Network Systems
Science & Advanced
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Biocomplexity Institute & Initiative

University of Virginia

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

March 7<sup>th</sup>, 2024

(data current to February 29<sup>th</sup> – March 6<sup>th</sup>) Biocomplexity Institute Technical report: TR BI-2024-20



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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



#### **Points of Contact**

Bryan Lewis brylew@virginia.edu

Srini Venkatramanan <a href="mailto:srini@virginia.edu">srini@virginia.edu</a>

Madhav Marathe marathe@virginia.edu

Chris Barrett
ChrisBarrett@virginia.edu

#### Model Development, Outbreak Analytics, and Delivery Team

Abhijin Adiga, Aniruddha Adiga, Hannah Baek, Chris Barrett, Parantapa Bhattacharya, Chen Chen, Da Qi Chen, Jiangzhuo Chen, Baltazar Espinoza, Galen Harrison, Stefan Hoops, Ben Hurt, Gursharn Kaur, Brian Klahn, Chris Kuhlman, Bryan Lewis, Dustin Machi, Madhav Marathe, Sifat Moon, Henning Mortveit, Mark Orr, Przemyslaw Porebski, SS Ravi, Erin Raymond, Samarth Swarup, Pyrros Alexander Telionis, Srinivasan Venkatramanan, Anil Vullikanti, Andrew Warren, Amanda Wilson, Dawen Xie



## 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

#### COVID-19 indicators remain elevated, trends are mixed between steady and decline

- Hospital admissions and Visits with Diagnosed COVID are higher than they were at this
  point last year
  - Hospital admissions peak was ~20% lower than last year, but the peak this year is broader.
- Wastewater continues to show high viral loads, though may be receding
- Together this suggest continued plateaus in activity with likely decline in coming weeks.

#### Influenza is remains elevated in VA and across the US

## RSV hospitalizations have reduced to minimal activity



## COVID-19 Surveillance

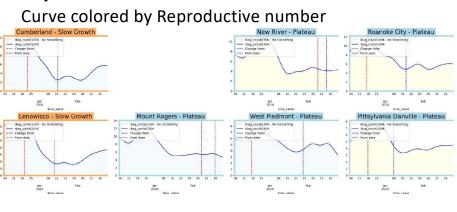


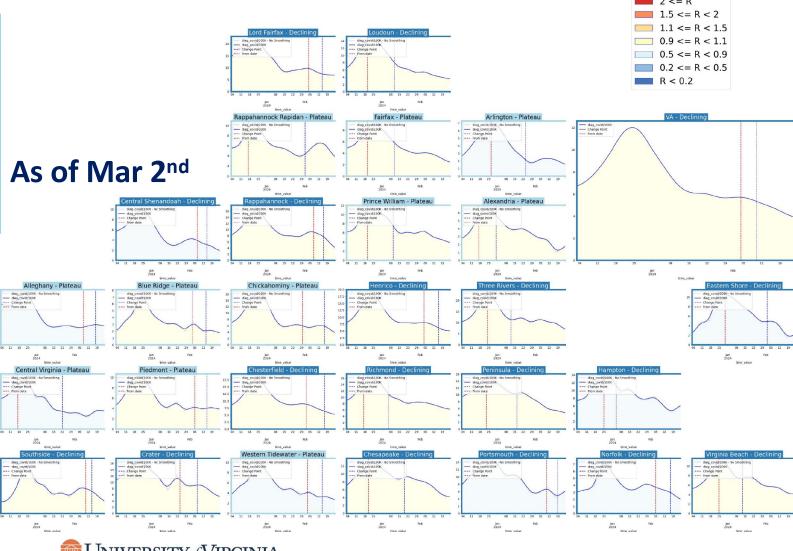
## District Diagnosed COVID Trajectories – last 10 weeks

Status	Number of Districts		
	<b>Current Week</b>	Last month	
Declining	17	9	
Plateau	16	24	
Slow Growth	2	2	
In Surge	0	0	

Curve shows smoothed Emergency Dept and Urgent Care visits with Diagnosed COVID-19 rate (per 100K) in each District

Trajectories of states in label & chart box





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2024-03-02

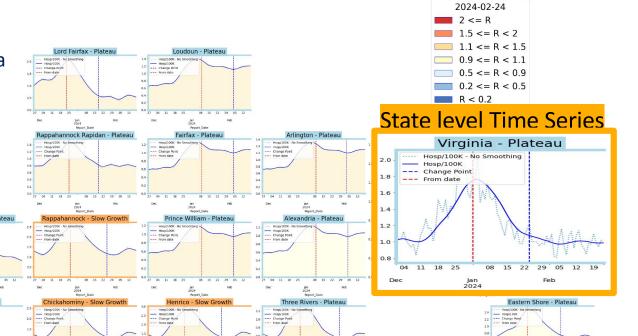
## District Hospital Trajectories – last 10 weeks

#### **Rt estimates from EpiNow2**

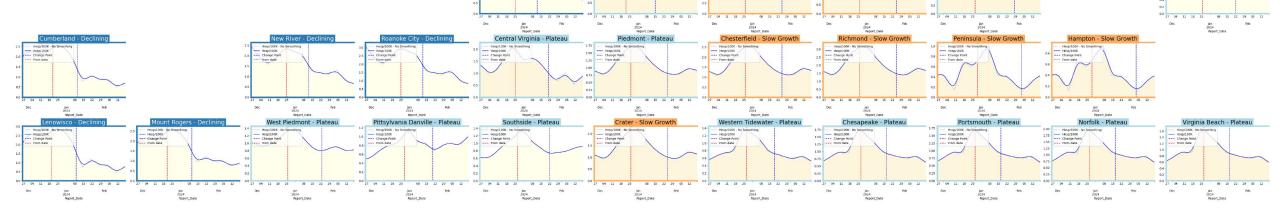
Status	Number of	Districts
Status	Current Week Last week	
Declining	6	8
Plateau	21	19
Slow Growth	8	8
In Surge	0	0

Hospitalization by county inferred from Facility data mapped to counties through Hospital Referral Regions.

As of Feb 24th



Curve shows smoothed hospitalization rate (per 100K) by district
Hosp rate curve colored by R<sub>e</sub> number



3/6/24

## Hospitalizations in VA by Age

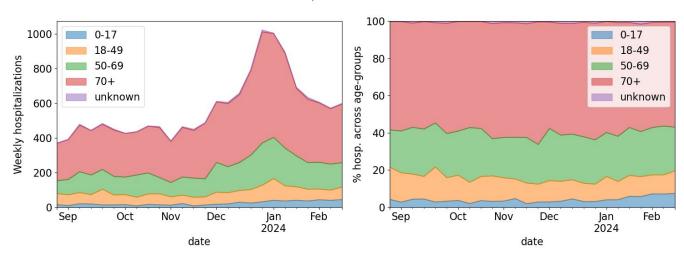
# Age distribution in hospitals showing slight shift towards younger age groups

- Overall hospitalizations stable across all age groups
- Pediatric hospitalizations remain high compared to summer and fall

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

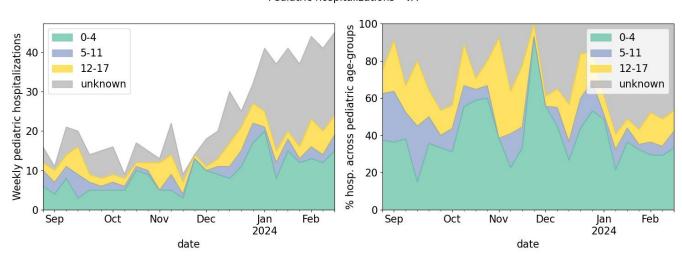
#### Virginia Hospitalizations by Age (all ages)





#### Pediatric Hospitalizations by Age (0-17yo)

Pediatric hospitalizations - VA

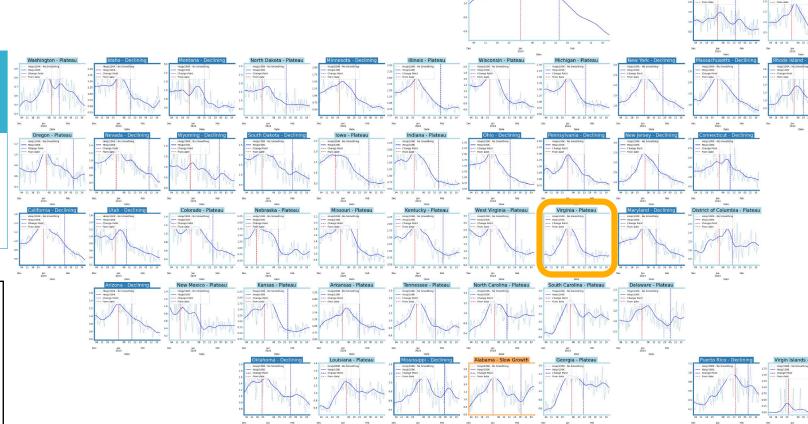


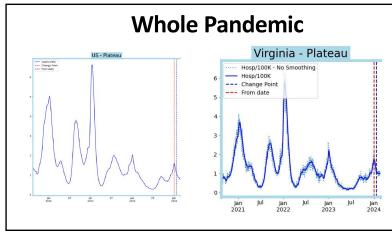
Data Source: <u>Delphi</u> and <u>HHS</u>

## United States Hospitalizations



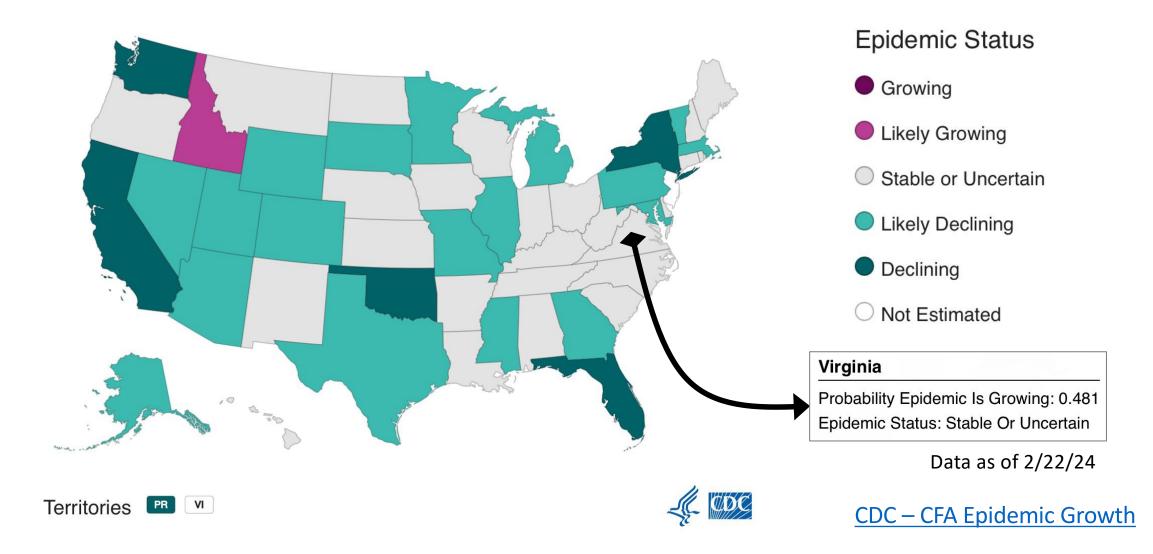
	Number of States		
Status _	Current Week	Last Week	
Declining	25	27	
Plateau	27	25	
Slow Growth	1	1	
In Surge	0	0	





3/6/24

## COVID-19 Hospitalizations – Epidemic Growth



## Estimating Daily Reproductive Number –

EpiNow2 estimation

#### Reproductive Estimate Summary, per data as of March 2<sup>nd</sup>, 2024

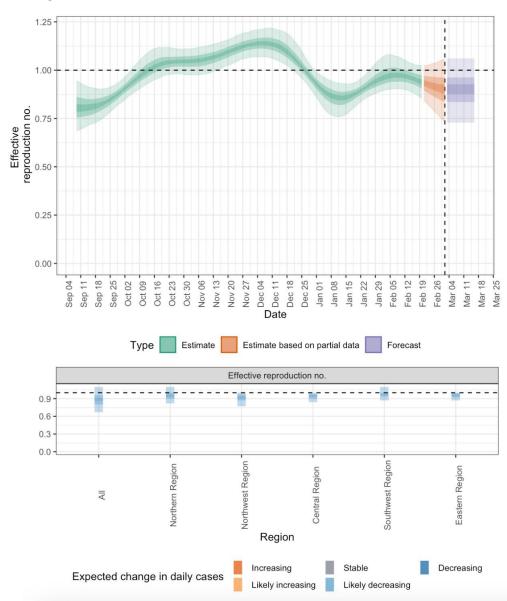
Region	Reproductive number estimate	Credible Interval	Trend forecast
State-wide	0.89	(0.67 - 1.1)	Likely decreasing
Central	0.94	(0.84 - 1)	Likely decreasing
Eastern	0.95	(0.87 - 1)	Likely decreasing
Northern	0.95	(0.82 - 1.1)	Likely decreasing
Northwest	0.92	(0.77 - 1)	Likely decreasing
Southwest	0.97	(0.87 - 1.1)	Likely decreasing

#### Methodology

- 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.
- COVID disease model parameters (including generation time and delay distributions) per CDC CFA blog: <a href="https://www.cdc.gov/forecast-outbreak-analytics/about/technical-blog-rt.html#anchor\_01204">https://www.cdc.gov/forecast-outbreak-analytics/about/technical-blog-rt.html#anchor\_01204</a>
- Uses confirmation date but report date biases are accounted for; estimated date of infection is inferred using Bayesian smoothing techniques and used to produce Rt estimates.
- Source data: <a href="https://data.virginia.gov/dataset/vdh-covid-19-publicusedataset-cli-by-healthdistrict">https://data.virginia.gov/dataset/vdh-covid-19-publicusedataset-cli-by-healthdistrict</a>

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

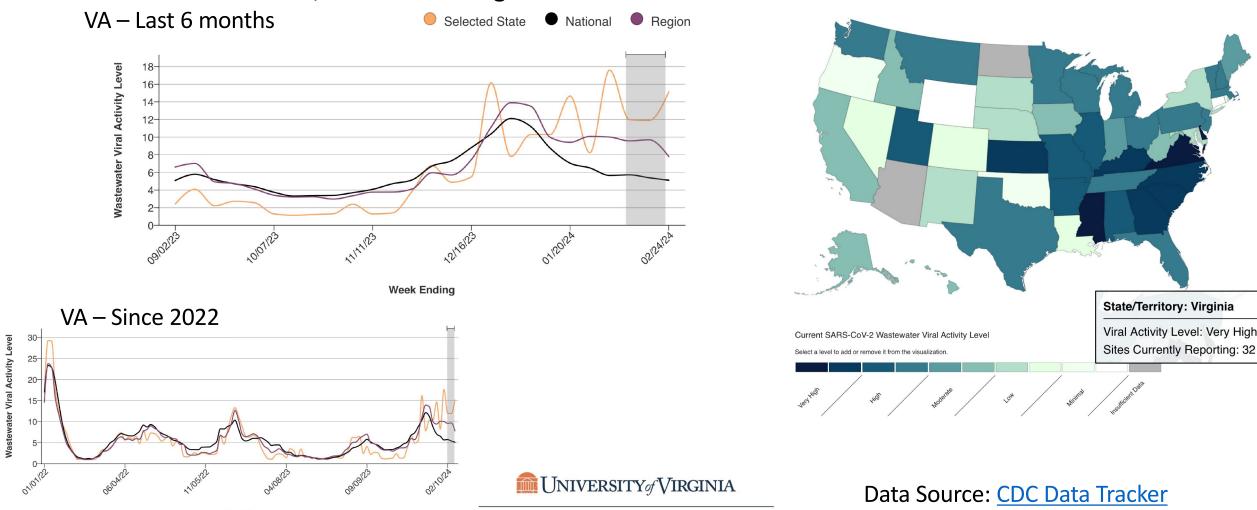
#### **R**<sub>e</sub> per confirmed ED diagnosis (last 6 months)



## Wastewater Monitoring – NWSS

#### Wastewater provides a coarse estimate of COVID-19 levels in communities

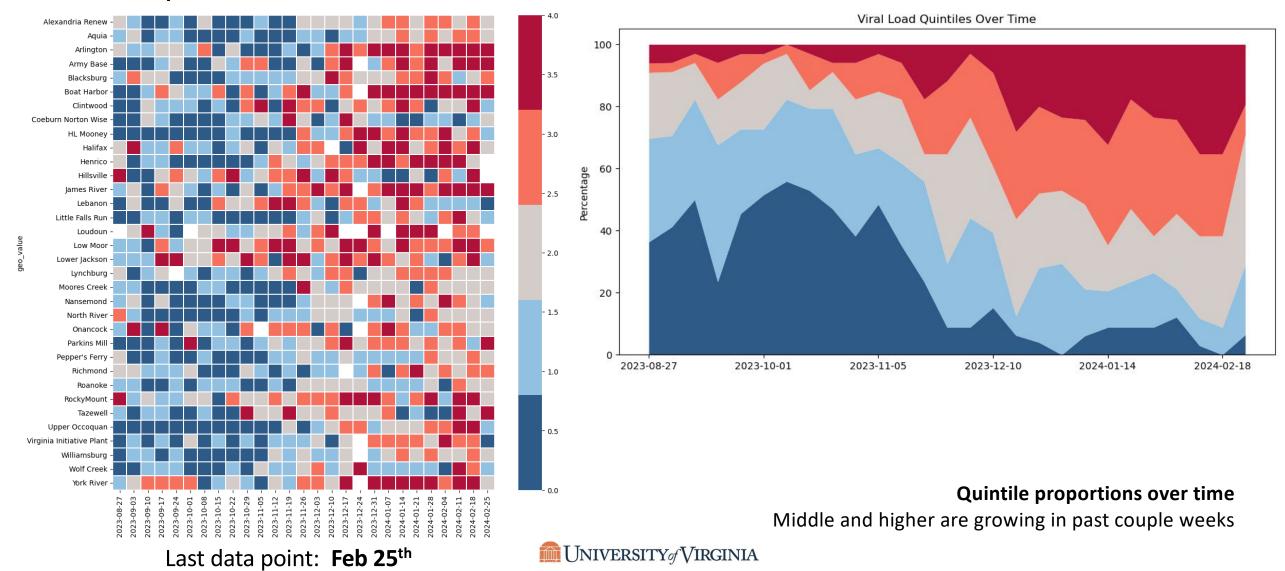
- VA back to "Moderate" after being "Very High" due to artifacts last week
- Pervious, well observed, levels below region and national levels



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## Wastewater Monitoring – VA Sites

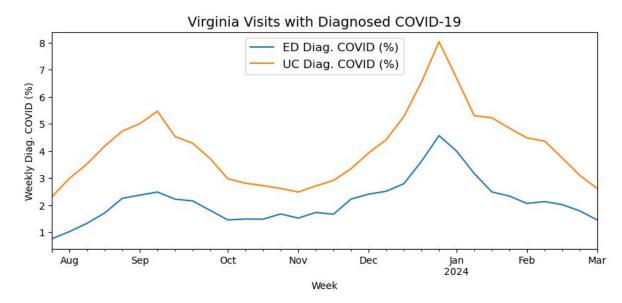
#### Wastewater provides COVID-19 levels in communities which correlate to disease burden

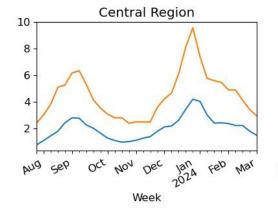


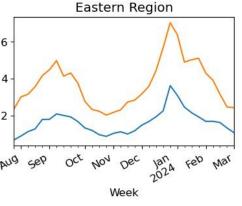
## ED & UC Visits with Diagnosed COVID-19

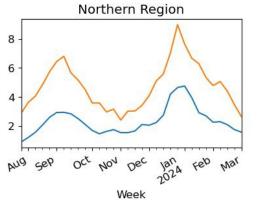
National Syndromic Surveillance Program (NSSP) reports diagnosed COVID-19 from multiple healthcare settings

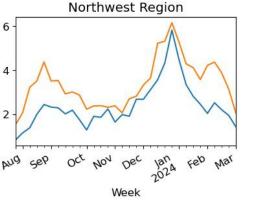
- Week ending March 5<sup>h</sup>, 2024
- Diagnosed visits are a smoother more specific indicator than COVID-like Illness
- COVID-19 Diagnosed visits show signs of further decline after a period so slowed decreases

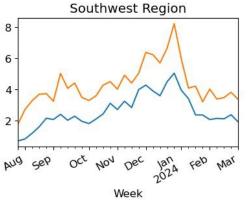










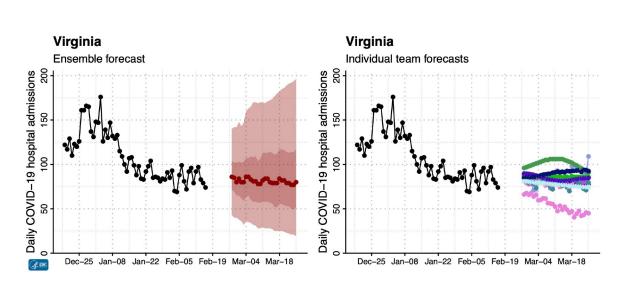


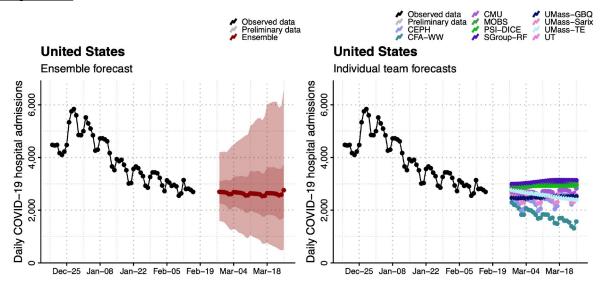
## Current COVID-19 Hospitalization Forecast

## 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) From February 26<sup>th</sup>







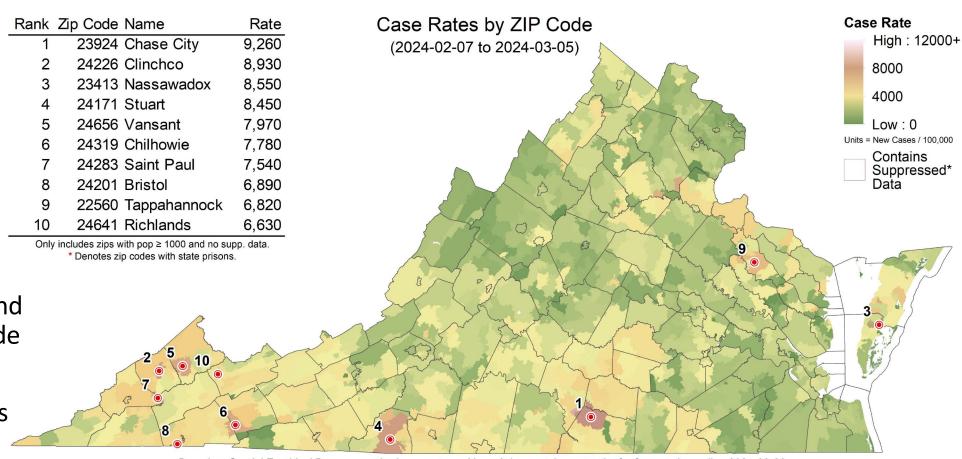
## COVID-19 Spatial Epidemiology



## ZIP Code Level Case Rates Since Last Meeting

## New cases per 100k in the last four weeks

- Divide rates by four to calculate average weekly incidence.
- No change in color scale from last meeting.
- Case rates continue to decline across the Commonwealth.
- Rates remain elevated in far Southwest Virginia, and in a few isolated Southside ZIP codes.
- No ZIP codes with prisons appear in this week's top 10.



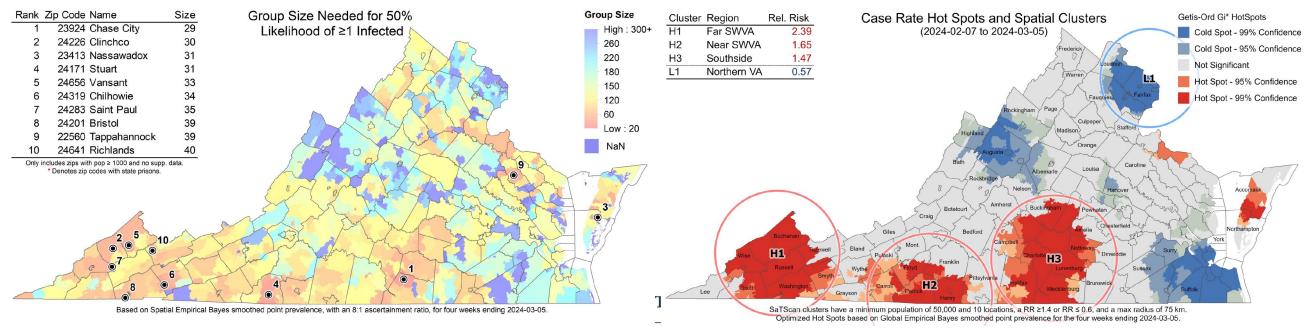
Based on Spatial Empirical Bayes smoothed case rates, with an 8:1 ascertainment ratio, for four weeks ending 2024-02-06.

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## Risk of Exposure / Spatial Clusters and Hot Spots

Case rates since last meeting by ZIP code used to calculate risk of encountering someone infected in a gathering of randomly selected people and find spatial hot spots

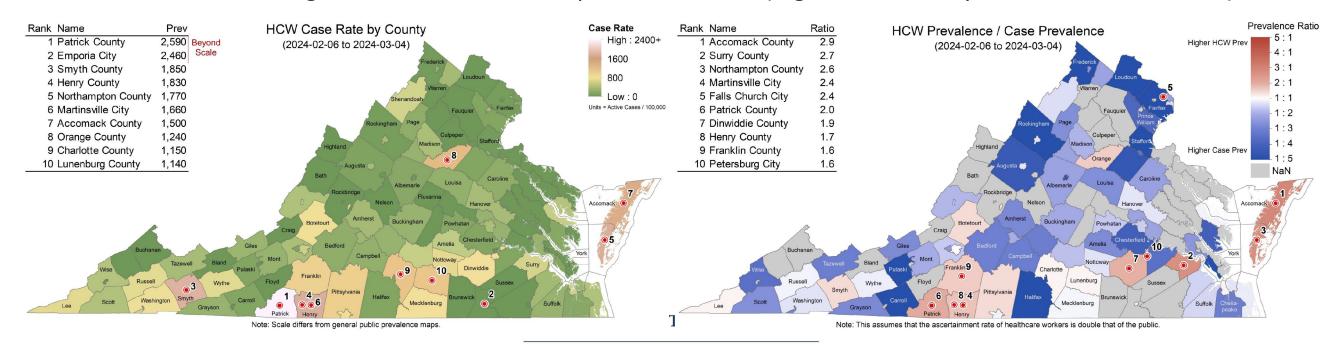
- **Group Size**: Assumes **8 undetected infections** per confirmed case (ascertainment rate from recent seroprevalence survey) and shows minimum size of a group with a 50% chance an individual is infected by ZIP code (e.g., in a group of 29 in Chase City, there is a 50% chance someone will be infected).
- **Spatial Clustering**: Getis-Ord Gi\* based hot spots compare clusters of ZIP codes with four-week case rates higher than nearby ZIP codes to identify larger areas with statistically significant deviations. SaTScan was used to corroborate this analysis and determine relative risk for identified clusters.



## COVID-19 among Healthcare Workers

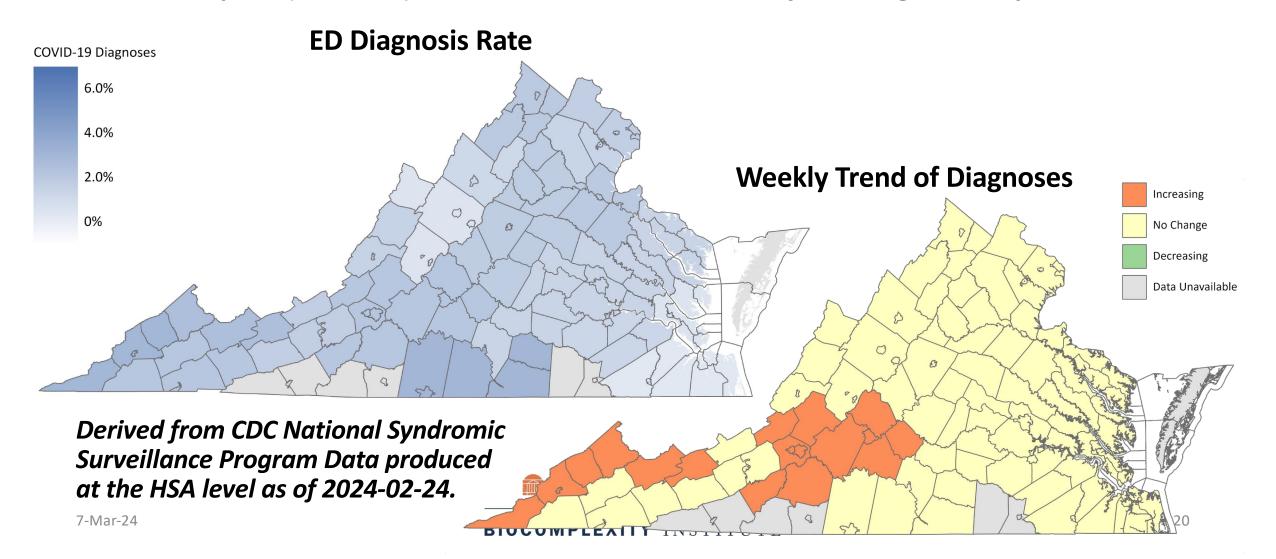
## COVID-19 case rates for the public and for healthcare workers (HCW) were compared to find regions where HCW suffered unusually high burdens of disease

- HCW Rate: Case rate among health care workers (HCW) over a four-week period ending January 8, 2024.
- **HCW Ratio**: Case rate among health care workers (HCW) over the same period using patient facing healthcare workers as the numerator, and the population's case rate as the denominator.
- The healthcare case to public case ratio is well below one in most counties. Only a few show an elevation in HCW cases and a high healthcare worker to public case ratio (e.g. Patrick, Henry, and Franklin Counties).



## Emergency Department Diagnosis Rate – COVID-19

Southside and Far SW report the highest rates, though these are only about half what they were at last report (now 3%). Far SW and the Roanoke-Lynchburg area report increases.



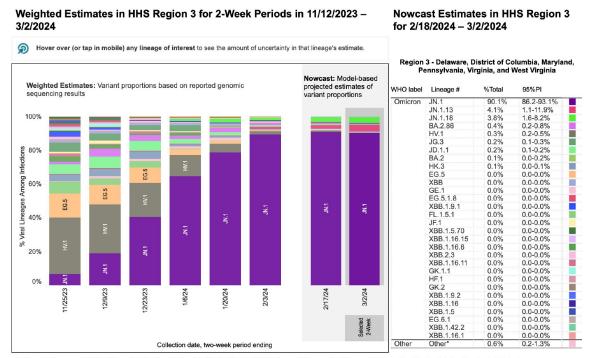
## COVID-19 Genomic Update



SARS-CoV2 Variants of Concern

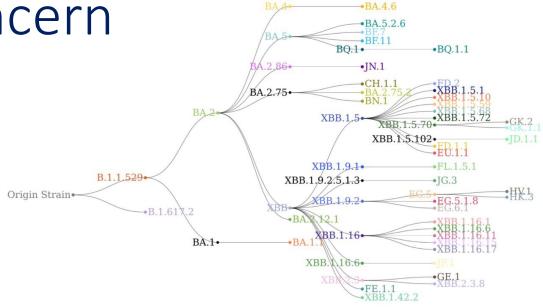
Emerging variants have potential to continue to alter the future trajectories of pandemic and have implications for future control

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



<sup>\*</sup> Enumerated lineages are US VOC and lineages circulating above 1% nationally in at least one 2-week period. "Other" represents the aggregation of lineages which are circulating <1% nationally during all 2-week periods displayed.
# While all lineages are tasked by CDC, those named lineages not enumerated in this graphic are aggregated with their parent lineages, based on Pango lineage definitions, described in more detail here:
https://www.pango.neworktfive-agengo-nemenclature-usless.

CDC Variant Tracking



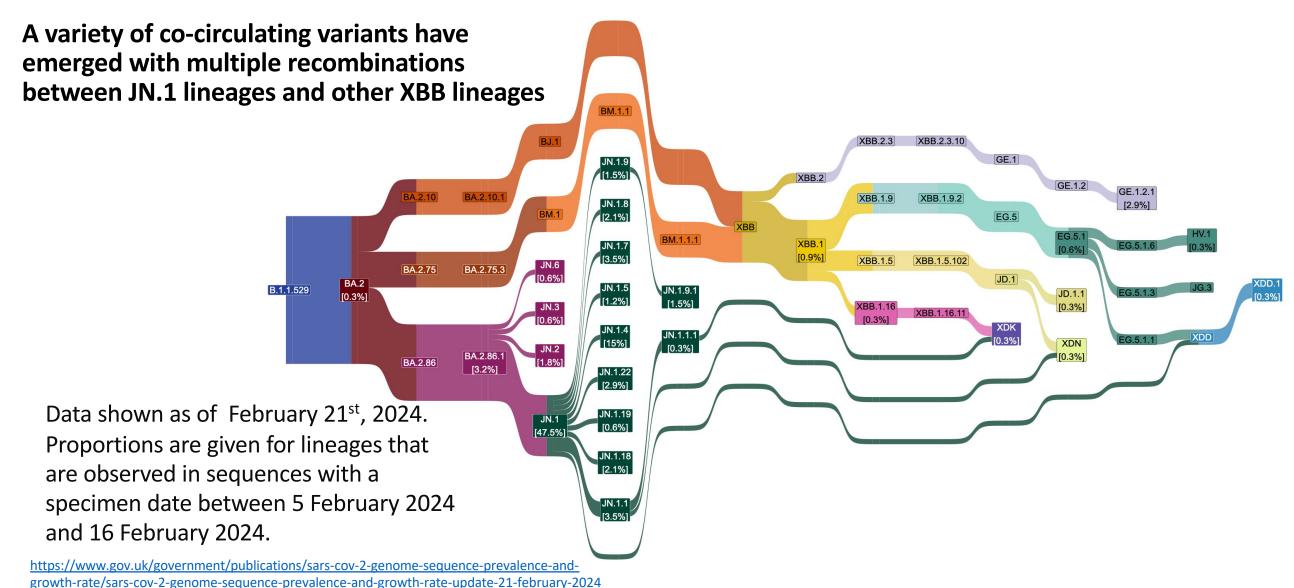
## **Omicron Updates\***

- JN.1 and descendants completely saturate
- Lineage HV.1 (XBB.1.9\*) down to 0.3% from 1%
- Other BA.2.86, JD.1.1, JG.3 remain top variants but are below 1%



<sup>\*</sup>percentages are CDC NowCast Estimates

## SARS-CoV2 Variants of Concern



16-Nov-23

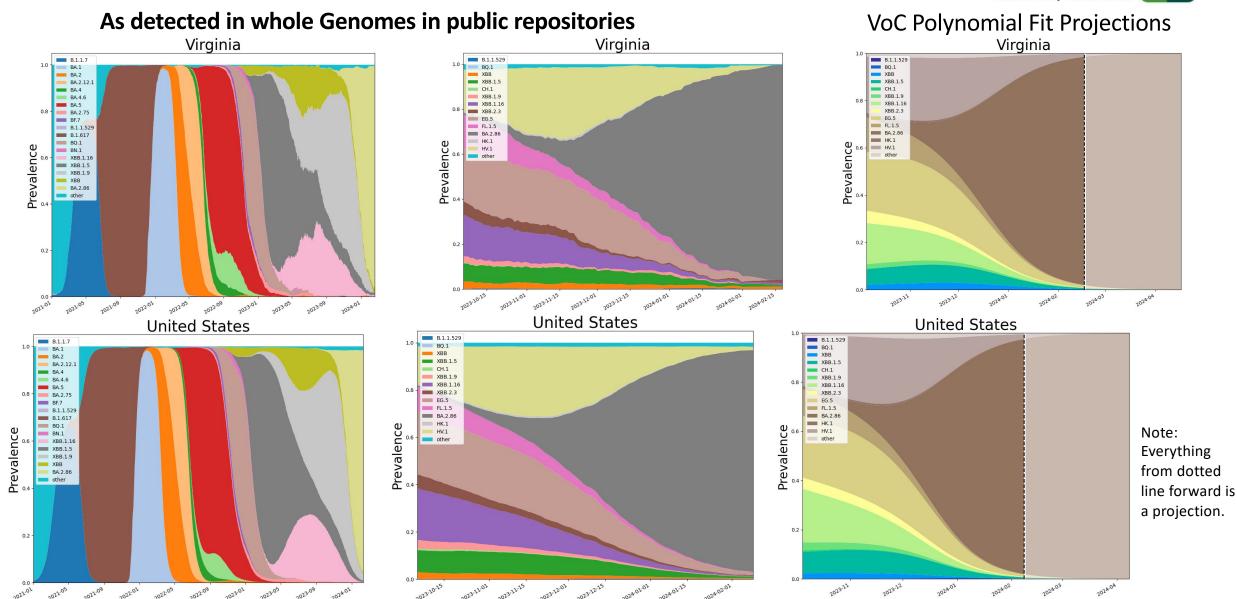
## SARS-CoV2 Omicron Sub-Variants

b-IVIar-24



24

Enabled by data from GISAID



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## SARS-CoV2 Omicron Sub-Variants

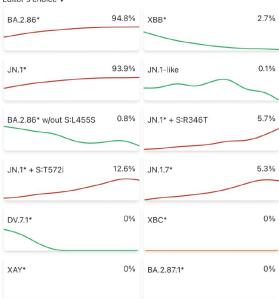
#### **COV-spectrum**

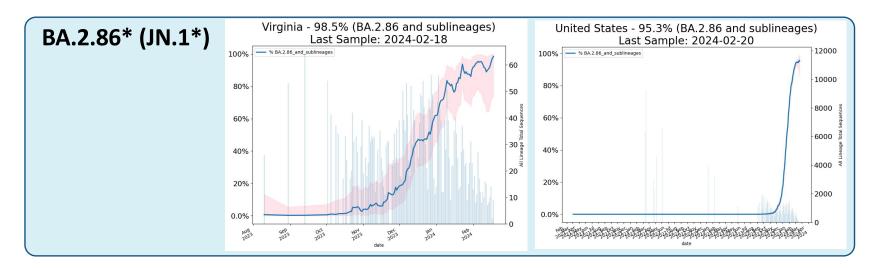
"Editor's choice" Variants to watch

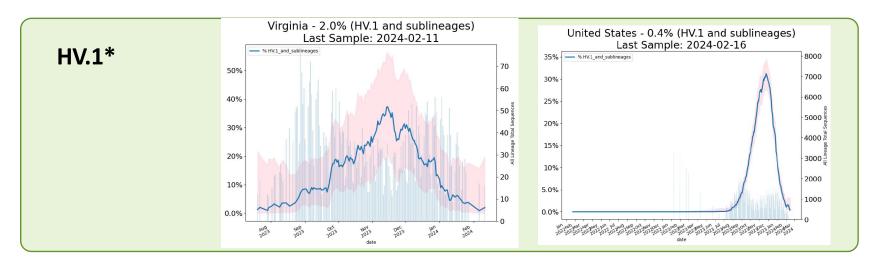
#### **Known variants**

Which variant would you like to explore?











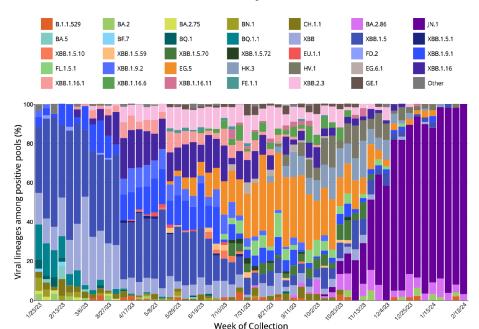
Enabled by data from GSAID

6-Mar-24 25

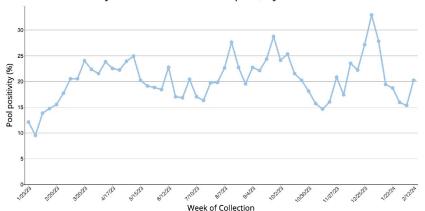
#### Global SARS-CoV2 Variant Status

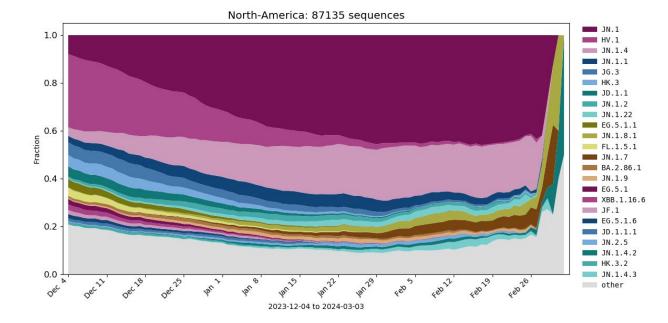
#### Traveller Surveillance

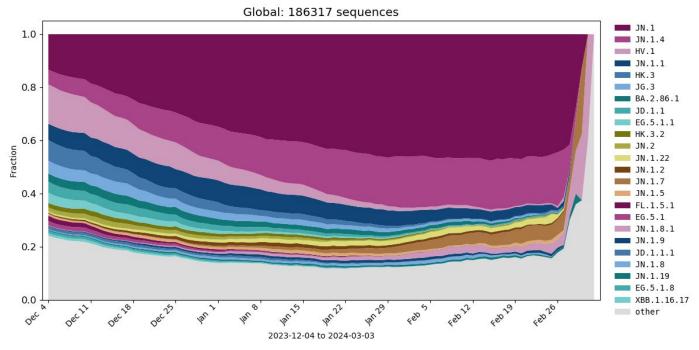
#### Variants Detected, by Collection Week



#### Positivity Rate for Pooled Samples, by Collection Week

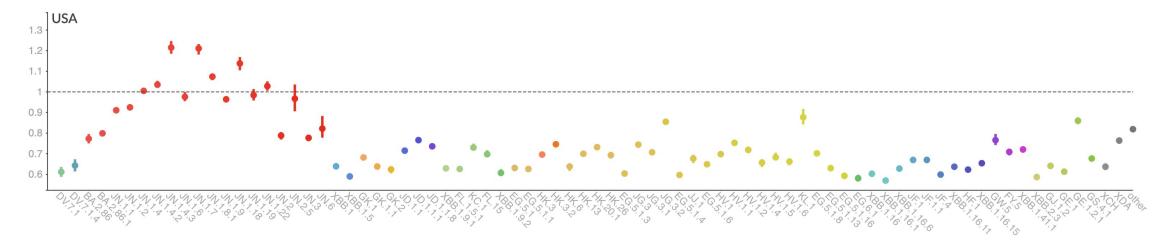






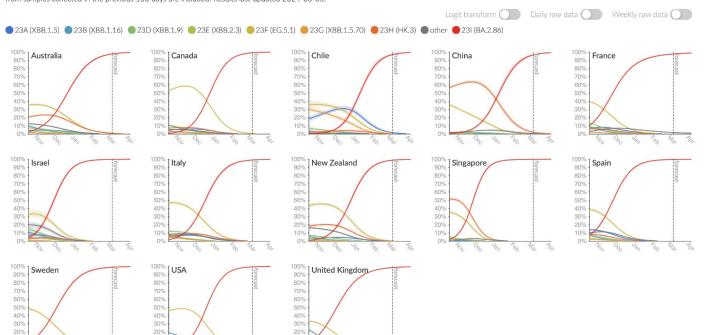
https://cov.lanl.gov/components/sequence/COV/sparks.comp https://covid.cdc.gov/covid-data-tracker/#traveler-genomic-surveillance

## Global SARS-CoV2 Variant Status



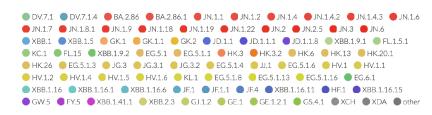
#### Clade frequencies over time

Each line represents the estimated frequency of a particular clade through time. Equivalent Pango lineage is given in parenthesis, eg clade 23A (lineage XBB.1.5). Only locations with more than 100 sequences from samples collected in the previous 150 days are included. Results last updated 2024-03-05.



#### Lineage growth advantage

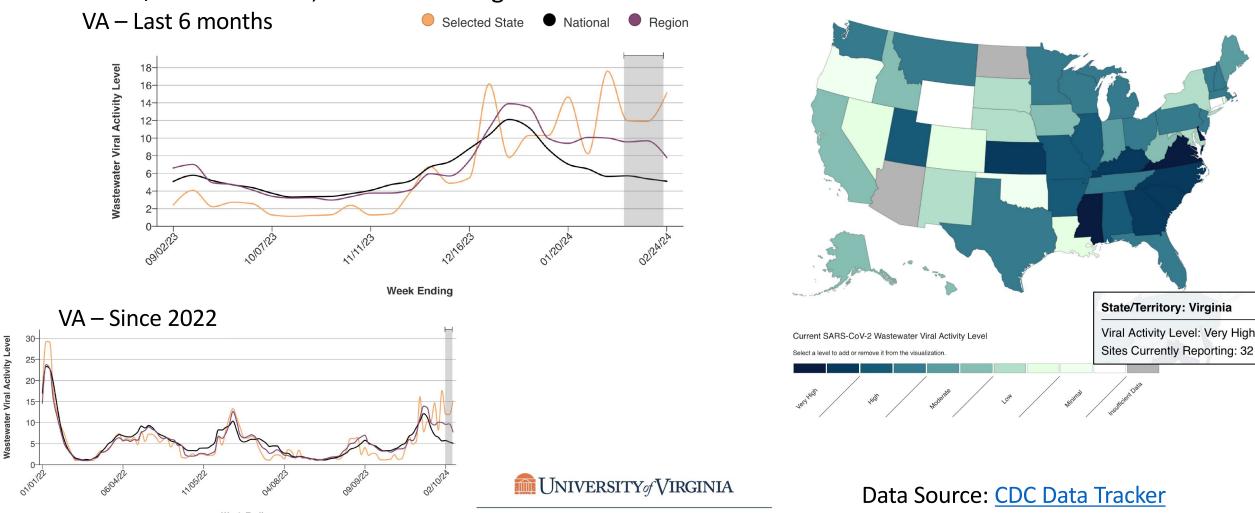
These plots show the estimated growth advantage for given Pango lineages relative to lineage JN.1. This describes how many more secondary infections a variant causes on average relative to lineage JN.1. Vertical bars show the 95% HPD. The "hierarchical" panel shows pooled estimate of growth rates across different locations. Results last updated 2024-03-05.



## Wastewater Monitoring – NWSS

#### Wastewater provides a coarse estimate of COVID-19 levels in communities

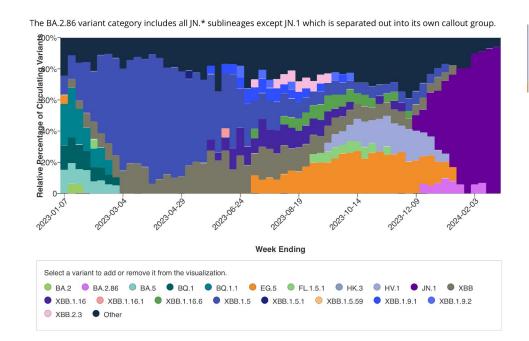
- VA back to "Moderate" after being "Very High" due to artifacts last week
- Pervious, well observed, levels below region and national levels



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### National Wastewater Variant Status

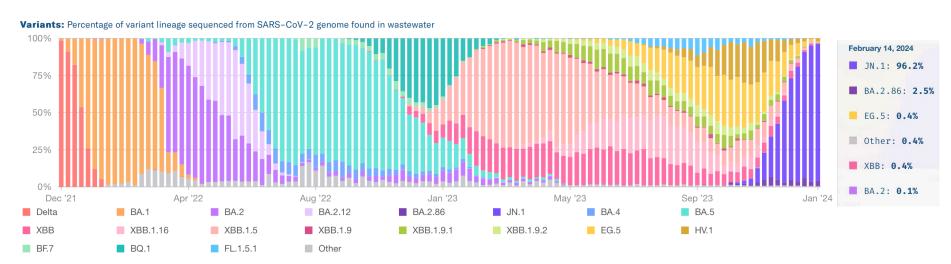
#### **CDC Wastewater**



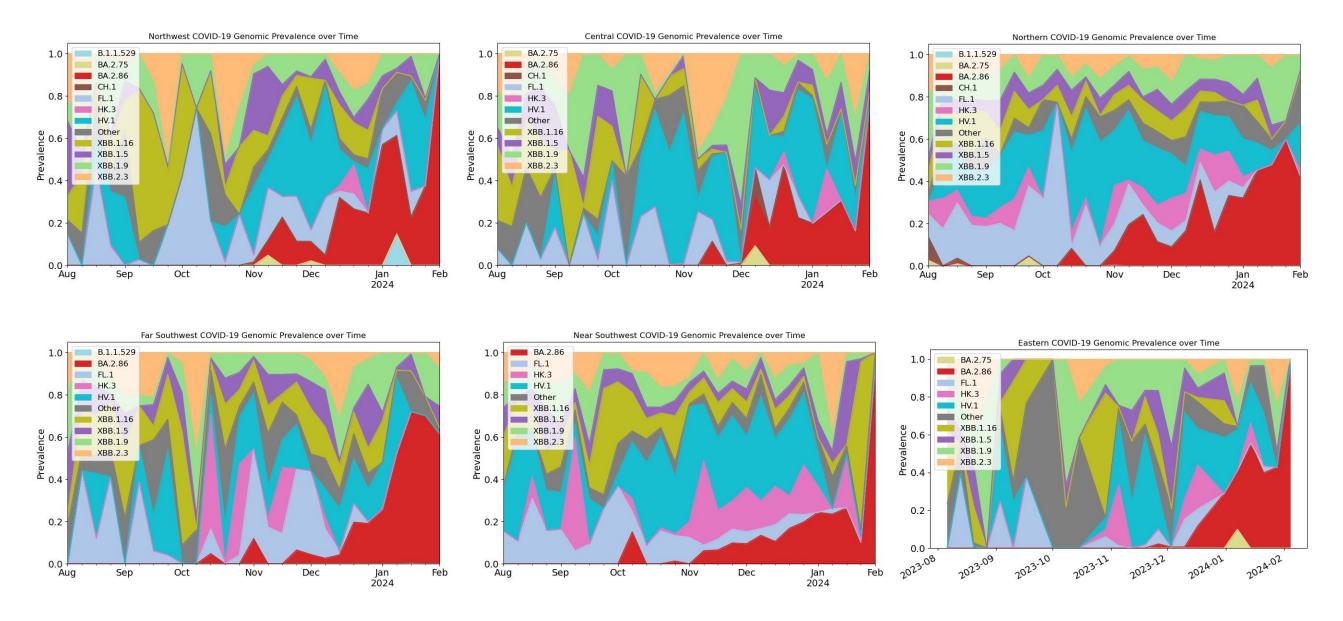
Week Ending: 2024-02-24

JN.1: 94% Other: 6%

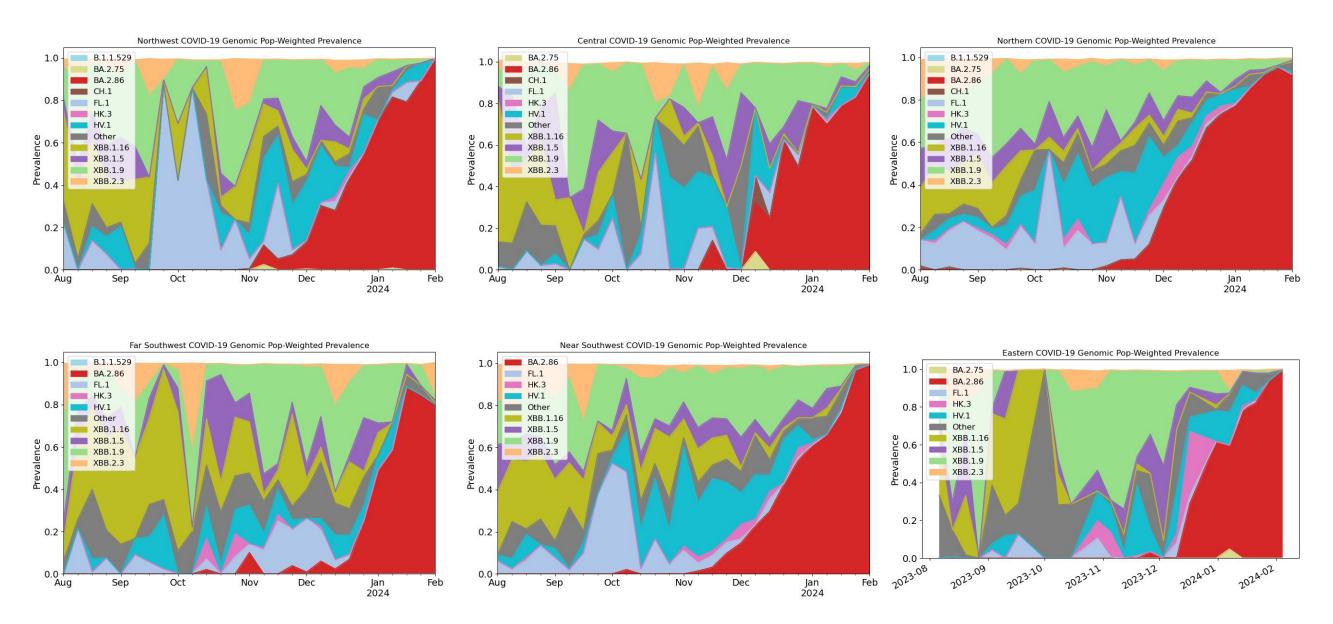
#### **Biobot Wastewater**



## Virginia Regional Wastewater Variant Status (median)

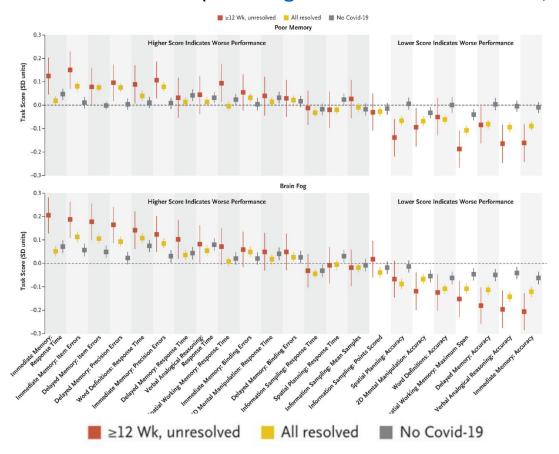


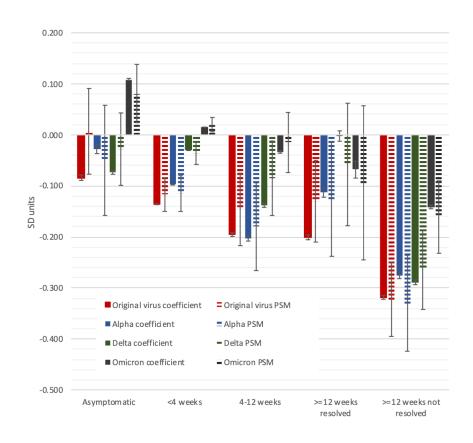
## Virginia Regional Population-Weighted Wastewater Variant Status



## Pandemic Pubs (March 7th, 2024)

**Long COVID Cognitive Effect**: Study of 800K in England, provided a cognitive assessment online and measured performance over time for those infected with COVID-19. Those with short times to resolution of symptoms experienced lower overall deficits. (New England Journal of Medicine, Feb 2024)





In this observational study, we found objectively measurable cognitive deficits that may persist for a year or more after Covid-19. We also found that participants with resolved persistent symptoms had small deficits in cognitive scores, as compared with the no–Covid-19 group, that were similar to those in participants with shorter-duration illness. Early periods of the pandemic, longer illness duration, and hospitalization had the strongest associations with global cognitive deficits.

## Pandemic Pubs (March 7<sup>th</sup>, 2024)

**Long COVID Prevented by Vaccination**: First of 2 studies summarized, Long COVID prevalence was 40-60% lower among vaccinated vs. unvaccinated in Michigan. Second study shows protective effect for adolescents against Long COVID across successive waves of SARS-CoV2 variants. (<u>Eric Topol, Ground Truths, Feb 2024</u>)

## **Two New Reports of Vaccination Protection Vs Long Covid**

From a study in the Annals of Epidemiology, Michiganders derived an important protective benefit against Long Covid: Long COVID prevalence was 40-60% lower among adults vaccinated (vs. unvaccinated) prior to their COVID-19. This level of protection is consistent with many recent reports and has not been emphasized enough regarding an added benefit of booster shots. The data were previously reviewed on Ground Truths here.

And a <u>new preprint report on protection in children and adolescents</u> which looked at different variants (Delta and Omicron) and cause and effect relationship for direct benefit of vaccination, summarized in the Table below. More protection was found in teens than children with the range of 60 to 75%.

Vaccine Effectiveness (in %) and 95 CI	Direct Effect	Indirect Effect
Delta stud	ly in adolescents	
95.4% (90.9, 97.7)	1.08 (0.75, 1.55)	0.04 (0.03, 0.05)
Omicron	study in children	
60.2% (40.3, 73.5)	1.24 (0.92, 1.66)	0.31 (0.23, 0.42)
Omicron st	udy in adolescents	
75.1% (50.4, 87.5)	0.91 (0.69, 1.19)	0.21 (0.16, 0.27)

#### **Solving the puzzle of Long Covid**

Long Covid provides an opportunity to understand how acute infections cause chronic disease

ZIYAD AL-ALY AND ERIC TOPOL Authors Info & Affiliations

SCIENCE - 22 Feb 2024 - Vol 383, Issue 6685 - pp. 830-832 - DOI: 10.1126/science.adl0867

Essay in <u>Science</u> advocating for addressing Long COVID <a href="https://www.science.org/doi/10.1126/science.adl0867">https://www.science.org/doi/10.1126/science.adl0867</a>

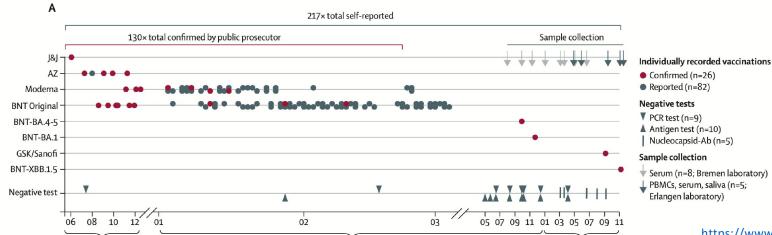


https://erictopol.substack.com/p/towards-solving-the-long-covid-puzzle

## Pandemic Pubs (March 7<sup>th</sup>, 2024)

**Hyper-Vaccination**: German man received 217 vaccinations over the course of 2.5 years. This Hyper-vaccination led to no adverse events and increased the quantity of antibodies and T-cells and did not negatively effect the quality of his immune response. (Lancet, March 2024)

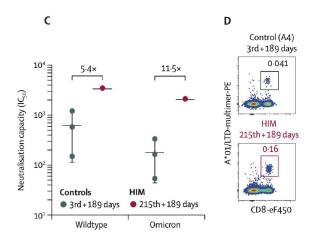
2023



2022

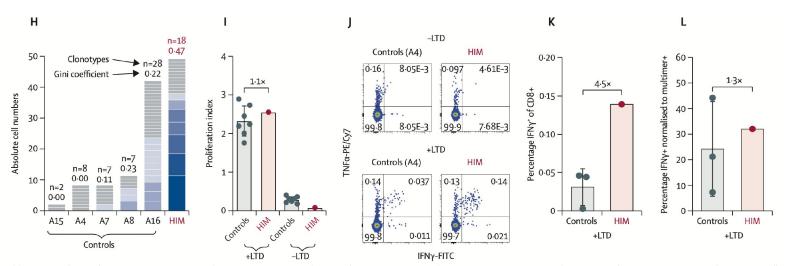
# Hypervaccination increases the quantity, but not the quality, of adaptive immunity

#### https://www.thelancet.com/pdfs/journals/laninf/PIIS1473-3099(24)00134-8.pdf



2021

(C) Neutralisation capacity against wildtype and Omicron spike-protein of HIM's and controls' sera in a pseudotype neutralisation assay. (D–E) Frequency of spike epitope (HLA-A\*01/LTD)-specific CD8+ T cells. n=5 controls.



(H) T-cell clonality of LTD-specific CD8+T cells determined by scRNAseq (10× Genomics, Pleasanton CA, USA). Segments of bars indicate individual clones (grey segments=1 cell; blue segments>1 cell). Numbers on top of the bars represent total number of clones and Gini coefficient to indicate clonality. (I) Proliferation index of LTD-specific CD8+T cells upon stimulation with LTD-peptide for 14 days. n=7 control samples were collected from day 76 to 568 after last spike-exposure (vaccination or infection). (I)—I) Cytokine expression of CD8+T cells upon stimulation (L) Normalisation of IFNy/TNFα expression. (K) Quantification of IFNy/White the LTD-specific fraction of CD8+T cells. Connected dots represent individual donors, (B,E). Data points represent individual donors, bars or solid lines and error bars indicate the mean +/- s.d. (C,G,I,K,L). Fold-differences to mean of controls are indicated (C,G,I,K,L). HIM-hypervaccinated individual from Magdeburg, Germany. J&L=Johnson & Johnson Ad26.COV2.S vaccine. AZ-ASTAZeneca Vaxzevria vaccine. Moderna=Spikevax vaccine. BNT Original=Pfizer-BioNTech Comirnaty original vaccine. BNT-BA 4-S=Comirnaty original/Omicron BA 4-S. BNT-BA 1.5 comirnaty original/Omicron BA 1.6 SK/Sanofi=Vidprevtyn Beta vaccine. BNT-XBB.1.5. nd=not detected. ICS0=half-maximal inhibitory concentration. LTD=LTDEMIAQY epitope. PE=phycoeytyrin. PBMC=peripheral blood mononuclear cells. A\*01/LTD-multimer-PE=peptide human leukocyte antigen (HLA) multimer for HLA-A\*01:01 presenting the LTD epitope peptide and conjugated to the PE dye. TN-like/SCM=naive-like and stem cell memory T cells. IEM=Refector memory T cells. IEMR=Refector memory T cells. EMRA=effector memory T cells after LTD-expection and conjugated to the PE dye. TN-like/SCM=naive-like and stem cell memory T cells. IEMR=Refector memory T cells. Superselation and construction.

## Influenza Update



#### FluView Interactive

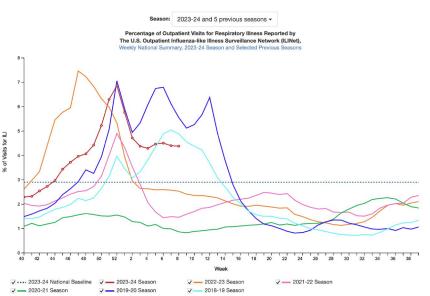
**Region 3** 

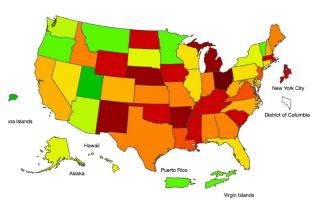
## Current Influenza Situation — ILI Activity

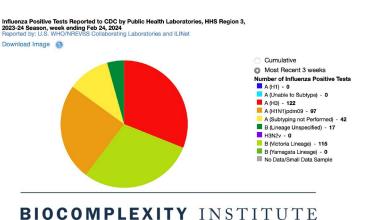
# All regions remain above threshold and many are steady

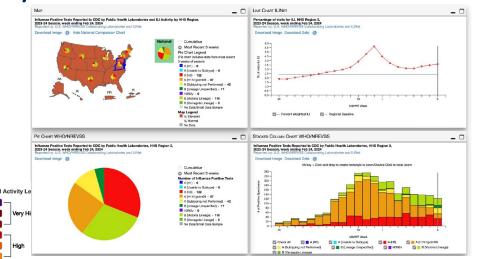
Virginia remains a "High" level of Influenza activity

National ILI activity has been at a steady high level for 6
weeks

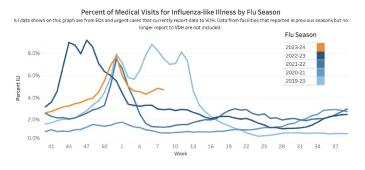


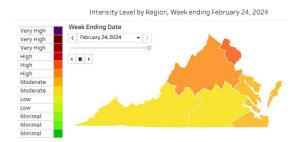






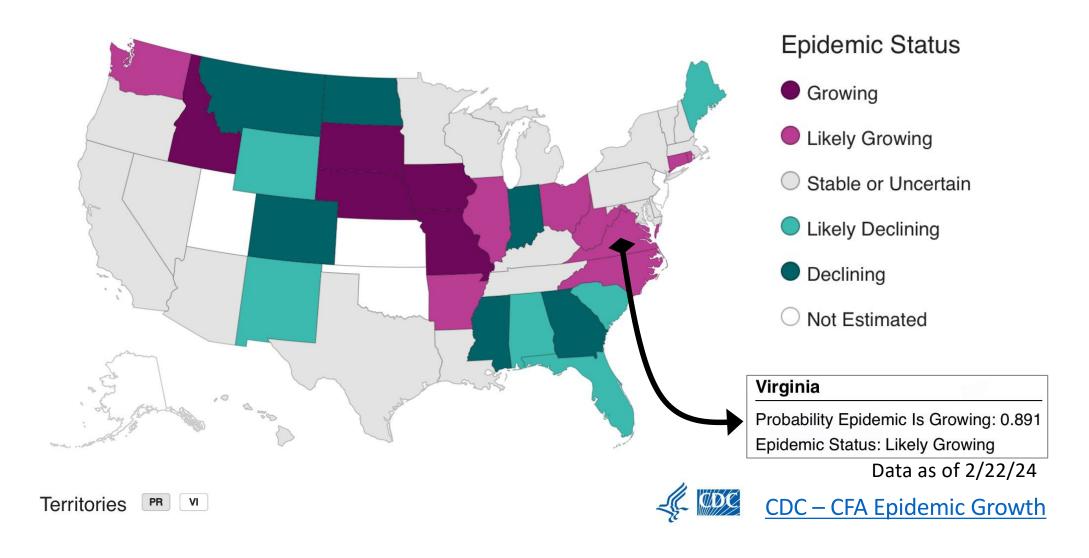
#### Virginia (ED & UC Visits – Feb24, 2024)





FluView Surveillance

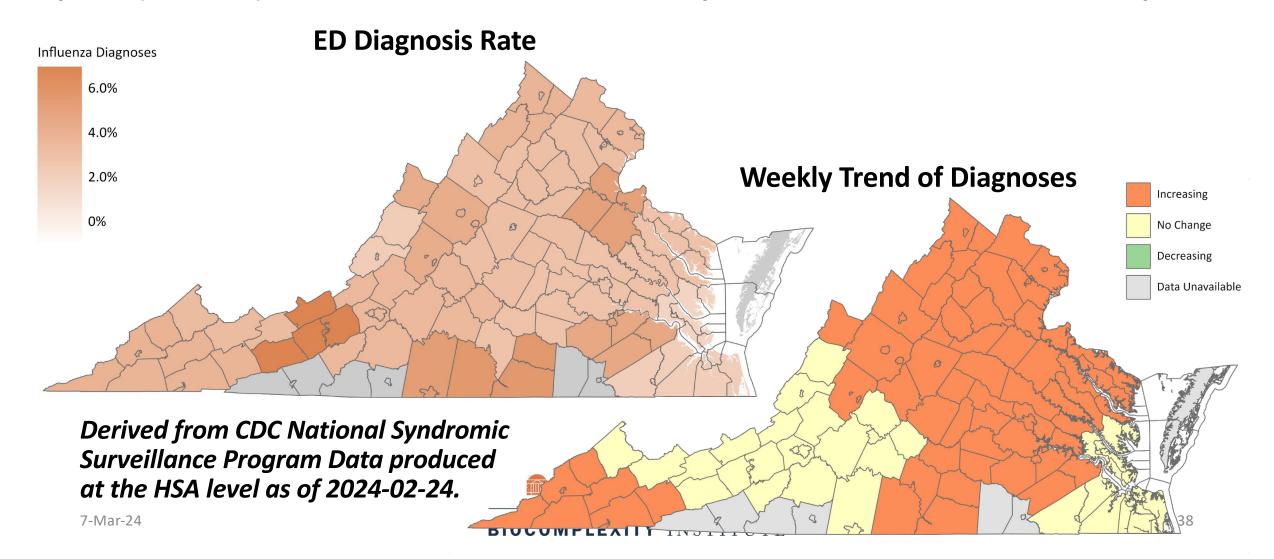
# Influenza Hospitalizations – Epidemic Growth





# Emergency Department Diagnosis Rate – Influenza

Flu diagnoses are still highest in the New River Valley, with rates rivaling last month's reports (over 6%). Most of the Commonwealth reported increases from the week prior.

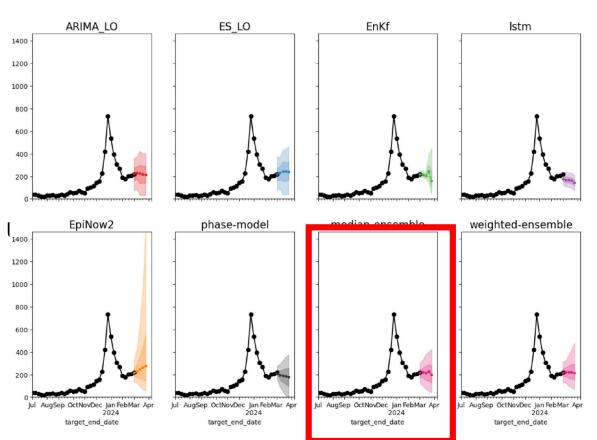


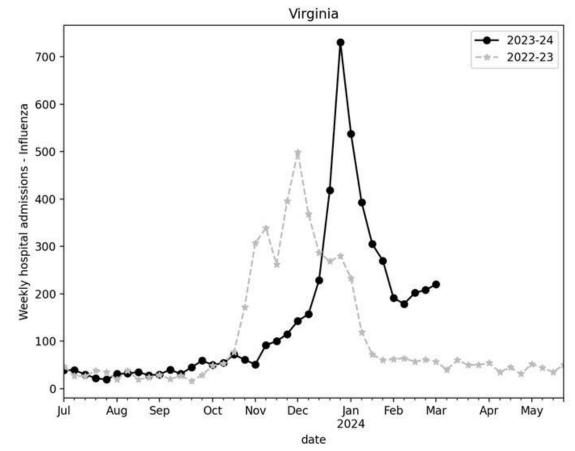
## Influenza Forecasts – Hospitalization Admissions

UVA forecast model only
Hospital Admissions for Influenza
and Forecast for next 4 weeks

National Flu Hospital Admissions
Weekly hospital admissions
Last update: March 2<sup>nd</sup>, 2024







Forecast from March 6<sup>th</sup> from data of Mar 2<sup>nd</sup>



### Current Influenza Hospitalization Forecast

#### Statistical models for submitting to <a href="CDC Influenza Forecasting Hub">CDC Influenza Forecasting Hub</a>

• Uses a variety of statistical and ML approaches to forecast weekly hospital admissions for the next 4 weeks for all

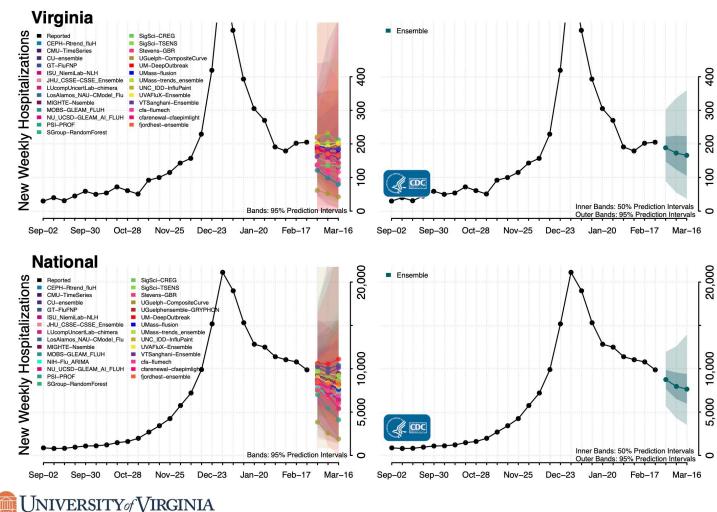
states in the US

Hospital Admissions for Influenza and Forecast for next 4 weeks (CDC Influenza Ensemble)

From February 28th

**CDC Flu Activity Surveillance** 

https://www.cdc.gov/flu/weekly/fluactivitysurv.htm





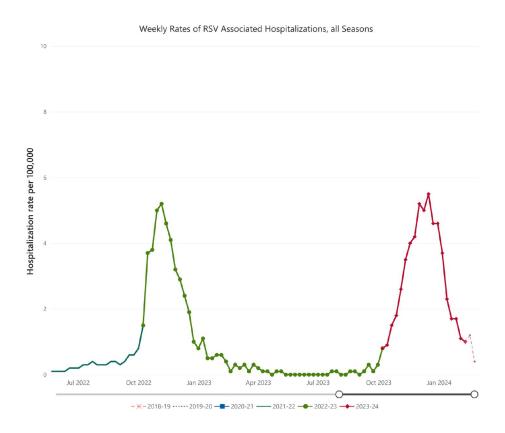
# RSV Update

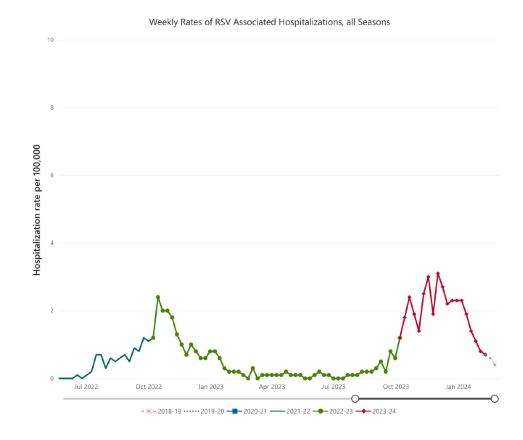


## Current RSV Situation – Hospitalization Rates (RSV-Net)

Maryland (RSV-Net)

Tennessee (RSV-Net)





#### Surveillance data as of:

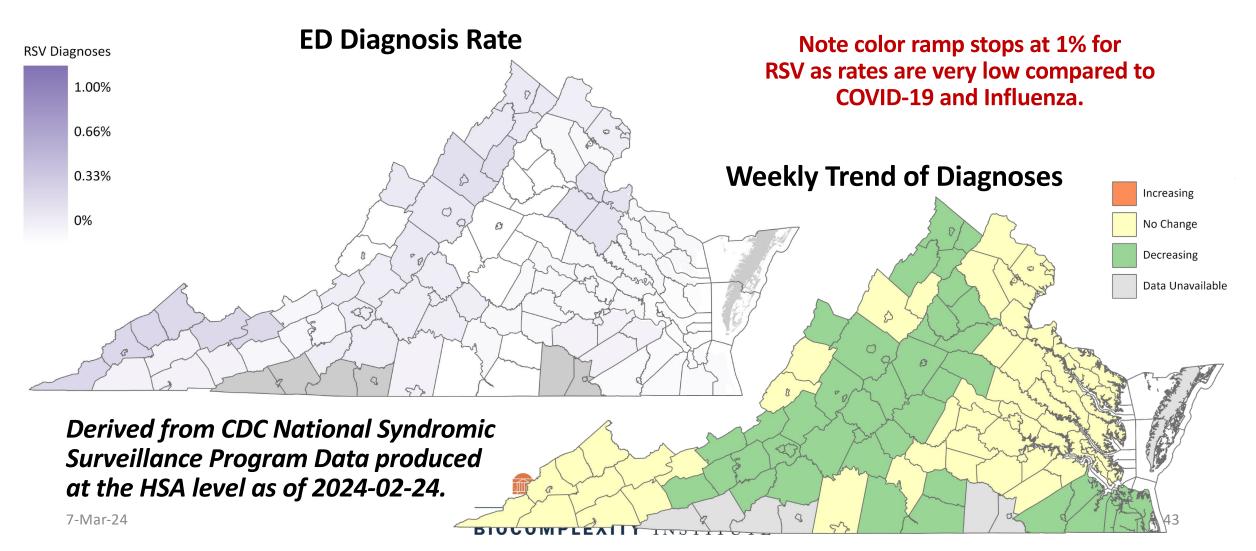
2/10 (last solid data)2/24 (last recent but likely to be updated)





## Emergency Department Diagnosis Rate – RSV

RSV rates are so low that a different color scale was required for maps. No counties report a diagnosis rate higher than 0.28%. Most counties continue to report weekly decreases.

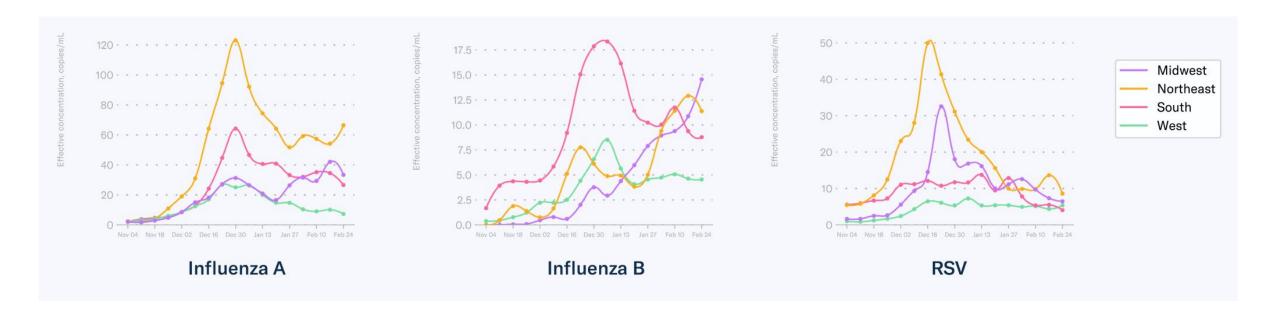


# Respiratory Illness Combined Update



### Combined Respiratory Illness Viruses - Wastewater

#### Regional Flu and RSV Wastewater Concentrations

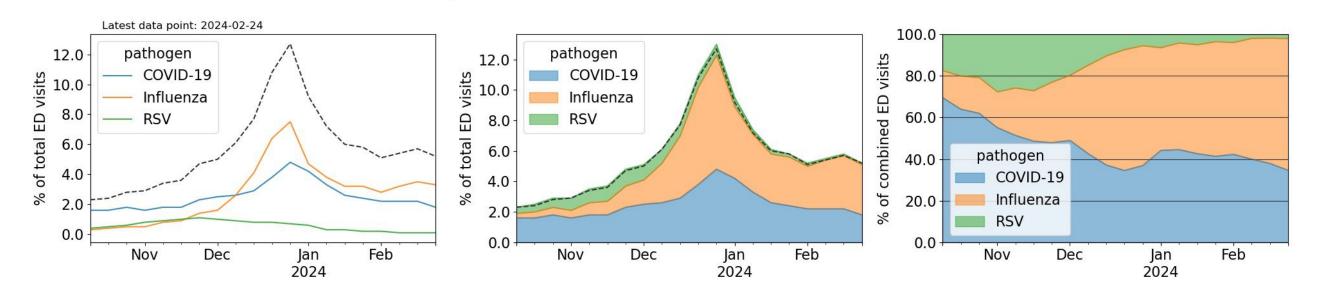






### Combined Respiratory Illness Viruses – NSSP VA ED Visit

Virginia - COVID-19, Influenza, and RSV ED visits - Source: NSSP



Data as of February 24th, 2024

## Key Takeaways

#### COVID-19 indicators remain elevated, trends are mixed between steady and decline

- Hospital admissions and Visits with Diagnosed COVID are higher than they were at this
  point last year
  - Hospital admissions peak was ~20% lower than last year, but the peak this year is broader.
- Wastewater continues to show high viral loads
- Together this suggest continued plateaus in activity with likely decline in coming weeks.

#### Influenza is remains elevated in VA and across the US

#### RSV hospitalizations have reduced to minimal activity



### Questions?

#### **Points of Contact**

Bryan Lewis brylew@virginia.edu

Srini Venkatramanan srini@virginia.edu

Madhav Marathe marathe@virginia.edu

Chris Barrett@virginia.edu

#### **Biocomplexity COVID-19 Response Team**

Aniruddha Adiga, Abhijin Adiga, Hannah Baek, Chris Barrett, Golda Barrow, Richard Beckman, Parantapa Bhattacharya, Jiangzhuo Chen, Clark Cucinell, Patrick Corbett, Allan Dickerman, Stephen Eubank, Stefan Hoops, Ben Hurt, Ron Kenyon, Brian Klahn, Bryan Lewis, Dustin Machi, Chunhong Mao, Achla Marathe, Madhav Marathe, Henning Mortveit, Mark Orr, Joseph Outten, Akhil Peddireddy, Przemyslaw Porebski, Erin Raymond, Jose Bayoan Santiago Calderon, James Schlitt, Samarth Swarup, Alex Telionis, Srinivasan Venkatramanan, Anil Vullikanti, James Walke, Andrew Warren, Amanda Wilson, Dawen Xie

