Network Systems Science & Advanced Computing

Biocomplexity Institute & Initiative

University of Virginia

Estimation of COVID-19 Impact in Virginia

September 14th, 2022

(data current to September 10th – September 12th)

Biocomplexity Institute Technical report: TR BI-2022-1766

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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

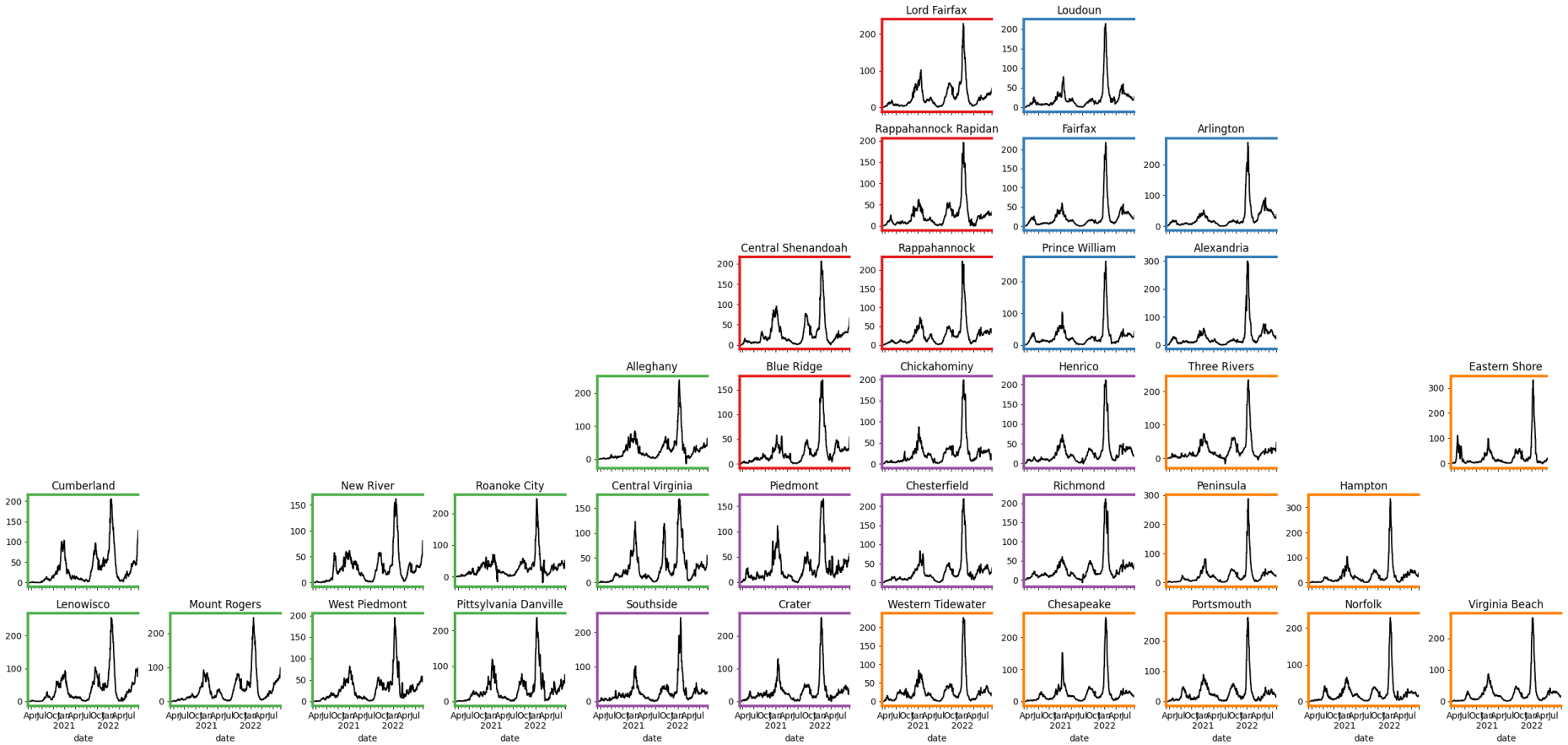
Projecting future cases precisely is impossible and unnecessary.
Even without perfect projections, we can confidently draw conclusions:

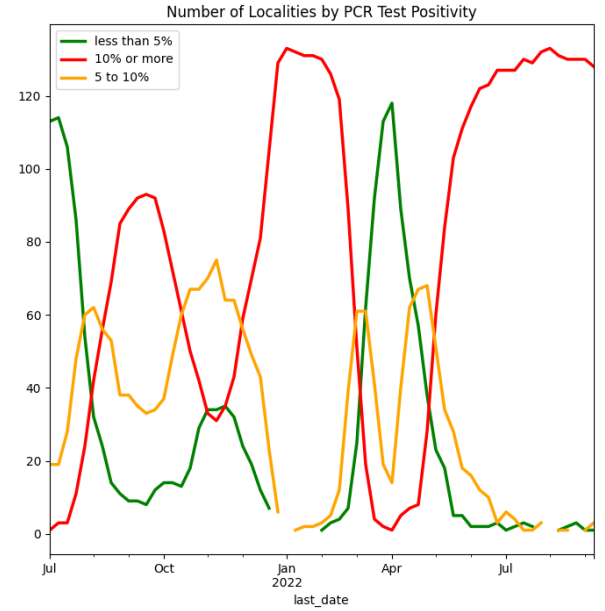
- **Case rates have remained flat as have hospitalizations**
- VA weekly case rate flat at 206 per 100K from 203 per 100K
  - US weekly case rate is down to 174 per 100K from 189 per 100K
  - VA hospital occupancy (rolling 7 day mean of 791 slightly down from 798 a week ago) currently on month plateau
- Sub-variant prevalence evolution as expected
- Projections from last week remain largely on target, though cases are diverging

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

Situation Assessment

Case Rates (per 100k) and Test Positivity





County level RT-PCR test positivity

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

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

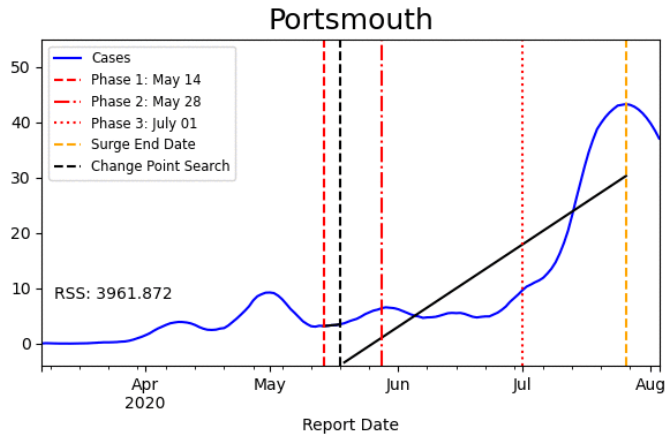
Red: >10.0% (and not "Green" or "Yellow")

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

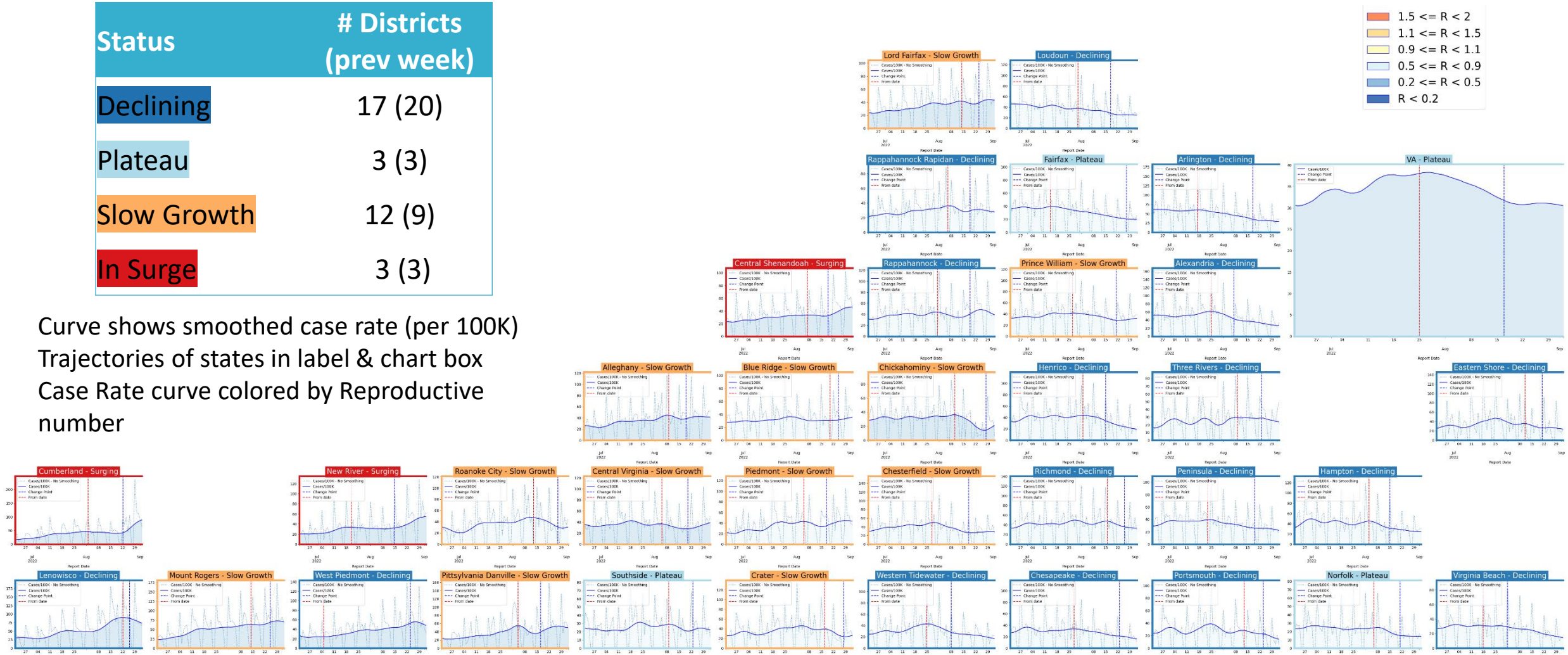


Trajectory	Description	Weekly Case Rate Slope (per 100k)	Weekly Hosp Rate Slope (per 100k)
Declining	Sustained decreases following a recent peak	slope < -0.88/day	slope < -0.07/day
Plateau	Steady level with minimal trend up or down	-0.88/day < slope < 0.42/day	-0.07/day < slope < 0.07/day
Slow Growth	Sustained growth not rapid enough to be considered a Surge	0.42/day < slope < 2.45/day	0.07/day < slope < 0.21/day
In Surge	Currently experiencing sustained rapid and significant growth	2.45/day < slope	0.21/day < slope

District Case Trajectories – last 10 weeks

Status	# Districts (prev week)
Declining	17 (20)
Plateau	3 (3)
Slow Growth	12 (9)
In Surge	3 (3)

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

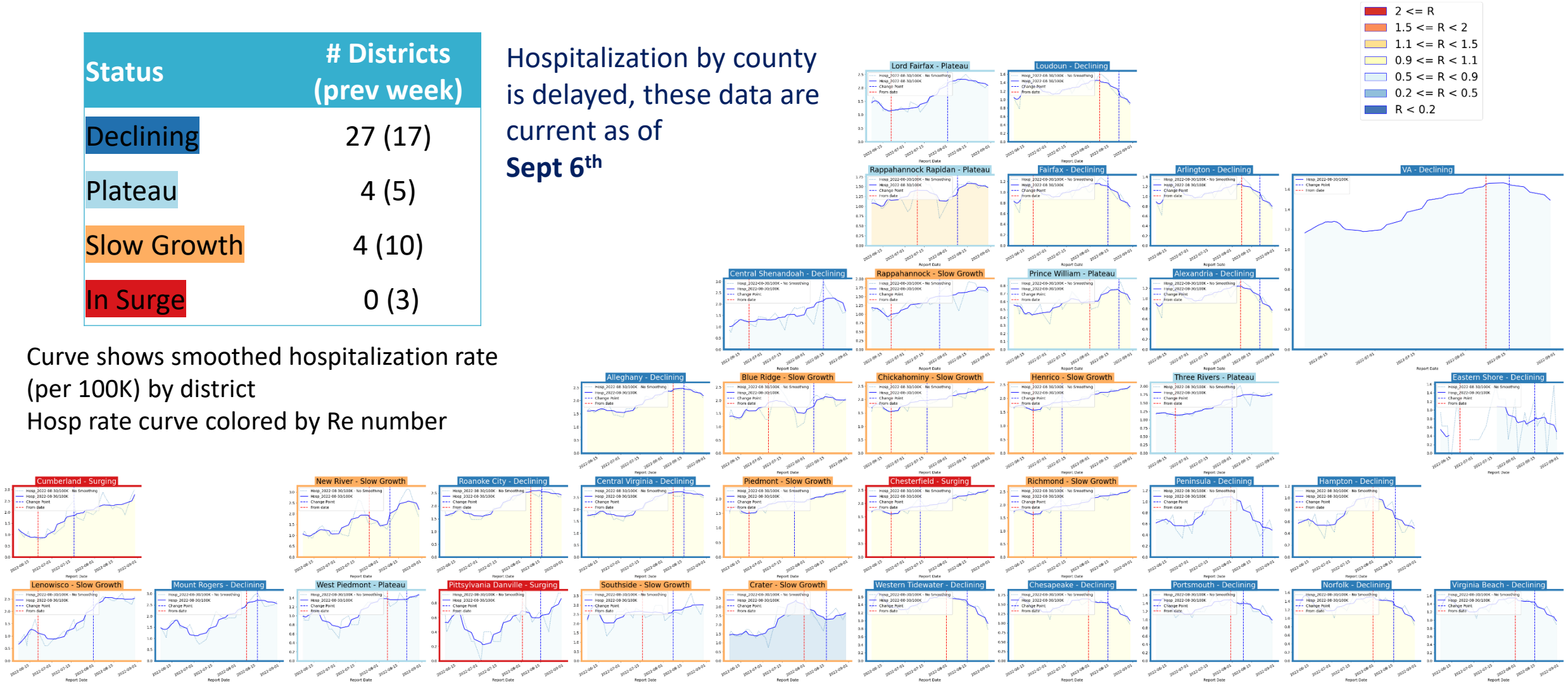


District Hospital Trajectories – last 10 weeks

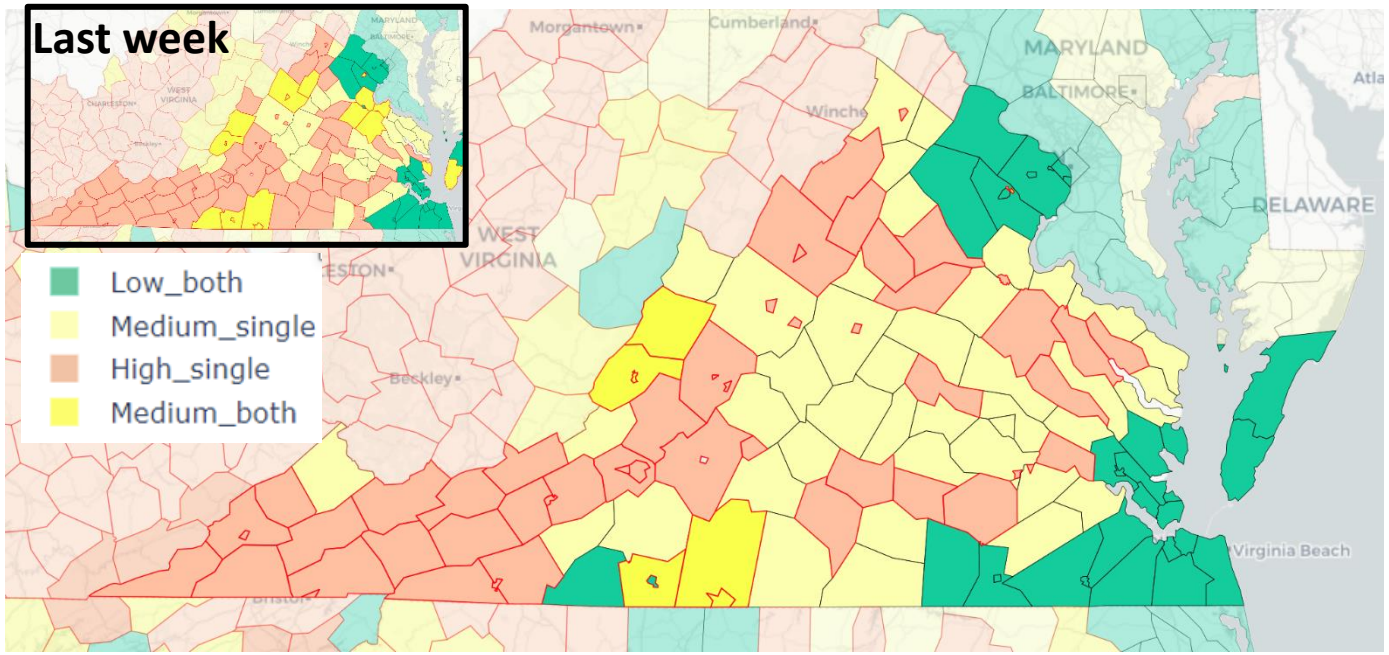
Status	# Districts (prev week)
Declining	27 (17)
Plateau	4 (5)
Slow Growth	4 (10)
In Surge	0 (3)

Hospitalization by county is delayed, these data are current as of **Sept 6th**

Curve shows smoothed hospitalization rate (per 100K) by district
Hosp rate curve colored by Re number



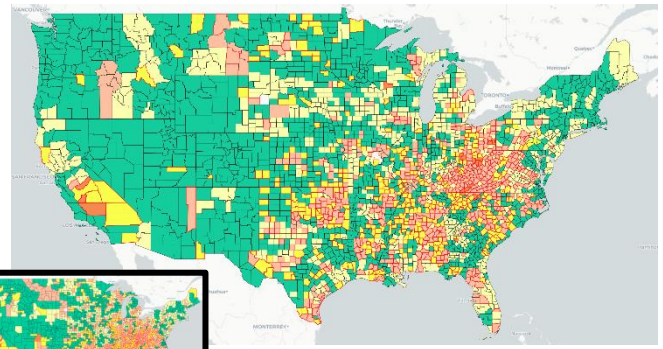
CDC's COVID-19 Community Levels

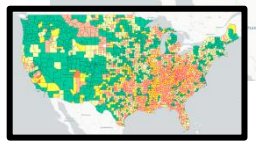


Red outline indicates county had 200 or more cases per 100k in last week

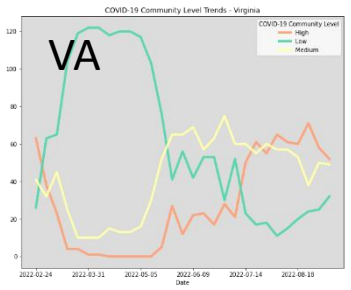
Pale color indicates either beds or occupancy set the level for this county

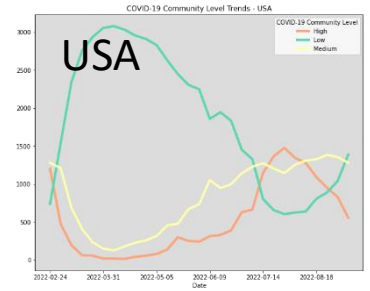
Dark color indicates both beds and occupancy set the level for this county





Last week





COVID-19 Community Levels – Use the Highest Level that Applies to Your Community

New COVID-19 Cases Per 100,000 people in the past 7 days	Indicators	Low	Medium	High
Fewer than 200	New COVID-19 admissions per 100,000 population (7-day total)	<10.0	10.0-19.9	≥20.0
	Percent of staffed inpatient beds occupied by COVID-19 patients (7-day average)	<10.0%	10.0-14.9%	≥15.0%
200 or more	New COVID-19 admissions per 100,000 population (7-day total)	NA	<10.0	≥10.0
	Percent of staffed inpatient beds occupied by COVID-19 patients (7-day average)	NA	<10.0%	≥10.0%

The COVID-19 community level is determined by the higher of the new admissions and inpatient beds metrics, based on the current level of new cases per 100,000 population in the past 7 days

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Data from: CDC Data Tracker Portal

District Trajectories with Community Levels

Community Level (Title Color)
- High
- High-Med
- Med-High
- Medium
- Med-Low
- Low-Med
- Low

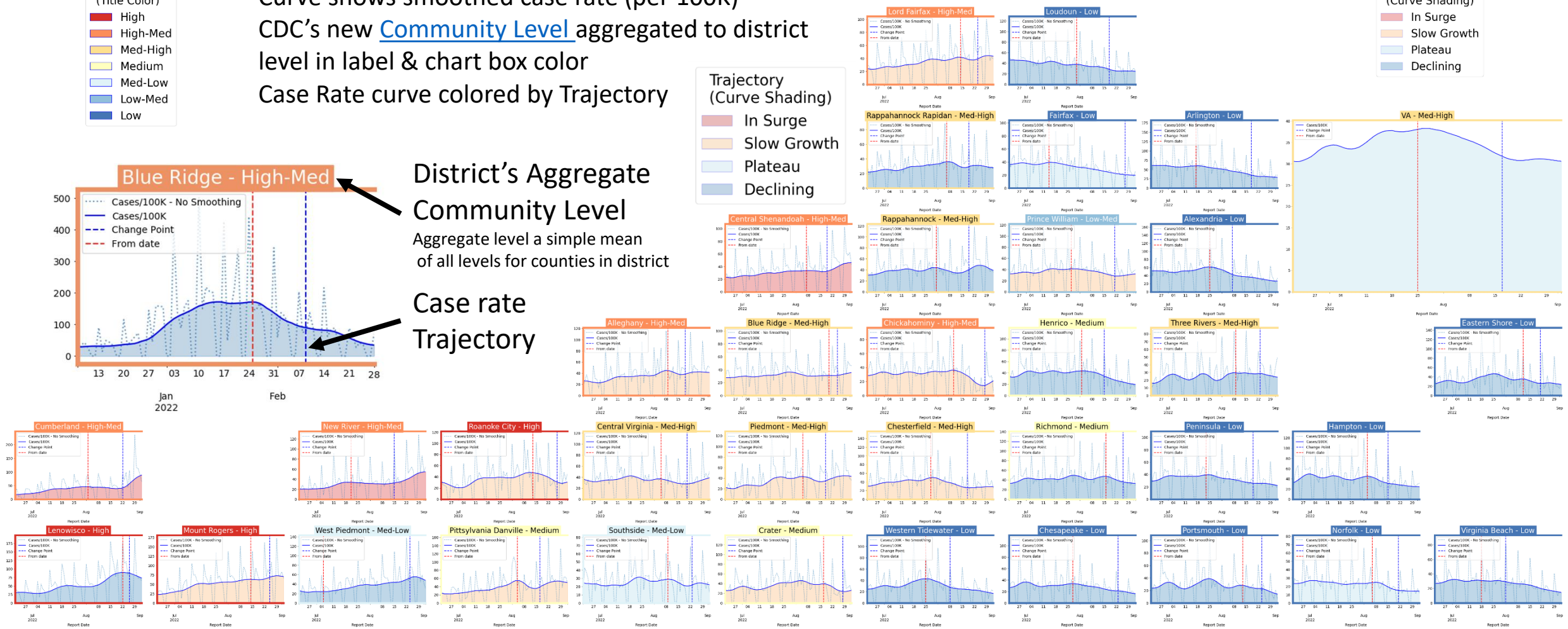
Curve shows smoothed case rate (per 100K)
CDC's new Community Level aggregated to district level in label & chart box color
Case Rate curve colored by Trajectory

Trajectory (Curve Shading)
- In Surge
- Slow Growth
- Plateau
- Declining

District's Aggregate Community Level

Aggregate level a simple mean of all levels for counties in district

Case rate Trajectory



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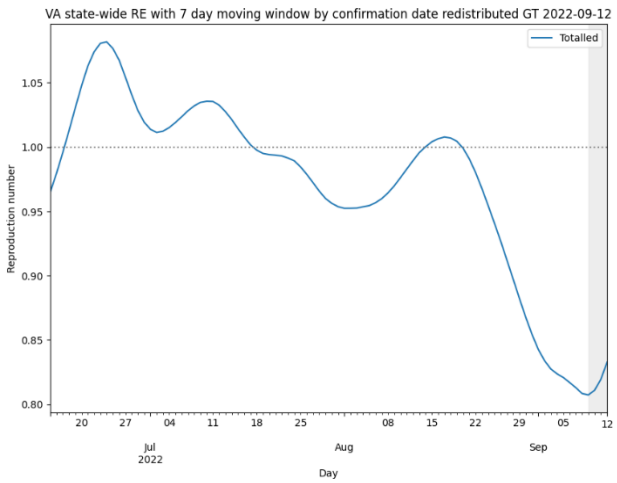
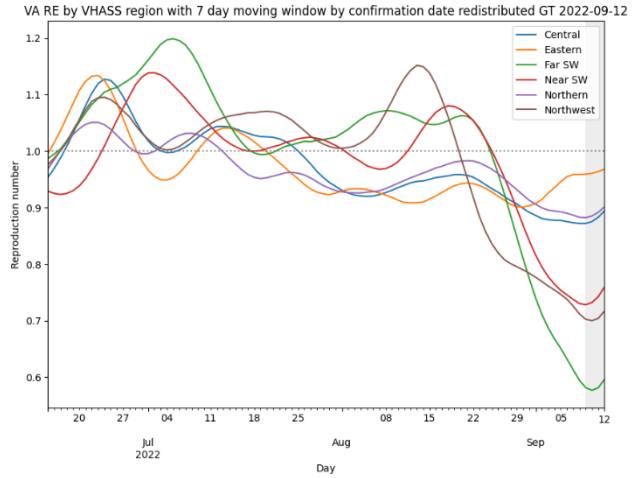
Estimating Daily Reproductive Number –
Redistributed gap

September 12th Estimates

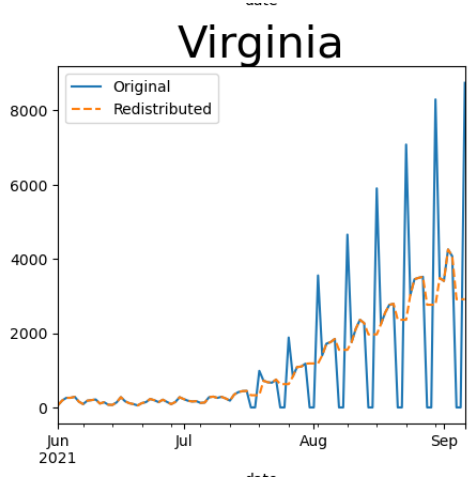
Region	Date Confirmed R_e	Date Confirmed Diff Last Week
State-wide	0.833	-0.048
Central	0.894	-0.014
Eastern	0.968	0.088
Far SW	0.596	-0.205
Near SW	0.759	-0.146
Northern	0.901	-0.011
Northwest	0.717	-0.146





Skipping Weekend Reports & holidays biases estimates

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



Methodology

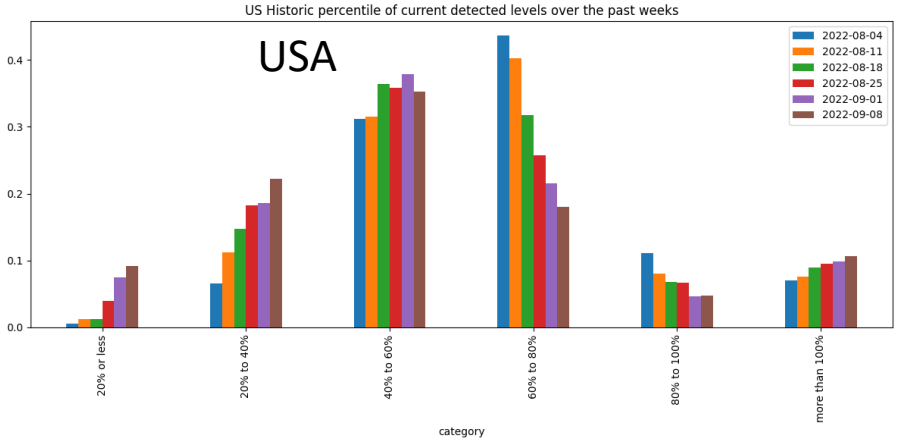
- Wallinga-Teunis method (EpiEstim[1]) for cases by **confirmation date**
- Serial interval: updated to discrete distribution from observations (mean=4.3, Flaxman et al, Nature 2020)
- Using Confirmation date since due to increasingly unstable estimates from onset date due to backfill

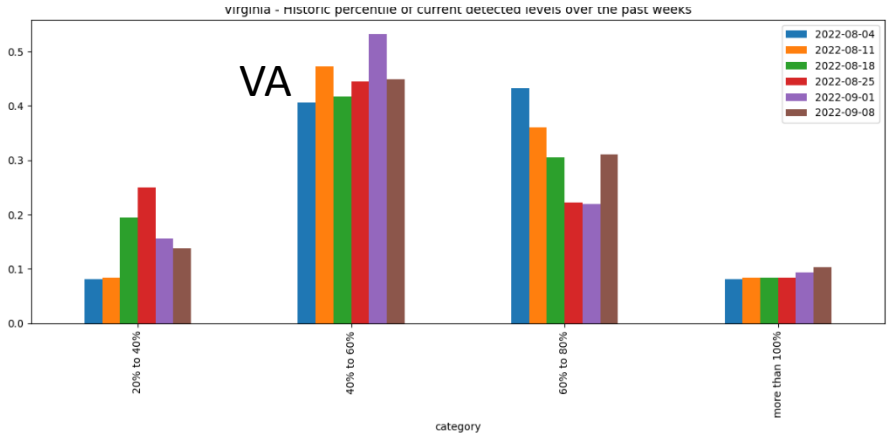
1. Anne Cori, Neil M. Ferguson, Christophe Fraser, Simon Cauchemez. A New Framework and Software to Estimate Time-Varying Reproduction Numbers During Epidemics. American Journal of Epidemiology, Volume 178, Issue 9, 1 November 2013, Pages 1505–1512, https://doi.org/10.1093/aje/kwt133

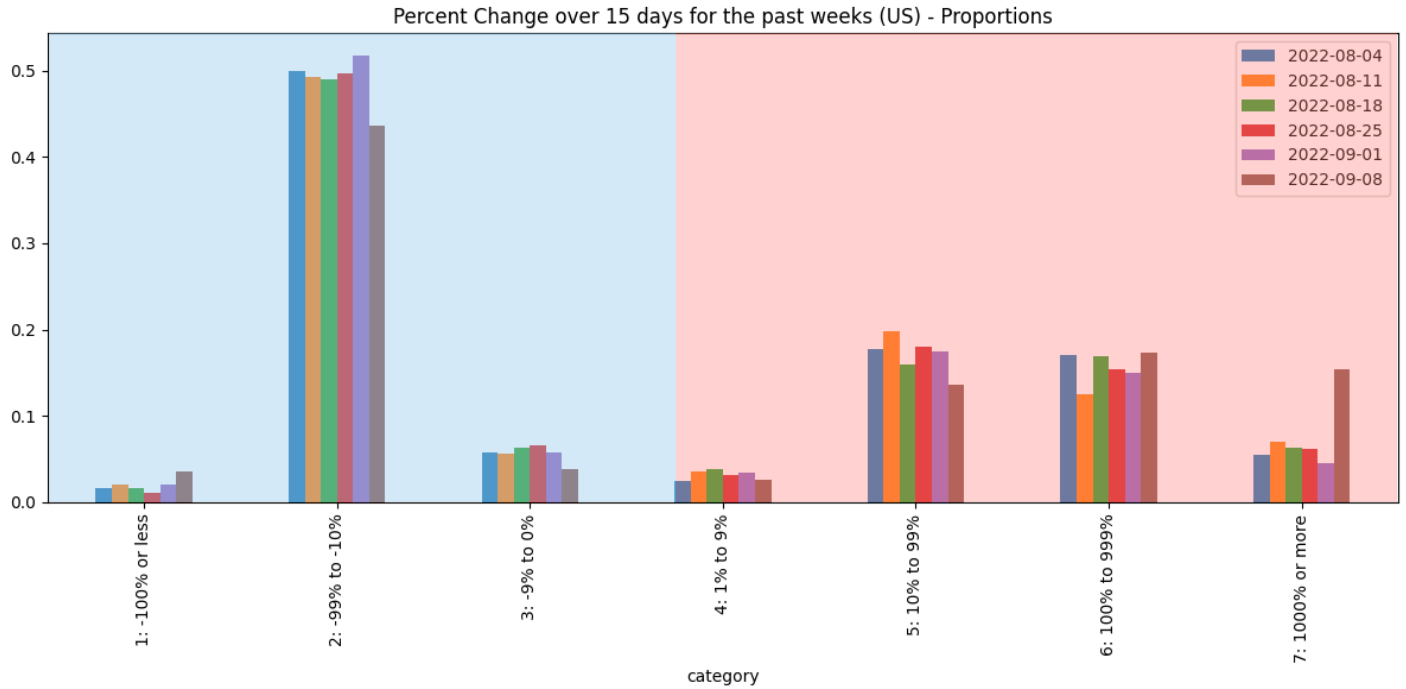
Wastewater Monitoring

Wastewater provides a coarse early warning of COVID-19 levels in communities

- Overall in the US, there is an increase in sites with increased levels of virus compared to 15 days ago
- Current virus levels are at or exceeding max of previous historical levels, has slowed, though more sites are entering upper quintiles







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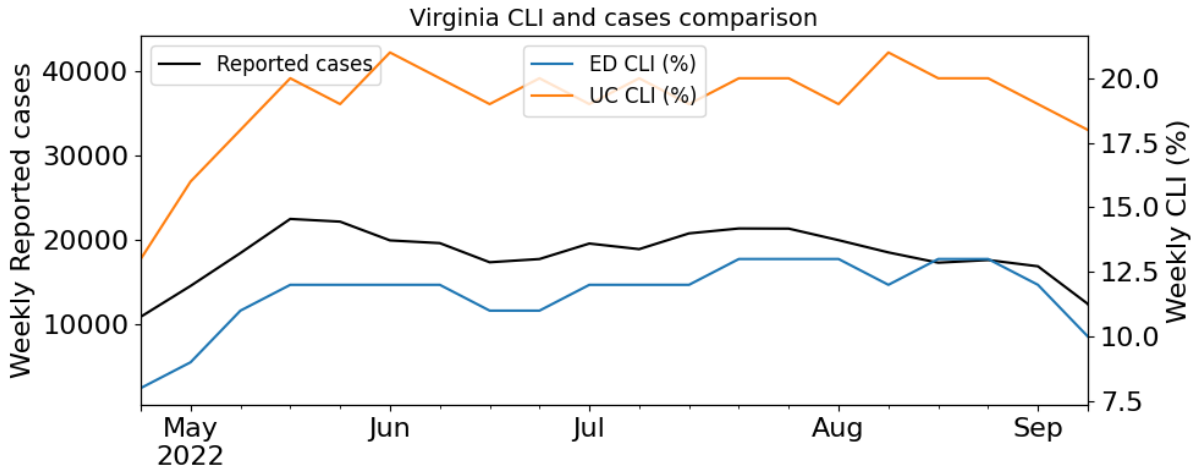
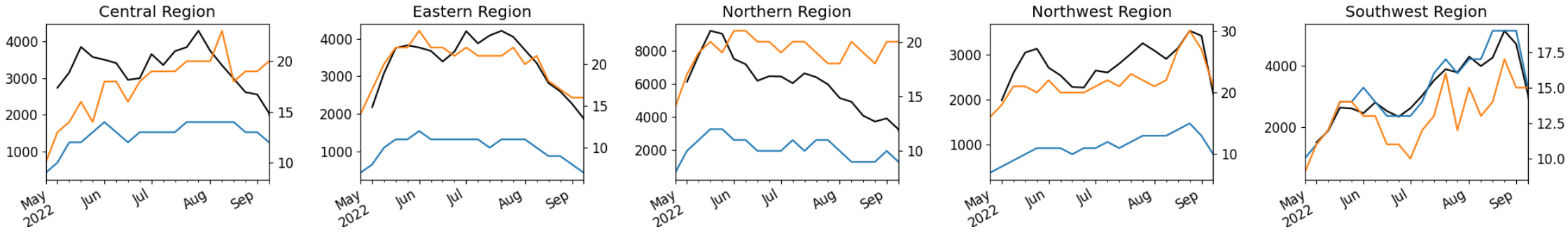
Data Source: CDC Data Tracker

COVID-like Illness Activity

COVID-like Illness (CLI) gives a measure of COVID transmission in the community

- Emergency Dept (ED)-based CLI is more correlated with case reporting
- Urgent Care (UC) is a leading indicator but prone to some false positives
- **Current trends in UC CLI have plateaued since May 2022, mixed by region**



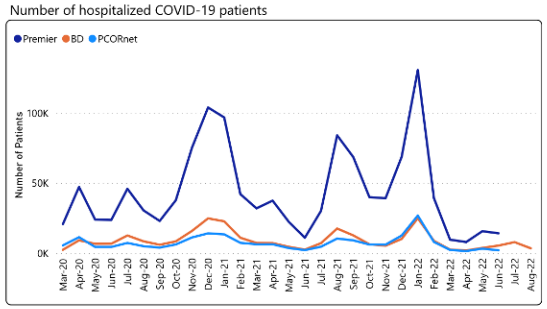


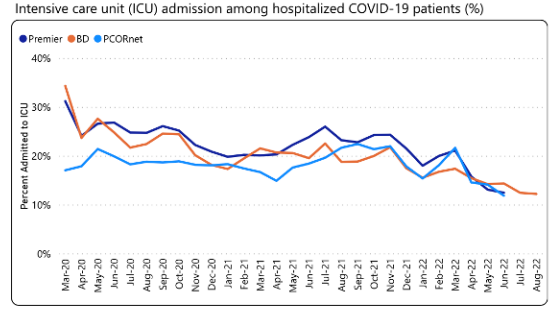
Hospitalizations and Severe Outcomes

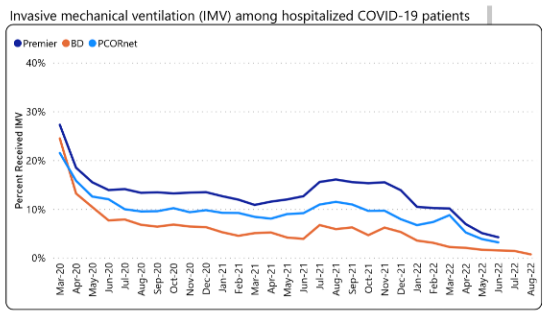
Data Source: [CDC Data Tracker]

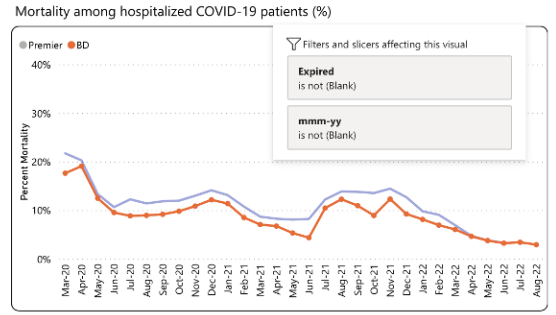
Proportion of most severe outcomes decreasing among those who are hospitalized

- ICU has declined from ~20% of hospitalized to nearly 10% since initial Omicron wave
- Also seen across all age-groups
- Similar levels of decline seen in VA
- Regionally more variation

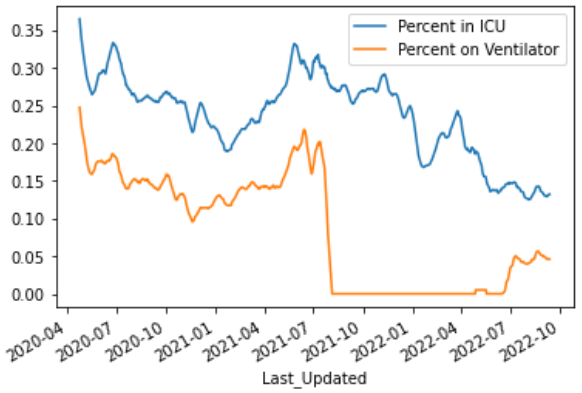




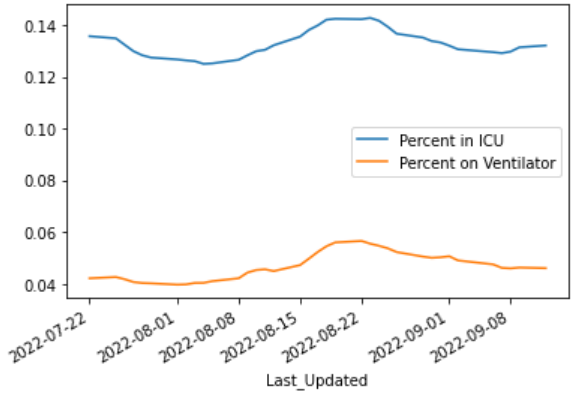




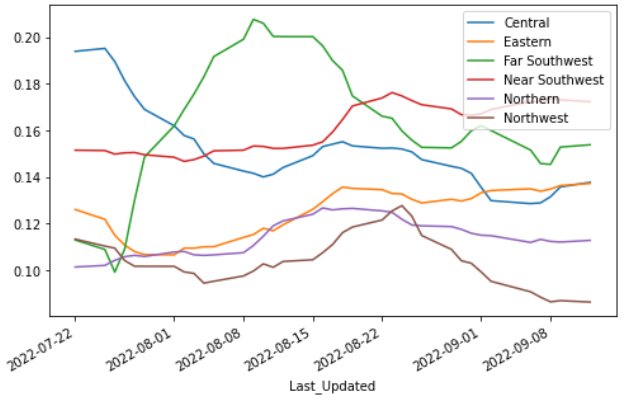
Virginia wide – full pandemic



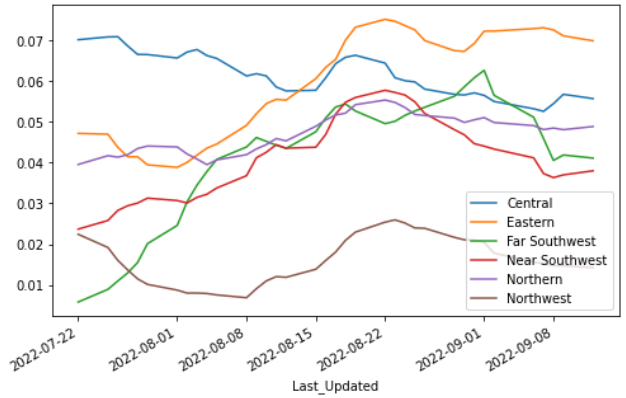
Virginia wide – recent



Virginia Regional ICU percent



Virginia Regional Ventilation %

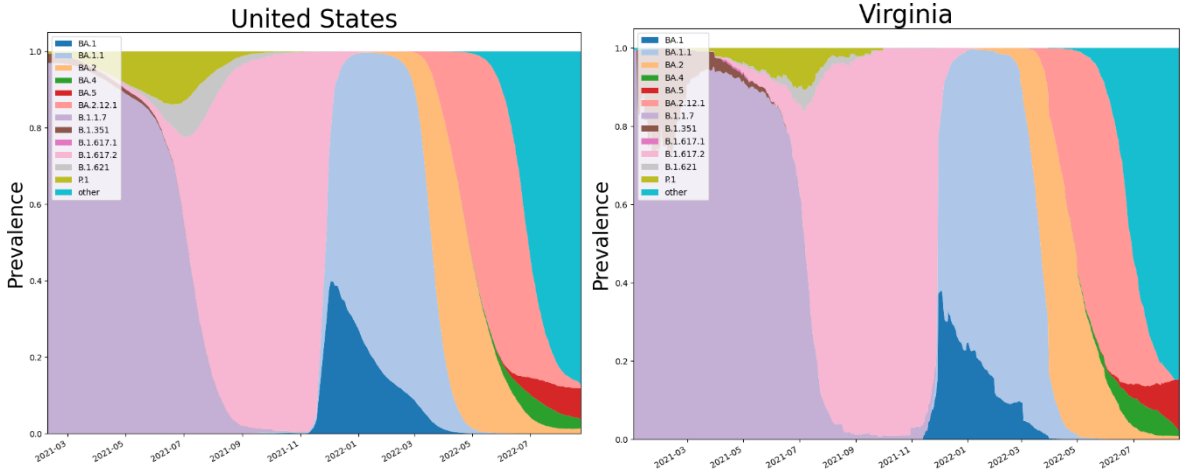


SARS-CoV2 Variants of Concern

GISAID outbreak.info

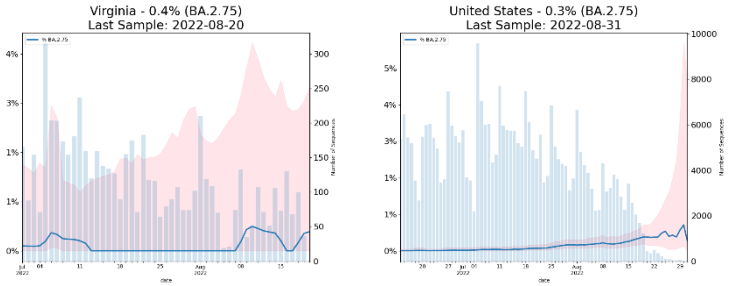
Emerging new variants will alter the future trajectories of pandemic and have implications for future control

- Emerging variants can:
  - Increase transmissibility
  - Increase severity (more hospitalizations and/or deaths)
  - Limit immunity provided by prior infection and vaccinations



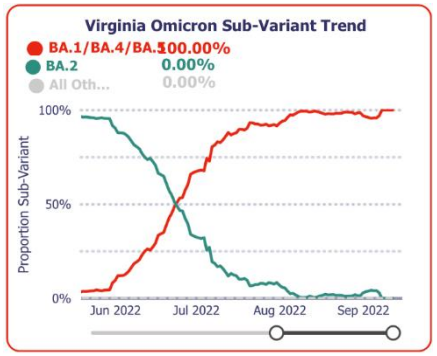
Omicron Updates (Region 3)

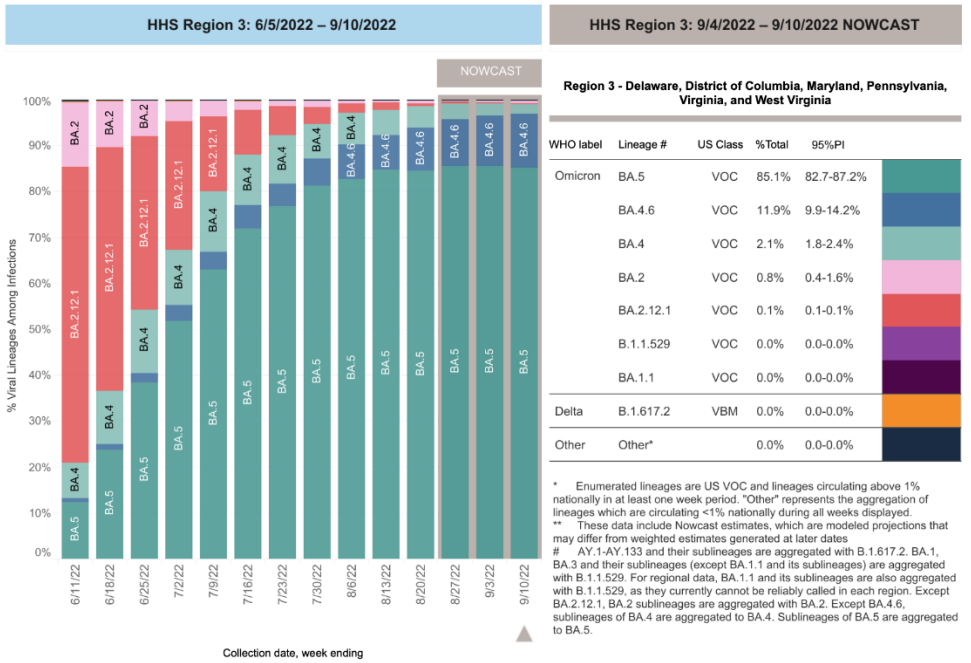
- BA.4 has declined as well, now contributing about 2%, but BA.4.6 remains in very slow growth moving to 12% from 11% last week
- BA.5 has stagnated if not slightly declined, nowcasted at 85% compared to 87% last week



BA.2.75 detected in US (very limited samples)

[Walgreen's SGTF]





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

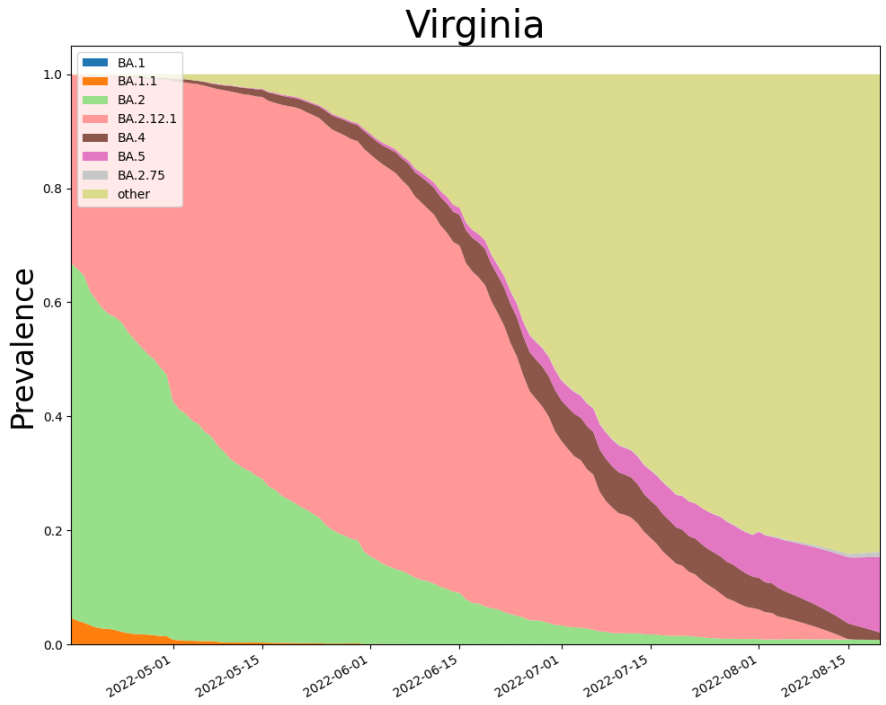
WHO label	Lineage #	US Class	%Total	95%PI
Omicron	BA.5	VOC	85.1%	82.7-87.2%
	BA.4.6	VOC	11.9%	9.9-14.2%
	BA.4	VOC	2.1%	1.8-2.4%
	BA.2	VOC	0.8%	0.4-1.6%
	BA.2.12.1	VOC	0.1%	0.1-0.1%
	B.1.1.529	VOC	0.0%	0.0-0.0%
	BA.1.1	VOC	0.0%	0.0-0.0%
Delta	B.1.617.2	VBM	0.0%	0.0-0.0%
Other	Other*		0.0%	0.0-0.0%

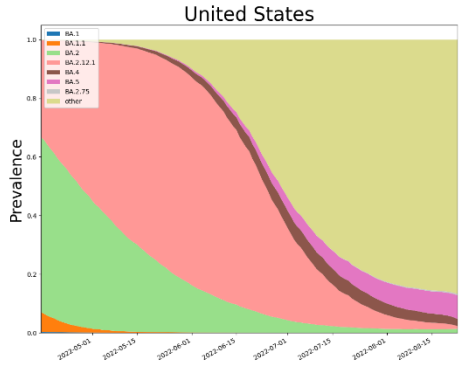
* Enumerated lineages are US VOC and lineages circulating above 1% nationally in at least one week period. "Other" represents the aggregation of lineages which are circulating <1% nationally during all weeks displayed.
** These data include Nowcast estimates, which are modeled projections that may differ from weighted estimates generated at later dates
# AY.1-AY.133 and their sublineages are aggregated with B.1.617.2. BA.1, BA.3 and their sublineages (except BA.1.1 and its sublineages) are aggregated with B.1.1.529. For regional data, BA.1.1 and its sublineages are also aggregated with B.1.1.529, as they currently cannot be reliably called in each region. Except BA.2.12.1, BA.2 sublineages are aggregated with BA.2. Except BA.4.6, sublineages of BA.4 are aggregated to BA.4. Sublineages of BA.5 are aggregated to BA.5.

CDC Variant Tracking

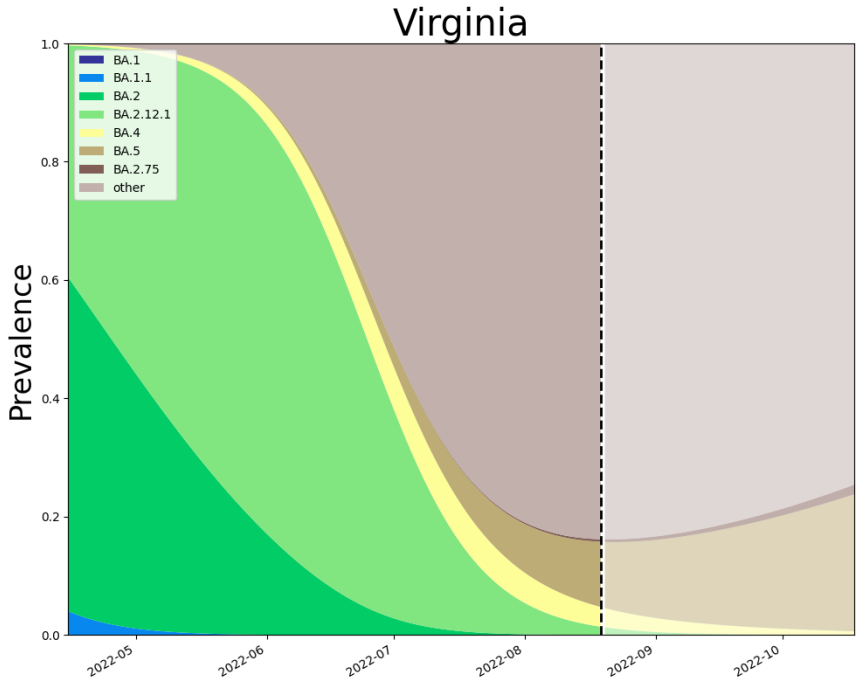
SARS-CoV2 Omicron and Sub-Variants

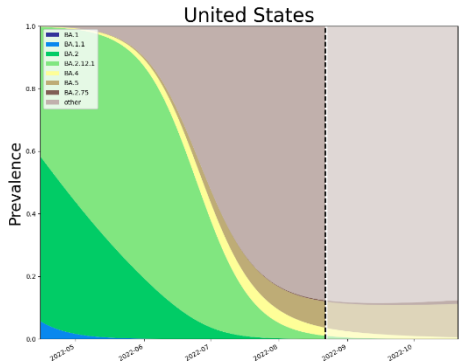
As detected in whole Genomes in public repositories





VoC Polynomial Fit Projections





Note: Data lags force projections to start in past. Everything from dotted line forward is a projection.

GISAID outbreak.info

Pandemic Pubs

1. Nasal immune response to Omicron enhanced but not completely restored to ancestral levels when boosted using single strain booster.
2. Hamsters: intranasal boost elicited high-magnitude serum neutralizing antibody responses and IgA responses in the upper respiratory tract. Protected against virus in the lower airways and against onward SARS-CoV-2 transmission.
3.Impaired diffusion from air to red blood cells in 39% patients (6 months after infection) and 31% (12 months).
4. Estimated 10 million children orphanaged due to primary and secondary caregiver deaths from covid worldwide

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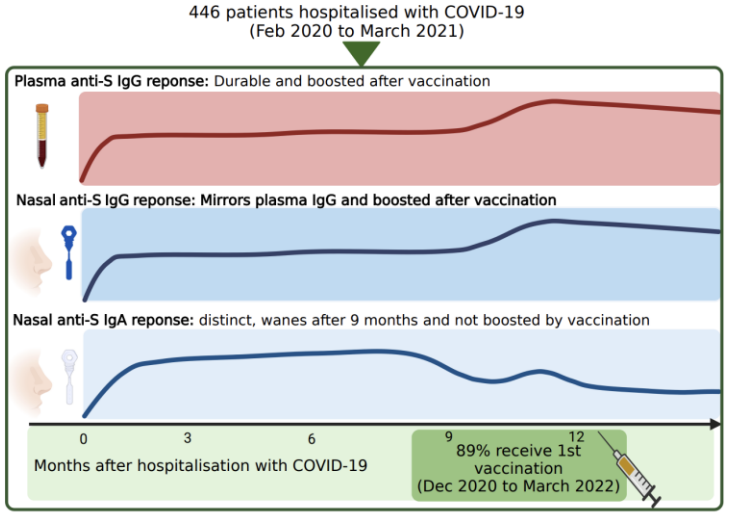

Plasma and nasosorption samples were prospectively collected from 446 adults hospitalised for COVID-19 between February 2020 and March 2021. IgA and IgG responses to NP and S of ancestral SARS-CoV-2, Delta and Omicron (BA.1) variants were measured by electrochemiluminescence and compared with plasma neutralisation data. **Nasal antibody induced by infection with pre-Omicron variants, bind Omicron virus in vitro better than plasma antibody. Although nasal and plasma IgG responses were enhanced by vaccination, Omicron binding responses did not reach levels equivalent to responses for ancestral SARS-CoV-2.** Results show that nasal IgA declines and has a minimal response to vaccination while plasma antibody responses to S antigen are well maintained and boosted by vaccination. Authors highlight the need to develop vaccines that enhance nasal immunity
https://www.medrxiv.org/content/10.1101/2022.09.09.22279759v1

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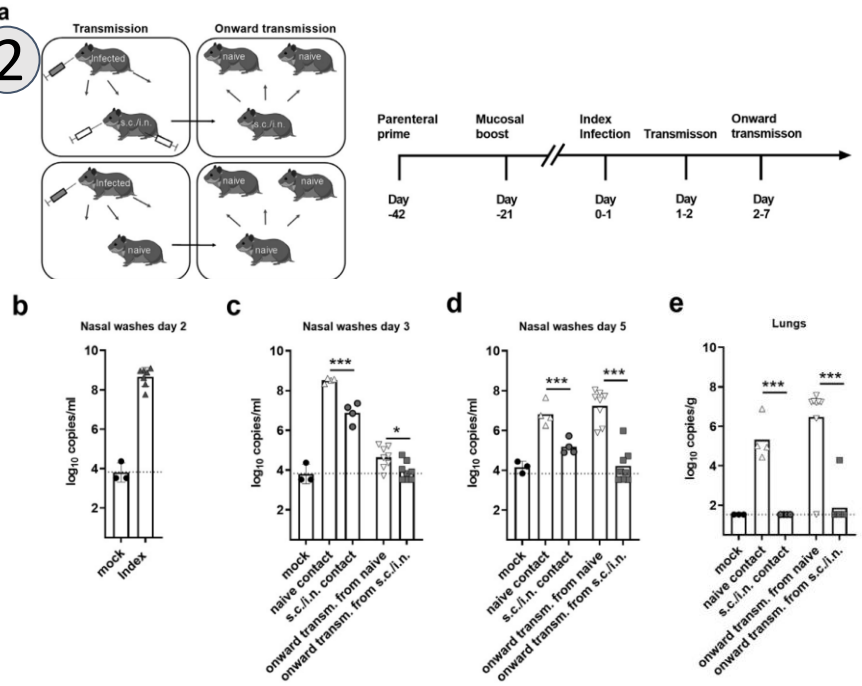

Center for Vaccine Research, Denmark: Study suggests mucosal booster strategy using protein-based subunit vaccines may be an effective means to protect against transmission of SARS-CoV-2 and potentially other respiratory viruses despite incomplete clearance of virus from the upper respiratory tract.
https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964(22)00430-3/fulltext

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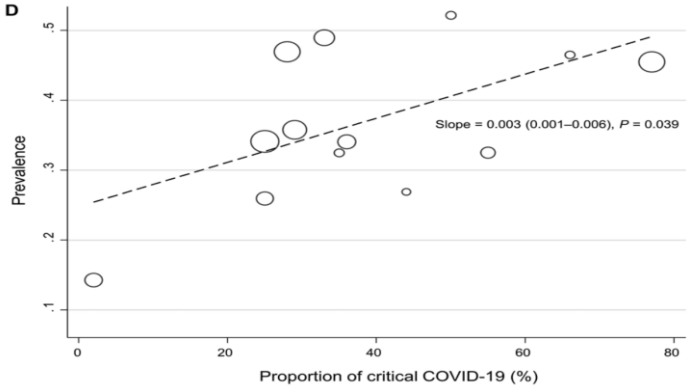

Systematic review and meta-analysis using a random-effects model to estimate the pooled prevalence of the pulmonary sequelae of COVID-19, as demonstrated by pulmonary function testing (PFT) and chest computed tomography (CT) performed at least 6 months after initial infection. A substantial number of COVID-19 survivors displayed pulmonary sequelae as part of PACS. Except for restrictive pulmonary dysfunction, the prevalence of these sequelae did not decrease until 1 year after initial infection. Of the 18,062 studies identified, 30 met eligibility criteria. Among these studies, 25 and 22 had follow-up PFT and chest CT data, respectively. **The follow-up durations were approximately 6 and 12 months in 18 and 12 studies, respectively. Impaired diffusion capacity was the most common abnormality on PFT (pooled prevalence 35%, 95% confidence interval [CI] 30–41%) with a prevalence of 39% (95% CI 34–45%) and 31% (95% CI 21–40%) in the 6-month and 12-month follow-up studies, respectively (P = 0.115)**
https://respiratory-research.biomedcentral.com/articles/10.1186/s12931-022-02163-x

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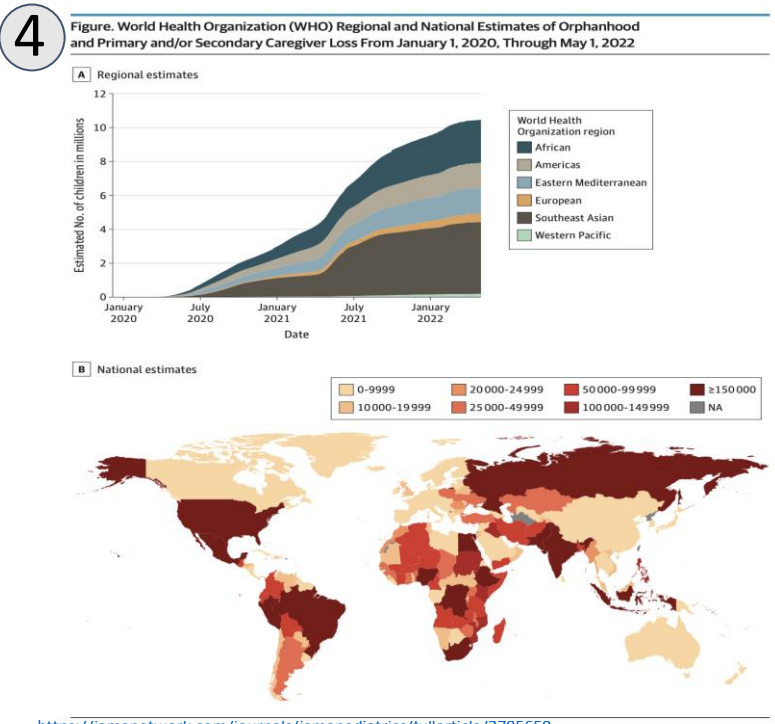

https://jamanetwork.com/journals/jamapediatrics/fullarticle/2795650

Pandemic Pubs (last week)

1. NIAID research indicates B-cell responses to booster vaccines may be impeded by recent infection
2. Data released by the CDC suggest a 4.2- and 4.5-fold neutralization increase from the BA.1 containing and BA.5 containing bivalent vaccines respectively
3. Further evidence of the protection conferred by vaccination against severe disease with BA.4 and BA.5
4. Survey of a population-representative sample of 3,042 U.S adults between June 30 and July 2, 2022, during the Omicron BA.5 surge, estimated 21.5% (95% CI 18.2, 24.7) of respondents with a SARS-CoV-2 infection more than 4 weeks prior reported long COVID symptoms

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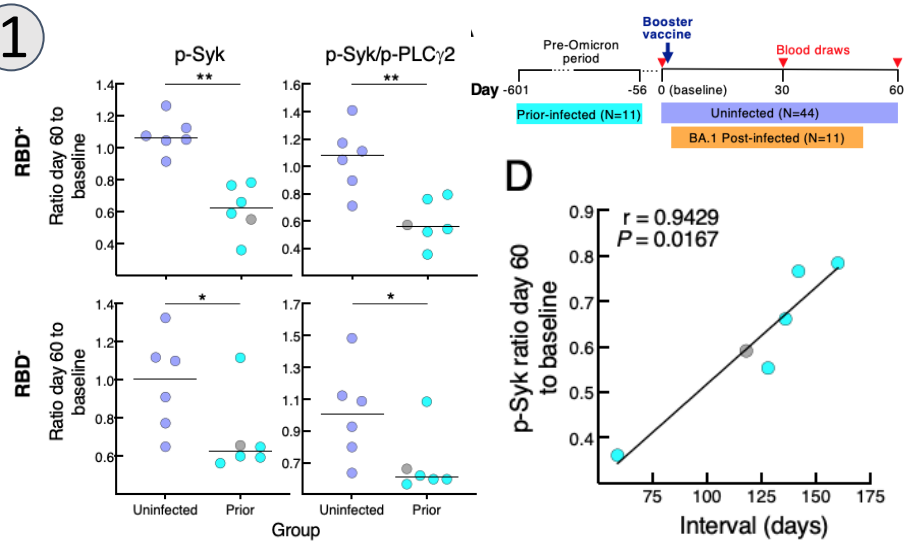

Researchers present evidence that the interval between prior infection and booster vaccination is a critical determinant of the immune response to the booster vaccine and that B cells of individuals who were recently infected are unresponsive to the booster vaccine. The findings identify timing relative to infection as a key factor in immune boosting. B-cell response to the booster vaccine was poor in magnitude and breadth in the prior-infected group while robust in the uninfected and post-infected groups, with the latter having an additional boost from the breakthrough infection. 66 adults scheduled to receive a third dose (booster) of either BNT162b2 or mRNA-1273 vaccine was recruited to donate blood at baseline (day 0) and days 30 and 60 post-vaccination. At day 60, participants were stratified into three groups based on exposure to SARS-CoV-2: uninfected (N=44) by nucleocapsid antibody serology, prior-infected (N=11) or post-infected (N=11) depending on whether exposure occurred prior to or after booster vaccination, respectively
https://www.medrxiv.org/content/10.1101/2022.08.30.22279344v1

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Table 3. Prevalence and characteristics of U.S. adults with long COVID, July 2022

	Had COVID more than one month ago	Long COVID	Crude Prevalence of Long COVID	Age and sex direct-standardized prevalence of long COVID*	Crude prevalence ratio (PR)	Adjusted prevalence ratio (aPR)**
	N (%)	N (%)	% (95% CI)	% (95% CI)	PR (95% CI)	aPR (95% CI)
Total	1036 (100.0)	222 (100.0)	21.5 (18.2, 24.7)			
Age						
18-24	70 (6.8)	17 (7.8)	24.8 (7.5, 42.0)	18.6 (8.8, 35.2)	1.1 (0.7, 1.7)	1.2 (0.7, 1.9)
25-34	250 (24.2)	58 (26.1)	23.2 (15.2, 31.2)	22.3 (15.2, 31.5)	Ref	Ref
35-44	178 (17.2)	43 (19.1)	23.9 (15.5, 32.3)	27.6 (19.3, 37.8)	1.0 (0.7, 1.5)	1.2 (0.9, 1.8)
45-54	171 (16.5)	37 (16.5)	21.6 (13.9, 29.3)	22.3 (15.6, 30.9)	0.9 (0.7, 1.3)	1.1 (0.7, 1.5)
55-64	185 (17.9)	41 (18.2)	21.9 (15.5, 28.3)	23.1 (17.2, 30.3)	0.9 (0.7, 1.4)	1.1 (0.8, 1.5)
65+	182 (17.6)	27 (12.2)	14.9 (10.5, 19.2)	14.8 (10.8, 19.9)	0.6 (0.4, 1.0)	0.7 (0.5, 1.1)
Gender						
Male	465 (44.9)	72 (32.4)	15.5 (11.6, 19.4)	15.5 (11.9, 20.2)	Ref	Ref
Female	528 (51.0)	144 (64.8)	27.3 (22.2, 32.4)	27.4 (22.8, 32.6)	1.8 (1.4, 2.3)	1.8 (1.4, 2.3)
Non-binary	43 (4.2)	6 (2.8)	14.2 (0.0, 31.8)	13.3 (4.8, 32.1)	0.9 (0.4, 1.9)	0.9 (0.4, 1.9)

NY researchers found that SARS-CoV-2 prevalence was higher among those 18-24 years old (aPR 2.2, 95% CI 1.8, 2.7) and among non-Hispanic Black (aPR 1.7, 95% CI 1.4 ,2.2) and Hispanic (aPR 2.4, 95% CI 2.0 , 2.9). SARS-CoV-2 prevalence was also higher among those with lower income (aPR 1.9, 95% CI 1.5, 2.3), lower education (aPR 3.7 95% CI 3.0,4.7), and those with comorbidities (aPR 1.6, 95% CI 1.4, 2.0).
https://www.medrxiv.org/content/10.1101/2022.09.04.22279588v1.article-info

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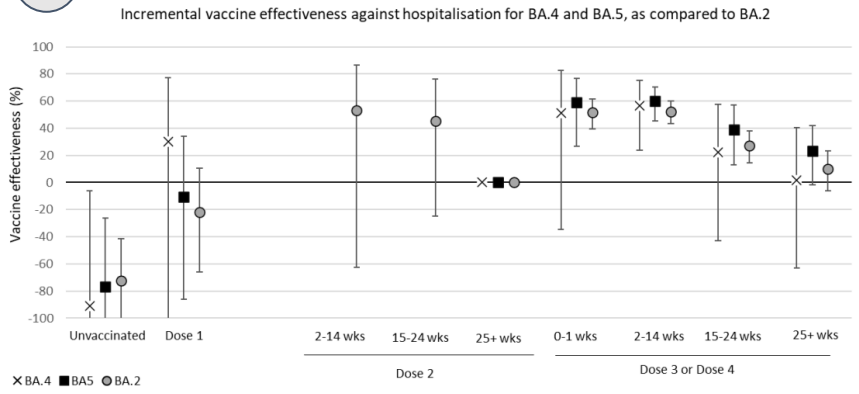

UKHSA study used a whole population test-negative case-control study design to estimate the effectiveness of the vaccines currently in use as part of the UK COVID-19 vaccination programme against hospitalisation following infection with BA.4 and BA.5 as compared to BA.2 during a period of co-circulation. 32,845 eligible tests from hospitalised individuals. Of these, 25,862 were negative (controls), 3,432 were BA.2, 273 were BA.4, 947 were BA.5 and 2,331 were either BA.4 or BA.5 cases. The incremental VE was 56.8% (95% C.I.; 24.0-75.4%), 59.9% (95% C.I.; 45.6-70.5%) and 52.4% (95% C.I.;43.2-60.1%) for BA.4, BA.5 and BA.2, respectively, at 2 to 14 weeks after a third or fourth dose. VE was estimated in those who had recently received a booster vaccine relative to those with waned immunity who had received their second dose 25 or more weeks ago therefore appear lower than absolute VE estimates and should not be directly compared to VE estimates which are relative to unvaccinated individuals.
https://www.medrxiv.org/content/10.1101/2022.08.31.22279444v1

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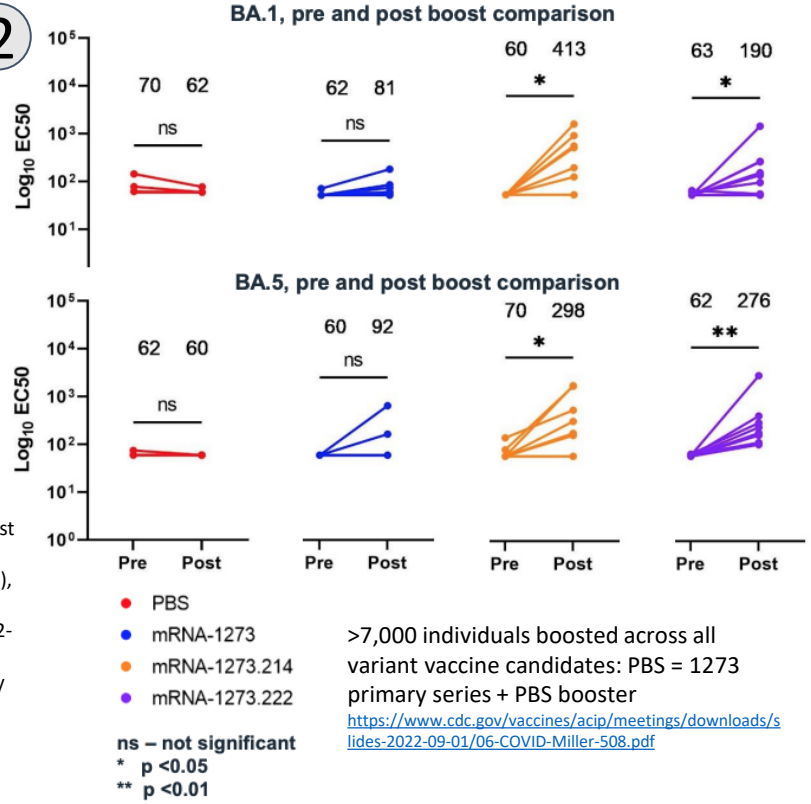
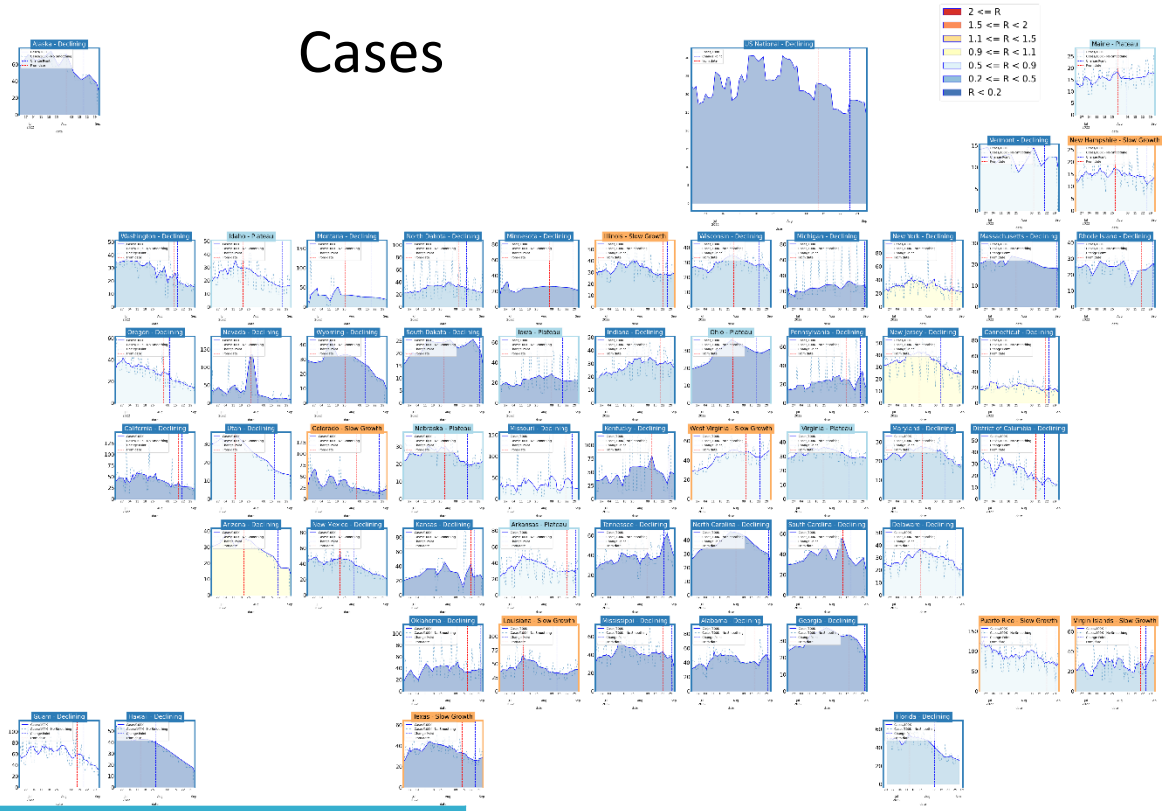
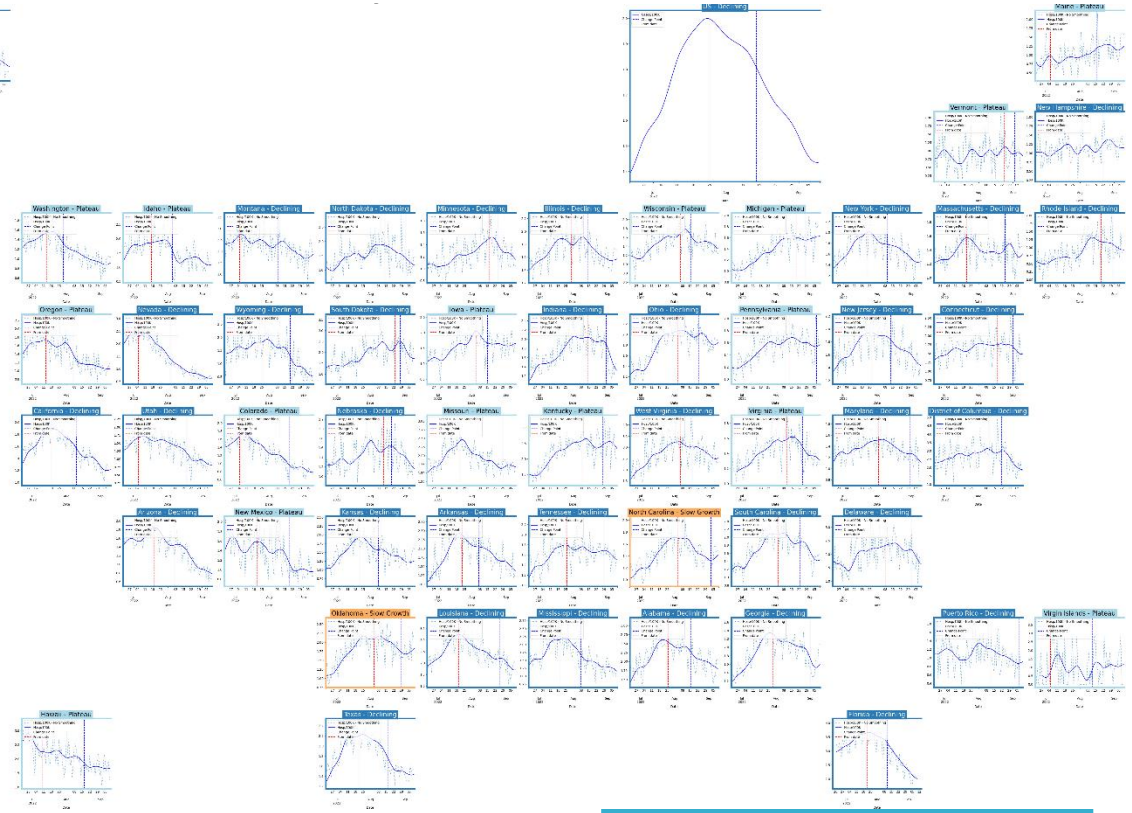


>7,000 individuals boosted across all variant vaccine candidates: PBS = 1273 primary series + PBS booster
https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2022-09-01/06-COVID-Miller-508.pdf

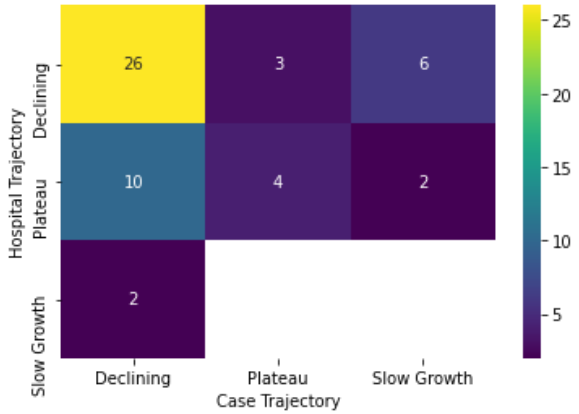
United States Case & Hospitalizations

Cases





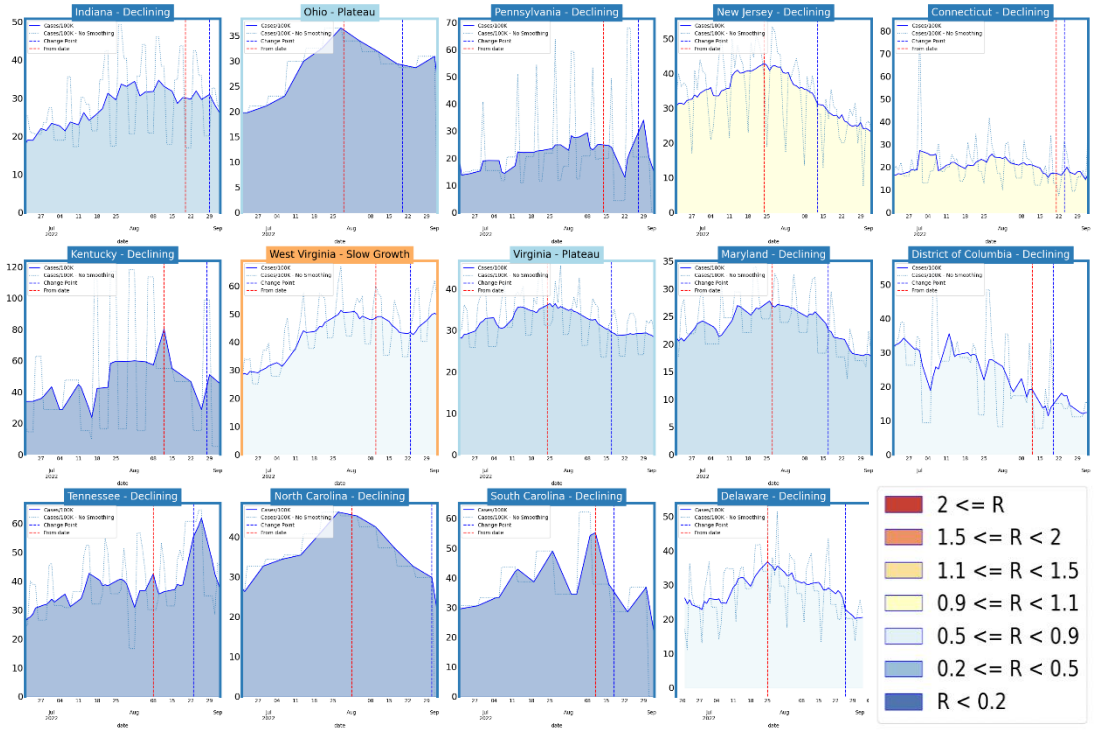
Status	# States
Declining	38 (43)
Plateau	7 (8)
Slow Growth	8 (3)
In Surge	0 (0)



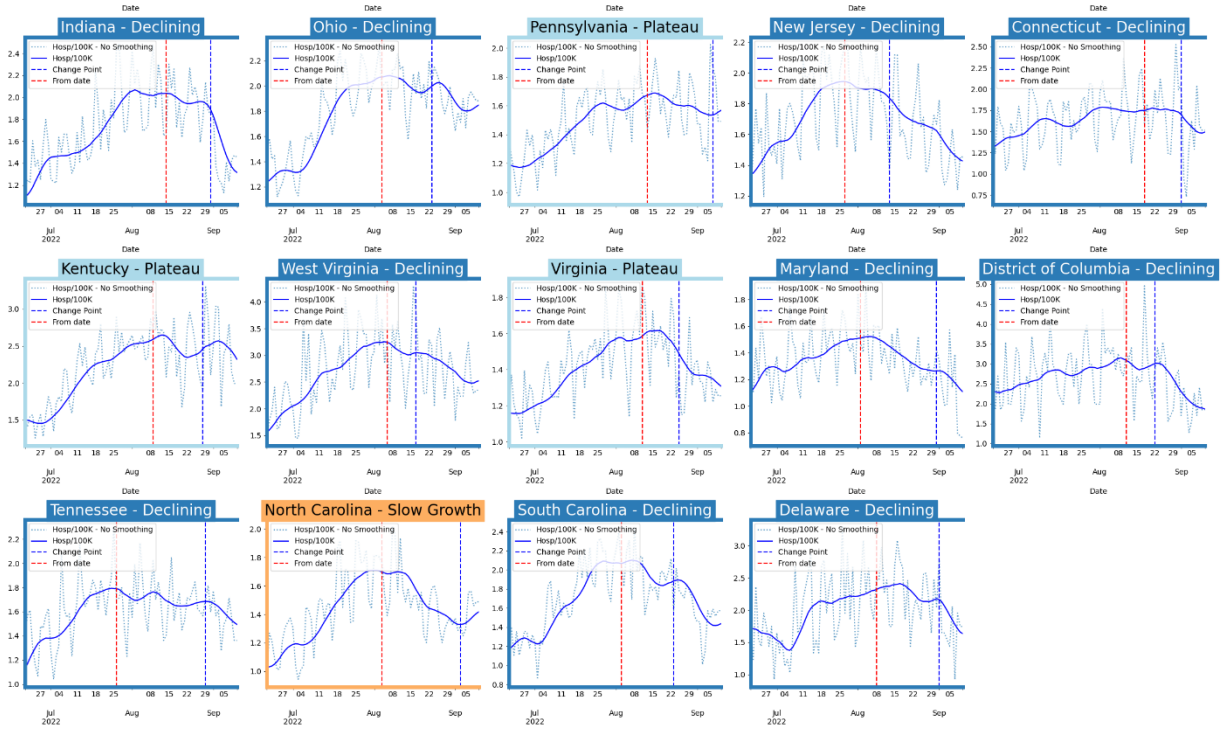
Status	# States
Declining	35 (22)
Plateau	16 (28)
Slow Growth	2 (3)
In Surge	0 (0)

Virginia and Her Neighbors

Cases



Hospitalizations



Using Ensemble Model to Guide Projections

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

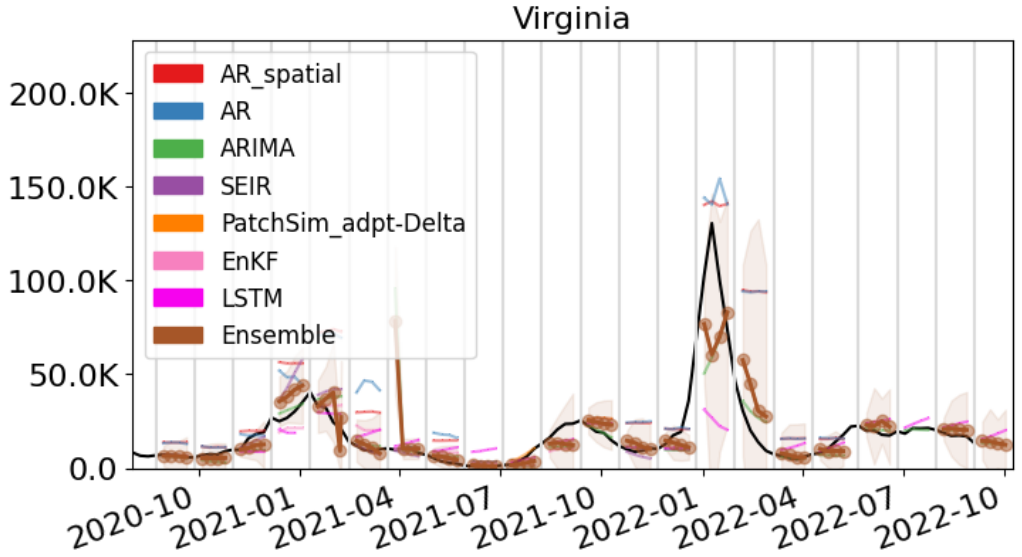
- Autoregressive (AR, ARIMA)
- Neural networks (LSTM)
- Kalman filtering (EnKF)

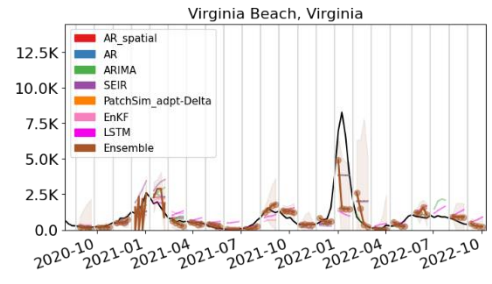
<u>Weekly forecasts</u> done at county level.

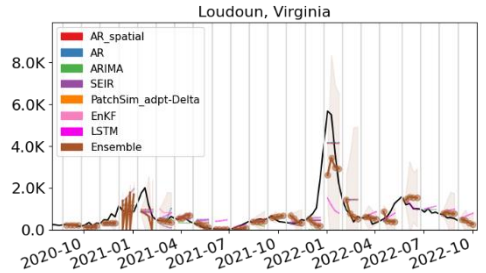
Models chosen because of their track record in disease forecasting and to increase diversity and robustness.

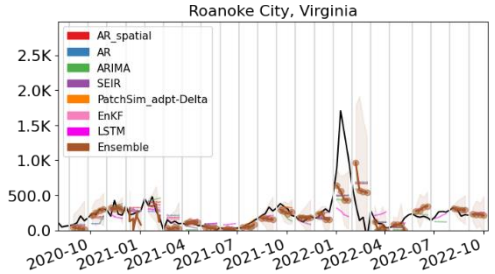
Ensemble forecast provides additional ‘surveillance’ for making scenario-based projections.

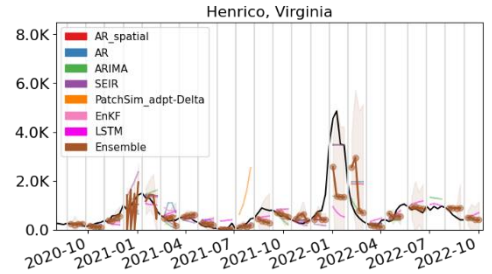
Also submitted to CDC Forecast Hub.









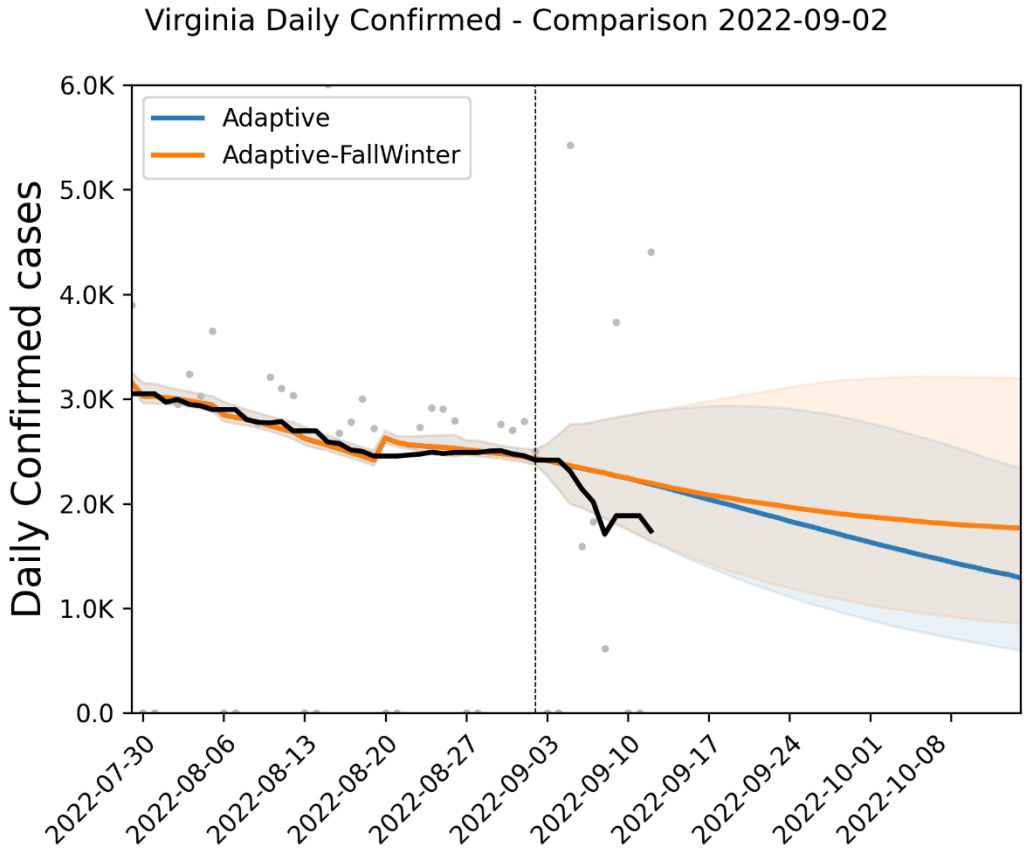


UNIVERSITY of VIRGINIA

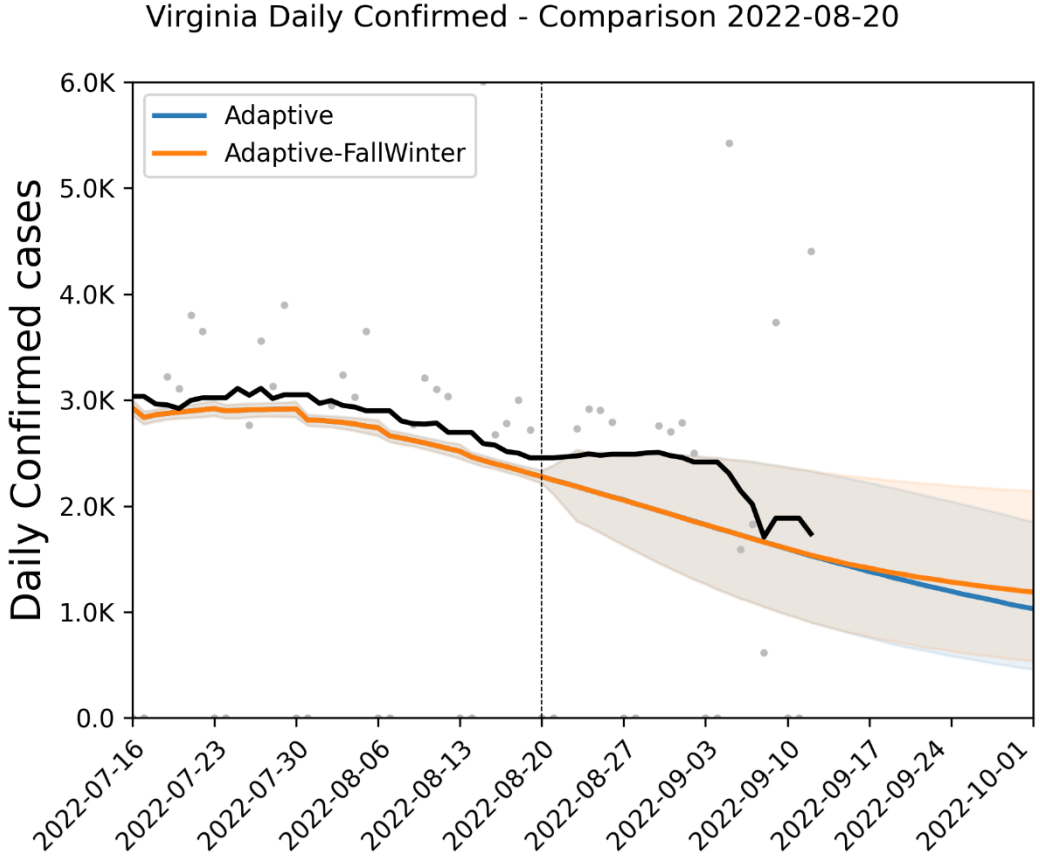
BIOCOMPLEXITY INSTITUTE

Case projection comparison

Projection from 1 weeks ago

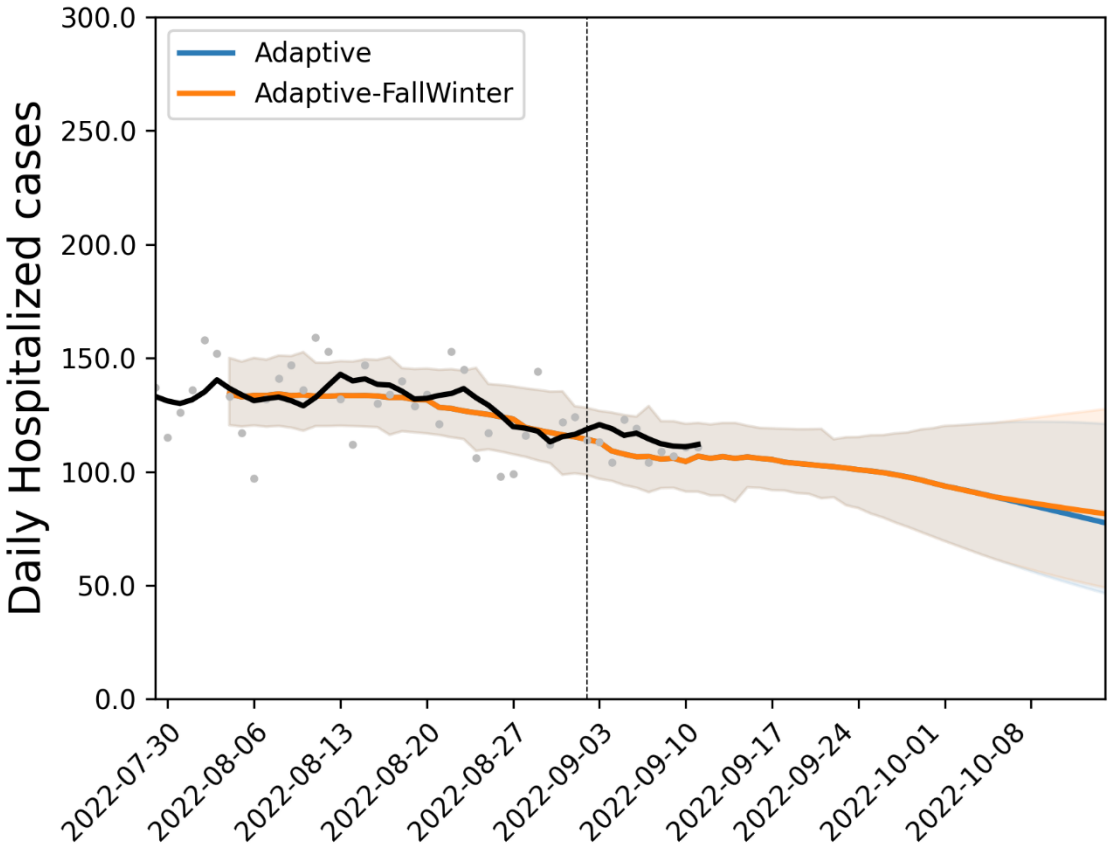


Projection from 3 weeks ago

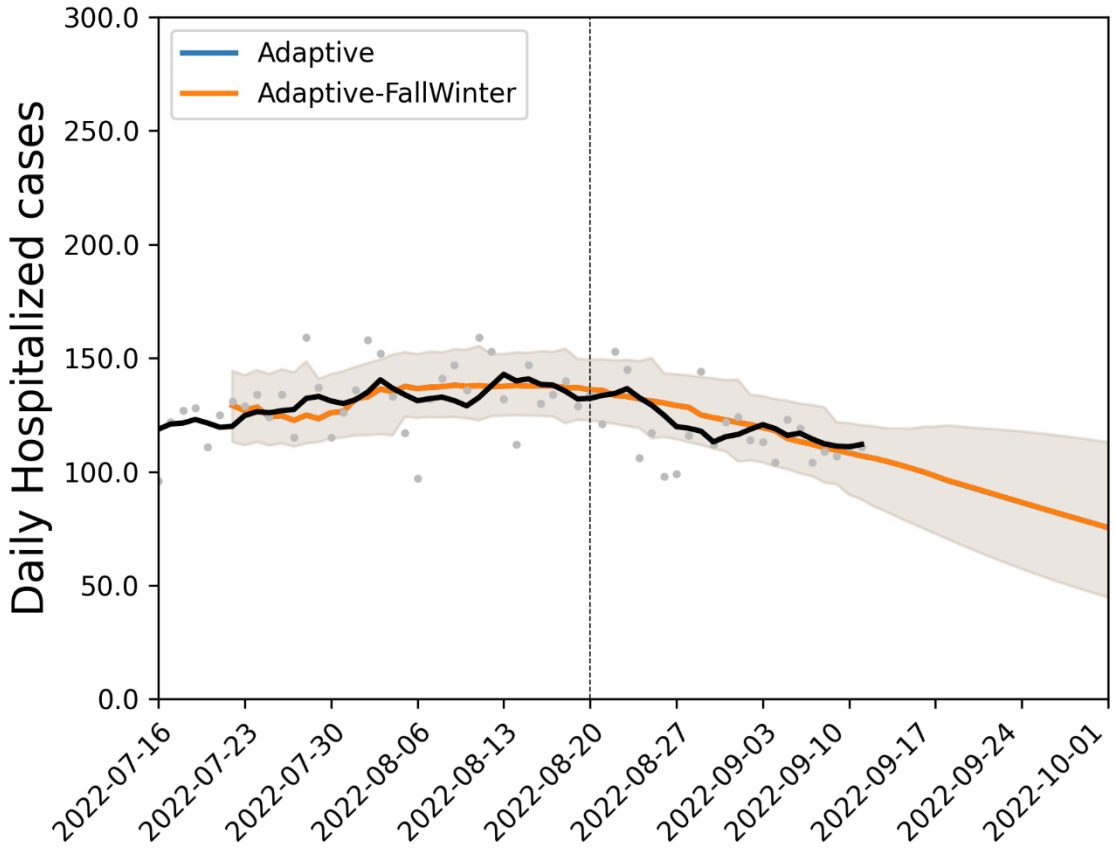


Hospitalization projection comparison

Projection from 1 weeks ago



Projection from 3 weeks ago

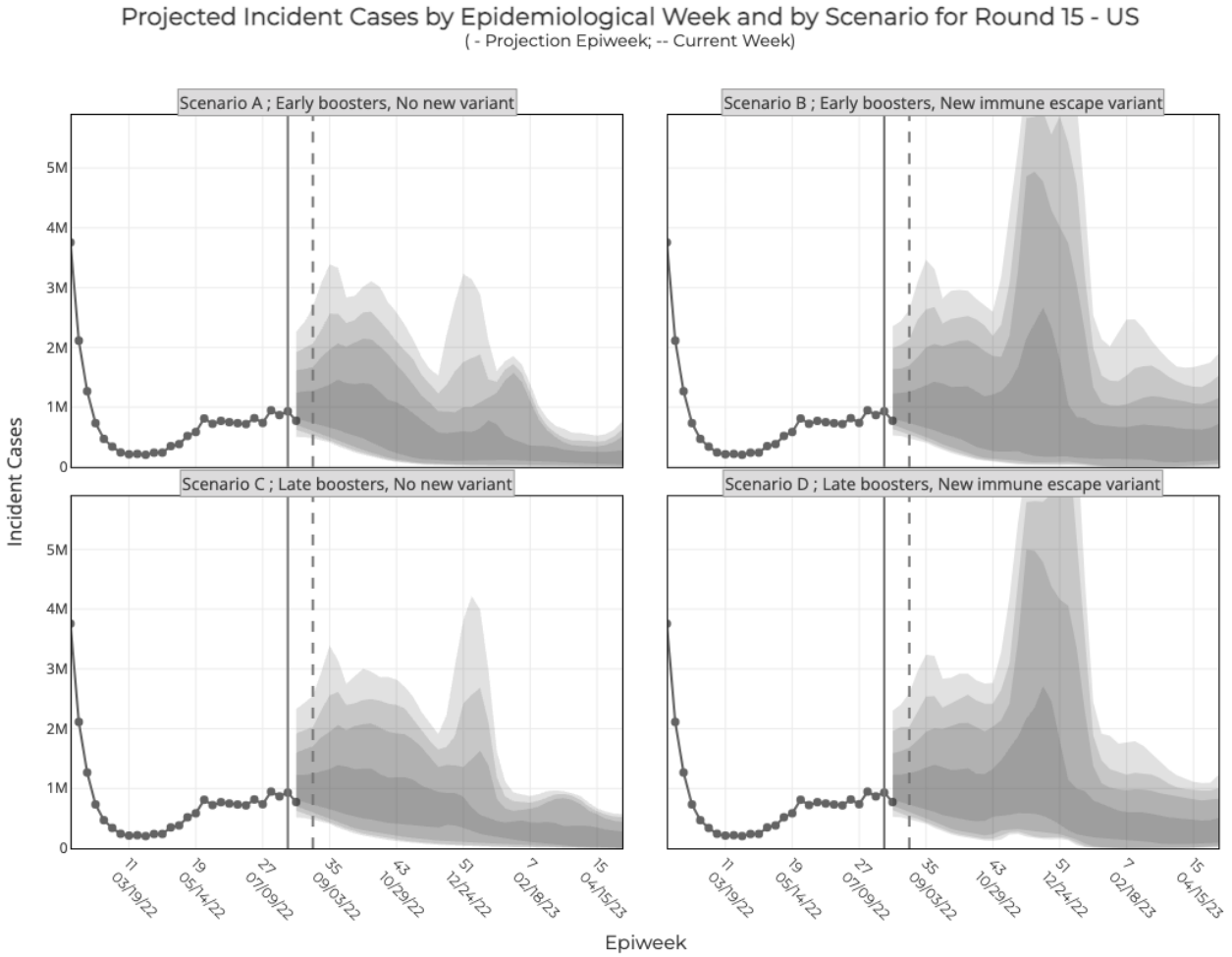


Scenario Modeling Hub – COVID-19 (Rd15), Flu (Rd1)

Collaboration of multiple academic teams to provide national and state-by-state level projections for 4 aligned scenarios

- Round 15 results published
  - Scenarios: Test benefits of reformulated fall boosters w/ and w/out a new variant
  - Timing of reformulated boosters is one of the axes
- Flu scenarios currently being generated
  - Impact of missed flu seasons on pre-season immunity
  - Testing different seasonal vaccine coverage and efficacy

https://covid19scenariomodelinghub.org/viz.html



Key Takeaways

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

- **Case rates have remained flat as have hospitalizations**
- VA weekly case rate flat at 206 per 100K from 203 per 100K
  - US weekly case rate is down to 174 per 100K from 189 per 100K
  - VA hospital occupancy (rolling 7 day mean of 791 slightly down from 798 a week ago) currently on month plateau
- Sub-variant prevalence evolution as expected
- Projections from last week remain largely on target, though cases are diverging

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

Additional Analyses

References

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

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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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