Network Systems Science & Advanced Computing

Biocomplexity Institute & Initiative

University of Virginia

Estimation of COVID-19 Impact in Virginia

September 28th, 2022

(data current to September 24th – September 27th)

Biocomplexity Institute Technical report: TR BI-2022-1769

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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

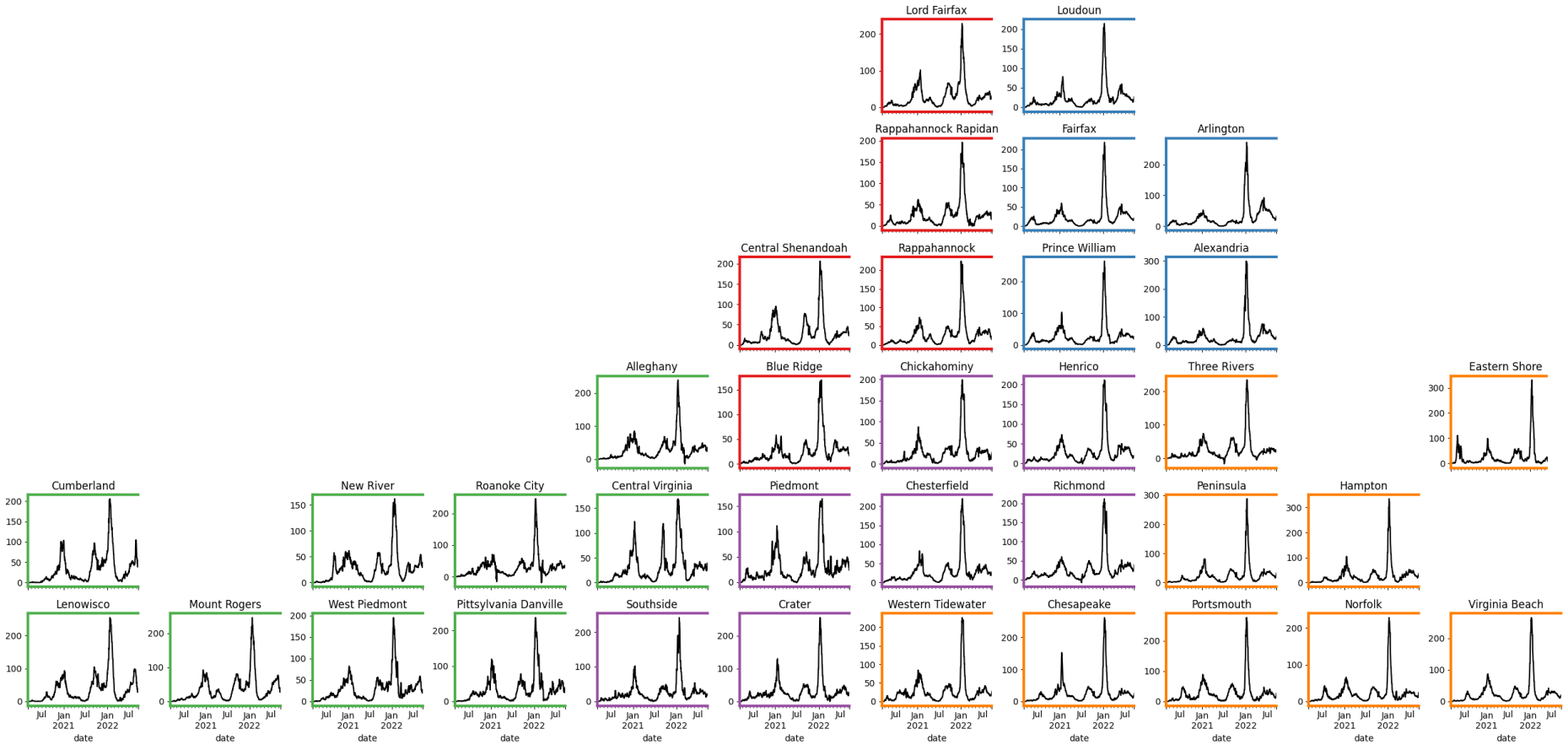
Projecting future cases precisely is impossible and unnecessary.
Even without perfect projections, we can confidently draw conclusions:

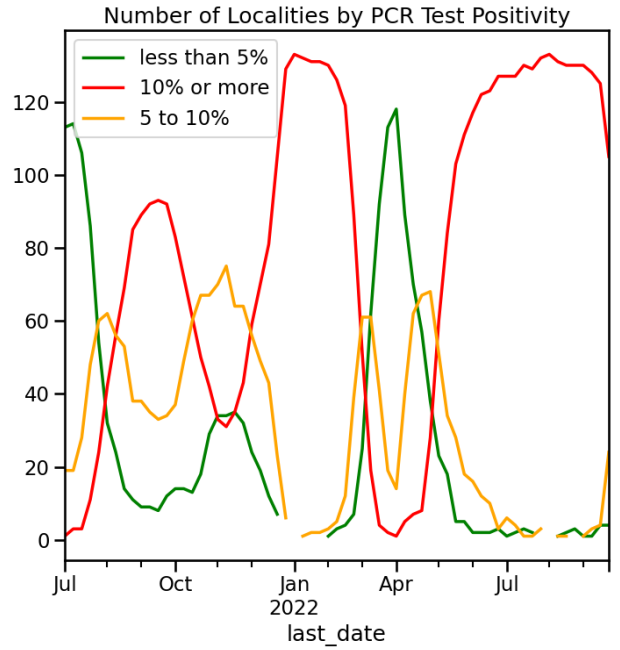
- **Case rates have continued to decline**
- VA weekly case rate is down at 109 per 100K from 132 per 100K
  - US weekly case rate is down to 105 per 100K from 116 per 100K
  - VA hospital occupancy (rolling 7 day mean of 599 slightly down from 660 a week ago) currently on month plateau
- Sub-variant prevalence evolution as expected
- Projections from last week remain largely on target, though FallWinter scenario will start to diverge soon

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)

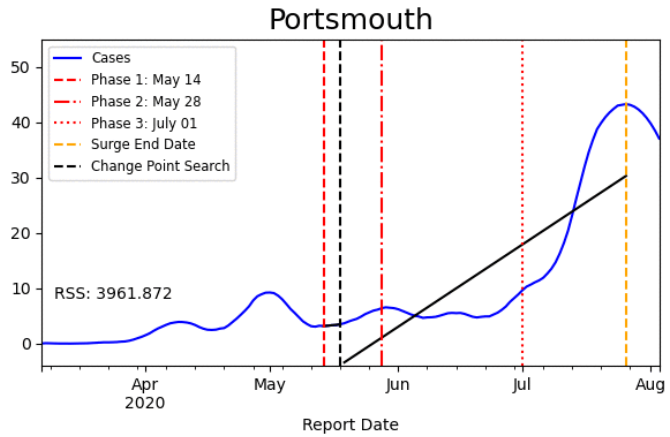
Red: >10.0% (and not "Green" or "Yellow")

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

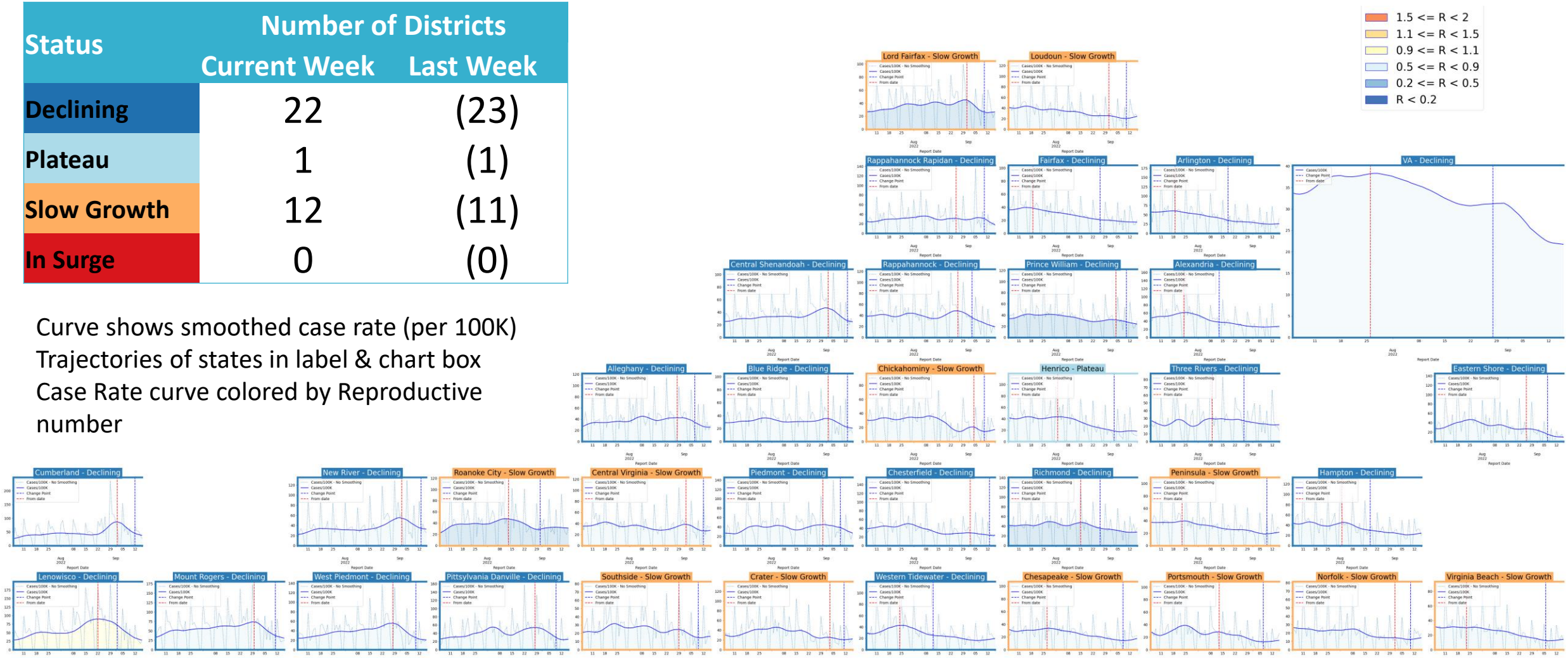


Trajectory	Description	Weekly Case Rate Slope (per 100k)	Weekly Hosp Rate Slope (per 100k)
Declining	Sustained decreases following a recent peak	slope < -0.88/day	slope < -0.07/day
Plateau	Steady level with minimal trend up or down	-0.88/day < slope < 0.42/day	-0.07/day < slope < 0.07/day
Slow Growth	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	Number of Districts	
	Current Week	Last Week
Declining	22	(23)
Plateau	1	(1)
Slow Growth	12	(11)
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

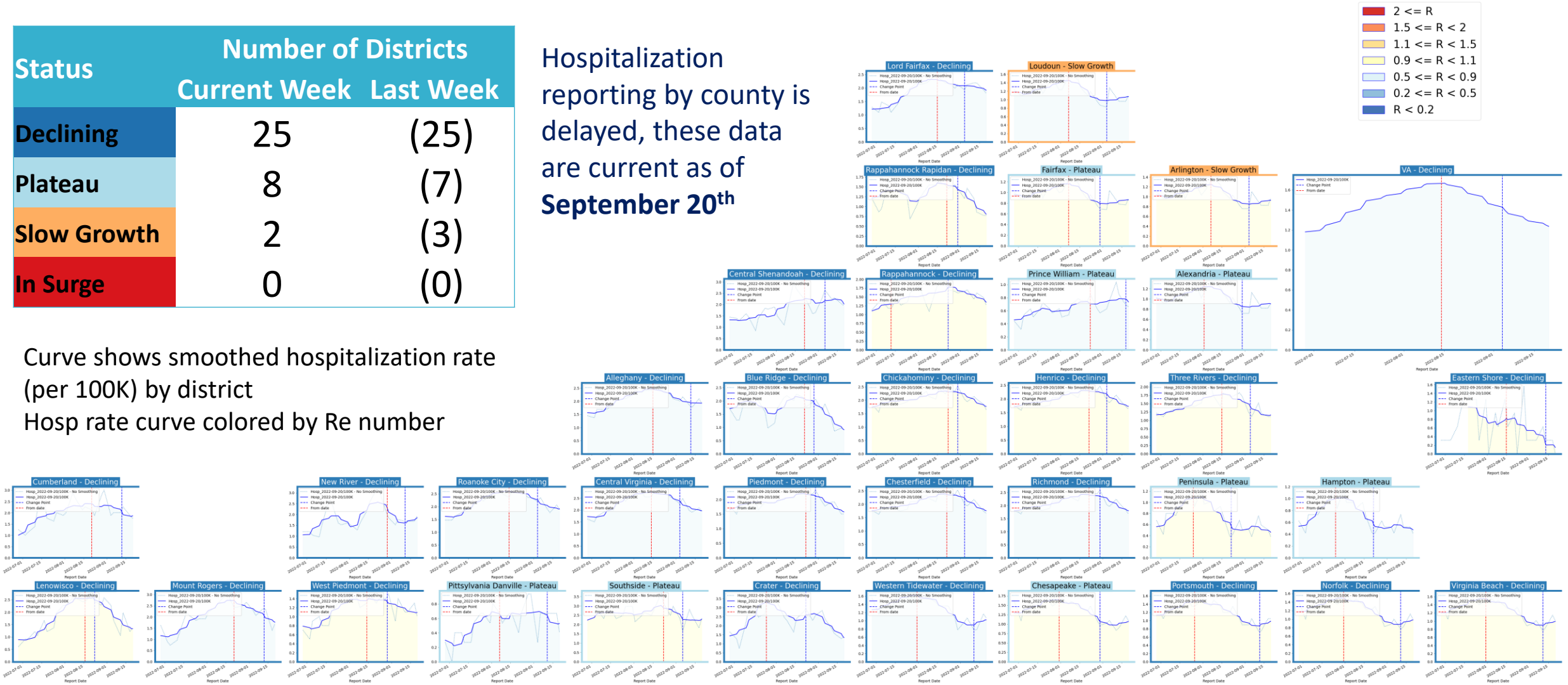


District Hospital Trajectories – last 10 weeks

Status	Number of Districts	
	Current Week	Last Week
Declining	25	(25)
Plateau	8	(7)
Slow Growth	2	(3)
In Surge	0	(0)

Hospitalization reporting by county is delayed, these data are current as of **September 20th**

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



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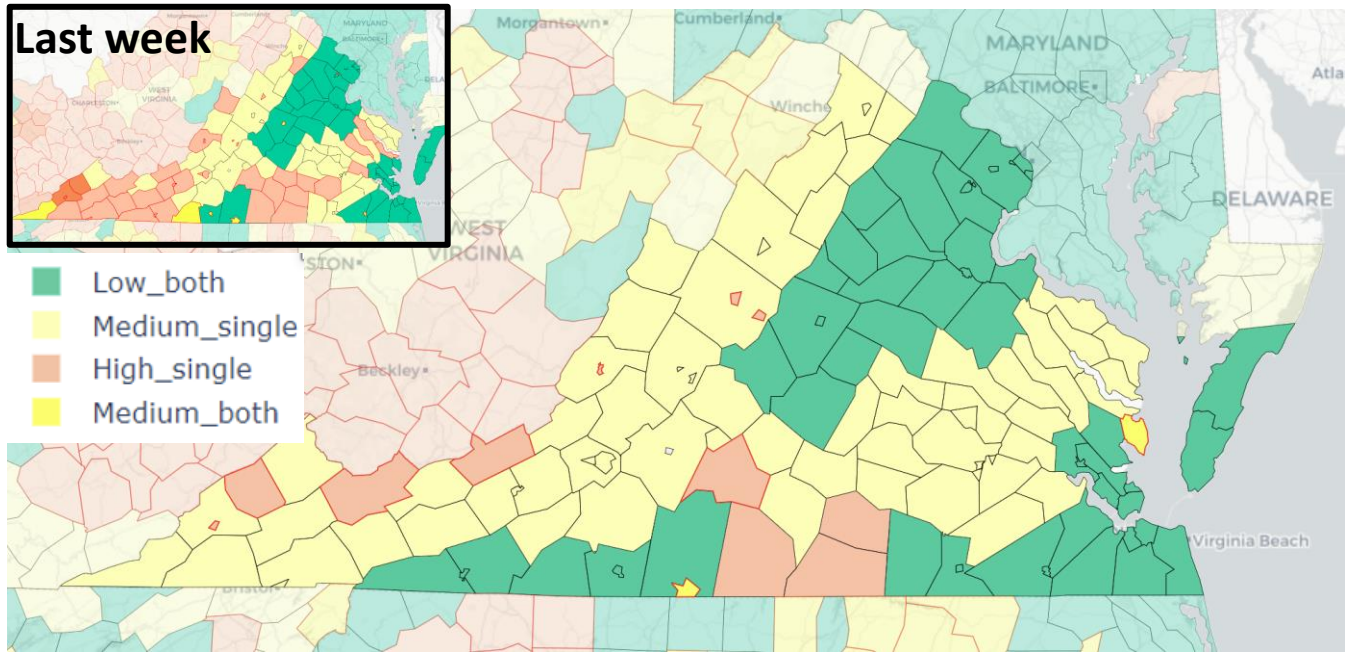
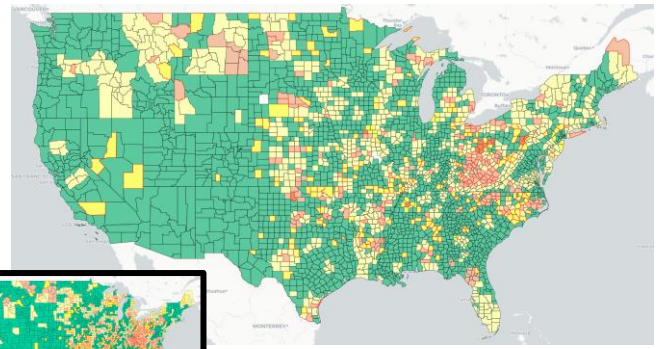
CDC's COVID-19 Community Levels

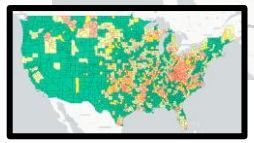


Red outline indicates county had 200 or more cases per 100k in last week

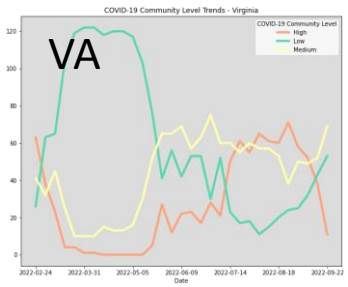
Pale color indicates either beds or occupancy set the level for this county

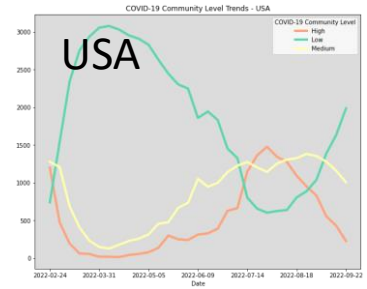
Dark color indicates both beds and occupancy set the level for this county





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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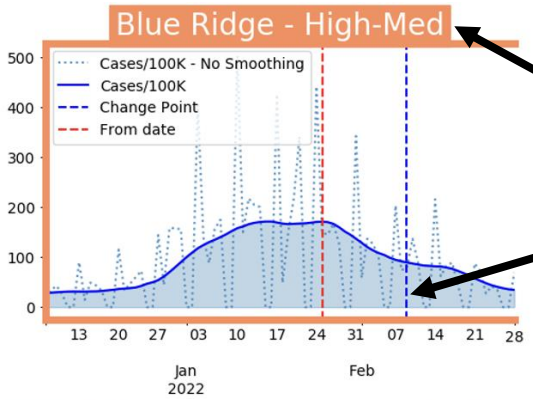
Data from: CDC Data Tracker Portal

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

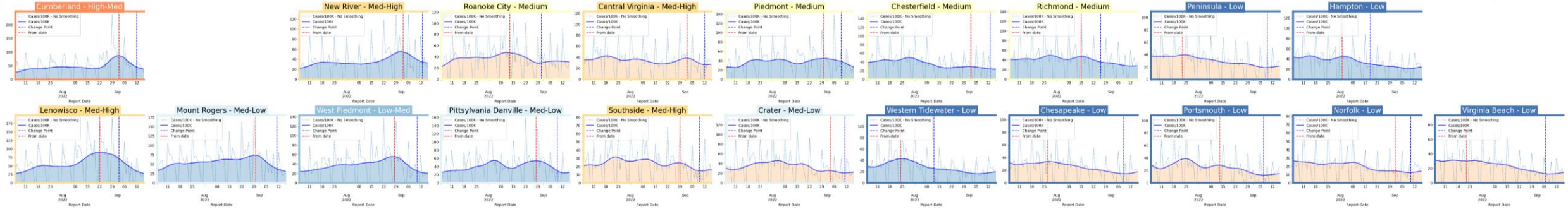
Trajectory (Curve Shading)
- In Surge
- Slow Growth
- Plateau
- Declining



District's Aggregate Community Level

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

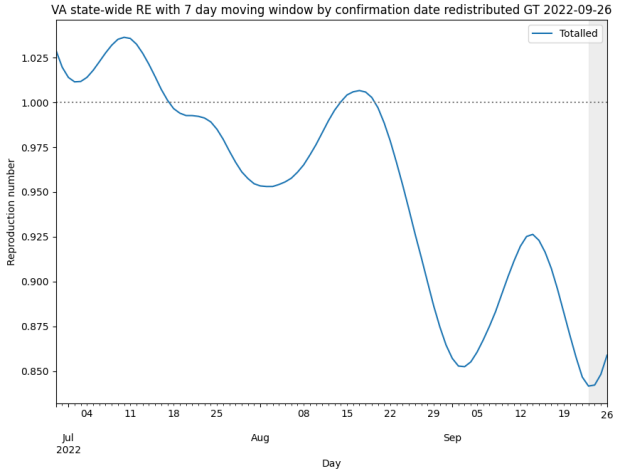
Case rate Trajectory

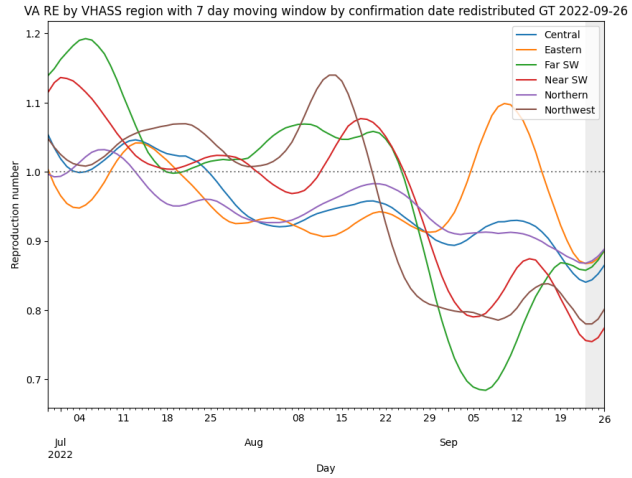


Estimating Daily Reproductive Number –
Redistributed gap

Sept 26th Estimates

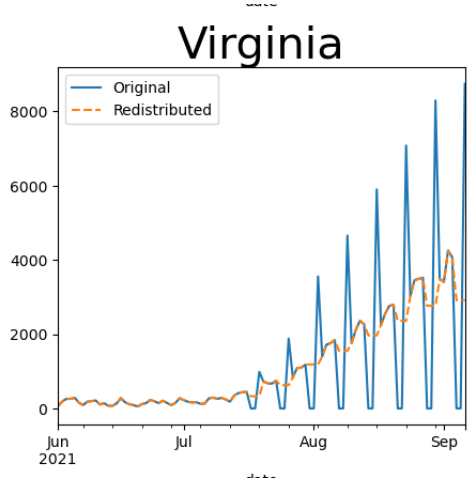
Region	Date Confirmed R_e	Date Confirmed Diff Last Week
State-wide	0.859	-0.041
Central	0.871	-0.009
Eastern	0.888	-0.139
Far SW	0.887	0.215
Near SW	0.776	-0.116
Northern	0.890	-0.012
Northwest	0.797	0.022





Skipping Weekend Reports & holidays biases estimates

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



Methodology

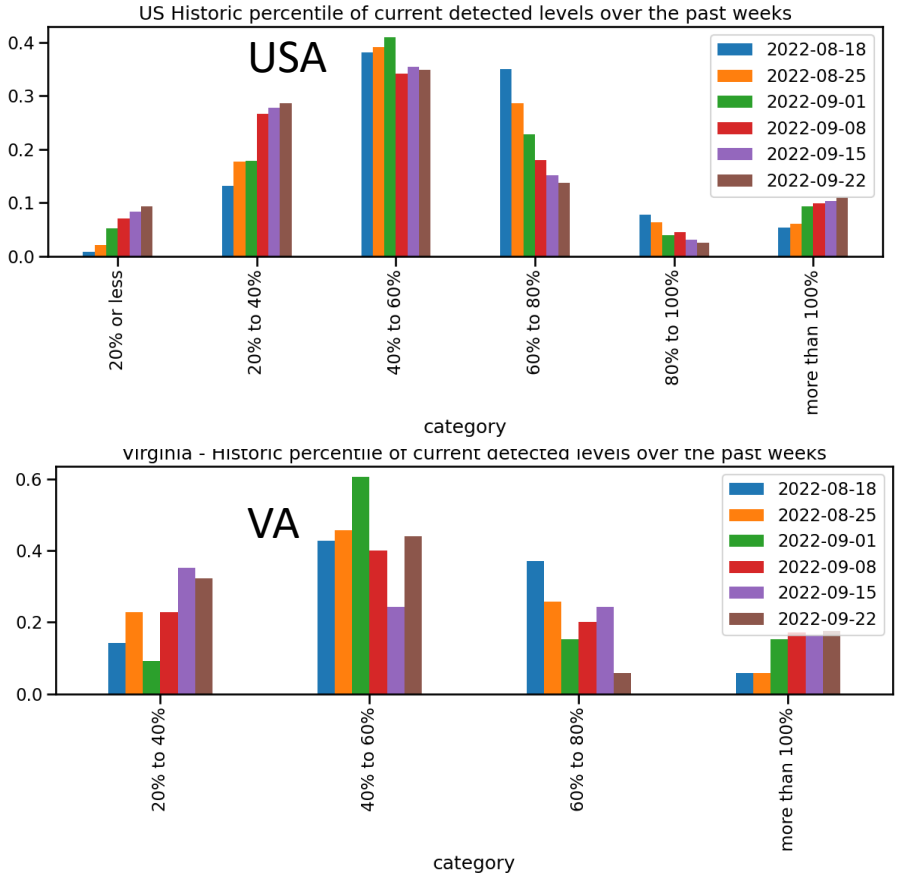
- Wallinga-Teunis method (EpiEstim[1]) for cases by **confirmation date**
- Serial interval: updated to discrete distribution from observations (mean=4.3, Flaxman et al, Nature 2020)
- Using Confirmation date since due to increasingly unstable estimates from onset date due to backfill

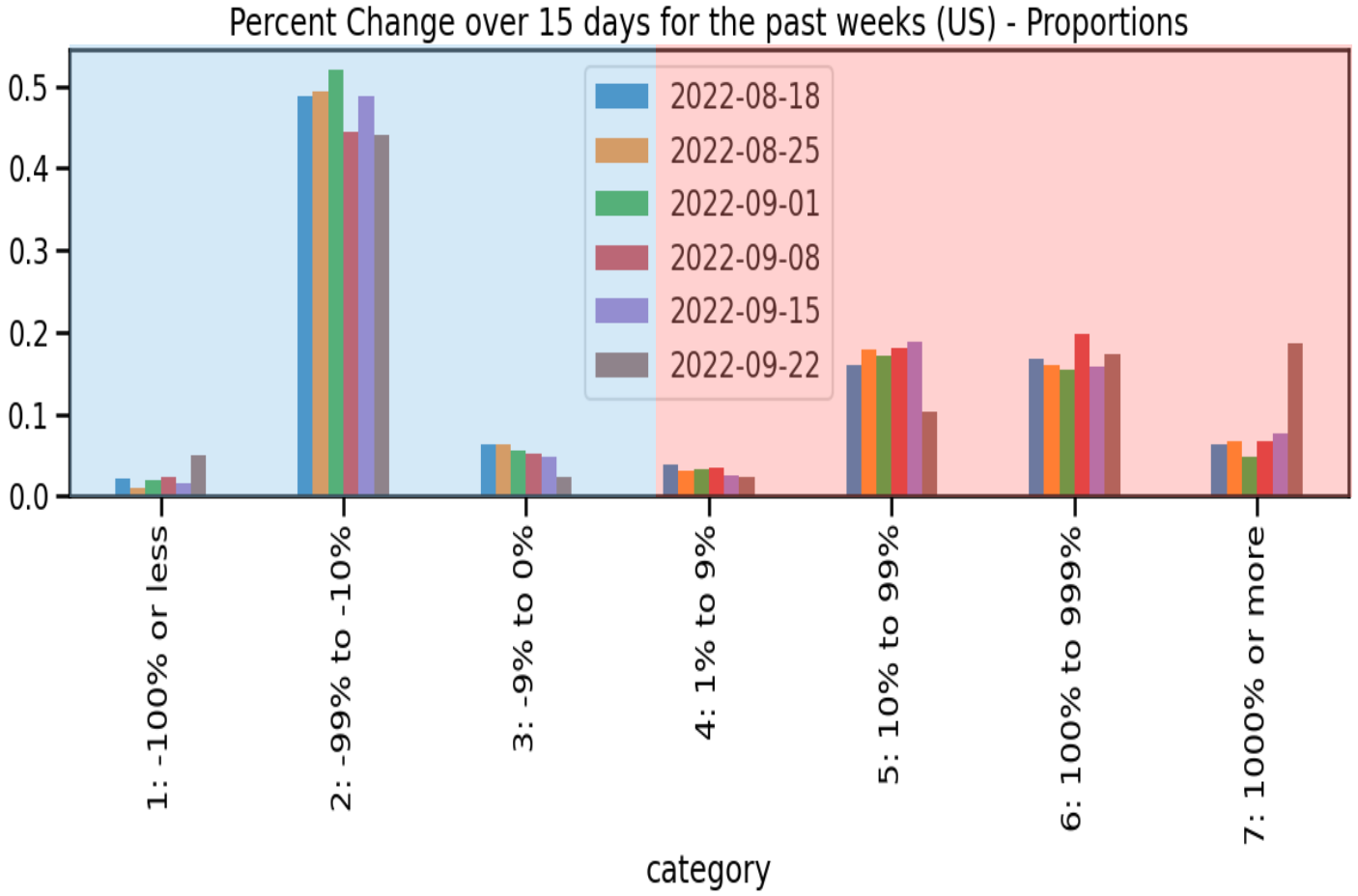
1. Anne Cori, Neil M. Ferguson, Christophe Fraser, Simon Cauchemez. A New Framework and Software to Estimate Time-Varying Reproduction Numbers During Epidemics. American Journal of Epidemiology, Volume 178, Issue 9, 1 November 2013, Pages 1505–1512, https://doi.org/10.1093/aje/kwt133

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



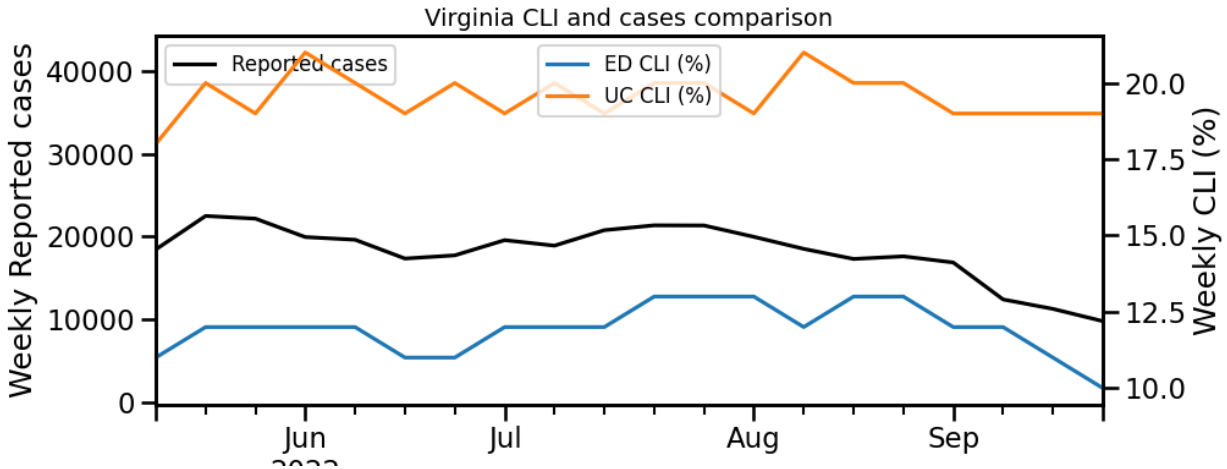


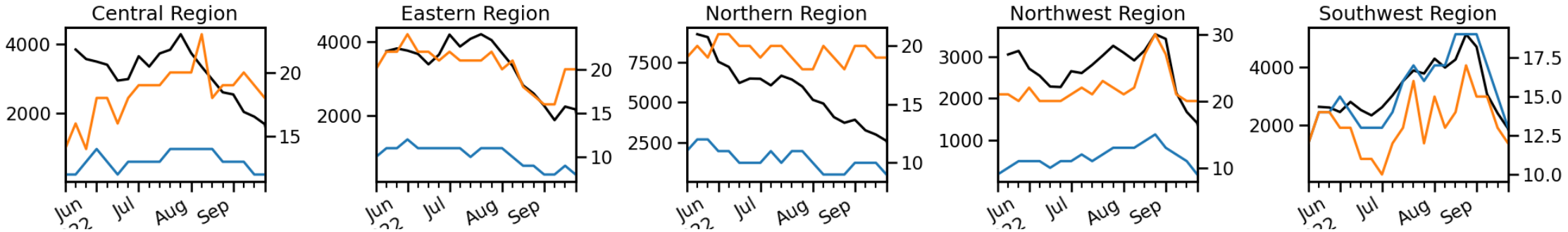
Data Source: [CDC Data Tracker]

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**



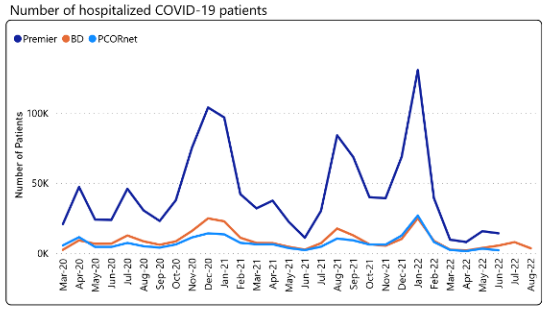


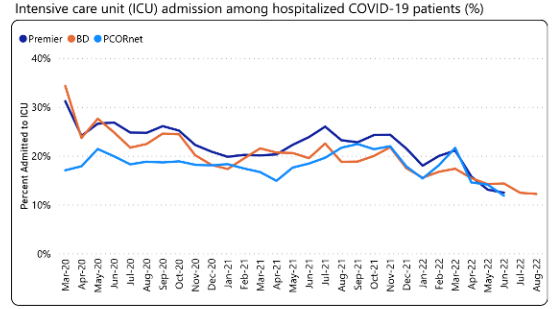
Hospitalizations and Severe Outcomes

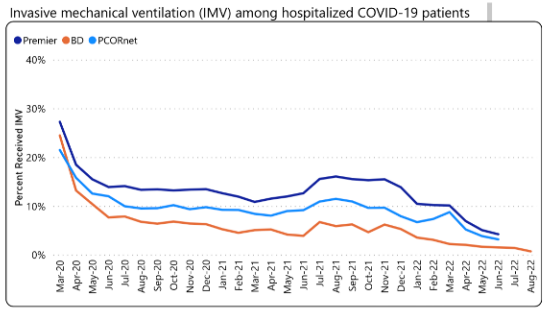
Data Source: [CDC Data Tracker]

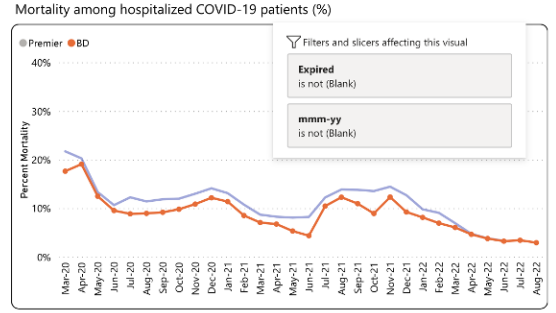
Proportion of most severe outcomes decreasing among those who are hospitalized

- 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

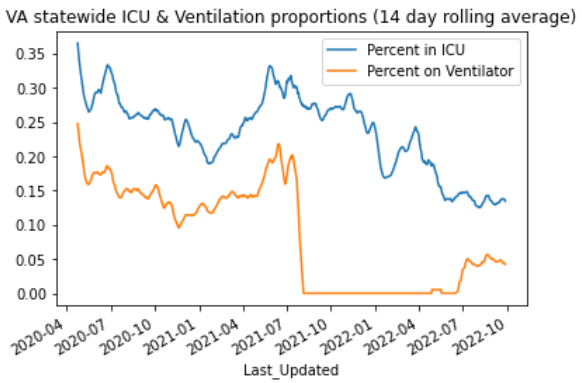




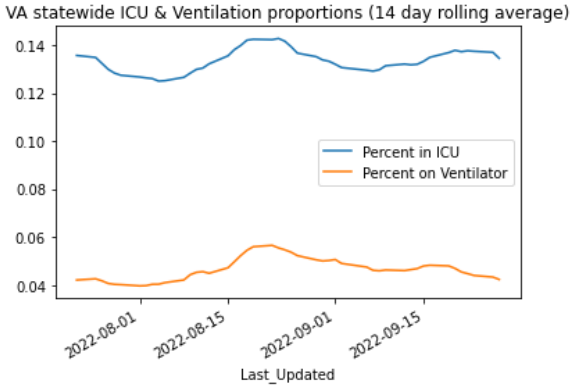




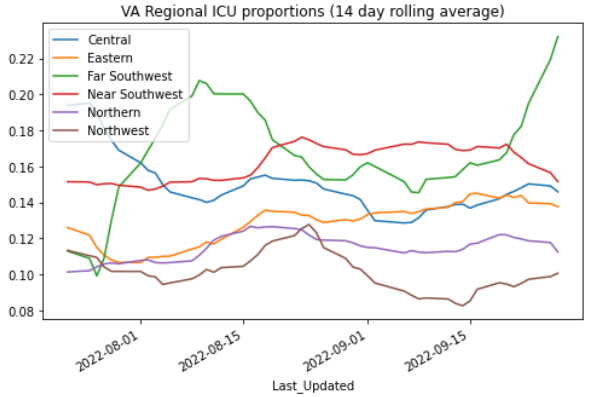
Virginia wide – full pandemic



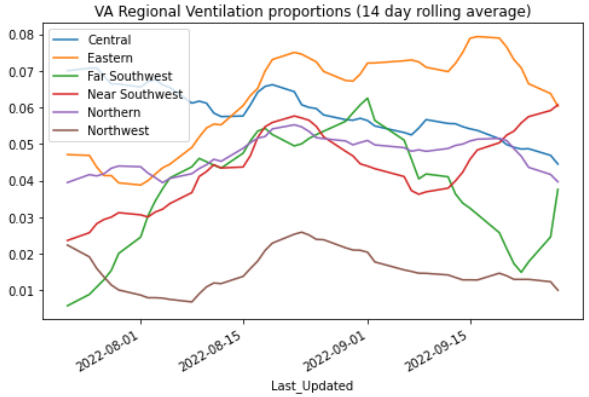
Virginia wide – recent



Virginia Regional ICU percent



Virginia Regional Ventilation %

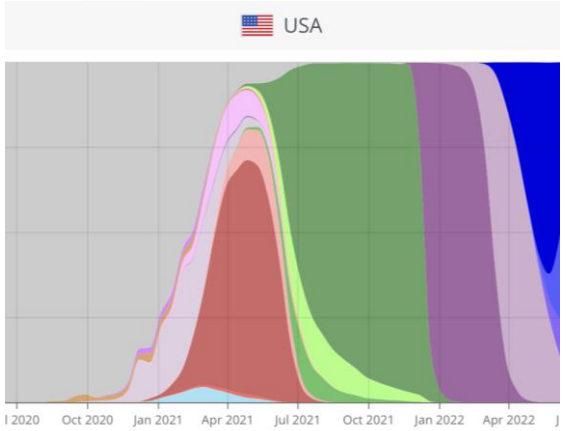


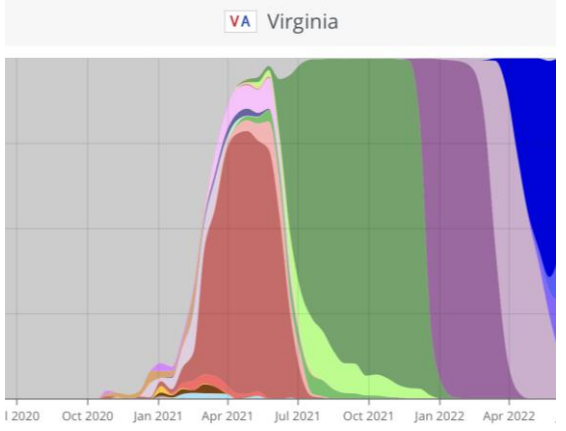
SARS-CoV2 Variants of Concern

GISAID outbreak.info

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

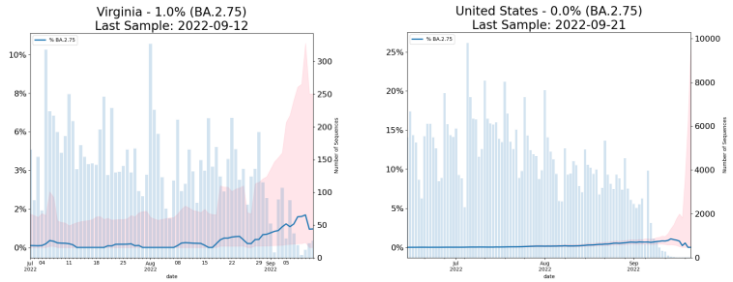
- Emerging variants can:
  - Increase transmissibility
  - Increase severity (more hospitalizations and/or deaths)
  - Limit immunity provided by prior infection and vaccinations





Omicron Updates (Region 3)

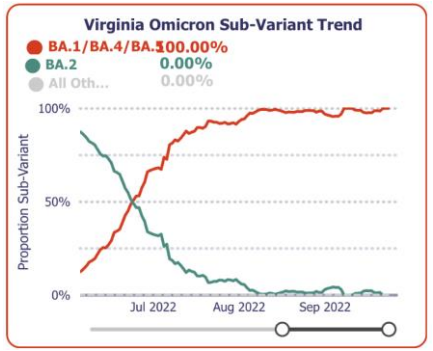
- BA.4 has declined as well, now contributing about 2%, but BA.4.6 remains in very slow growth moving to 15% from 13% last week
- BA.5 has stagnated if not slightly declined, nowcasted at 80% compared to 82% last week
- BA.2.72.2 showing some signs as being a potential candidate for future variant, as it has recently been shown to have significant immune escape

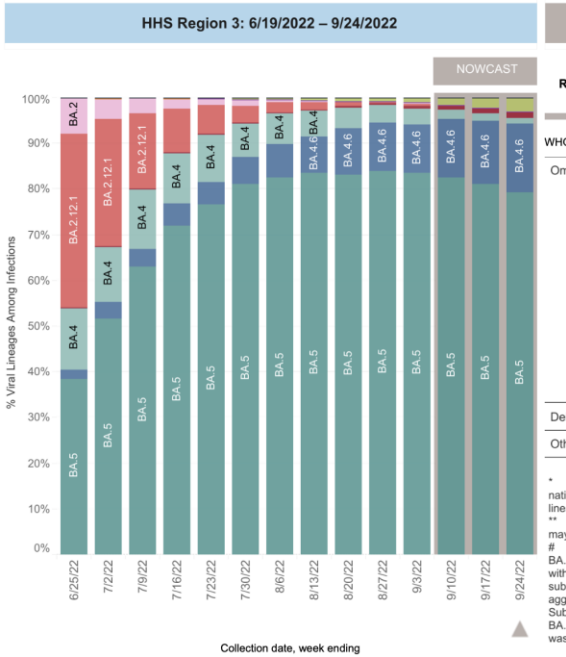


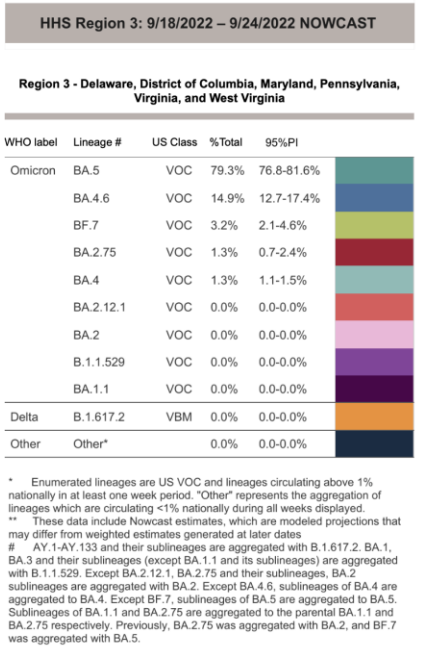
30-Sep-22

BA.2.75 detected in US (very limited samples)

Walgreen's SGTF







WHO label	Lineage #	US Class	%Total	95%PI
Omicron	BA.5	VOC	79.3%	76.8-81.6%
	BA.4.6	VOC	14.9%	12.7-17.4%
	BF.7	VOC	3.2%	2.1-4.6%
	BA.2.75	VOC	1.3%	0.7-2.4%
	BA.4	VOC	1.3%	1.1-1.5%
	BA.2.12.1	VOC	0.0%	0.0-0.0%
	BA.2	VOC	0.0%	0.0-0.0%
	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. Except BA.2.12.1, BA.2.75 and their sublineages, BA.2 sublineages are aggregated with BA.2. Except BA.4.6, sublineages of BA.4 are aggregated to BA.4. Except BF.7, sublineages of BA.5 are aggregated to BA.5. Sublineages of BA.1.1 and BA.2.75 are aggregated to the parental BA.1.1 and BA.2.75 respectively. Previously, BA.2.75 was aggregated with BA.2, and BF.7 was aggregated with BA.5.

CDC Variant Tracking

Pandemic Pubs

1. Representative survey estimates 7.3% of the US adult population (~18.5 million) reported having long COVID by July
2. A propensity matched cohort from the UK found that 2+ doses of vaccine decreased adjusted long COVID risk by 41% (95% CI 31%-50%)
3. BA.2.75.2 neutralised, on average, at titers ~6.5-times lower than BA.5, making BA.2.75.2 the most neutralisation resistant variant evaluated to date
4. Retrospective cohort study of 6,245,282 older adults (age ≥65 years) who had medical encounters between 2/2020–5/2021, indicates that people with COVID-19 were at significantly increased risk for a new diagnosis of Alzheimer's disease within 360 days after the initial COVID-19 diagnosis

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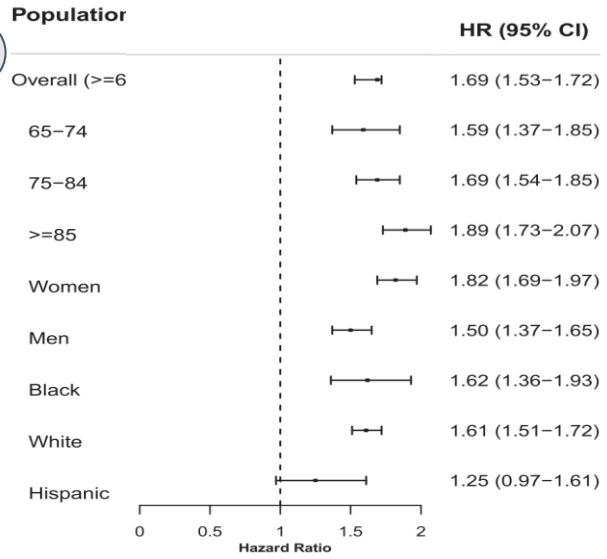

https://content.iospress.com/articles/journal-of-alzheimers-disease/jad220717

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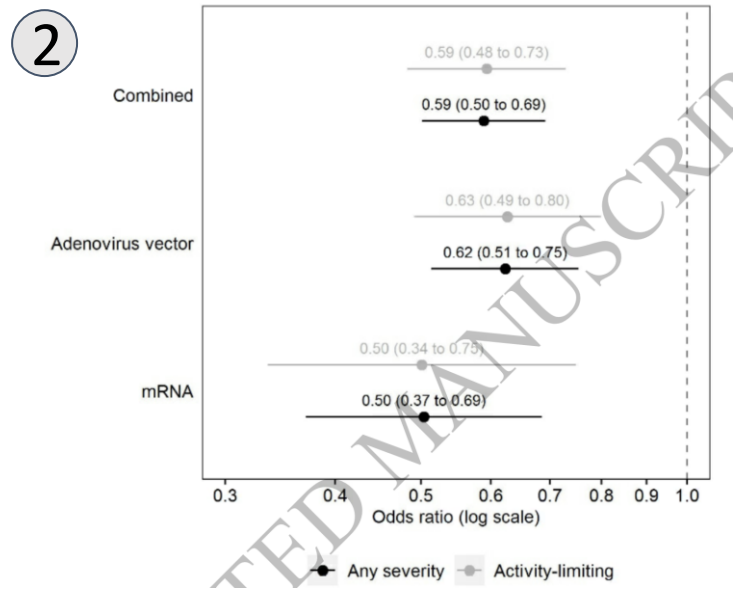
Prevalence of Long COVID Among All Respondent (with or without COVID)

	Total	Long COVID	Crude Prevalence of Long COVID % (95% CI)	Age and sex direct-standardized prevalence of long COVID* % (95% CI)	Crude prevalence ratio (PR) PR (95% CI)	Adjusted prevalence ratio (aPR)** aPR (95% CI)	Estimated Number with Long COVID
	Weighted N (%)	Weighted N (%)					
Total	3,042 (100.0)	222 (100.0)	7.3 (6.1, 8.5)				18,533,864
Age							
18-24	365 (12.0)	17 (7.8)	4.8 (0.9, 8.6)	4.4 (1.8 - 10.0)	**0.45 (0.27, 0.76)**	**0.50 (0.30, 0.84)**	1,445,641
25-34	547 (18.0)	58 (26.1)	10.6 (6.6, 14.6)	10.0 (6.8 - 14.6)	Ref	Ref	4,837,339
35-44	495 (16.3)	43 (19.1)	8.6 (5.3, 11.9)	9.0 (6.1 - 13.1)	0.81 (0.56, 1.18)	0.87 (0.60, 1.26)	3,539,968
45-54	498 (16.4)	37 (16.5)	7.4 (4.6, 10.2)	7.4 (5.1 - 10.7)	0.70 (0.47, 1.03)	0.72 (0.49, 1.07)	3,058,088
55-64	508 (16.7)	41 (18.2)	8.0 (5.5, 10.5)	8.3 (6.0 - 11.2)	0.75 (0.51, 1.10)	0.80 (0.55, 1.18)	3,373,163
65+	629 (20.7)	27 (12.2)	4.3 (3.0, 5.6)	4.2 (3.0 - 5.8)	**0.41 (0.26, 0.63)**	**0.43 (0.27, 0.66)**	2,261,131
Gender							
Male	1,443 (47.4)	72 (32.4)	5.0 (3.6, 6.3)	5.0 (3.8 - 6.5)	Ref	Ref	6,004,972
Female	1,516 (49.8)	144 (64.8)	9.5 (7.5, 11.5)	9.4 (7.7 - 11.6)	**1.90 (1.45, 2.50)**	**1.84 (1.40, 2.42)**	12,009,944

NY researchers conducted a population-representative survey, June 30-July 2, 2022, of a random sample of 3,042 United States adults. Using questions developed by the United Kingdom's Office of National Statistics, we estimated the prevalence by sociodemographics, adjusting for gender and age. An estimated 7.3% (95% CI: 6.1-8.5%) of all respondents reported long COVID, approximately 18,533,864 adults. One-quarter (25.3% [18.2-32.4%]) of respondents with long COVID reported their day-to-day activities were impacted 'a lot' and 28.9% had SARS-CoV-2 infection >12 months ago.
https://www.medrxiv.org/content/10.1101/2022.09.12.22279862v1

2



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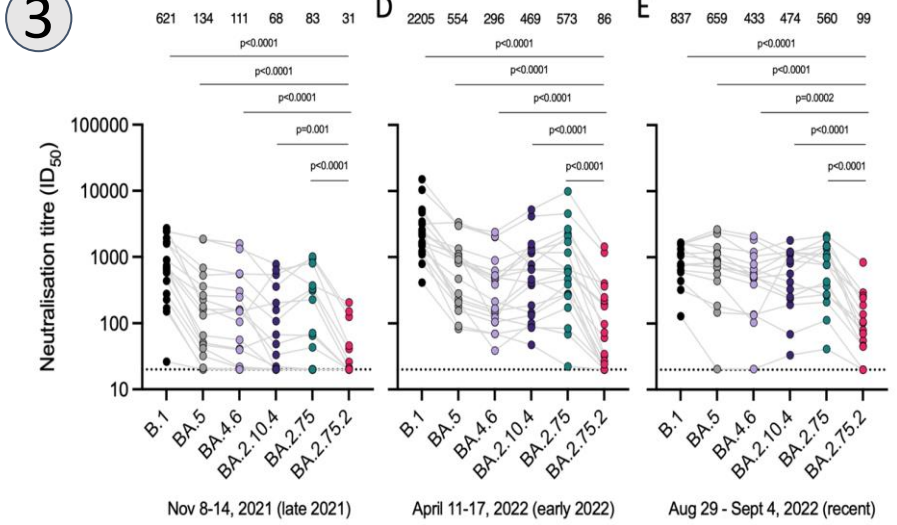


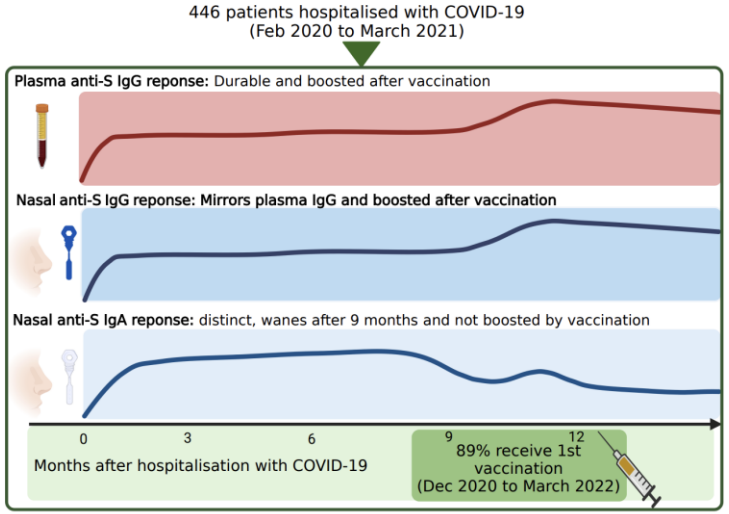
In 18 random blood donor samples in Stockholm, sampled recently BA.2.75.2 was neutralised, on average, five-fold less potently than BA.5. These are recent samples in a city that has good vaccine coverage and likely relatively high prior infection rates. Researchers also report the sensitivity of emerging omicron sublineages BA.2.75.2, BA.4.6, and BA.2.10.4 to neutralisation by a panel of clinically relevant and pre-clinical monoclonal antibodies, as well as by serum from blood donated in Stockholm, Sweden.
https://www.biorxiv.org/content/10.1101/2022.09.16.508299v2
https://twitter.com/benjmurrell/status/1570862185819303937?s=12&t=sL45iDMQ7GGmC2KakXPNZg

Oxford researchers investigated Long Covid incidence by vaccination status in a random sample of UK adults from April 2020 to November 2021. Persistent symptoms were reported by 9.5% of 3,090 breakthrough SARS-CoV-2 infections and 14.6% of unvaccinated controls (adjusted odds ratio 0.59, 95% CI: 0.50-0.69), emphasising the need for public health initiatives to increase population-level vaccine uptake. Matched study participants who were double-vaccinated at time of infection to control participants who were unvaccinated when infected and remained so at their first follow-up visit ≥12 weeks later. Most double-vaccinated participants (3,057, 98.9%) were infected after 17 May 2021, when the Delta variant dominated in the UK, while nearly all unvaccinated participants (3,082, 14 99.7%) were infected before this date.
https://academic.oup.com/ofid/advance-article/doi/10.1093/ofid/ofac464/6696170?login=false
https://twitter.com/DFisman/status/1570901408211402752

Pandemic Pubs (last week)

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 orphaned due to primary and secondary caregiver deaths from COVID worldwide.

1



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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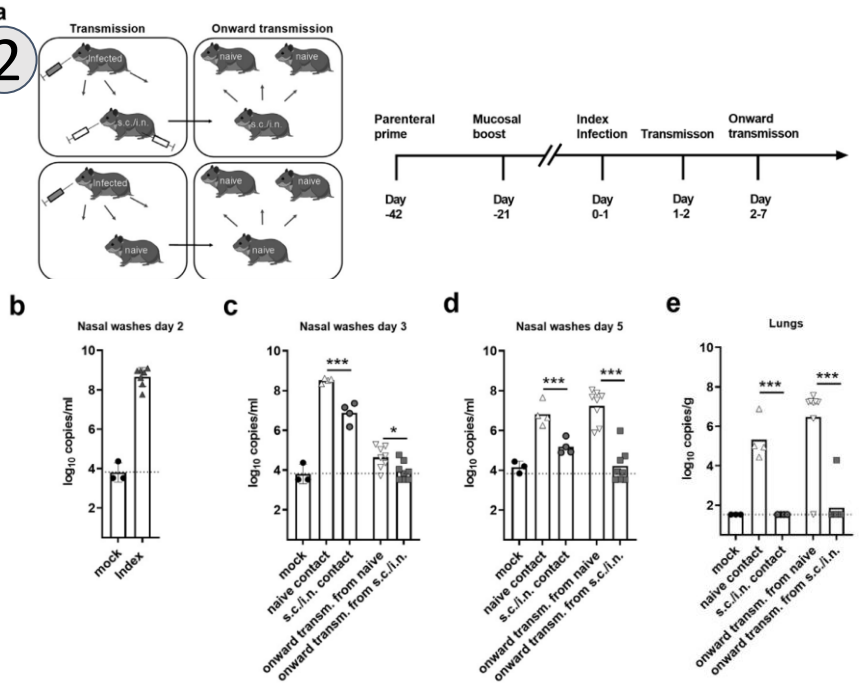
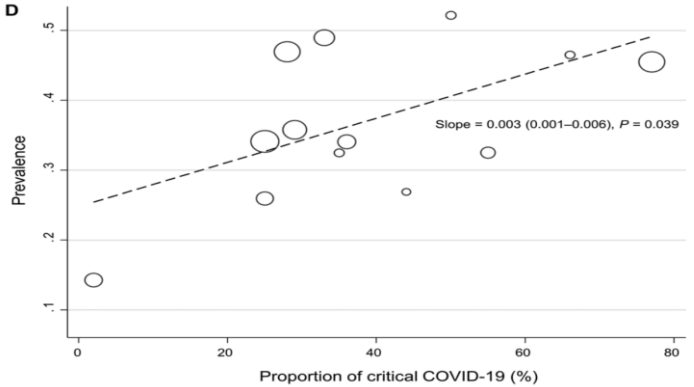


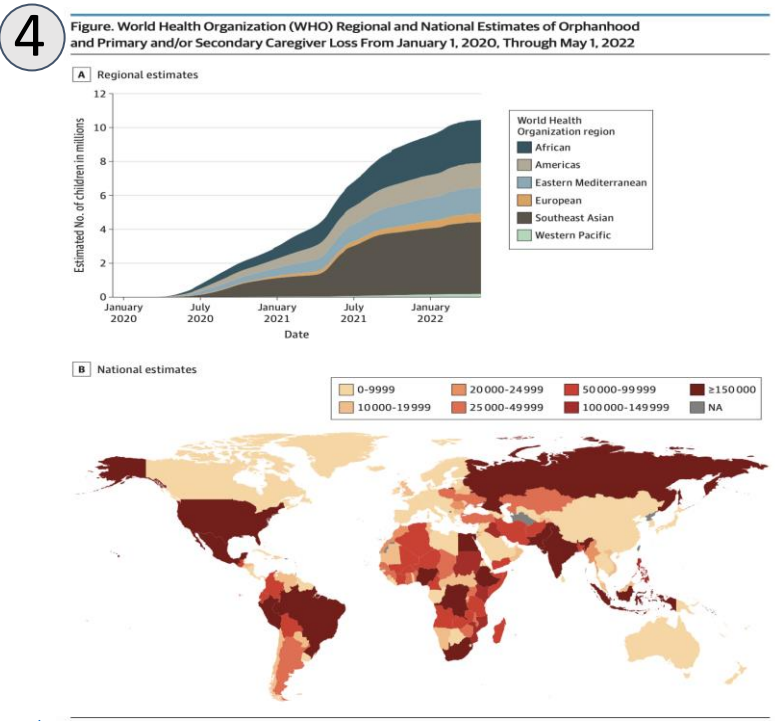
Center for Vaccine Research, Denmark: Study suggests mucosal booster strategy using protein-based subunit vaccines may be an effective means to protect against transmission of SARS-CoV-2 and potentially other respiratory viruses despite incomplete clearance of virus from the upper respiratory tract.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

3



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

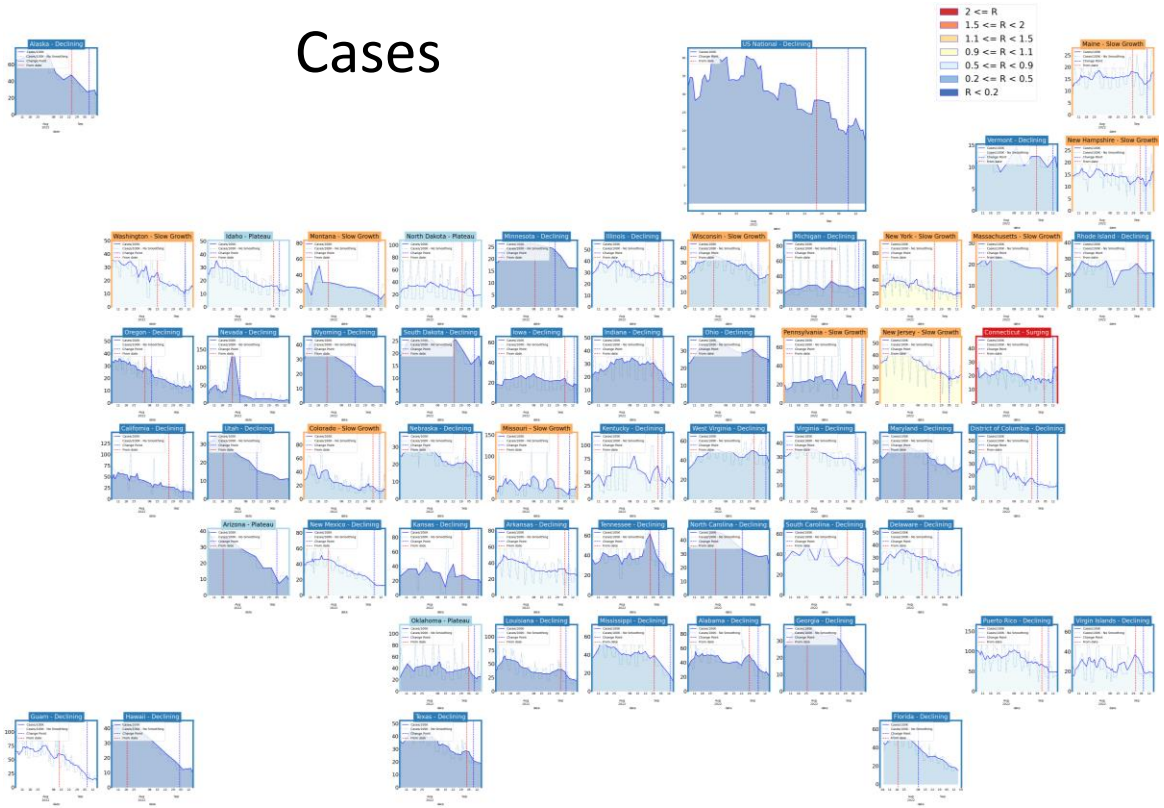
4

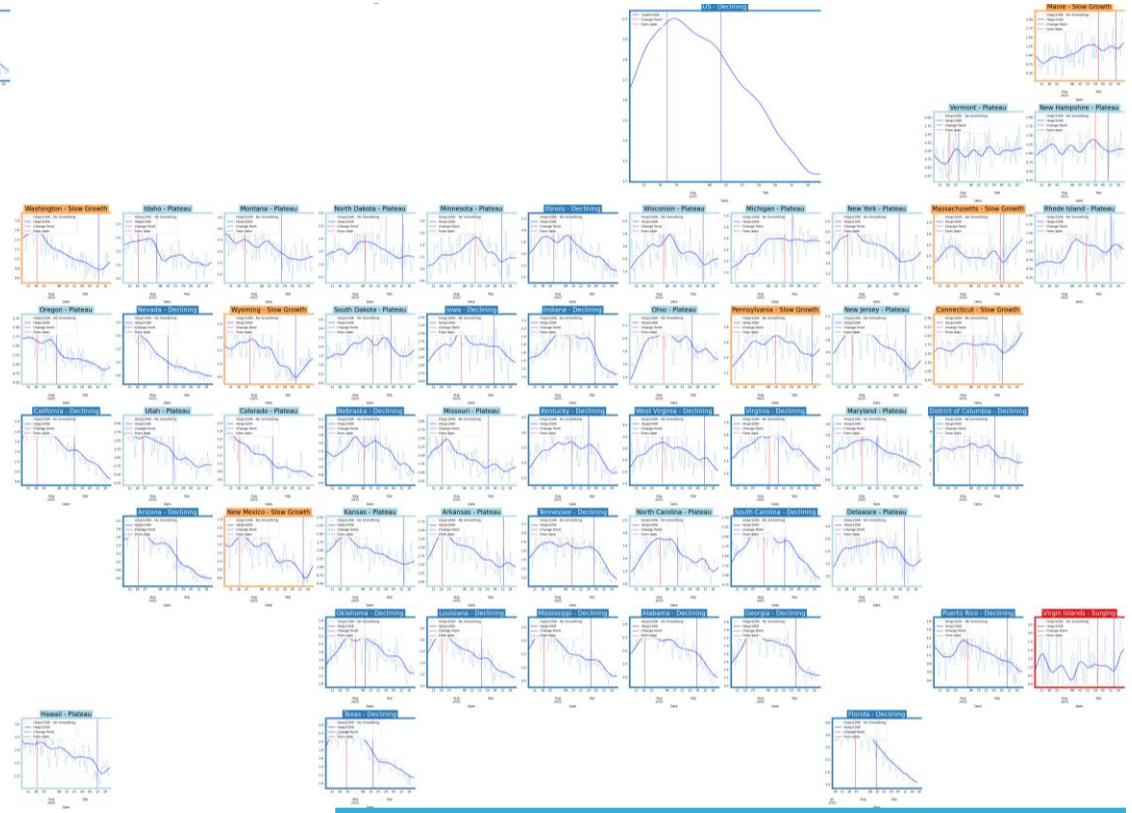


https://jamanetwork.com/journals/jamapediatrics/fullarticle/2795650

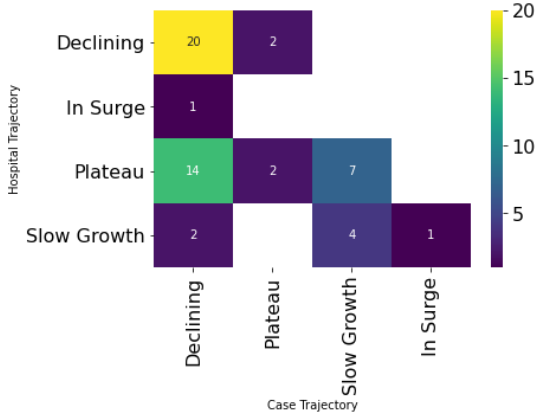
United States Case & Hospitalizations

Cases





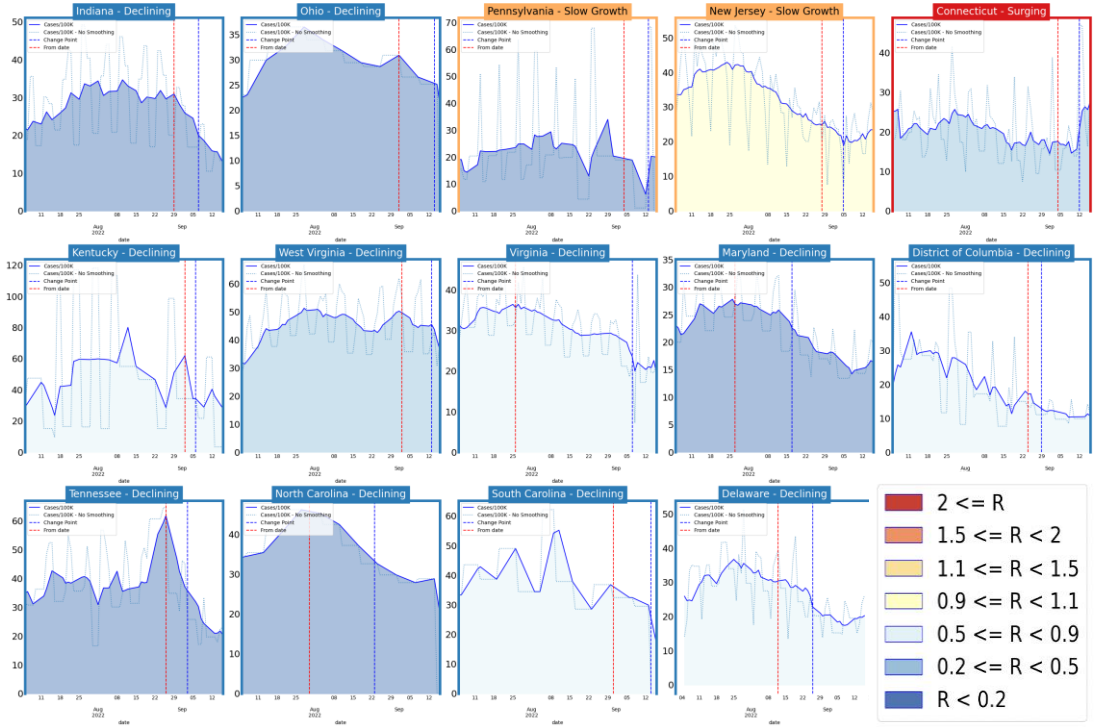
Status	Number of States	
	Current Week	Last Week
Declining	38	(40)
Plateau	4	(4)
Slow Growth	11	(9)
In Surge	1	(1)



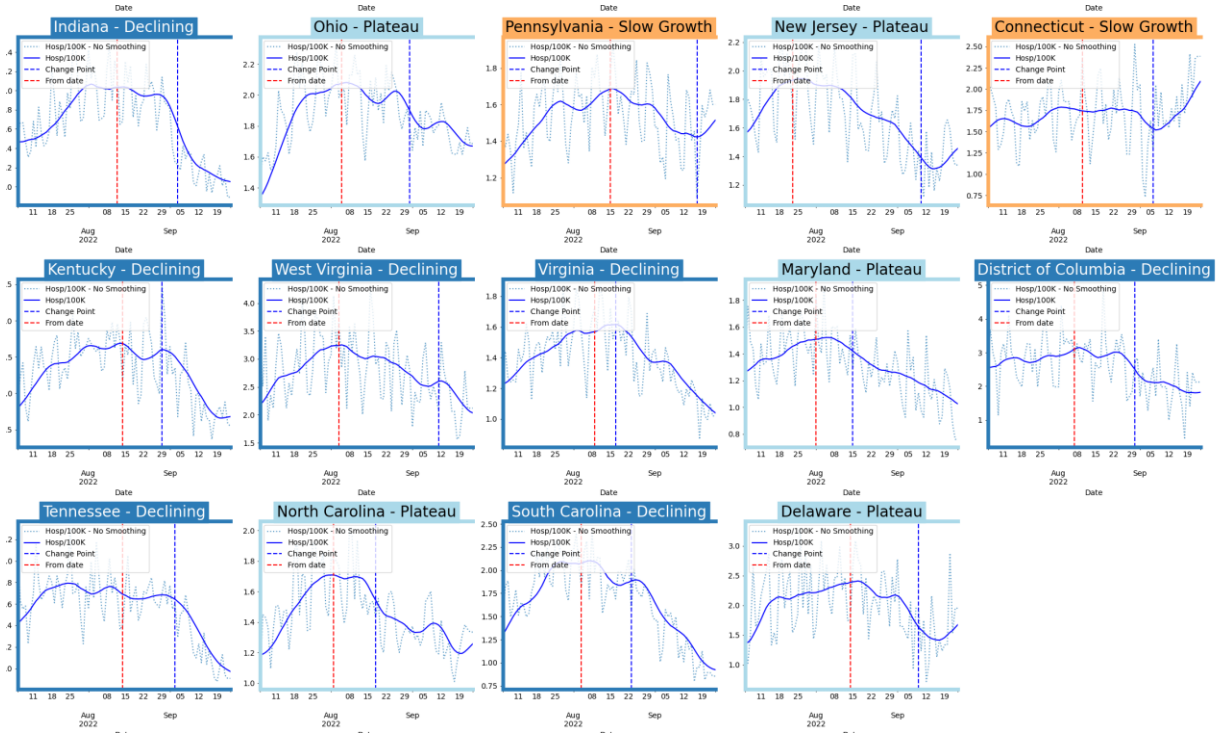
Status	Number of States	
	Current Week	Last Week
Declining	22	(35)
In Surge	1	(0)
Plateau	23	(12)
Slow Growth	7	(6)

Virginia and Her Neighbors

Cases

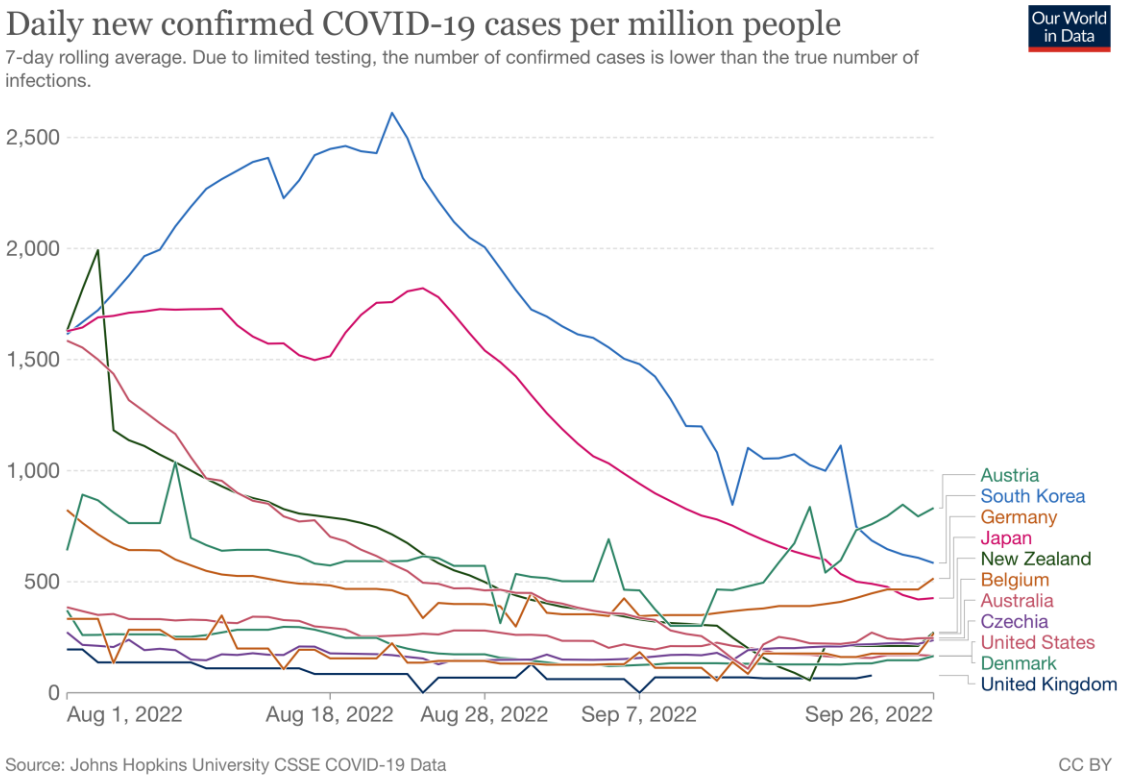


Hospitalizations

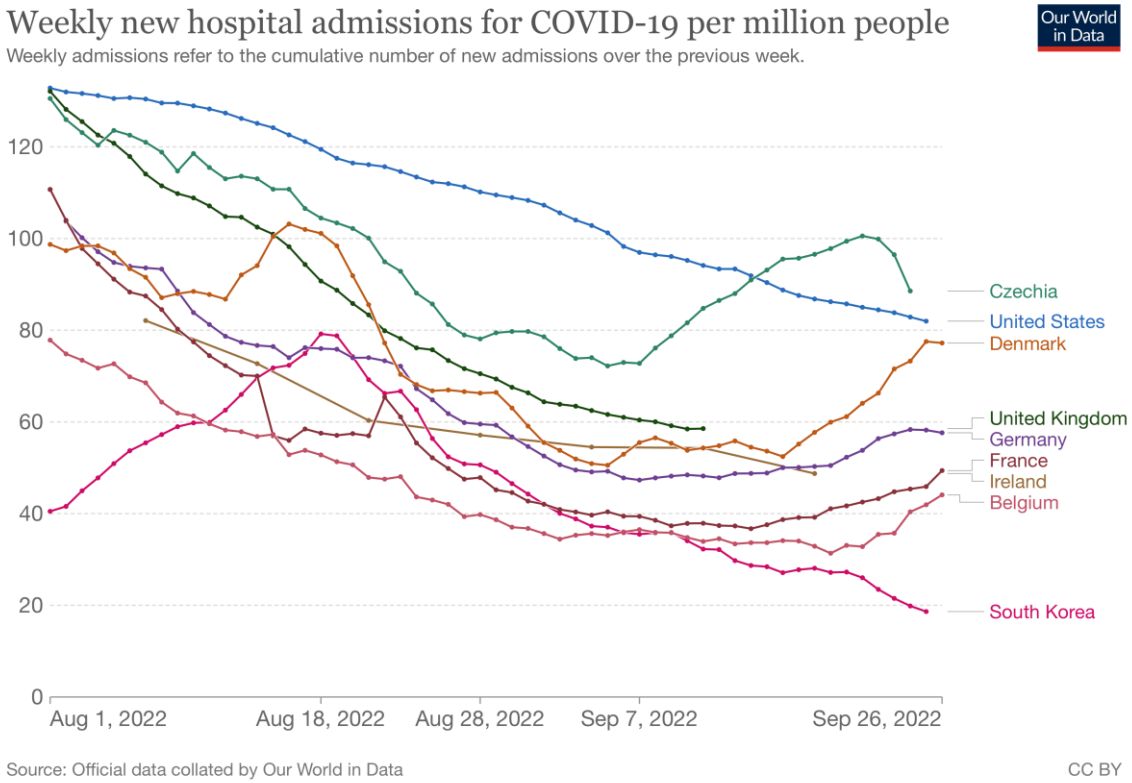


Around the World – Various trajectories

Confirmed cases



Hospitalizations



[Our World in Data]

Using Ensemble Model to Guide Projections

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

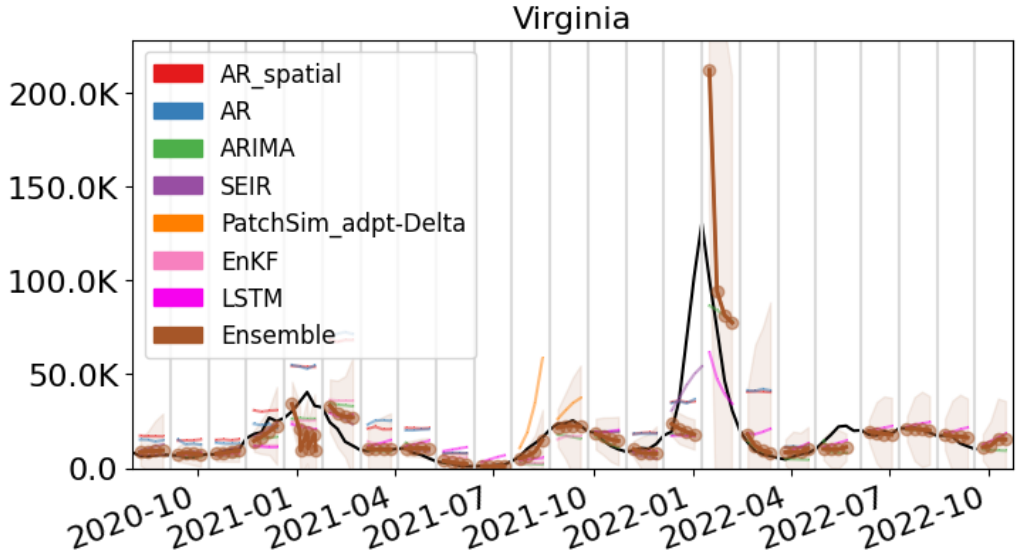
- Autoregressive (AR, ARIMA)
- Neural networks (LSTM)
- Kalman filtering (EnKF)

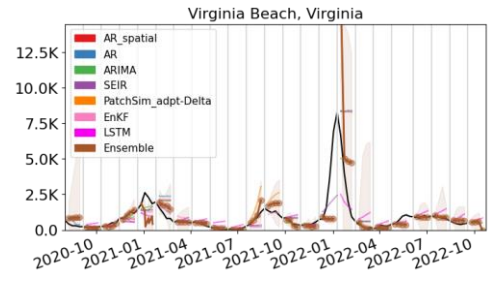
<u>Weekly forecasts</u> done at county level.

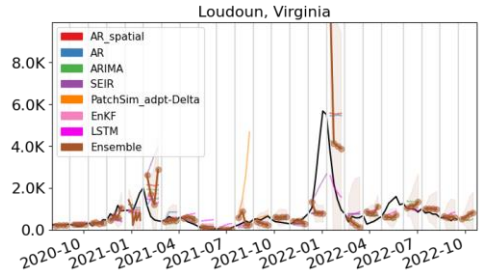
Models chosen because of their track record in disease forecasting and to increase diversity and robustness.

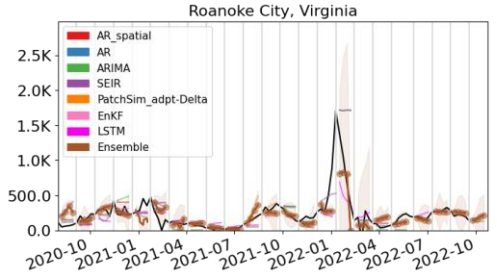
Ensemble forecast provides additional ‘surveillance’ for making scenario-based projections.

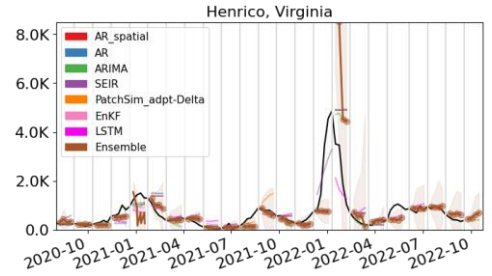
Also submitted to CDC Forecast Hub.







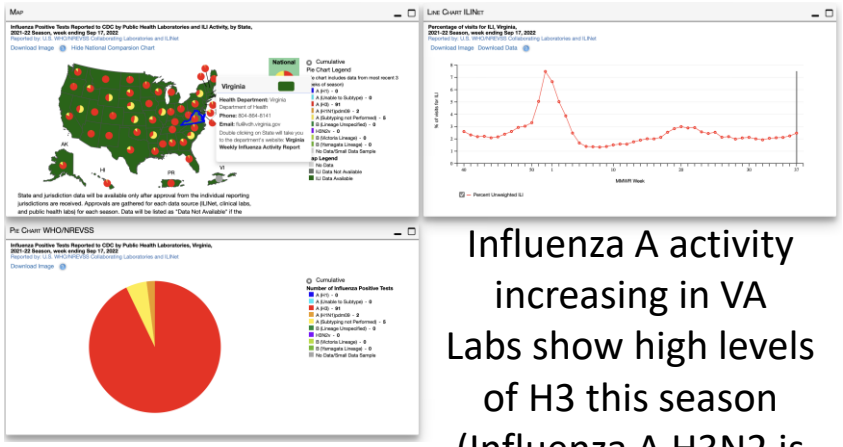




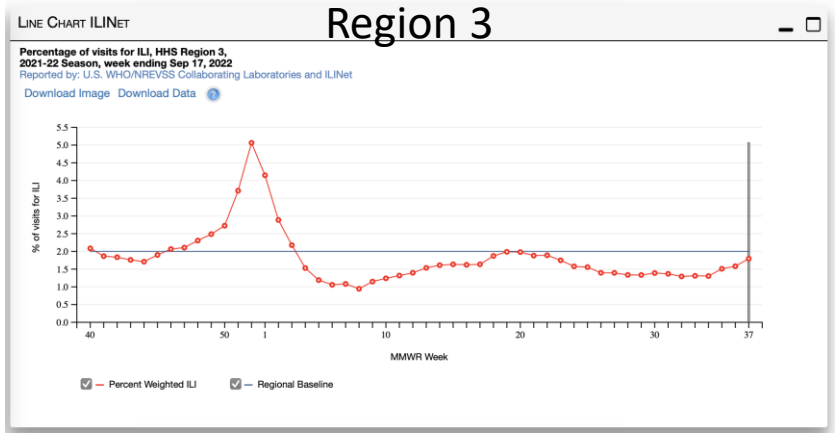
Current Influenza Hospitalization Forecast

Statistical models for submitting to CDC FluSight forecasting challenge

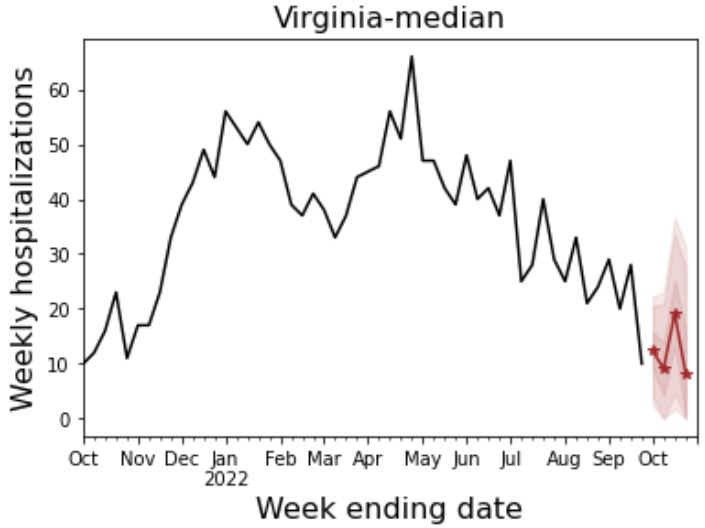
- Similar to COVID-19 case forecasts, uses a variety of statistical and ML approaches to forecast weekly hospital admissions for the next 4 weeks for all states in the US

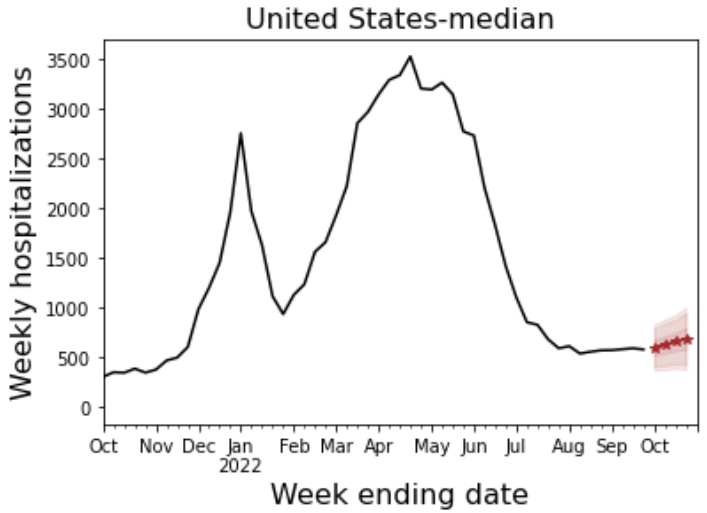


Influenza A activity increasing in VA
Labs show high levels of H3 this season (Influenza A H3N2 is more severe)



Hospital Admissions for Influenza and Forecast for next 4 weeks (UVA ensemble)



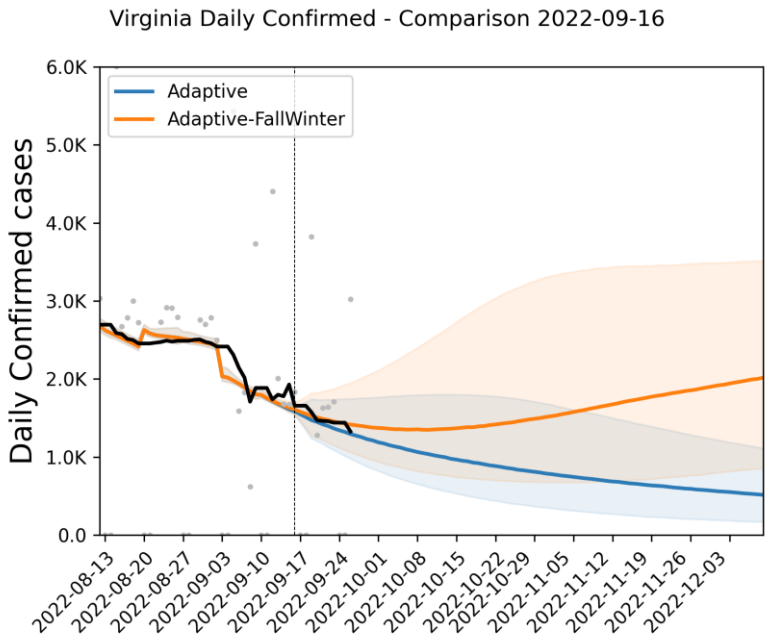


Initial forecasts have wide uncertainty due to noisiness in data due to low numbers of hospitalizations

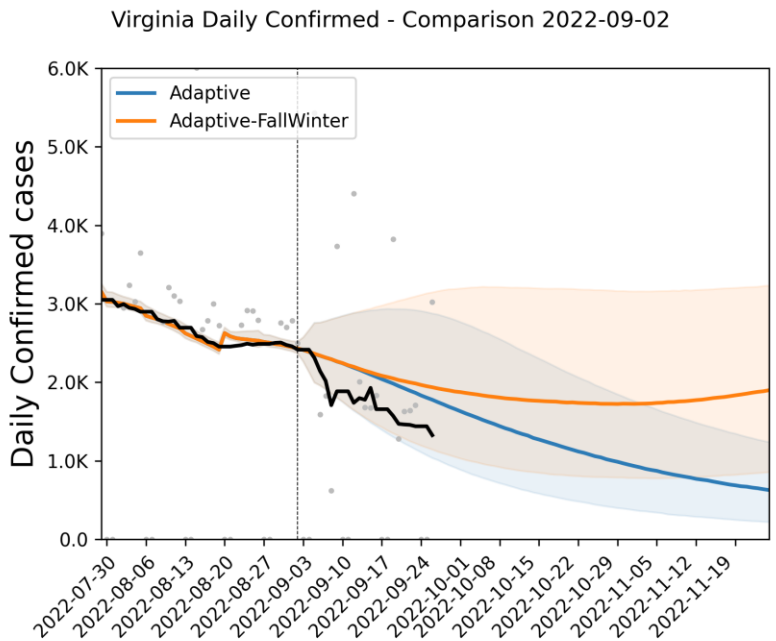
Previous projections comparison - Cases

- Previous projections continue to track observed cases
- Projection from 2 weeks ago projected continued decline but cases plateaued
- Projection from 4 weeks ago projected slower decline better capturing recent plateau

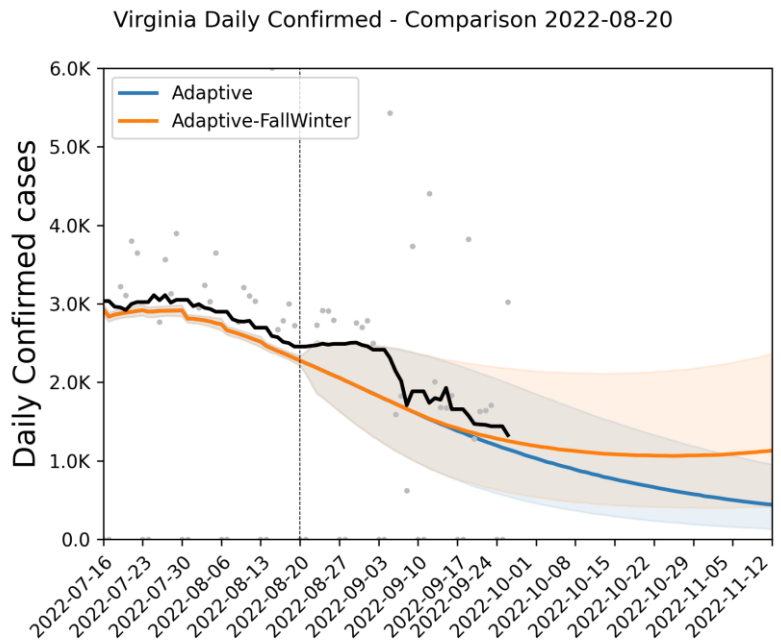
Projection from 1 weeks ago



Projection from 3 weeks ago



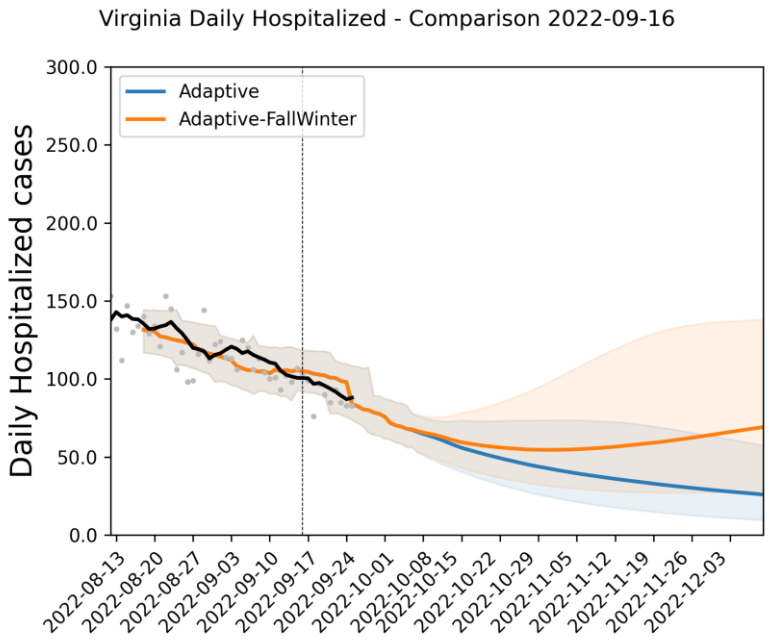
Projection from 5 weeks ago



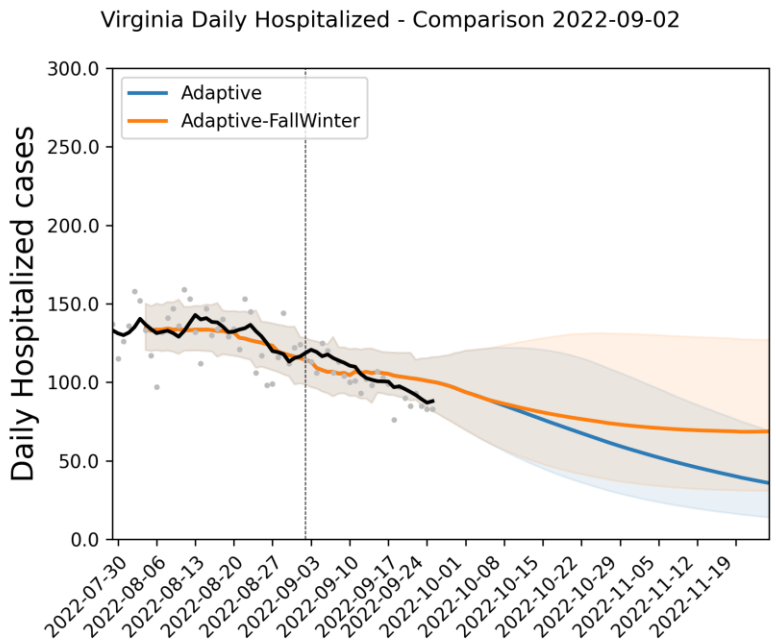
Previous projections comparison - Hospitalizations

- Previous projections have tracked observed hospitalizations well
- Projection from 2 weeks ago projected continued decline
- Projection from late July anticipated a plateau giving way to gentle decline

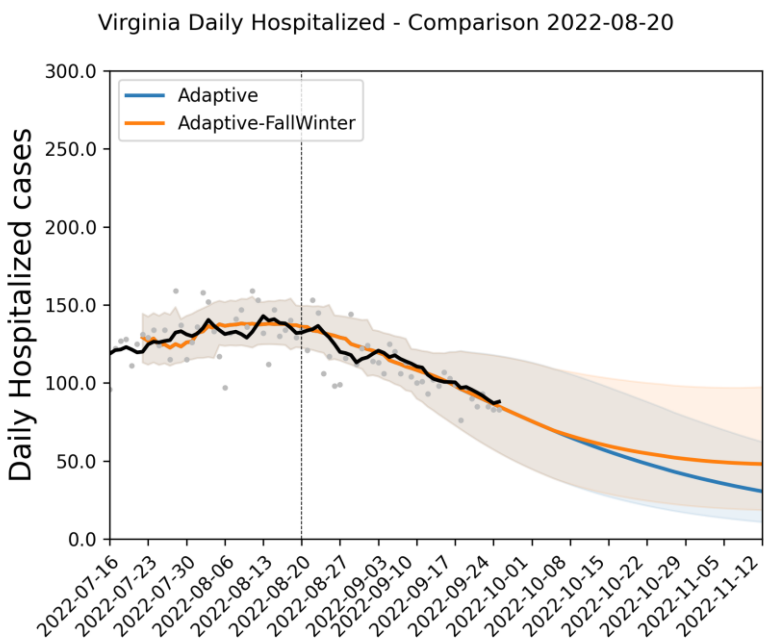
Projection from 1 weeks ago



Projection from 3 weeks ago



Projection from 5 weeks ago

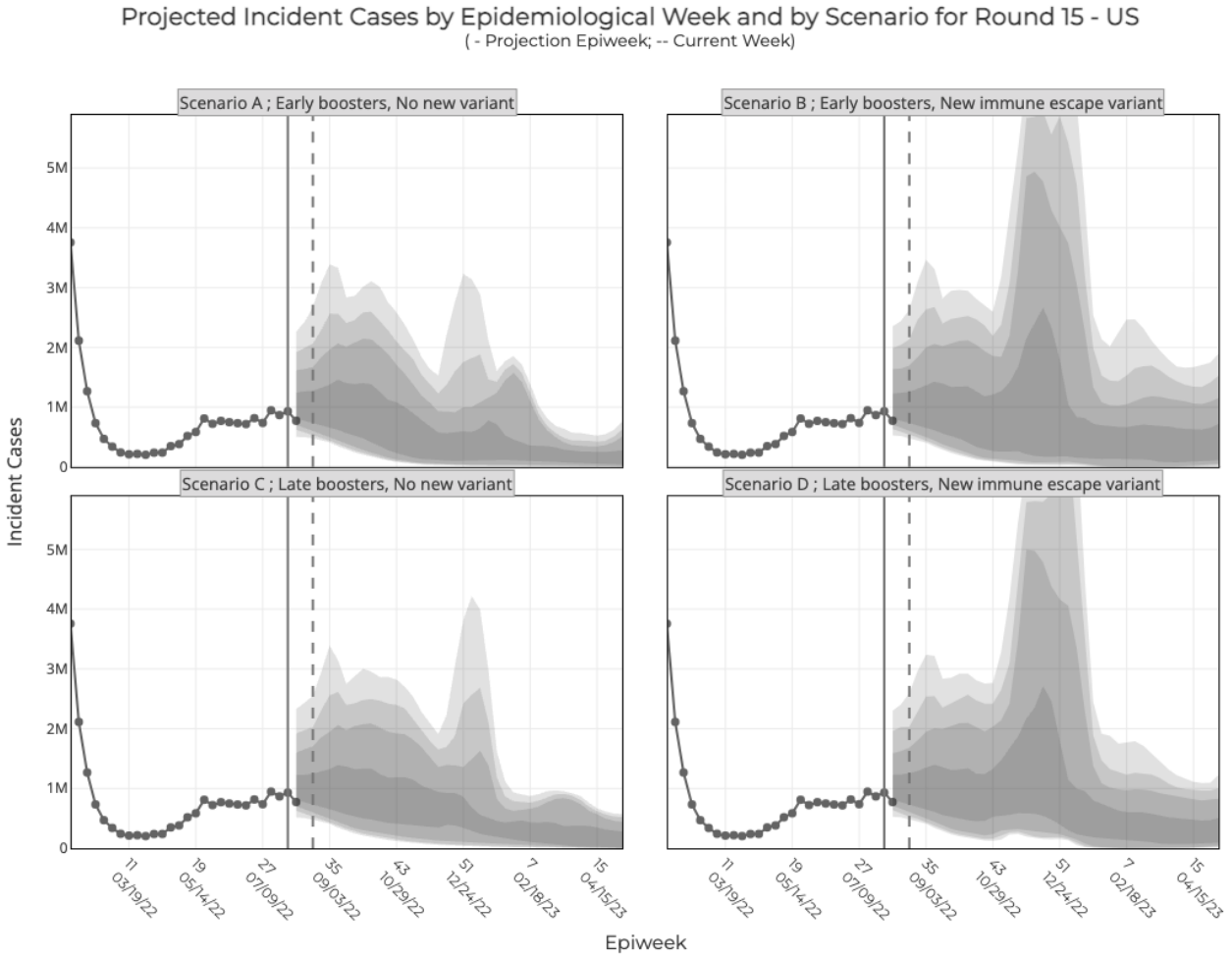


Scenario Modeling Hub – COVID-19 (Rd15), Flu (Rd1)

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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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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