Network Systems Science & Advanced Computing Biocomplexity Institute & Initiative University of Virginia

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

December 14th, 2023

(data current to Dec 1st – Dec 13th) Biocomplexity Institute Technical report: TR BI-2023-286

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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 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

Most COVID-19 indicators show continued growth

- Case and Hospitalization growth may be slowing but remain elevated
- Other indicators are mixed with some plateaus and some growth
- Wastewater indicators have receded from growth of past weeks; some sites remain high
- Together this suggest continued slow growth which may accelerate going forward.

Other Respiratory diseases (Flu, RSV) are active



COVID-19 Surveillance



Case Rates (per 100k)





District Case Trajectories – last 10 weeks

<u>Rt estimates from EpiNow2</u>

Status	Number of Districts		
	Current Week	Last month	
Declining	3	(9)	
Plateau	3	(9)	
Slow Growth	22	(17)	
In Surge	7	(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





District Hospital Trajectories – last 10 weeks

Rt estimates from EpiNow2



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

As of Dec 9th



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



13-Dec-2023

COVID-19 Spatial Epidemiology



ZIP Code level case rate since last meeting

New cases per 100k in the last four weeks

- Rates are for the weeks since last meeting.
 Divide rates by four to calculate average weekly incidence.
- Case rates remain highly elevated in the Southwest, particularly west of Martinsville.
- Other areas of higher burden include Hanover, as well as Augusta and Pittsylvania Counties.
- Hanover is the only prison containing ZIP code in the top 10.



Based on Spatial Empirical Bayes smoothed case rates, with an 8:1 ascertainment ratio, for four weeks ending 2023-12-12.

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Risk of Exposure 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 15 in Laurel Fork, 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.



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 December 11.
- HCW Ratio: Case rate among health care workers (HCW) over the same period using patient facing health care workers as the numerator, and the population's case rate as the denominator.
- High HCW regions are sporadically spread across Virginia. But Patrick County, King and Queen County, and Martinsville appear on both top 10 lists. They have high HCW rates, despite comparably low case rates.



COVID-19 Broader Context



United States Hospitalizations



United States Hospitalizations – Epidemic Growth



13-Dec-2023

Around the World – Hospital Admissions



Data source: Official data collated by Our World in Data

<u>CC BY</u>





COVID-19 Growth Metrics



Estimating Daily Reproductive Number – VDH report dates – EpiNow2 estimation Re from VDH

Reproductive Estimate Summary as of December 12, 2023

Region	Reproductive number estimate	Credible Interval	Trend forecast
State-wide cases	1.2	1.0 - 1.3	Increasing
State-wide hosp	1.0	0.88 - 1.1	Stable
Central	1.1	0.95 - 1.3	Likely increasing
Eastern	1.2	1.1 - 1.5	Increasing
Far SW	1.1	0.93 - 1.4	Likely increasing
Near SW	1.0	0.79 - 1.2	Stable
Northern	1.2	1.0 - 1.4	Increasing
Northwest	1.1	0.90 - 1.3	Likely increasing

Re from VDH Cases (last 6 months)



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.
- Serial interval, generation time, and incubation period per CDC CFA: <u>https://www.cdc.gov/forecast-outbreak-analytics/about/technical-blog-rt.html</u>.
- Uses confirmation date but report date biases are better accounted for; estimated date of infection is inferred using Bayesian smoothing techniques and used to produce Rt estimates.
- Note: most recent data point for hospitalizations is 3 days prior to that of cases (HHS hospitalization through 12/09/23 vs. VDH case data through 12/12/23).



Wastewater Monitoring – VA Sites

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

13-Dec-2023

Some VA sites (esp. Eastern) are starting to shift to higher quintiles in wastewater percentile groups •



Wastewater Monitoring – NWSS

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

- VA currently "Very High" (may be due to limited reporting in recent weeks)
- Pervious, well observed, levels below region and national levels





Current SARS-CoV-2 Wastewater Viral Activity Level

select a level to add or remove it from the visualization.

Data Source: CDC Data Tracker

Region Level Viral Activity Level



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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





Pediatric hospitalizations - VA



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

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
- CLI remains reduced and plateaued in most regions, with Southwest showing slow continued growth
- Levels returning to spring-time levels in most regions







Wastewater, ED visits, and Test positivity

Wastewater: Effective SARS-CoV-2 virus concentration (copies / mL of sewage)



Weekly Emergency Department Visits by Viral Respiratory Illness Type and State, as a Percent of All Emergency Department Visits

Make a selection from the filters to change the visualization information.



- National WW signals have increased over the past two weeks
- ED visits for COVID are beginning to increase



Weekly Emergency Department Visits by Age Group and Respiratory Illness, as a Percent of All Emergency Department Visits



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

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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)







COVID-19 Genomic Update



SARS-CoV2 Variants of Concern

Nowcast Estimates in HHS Region 3

for 11/26/2023 - 12/9/2023

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

Weighted Estimates in HHS Region 3 for 2-Week Periods in 8/20/2023 –



* 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 tracked by COC, how a manufilineages not annot a graphic are aggregated with their parent lineages, based on Pango lineage definitions, described in more detail here: https://www.pango-enversichture-systems/tatement-of-comcatare-rulew.



Omicron Updates*

- New lineage HV.1 (XBB.1.9*) up to 35% from 34%
- BA.2.86* lineages (including JN.1) are up to 16.4% from 9%
- JD.1.1 (XBB.1.5) remains at 9%
- EG.5 (XBB.1.9) down to 9% from 12%
- HK.3 holding at 7% for several weeks
- JG.3 (XBB.1.9) now tracked at 6%
- FL.1.5.1 (XBB.1.9) down to 5% from 7%

12/9/2023





cov-2-genome-sequence-prevalence-and-growth-rate-update-6-december-2023

SARS-CoV2 Omicron Sub-Variants

Enabled by data from GISAID

covSPECTRUM



16-Nov-23

SARS-CoV2 Omicron Sub-Variants

<u>COV-spectrum</u> "Editor's choice" Variants to watch

Known variants



Enabled by data from CISAD





15-Dec-23

Global SARS-CoV2 Variant Status





2023-09-13 to 2023-12-12

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

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

National Wastewater Variant Status



https://www.cdc.gov/nwss/rv/COVID19-variants.html https://biobot.io/data/



Select a variant to add or remove it from the visualization.



Virginia Wastewater Variant Status





Near Southwest COVID-19 Genomic Prevalance over Time

Eastern COVID-19 Genomic Prevalance over Time



COVID-19 Literature Updates



Pandemic pubs



Calculations with an indoor air transmission model showed that given a range of viral load following symptom onset, a susceptible person would inhale an infectious dose within 6 to 37 min after an infected person entered a room with normal ventilation.



Properties of viral load were calculated from cultured aerosol samples.

Pandemic pubs





Administration of an updated monovalent mRNA vaccine (XBB.1.5 MV) to uninfected individuals boosted serum virus-neutralization antibodies significantly against not only XBB.1.5 (27.0-fold) and the currently dominant EG.5.1 (27.6-fold) but also key emergent viruses like HV.1, HK.3, JD.1.1, and JN.1 (13.3-to-27.4-fold)

Anitgenic cartography shows discernible shortening of antigenic distances between D614G and other SARS-CoV-2 variants after a shot of XBB.1.5 monovalent vaccine (Figures 3b and 3d) was indicative of the significant boost in antibody potency and breadth.

Shortening of these antigenic distances after XBB.1.5 infection was also similar (Figure 3c) to that of XBB.1.5 vaccine booster (Figure 3b), suggesting that infection and vaccination resulted in comparable enhancement of antibody responses.

Third, the emergent subvariants HV.1, HK.3, and JD.1.1 clustered together but were more distant than XBB.1.5 and EG.5.1 (Figure 3), demonstrating not only their antigenic similarity but also their greater antibody resistance compared to their predecessors.

Lastly, JN.1 was antigenically distinct and more distant.

Pandemic pubs



JN.1 sublineage of BA.2.86 bears watching due to immune escape, displayed growth, and mutation profile

Antigenic Cartography (Mouse immunized by Spike mRNA)



Updated Booster & Variants of Concern

Figure 2. Analysis of Neutralizing Antibody Titers Against Ancestral SARS-CoV-2 (D614G) and BA.4/BA.5, XBB.1.5, XBB.1.16, XBB.2.3.2, EG.5.1, FL.1.5.1 and BA.2.86 Variants in a Randomly-selected Subset of Participants Who Received Monovalent mRNA-1273.815



https://www.medrxiv.org/content/10.1101/2023.08.22.23293434v2

Phase 2/3 participants in updated booster trial show significantly increased neutralization levels for XBB.2.3.2, EG.5.1, FL.1.5.1 and BA.2.86.

The occurrence of solicited adverse reactions and unsolicited adverse events were overall similar to those previously reported for the original mRNA-1273 50- μ g and omicron BA.4/BA.5-containing bivalent mRNA-1273 vaccines.

Influenza Update



Current Influenza Situation – ILI Activity

Region 3 Influenza Activity is above threshold

Season: 2023-24 and 5 previous seasons -

Percentage of Outpatient Visits for Respiratory Illness Reported by The U.S. Outpatient Influenza-like Illness Surveillance Network (ILINet), Weekly National Summary, 2023-24 Season and Selected Previous Seasons

2022-23 Seaso

2018-19 Seaso

- Virginia is now in "Moderate" level of Influenza activity
- National ILI activity remains above threshold after and continues to grow
- Most regions are over threshold, with the most activity in the southern states

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2021-22 Seasor



Region 3



2020-21 Seaso

•••• 2023-24 National Baseline 🔽 — 2023-24 Season

🔽 — 2019-20 Seasor

for ILI

Current Influenza Situation – Hospitalization Admissions







United States



- Influenza Hospitalizations continue to rise
- US and Virginia are in steady growth
- Some of Virginia's neighbors have entered exponential growth phase
- Others remain in steady state this week



United States Hospitalizations – Epidemic Growth







Influenza Forecasts – Hospitalization Admissions



Forecast from Dec 9th Hospital Admissions for Influenza and Forecast for next 4 weeks

http://flux-forecasting.pods.uvarc.io



United States

Virginia



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Current Influenza Hospitalization Forecast

Statistical models for submitting to CDC Influenza 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 Influenza and Forecast for next 4 weeks (CDC Influenza Ensemble)

From December 8th

CDC Flu Activity Surveillance

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

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Current RSV Situation – Hospitalization Rates (RSV-Net)

Maryland (RSV-Net)



Data last updated: 12/06/2023 | Accessibility: Select (Enter) the graph area and press Alt + Shift + F11 to view the data as a table.

Tennessee (RSV-Net)

11/18 (last solid data)

12/2 (last recent but likely to be updated)





Current RSV Situation – Wastewater in VA





Current RSV Situation – Vaccinations

Figure 1A. Cumulative Percentage of Adults 60 Years and Older Vaccinated with RSV Vaccine, 2023-2024^{*,†,‡,±} Data Source: National Immunization Survey–Adult COVID Module



Demographic Level: Overall Name:	s (60+)		
Jurisdiction	Vaccination & Intent	Estimate (%)	95% CI (%)
National	Vaccinated	15.9%	14.6 - 17.2
National	Definitely will get a vaccine	15.6%	13.3 - 18.0
National	Probably will get a vaccine or are unsure	40.3%	37.1 - 43.5
National	Definitely or probably will not get a vaccine	28.1%	25.3 - 30.9

- RSV Vaccination of 60+ nears 17% and exceeds National and Regional levels
- Another 16% still "definitely" intending to get vaccine
- Now 28% not planning on vaccinating





Scenario Modeling Hub – RSV (Round 1) in prep

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

- Round Designed to explore impacts of newly available treatments (monoclonal antibodies and vaccines)
- Based on data till November 12th, 2023

Scenario Dimensions:

No interventions vs. levels of treatments for infants vs. seniors:

Infants: Optimistic vs. Pessimistic - coverage (80% vs. 20%) and VE (80% vs, 60%)

Seniors: Optimistic vs. Pessimistic - coverage (40% vs. 20%) and VE (90% vs. 70%)

https://github.com/midas-network/rsv-scenario-modeling-hub

	Optimistic senior protection Vaccine is administered from Sep-June to seniors 60+ yrs - coverage saturates at 40% of the 2021-22 state- and age-specific flu vaccine coverage - VE against hospitalization is 90%	Pessimistic senior protection Vaccine is administered from Sep-June to seniors 60+ yrs - coverage saturates at 20% of the 2021-22 state-and age-specific flu vaccine coverage - VE against hospitalization is 70%	No senior intervention
Optimistic infant protection Long-acting monoclonals target infants < 6 months during RSV season (Oct-Mar) - coverage saturates at 60% of the 2021-22 state- and age-specific flu vaccine coverage - VE against hospitalization is 80%	Scenario A	Scenario B	
Pessimistic infant protection Long-acting monoclonals target infants < 6 months during RSV season (Oct-Mar) -coverage saturates at 20% of the 2021-22 state- and age-specific flu vaccine coverage - VE against hospitalization is 60%	Scenario C	Scenario D	
No infant intervention beyond what was used in prior years (limited supply of palivizumab, targeting ~2% of birth cohort at high risk)			Scenario E (counterfactual)

Scenario Modeling Hub – RSV (Round 1)

Preliminary Results based UVA-EpiHiper Model

- Hospitalizations of 0-1 year olds can be reduced 5-10% through high levels of treatments
- Hospitalization of 65+ year olds can be reduced 7-22%

Conservative assumptions

- Treatments and vaccinations don't interrupt transmission (unlikely, but no evidence yet to prove it)
- Vaccination coverage a fraction of seasonal influenza vaccines



Scenario Modeling Hub – Influenza (Round 4)

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

- Round Designed to explore a season dominated by H3 vs. H1 with different levels of seasonal flu vaccination coverage
- Based on data till September 2nd, 2023

Scenario Dimensions:

Influenza type A/H3 vs. A/H1:

- H3 higher hospitalization rates with vax efficacy weaker in older groups
- H1 lower hospitalization rates and efficacy even across age groups

Vaccination levels (compared to 2021-22 season):

Low (20% less) vs. Business as Usual (same) vs. Higher (20% more)

https://fluscenariomodelinghub.org/viz.html

	Season dominated by influenza A/H3N2, indexed on age distribution of 2017-18 season. VE = 40% against medically attended illnesses and hospitalizations, VE drops in older age groups	Season dominated by influenza A/H1N1, indexed on age distribution of 2019-20 season. VE = 40% against medically attended illnesses and hospitalizations, similar VE across all age groups
 Higher than Usual Vaccine Coverage Vaccine coverage is 20% higher than in the 2021-22 flu season in all age groups and jurisdictions. (20% is a relative change, ie a 50% coverage for age group <i>a</i> and jurisdiction <i>j</i> in 2021-22 translates to a 50%*1.20=60% coverage for 2023-24). Overall, the US coverage is about 60% in this scenario. 	Scenario A	Scenario B
 Business as Usual Vaccine Coverage Vaccine coverage is the same as in the 2021-22 flu season in all age groups and jurisdictions. Overall, the US coverage is about 50% in this scenario. 	Scenario C	Scenario D
 Low Vaccine Coverage Vaccine coverage is 20% lower than in the 2021-22 flu season in all age groups and jurisdictions. Overall, the US coverage is about 40% in this scenario. 	Scenario E	Scenario F

Scenario Modeling Hub – Influenza (Round 4)

- H1N1 season seems to have emerged
- Projections remain relatively on track

Projected Incident Hospitalization by Epidemiological Week and by Scenario for Round 1 - 2023/2024 Scenario B: High vaccine coverage, A/H1N1 dominan Scenario D: Business as usual vaccine coverage, A/H1N1 dominan ist Peak - Max: 918 - Max: 918 ast Peak - 2022-2023 Season: 469 ast Peak - 2022-2023 Season: 469 Past Peak - Min: 35 - Min: 35 Scenario F: Low vaccine coverage, A/H1N1 dominanc - Max: 918 ast Peak - 2022-2023 Season: 469 Sep 2023 Nov 2023 Jan 2024 Mar 2024 May 2024 Epiweek

Virginia Hospitalizations

Scenario B: High vaccine coverage, A/H1N1 dominance 35k - 2022-2023 Season: 26333 25k 15k ast Peak - Min: 13147 Scenario F: Low vaccine coverage, A/H1N1 dominance Past Peak - Max: 3438 35k ak - 2022-2023 Season: 26333 15k ast Peak - Min: 13147 Sep 2023 Nov 2023 Jan 2024 Mar 2024 May 2024

Projected Incident Hospitalization by Epidemiological Week and by Scenario for Round 1 - 2023/2024 (- Start Projection Epiweek; -- Current Date) Scenario D: Business as usual vaccine coverage, A/H1N1 dominanc Past Pe - Max: 34385 - 2022-2023 Season: 2633 Past Peak - Min: 13147



United States Hospitalizations

Epiweek





16-Nov-23

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

- 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 https://covid19scenariomodelinghub.org/viz.html

	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%)

— USC-SIkJalpha — Ensemble LO

Key Takeaways

COVID-19 Activity levels remain in an undulating plateau

- Cases and hospitalizations have remained flat for a month
- Other indicators continue to point towards this continuing but with some increased activity in Southwest
- Wastewater based indicators similar mix of viral loads as in previous weeks

Genomic Surveillance maintains high diversity with no dominating variant

Influenza Activity is picking up Nationally, still low in Virginia

• Recent hospitalization surveillance from the 15th shows growth

Together this suggests continued COVID-19 plateaus in near term

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Questions?

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