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

Estimation of COVID-19 Impact in Virginia

December 14^{th} , 2022

(data current to December 6th – December 13th) Biocomplexity Institute Technical report: TR BI-2022-1891





BIOCOMPLEXITY INSTITUTE

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 srini@virginia.edu

Madhav Marathe marathe@virginia.edu

Chris Barrett ChrisBarrett@virginia.edu

Model Development, Outbreak Analytics, and Delivery Team

Przemyslaw Porebski, Joseph Outten, Brian Klahn, Alex Telionis, Srinivasan Venkatramanan, Bryan Lewis, Aniruddha Adiga, Hannah Baek, Chris Barrett, Jiangzhuo Chen, Patrick Corbett, Stephen Eubank, Galen Harrison, Ben Hurt, Dustin Machi, Achla Marathe, Madhav Marathe, Mark Orr, Akhil Peddireddy, Erin Raymond, James Schlitt, Anil Vullikanti, Lijing Wang, James Walke, Andrew Warren, Amanda Wilson, Dawen Xie



Overview

- Goal: Understand impact of COVID-19 mitigations in Virginia
- Approach:
 - Calibrate explanatory mechanistic model to observed cases
 - Project based on scenarios for next 4 months
 - Consider a range of possible mitigation effects in "what-if" scenarios

• Outcomes:

- Ill, Confirmed, Hospitalized, ICU, Ventilated, Death
- Geographic spread over time, case counts, healthcare burdens



Key Takeaways

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

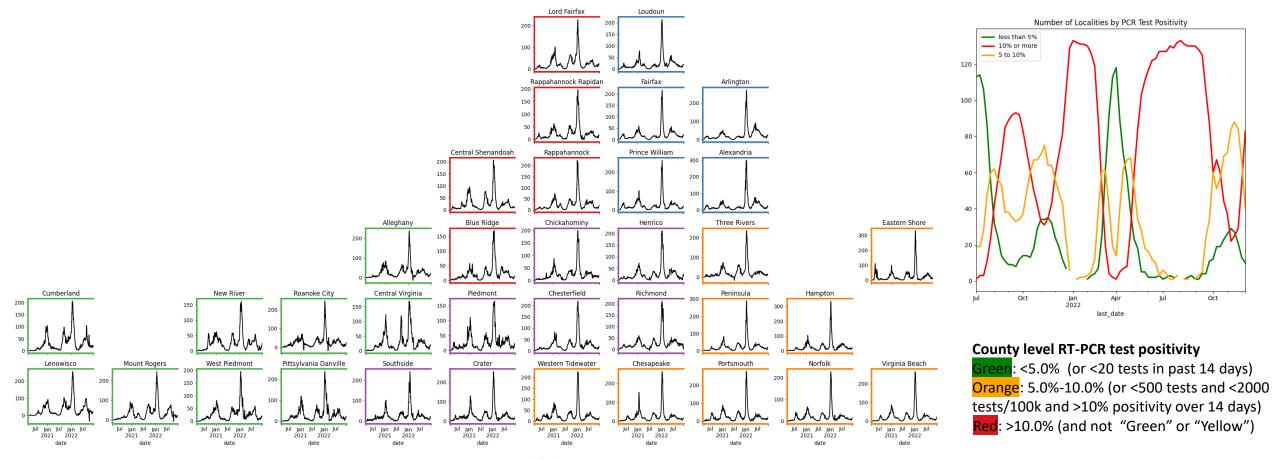
- Case rates and hospitalizations starting to rise rapidly
- VA weekly case rate is up to at 95/100K from 81/100K
 - US weekly case rate up sharply to 126 per 100K from 74 per 100K, and hospitalizations continue to quickly rise
- VA hospital occupancy is quickly rising (rolling 7 day mean of 694 from 644 a week ago); highest since early Sept
 - Influenza weekly hospital admissions remain high (~300 a week) but are now declining
- Projections anticipate increases in cases and hospitalizations in coming weeks
 - Combined hospitalizations due to Influenza and COVID-19 are expected to have a steady increase
- Model updates:
 - Model now fitted with Adaptive-Variant X, assumes this as the base case, since current growth can be attributed to rise of swarm of variants with more immune escape, Fall-Winter effects continue to add additional growth

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

Situation Assessment



Case Rates (per 100k) and Test Positivity



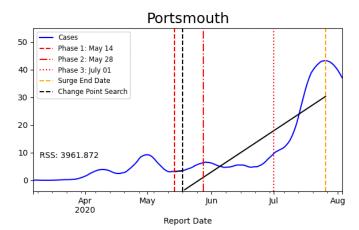


District Trajectories

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



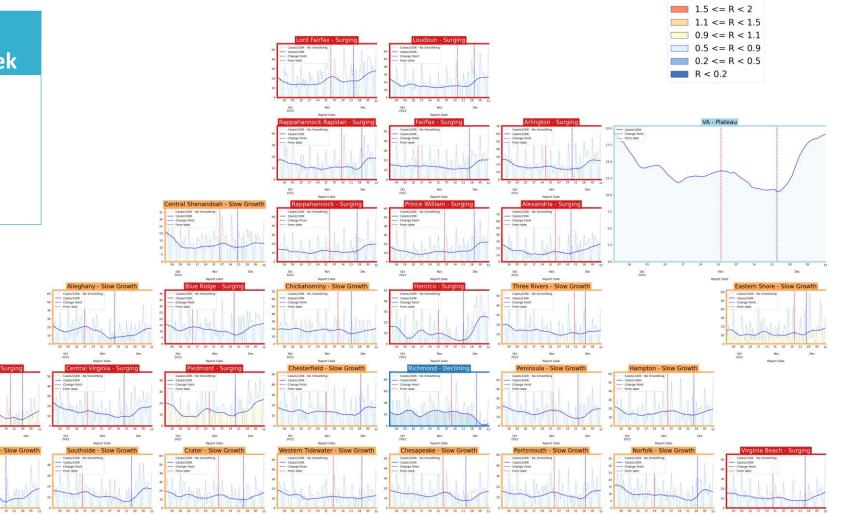
Trajectory	Description	Weekly Case Rate Slope (per 100k)	Weekly Hosp Rate Slope (per 100k)
Declining	Sustained decreases following a recent peak	slope < -0.88/day	slope < -0.07/day
Plateau	Steady level with minimal trend up or down	-0.88/day < slope < 0.42/day	-0.07/day < slope < 0.07/day
Slow Growth	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		
Status	Current Week	Last Week	
Declining	1	(2)	
Plateau	1	(3)	
Slow Growth	17	(15)	
In Surge	16	(15)	

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



MUNIVERSITY of VIRGINIA

District Hospital Trajectories – last 12 weeks

Status	Number of Districts		
Status	Current Week	Last Week	
Declining	4	(23)	
Plateau	1	(5)	
Slow Growth	30	(7)	
In Surge	0	(0)	

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

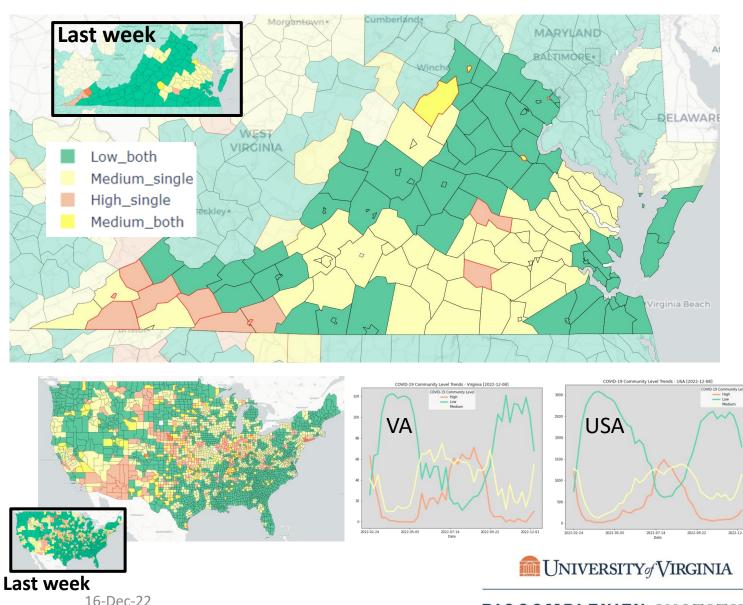


MUNIVERSITY of VIRGINIA

BIOCOMPLEXITY INSTITUTE

2022-12-06 2 <= R

CDC's COVID-19 Community Levels



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

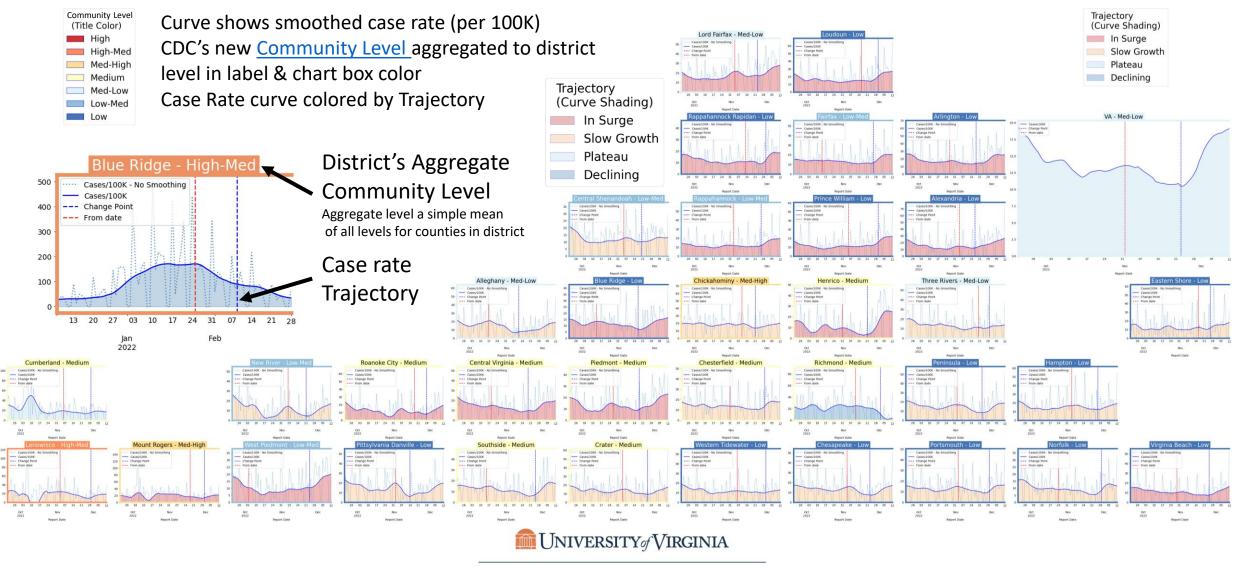
Pale color indicates either beds or occupancy set the level for this county

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

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

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

District Trajectories with Community Levels



Estimating Daily Reproductive Number – Redistributed gap

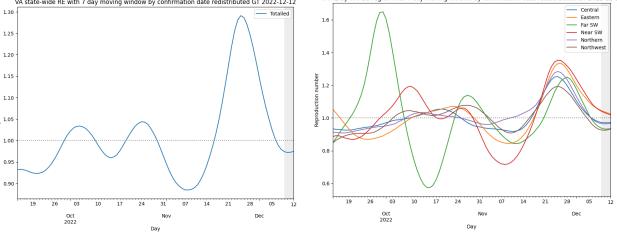
November 28th Estimates

Region	Date Confirmed R _e	Date Confirmed Diff Last Week
State-wide	0.973	-0.094
Central	0.970	-0.073
Eastern	1.026	-0.079
Far SW	0.946	-0.142
Near SW	1.019	-0.086
Northern	0.966	-0.119
Northwest	0.938	-0.058

Methodology

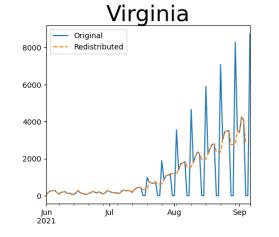
- Wallinga-Teunis method (EpiEstim¹) for cases by <u>confirmation date</u>
- Serial interval: updated to discrete distribution from observations (mean=4.3, Flaxman et al, Nature 2020)
- Using Confirmation date since due to increasingly unstable estimates from onset date due to backfill

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



VA RE by VHASS region with 7 day moving window by confirmation date redistributed GT 2022-12-12

Skipping Weekend Reports & holidays biases estimates Redistributed "big" report day to fill in gaps, and then estimate R from "smoothed" time series



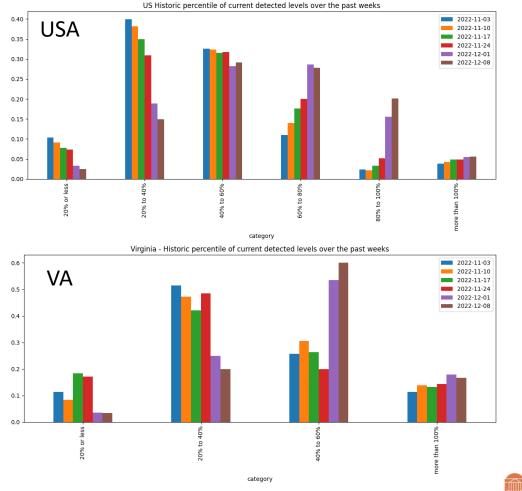
12

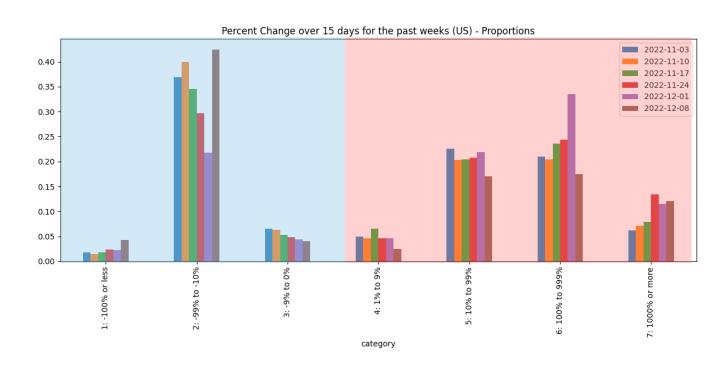
16-Dec-22

Wastewater Monitoring

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

- Overall in the US, there is an increase in sites with increased levels of virus compared to 15 days ago
- Growth seen in the category where current virus levels are at or exceeding max of previous historical levels





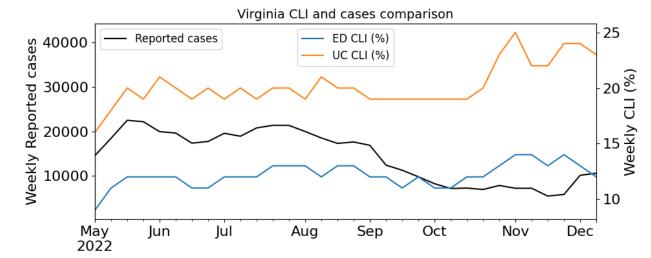


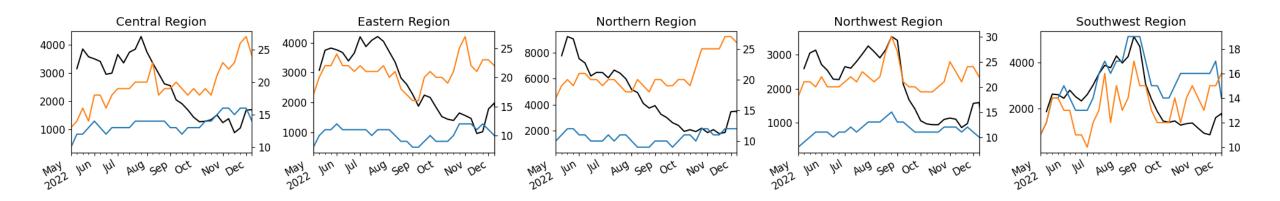
Data Source: CDC Data Tracker

COVID-like Illness Activity

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

- Emergency Dept (ED) based CLI is more correlated with case reporting
- Urgent Care (UC) is a leading indicator but may be influenced by testing for other URIs
- After 5 months of plateau, UC CLI remains higher than previous levels statewide



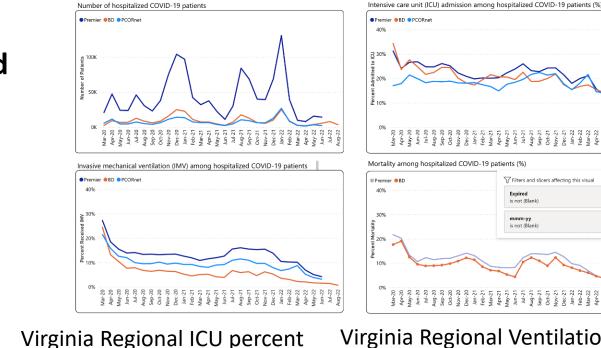


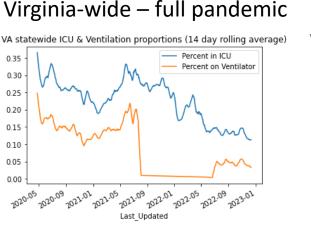
MUNIVERSITY of VIRGINIA

Hospitalizations and Severe Outcomes Data Source: CDC Data Tracker

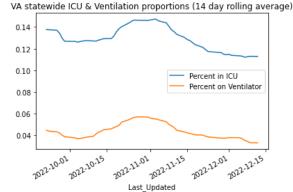
Proportion of most severe outcomes decreasing among those who are hospitalized

- ICU has declined from ~20% of hospitalized to 10-15% since initial Omicron wave
- Seen across all age-groups
- Recent rises in these rates have subsided in \bullet the past week



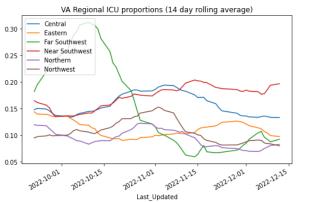


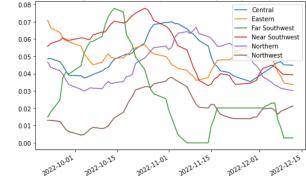
Virginia-wide – recent



Virginia Regional ICU percent

Virginia Regional Ventilation % VA Regional Ventilation proportions (14 day rolling average



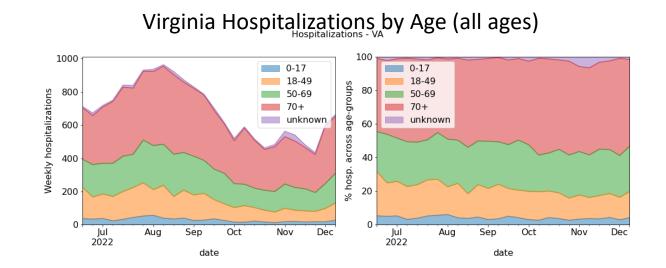


Hospitalizations in VA by Age

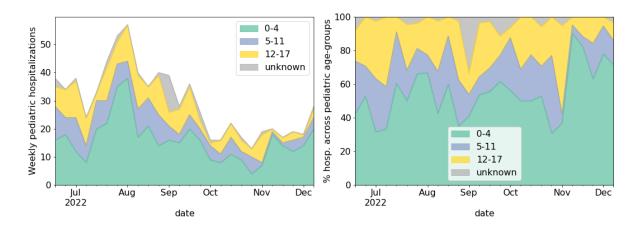
Age distribution in hospitals relatively stable

- Uptick in hospitalizations felt across most age-groups, including pediatric
- Majority of pediatric hospitalizations has been in 0-4-yo

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







Data Source: Delphi and HHS

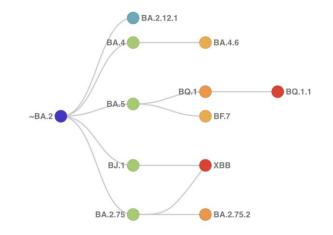
SARS-CoV2 Variants of Concern

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

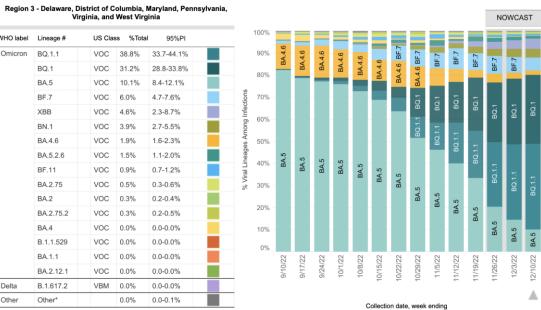
Omicron Updates

- BQ.1 and BQ.1.1 continue to dominate at 39% and 31% respectively (up from 31% and 34%)
- BA.2.75.* family variants (includes BN.1) remain steady at nearly a 5%
- BF.7 and BA.4.6 have been slowly shrinking to 6% and 2%
- BA.5.2.6 and BF.11 and account for relatively smaller shares (2% and 4% respectively)
- XBB and subvariants remain significant, steady at 5%



HHS Region 3: 12/4/2022 – 12/10/2022 NOWCAST

HHS Region 3: 9/4/2022 – 12/10/2022



* Enumerated lineages are US VOC and lineages circulating above 1% nationally in at least one week period. "Other" represents the aggregation of lineages which are circulating <1% nationally during all weeks displayed.

BA.1, BA.3 and their sublineages (except BA.1.1 and its sublineages) are aggregated with B.1.1.529. Except BA.2.12.1, BA.2.75, BA.2.75, B.N.1,XBB and their sublineages, BA.2 sublineages are aggregated with BA.2. Except BA.7, BF.11, BA.5.2.6, BQ.1 and BQ.1.1, sublineages of BA.5 are aggregated to BA.4. Except BF.7, BF.11, BA.5.2.6, BQ.1 and BQ.1.1, sublineages of BA.5 are aggregated to BA.5. For all the lineages listed in the above table, their sublineages are aggregated to the listed parental lineages respectively. Previously, XBB was aggregated with other. Lineages BA.2.75.2, XBB, BN.1, BA.4.6, BF.7, BF.11, BA.5.2.6 and BQ.1.1 contain the spike substitution R346T.

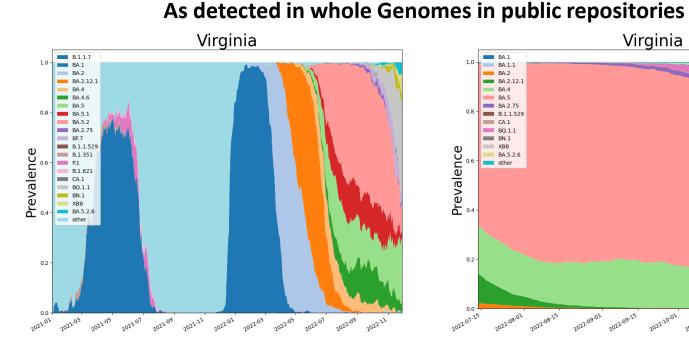


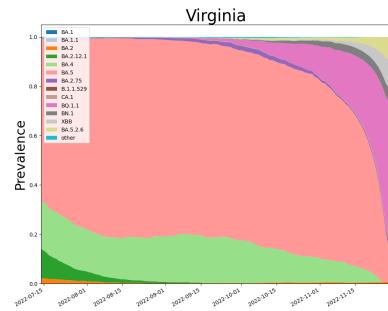
17

^{*} These data include Nowcast estimates, which are modeled projections that may differ from weighted estimates generated at later dates

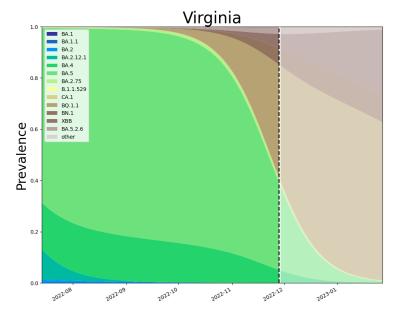
SARS-CoV2 Omicron Sub-Variants

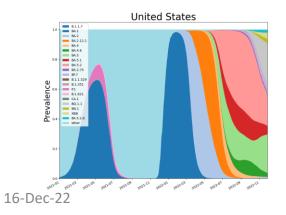


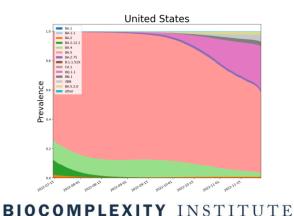




VoC Polynomial Fit Projections







United States Prevalence

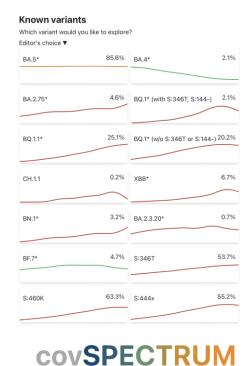
Note: Data lags force projections to start in past. Everything from dotted line forward is a projection.

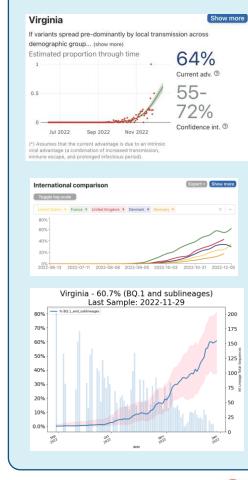
18

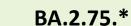
SARS-CoV2 Omicron Sub-Variants

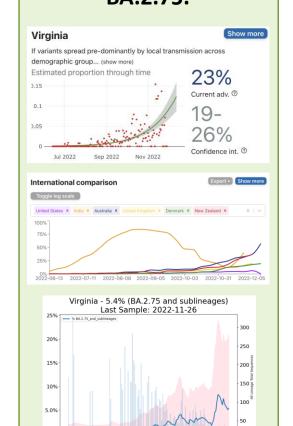
BQ.1.*

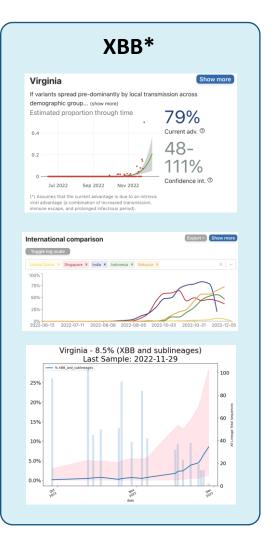
<u>COV-spectrum</u> "Editor's choice" Variants to watch











MUNIVERSITY / VIRGINIA

NIG

489 -072

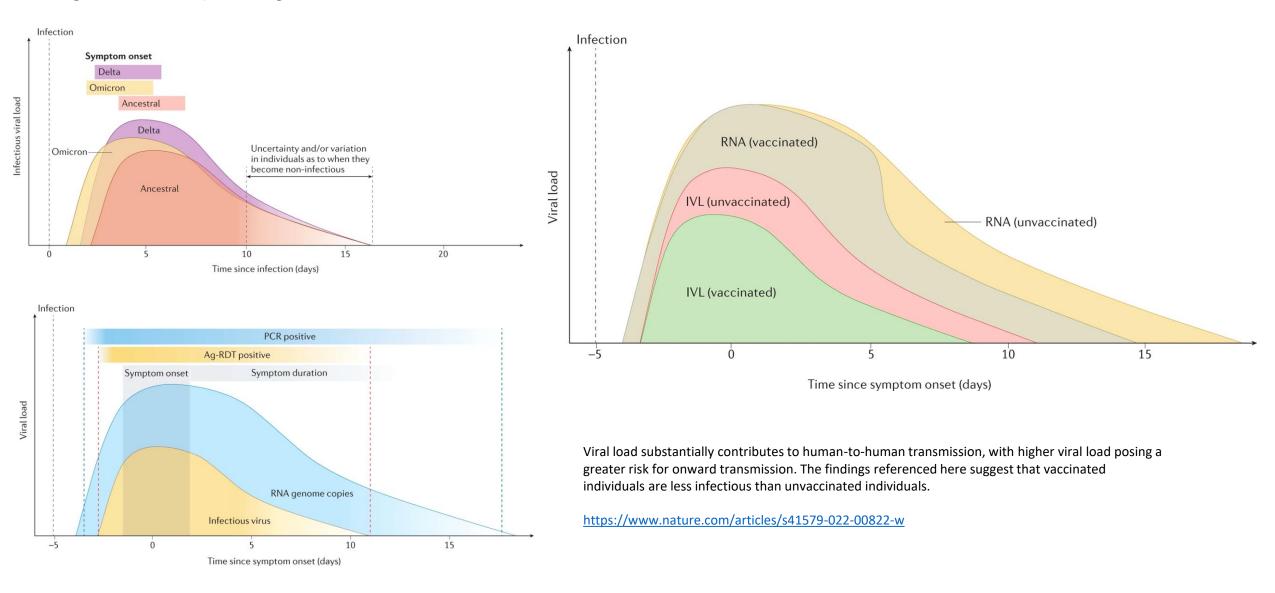
BIOCOMPLEXITY INSTITUTE

16-Dec-22

Enabled by data from **GISAID**

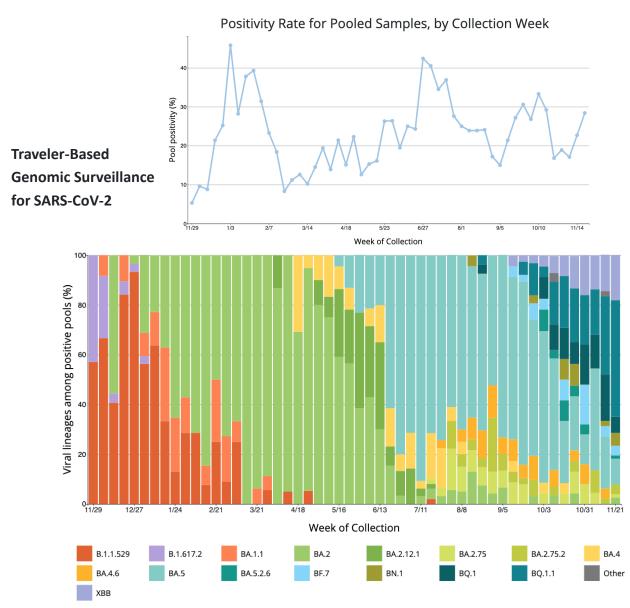
Pandemic Pubs (Dec 13th, 2022)

1. Higher viral load poses a greater risk for onward transmission

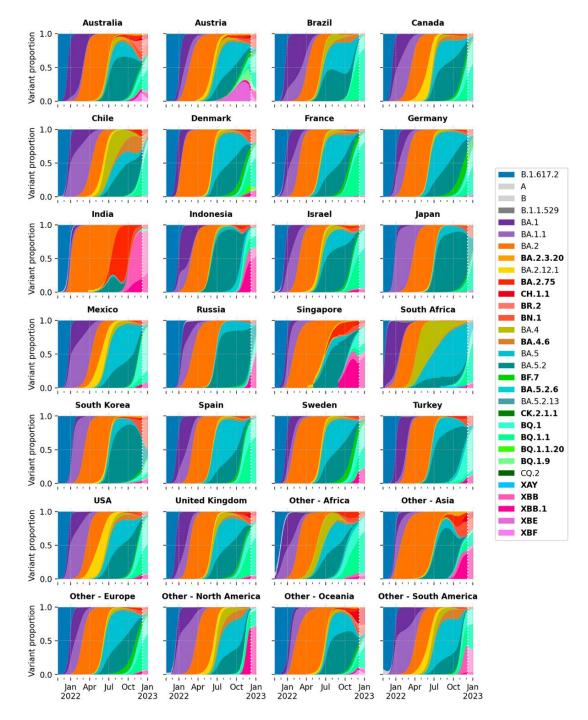


Pandemic Pubs (Dec 13th, 2022)

2. Variants around the world

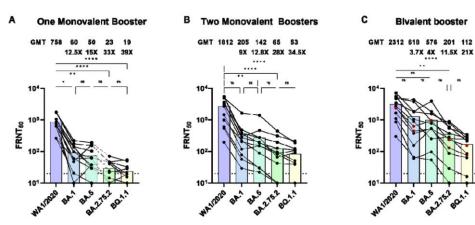


https://covid.cdc.gov/covid-data-tracker/#traveler-genomic-surveillance https://github.com/gerstung-lab/SARS-CoV-2-International



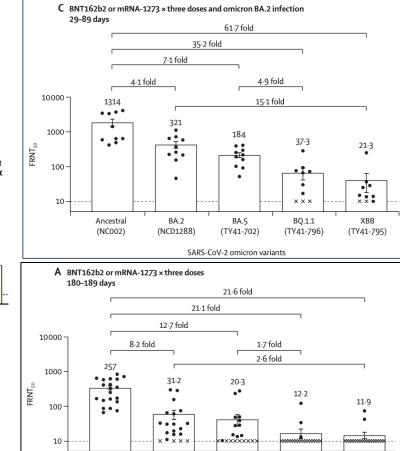
Pandemic Pubs (Dec 13th, 2022)

3. Immune escape updates on incoming variants



Previous: Researchers at Emory, Stanford, and NIAID evaluated serum samples from individuals who had received either one or two monovalent boosters or the bivalent booster to determine neutralizing activity against wild-type and Omicron subvariants BA.1, BA.5, BA.2.75.2, and BQ.1.1. Monovalent booster cohort: relative to WA1/2020, observed a reduction in neutralization titers of 9-15-fold against BA.1 and BA.5 and 28-39-fold against BA.2.75.2 and BQ.1.1. In the BA.5-containing bivalent booster cohort, the neutralizing activity improved against all the Omicron subvariants. Relative to wildtype observed a reduction in neutralization titers of 3.7- and 4-fold against BA.1 and BA.5, respectively, and 11.5- and 21-fold against BA.2.75.2 and BQ.1.1, respectively. These data suggest that the bivalent mRNA booster vaccine broadens humoral immunity against the Omicron subvariants.

https://www.biorxiv.org/content/10.1101/2022.10.31.5146 36v1



Current: Researchers in Japan and the US recently characterized the immune escape properties of variants BQ.1.1 and XBB, both show higher immune evasion abilities than earlier omicron variants. Groups included individuals (180–189 days after the third dose; n=20) who received three doses of the monovalent mRNA vaccine BNT162b2 (Pfizer–BioNTech) or mRNA-1273 (Moderna), or both; individuals (33–57 days after the fourth dose; n=20) who received four doses of the monovalent mRNA vaccine BNT162b2 or mRNA-1273, or both; and individuals (29–89 days after the infection; n=10) who received three doses of monovalent BNT162b2 or mRNA-1273 before the BA.2 breakthrough infection. Using a live-virus neutralisation assay, to determine the 50% focus reduction neutralisation titre (FRNT50)

BA.2

(NCD1288)

BA.5

(TY41-702)

BO.1.1

(TY41-796)

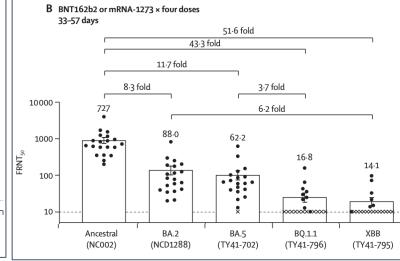
XBB

(TY41-795)

https://www.thelancet.com/action/showPdf?pii=S1473-3099%2822%2900816-7

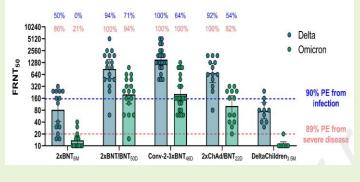
Ancestral

(NC002)



Previous: Italian study provides an analysis of 44 individuals antibody neutralization against omicron and other variants deriving analytic serologic cut-offs that correlate with protection, using a common highthroughput assay targeting anti-SARS-CoV-2 Spike antibodies. Their findings confirm published models for the prediction of protection efficacy. This model provides a useful touchstone for calibrating protection according to immune waning kinetics. https://papers.ssrn.com/sol3/papers.cfm?abstract_id=4016530

Proportion of individuals predicted to be protected from infection and severe disease



Pandemic Pubs (Dec 7th, 2022)

1. Recent studies highlight the benefit of Paxlovid in reduction of risk associated with hospitalization and long term symptoms

Events per 100,000 person-days No. of Characteristic Adjusted HR (95% CI)[†] participants No. hospitalized Overall Exposed[§] Unexposed[§] Total 0.49 (0.46-0.53) 693,084 5,229 25.31 15.88 29.05 COVID-19 vaccination status[¶] Figure 2a. Post-acute sequelae of COVID-19 Vaccinated (\geq 3 mRNA doses) 0.50 (0.45-0.55) 310,196 2,126 22.98 24.37 Vaccinated (2 mRNA doses) 0.50 (0.42-0.58) 149,498 1,086 Unvaccinated 29.05 0.50 (0.43-0.59) 170,789 1,477 1.00 UHC** and a second and a s 0 0.89(0.58 - 1.36)52,592 106 6.73 Survival probabilities 96'0 56'0 0.57 (0.45-0.71) 200,116 503 8.40 ≥2 0.47 (0.44-0.51) 440,376 35.29 4,620 Previous infection^{††} No 0.48 (0.44-0.51) 589,147 4,715 26.86 Control group Yes 0.76 (0.60-0.98) 103,937 514 16.56 Nirmatrelvir Immunocompromised^{§§} No 0.49 (0.45-0.53) 628,706 3,770 20.09 Yes 0.50 (0.44-0.58) 64,378 1,459 77.01 Month of COVID-19 diagnosis Apr 2022 0.54 (0.40-0.71) 60,001 450 25.16 40 50 60 70 80 90 May 2022 0.57 (0.48-0.67) 139,062 979 23.61 Days Jun 2022 0.51 (0.43-0.60) 143,706 23.48 1,006 Jul 2022 0.46 (0.40-0.53) 184,153 1,432 26.09 30.94 15.65 32.93 Aug 2022 0.44 (0.38-0.51) 166,162 1,362 27.52 15.60

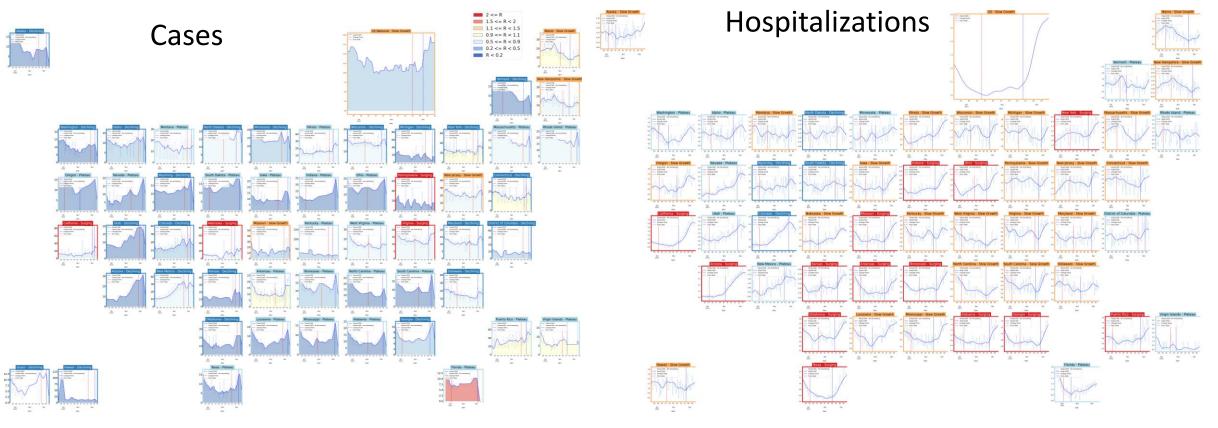
TABLE 2. Adjusted hazard ratios for COVID-19-associated hospitalization based on Paxlovid prescription receipt (exposure) — Cosmos,* United States, April–September 2022

Two recent studies:

1) Researchers at the CDC found that "persons who were prescribed Paxlovid within 5 days of diagnosis had a 51% lower hospitalization rate within 30 days after diagnosis than those who were not prescribed Paxlovid".

2) Researchers at Veterans Research and Education Foundation used the healthcare databases of the US Department of Veterans Affairs to identify users of the health system who had a SARS-CoV-2 positive test between March 01, 2022 and June 30, 2022, were not hospitalized on the day of the positive test, had at least 1 risk factor for progression to severe COVID-19 illness and survived the first 30 days after SARS-CoV-2 diagnosis. Compared to the control group, treatment was associated with reduced risk of PASC (HR 0.74 95% CI (0.69, 0.81), including reduced risk of sequelae in the cardiovascular system https://www.medrxiv.org/content/10.1101/2022.11.03.22281783v1 https://www.medrxiv.org/content/10.1101/2022.11.03.22281783v1

United States Cases & Hospitalizations



Status	Number of States		
วเลเนร	Current Week	Last Week	
Declining	23	(25)	
Plateau	23 (19)		
Slow Growth	0	(3)	
In Surge	4	(7)	

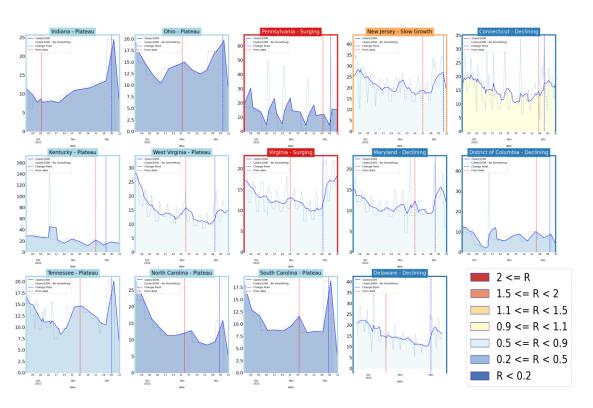


Status	Number of States		
Status	Current Week	Last Week	
Declining	1	(5)	
Plateau	11	(29)	
Slow Growth	22	(15)	
In Surge	19	(4)	

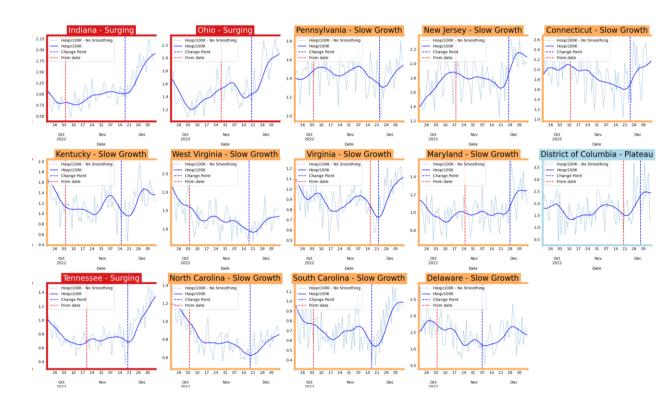
16-Dec-22

Virginia and Her Neighbors

Cases



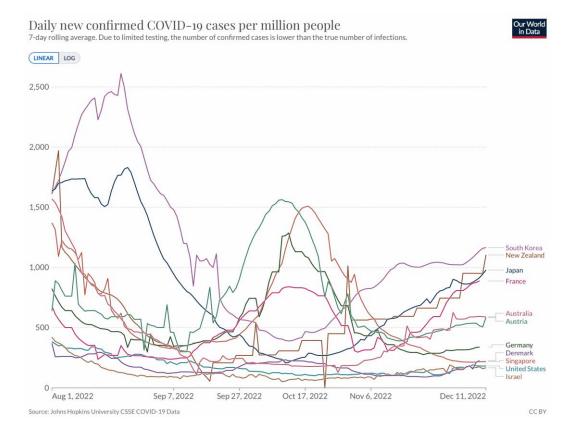
Hospitalizations



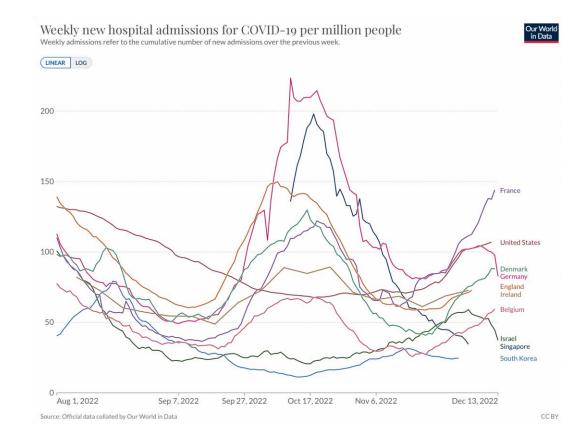


Around the World – Various trajectories

Confirmed cases



Hospitalizations





16-Dec-22

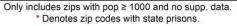


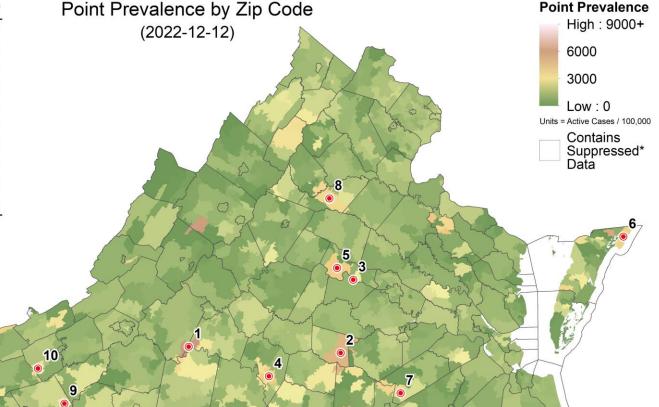
Zip code level weekly Case Rate (per 100K)

Case Rates in the last week by zip code

- Statewide case rates are growing slowly.
 Map now shows more yellows and even some oranges and reds.
- Chincoteague Island is still in the top five, and reports even higher rates than on Nov 29.
- Two prisons appear in this week's top 10. Goochland appeared in the Nov 29 report also.
- Some counts are low and suppressed to protect anonymity. They are shown with a red outline.

Rank	Zip Code	Name	Prev
1	24571	Lynch Station	6,650
2	23824	Blackstone	5,360
3	23160	State Farm*	5,110
4	23967	Saxe	4,680
5	23063	Goochland*	4,330
6	23336	Chincoteague Is.	4,140
7	23867	Jarratt	3,960
8	22960	Orange	3,630
9	24352	Laurel Fork	3,220
10	24324	Draper	3,190





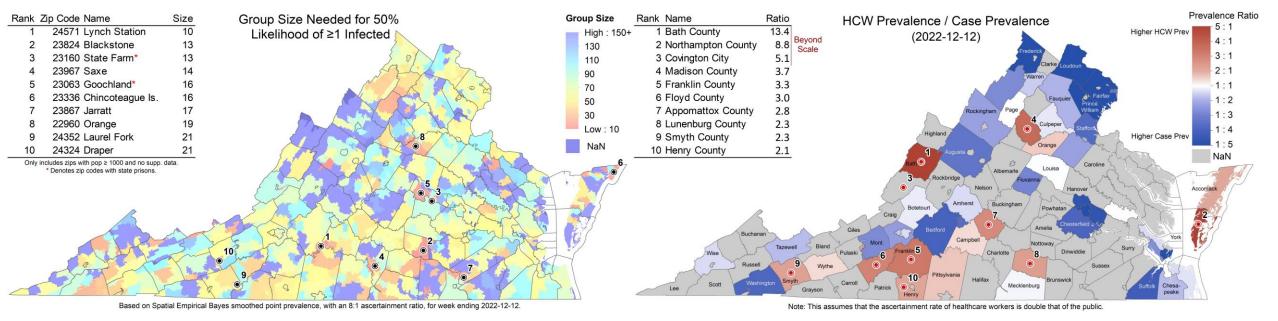
Based on Spatial Empirical Bayes smoothed point prevalence, with an 8:1 ascertainment ratio, for week ending 2022-12-12.

UNIVERSITY of VIRGINIA

Risk of Exposure by Group Size and HCW prevalence

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

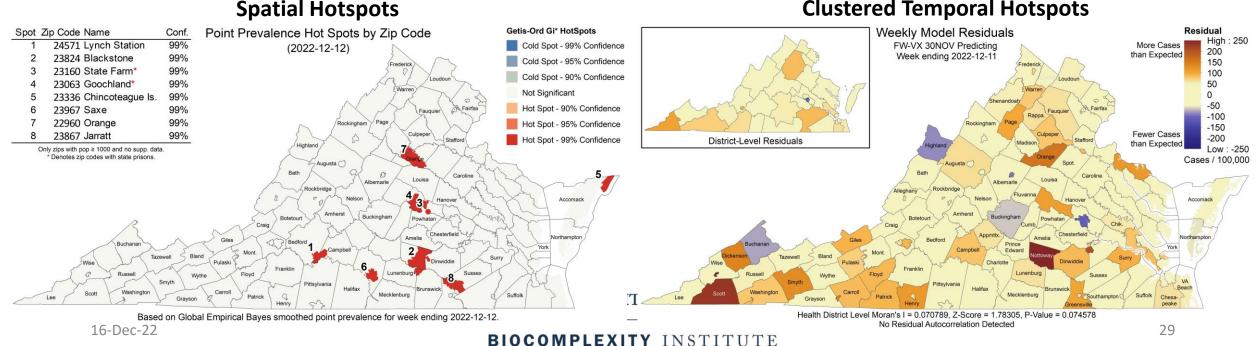
- **Group Size**: Assumes **8 undetected infections** per confirmed case (ascertainment rate from recent seroprevalence survey) and shows minimum size of a group with a 50% chance an individual is infected by zip code (e.g., in a group of 10 in Lynch Station, there is a 50% chance someone will be infected).
- HCW ratio: Case rate among health care workers (HCW) in the last week using patient facing health care workers as the numerator / population's case prevalence. Note areas south of Roanoke/Lynchburg + Bath.



Current Hot-Spots

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

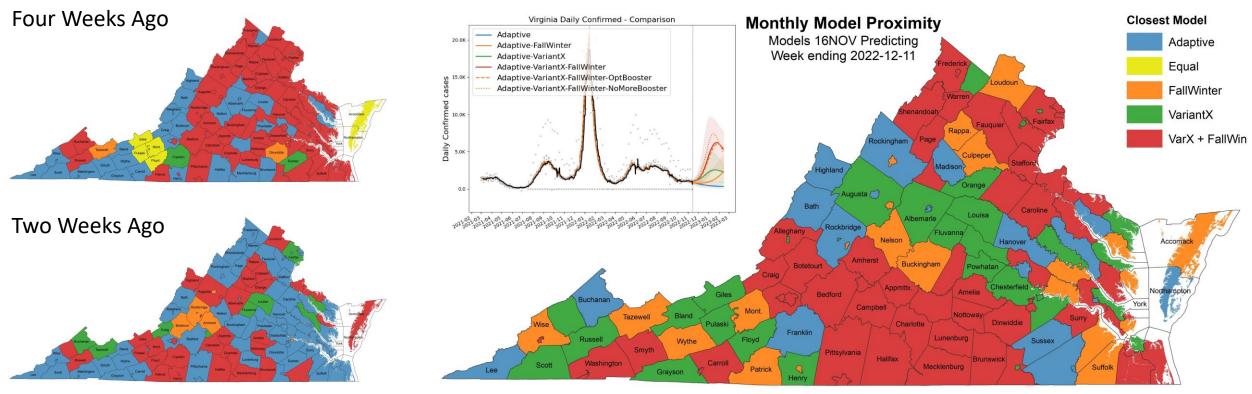
- Spatial: Getis-Ord Gi* based hot spots compare clusters of zip codes with weekly case prevalence higher than nearby zip codes to identify larger areas with statistically significant deviations
- **Temporal**: The weekly case rate (per 100K) projected last week compared to observed by county, which highlights temporal fluctuations that differ from the model's projections.
- Spatial hotspots remain sporadic. Temporal hotspots are primarily found in Southwest VA, plus Crater and Rapp./Rapidan, which all saw more cases than models expected. Richmond saw fewer cases than expected.



Clustered Temporal Hotspots

Scenario Trajectory Tracking

Which scenario from a month ago did projection for each county track closest?



- One-month projections separate the scenarios more clearly and reveals larger overall patterns.
- For the past month Adaptive had been gaining counties and outperforming other scenarios. This week the trend reversed. VariantX-FallWinter was the most accurate statewide as well as in 60 counties.

16-Dec-22

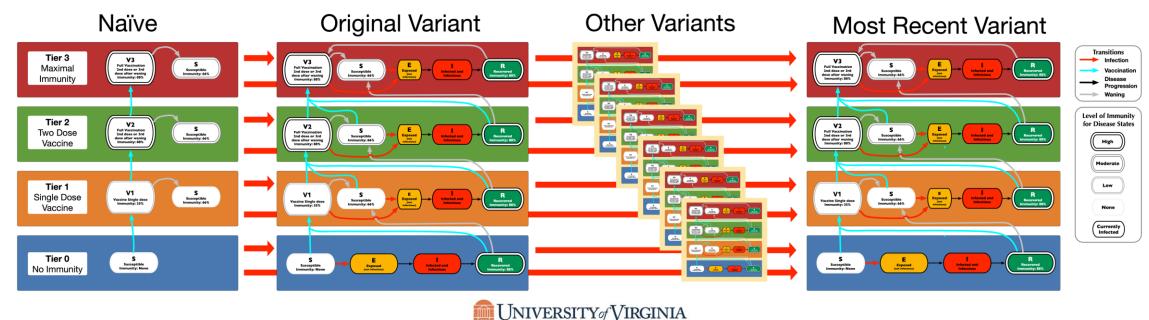
Model Update – Adaptive Fitting



Model Structure Extended for more sub-variants

Omicron sub-variants escape immunity induced by previous sub-variants

- Multiple strain support allows representation of differential protection based on immunological history (BA.1, BA.2, BA.2.12.1, BA.4/5, and future variants (VariantX))
- Each sub-variant has differing levels of immune escape to previous sub-variants, the prevalences are based on observations for fitting purposes, and projections use estimated future prevalences
- Adaptive fitting approach continues to use simulation to generate the full distribution of immune states across the population



Adaptive Fitting Approach

Each county fit precisely, with recent trends used for future projection

 Allows history to be precisely captured, and used to guide bounds on projections

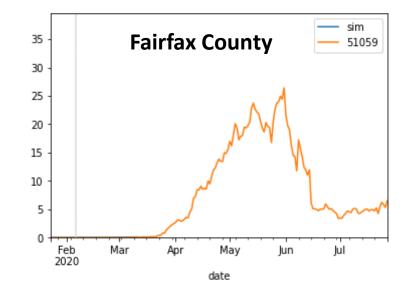
Model: An alternative use of the same meta-population model, PatchSim with multiple tiers of immunity

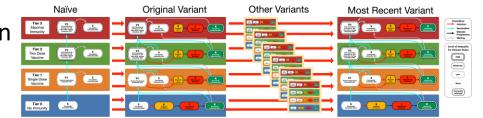
- Allows for future "what-if" Scenarios to be layered on top of calibrated model
- Allows for waning of immunity and for partial immunity against different outcomes (eg lower protection for infection than death)

External Seeding: Steady low-level importation

 Widespread pandemic eliminates sensitivity to initial conditions, we use steady 1 case per 10M population per day external seeding







Calibration Approach

- Data:
 - County level case counts by date of onset (from VDH)
 - Confirmed cases for model fitting
- Calibration: fit model to observed data and ensemble's forecast
 - Tune transmissibility across ranges of:
 - Duration of incubation (5-9 days), infectiousness (3-7 days)
 - Undocumented case rate (1x to 7x) guided by seroprevalence studies
 - Detection delay: exposure to confirmation (4-12 days)
 - Approach captures uncertainty, but allows model to precisely track the full trajectory of the outbreak
- **Project:** future cases and outcomes generated using the collection of fit models run into the future
 - Mean trend from last 7 days of observed cases and first week of ensemble's forecast used
 - Outliers removed based on variances in the previous 3 weeks
 - 2 week interpolation to smooth transitions in rapidly changing trajectories
- **Outcomes**: Data driven by shift and ratio that has least error in last month of observations
 - Hospitalizations: 3 days from confirmation, 6.8% of cases hospitalized
 - Deaths: 11 days from confirmation, 1.45% of cases die



COVID-19 in Virginia:



Dashboard Updated: 12/14/2022 Data entered by 5:00 PM the prior day.

	Cases, Hospitalizations and Deaths				
Total Cases*Total HospitalTotal2,171,414Admissions**Deaths					
(New Case		57,	971	22,	568
Confirmed† 1,529,714	Probable [†] 641,700	Confirmed† 54,382	Probable† 3,589	Confirmed† 18,711	Probable† 3,857

* Includes both people with a positive test (Confirmed), and symptomatic with a known exposure to COVID-19 (Probable). ** Hospitalization of a case is captured at the time VDH performs case investigation. This underrepresents the total number of hospitalizations in

Virginia. ^New cases represent the number of confirmed and probable cases reported to VDH in the past 24 hours.

YUDH adopted the updated CDC COVID-19 confirmed and probable surveillance case definitions on September 1st, 2021. Found here: https://ndc.services.cdc.gov/case-definitions/coronavirus-disease-2019-2021/

Source: Cases - Virginia Electronic Disease Surveillance System (VEDSS), data entered by 5:00 PM the prior day.

Out	tbreaks
Total Outbreaks*	Outbreak Associated Cases
10,351	170,303

* At least two (2) lab confirmed cases are required to classify an outbreak.

Testing (PCR Only)		
Testing Encounters PCR Only*	Current 7-Day Positivity Rate PCR Only**	
15,584,461	13.4%	

* PCR" refers to "Reverse transcriptase polymerase chain reaction laboratory testing."
** Lab reports may not have been received yet. Percent positivity is not calculated for days with incomplete data

	n Inflammatory e in Children
Total Cases*	Total Deaths
180	1

*Cases defined by CDC HAN case definition: https://emergency.cdc.gov/han/2020/han00432.asp

Accessed 9:30am December 14, 2022 https://www.vdh.virginia.gov/coronavirus/



Scenarios – Transmission Conditions

- Variety of factors continue to drive transmission rates
 - Seasonal impact of weather patterns, travel and gatherings, fatigue and premature relaxation of infection control practices
- Waning Immunity: Omicron waning with a mean of 4 months

• Projection Condition Ingredients:

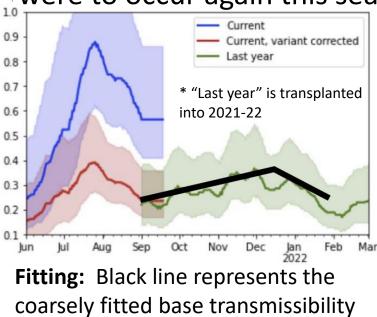
- Adaptive: Controls remain as currently experienced into the future with NO influence from other conditions (eg seasonal, variants, etc.)
- Seasonal (Fall-Winter boosting): Controls remain the same, however, seasonal forcing similar to past Fall-Winter waves is added from Sept-Feb
- Vaccine Booster Campaign (Booster): Reformulated booster available this fall provides improved immunity against Omicron sub-variants
- New Variants (VariantX): As of yet unidentified novel sub-variant with similar immune escape but no transmission advantage emerges 4 months after the last significant sub-variant and grows at a similar rate



Scenarios – FallWinter

September – February saw strong waves of transmission for both years

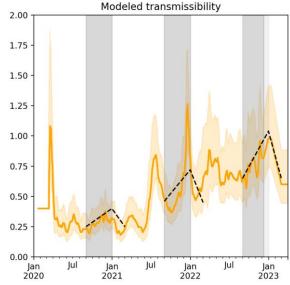
- Based on analyses of the past 2 seasons we generate a "coarse baseline transmission boost"
 - In 2021 the distribution of fitted model transmissibility was nearly identical between these periods when corrected for Delta's increased transmissibility
- FallWinter captures these "transmission drivers" from the past and uses them as if they were to occur again this season



16-Dec-22

2022 FallWinter has kept pace with observed relative increases:

- 2022's relative increase in transmission has been roughly the same this year as previous years
- Overall, the transmission rates are higher this year but the increased immunity has kept cases relatively stable



MUNIVERSITY / VIRGINIA

Scenarios – Optimistic vs. Pessimistic Booster Coverage

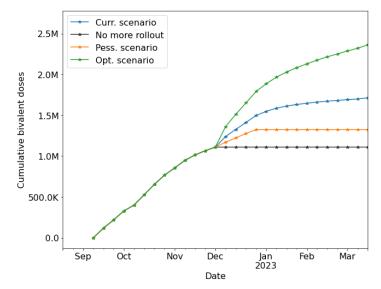
Reformulated Boosters available now

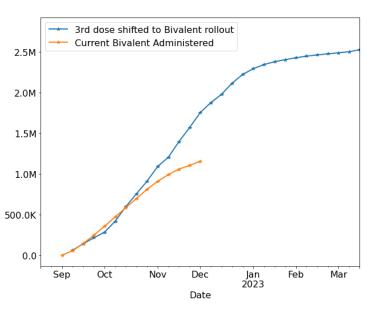
- Assume vax efficacy for BA.4/5 and previous variants is 80% against symptomatic illness
- Campaign follows current ground truth to present
- Variant X has same immune escape to these vaccines as against BA.5 (33%)

Current pace: Follows 3rd dose rollout, but maintains current pace relative to it (eg if slower, same slower rate continues into future)

Optimistic pace: 25% higher than previous 3rd dose schedule

No More: No further Bivalent boosters administered



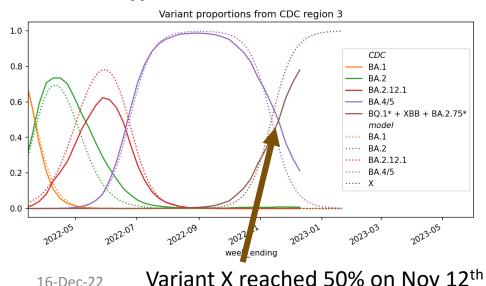


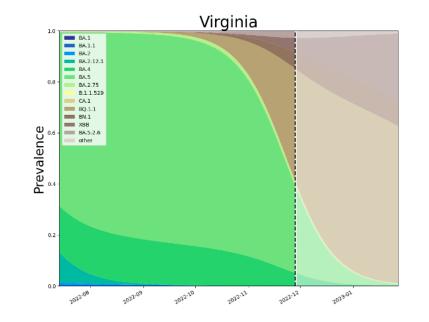
Scenarios – Variant X

Omicron sub-variants seem to be emerging and then dominating with some regularity

- An increasingly complex soup of variants with demonstrated growth advantages in other countries and states continues to grow
- BQ.1.1, XBB, and 2.75.* (including BN.1) have shown evidence of significant immune escape, BQ.1.1 currently dominating in US and VA, while others continue to grow slowly
- VariantX represents the next variant or the potential swarm of several. We assume similar growth and level of immune escape against previous sub-variants as BA.4/5 (same transmissibility and 30% immune escape against BA.4/5, higher for other sub-variants).

Sub-Variants with Fitted Prevalences and Hypothetical Future waves





Projection Scenarios – Combined Conditions

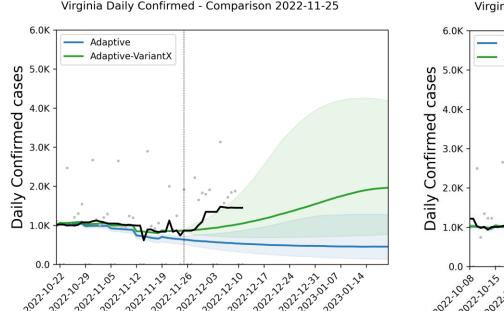
Name	Txm	Variant	Booster	Description		
Adaptive	С	SQ	Current	Likely trajectory based on conditions remaining similar to the current experience, includes immune escape due to Omicron		
Adaptive-FallWinter	FallWinter	SQ	Current	Like Adaptive, with seasonal forcing of FallWinter added on		
Adaptive-VariantX	С	х	Current	Like Adaptive, with emergence of a speculative unknown variant 4 months after BA.4/5 with similar level of immune escape and equal transmissibility		
Adaptive-VariantX-FallWinter	FallWinter	х	Current	Like Adaptive-VariantX but with the seasonal force of FallWinter added on		
Adaptive-VariantX-FallWinter- OptBooster	FallWinter	х	Optimistic	Like Adaptive-VariantX-Fall Winter but with Optimistic Booster (25% more than 3 rd dose rollout)		
Adaptive-VariantX-FallWinter- NoMoreBooster	FallWinter	х	No More	Like Adaptive-VariantX-FallWinter but with no additional Booster doses		
Fall	C = Current levels persist into the future FallWinter = Transmission rates learned from Sept through February of past seasons are estimated and added as a seasonal boosting to baseline transmission rates					
	SQ = Status quo prevalences remain the same (e.g. no significant major driving of transmission anticipated) X = Novel sub-variant scenario, new variant emerges reaches dominance in near term, 30% immune escape					
	Current = Current pace relative to 3 rd dose rollout is maintained in the future Optimistic = Starting this week, additional 25% over the 3 rd dose rollout is maintained into the future					
16-Dec-22 No	No More = Starting this week, no additional doses of the booster are administered 39					

Model Results



Previous projections comparison - Cases

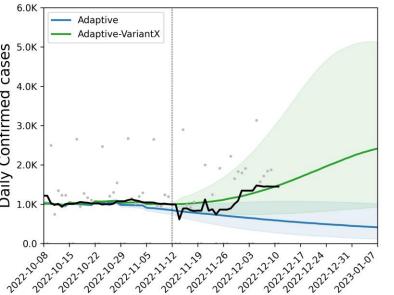
- Previous projections continue to track observed cases
- Slight decrease 2 weeks ago suppressed growth thus model underpredicted cases
- Flat cases 4 weeks ago allowed Variant X scenario to track observed growth
- July-based long-term projection remains eerily prescient



Previous round (2 weeks ago)

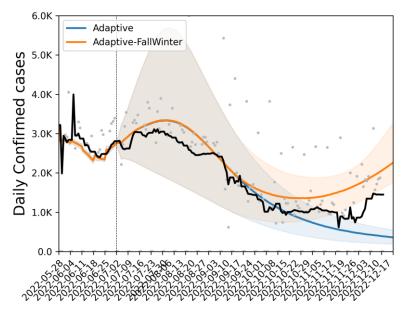
Projection from 4 weeks ago

Virginia Daily Confirmed - Comparison 2022-11-12



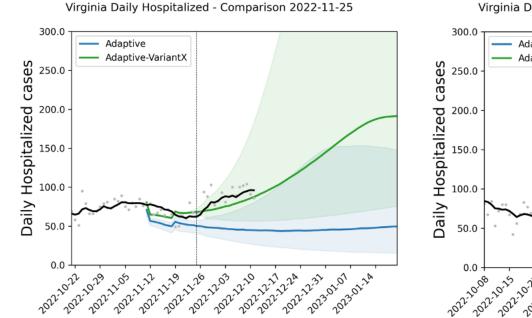
Projection from 5 months ago

Virginia Daily Confirmed - Comparison 2022-07-02



Previous projections comparison - Hospitalizations

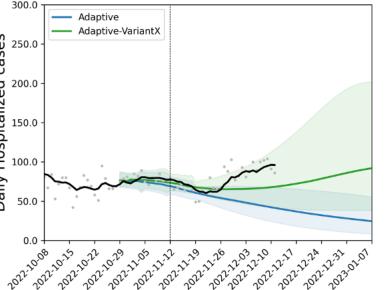
- Previous projections have tracked observed hospitalizations well
- Projection from 2 weeks ago had enough growth in hospitalizations to track well
- Projection from 4 weeks ago had declines which delayed the growth
- Projection from early July anticipated a Fall-Winter rise that has tracked well



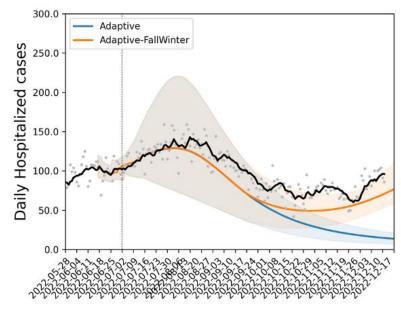
Previous round (2 weeks ago)

Projection from 4 weeks ago

Virginia Daily Hospitalized - Comparison 2022-11-12



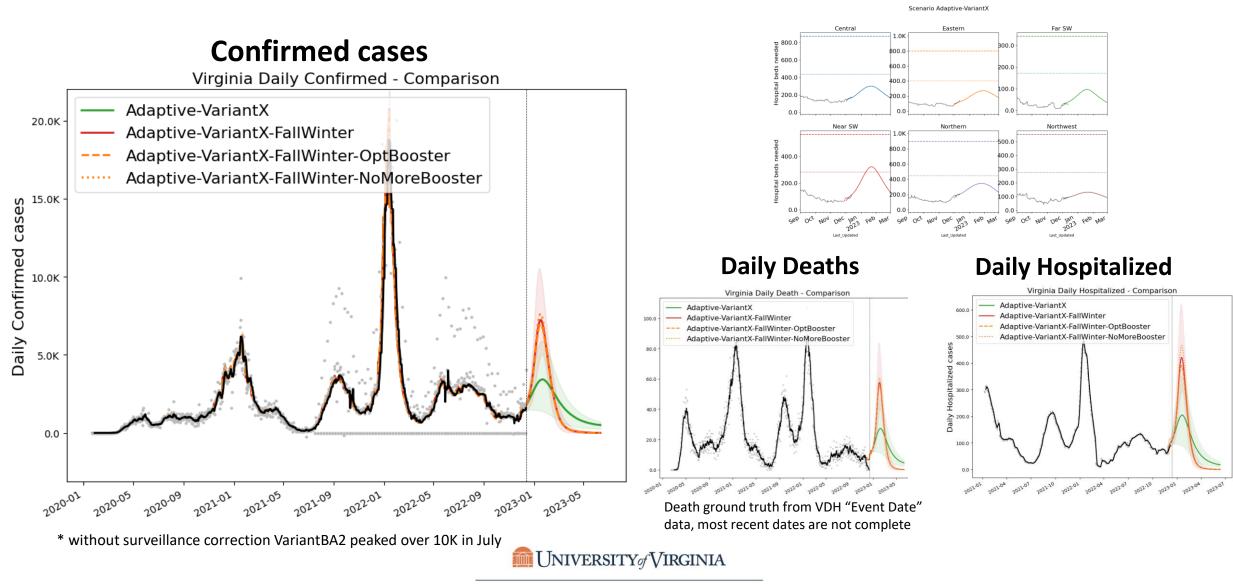
Projection from 5 months ago



Virginia Daily Hospitalized - Comparison 2022-07-02

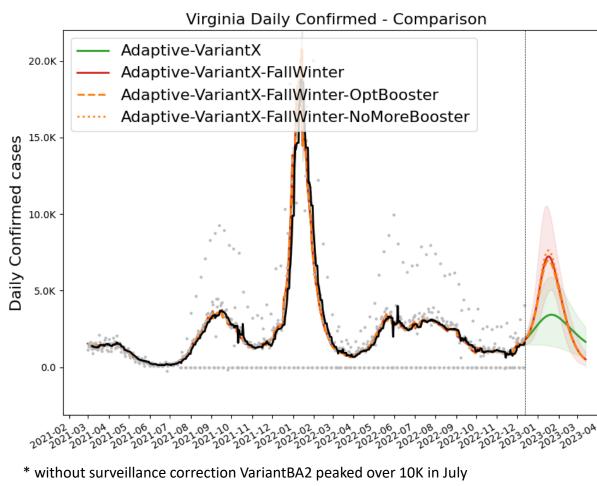
Outcome Projections

Estimated Hospital Occupancy



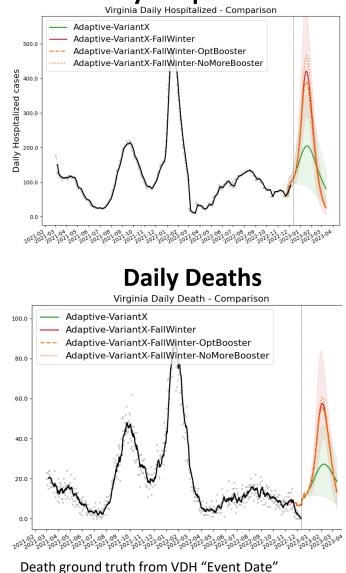
Outcome Projections – Closer Look

Confirmed cases





Daily Hospitalized



data, most recent dates are not complete

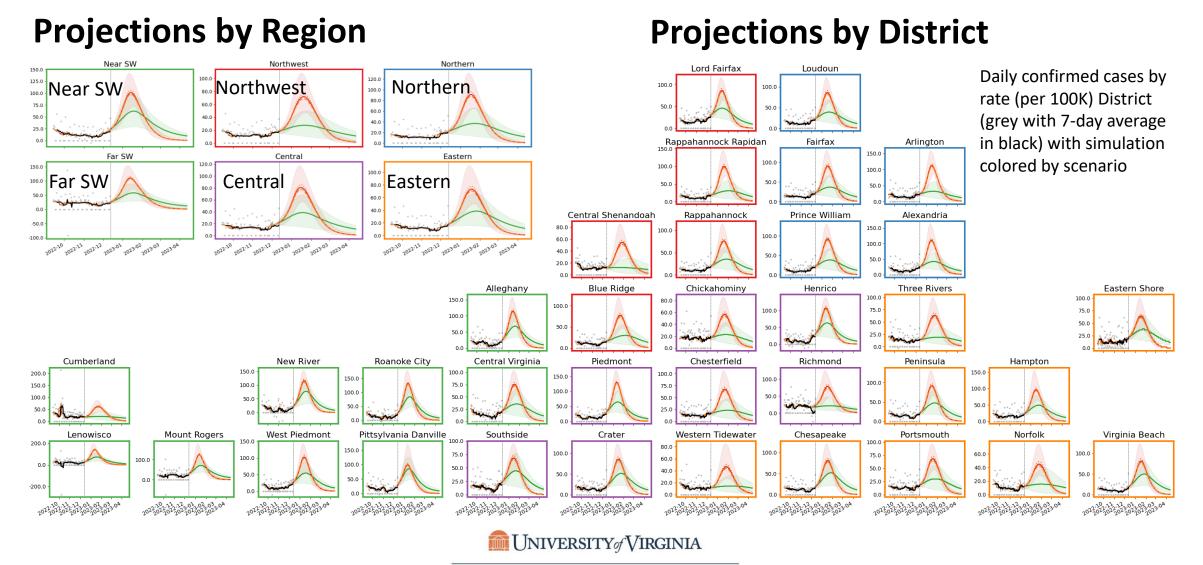
16-Dec-22

Detailed Projections: Cases for All Scenarios

Projections by Region Projections by District Northern Lord Fairfax Loudour Daily confirmed cases) Near SW 250.0 Northern Northwest 200.0 200.0 200.0 200.0 150.0 200 0 150.0 by rate (per 100K) 150.0 100.0 100 100. 100.0 100.0 District (grey with 7-day 50.0 50.0 average in black) with Rappahannock Rapidan -50.0 Fairfax Arlington 300.0 200.0 Far SW Central Fastern 200.0 simulation colored by 200.0 Eastern Far SW Central 200.0 250.0 100 200.0 100.0 100.0 200.0 scenario 150.0 100.0 150.0 100.0 Central Shenandoah Rappahannock Prince William Alexandria 50.0 300.0 400.0 200.0 200 0 200.0 200.0 100.0 100.0 Blue Ridge Chickahominv Henrico Three Rivers Eastern Shore Alleghany 200.0 200.0 300.0 200.0 200.0 100.0 200.0 100.0 100.0 100 (100.0 100.0 0.0 -100 Roanoke City Central Virginia Chesterfield Cumberland New River Piedmont Richmond Peninsula Hampton 200.0 400 0 300.0 200.0 150.0 200.0 200.0 150.0 200.0 300.0 100.0 200.0 100.0 200.0 100.0 100.0 50.0 100.0 100.0 50.0 100.0 -100.0 Pittsylvania Danville Lenowisco Mount Rogers West Piedmont Southside Crater Western Tidewater Chesapeake Portsmouth Norfolk Virginia Beach 300.0 300. 300.0 200.0 200.0 200.0 200.0 200.0 200.0 200.0 200.0 200.0 200.0 200.0 100 (-200.0

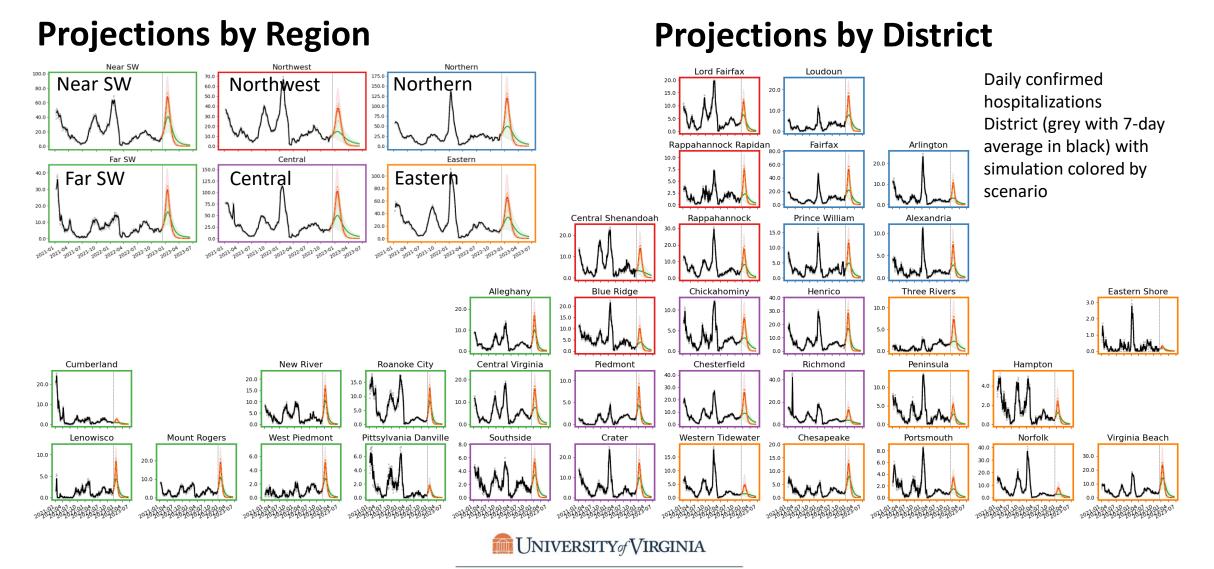
MUNIVERSITY of VIRGINIA

Detailed Projections: Cases for All Scenarios - Closer Look

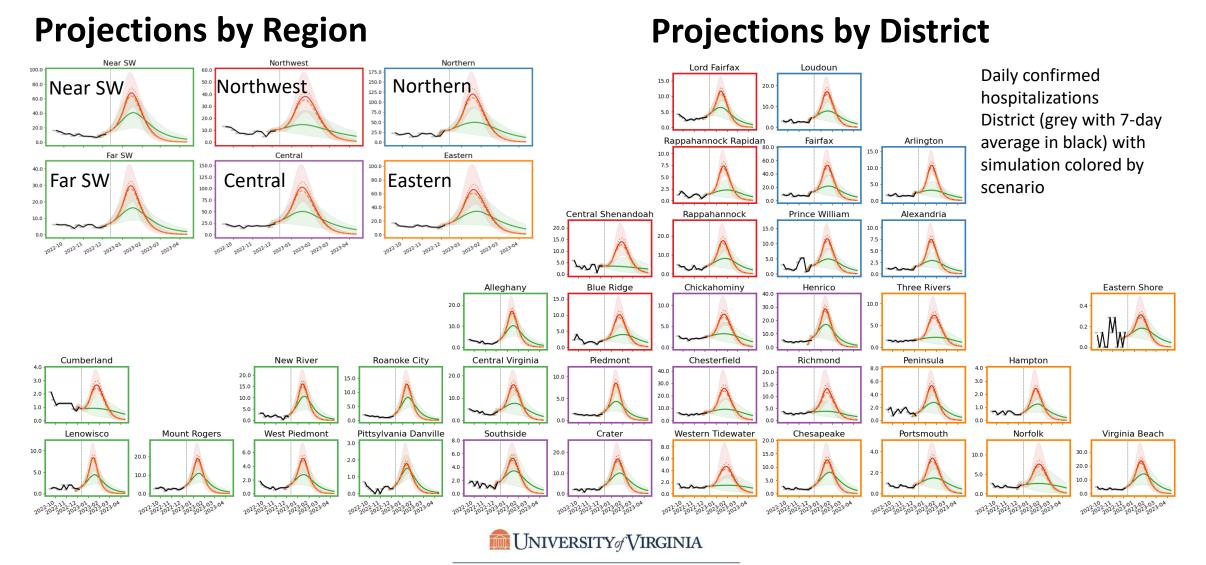


16-Dec-22

Detailed Projections: Hospitalizations for All Scenarios

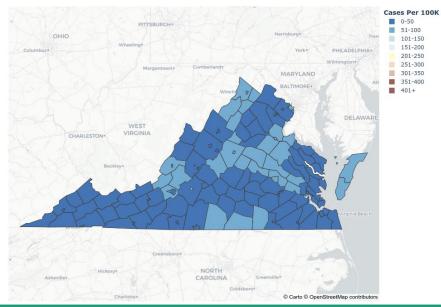


Detailed Projections: Hosps for All Scenarios - Closer Look

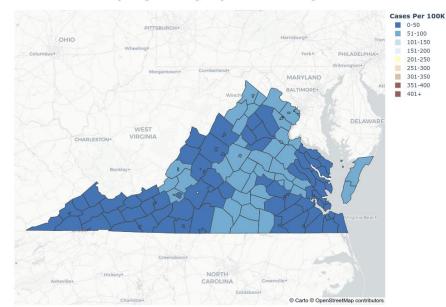


16-Dec-22

Adaptive Weekly Projections (Adaptive) 07-Dec-2022

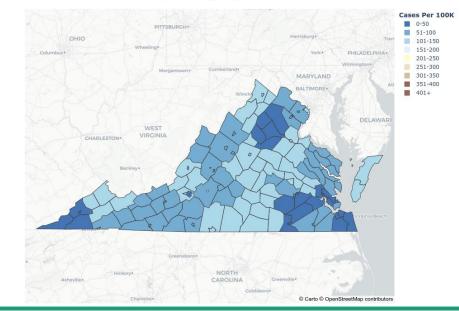


Weekly Projections (Adaptive-FallWinter) 07-Dec-2022

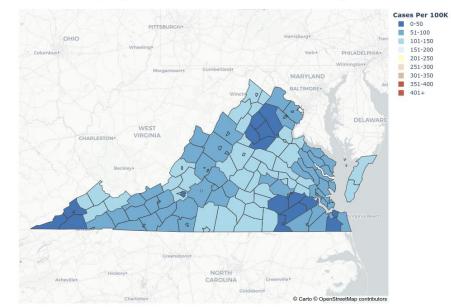


VariantX

Weekly Projections (Adaptive-VariantX) 07-Dec-2022



Weekly Projections (Adaptive-VariantX-FallWinter) 07-Dec-2022



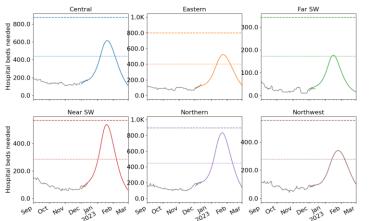
Adaptive-Fall-Winter

Hospital Demand and Bed Capacity by Region

Capacities by Region

COVID-19 capacity ranges from 80% (dots) to 120% (dash) of total beds

Adaptive – VariantX & Fall Winter



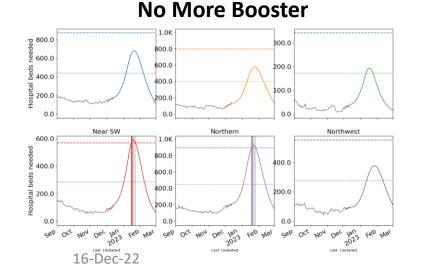
Adaptive – VariantX & Fall Winter

Length of Stay more variable with Omicron, occupancy projections may vary as a result, ad-hoc estimation performed per region Length of Stay Estimates

Central	6
Eastern	6
Far SW	4
Near SW	9
Northern	5
Northwestern	9

Estimated LOS shortened slightly to better fit observed data

Projections show continued declines and with expanded capacities and adjusted length of stay, no capacities exceeded





MUNIVERSITY of VIRGINIA

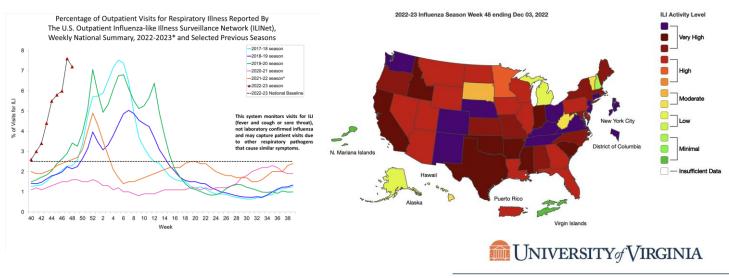
Influenza Update



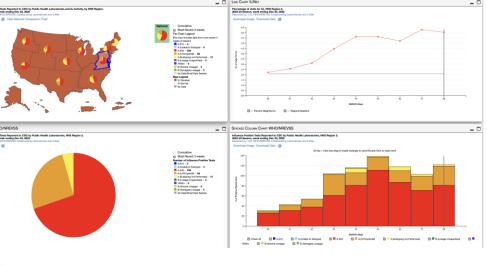
Current Influenza Situation – ILI Activity

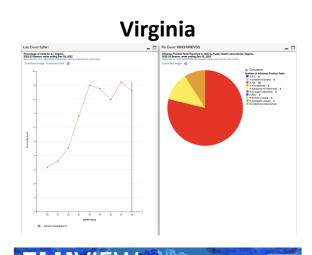
Influenza Activity is Higher than Usual

- Virginia at "Very High" activity along with many states across the US
- In VA ILI Activity remains at the 8-9% for several weeks
- National ILI activity has reached a peak rivaling the previously most intense season in the last decade (2017-18)
- After starting with high proportions of H3N2 typed influenza, H1N1pdm09 now represents ~1/4 of all infections nationally, though remain H3 dominates in VA



Region 3



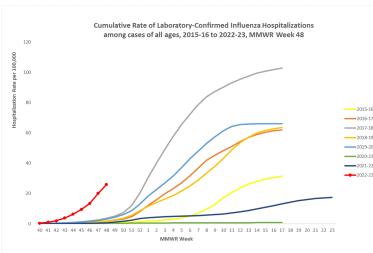


Current Influenza Situation - Hospitalizations

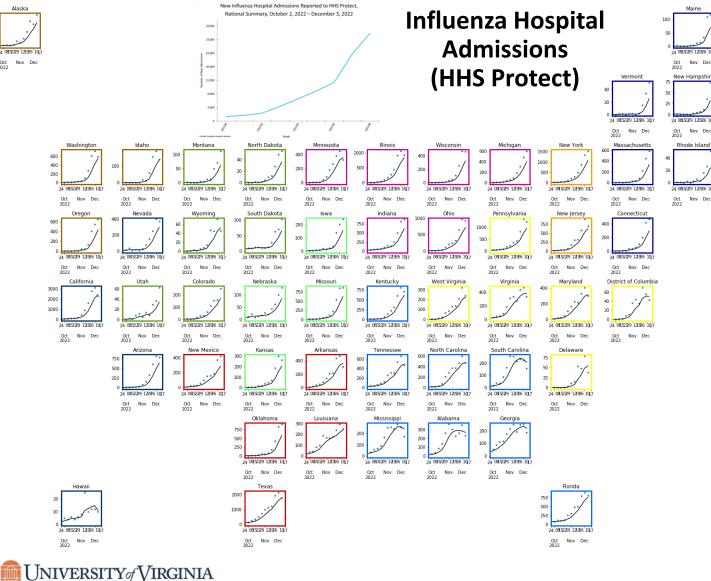
Oct Nov Dec

Influenza A hospitalizations continue rapid growth

- National level of influenza hospitalizations ٠
- Nearly all states have doubled their ٠ hospitalizations due to influenza in the last couple weeks
- Virginia shows leveling off in the last • weeks



**In this figure, weekly rates for all seasons prior to the 2022-23 season reflect end-of-season rates. For the 2022-23 season, rates for recent hospital admissions are subject to reporting delays. As hospitalization data are received each week, prior case counts and rates are updated accordingly

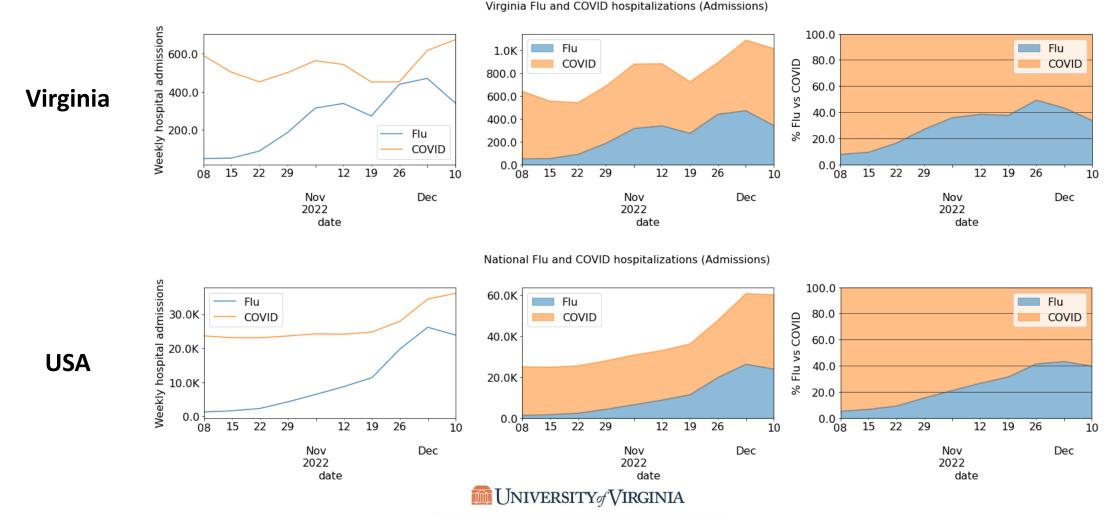


BIOCOMPLEXITY INSTITUTE

16-Dec-22

Current Combined Hospitalizations (COVID-19 & Influenza)

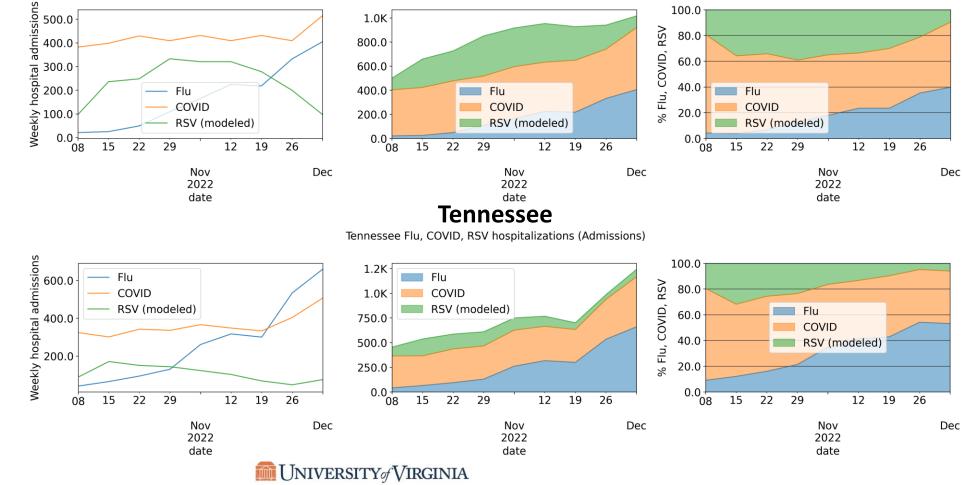
COVID-19 and Influenza Weekly Hospitalizations (HHS Protect)



Current Combined Hospitalizations (COVID-19, Flu & RSV)

COVID-19, Influenza, and RSV Weekly Hospitalizations

RSV Hospitalizations captured by RSV-Net which has lagged reporting and does not cover Virginia, thus her closest neighbors are shown for comparison



Maryland

Maryland Flu, COVID, RSV hospitalizations (Admissions)

Current Influenza Hospitalization Forecast

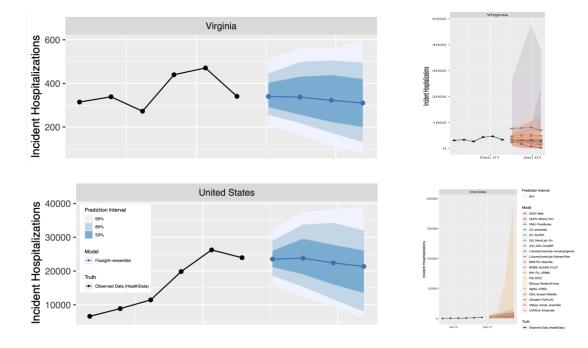
Statistical models for submitting to CDC FluSight forecasting challenge

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

Hospital Admissions for Influenza and Forecast for next 4 weeks (UVA ensemble) Virginia-no-bfill 700 Weekly hospitalizations Oct Oct Jan 2023 Jan 2022 Apr lul Week ending date United States-no-bfill 50000 S izatior 40000 hospitali 30000 50000 Weekly 10000 Oct Jan 2022 Oct Apr Jan 2023

Week ending date

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



UNIVERSITY / VIRGINIA



Combined ILI and COVID-19 Hospitalizations

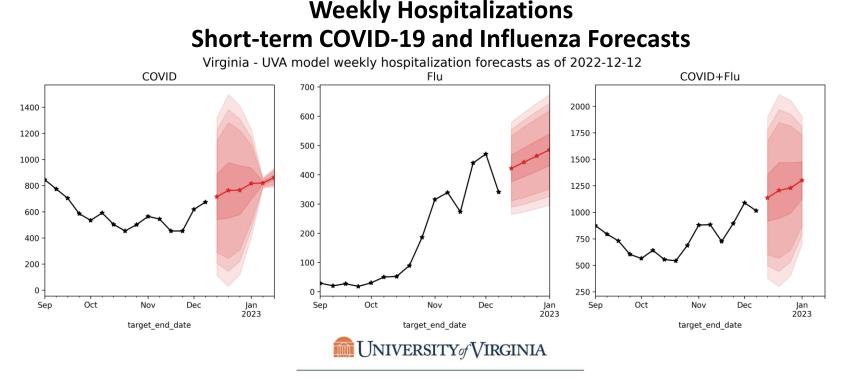
Ensemble methodology that combines the Adaptive with machine learning and statistical models such as:

• Autoregressive (AR, ARIMA), Neural networks (LSTM), Kalman filtering (EnKF), G-model (phase), Holt-Winters

<u>Weekly forecasts of hospitalizations</u> done at state level.

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

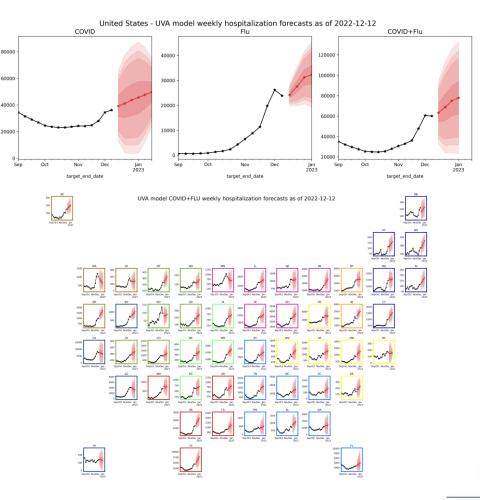
Both are regularly submitted to CDC Forecast Hubs



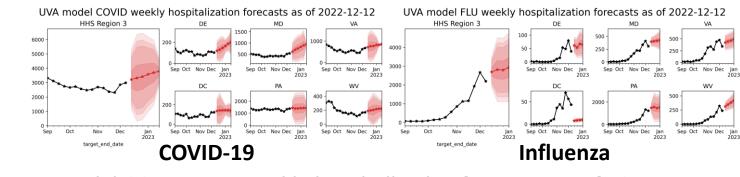
Combined ILI and COVID-19 Hospitalizations

National

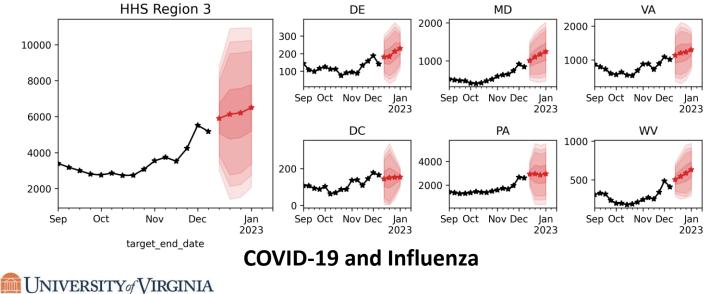
Short-term COVID-19 and Influenza Forecasts



HHS Region 3 Short-term COVID-19 and Influenza Forecasts



UVA model COVID+FLU weekly hospitalization forecasts as of 2022-12-12



National Modeling Hub Updates



Scenario Modeling Hub – COVID-19 (Round 16)

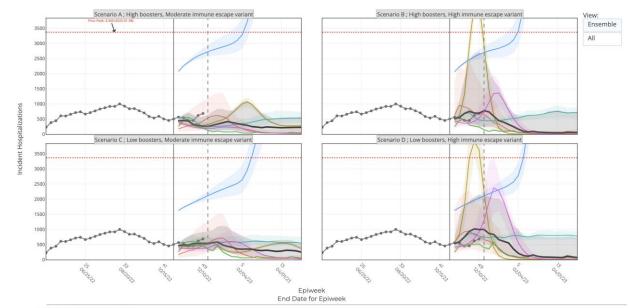
Collaboration of multiple academic teams to provide national and stateby-state level projections for 4 aligned scenarios

- Round 16 results published
- High escape scenarios tracking best

	"Level 5" Variants	"Level 6/7" Variants		
Accelerating uptake levels of reformulated boosters	*Level 5* Variants Scenario A • Variants have a 25% immune escape from BA.5.2 • Seeding based on combined observed prevalence of Level 5 variants at the start of the projection period • No change in severity given symptomatic infection	"Level 6/7" Variants Scenario B - Variants have a 50% immune escape from BA.5.2 - Seeding based on combined observed prevalence of Level 6 and 7 variants at the start of the projection period - No change in severity given symptomatic infection		
	Accelerating uptake levels of reformulated boosters, with coverage plateauing at 90% of flu vaccination levels by February 1st, 2023 - Teams are free to use available data and information from current and previous rollouts as tehy see fit to define rates - Teams should assume increasing uptake through October and November as necessary to reach the projected February 1st, 2022 plateau	Accelerating uptake levels of reformulated boosters, with coverage plateauing at 90% of flu vaccination levels by February 1st, 2023 - Teams are free to use available data and information from current and previous rollouts as terby see fit to define rates - Teams should assume increasing uptake through October and November as necessary to reach the projected February 1st, 2022 plateau		
Current uptake levels of reformulated boosters	*Level 5* Variants Scenario C • Variants have a 25% immune escape from BA.5.2 • Seeding based on combined observed prevalence of Level 5 variants at the start of the projection period • No change in severity given symptomatic infection	*Level 6/7* Variants Scenario D - Variants have a 50% immune escape from BA52 - Seeding based on combined observed prevalence of Level 6 and 7 variants at the start of the projection period - No change in severity given symptomatic infection		
	Current uptake levels of reformulated boosters, with coverage plateauing at booster 1 levels by the end of the simulation - Teams are free to use available data and information from current and previous rollouts as tehy see fit to define rates	Current uptake levels of reformulated boosters, with coverage plateauing at booster I levels by the end of the simulation - Teams are free to use available data and information from current and previous rollouts as tehy see fit to define rates		
	 Based on current rates, plateau date is flexible as long as it occurs before the end of the simulation (Teams can adjust rates up if needed to achieve adequate coverage by target date) 	 Based on current rates, plateau date is flexible as long as it occurs before the end of the simulation (Teams can adjust rates up if needed to achieve adequate coverage by target date) 		

https://covid19scenariomodelinghub.org/viz.html

Projected Incident Hospitalizations by Epidemiological Week and by Scenario for Round 16 - Virginia (- Projection Epiweek; -- Current Week)



Double-click on a model name to only display it. Click on a model name to remove it or add it from the elot display.

Zoom in the graph by click and drag (double-click to zoom-out) Ensemble_LOP_untrimmed

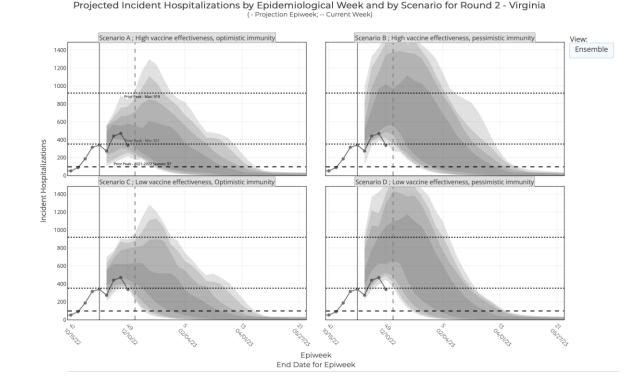
Scenario Modeling Hub – Influenza (Round 2)

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

- Round 2 is more calibrated and similar to Round 1
- Round 3 in progress (prelim results)

	Optimistic flu prior immunity	Pessimistic flu prior immunity		
High Vaccine	Scenario A	Scenario B		
Effectiveness	Optimistic flu prior immunity - No	Pessimistic flu prior immunity		
	impact of missed flu seasons due to the COVID-19 pandemic on prior immunity.* - Same amount of prior immunity as in a typical, pre-COVID19 pandemic prior season.	Substantial impact of missed flu seasons due to the COVID-19 pandemic on prior immunity.* - 50% lower immunity than a typical, pre- COVID19 pandemic season.		
		High Vaccine Effectiveness - VE = 50% against medically attended		
	High Vaccine Effectiveness - VE = 50% against medically attended influenza illnesses and hospitalizations (comparable to 2015-16 season).	influenza illnesses and hospitalizations (comparable to 2015-16 season).		
Low Vaccine	Scenario C	Scenario D		
Effectiveness	Optimistic flu prior immunity	Pessimistic flu prior immunity		
	impact of missed flu seasons due to the COVID-19 pandemic on prior immunity.* - Same amount of prior immunity as in a typical, pre-COVID19 pandemic prior season.	Substantial impact of missed flu seasons due to the COVID-19 pandemic on prior immunity.* - 50% lower immunity than a typical, pre- COVID19 pandemic season.		
		Low Vaccination Protection		
	Low Vaccine Effectiveness - VE = 30% against medically attended influenza illnesses and hospitalizations (comparable to 2018-19 season).	 - VE = 30% against medically attended influenza illnesses and hospitalizations (comparable to 2018-19 season). 		

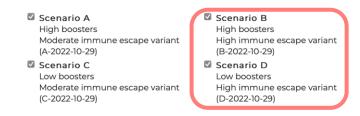
https://fluscenariomodelinghub.org/viz.html



Combined – COVID-19 and Influenza

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

• COVID-19 Scenarios – Round 16



• Influenza Scenarios – Round 3 (prelim)

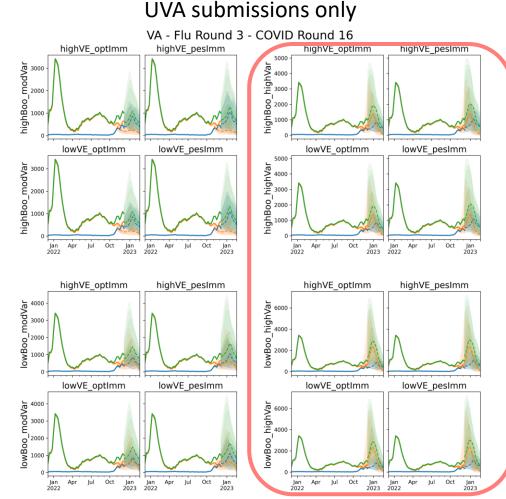
\checkmark	Scenario A	\checkmark	Scenari
	High vaccine effectiveness		High vac
	optimistic immunity		pessimis
	(A-2022-11-13)		(B-2022-
\checkmark	Scenario C	\checkmark	Scenari
	Low vaccine effectiveness		Low vac
	Optimistic immunity		pessimis

 Scenario B High vaccine effectiveness pessimistic immunity (B-2022-11-13)
 Scenario D Low vaccine effectiveness pessimistic immunity

Round 16 of COVID-19 is published and Round 2 is published, but a quick update Round 3 is now in preliminary results stage

(D-2022-11-13)

Combined Hospitalizations (VA)



Four COVID-19 scenarios crossed with four Influenza Scenarios

COVID scenarios with high immune escape seem to track best

(C-2022-11-13)

62

Key Takeaways

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

- Case rates and hospitalizations starting to rise rapidly
- VA weekly case rate is up to at 95/100K from 81/100K
 - US weekly case rate up sharply to 126 per 100K from 74 per 100K, and hospitalizations continue to quickly rise
- VA hospital occupancy is quickly rising (rolling 7 day mean of 694 from 644 a week ago); highest since early Sept
 - Influenza weekly hospital admissions remain high (~300 a week) but are now declining
- Projections anticipate increases in cases and hospitalizations in coming weeks
 - Combined hospitalizations due to Influenza and COVID-19 are expected to have a steady increase
- Model updates:
 - Model now fitted with Adaptive-Variant X, assumes this as the base case, since current growth can be attributed to rise of swarm of variants with more immune escape, Fall-Winter effects continue to add additional growth

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

References

Venkatramanan, S., et al. "Optimizing spatial allocation of seasonal influenza vaccine under temporal constraints." *PLoS Computational Biology* 15.9 (2019): e1007111.

Arindam Fadikar, Dave Higdon, Jiangzhuo Chen, Bryan Lewis, Srinivasan Venkatramanan, and Madhav Marathe. Calibrating a stochastic, agent-based model using quantile-based emulation. SIAM/ASA Journal on Uncertainty Quantification, 6(4):1685–1706, 2018.

Adiga, Aniruddha, Srinivasan Venkatramanan, Akhil Peddireddy, et al. "Evaluating the impact of international airline suspensions on COVID-19 direct importation risk." *medRxiv* (2020)

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

Virginia Department of Health. COVID-19 in Virginia. <u>http://www.vdh.virginia.gov/coronavirus/</u>

Biocomplexity Institute. COVID-19 Surveillance Dashboard. <u>https://nssac.bii.virginia.edu/covid-19/dashboard/</u>

Google. COVID-19 community mobility reports. <u>https://www.google.com/covid19/mobility/</u>

Biocomplexity page for data and other resources related to COVID-19: <u>https://covid19.biocomplexity.virginia.edu/</u>



Questions?

Points of Contact

Bryan Lewis brylew@virginia.edu

Srini Venkatramanan srini@virginia.edu

Madhav Marathe marathe@virginia.edu

Chris Barrett ChrisBarrett@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

