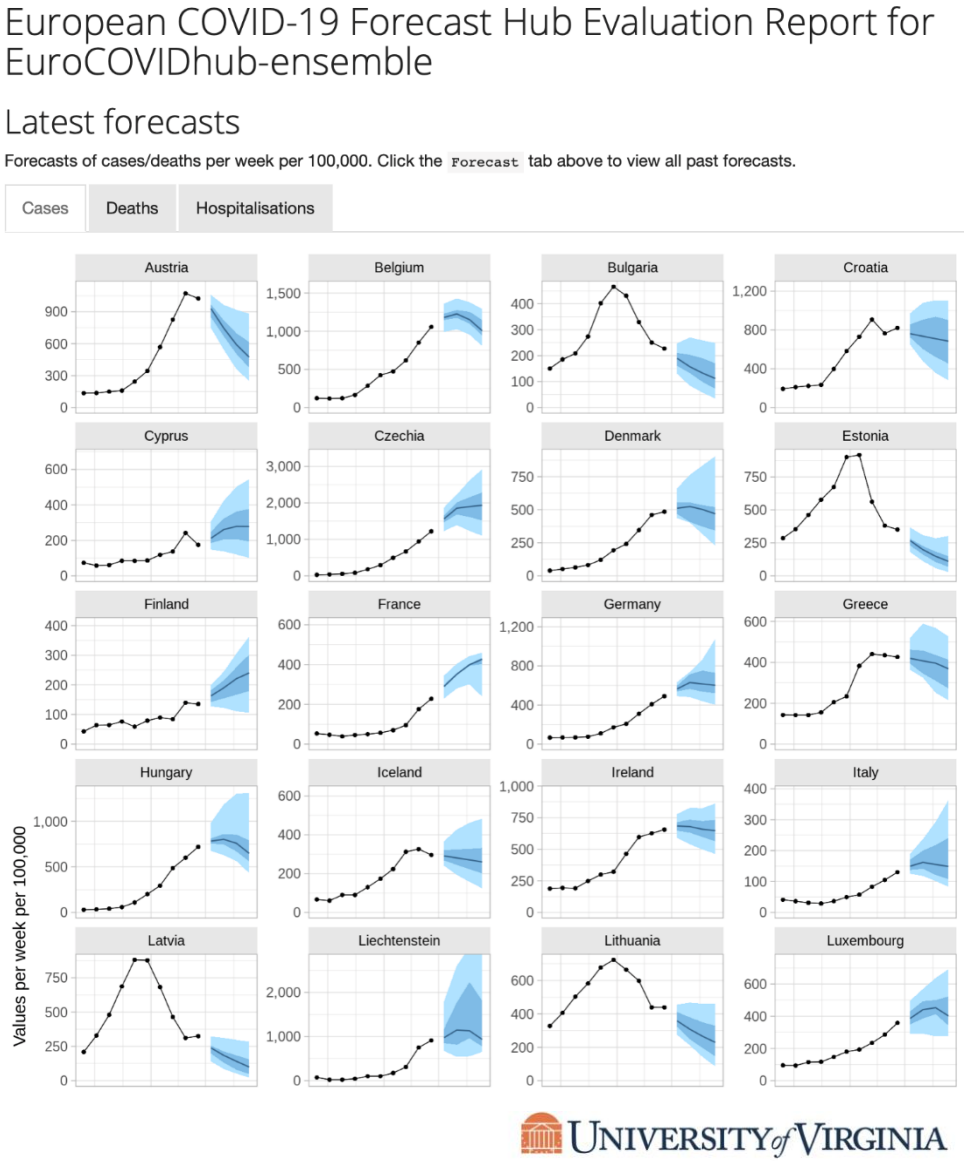
Virginia Counties

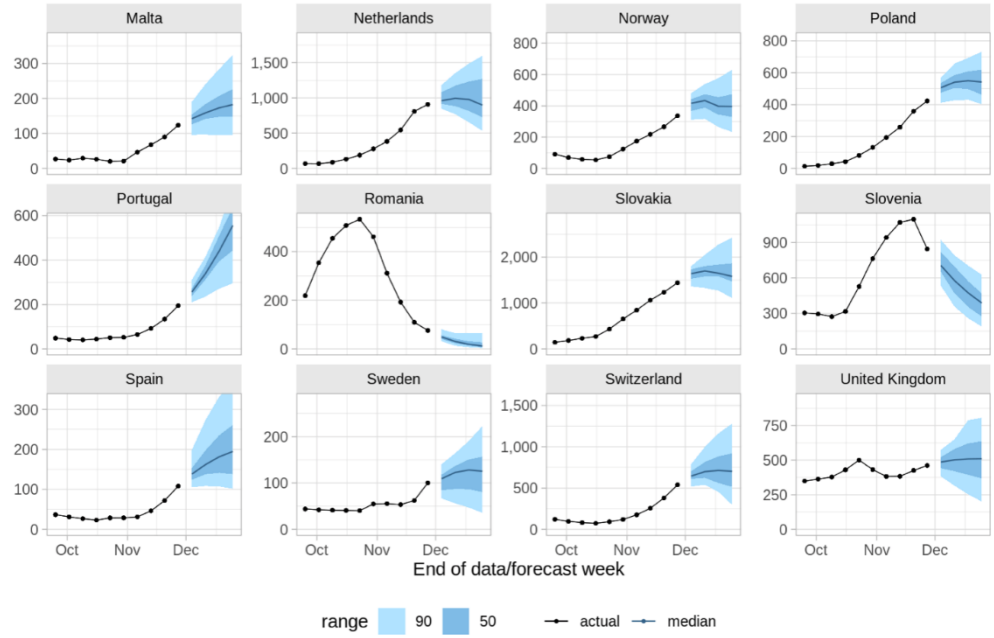
- Counties with higher vax coverage slightly lower rates



European Nations

- Cases continue to climb in most European nations
- Short term more mixed as some countries have experienced more of a decline
- Some are renewing control measures





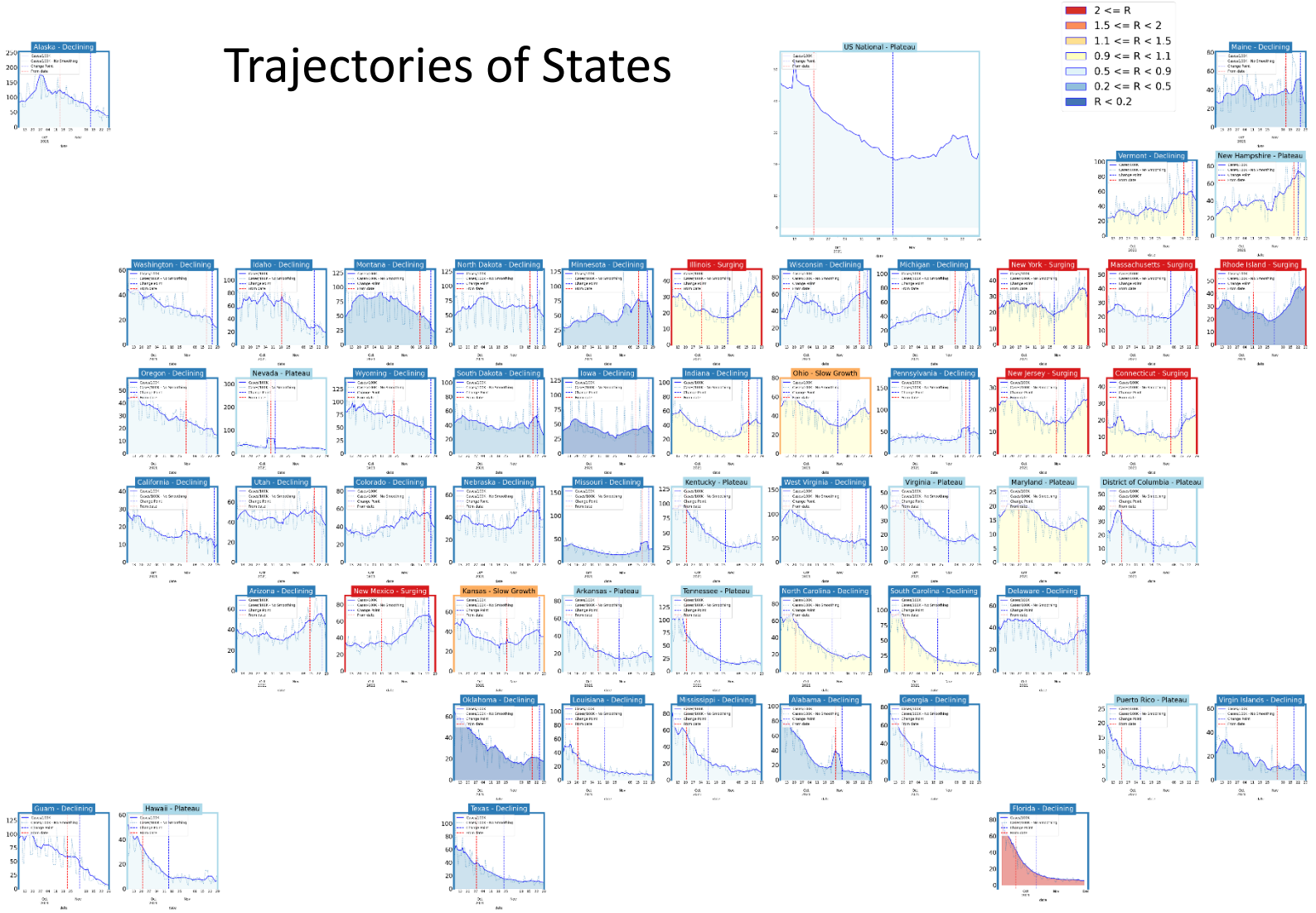
UVA-Ensemble model contributes to these forecasts
https://covid19forecasthub.eu/reports.html

United States Overall

- Declines still outnumber growth but the gap has closed
- Significant number of states in growth
- Case rates remain moderate to high in most states

Status	# States (2 weeks ago)
Declining	35 (25)
Plateau	10 (10)
Slow Growth	2 (6)
In Surge	7 (13)

Trajectories of States



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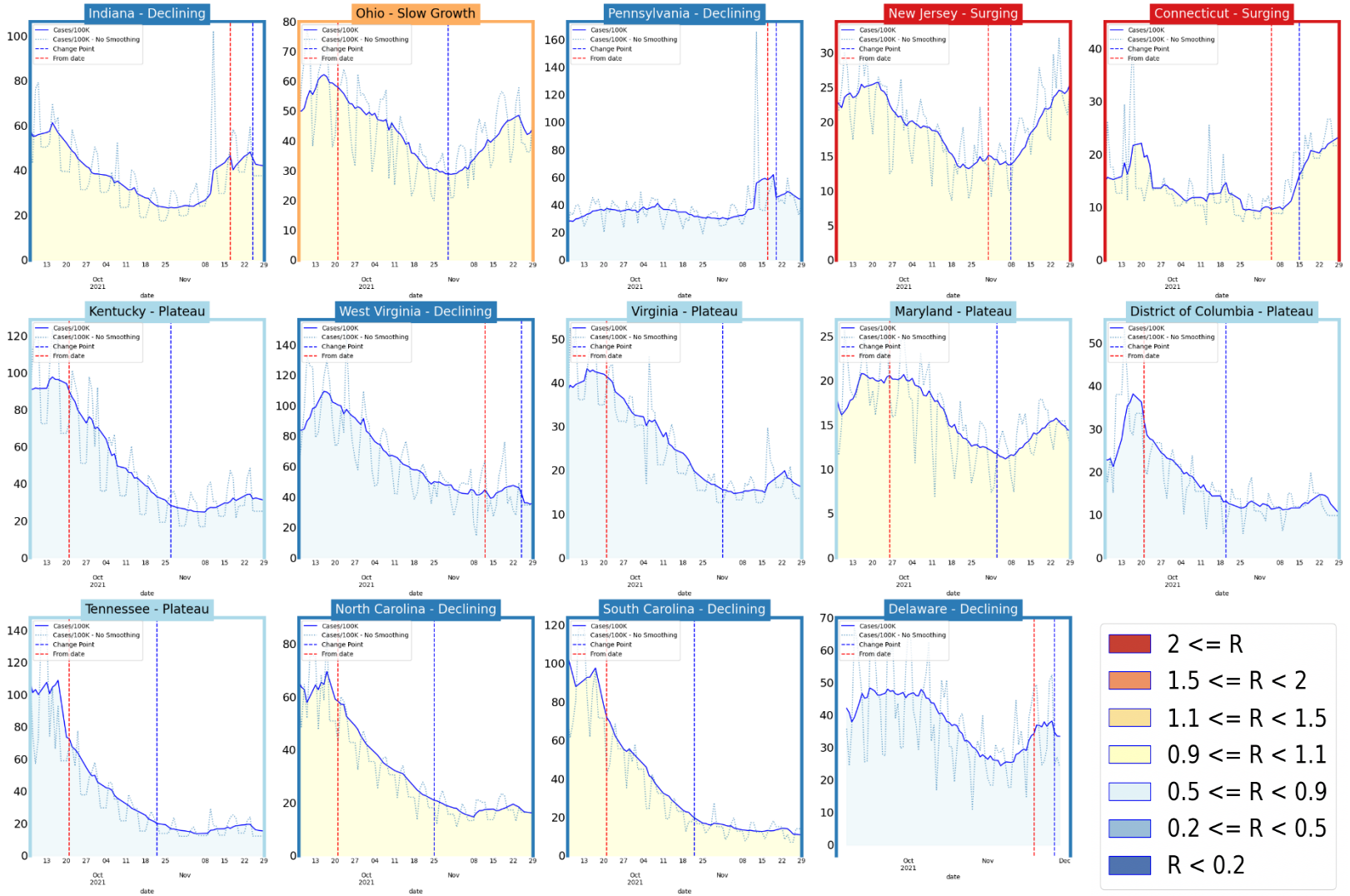
Virginia and Her Neighbors

- Neighbors now shifting to growth
- Declines remain in neighbors to the south
- Case rates have mostly moderated but some remain high
- Signs of slowing declines and plateaus emerging



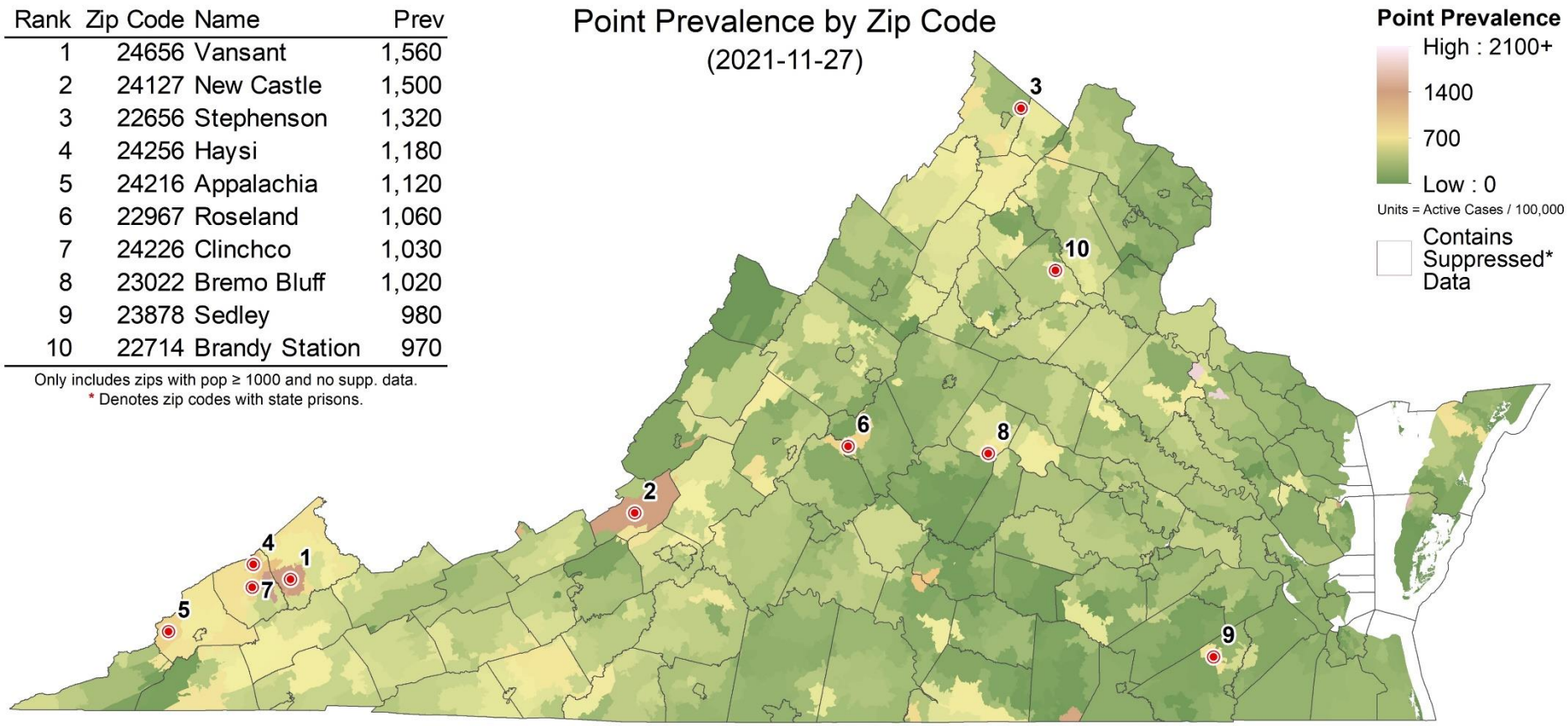
Zip code level weekly Case Rate (per 100K)

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	24656	Vansant	1,560
2	24127	New Castle	1,500
3	22656	Stephenson	1,320
4	24256	Haysi	1,180
5	24216	Appalachia	1,120
6	22967	Roseland	1,060
7	24226	Clinchco	1,030
8	23022	Bremo Bluff	1,020
9	23878	Sedley	980
10	22714	Brandy Station	970

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 2021-11-27.

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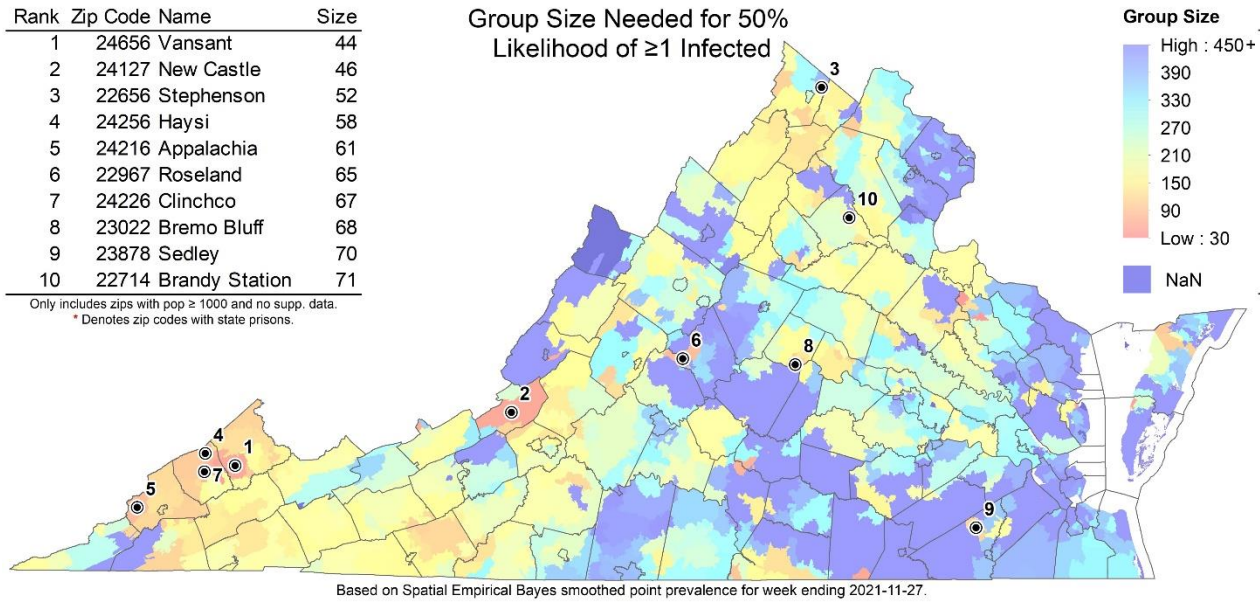
Risk of Exposure by Group Size and HCW prevalence

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

- **Group Size**: Assumes 2 undetected infections per confirmed case (ascertainment rate from recent seroprevalence survey), and shows minimum size of a group with a 50% chance an individual is infected by zip code (eg in a group of 44 in Vansant, 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

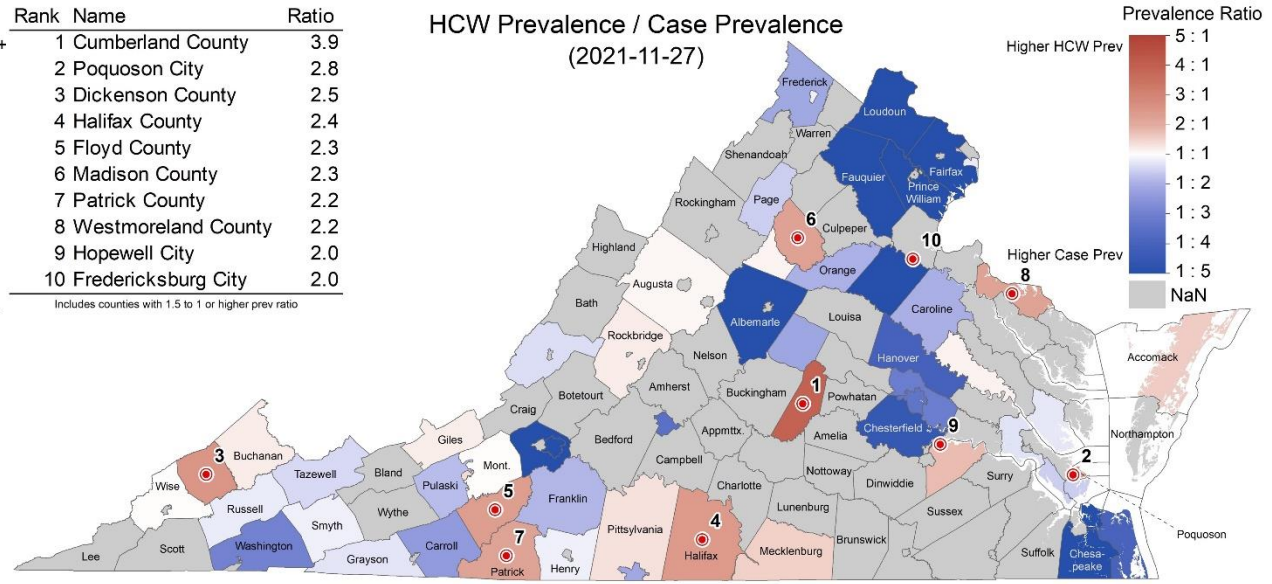
Rank	Zip Code	Name	Size
1	24656	Vansant	44
2	24127	New Castle	46
3	22656	Stephenson	52
4	24256	Haysi	58
5	24216	Appalachia	61
6	22967	Roseland	65
7	24226	Clinchco	67
8	23022	Bremo Bluff	68
9	23878	Sedley	70
10	22714	Brandy Station	71

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



Rank	Name	Ratio
1	Cumberland County	3.9
2	Poquoson City	2.8
3	Dickenson County	2.5
4	Halifax County	2.4
5	Floyd County	2.3
6	Madison County	2.3
7	Patrick County	2.2
8	Westmoreland County	2.2
9	Hopewell City	2.0
10	Fredericksburg City	2.0

Includes counties with 1.5 to 1 or higher prev ratio



Current Hot-Spots

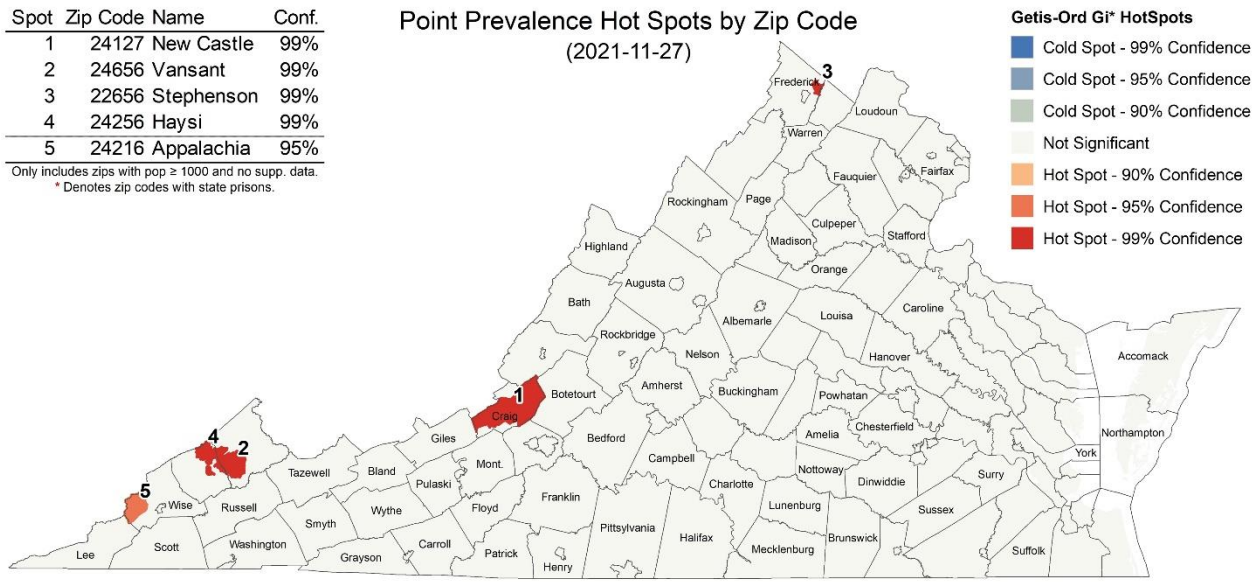
Case rates that are significantly different from neighboring areas or model projections

- **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

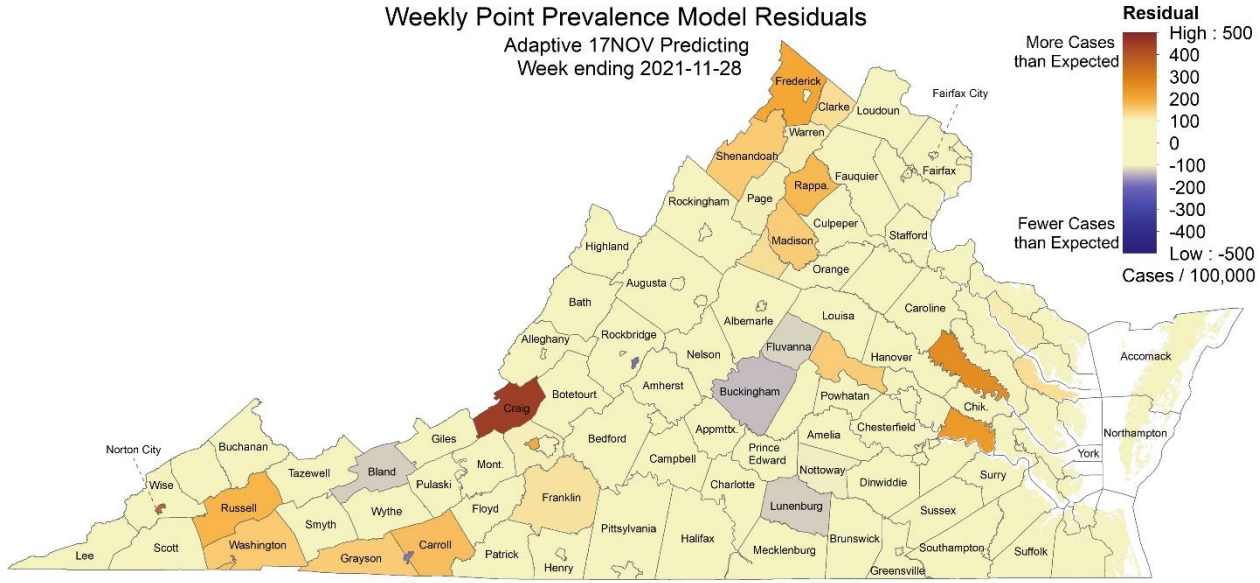
Spot	Zip Code	Name	Conf.
1	24127	New Castle	99%
2	24656	Vansant	99%
3	22656	Stephenson	99%
4	24256	Haysi	99%
5	24216	Appalachia	95%

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



Based on Global Empirical Bayes smoothed point prevalence for week ending 2021-11-27.

Clustered Temporal Hotspots

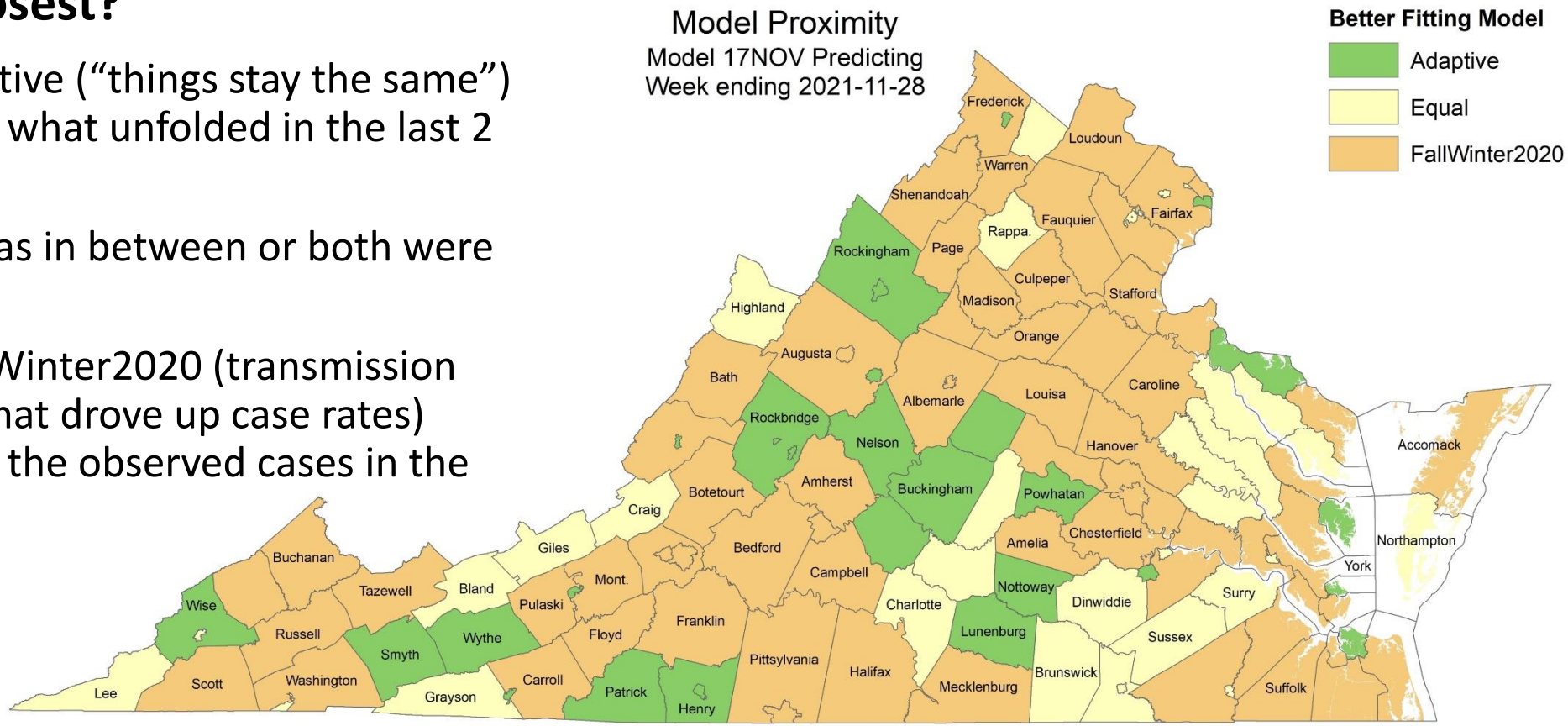


Moran's I = 0.030827, Z-Score = 1.701706, P-Value = 0.08881
No Residual Autocorrelation Detected

Scenario Trajectory Tracking

Which scenario from last projection did each county track closest?

- Green means the Adaptive ("things stay the same") scenario was closest to what unfolded in the last 2 weeks
- Yellow means reality was in between or both were very similar
- Orange means the FallWinter2020 (transmission drivers from last year that drove up case rates) scenario was closest to the observed cases in the last 2 weeks

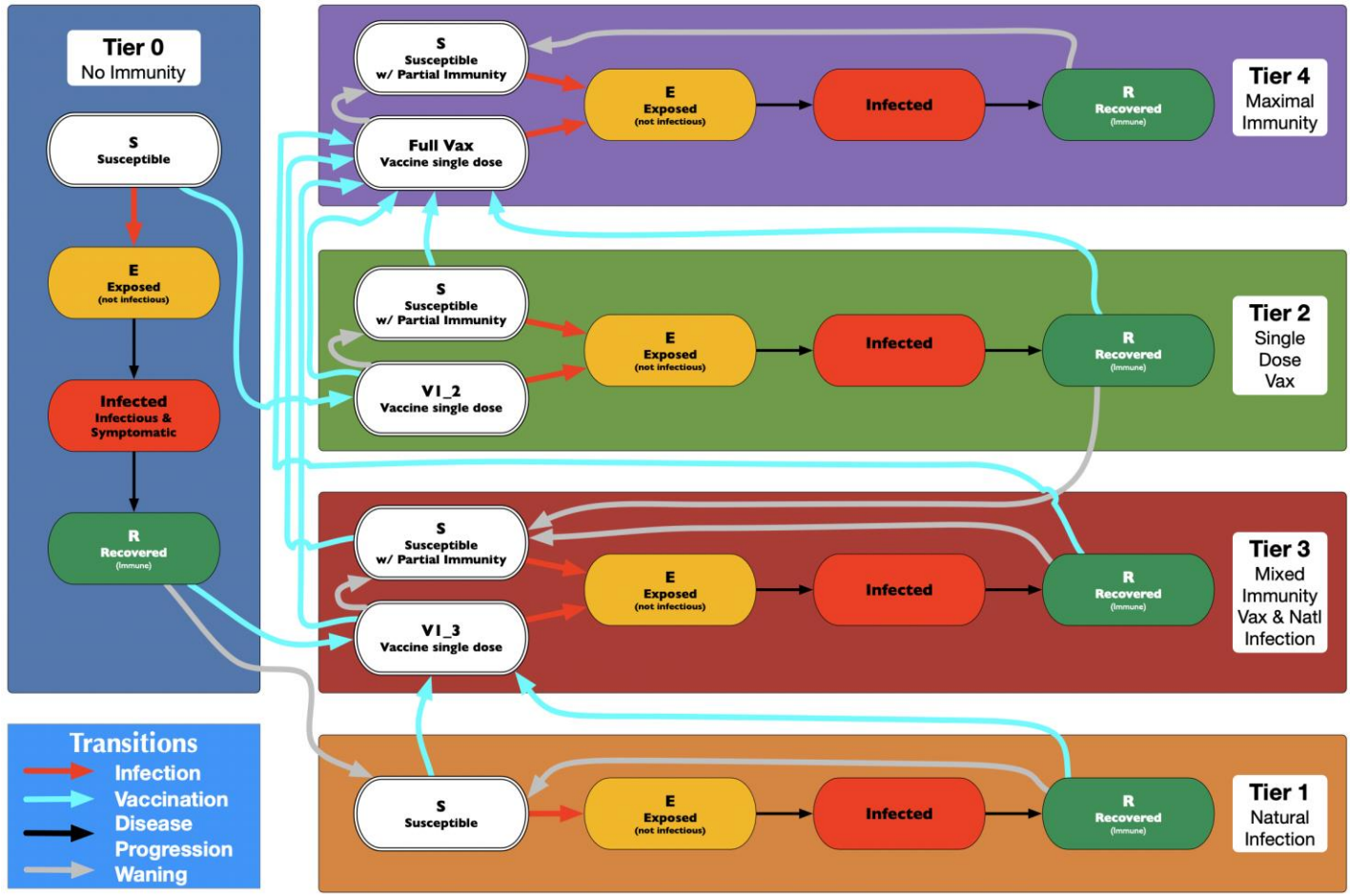


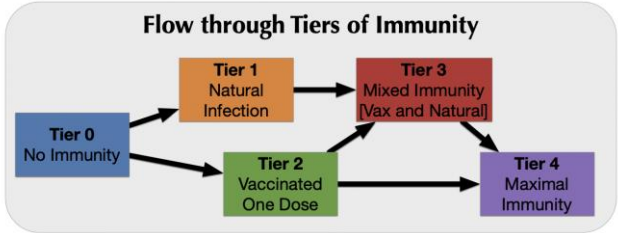
Model Update – Adaptive Fitting

New Model Structure Focused on Tiers of Immunity

Uncertainty surrounds the rate of waning immunity

- New model structure built to better track levels and timing of waning
- Outcomes vary based on age and immune history, for partial immunity protection against hospitalization and death is stronger than No Immunity but weaker than Maximal Immunity
- Use same Adaptive fitting approach with vaccine schedules and simulated infections driving movement across the tiers
- Different Scenarios can also be applied





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Adaptive Fitting Approach

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

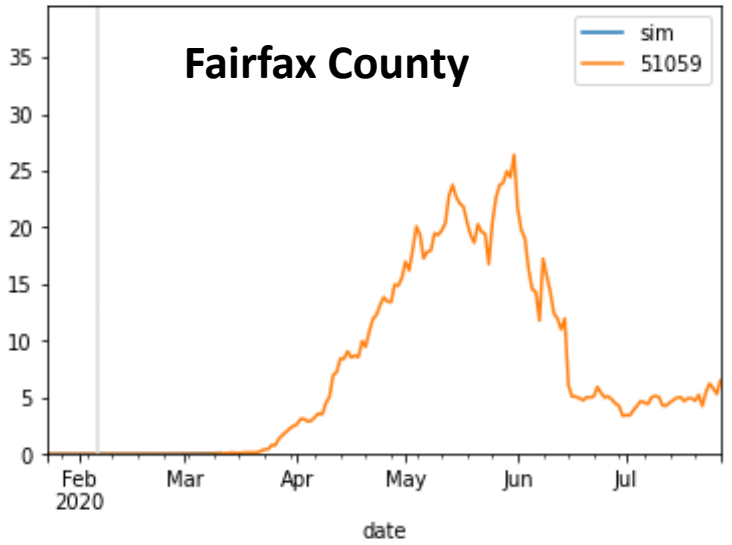
- Allows history to be precisely captured, and used to guide bounds on projections

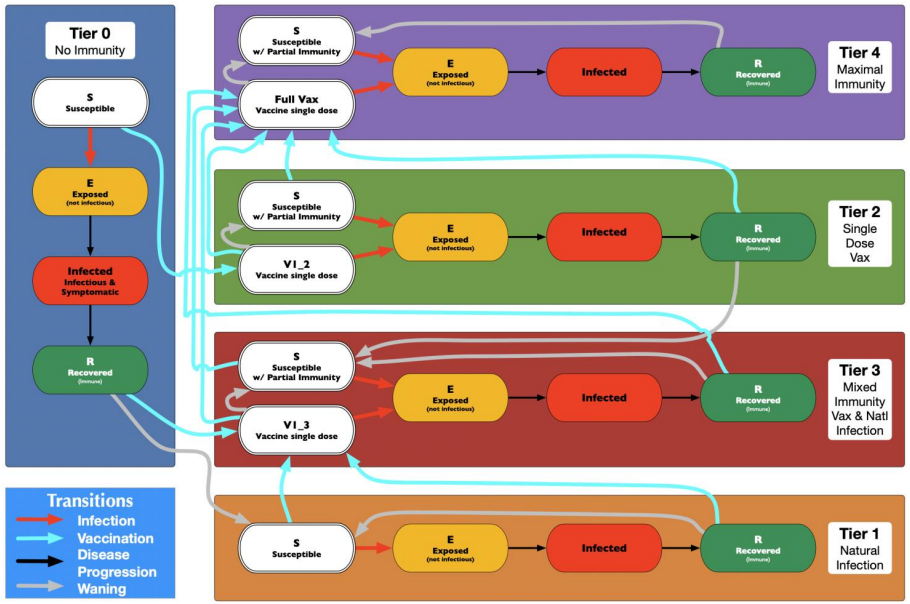
Model: An alternative use of the same meta-population model, PatchSim with multiple tiers of immunity

- Allows for future "what-if" Scenarios to be layered on top of calibrated model
- Allows for waning of immunity and for partial immunity against different outcomes (eg lower protection for infection than death)

External Seeding: Steady low-level importation

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





Using Ensemble Model to Guide Projections

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

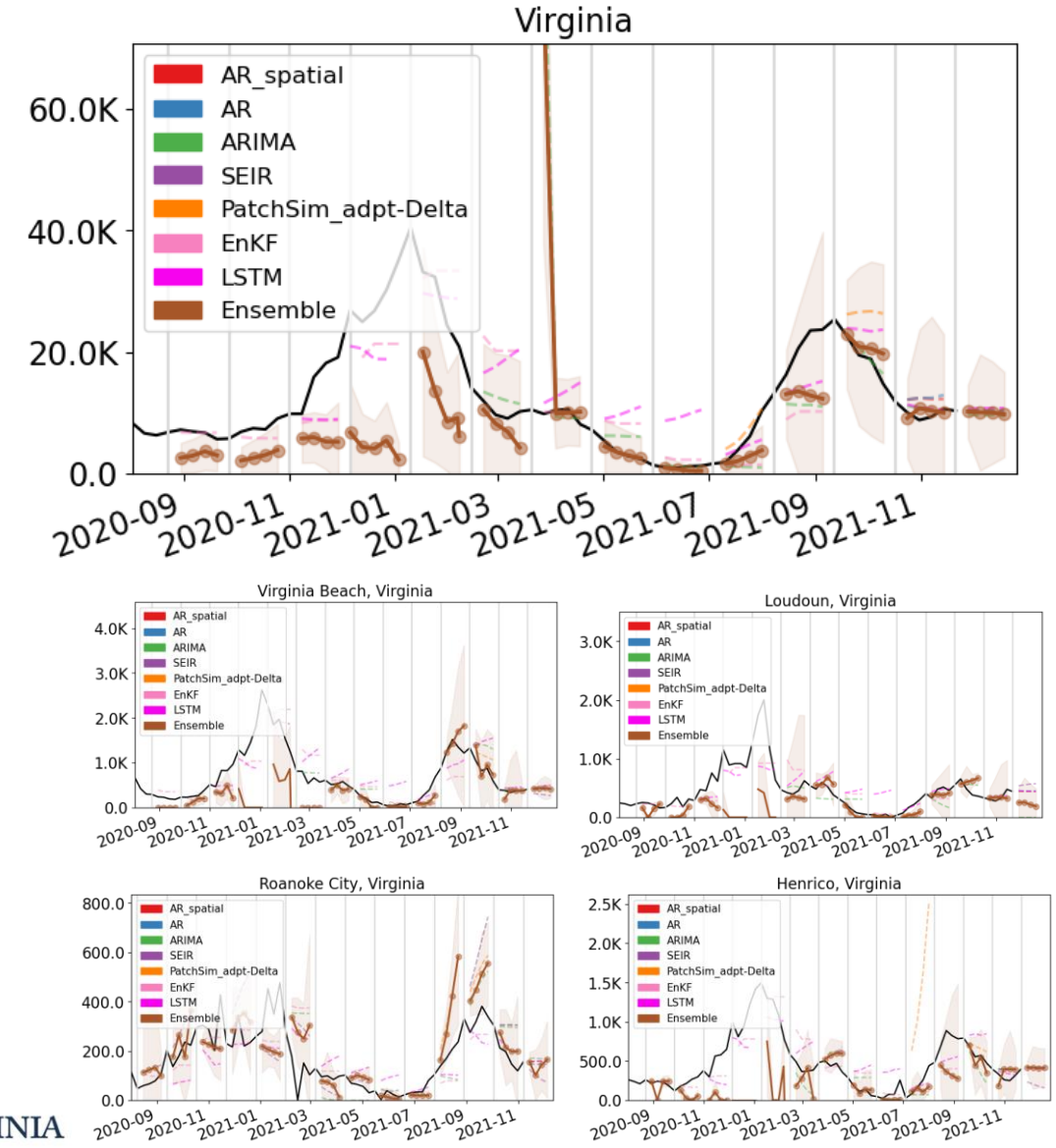
- Autoregressive (AR, ARIMA)
- Neural networks (LSTM)
- Kalman filtering (EnKF)

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

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

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

Also submitted to CDC Forecast Hub.



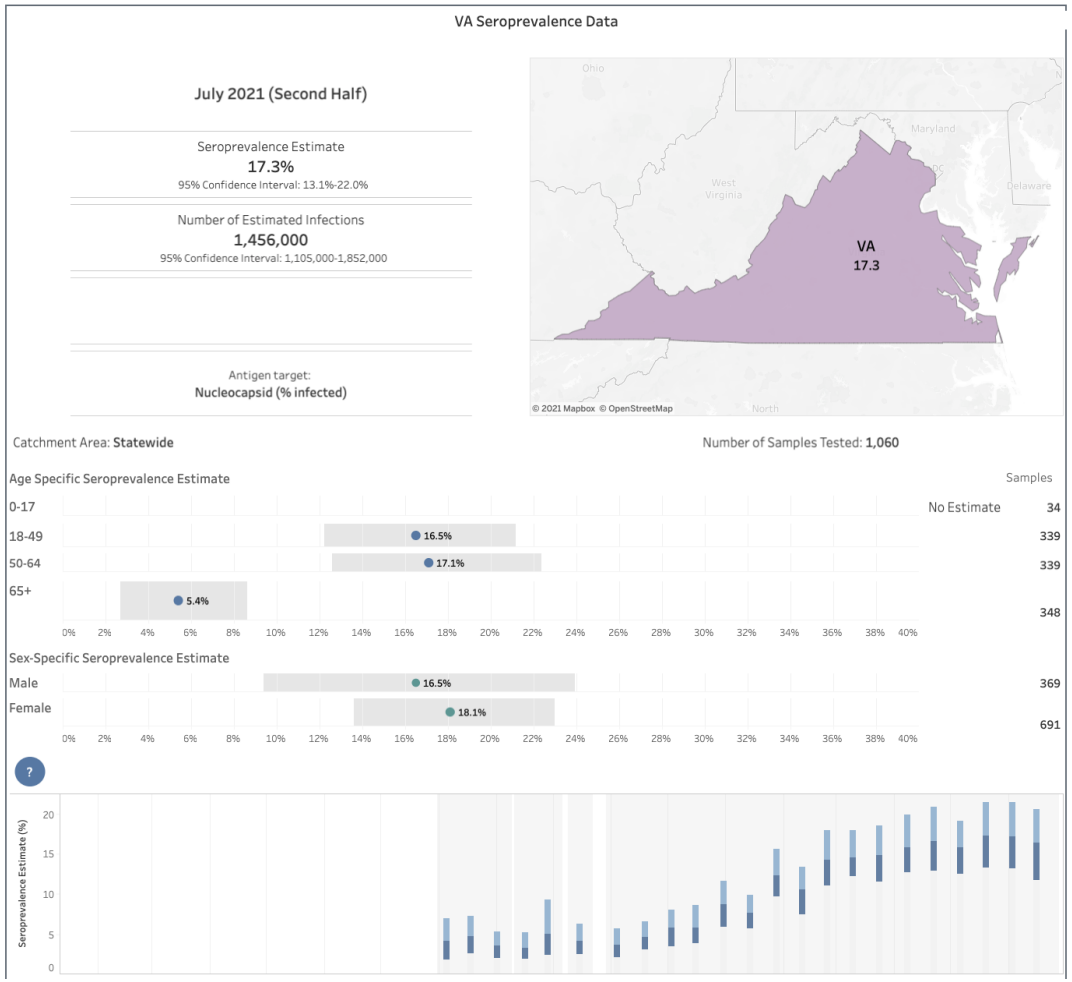
Seroprevalence updates to model design

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

- CDC Nationwide Commercial Laboratory Seroprevalence Survey

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

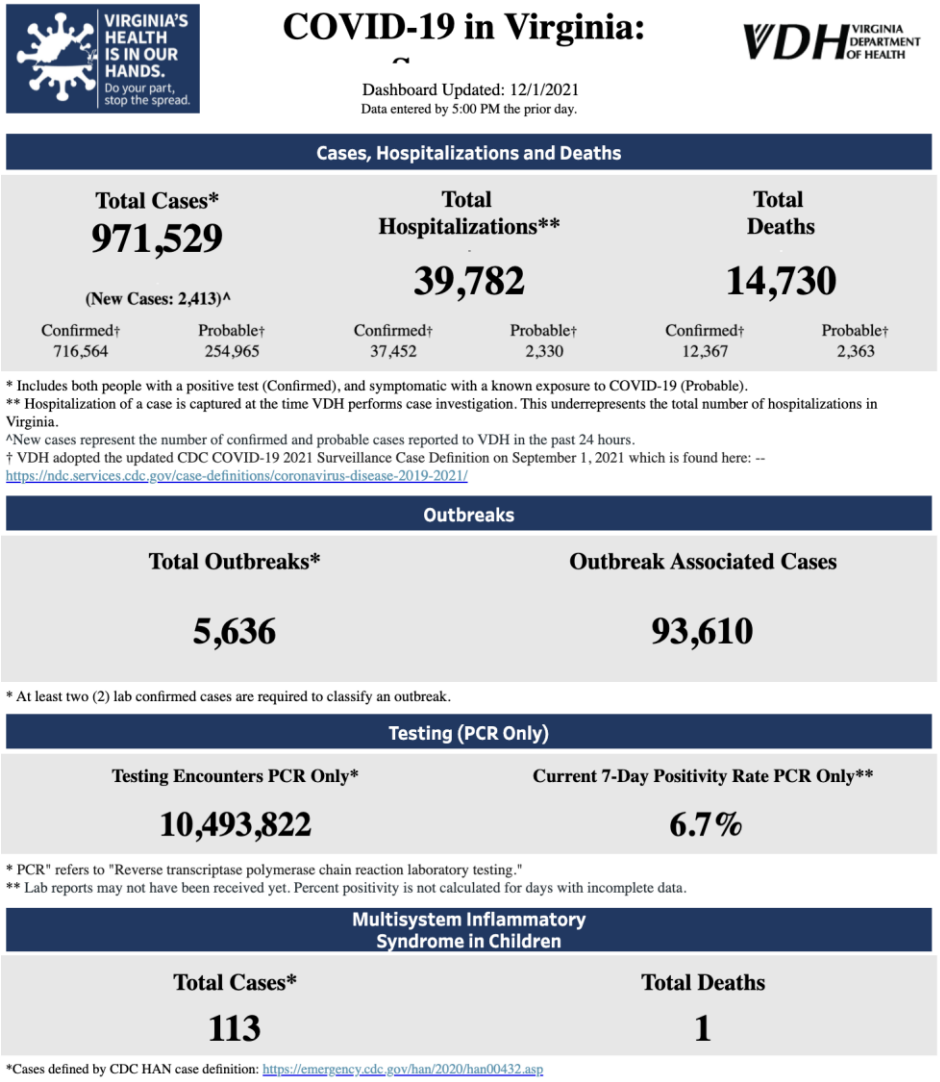
- Thus for 2x there are 2 total infections in the population for every confirmed case recently
- This measure now fully tracks the estimated ascertainment over time
- Uncertainty design has been shifted to these bounds (previously higher ascertainments as was consistent earlier in the pandemic were being 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: 12/1/2021
Data entered by 5:00 PM the prior day.

Cases, Hospitalizations and Deaths

Total Cases*	Total Hospitalizations**	Total Deaths
971,529	39,782	14,730
(New Cases: 2,413)^		

Confirmed†	Probable†	Confirmed†	Probable†	Confirmed†	Probable†
716,564	254,965	37,452	2,330	12,367	2,363

* 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
5,636	93,610

* 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**
10,493,822	6.7%

* 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
113	1

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

Accessed 10:30am December 1, 2021
https://www.vdh.virginia.gov/coronavirus/

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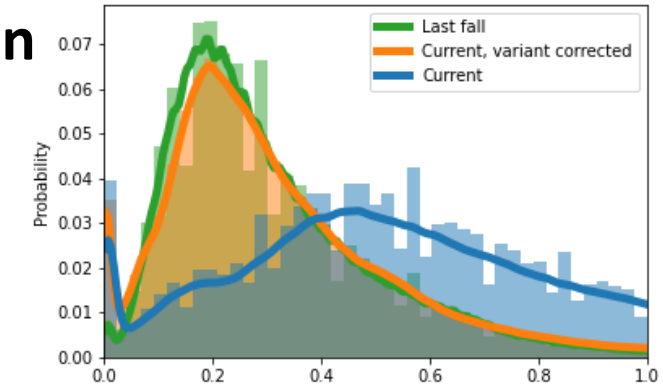
Scenarios – Transmission Conditions

- 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-FallWinter:** 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

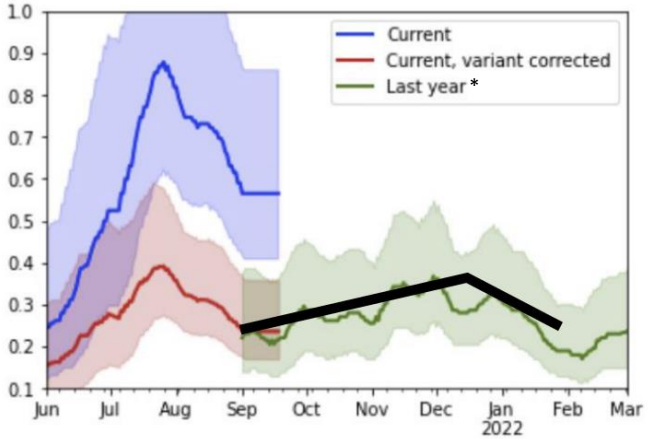
Scenarios – FallWinter2020 Description

September 2020 – February 2021 saw a strong wave of transmission

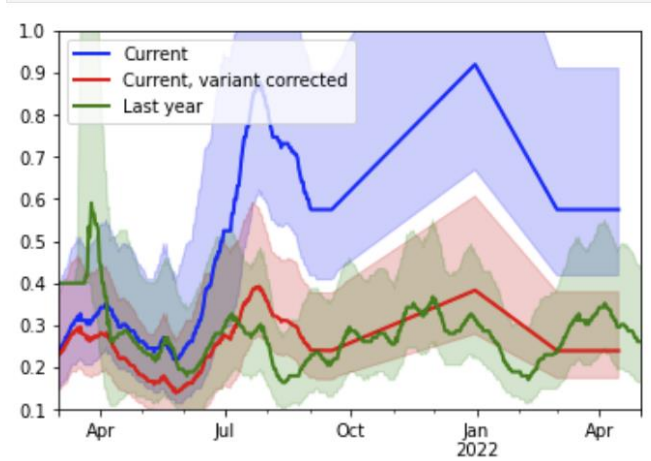


- We analyze previous Fall-Winter's wave vs. current Delta driven wave and observe surprising similarities
  - The distribution of fitted model transmissibility is nearly identical between these periods when corrected for Delta's increased transmissibility
- **FallWinter2020** tries to capture the "transmission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

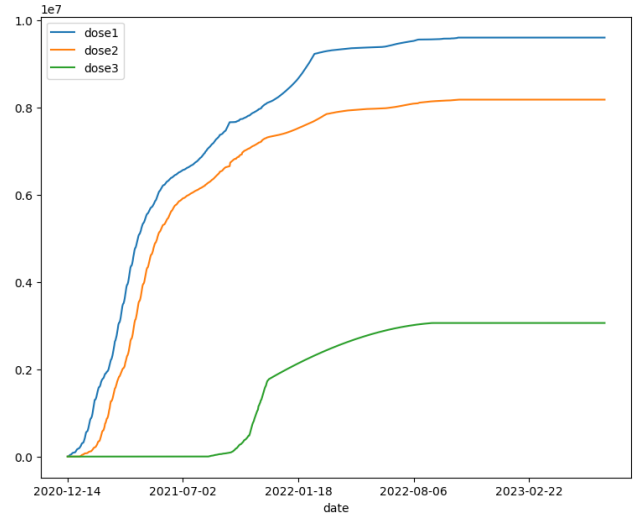
Vaccine Characteristics

- **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)

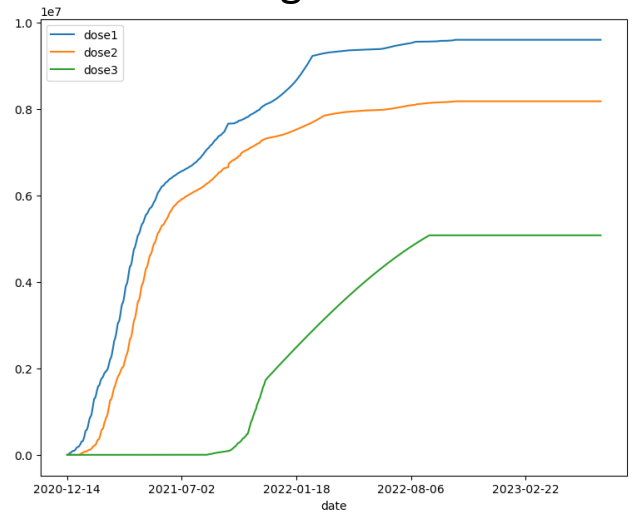
Vaccine Administration Scenarios

- **Status quo (no label):**
  - **Eventual coverage**: COVIDcast corrected acceptance estimates (statewide mean is ~80% adults, 65% of population) reached by end of January.
  - **Children (5-11):** Follow rates of 12-16 year olds, max out at 80% of adult acceptance
  - **3rd doses:** Top out with total coverage of 40%
- **Optimistically High Boosting (HighBoost):**
  - **Eventual coverage**: COVIDcast corrected acceptance estimates (statewide mean is ~80% adults, 65% of population) reached by end of January.
  - **Children (5-11):** Follow rates of 12-16 year olds, max out at 80% of adult acceptance
  - **3rd doses:** Top out with total coverage of 70%
- Acceptance at county level = regional acceptance +/- relative current vax
- Front-loaded rollout (two-thirds of the remaining in half the time)

Status Quo



High Boost



Projection Scenarios – Combined Conditions

Name	Txm Controls	Vax	Description
Adaptive	C	SQ	Likely trajectory based on conditions remaining similar to the current experience
Adaptive-HighBoost	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-FallWinter	FallWinter 2020	SQ	Transmission rates coarsely follow the rates from last September through this February but are boosted by Delta's enhanced transmissibility

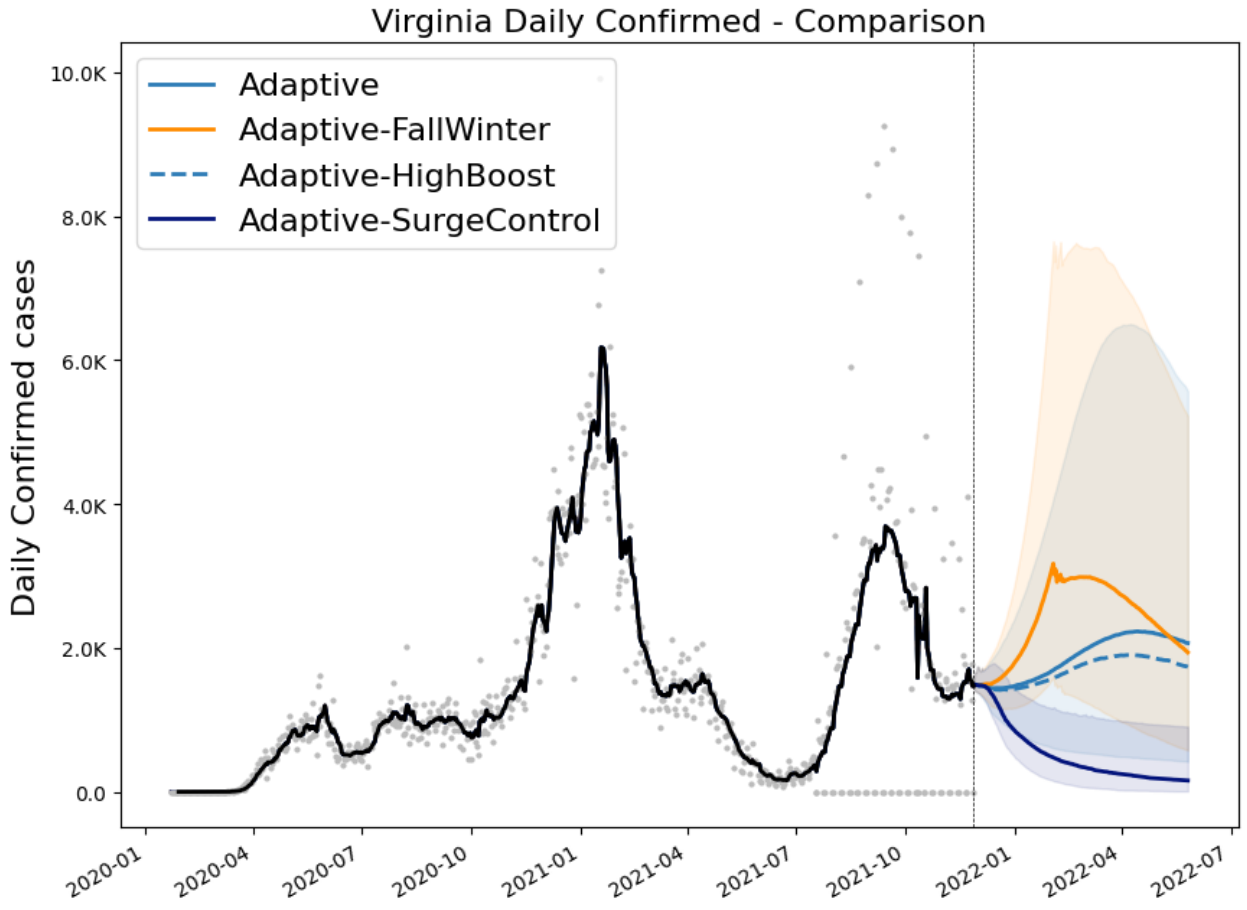
Transmission Controls:
C = Current levels persist into the future
25% = Transmission rates are reduced by 25% with a gradual introduction, concluding in 4 weeks
FallWinter2020 = Transmission rates from Sept 2020 – Feb 2021 are coarsely replayed but boosted by Delta's increased transmissibility

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

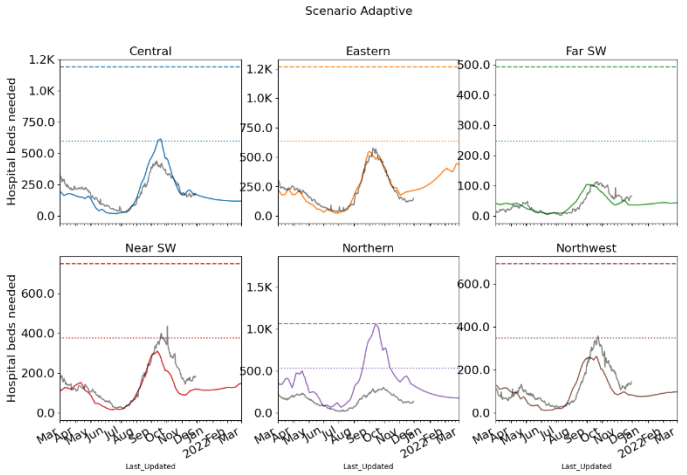
Model Results

Outcome Projections

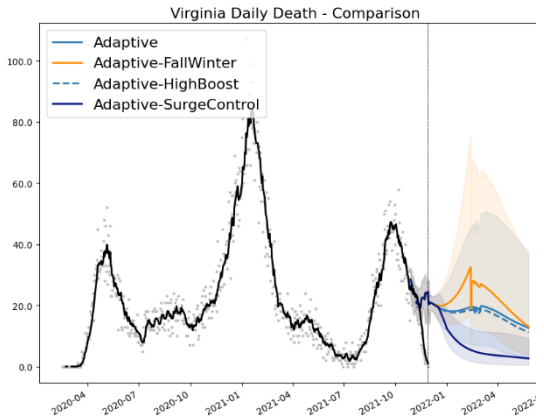
Confirmed cases



Estimated Hospital Occupancy

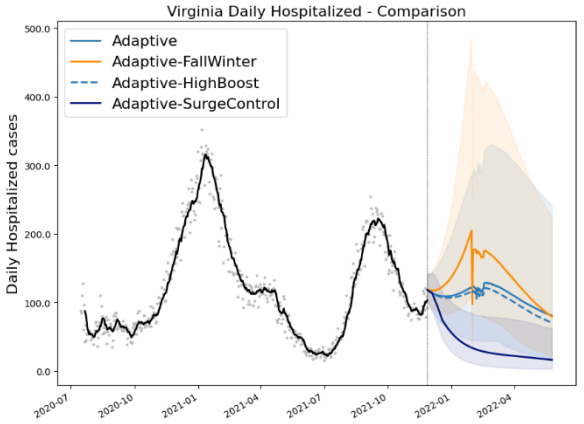


Daily Deaths



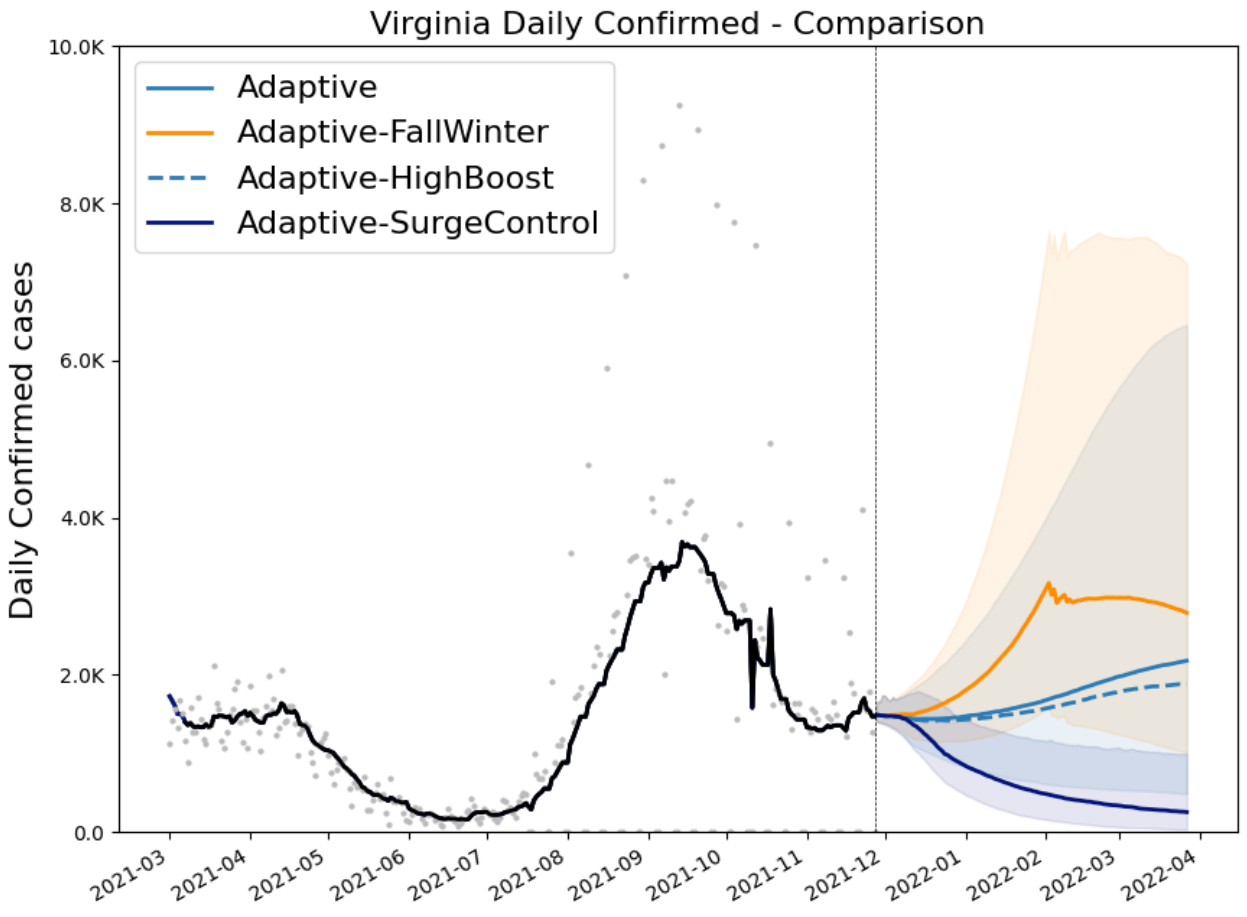
Death ground truth from VDH "Event Date" data, most recent dates are not complete

Daily Hospitalized

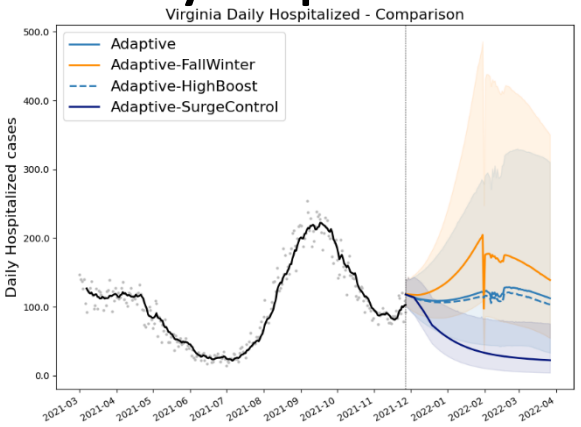


Outcome Projections – Closer Look

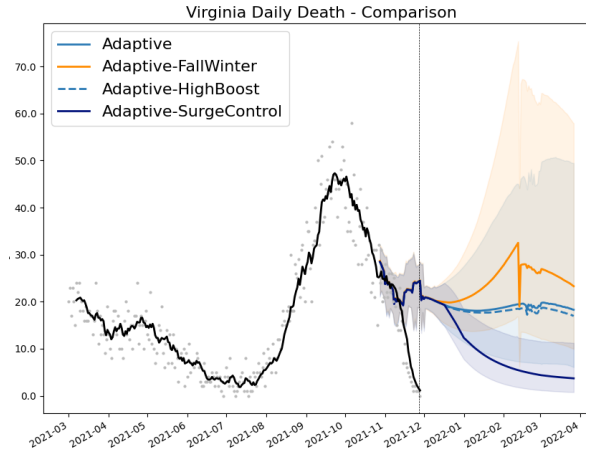
Confirmed cases



Daily Hospitalized



Daily Deaths



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

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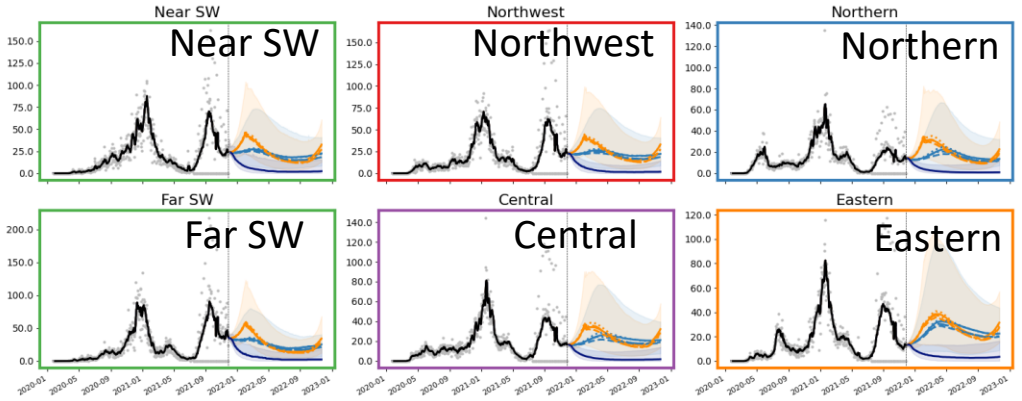
Detailed Projections: All Scenarios

Projections by Region

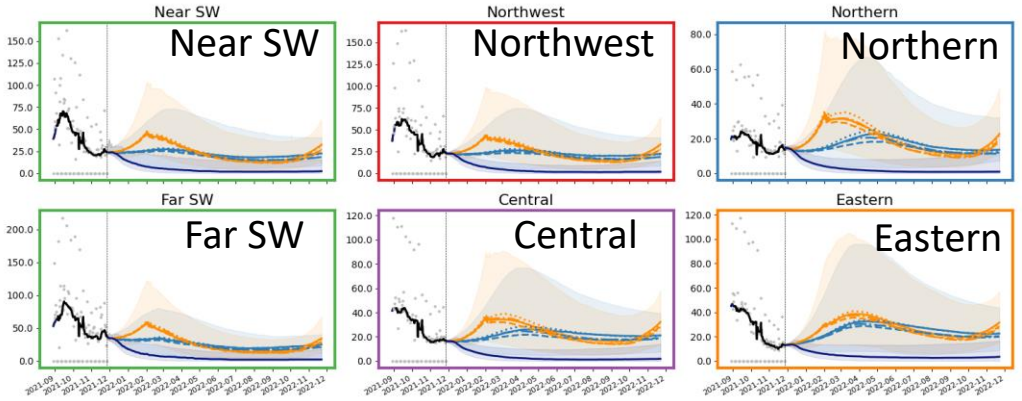


Projections by District

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



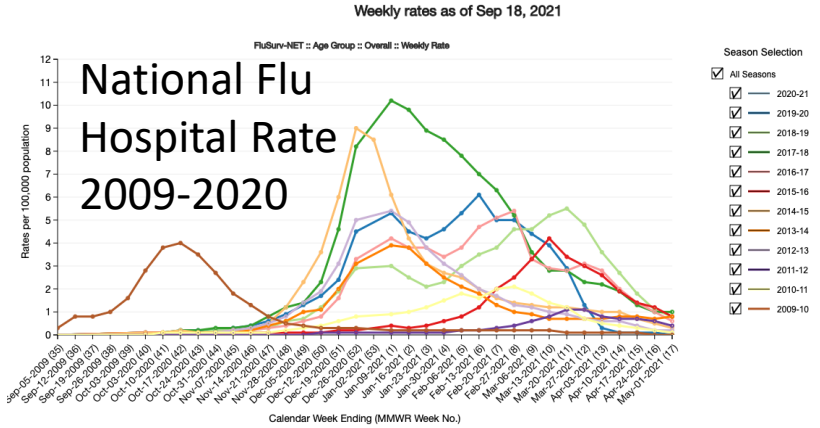
Projections by District

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

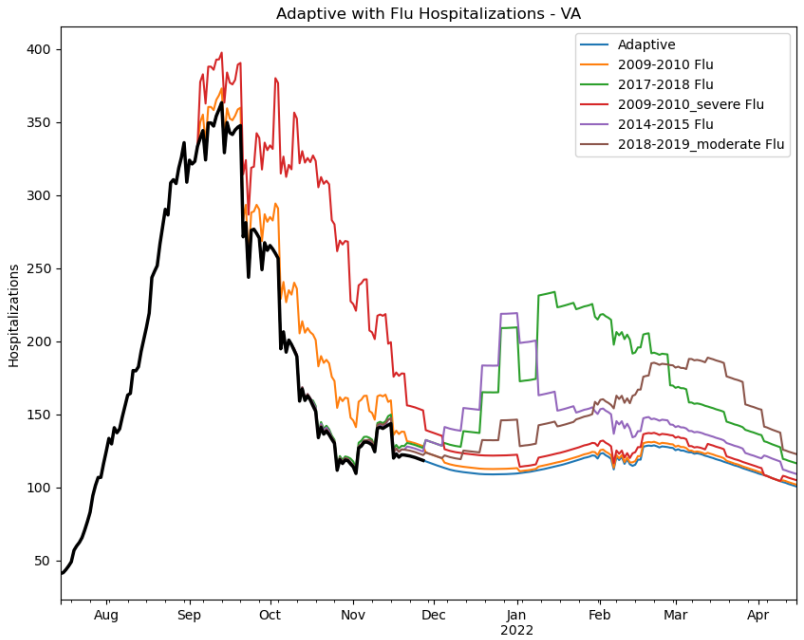
2017-18 – Timing and severity of 2017-18 season

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

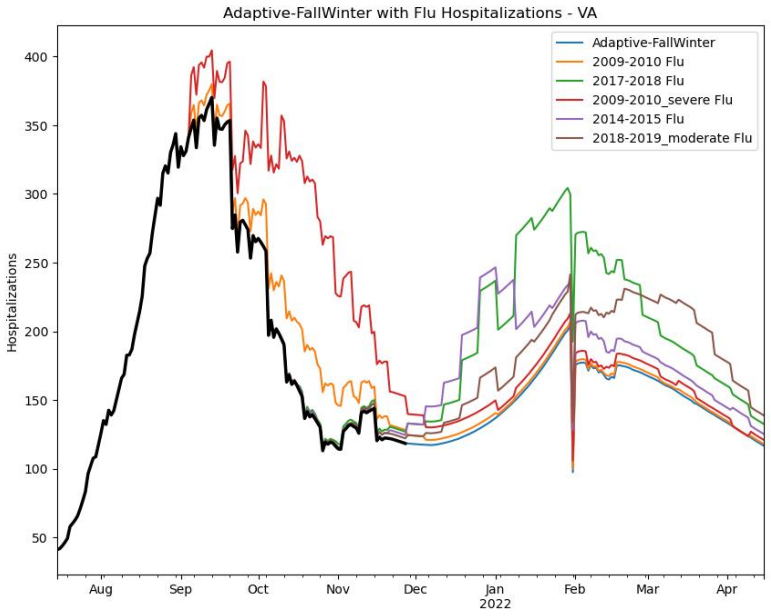
2014-15 – Timing and severity of 2014-15 season

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

Adaptive



Adaptive – FallWinter2020

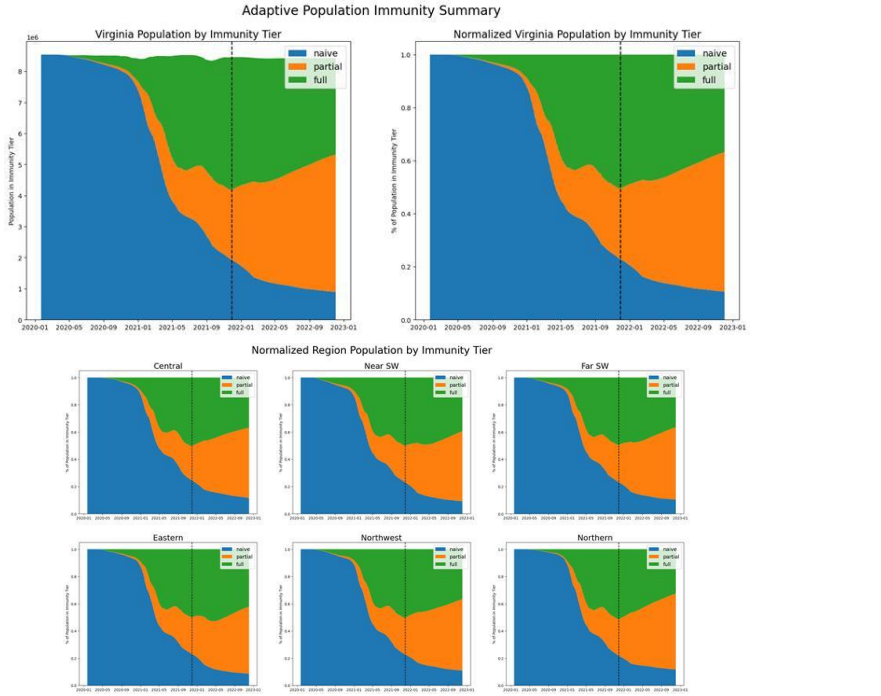


UNIVERSITY of VIRGINIA
BIOCOMPLEXITY INSTITUTE

Virginia's Population Immunity

Different levels of immunity exist across the population

- Duration of immunity from infection with SARS-CoV2 still not well understood
  - Currently model is parameterized with a 6 month waning rate that moves individuals from their vaccinated or naturally immune states to a partially immune state with limited protection (eg 60% vs. 95% protection)
  - Immune escape can further reduce the protection experienced by Partial and Full immunity
- Levels of Immunity:
  - **No immunity:** No protection from vaccines
  - **Partial Immunity:** Waned immunity from both vaccines and natural in all the various combinations (1 or 2 doses, naïve and breakthrough infection, etc.)
  - **Full Immunity:** Maximal immunity from non-waned 2 doses or 3rd dose boosted vaccination or recent infection.
- Population immunity depends on a very high proportion of the population getting vaccinated
  - Current models track measured seroprevalence



Region	No Immunity	Partial Immunity	Full Immunity
Central	25%	25%	50%
Eastern	23%	27%	50%
Far SW	23%	27%	50%
Near SW	23%	27%	50%
Northern	22%	27%	51%
Northwest	23%	27%	50%
Virginia	**22%**	**27%**	**51%**

* As of Nov 27th, 2021 for entire population

Key Takeaways

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

- **Case rates after holiday break decline after brief rise with a mix of activity across the commonwealth; holiday effects caused brief dips in activity last year**
- VA 7-day mean daily case rate receded to 16.7/100K from 20/100K; US is down to 25/100K (from 29/100K)
- Projections show a flattening with eventual rise should current low transmission drivers persist
- As seasonal factors mount trajectories may shift towards the FallWinter2020 scenario with more rapid near-term growth; this scenario shows considerable growth is still possible.
- Recent updates:
  - Overhauled model structure to better capture different tiers of immunity and the effects of waning
  - Analysis of the effects of further booster coverage

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

Additional Analyses

Overview of relevant on-going studies

Other projects coordinated with CDC and VDH:

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

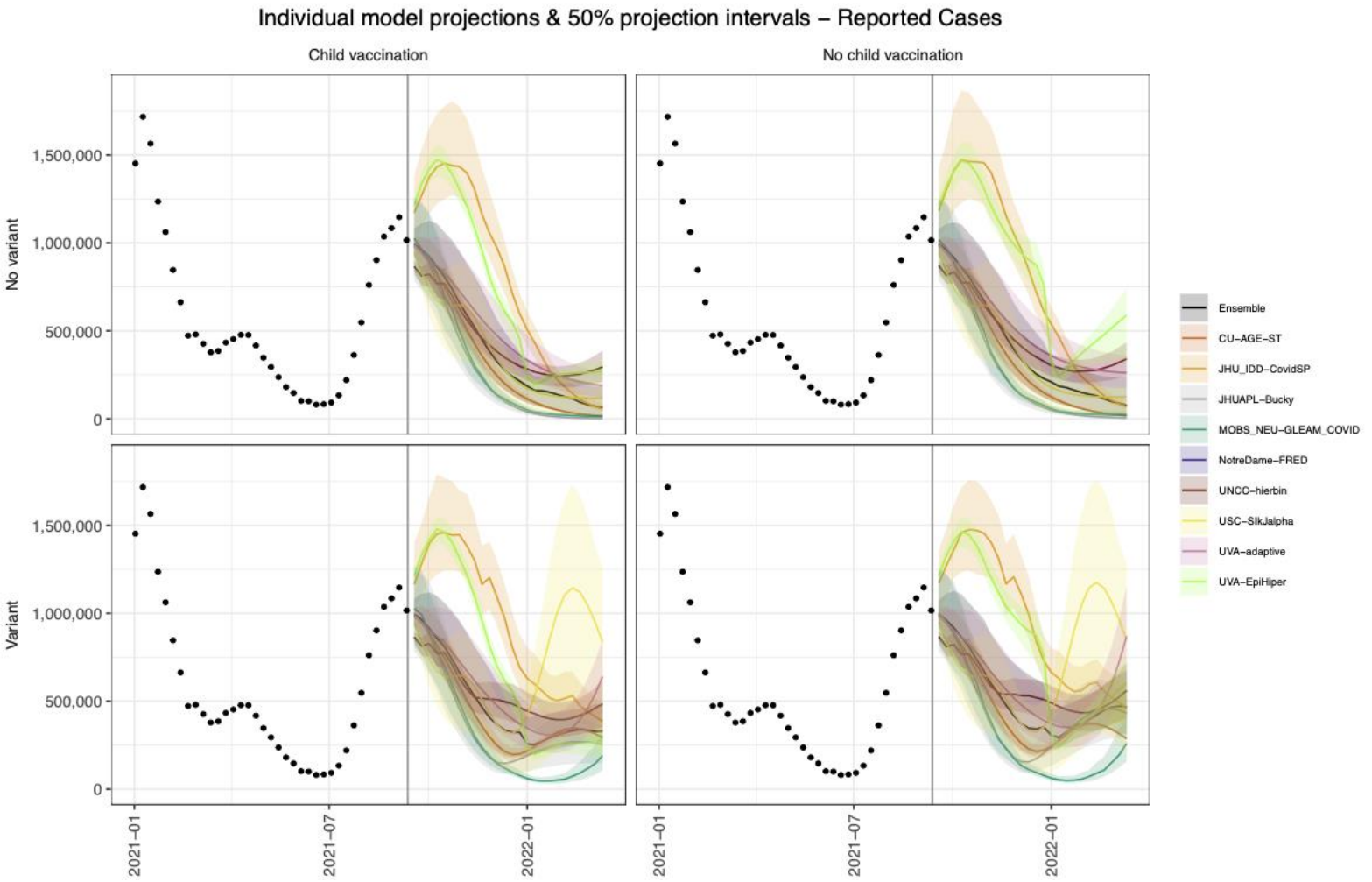
COVID-19 Scenario Modeling Hub

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

Preliminary Analysis of Impact of Waning and 3rd doses

Study to assess impact of waning rate and 3rd dose coverage levels

Waning rate: Duration population remains in an immune state (Vax or Recovered) until becoming susceptible

- Pessimistic: Mean duration 6 months
- Optimistic: Mean duration 1 year

3rd Dose Coverage: Proportion of Fully Vaccinated that receive a 3rd dose and return to full protection

- High: 70% coverage
- Low: 40% coverage

Scenario	Waning Rate	3rd Dose Coverage
A: optWan_highBoo	1 year	70%
B: optWan_lowBoo	1 year	40%
C: pessWan_highBoo	6 months	70%
D: pessWan_lowBoo	6 months	40%

Partial Protection for:

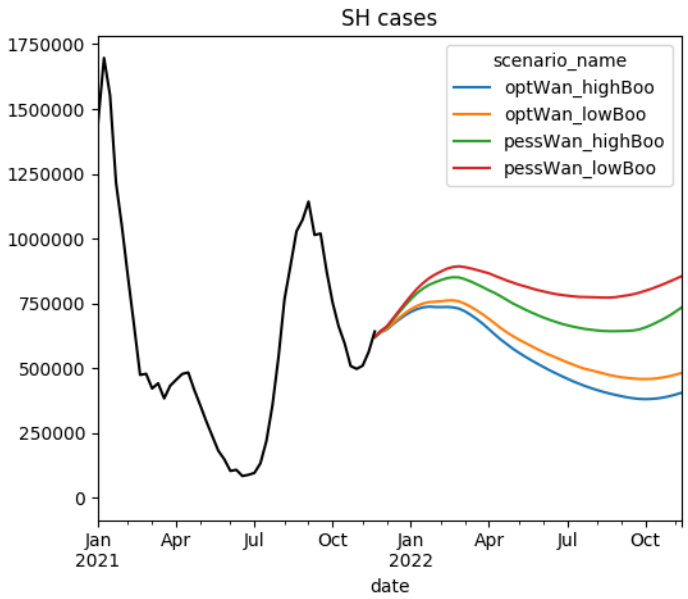
Optimistic Waning

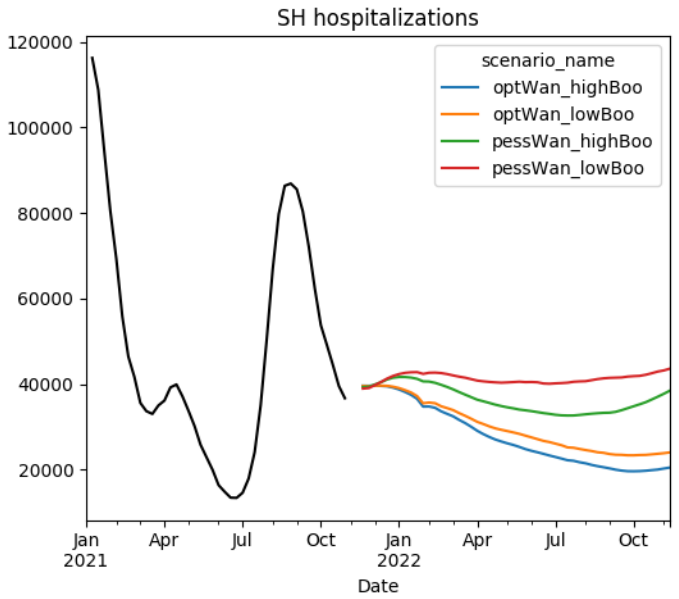
Protection against	Less than 65	65 +
Infection	60%	40%
Hospitalization	90%	80%
Death	95%	90%

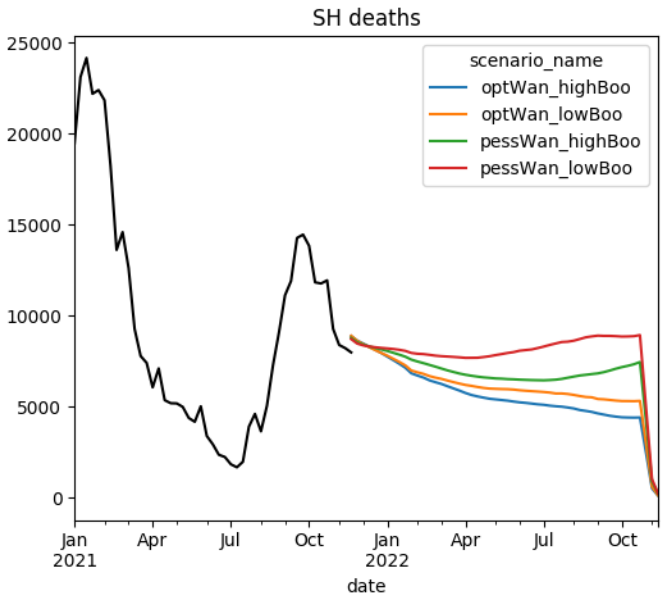
Pessimistic Waning

Protection against	Less than 65	65 +
Infection	50%	30%
Hospitalization	80%	70%
Death	90%	85%

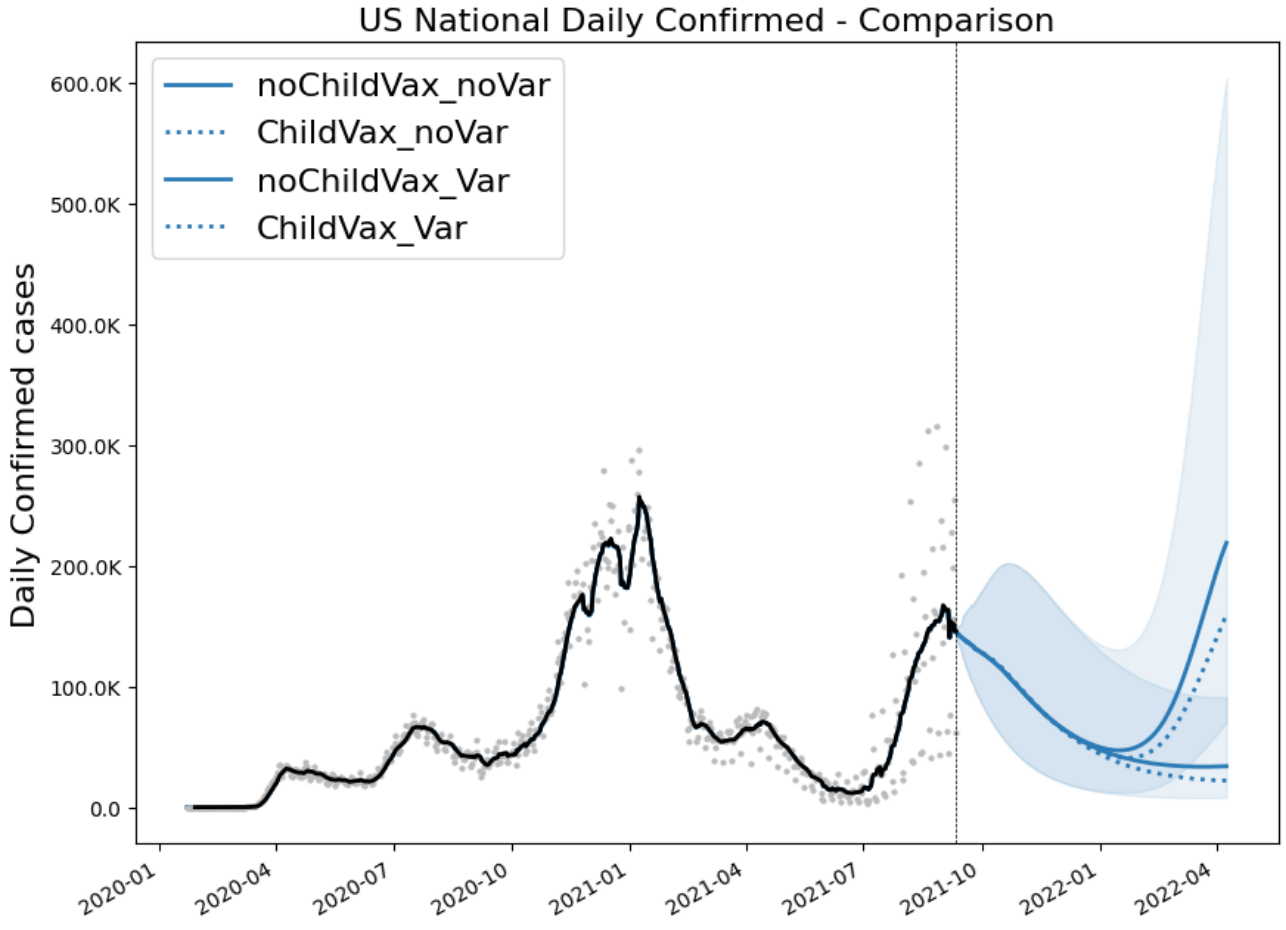
Preliminary Analysis of Impact of Waning and Boosters

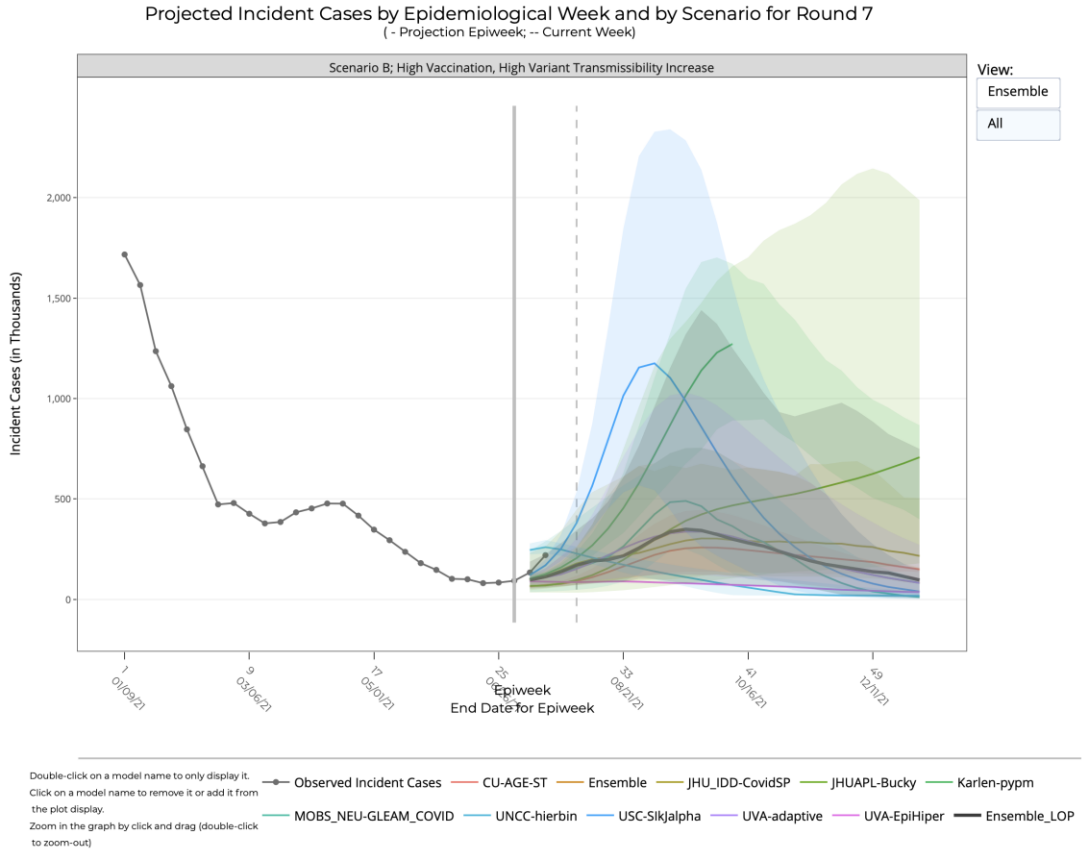






Modeling Hub – Round 9 Prelim Results

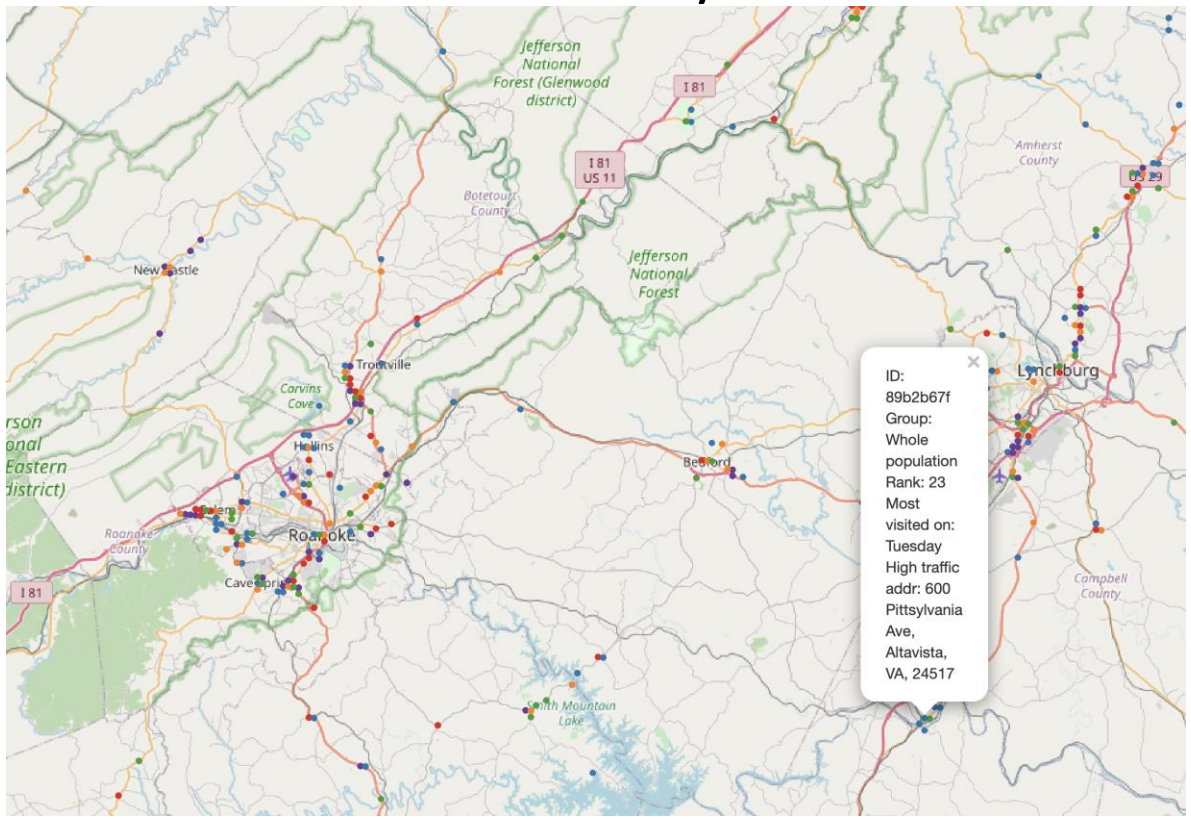




https://covid19scenariomodelinghub.org/viz.html

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

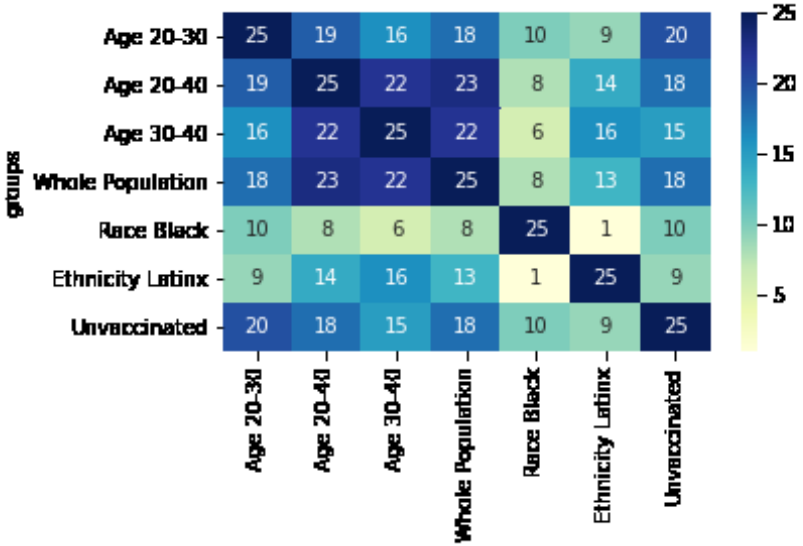
Goal: Provide frequently visited locations based on populations and vaccination levels one desires to reach

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

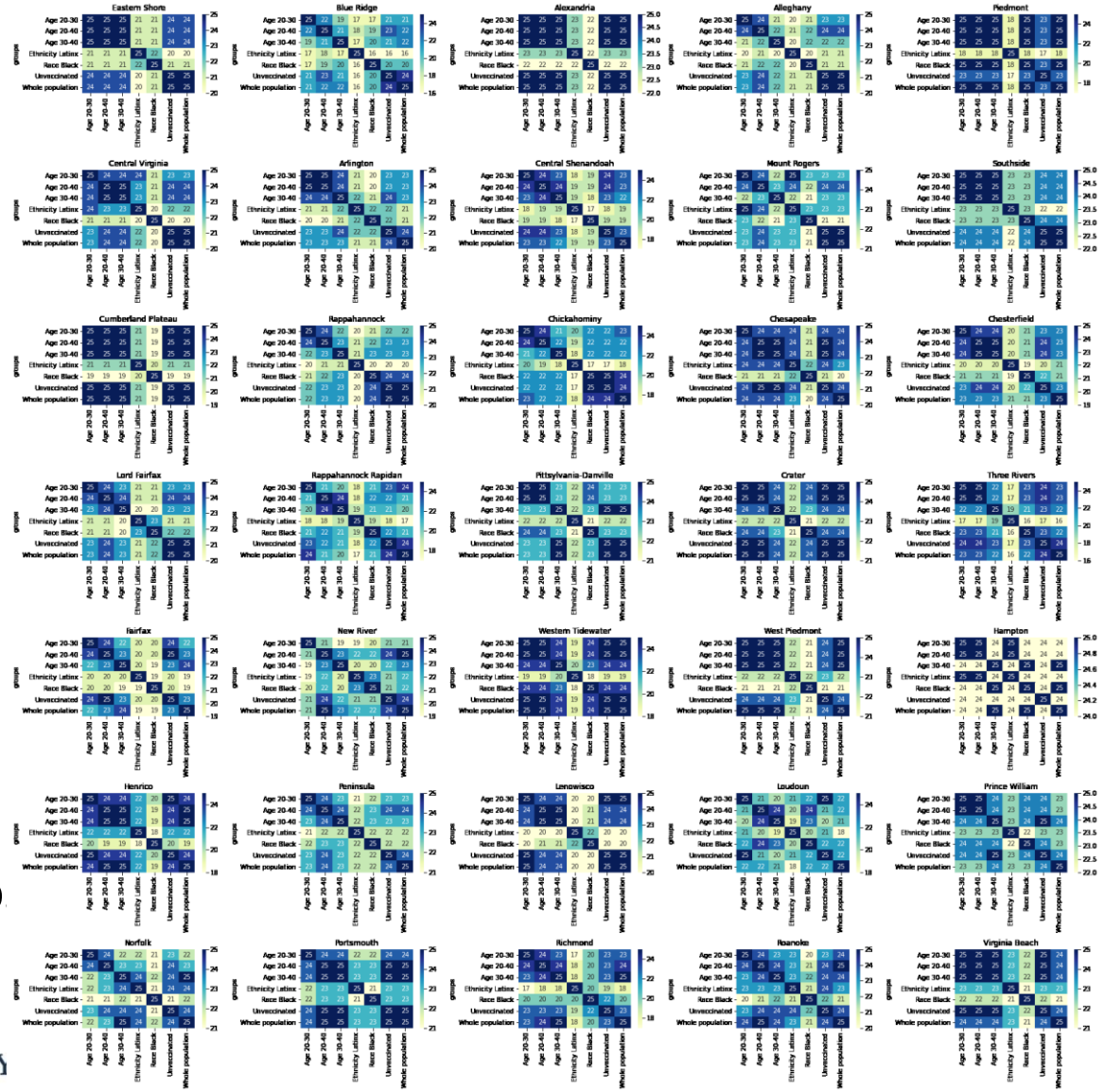
Data Recommended Mobile Vax Clinic Sites

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

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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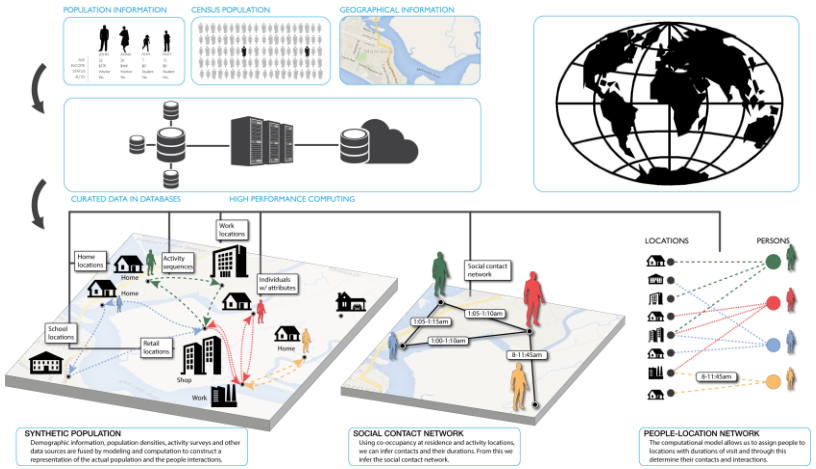
Supplemental Slides

Agent-based Model (ABM)

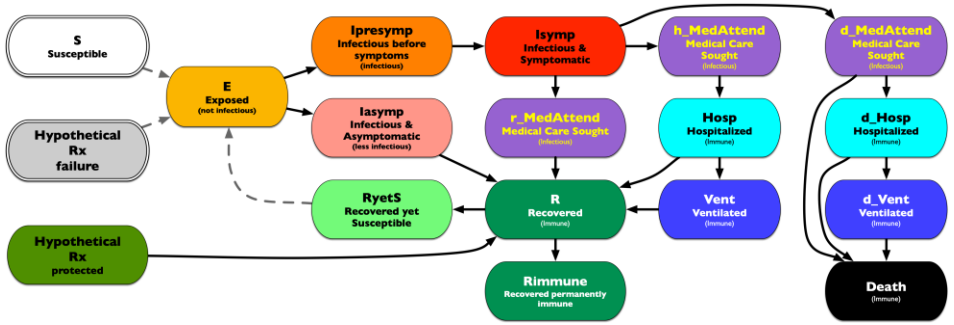
EpiHiper: Distributed network-based stochastic disease transmission simulations

- 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