Network Systems Science & Advanced Computing

Biocomplexity Institute & Initiative

University of Virginia

Foresight and Analysis of Infectious Disease Threats to Virginia's Public Health

August 10th, 2023

(data current to July 29th – Aug 8th)

Biocomplexity Institute Technical report: TR BI-2023-233

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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 current and emerging Infectious Disease threats to the Commonwealth of Virginia using modeling and analytics

- **Approach:**
  - Provide analyses and summaries of current infectious disease threats
  - Survey existing forecasts and trends in these threats
  - Analyze and summarize the current situation and trends of these threats in the broader context of the US and world
  - Provide broad overview of other emerging threats

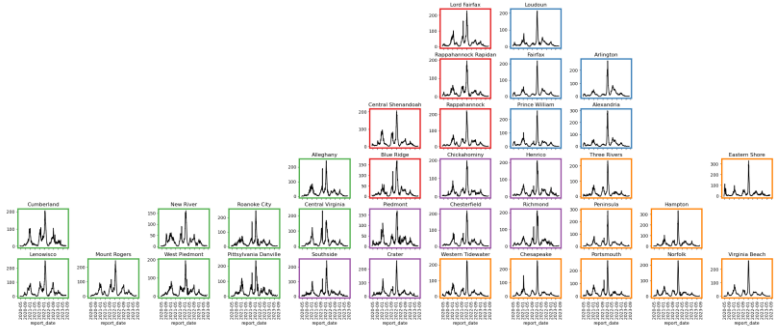
Key Takeaways

- Upticks in cases and hospitalizations hint at a late summer wave
- Hospitalizations have increased ~12% in recent week from prolonged plateau
- Other indicators from wastewater, ED visits show sustained growth through July
- Genomic surveillance hinting at the possible role of EG.5

- Literature review: Recent publications using wastewater surveillance
- National modeling updates

COVID-19 Surveillance

Case Rates (per 100k)



Whole pandemic

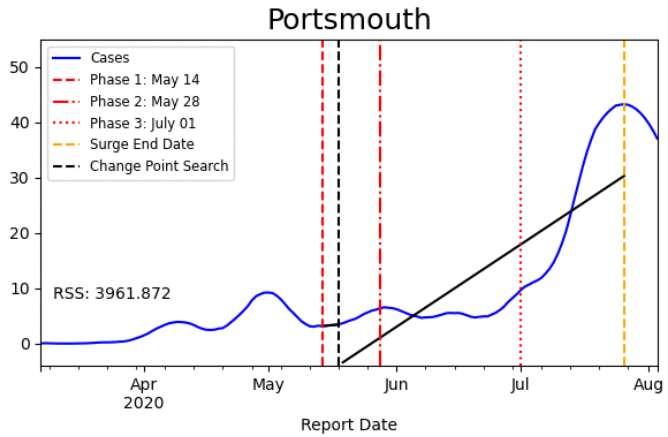
Since December 2021

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

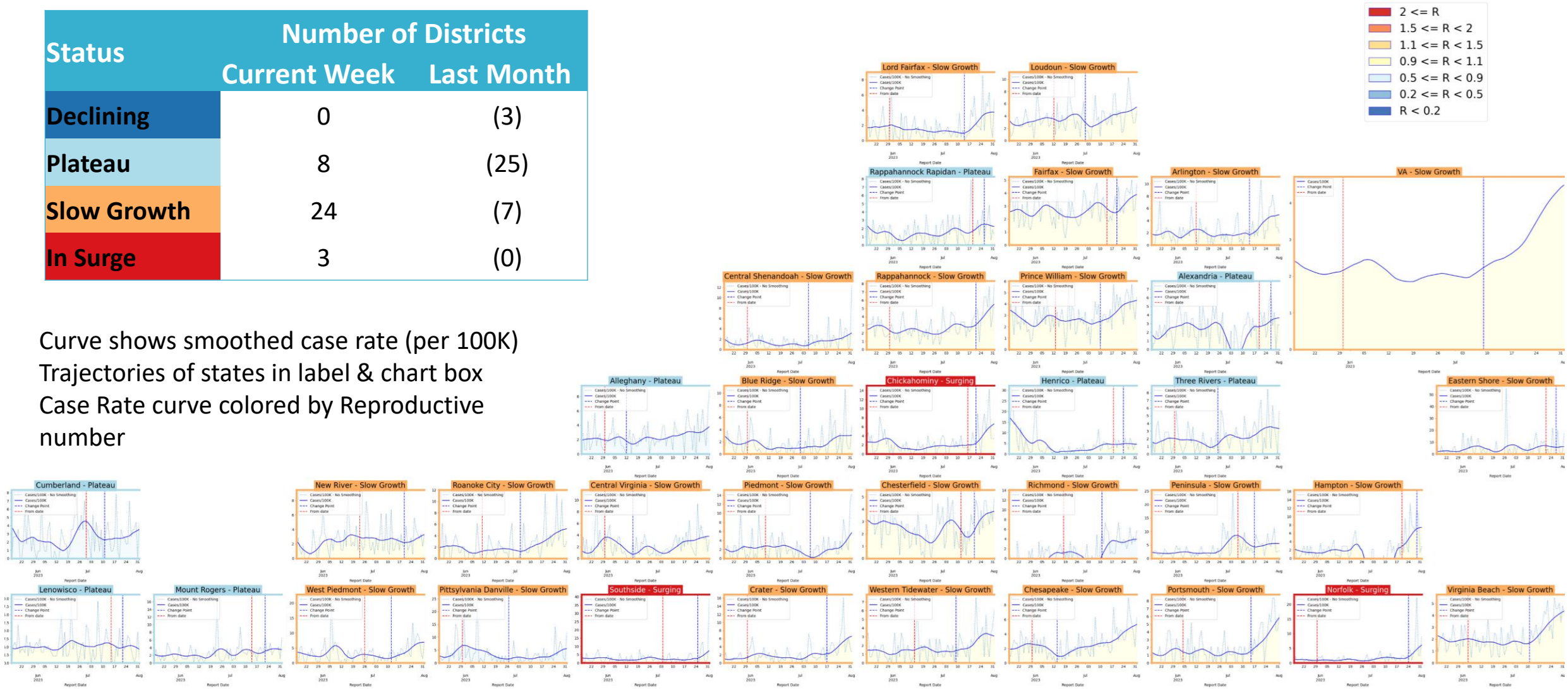


Trajectory	Description	Weekly Case Rate Slope (per 100k)	Weekly Hosp Rate Slope (per 100k)
Declining	Sustained decreases following a recent peak	slope < -0.88/day	slope < -0.07/day
Plateau	Steady level with minimal trend up or down	-0.88/day < slope < 0.42/day	-0.07/day < slope < 0.07/day
Slow Growth	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 Month
Declining	0	(3)
Plateau	8	(25)
Slow Growth	24	(7)
In Surge	3	(0)

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



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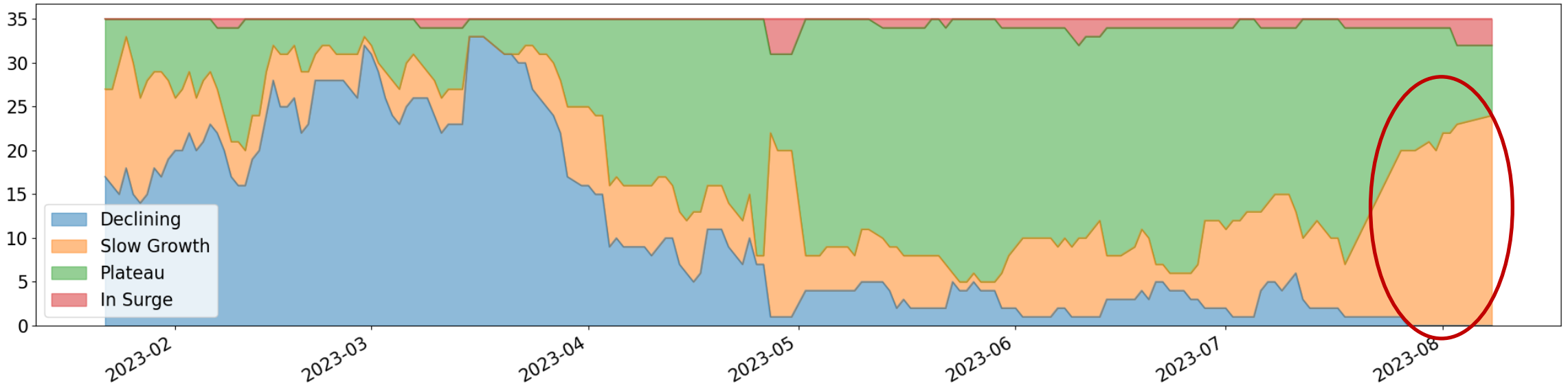
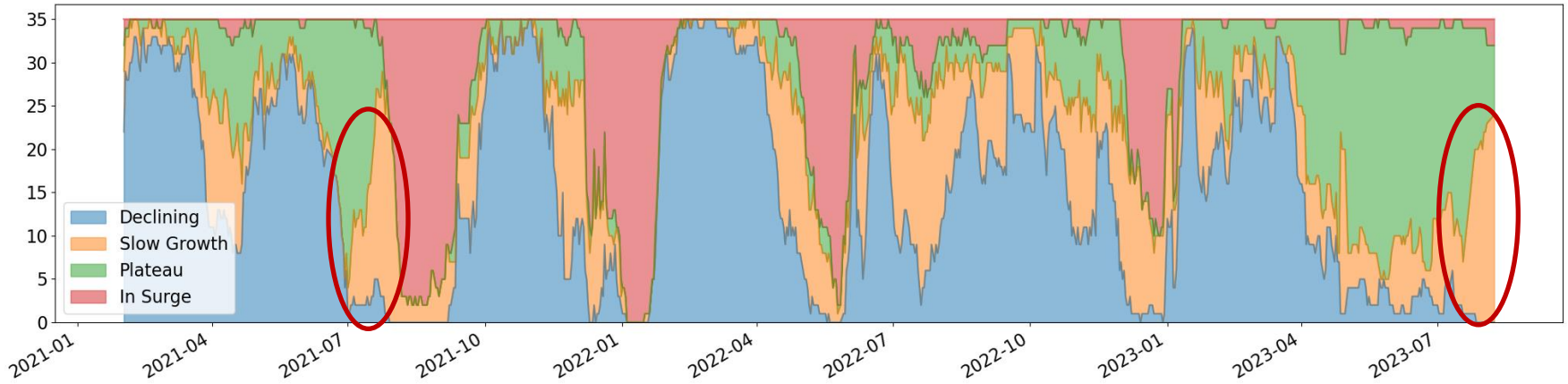
District Case Trajectories – Recent 6 months





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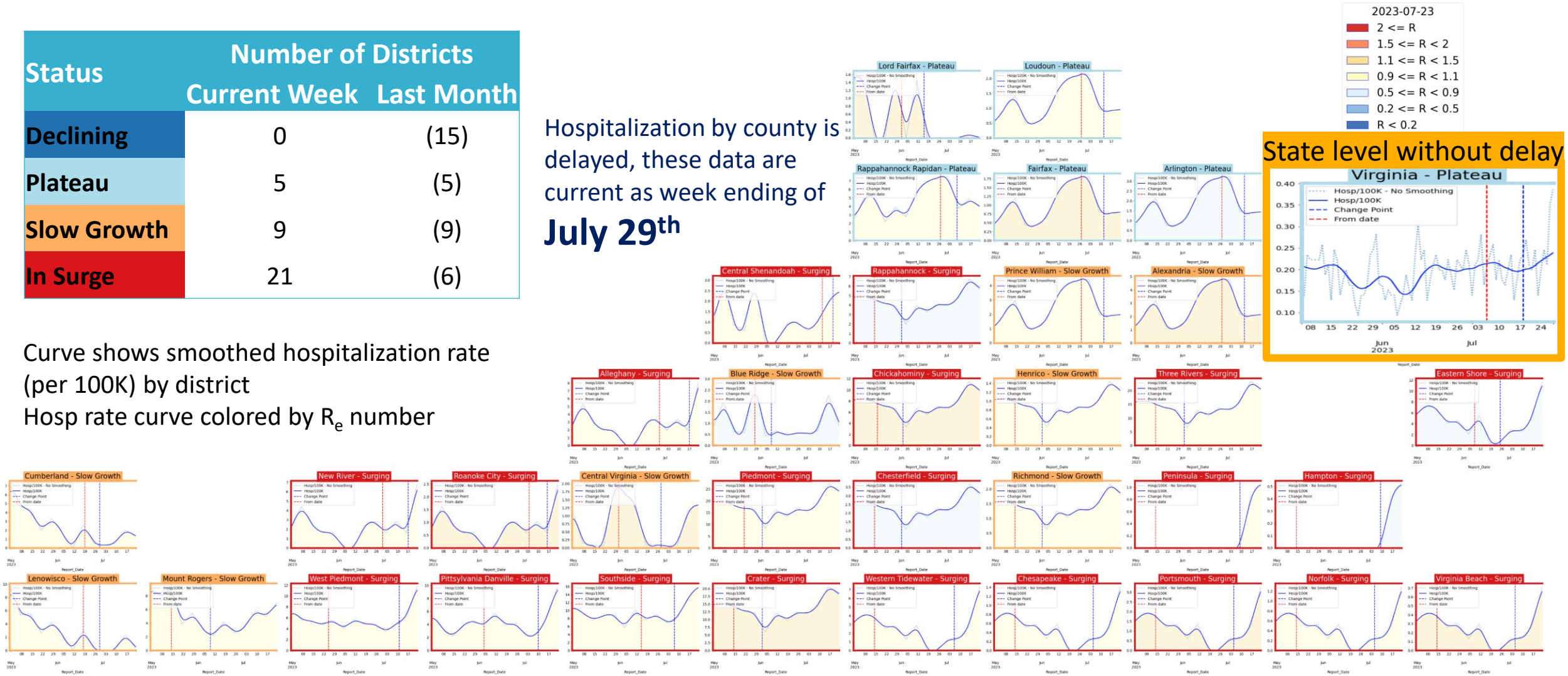
District Hospital Trajectories – last 10 weeks

Status	Number of Districts	
	Current Week	Last Month
Declining	0	(15)
Plateau	5	(5)
Slow Growth	9	(9)
In Surge	21	(6)

Hospitalization by county is delayed, these data are current as week ending of **July 29th**

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



State level without delay

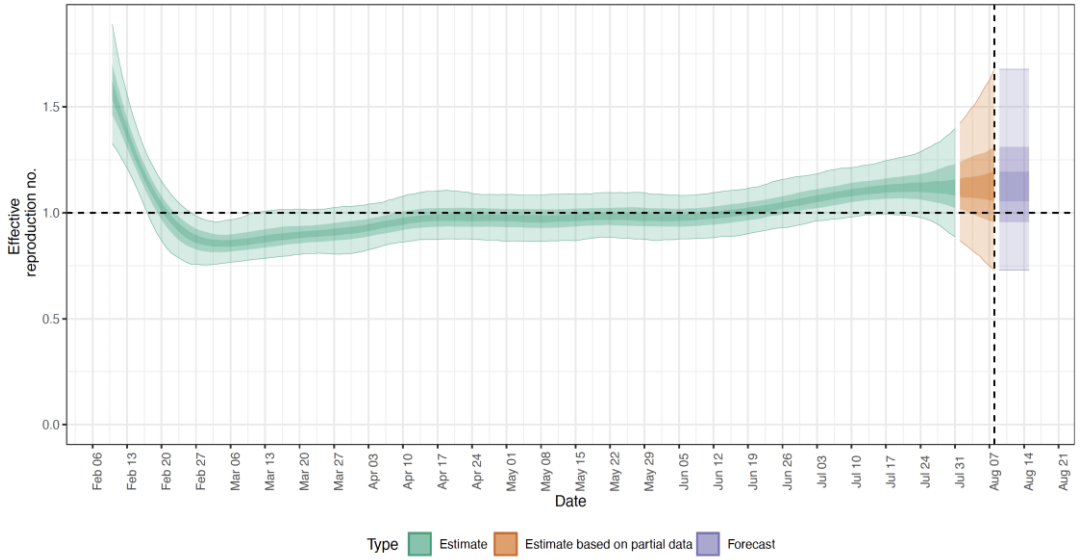
COVID-19 Growth Metrics

Estimating Daily Reproductive Number –
VDH report dates – EpiNow2 estimation

August 8th Estimates

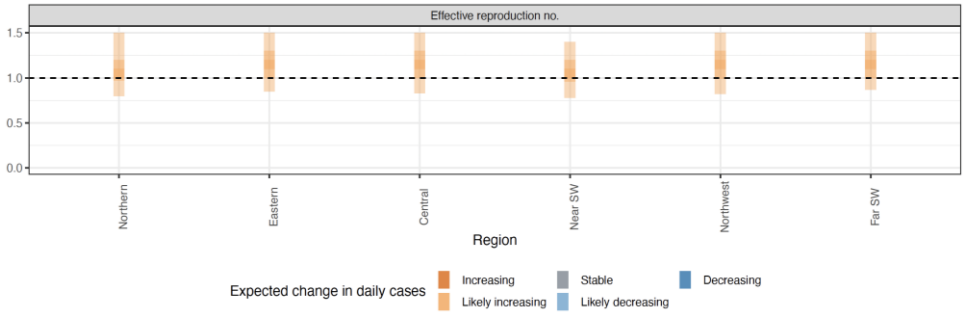
Region	Reproductive number estimate	Confidence interval	Trend forecast
State-wide cases	1.10	0.73 - 1.7	Likely increasing
State-wide hosp	1.00	0.95 - 1.1	Likely increasing
Central	1.10	0.84 - 1.5	Likely increasing
Eastern	1.10	0.85 - 1.5	Likely increasing
Far SW	1.10	0.88 - 1.5	Likely increasing
Near SW	1.10	0.79 - 1.5	Likely increasing
Northern	1.10	0.81 - 1.4	Likely increasing
Northwest	1.10	0.87 - 1.4	Likely increasing

R_e from VDH Cases (last 6 months)



Methodology

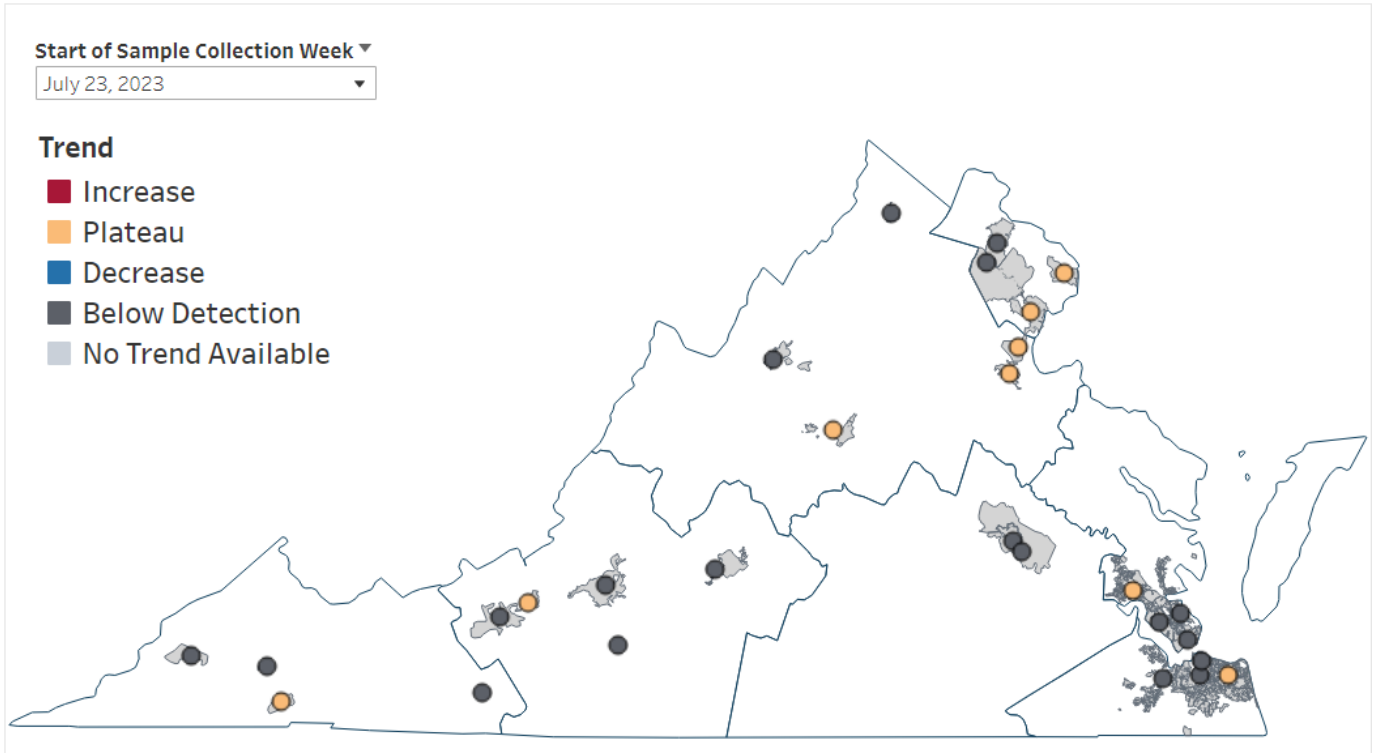
- Time-varying reproduction number estimates on cases by estimated date of infection produced by EpiNow2 for R.
- Uncertainty is propagated from all inputs into the final parameter estimates, helping mitigate spurious findings.
- Sam Abbott, Joel Hellewell, Katharine Sherratt, Katelyn Gostic, Joe Hickson, Hamada S. Badr, Michael DeWitt, Robin Thompson, EpiForecasts, Sebastian Funk (2020). **EpiNow2**: Estimate Real-Time Case Counts and Time-Varying Epidemiological Parameters. doi:10.5281/zenodo.3957489.
- **Note: Estimates based on past 6 months of data; most recent data point for hospitalizations is 10 days prior to that of cases (HHS hospitalization through 7/29/23 vs. VDH case data through 8/8/23).**

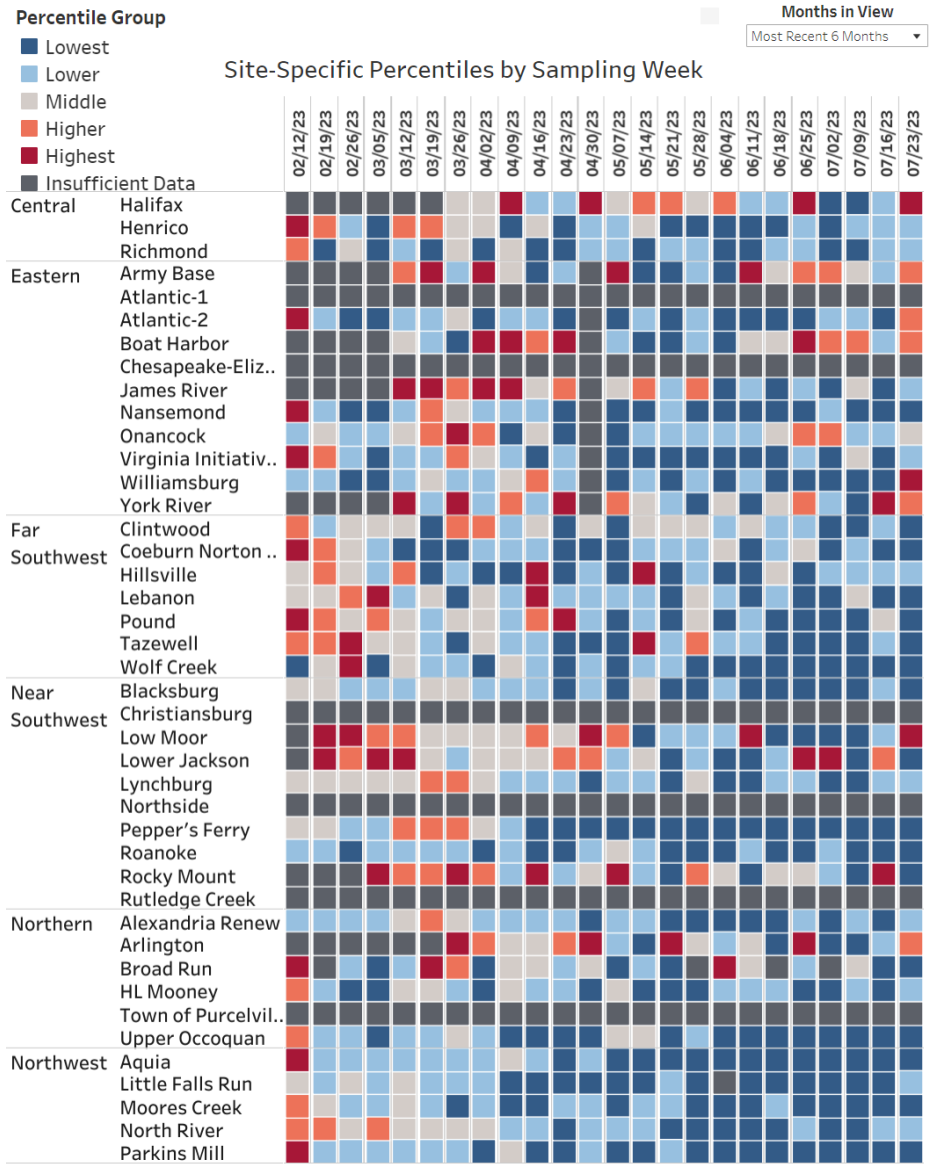


EpiNow2 home: https://epiforecasts.io/EpiNow2/

VA Wastewater Data Update

Multiple sites in the Eastern region in the top two percentile groups





[VDH COVID-19 Wastewater Surveillance]

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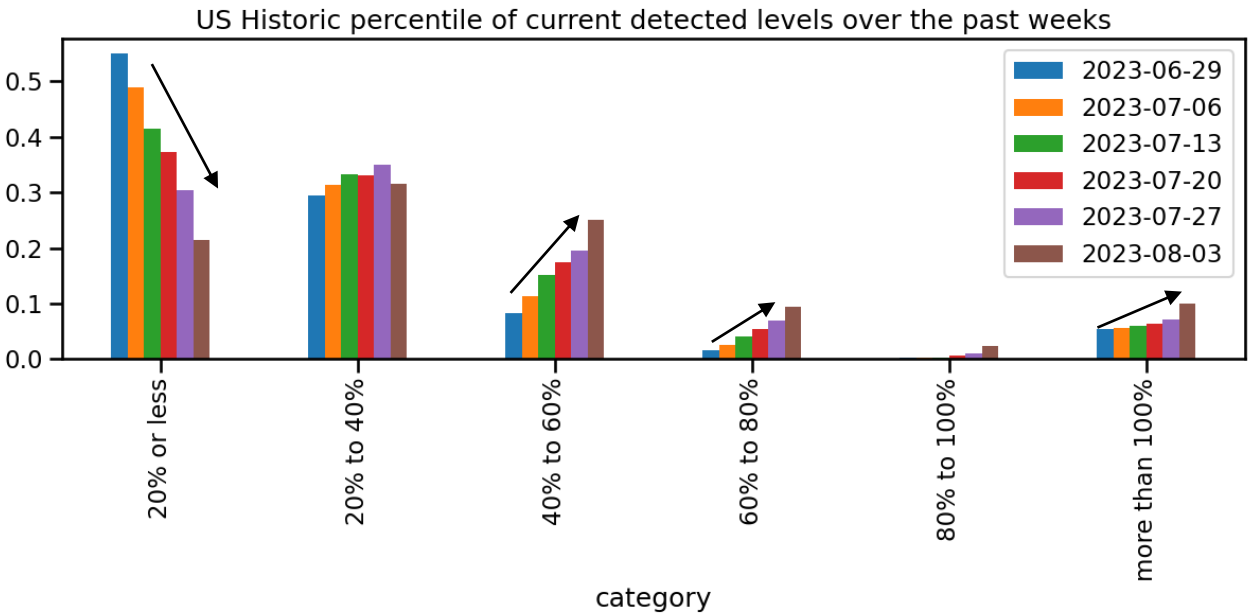
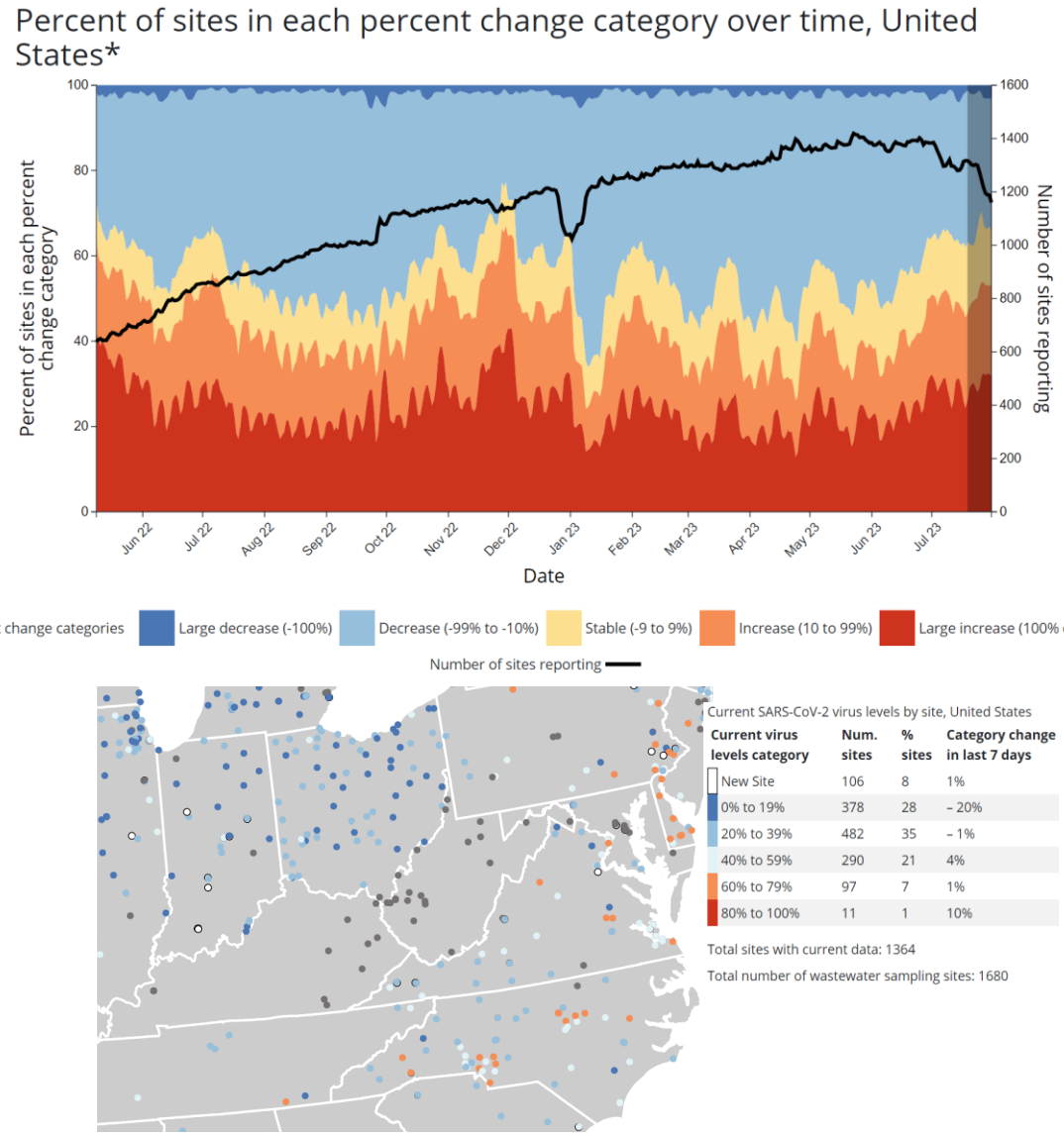
US Wastewater Monitoring

Wastewater provides a coarse estimate of COVID-19 levels in communities and can be a good indicator of activity levels

Increasing percent of sites in the higher trend categories



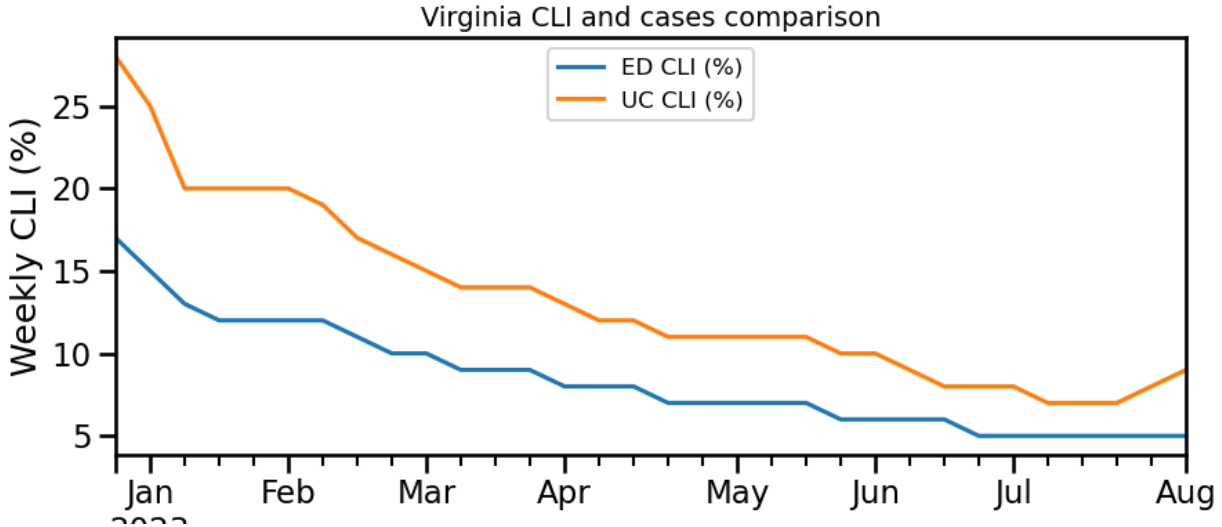


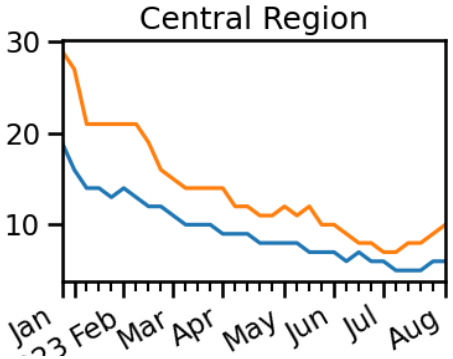
COVID-19 Severity Metrics

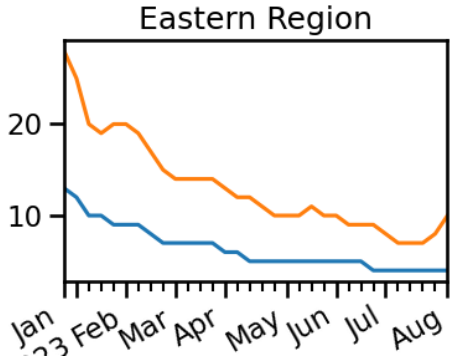
COVID-like Illness Activity

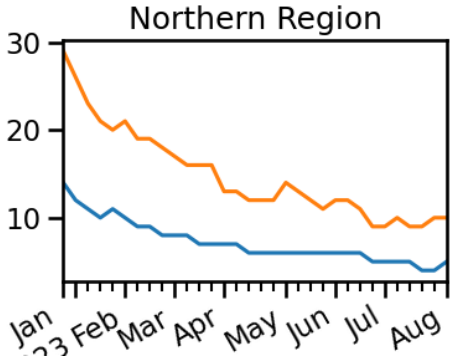
COVID-like Illness (CLI) gives a measure of COVID transmission in the community

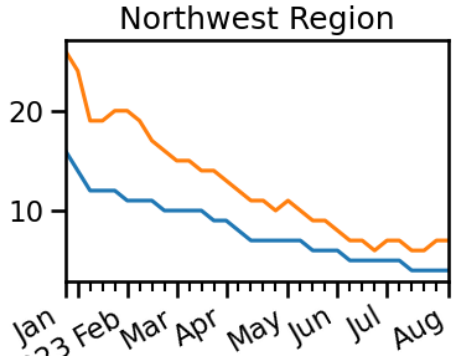
- Emergency Dept (ED) based CLI is more correlated with case reporting
- Urgent Care (UC) is a leading indicator but may be influenced by testing for other URIs
- Beginning to see upticks in UC CLI(%) especially in Central and Eastern Regions

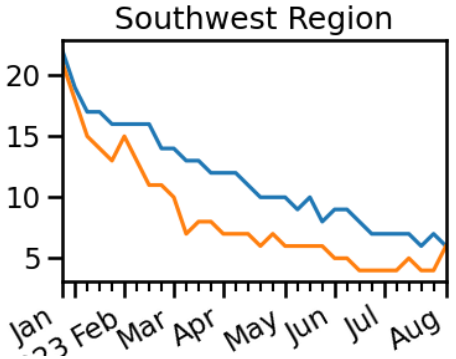








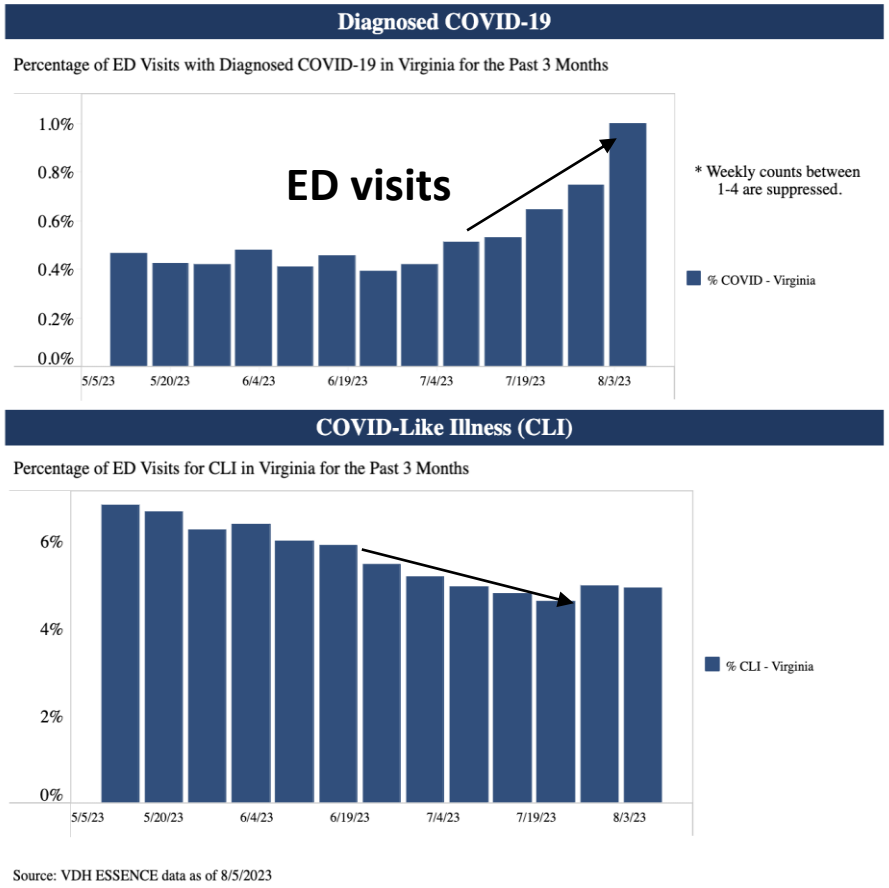


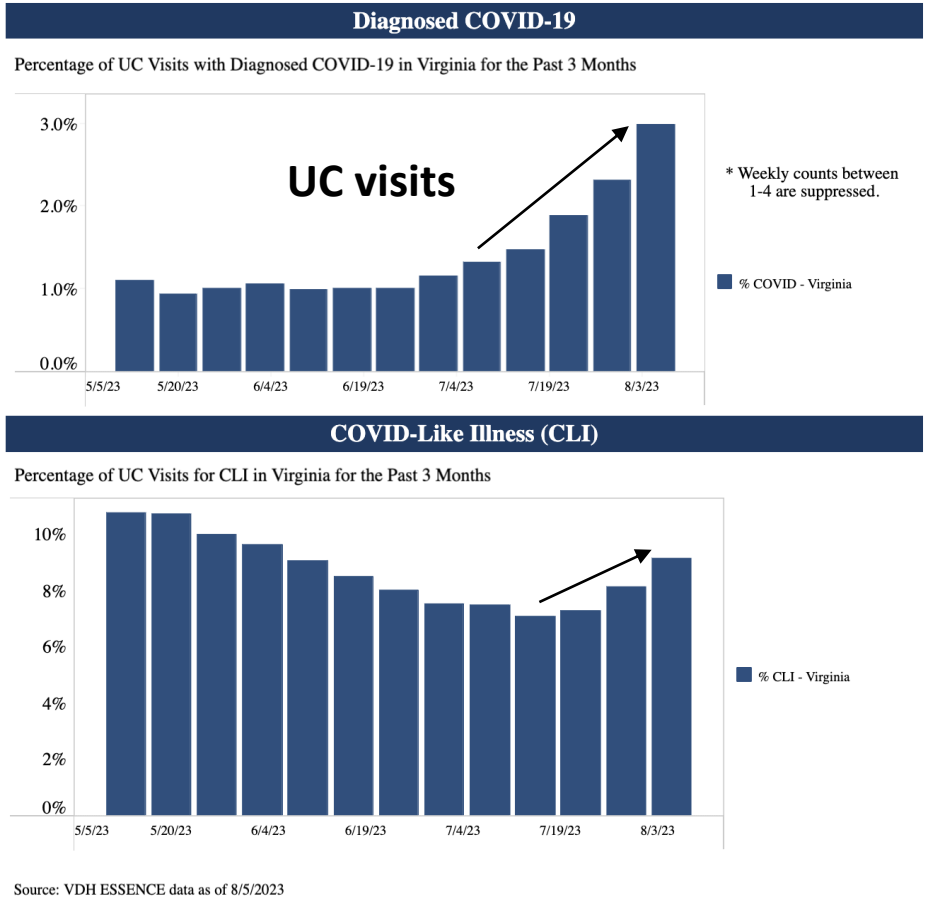


Diagnosed with COVID-19 in ED and UC visits

% of ED visits with Diagnosed COVID-19 showing sustained trend over the past month

https://www.vdh.virginia.gov/coronavirus/see-the-numbers/covid-19-data-insights/covid-like-illness-visits/





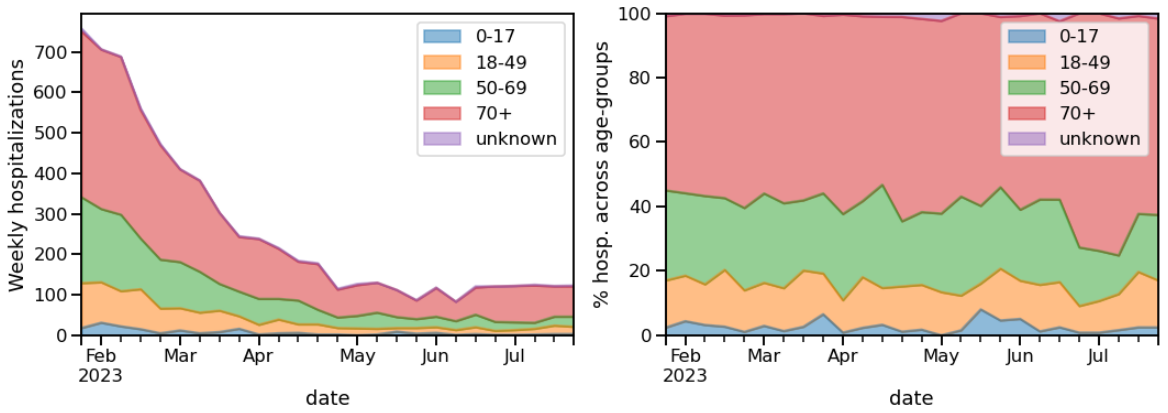
Hospitalizations in VA by Age

Age distribution in hospitals relatively stable

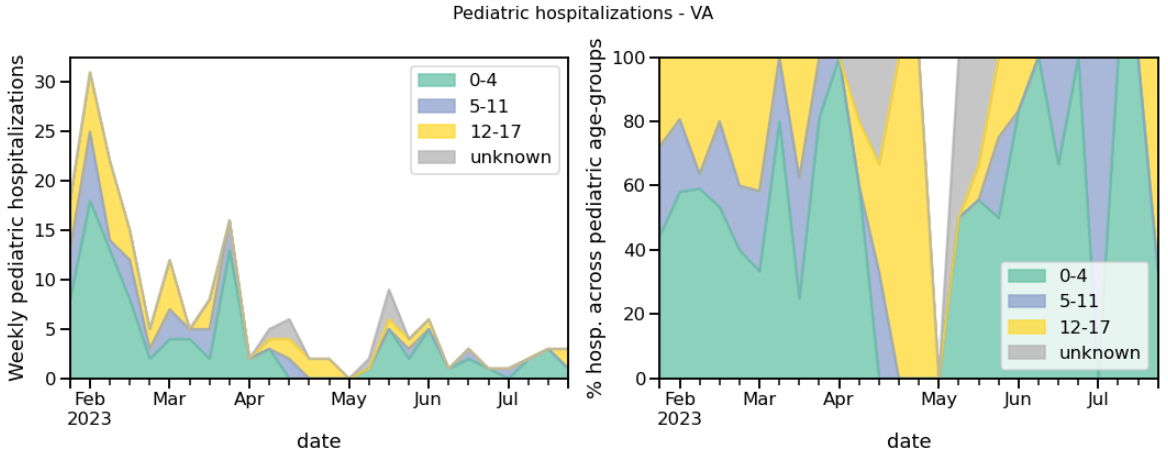
- Pediatric hospitalizations level off after uptick last week
- Nearly 60% of hospitalizations are occurring in the 70+ population

Note: These data are lagged and based on HHS hospital reporting

Virginia Hospitalizations by Age (all ages)

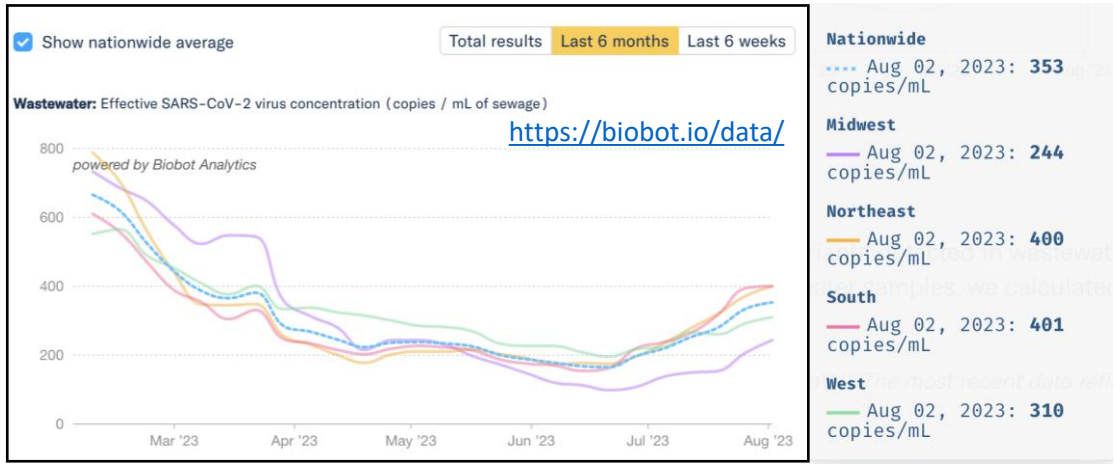


Pediatric Hospitalizations by Age (0-17yo)

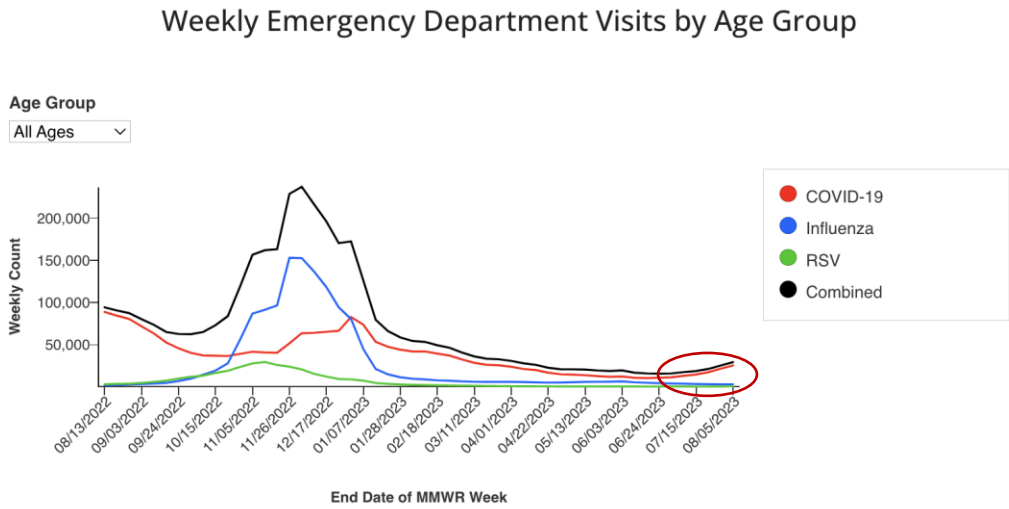


Data Source: Delphi and HHS

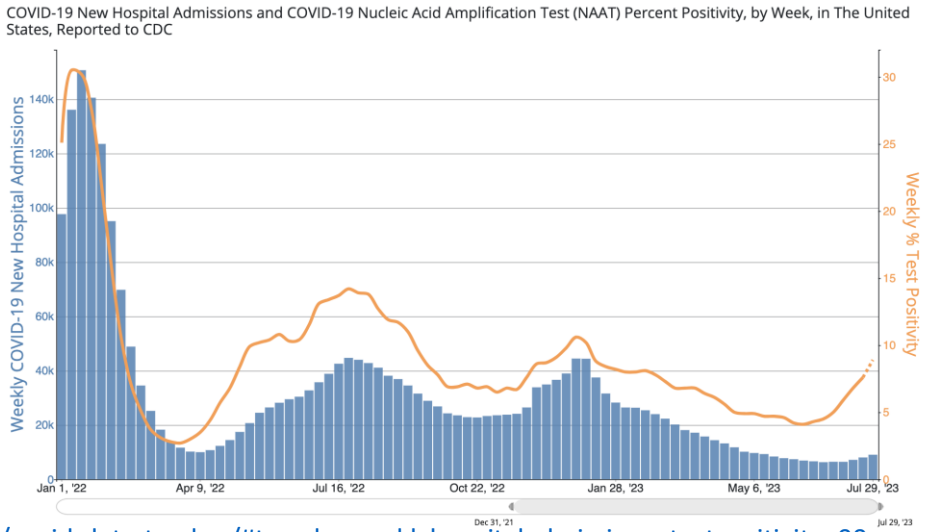
Wastewater, ED visits, and Test positivity



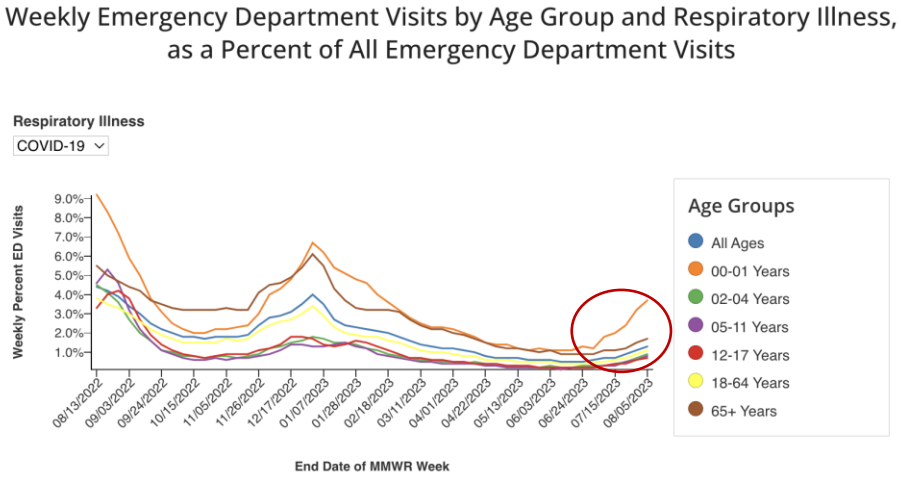
https://biobot.io/data/



- All three signals show sustained growth trends since July 2023
- National testing volumes reported to CDC have shrunk from 275k/day (July 2022) to 30k/day



https://covid.cdc.gov/covid-data-tracker/#trends_weeklyhospitaladmissions_testpositivity_00



https://www.cdc.gov/ncird/surveillance/respiratory-illnesses/index.html

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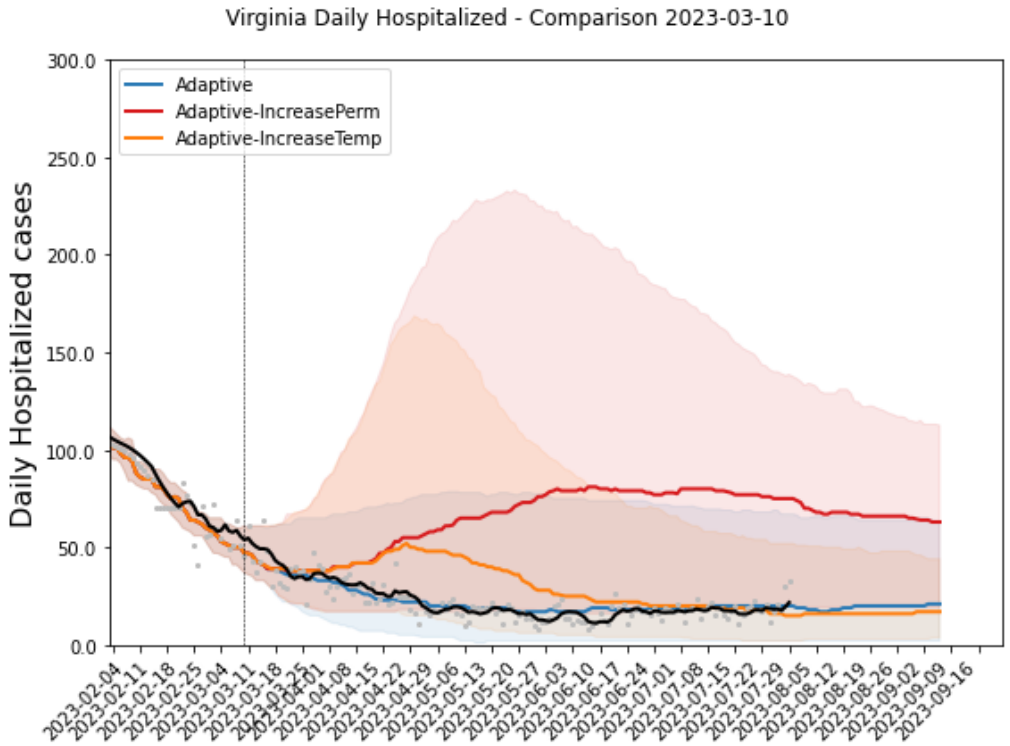
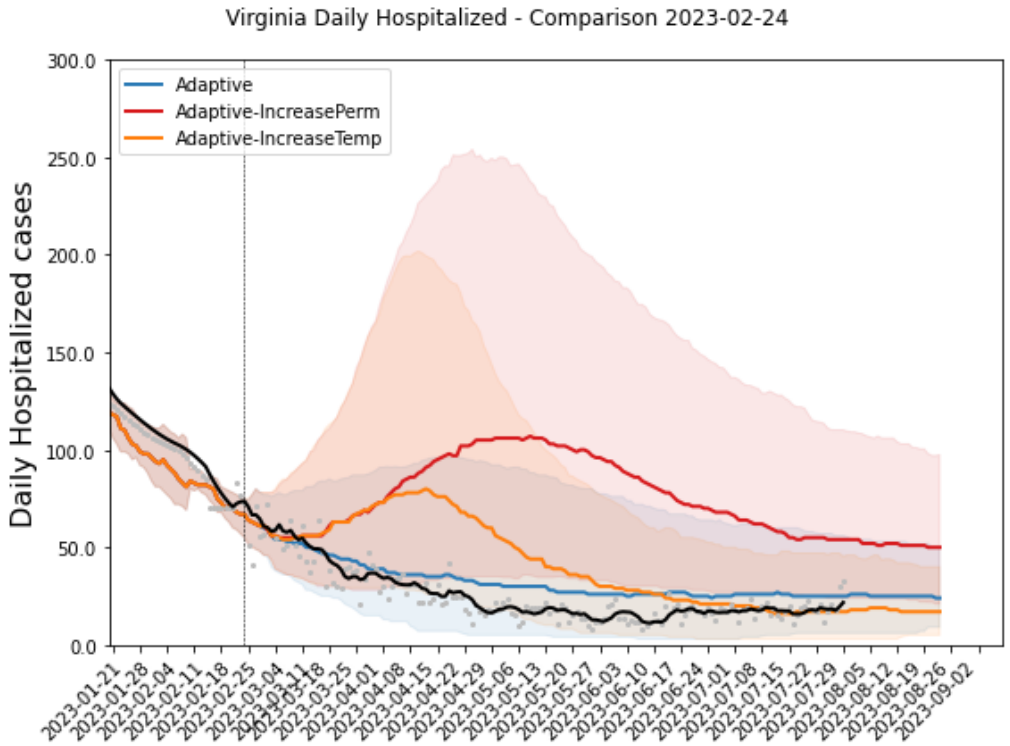
Past projections – Hospitalizations

- Projections mostly tracked the plateau phase since March 10th
- Slight deviations noticeable from projections 5 months ago

Previous round – 22 weeks ago



Previous round –20 weeks ago



COVID-19 Spatial Epidemiology

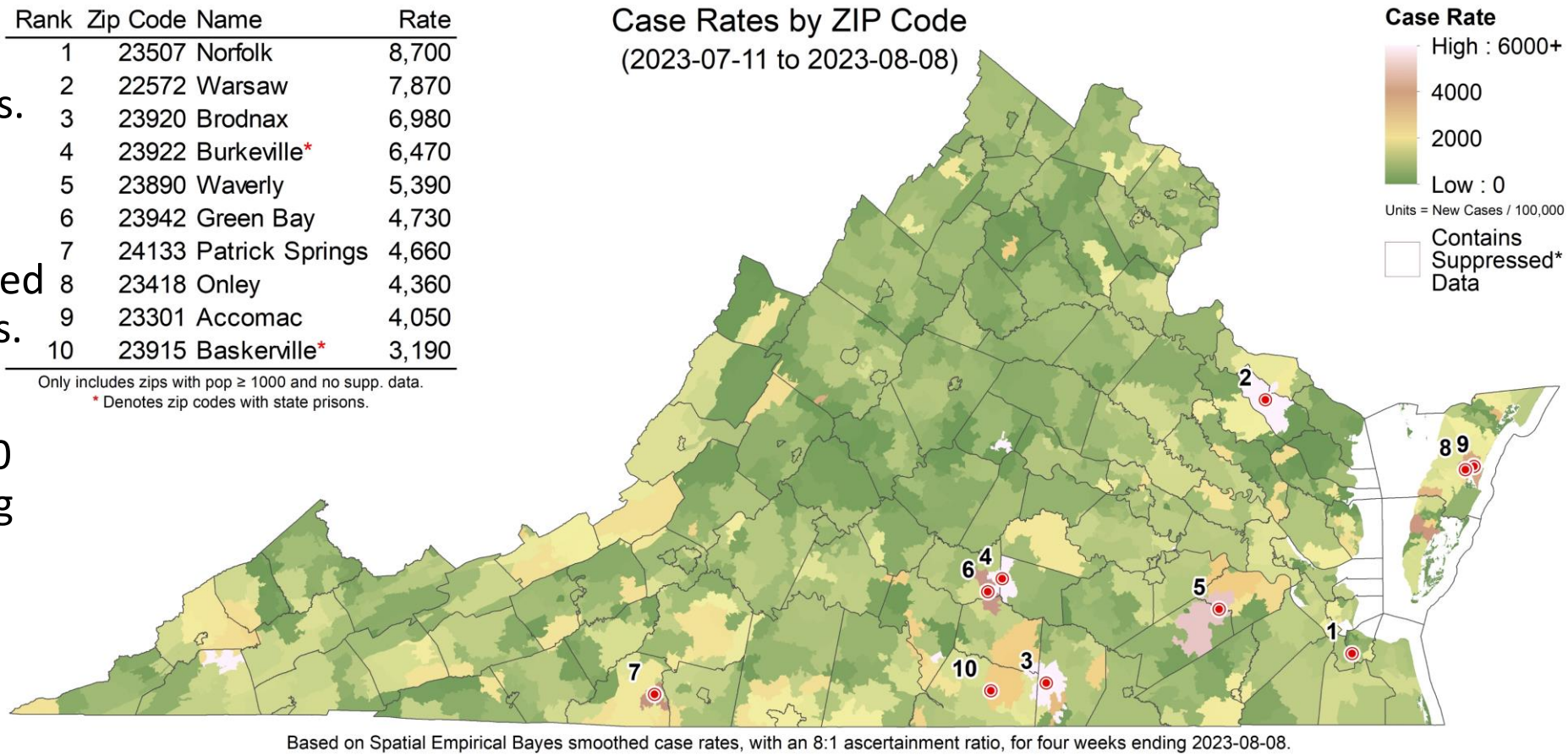
ZIP Code level case rate per 100K over last four weeks

New cases per 100k in the last fortnight by ZIP code

- Statewide COVID19 case rates have grown since early July, but remain low relative to past surges.
- Divide rates by four to calculate average weekly incidence. Norfolk averaged 2,175 / 100k weekly cases.
- Nassawadox has finally dropped out of the top 10 after two months of being near number 1.
- Burkeville and Baskerville represent the prison-containing ZIP codes in this week's top 10.

Rank	Zip Code	Name	Rate
1	23507	Norfolk	8,700
2	22572	Warsaw	7,870
3	23920	Brodnax	6,980
4	23922	Burkeville*	6,470
5	23890	Waverly	5,390
6	23942	Green Bay	4,730
7	24133	Patrick Springs	4,660
8	23418	Onley	4,360
9	23301	Accomac	4,050
10	23915	Baskerville*	3,190

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



Based on Spatial Empirical Bayes smoothed case rates, with an 8:1 ascertainment ratio, for four weeks ending 2023-08-08.

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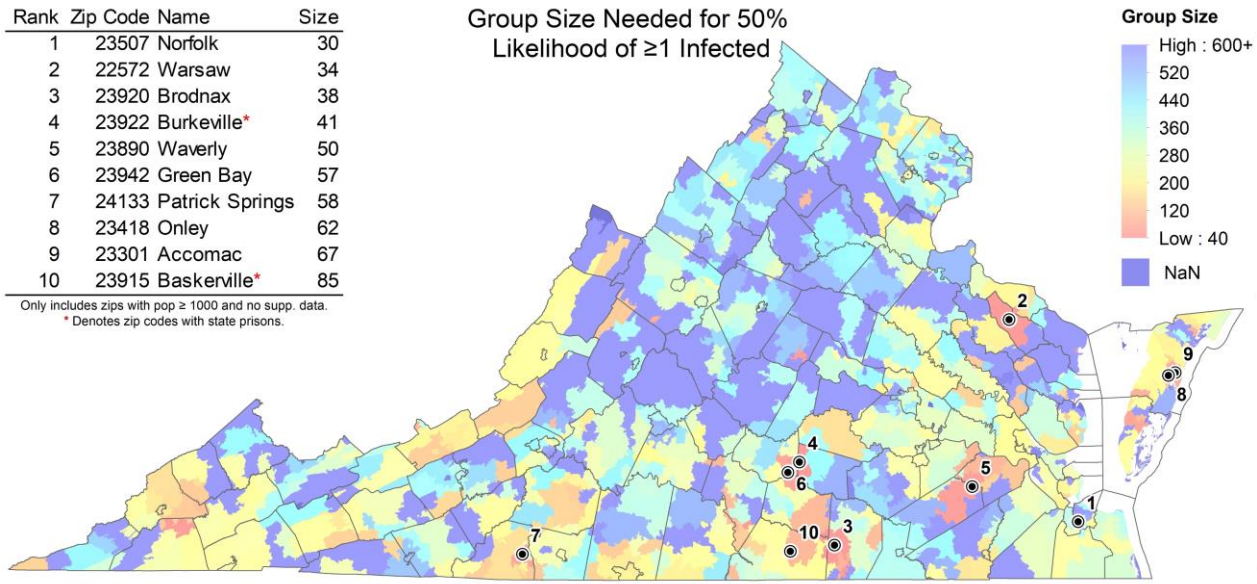
Risk of Exposure by Group Size and HCW prevalence

Case prevalence in the last four weeks by zip code used to calculate risk of encountering someone infected in a gathering of randomly selected people

- **Group Size**: Assumes **8 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 (e.g., in a group of 30 in Norfolk, there is a 50% chance someone will be infected).
- **HCW ratio**: Case rate among health care workers (HCW) in the last four weeks using patient facing health care workers as the numerator / population's case prevalence. High HCW rates are found west of Richmond.

Rank	Zip Code	Name	Size
1	23507	Norfolk	30
2	22572	Warsaw	34
3	23920	Brodnax	38
4	23922	Burkeville*	41
5	23890	Waverly	50
6	23942	Green Bay	57
7	24133	Patrick Springs	58
8	23418	Onley	62
9	23301	Accomac	67
10	23915	Baskerville*	85

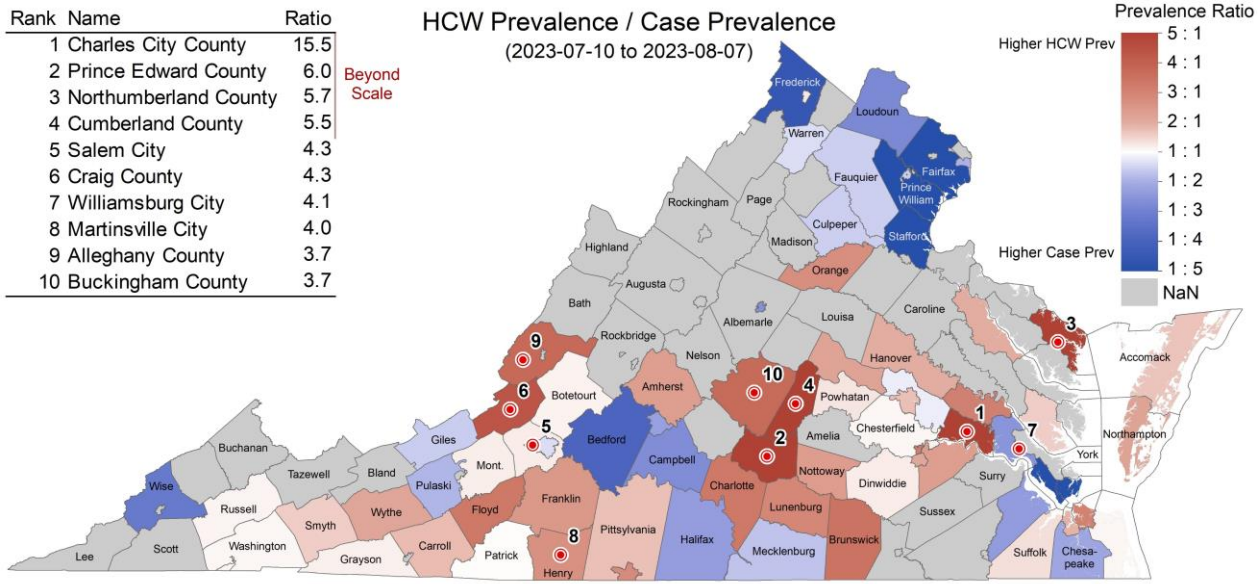
Only includes zips with pop ≥ 1000 and no supp. data.
* Denotes zip codes with state prisons.



Based on Spatial Empirical Bayes smoothed point prevalence, with an 8:1 ascertainment ratio, for four weeks ending 2023-08-08.

Rank	Name	Ratio
1	Charles City County	15.5
2	Prince Edward County	6.0
3	Northumberland County	5.7
4	Cumberland County	5.5
5	Salem City	4.3
6	Craig County	4.3
7	Williamsburg City	4.1
8	Martinsville City	4.0
9	Alleghany County	3.7
10	Buckingham County	3.7

Beyond Scale



Note: This assumes that the ascertainment rate of healthcare workers is double that of the public.

Current Hot-Spots

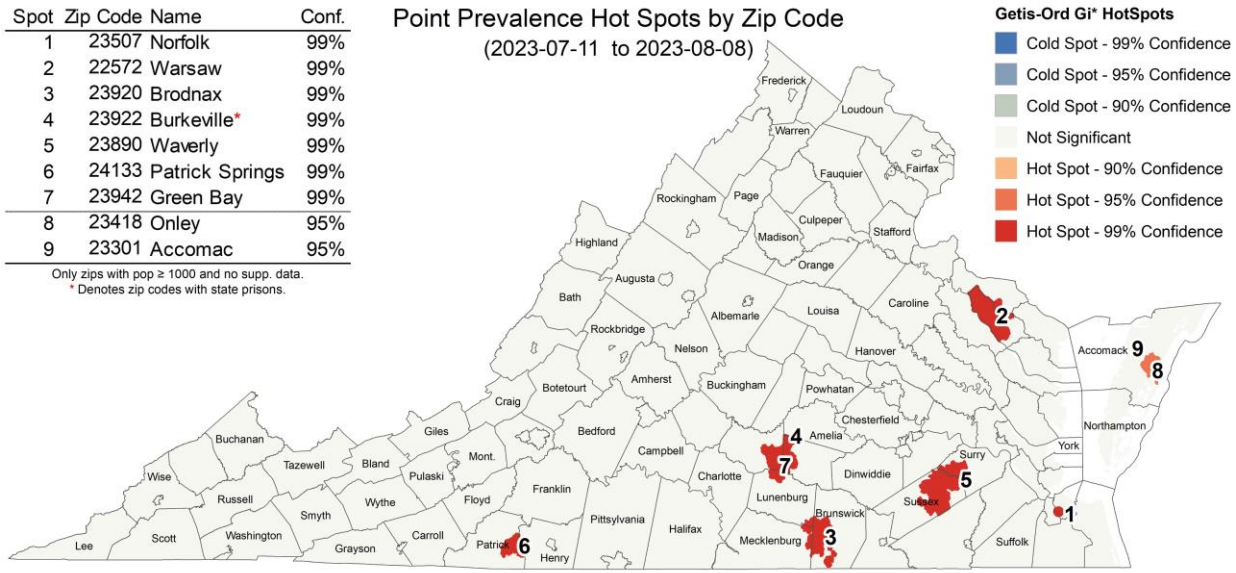
Case rates that are significantly different from neighboring areas or model projections

- **Spatial**: Getis-Ord Gi* based hot spots compare clusters of zip codes with four-week case prevalence higher than nearby zip codes to identify larger areas with statistically significant deviations
- **Temporal**: The cumulative case rate (per 100K) projected in March compared to those observed by county, which highlights temporal fluctuations that differ from the model's projections.
- Spatial hotspots were found sporadically across Virginia. Model overpredictions were seen in Southside, New River, and Crater. Lenowisco, Pittsylvania-Danville, and Eastern Shore saw more cases than expected.

Spatial Hotspots

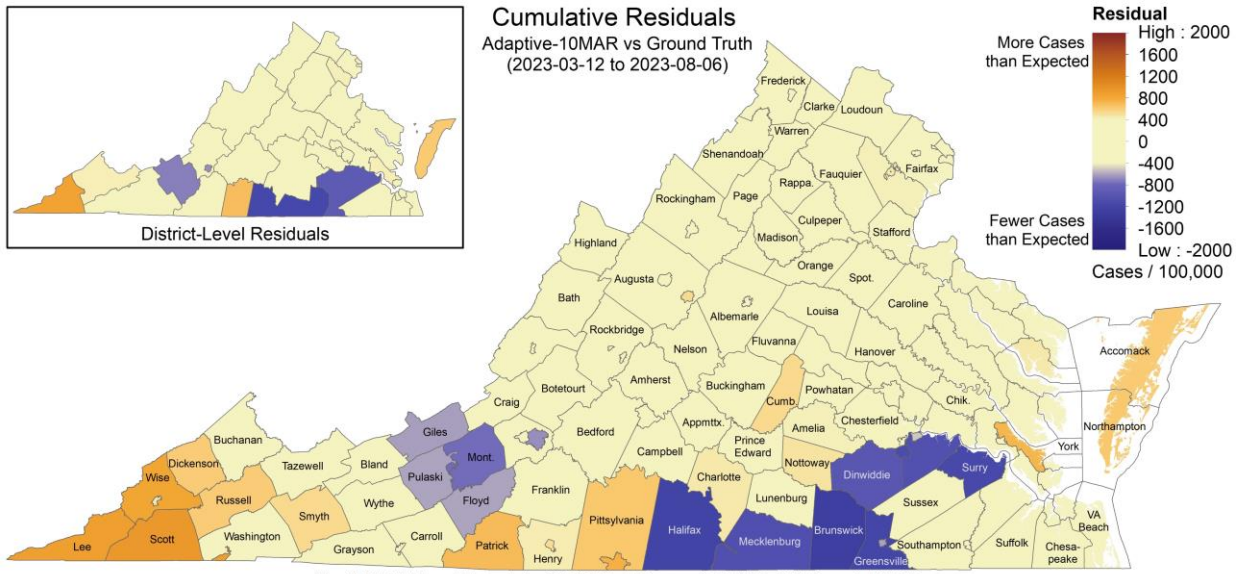
Spot	Zip Code	Name	Conf.
1	23507	Norfolk	99%
2	22572	Warsaw	99%
3	23920	Brodnax	99%
4	23922	Burkeville*	99%
5	23890	Waverly	99%
6	24133	Patrick Springs	99%
7	23942	Green Bay	99%
8	23418	Onley	95%
9	23301	Accomac	95%

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



Based on Global Empirical Bayes smoothed point prevalence for the four weeks ending 2023-08-08.

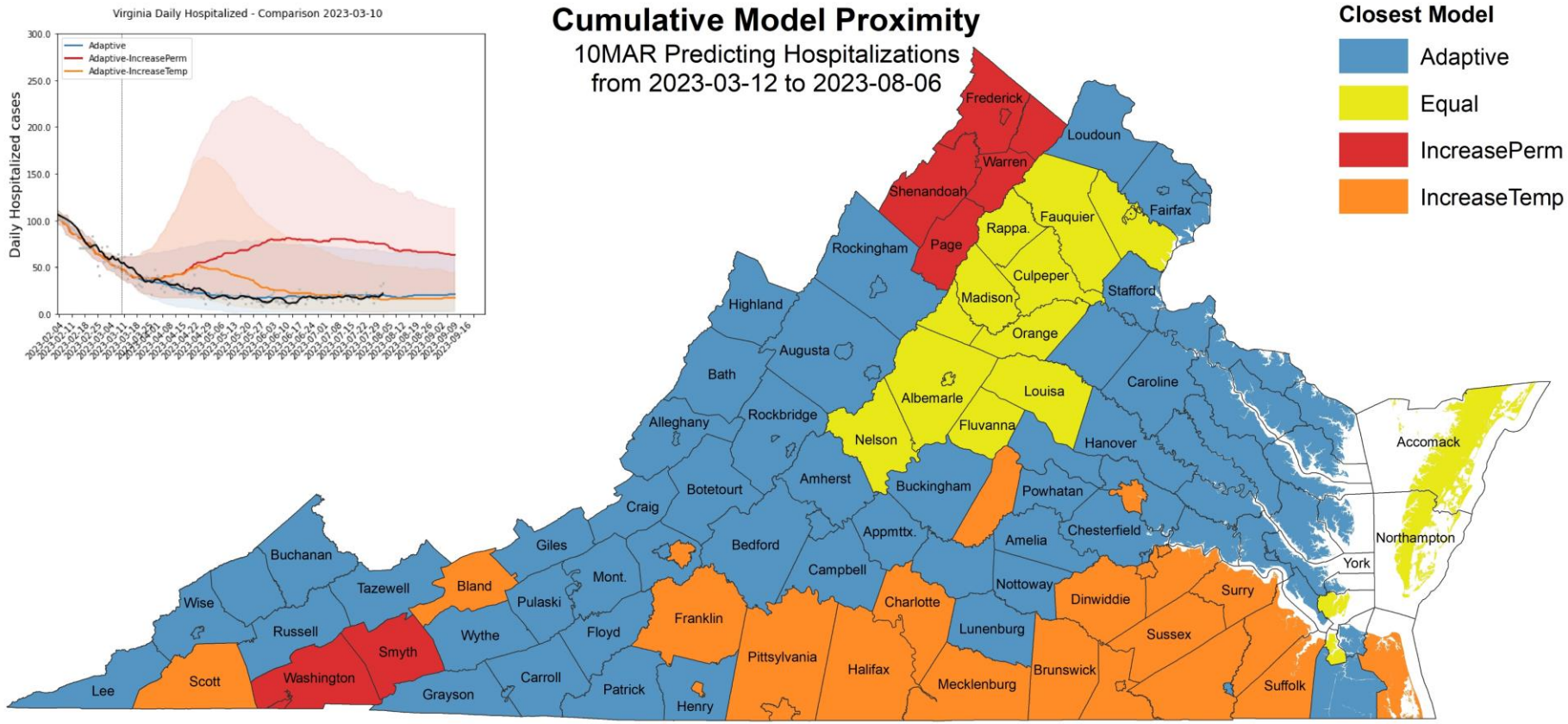
Clustered Temporal Hotspots



Health District Level Moran's I = 0.013169, Z-Score = 0.732633, P-Value = 0.463782
No Residual Autocorrelation Detected

Hospitalization Scenario Trajectory Tracking

Which scenario from March 10 did each county track closest?

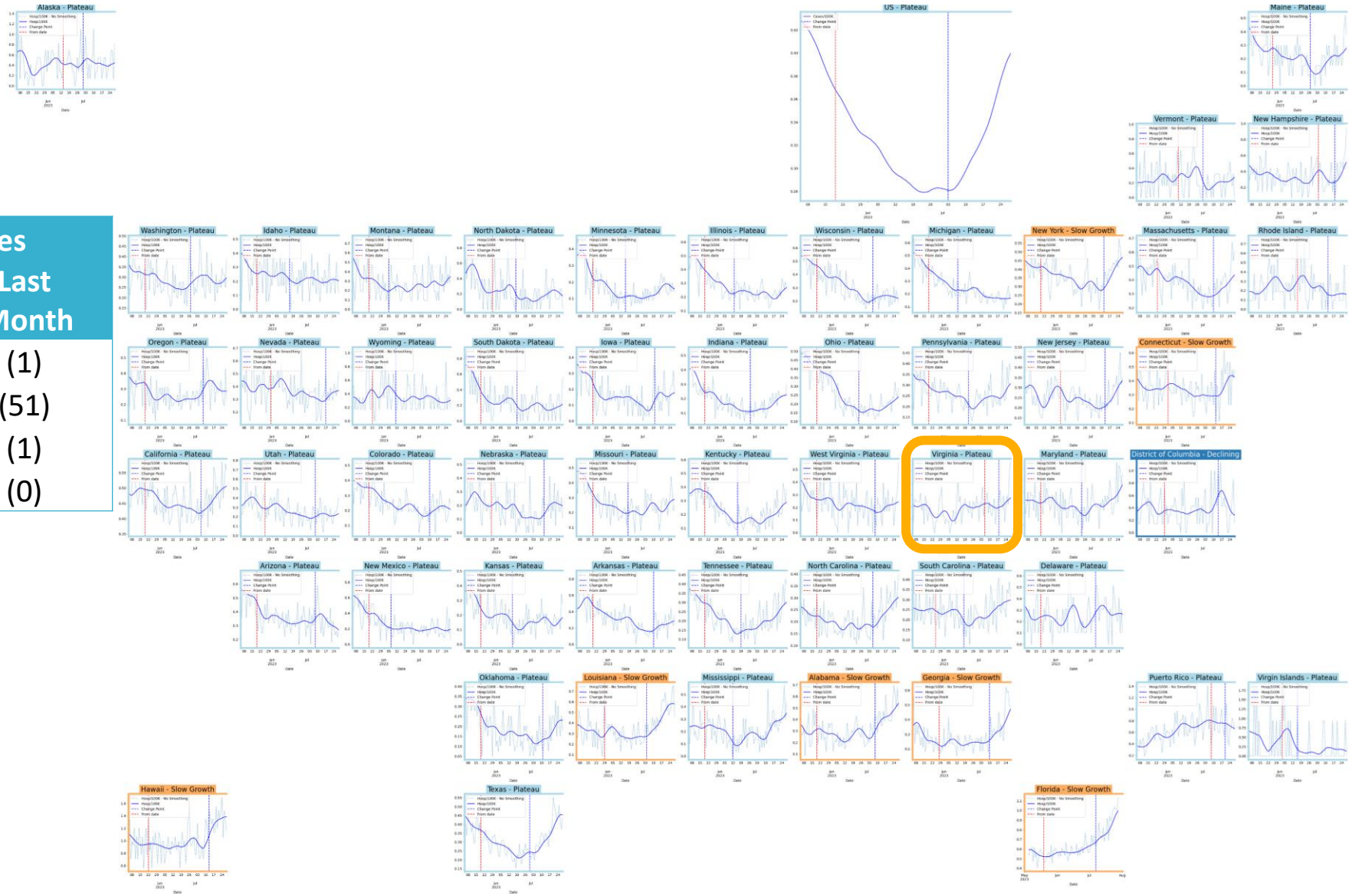


- A band of counties from Suffock to Franklin are tracking IncreaseTemp most closely.
- The northern Shenandoah Valley and areas near Bristol are tracking IncreasePerm more closely.
- Other areas of the Commonwealth are largely the same as last reported, mostly tracking Adaptive.

COVID-19 Broader Context

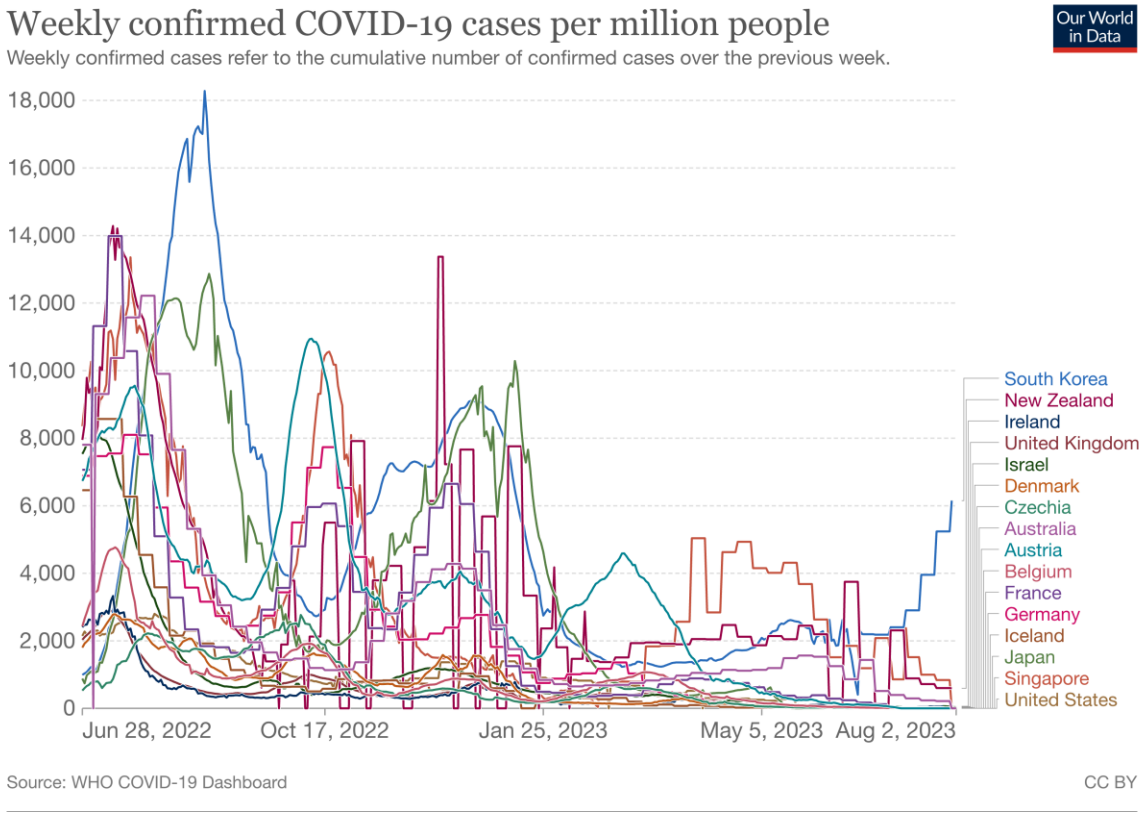
United States Hospitalizations

Status	Number of States	
	Current Week	Last Month
Declining	1	(1)
Plateau	45	(51)
Slow Growth	7	(1)
In Surge	0	(0)

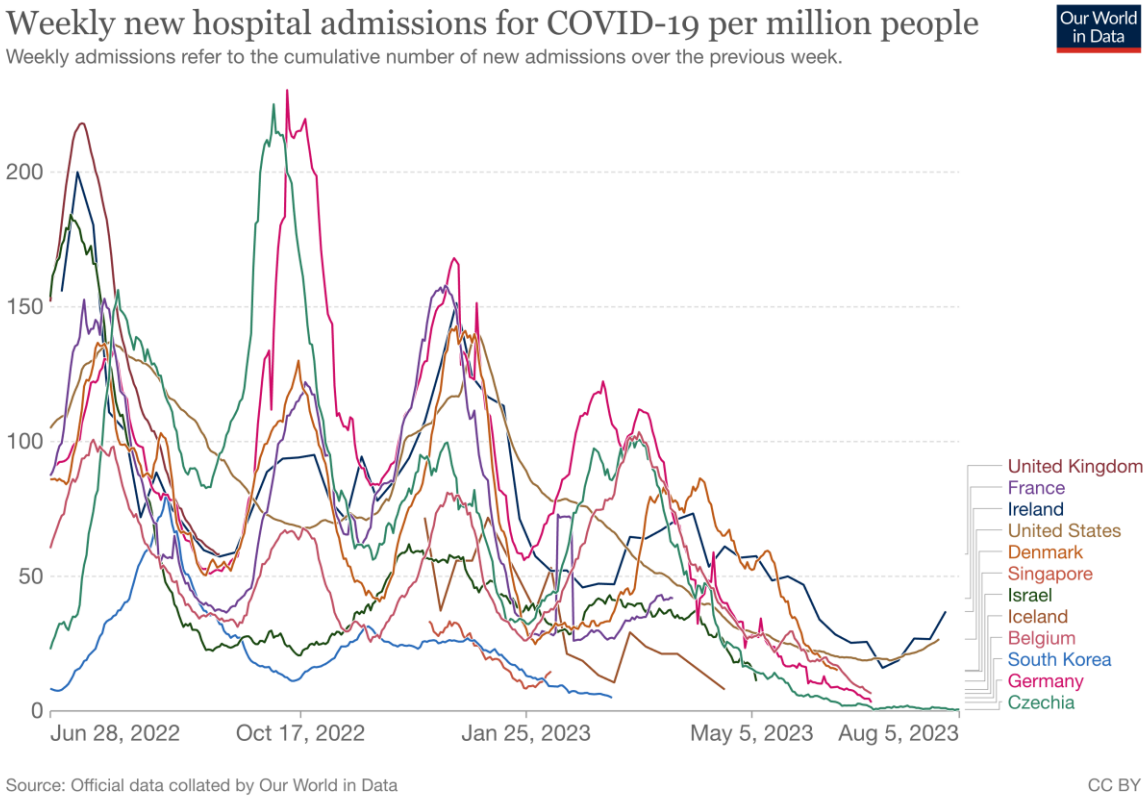


Around the World – Various trajectories

Confirmed cases



Hospitalizations



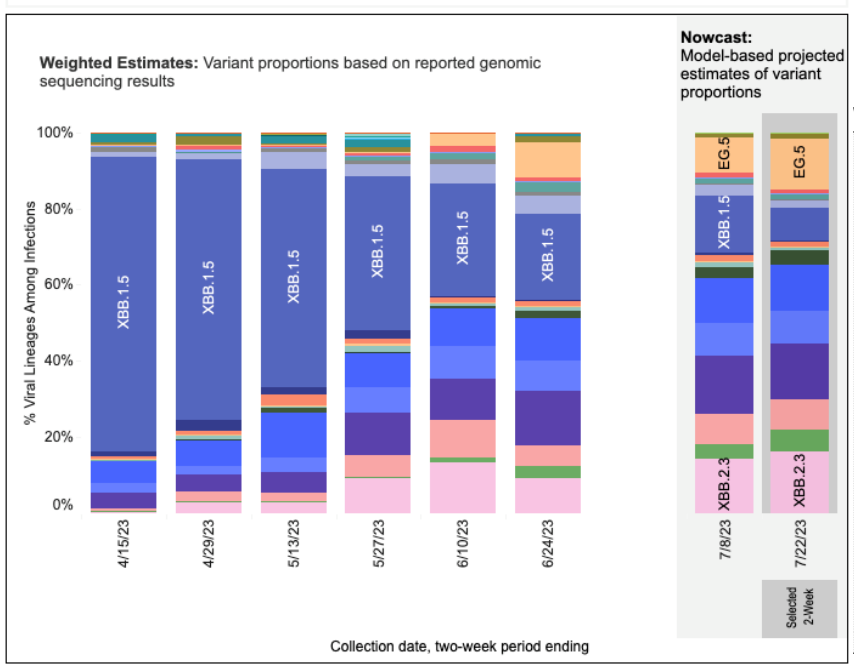
Our World in Data [Our World in Data]

COVID-19 Genomic Update

SARS-CoV2 Variants of Concern

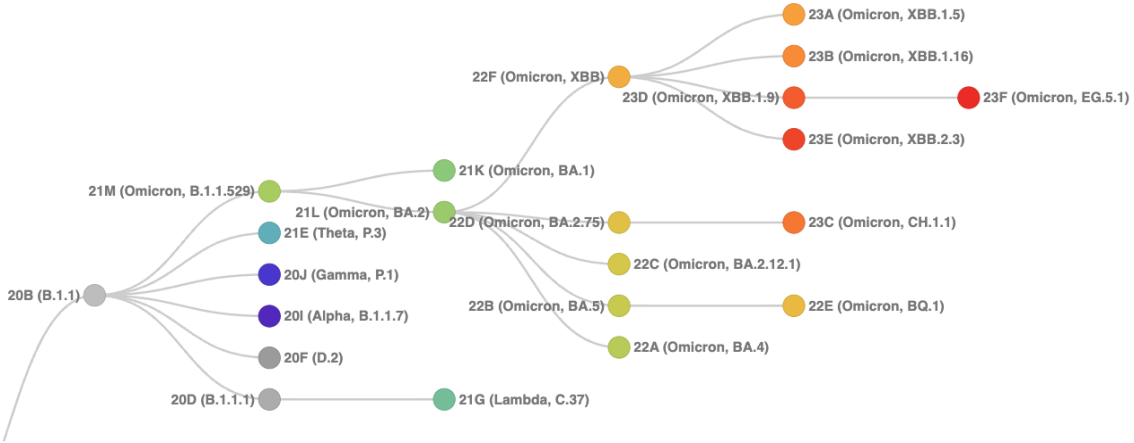
Emerging variants have potential to continue to alter the future trajectories of pandemic and have implications for future control

- **Variants have been observed to:** increase transmissibility, increase severity (more hospitalizations and/or deaths), and limit immunity provided by prior infection and vaccinations



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

WHO label	Lineage #	%Total	95%PI
Omicron	XBB.2.3	16.2%	11.6-22.1%
	XBB.1.16	14.4%	10.3-19.6%
	EG.5	13.4%	8.4-20.6%
	XBB.1.9.1	12.1%	7.0-19.7%
	XBB.1.9.2	8.6%	5.8-12.6%
	XBB.1.5	8.5%	6.4-11.2%
	XBB.1.16.1	8.1%	6.6-9.8%
	XBB.1.16.6	5.8%	2.4-12.5%
	XBB.1.5.72	3.8%	1.8-7.8%
	XBB	2.4%	1.5-3.7%
	FE.1.1	1.7%	0.8-3.5%
	CH.1.1	1.5%	0.4-4.4%
	XBB.1.5.10	1.1%	0.5-2.3%
	XBB.1.5.68	0.9%	0.5-1.8%
	EU.1.1	0.9%	0.4-1.9%
	XBB.1.5.1	0.3%	0.2-0.5%
	XBB.1.5.59	0.2%	0.1-0.8%
	FD.2	0.0%	0.0-0.0%
	BQ.1.1	0.0%	0.0-0.0%
	BN.1	0.0%	0.0-0.0%
	BA.2	0.0%	0.0-0.0%
	BA.5	0.0%	0.0-0.0%
	BQ.1	0.0%	0.0-0.0%
	BA.2.75	0.0%	0.0-0.0%
Other	Other*	0.1%	0.0-0.2%



https://clades.nextstrain.org

Omicron Updates*

- New lineage EG.5 up to 13.4 from 9%
- XBB.1.9* (EG.5^c) up to 20 from 17%
- XBB.1.16* holding steady at 28%, shifting internal structure
- XBB.1.5.72 new variant increasing to 3.8%
- New lineage XBB.2.3 down to 16.2 from 16.4%

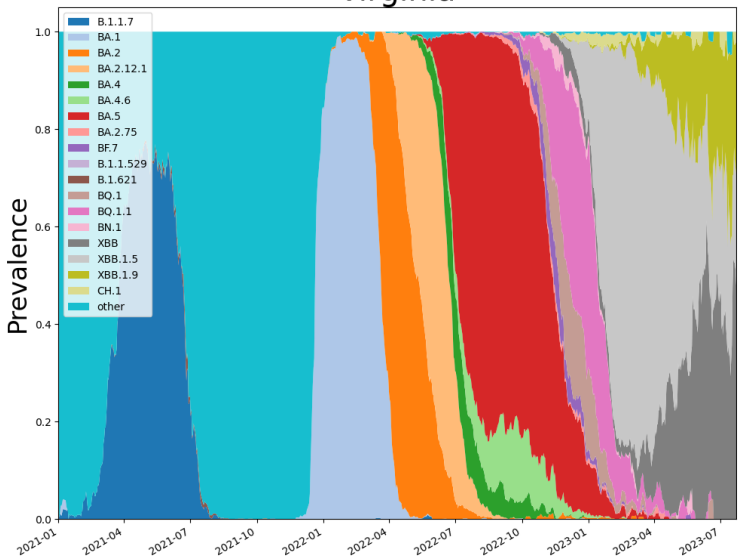
*percentages are CDC NowCast Estimates

SARS-CoV2 Omicron Sub-Variants

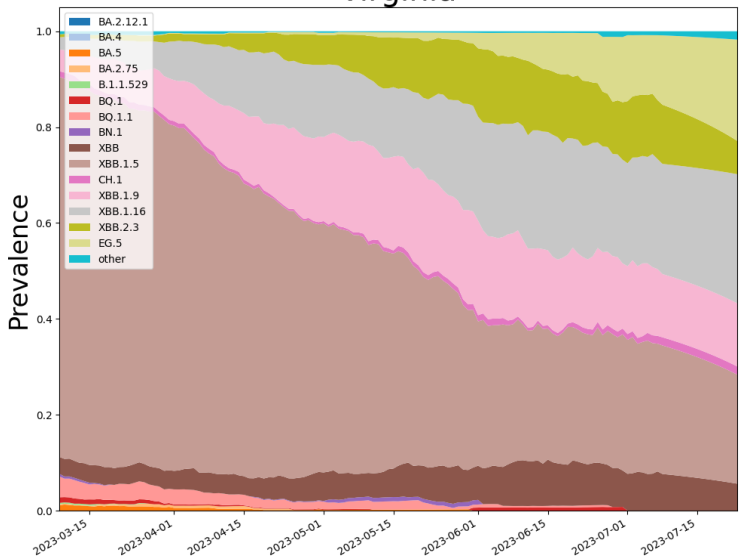
covSPECTRUM
Enabled by data from GISAID

As detected in whole Genomes in public repositories

Virginia

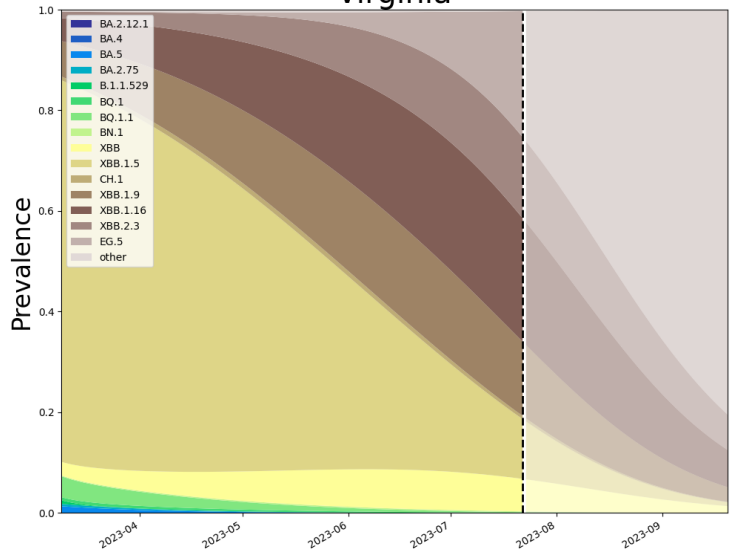


Virginia

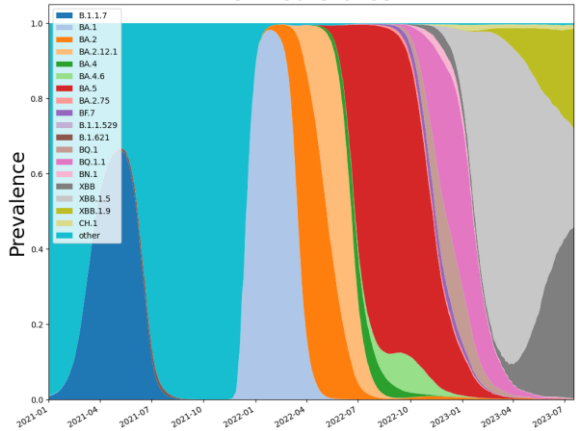


VoC Polynomial Fit Projections

Virginia



United States



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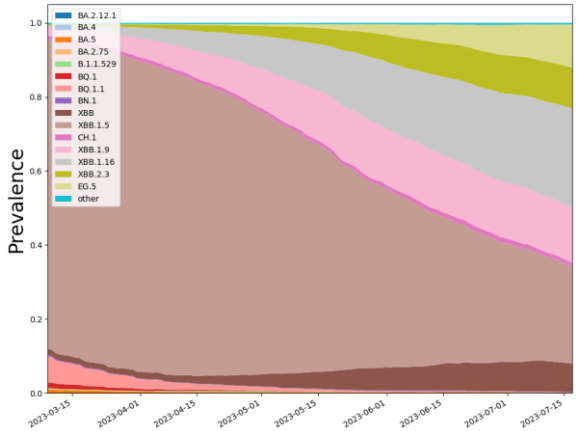

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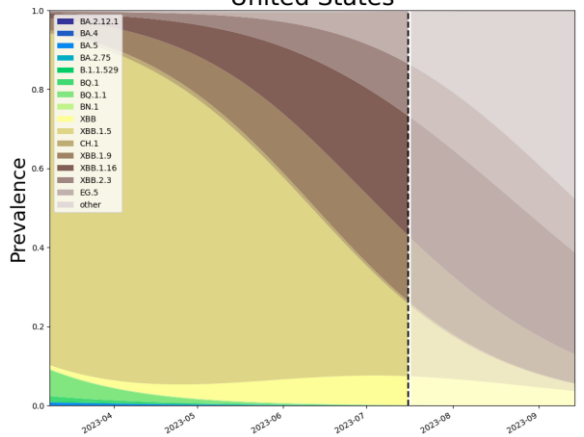


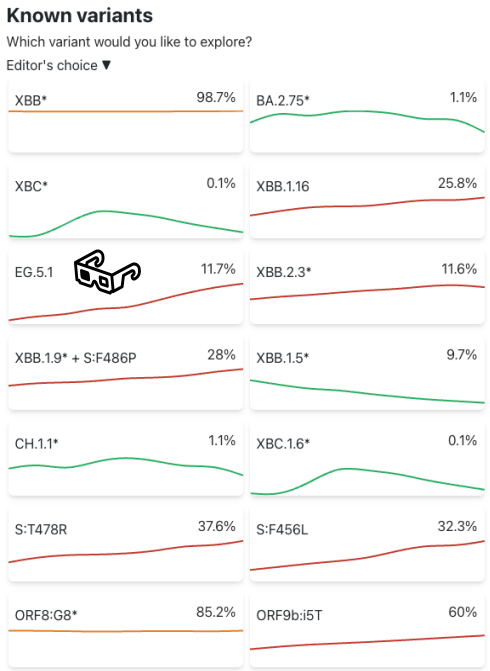
Note: Everything from dotted line forward is a projection.

SARS-CoV2 Omicron Sub-Variants

[COV-spectrum](#)

"Editor's choice"

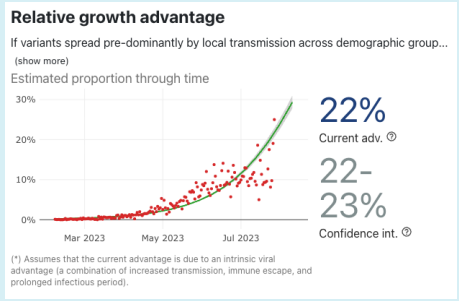
Variants to watch

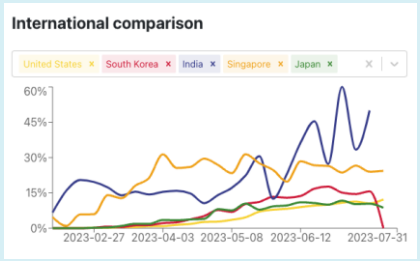


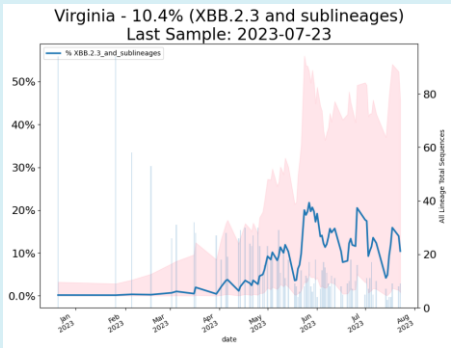
covSPECTRUM

Enabled by data from GISAID

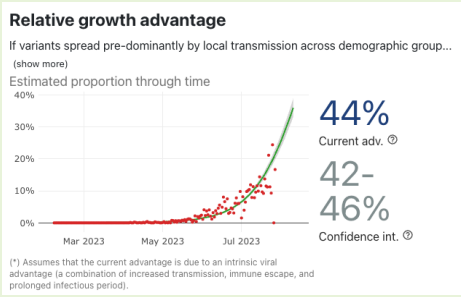
XBB.2.3*

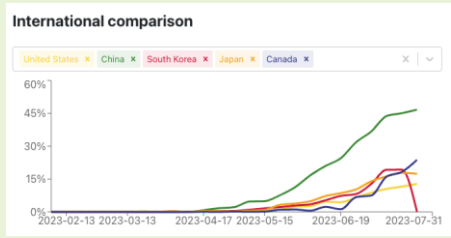


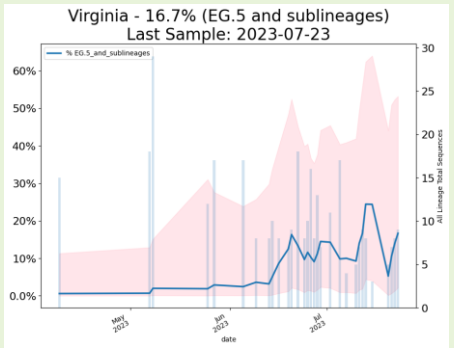




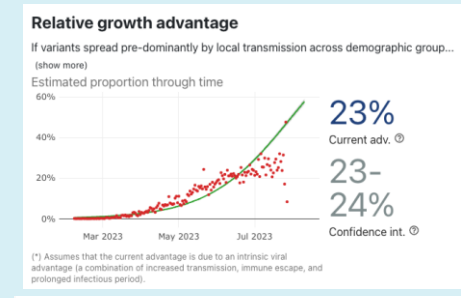
EG.5*

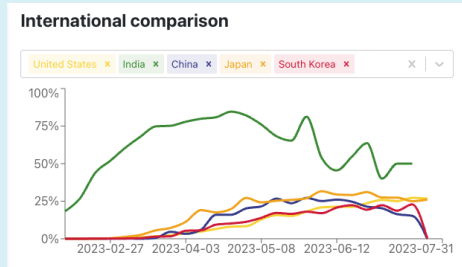


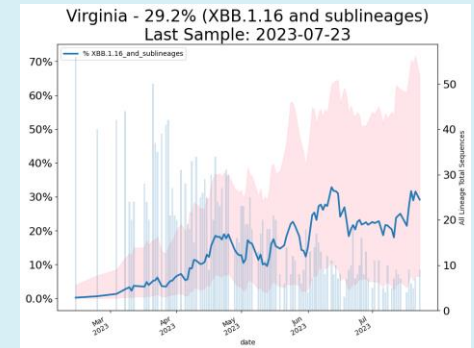




XBB.1.16*







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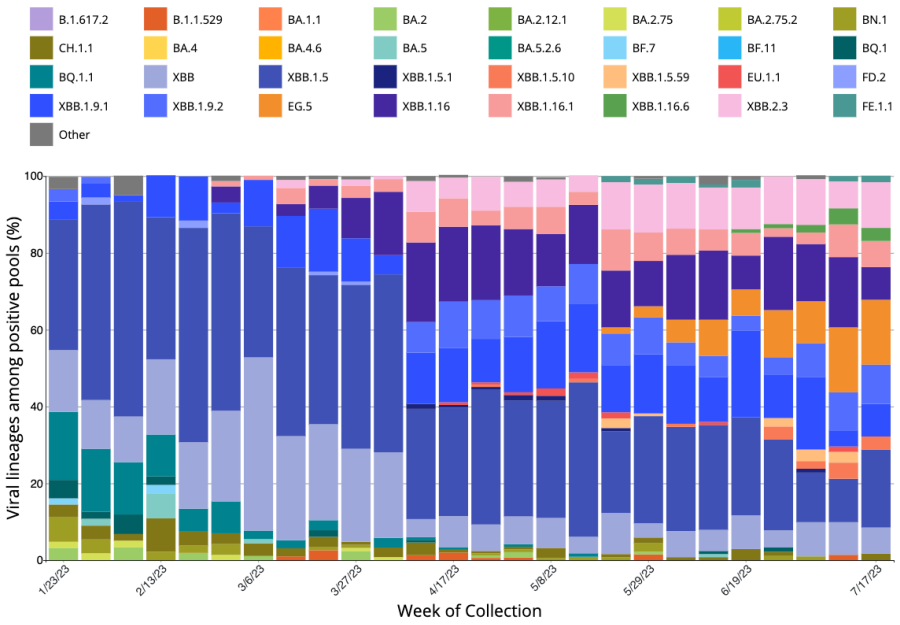
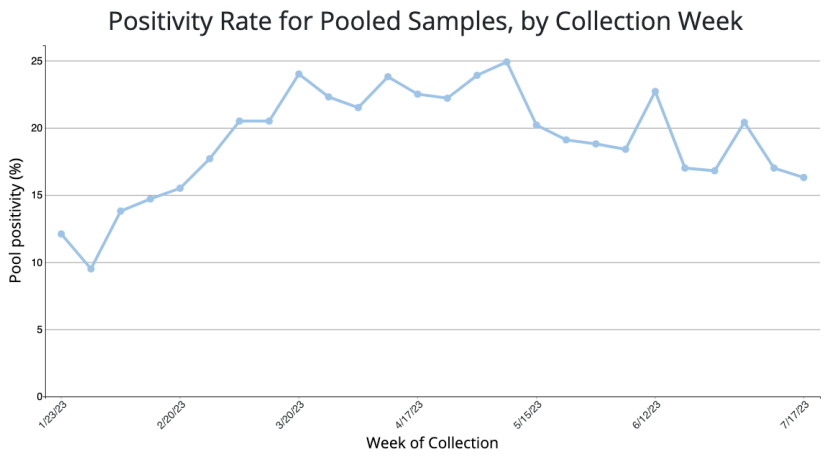
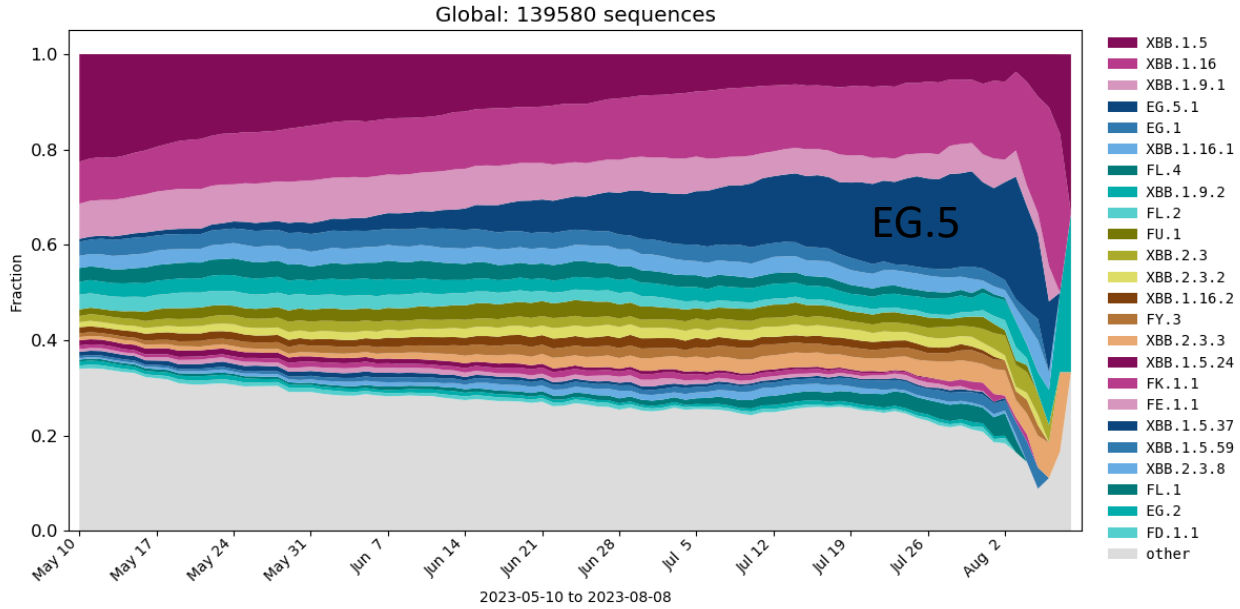
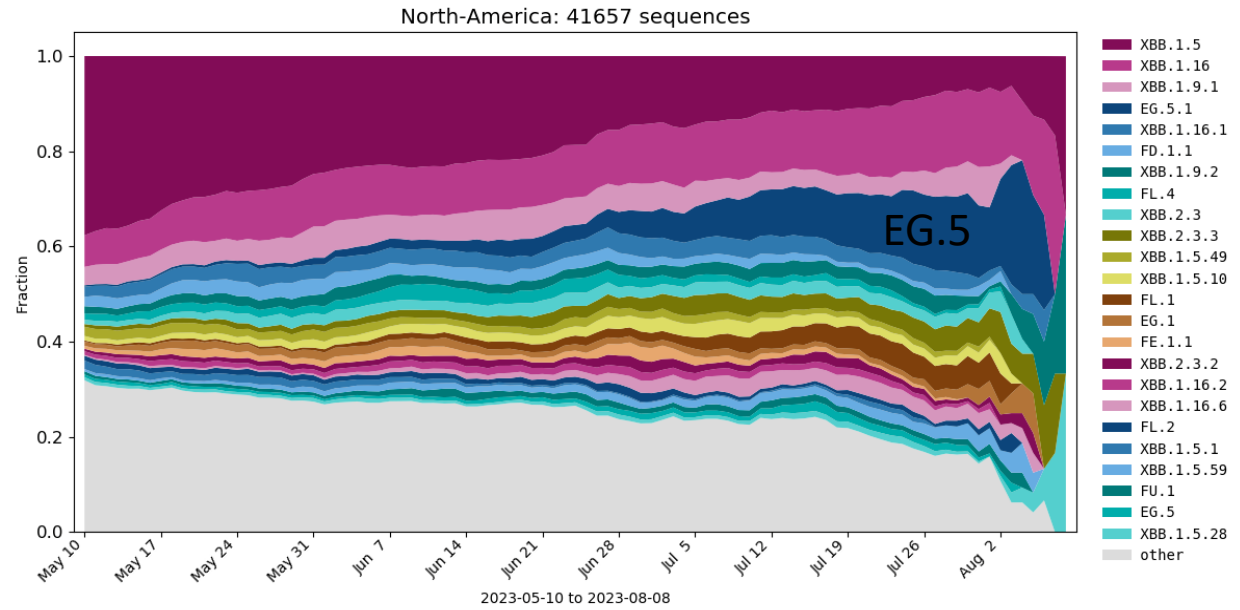
Global SARS-CoV2 Variant Status

Traveller Surveillance





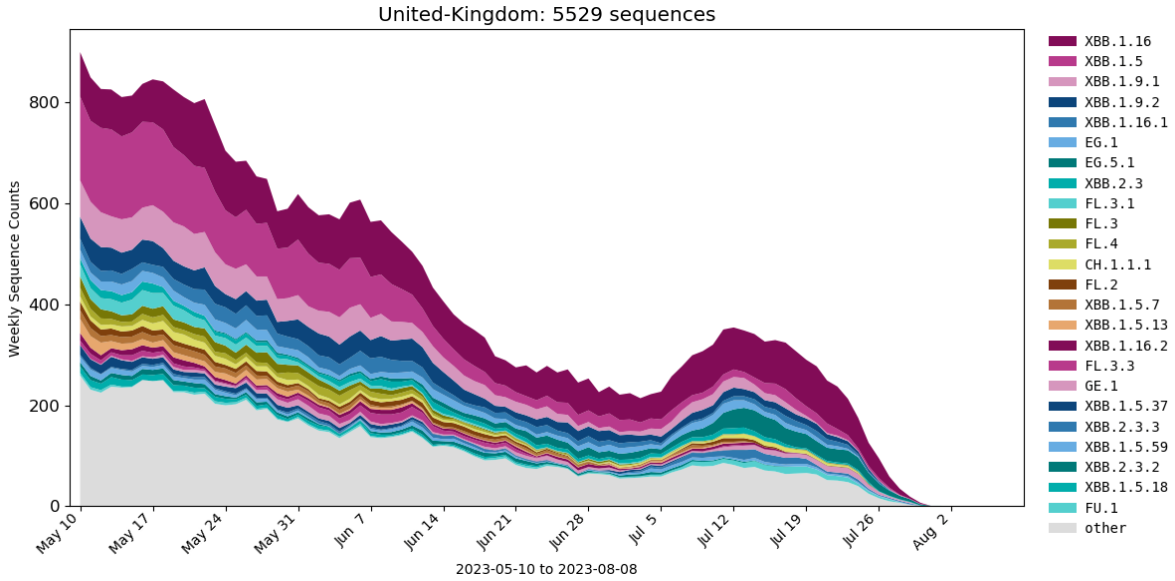


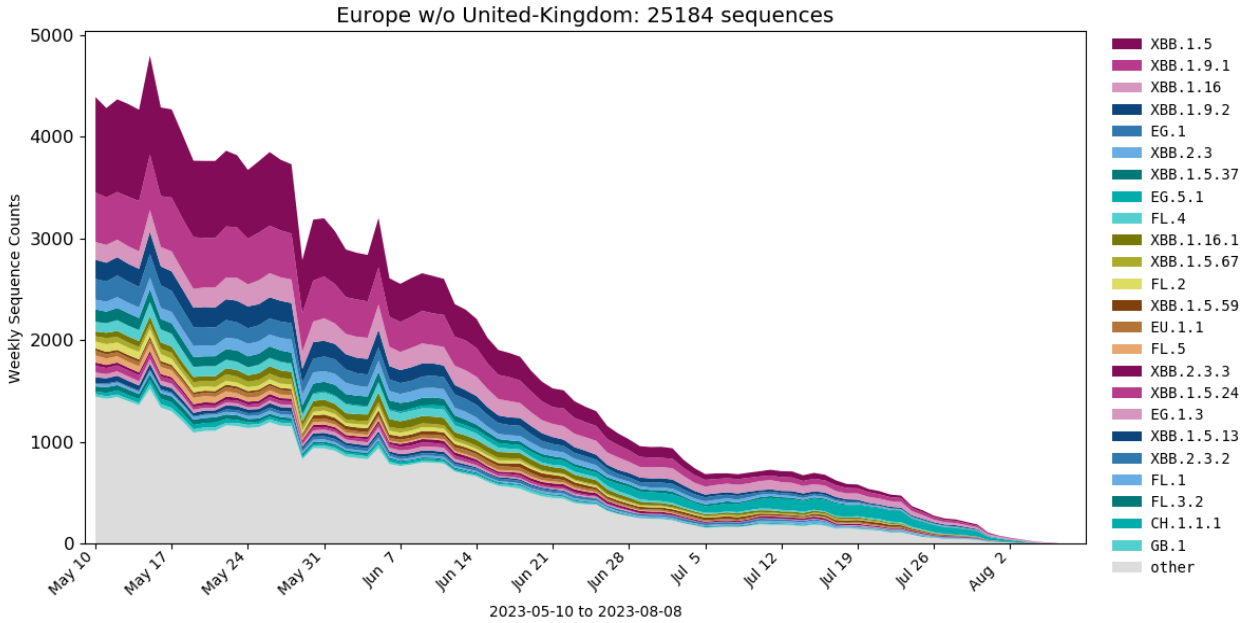


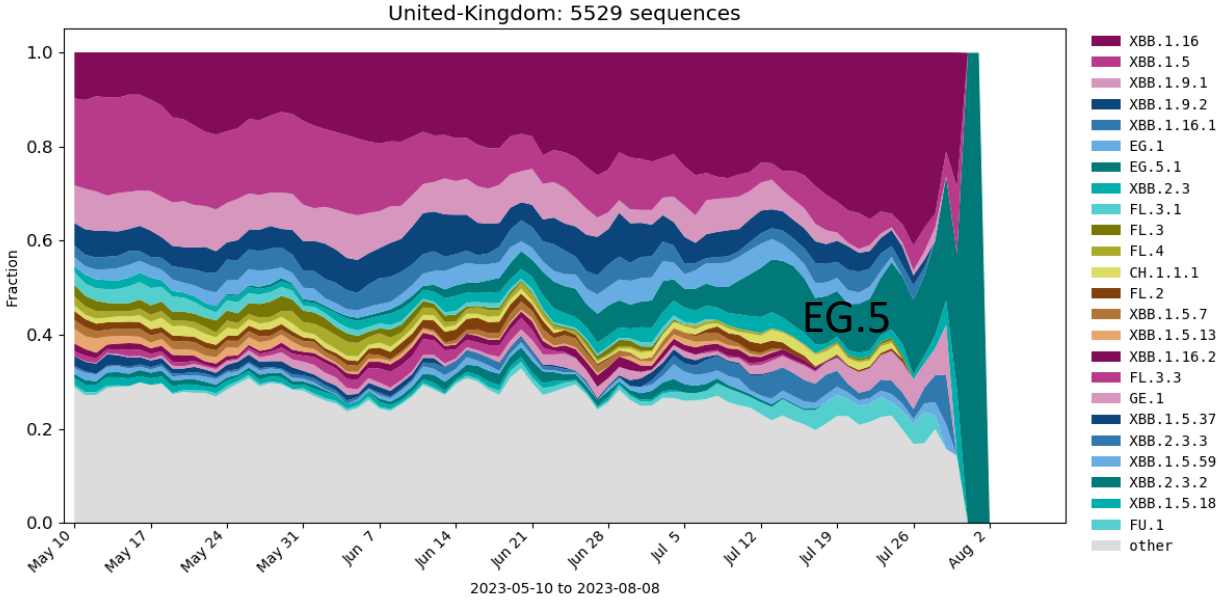
https://cov.lanl.gov/components/sequence/COV/sparks.comp

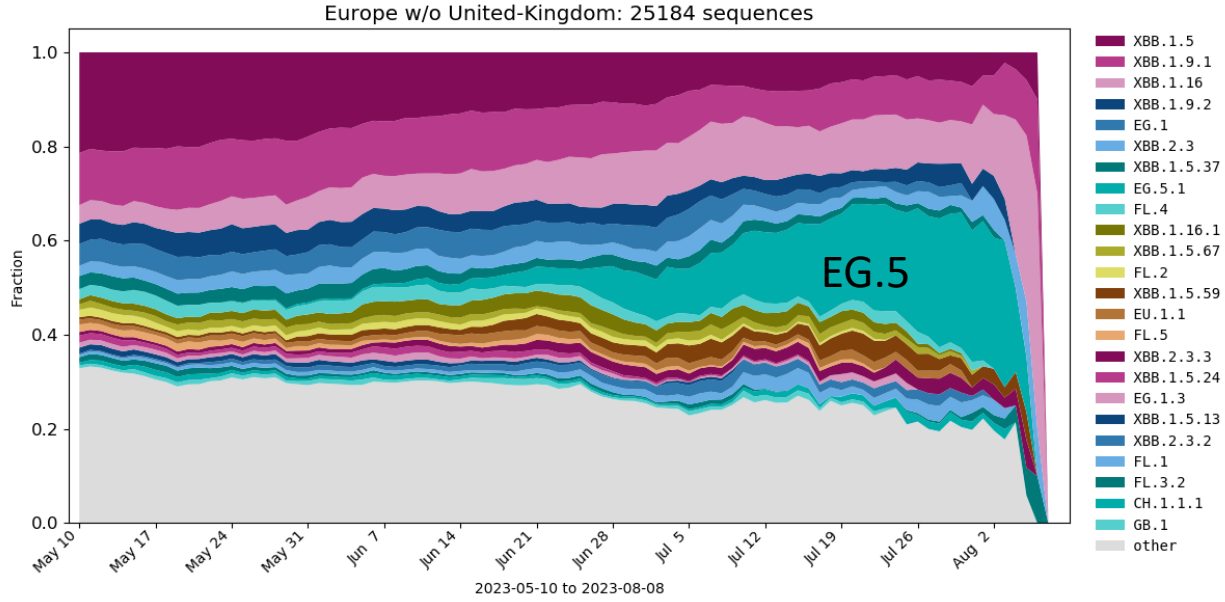
https://covid.cdc.gov/covid-data-tracker/#traveler-genomic-surveillance

Global SARS-CoV2 Variant Status









https://cov.lanl.gov/components/sequence/COV/sparks.comp

https://covid.cdc.gov/covid-data-tracker/#traveler-genomic-surveillance

Pandemic pubs – Wastewater surveillance (1)

https://www.pnas.org/doi/10.1073/pnas.2216021120

- North Carolina statewide analysis (62 weeks from 19 sites)
- Characterization around Delta and Omicron surges
- Findings:
  - Average lead time over cases – 4 to 7 days
  - Correlations similar across normalizations and alignment
  - Novel algorithm (Covid-SURGE) combining indicators

RESEARCH ARTICLE | POPULATION BIOLOGY

Separating signal from noise in wastewater data: An algorithm to identify community-level COVID-19 surges in real time

Aparna Keshaviah, Ian Huff, Xindi C. Hu, +9, and Isabel Musse Authors Info & Affiliations

Edited by Alan Hastings, University of California, Davis, CA; received October 7, 2022; accepted June 11, 2023

July 25, 2023 | 120 (31) e2216021120 | https://doi.org/10.1073/pnas.2216021120

Figure S1. North Carolina Wastewater Monitoring Network sites analyzed

Period	True positive rate, %			Maximum false positive rate, %		
	Criteria 1, 2, and 3	Criteria 1 and 2	Criterion 1 only	Criteria 1, 2, and 3	Criteria 1 and 2	Criterion 1 only
Delta surge (n = 19 sites)	*84*	74	84	*5*	5	12
Omicron surge (n = 19 sites)	*79*	79	84	*14*	14	27
Across both surges (n = 38 periods)	***82***	**76**	**84**		**7**	**15**
-In 5 sites (10 periods) with small WWTPs (3,500 to 15,527 served)	*80*			*3*		
-In 10 sites (20 periods) with medium WWTPs (49,384 to 151,589 served)	*75*			*10*		
-In 4 sites (8 periods) with large WWTPs (173,000 to 550,000 served)	*100*			5		

Covid-SURGE schematic

Criterion 1: Was the wastewater concentration higher than any concentration measured over the past month?

Criterion 2.1: Did the concentration represent a 100% increase or more from the previous sample?
Criterion 2.2: Did the concentration represent a percent increase that was higher than any observed over the past month?

Criterion 3: Did the wastewater concentration become detectable after one month of concentrations below the limit of detection?

Flag as a community-level surge if:
[Criteria 1 and 2.1] OR [Criteria 1 and 2.2] OR [Criteria 3] were met

Challenges:

- Defining ground truth "surge" dates – visual inspection + inflection points analyses on historical WW data
- Deriving best combination of indicators – manual process optimized for Delta surge

Pandemic pubs – Wastewater surveillance (2)

https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2807632

- NWSS based study of 268 counties in 22 states (Jan-Sep 2022)
- Association with “high” community level of case/hospitalization rates
- Findings:
  - Metrics based on percentile (levels) and 15-d % change (trends)
  - High association in Q1 of 2022 – AUC and logistic regression
  - Subsequent decline due to home testing and vaccinations

Original Investigation | Public Health

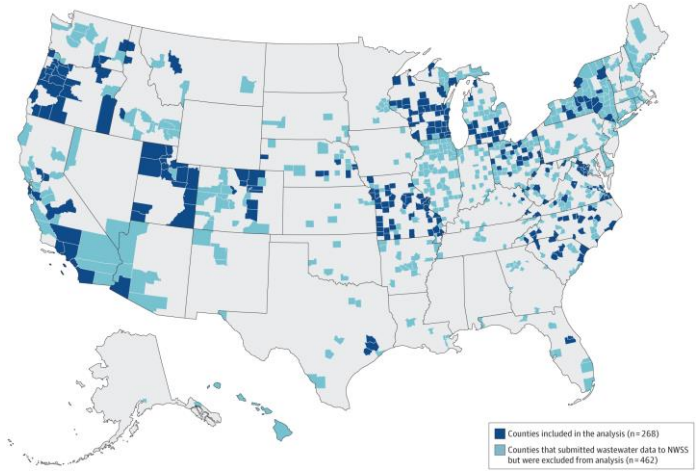
July 26, 2023

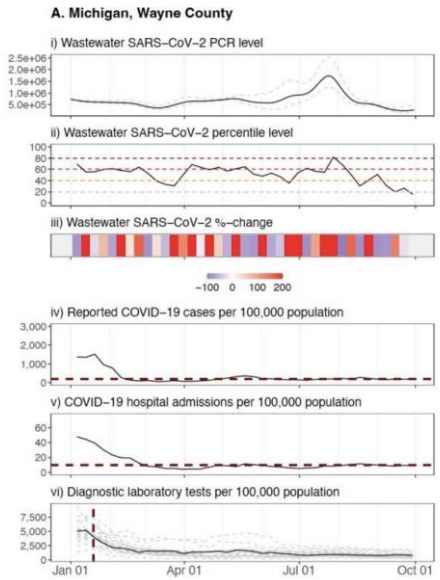
Use of Wastewater Metrics to Track COVID-19 in the US

Meri R. J. Varkila, MD[1]; Maria E. Montez-Rath, PhD[2]; Joshua A. Salomon, PhD[3]; et al

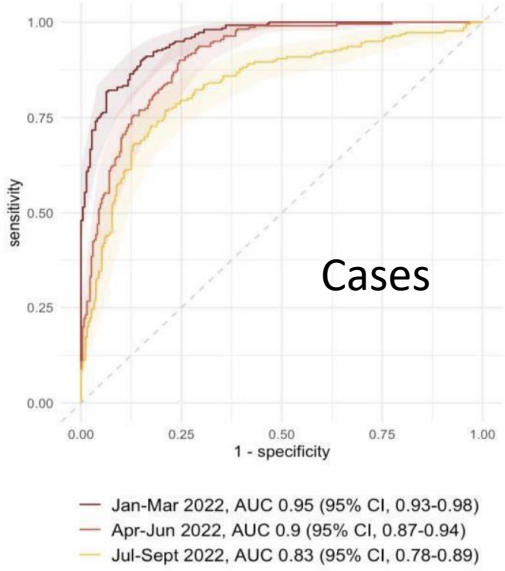
» Author Affiliations | Article Information

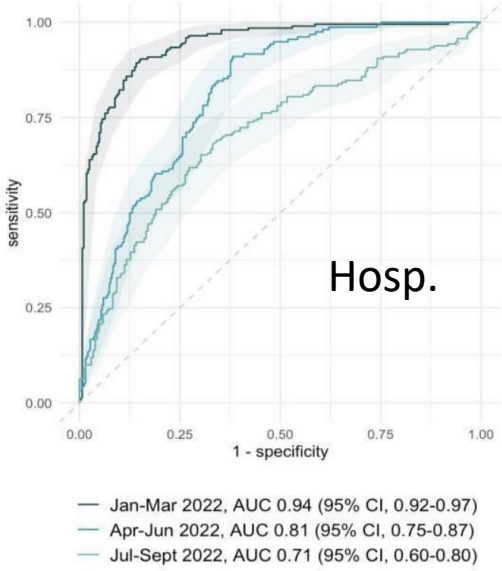
JAMA Netw Open. 2023;6(7):e2325591. doi:10.1001/jamanetworkopen.2023.25591





Wastewater Percentile in Reference to Clinical Case Metrics in Large US Counties (n=38)





Challenges:

- Benchmarking for newer sites with little historical data
- Lower utility for predicting surges/transitions

Pandemic pubs – Wastewater surveillance (3)

- Biobot county-level data for 159 counties (Jun 2021 – Jan 2023)
- Predicting weekly new hospital admissions using random forest
- Findings:
  - MAE within 4-6 patients/100k. NMAE within 0.2-0.4
  - RNA concentration - most crucial explanatory factor
  - Progressively learning model performs better

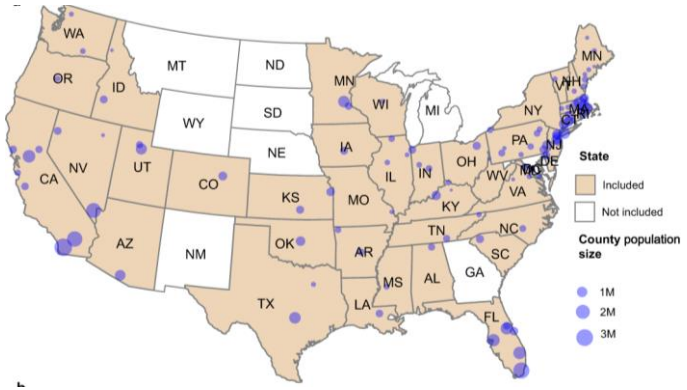
https://www.nature.com/articles/s41467-023-40305-x

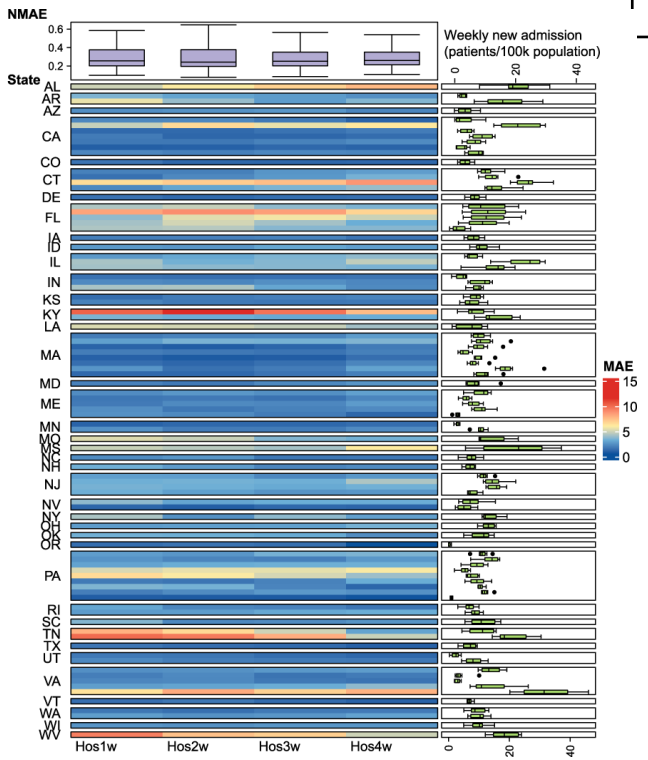
Article | Open Access | Published: 28 July 2023

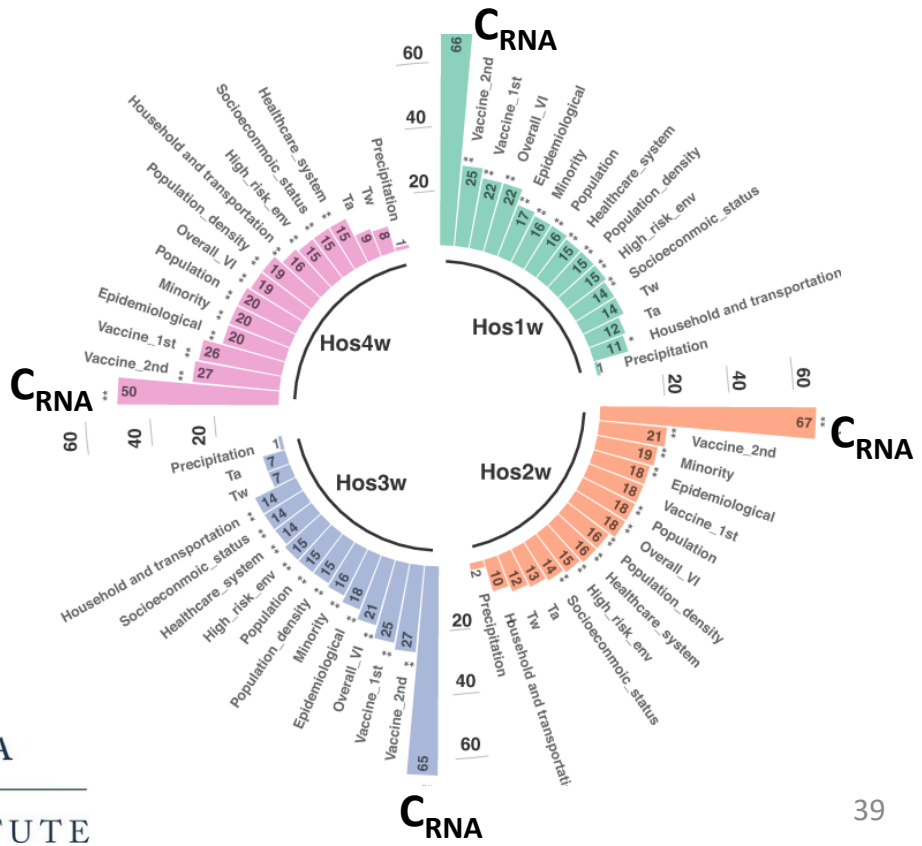
Wastewater-based epidemiology predicts COVID-19-induced weekly new hospital admissions in over 150 USA counties

Xuan Li, Huan Liu, Li Gao, Samendra P. Sherchan, Ting Zhou, Stuart J. Khan, Mark C. M. van Loosdrecht & Qilin Wang

Nature Communications **14**, Article number: 4548 (2023) | Cite this article







Challenges:

- Unclear what the implication of MAE is for various counties
- Does not include other useful signals (e.g., cases, CLI)

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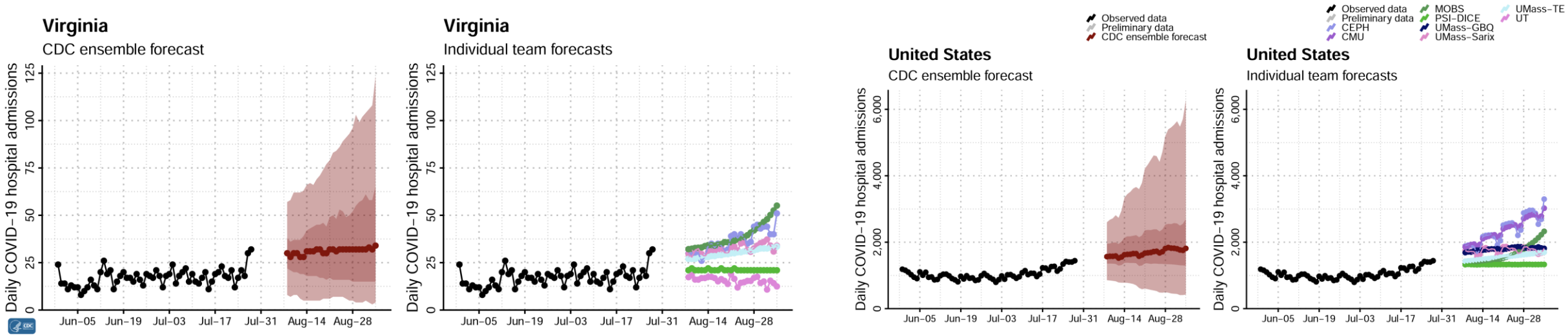
National Modeling Hub Updates

Current COVID-19 Hospitalization Forecast

Statistical models for submitting to CDC COVID Forecasting Hub

- Uses a variety of statistical and ML approaches to forecast weekly hospital admissions for the next 4 weeks for all states in the US

Hospital Admissions for COVID-19 and Forecast for next 4 weeks (CDC COVID Ensemble)



Scenario Modeling Hub – COVID-19 (Round 17)

Collaboration of multiple academic teams to provide national and state-by-state level projections for 6 aligned scenarios

https://covid19scenariomodelinghub.org/viz.html

- Preliminary Results
- Round Designed to explore different seasonal vaccination levels and the impact of Immune Escape

Scenario Dimensions:

Immune Escape (IE):

Slower IE (20%/yr) vs.
Faster IE (50%/yr)

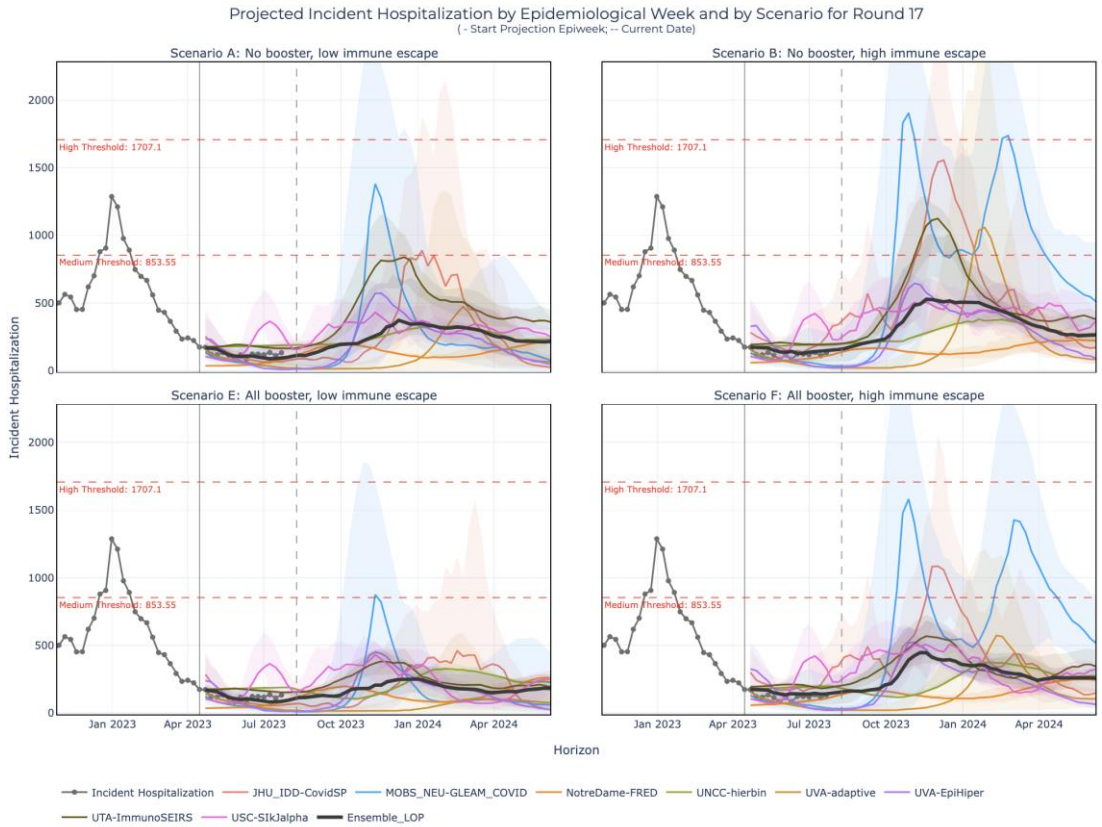
Vaccination levels:

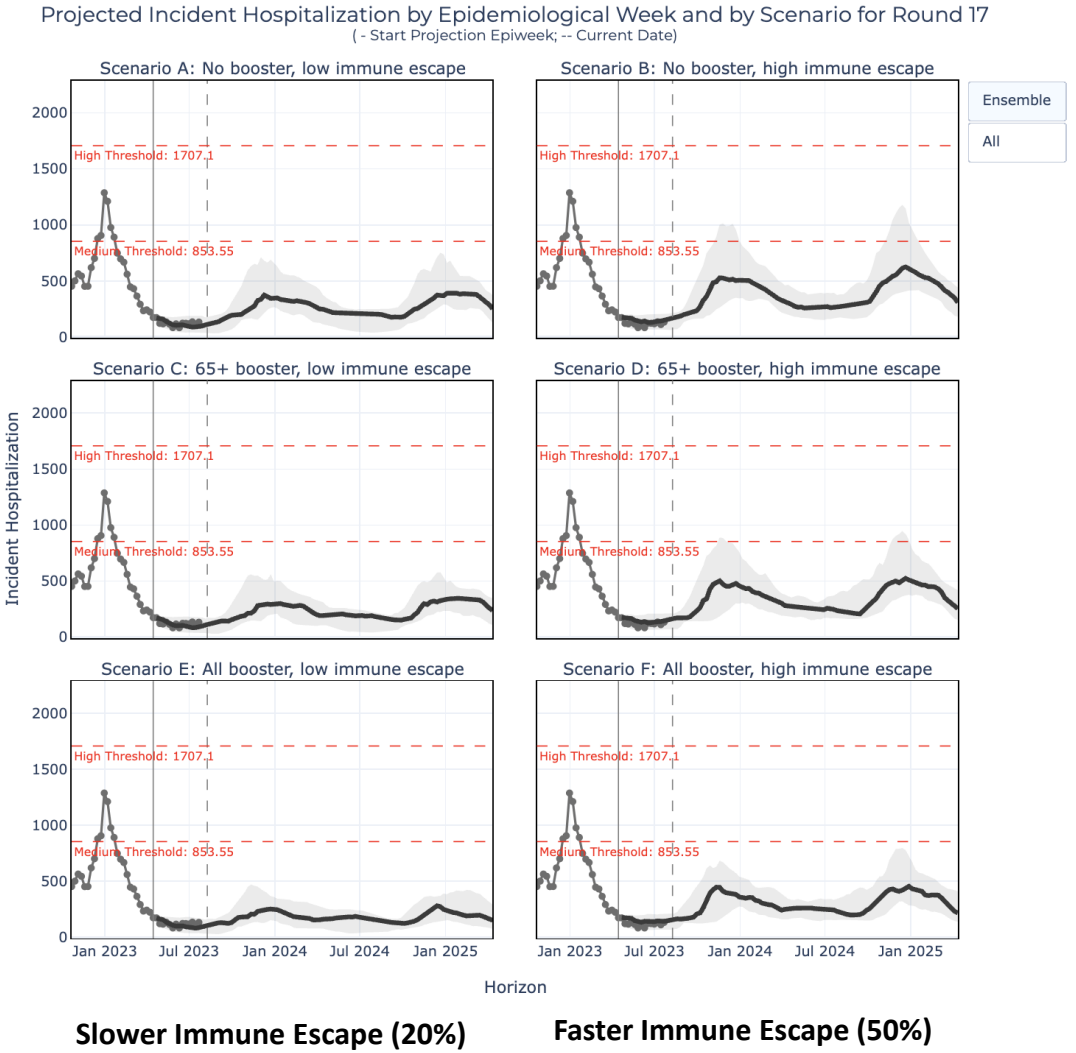
None vs.
Vulnerable and 65 + vs.
Broader population of eligible

	Low immune escape • Immune escape occurs at a constant rate of **20% per year**	**High immune escape** • Immune escape occurs at a constant rate of **50% per year**
No vaccine recommendation • Uptake negligible or continues at very slow levels based on existing 2022 booster trends	Scenario A	Scenario B
Reformulated annual vaccination recommended for 65+ and immunocompromised • Reformulated vaccine has **65% VE against variants circulating on June 15** • Vaccine becomes **available September 1** • Uptake in 65+ same as first booster dose recommended in September 2021 • Uptake in individuals under 65 negligible or continues to trickle based on 2022 booster trends	Scenario C	Scenario D
Reformulated annual vaccination recommended for all currently eligible groups • Reformulated vaccine has **65% VE against variants circulating on June 15** • Vaccine becomes **available September 1** • 65+ uptake same as first booster dose recommended in September 2021 • Coverage in individuals under 65+ saturates at levels of the 2021 booster (approximately 34% nationally)	Scenario E	Scenario F

SMH – COVID-19 (Round 17) – Virginia Results

- To date, immune escape evolution has been slow. Booster campaign size remains unknown.
- Significant variation in Fall-Winter 2023 outlook across models

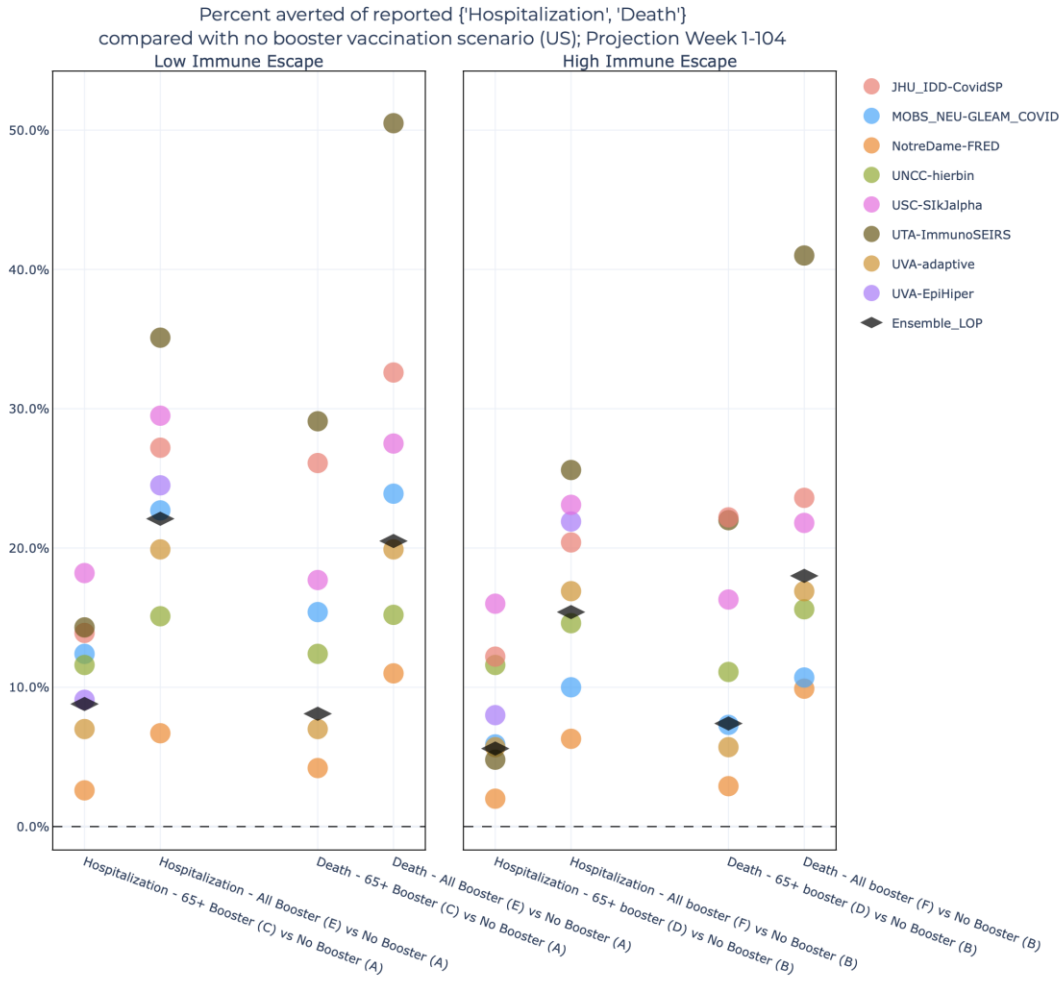




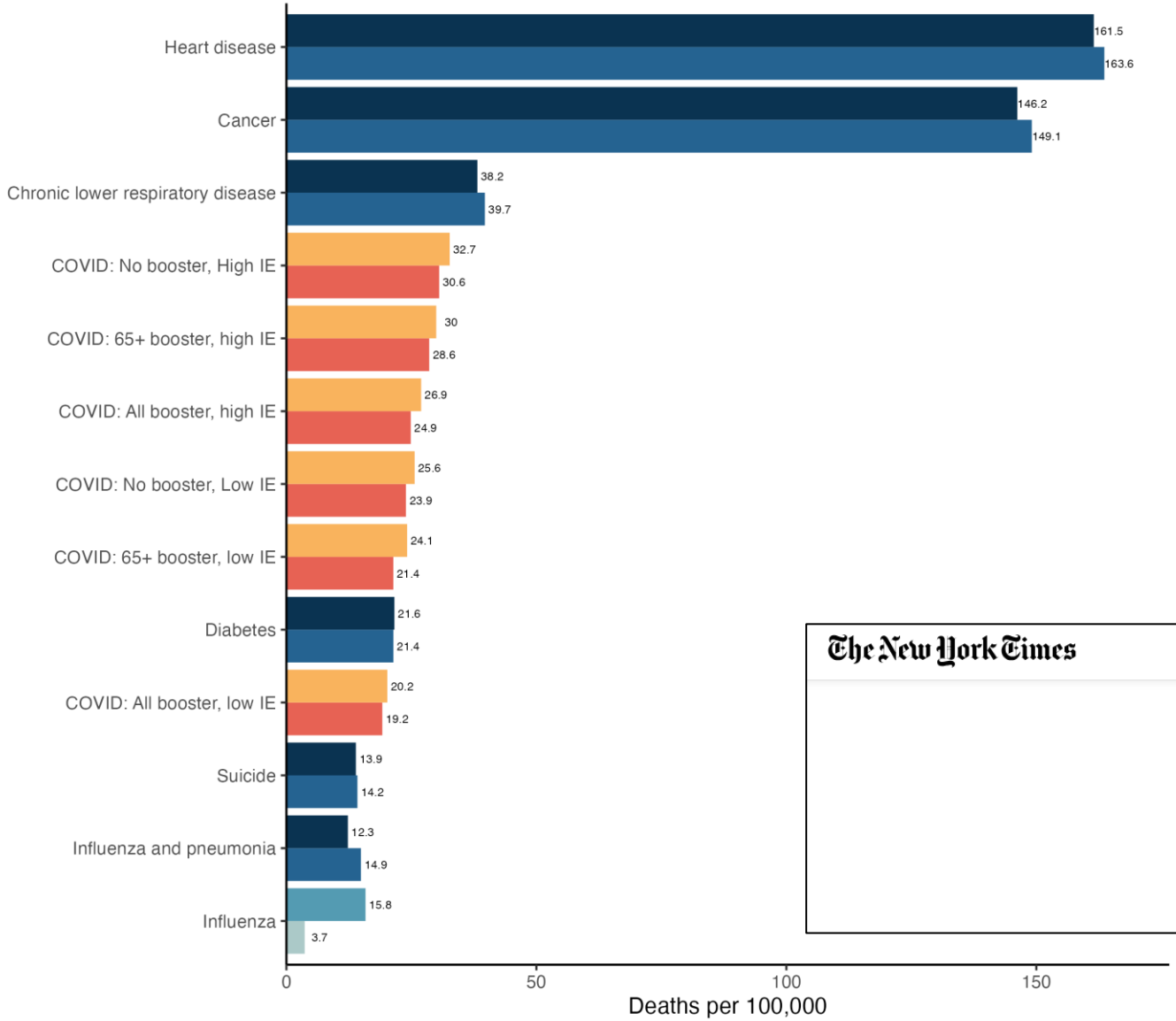
Slower Immune Escape (20%) **Faster Immune Escape (50%)**

SMH – COVID-19 (Round 17) – Results – Booster Impact

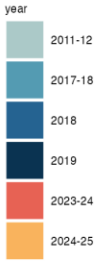
- Models estimate potential reduction in hospitalizations ranging from 35% - 15% for a whole population campaign and 8% - 18% for a 65+ only campaign
- Reductions in deaths are higher with ensemble estimates of 22% reduction for whole population and 18% reduction for 65+
- Reductions are smaller for the high immune escape scenarios



SMH – COVID-19 (Round 17) – Broader context



Across scenarios, COVID-19 is likely to be among the top 10 causes of mortality in the United States



The New York Times

HEALTH | Amid Signs of a Covid Uptick, Researchers Brace for the 'New Normal'

The range of estimated deaths would place Covid somewhere between liver disease and diabetes for causes of death. "Even in that most optimistic scenario, we're getting into the range of mortality that we see for top 10 causes of death in the United States," Dr. Lessler said.

Key Takeaways

- Upticks in cases and hospitalizations hint at a late summer wave
- Hospitalizations have increased ~12% in recent week from prolonged plateau
- Other indicators from wastewater, ED visits show sustained growth through July
- Genomic surveillance hinting at the possible role of EG.5

- Literature review: Recent publications using wastewater surveillance
- National modeling updates

Questions?

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