Network Systems
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Biocomplexity Institute & Initiative

University of Virginia

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

April 13th, 2023

(data current to April 6th – April 12th) Biocomplexity Institute Technical report: TR BI-2023-52



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

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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 broader overview of other emerging threats

Key Takeaways

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

- Case rates and hospitalizations from COVID-19 continue declines but rate has slowed and have seemingly entered a plateau
 - Hospital occupancy down to levels last seen in early May of 2022
- Nearly all indicators point to this trend continuing in near term
- Influenza hospitalizations remain very low and ILI activity remains below seasonal threshold

Model Updates

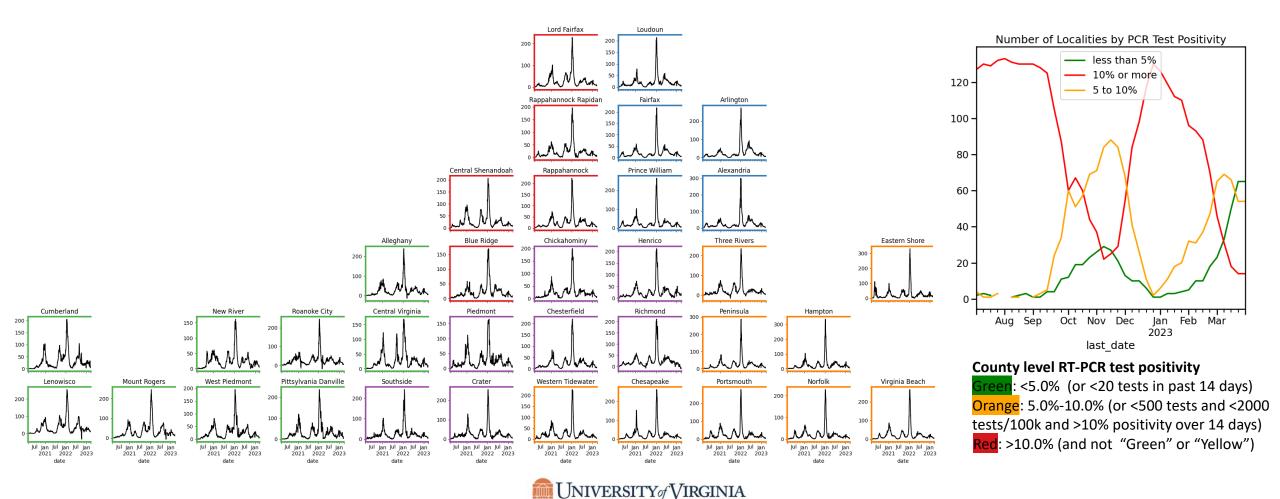
• Projected Trajectories from previous rounds remain on target, no new projections made this round



COVID-19 Surveillance



Case Rates (per 100k) and Test Positivity

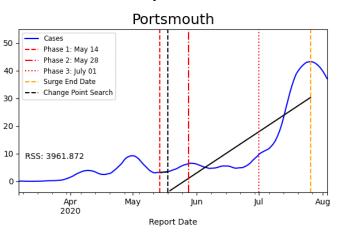


District Trajectories

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

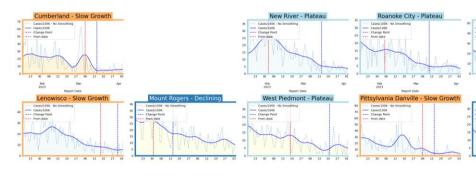


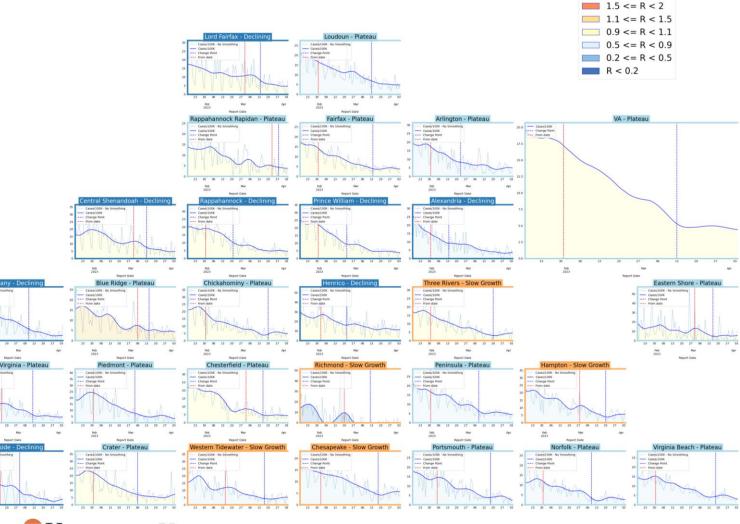
Trajectory	Description	Weekly Case Rate Slope (per 100k)	Weekly Hosp Rate Slope (per 100k)
Declining	Sustained decreases following a recent peak	slope < -0.88/day	slope < -0.07/day
Plateau	Steady level with minimal trend up or down	-0.88/day < slope < 0.42/day	-0.07/day < slope < 0.07/day
Slow Growth	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	9	(10)	
Plateau	18	(18)	
Slow Growth	8	(7)	
In Surge	0	(0)	

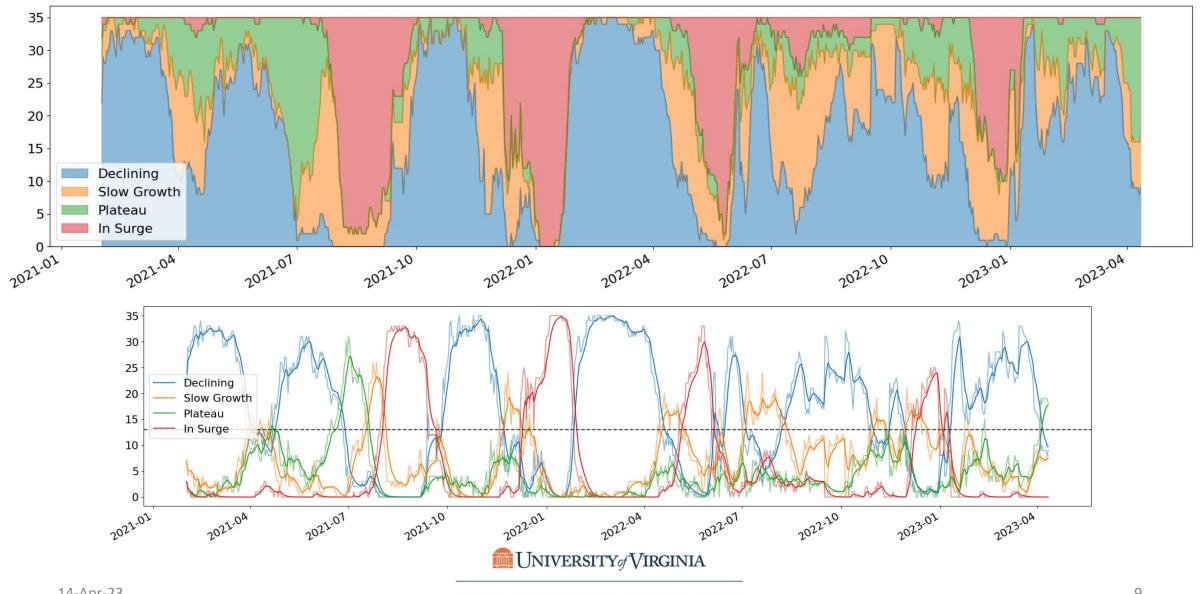
Curve shows smoothed case rate (per 100K)
Trajectories of states in label & chart box
Case Rate curve colored by Reproductive
number



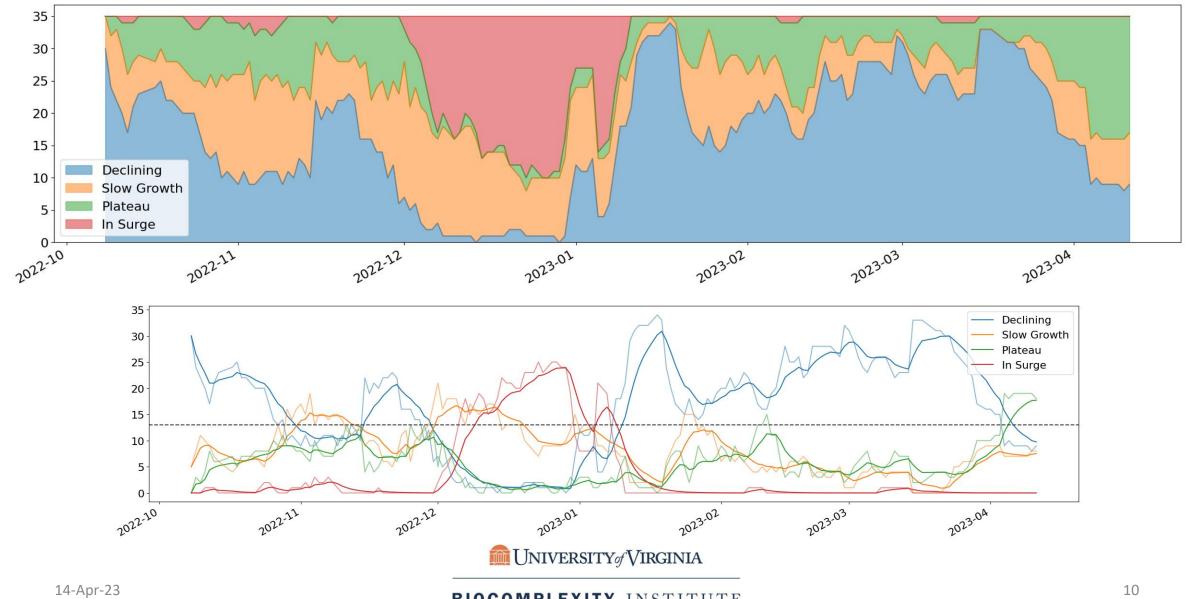


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District Case Trajectories – Full History



District Case Trajectories – Recent 6 months



District Hospital Trajectories – last 10 weeks

Hospitalization by county is

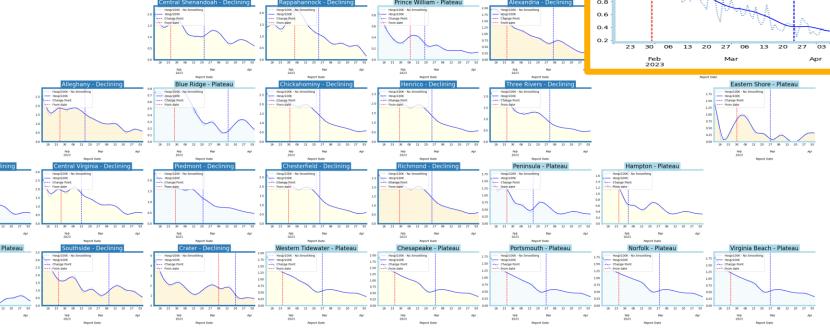
delayed, these data are

current as of

April 5th

Status	Number of Districts		
Status	Current Week	Last Week	
Declining	9	(9)	
Plateau	15	(14)	
Slow Growth	1	(2)	
In Surge	0	(0)	

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





2023-04-05

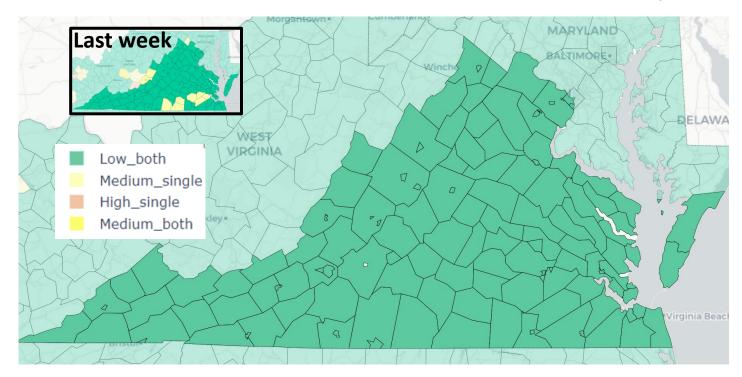
State level without delay

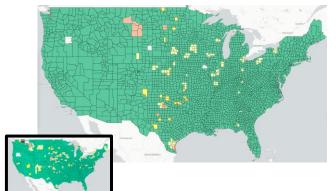
Hosp/100K - No Smoothing

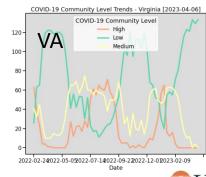
Change Point

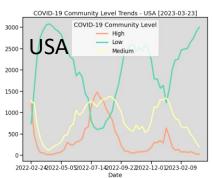
Virginia - Plateau

CDC's COVID-19 Community Levels









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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

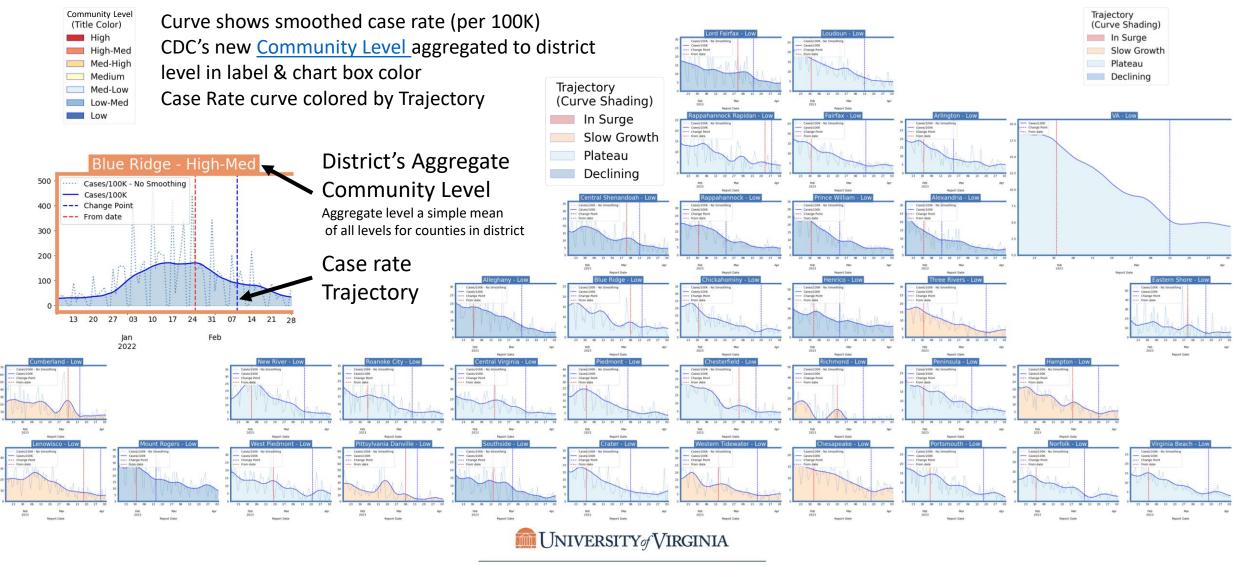
COVID-1	9 Community Levels – Use the Highest L	evel that Applies	to Your Commur	nity
New COVID-19 Cases Per 100,000 people in the past 7 days	Indicators	Low	Medium	High
	New COVID-19 admissions per 100,000 population (7-day total)	<10.0	10.0-19.9	≥20.0
Fewer than 200	Percent of staffed inpatient beds 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

Data from: CDC Data Tracker Portal

Last week

District Trajectories with Community Levels



COVID-19 Growth Metrics



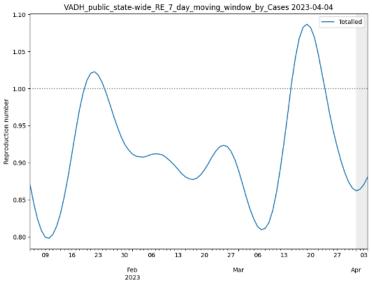
Estimating Daily Reproductive Number – VDH report dates

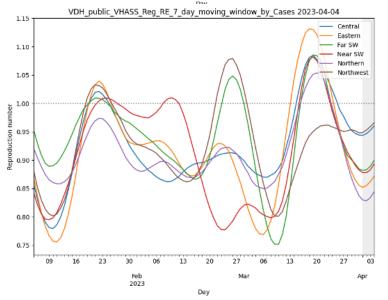
April 4th Estimates

Region	Date Confirmed R _e	Date Confirmed Diff Last Week
State-wide	0.894	-0.133
Central	0.972	-0.022
Eastern	0.878	-0.188
Far SW	0.904	-0.158
Near SW	0.905	-0.146
Northern	0.872	-0.152
Northwest	0.948	0.020

Methodology

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

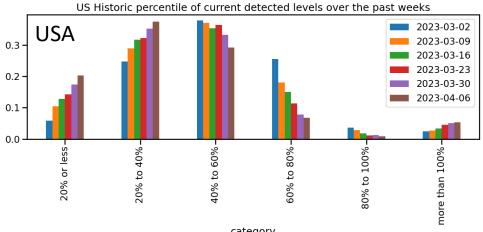


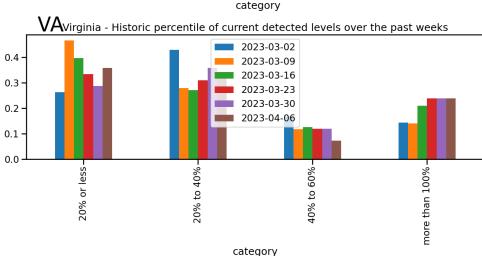


^{1.} Anne Cori, Neil M. Ferguson, Christophe Fraser, Simon Cauchemez. A New Framework and Software to Estimate Time-Varying Reproduction Numbers During Epidemics. American Journal of Epidemiology, Volume 178, Issue 9, 1 November 2013, Pages 1505–1512, https://doi.org/10.1093/aje/kwt133

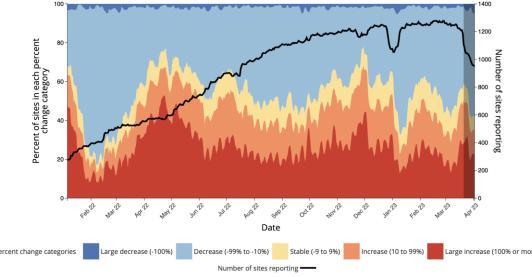
Wastewater Monitoring

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

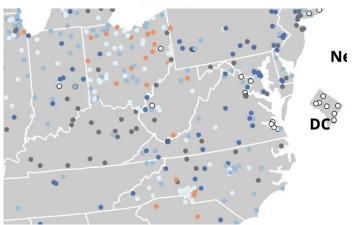




Percent of sites in each percent change category over time, United States*



*The darker bar on the right side of the figure highlights the most recent 2 weeks, which may be subject to reporting delays. The actual number of sites reporting during those 2 weeks will likely increase as historical data are added



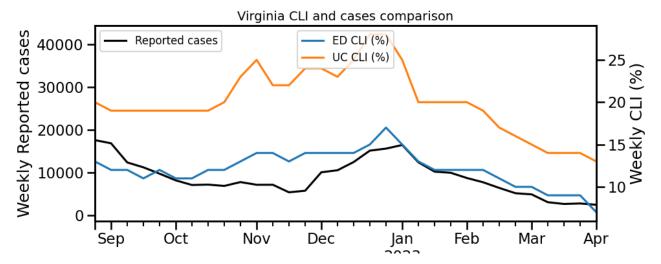
Data Source: CDC Data Tracker

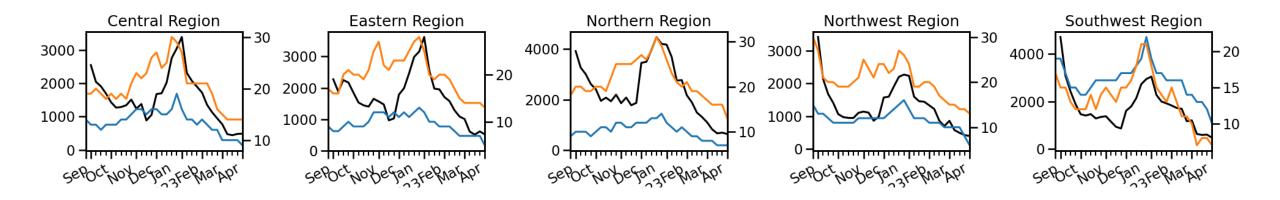
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COVID-like Illness Activity

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
- Levels continue to decline into lowest levels in past 7 months







COVID-19 Severity Metrics



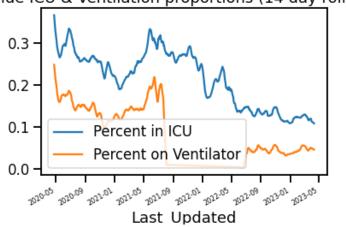
Hospitalizations and Severe Outcomes

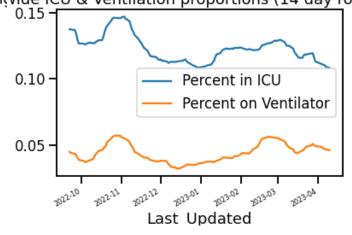
Proportion of most severe outcomes decreasing among those who are hospitalized

- ICU has declined from ~20% of hospitalized to 10-15% since initial Omicron wave
- Levels remain near all time lows, though have entered an oscillating plateau
- Regional trends are similar to state levels

Virginia-wide – full pandemic

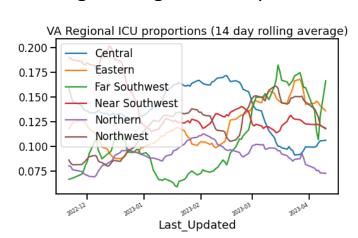
vide ICU & Ventilation proportions (14 day rollingvide ICU & Ventilation proportions (14 day rolling



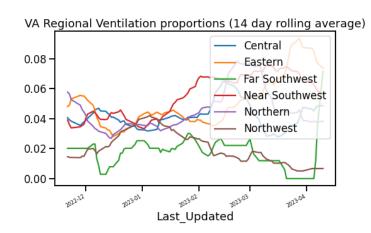


Virginia-wide – recent

Virginia Regional ICU percent



Virginia Regional Ventilation %



19

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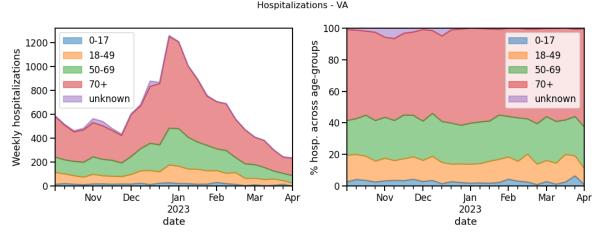
Hospitalizations in VA by Age

Age distribution in hospitals relatively stable

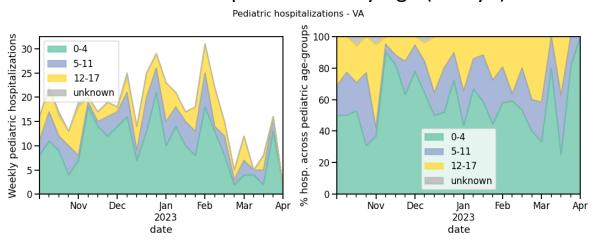
- Uptick in hospitalizations mostly fueled by 70+ age group
- Pediatric hospitalizations level off after uptick last week

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

Virginia Hospitalizations by Age (all ages)



Pediatric Hospitalizations by Age (0-17yo)



14-Apr-23 Data Source: <u>Delphi</u> and <u>HHS</u>

COVID-19 Spatial Epidemiology

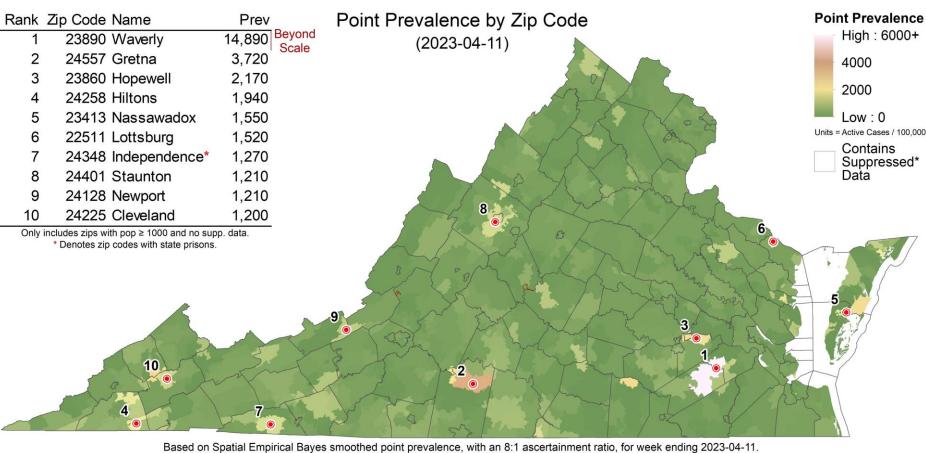


Zip code level weekly Case Rate (per 100K)

Case Rates in the last week by zip code

Statewide point prevalence levels remain low.

- Waverly is alone in reporting unusually high rates, likely reporting artifact.
- Independence, VA is the only locale with a prison in this week's top 10.
- High values are sporadic and spread across the Commonwealth.
- Some counts are low and suppressed to protect anonymity. They are shown with a red outline.

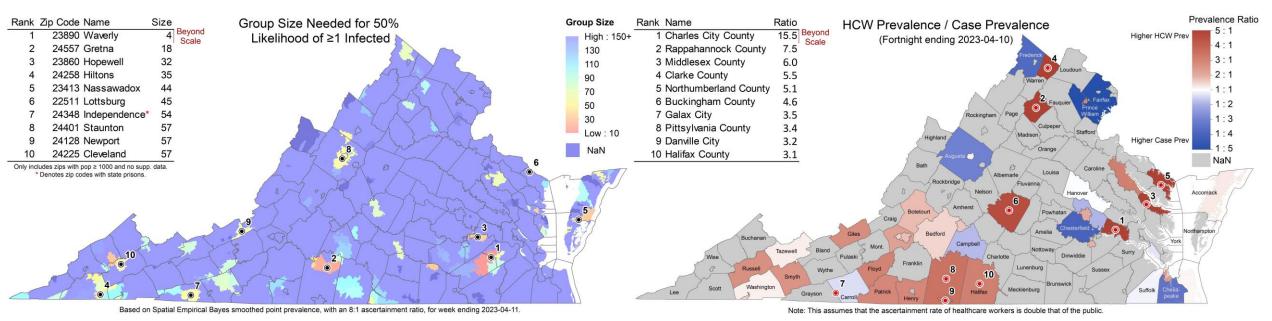


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Risk of Exposure by Group Size and HCW prevalence

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

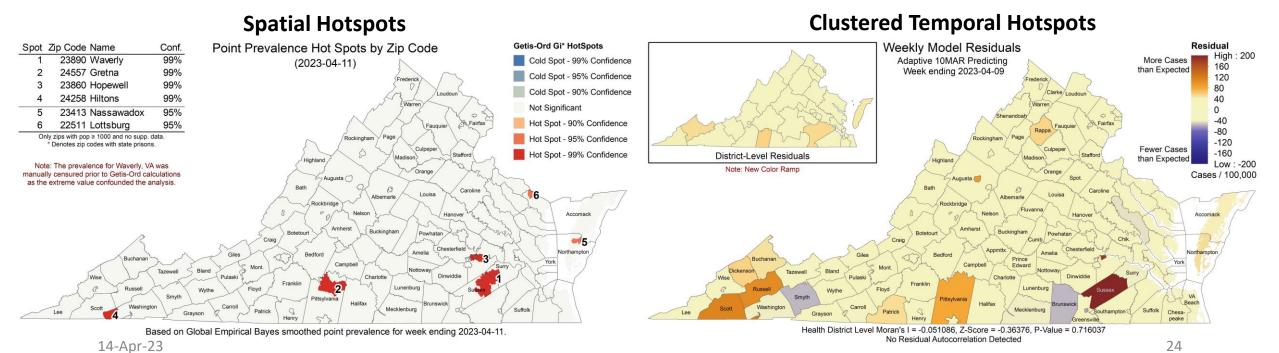
- **Group Size**: Assumes **8 undetected infections** per confirmed case (ascertainment rate from recent seroprevalence survey) and shows minimum size of a group with a 50% chance an individual is infected by zip code (e.g., in a group of 4 in Waverly, there is a 50% chance someone will be infected).
- **HCW ratio**: Case rate among health care workers (HCW) in the last fortnight using patient facing health care workers as the numerator / population's case prevalence. Pittsylvania and Halifax have significant HCW cases.



Current Hot-Spots

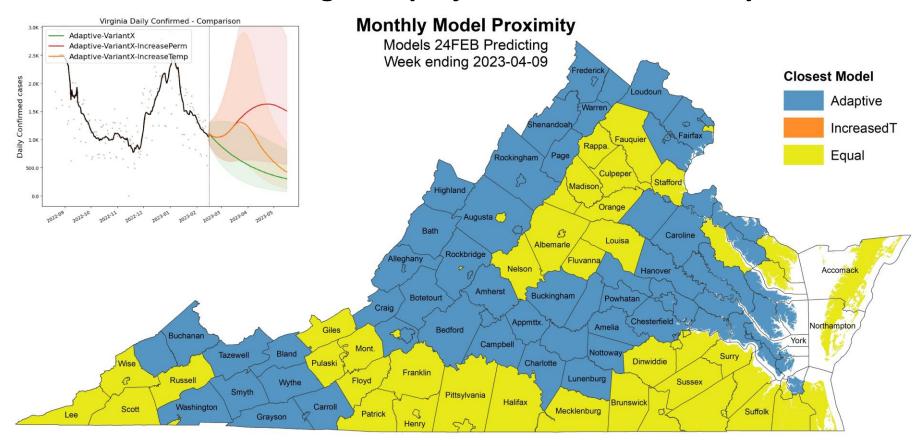
Case rates that are significantly different from neighboring areas or model projections

- 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 month compared to those observed by county, which highlights temporal fluctuations that differ from the model's projections.
- Spatial hotspots were sporadic. Note manual adjustment of Waverly due to extreme values. The models slightly underpredicted the Cumberland Plateau, Pittsylvania / Danville, and Crater Health Districts.



Scenario Trajectory Tracking

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



- Six-week projections separate the scenarios more clearly and reveals larger overall patterns.
- Most counties tracked the Adaptive (current course) scenario from late February.
- Not even one tracked the Increased Transmission scenarios better than the Adaptive.

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COVID-19 Broader Context



United States Hospitalizations



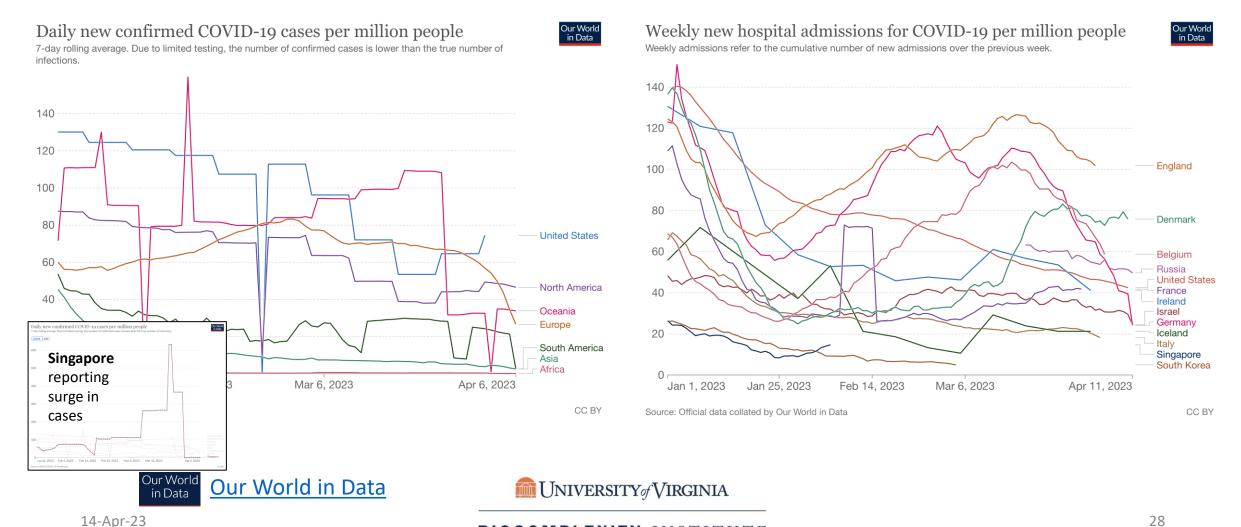
Status	Number of States		
Status	Current Week	Last Week	
Declining	18	(13)	
Plateau	34	(33)	
Slow Growth	0	(6)	
In Surge	1	(1)	



Around the World – Various trajectories

Confirmed cases

Hospitalizations



COVID-19 Genomic Update

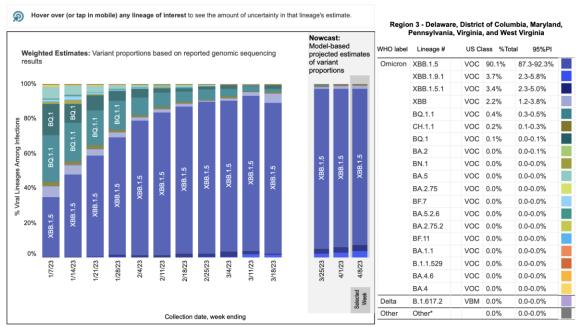


SARS-CoV2 Variants of Concern

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

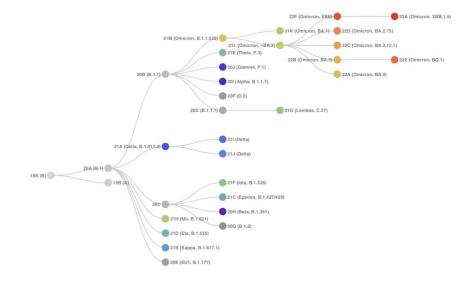
 Variants have been observed to: increase transmissibility, increase severity (more hospitalizations and/or deaths), and limit immunity provided by prior infection and vaccinations

Weighted and Nowcast Estimates in HHS Region 3 for Weeks of 1/1/2023 – Nowcast Estimates in HHS Region 3 for 4/2/2023 – 4/8/2023



^{*} 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.

CDC Variant Tracking



https://clades.nextstrain.org

Omicron Updates*

- XBB.1.5 proportions have fallen to 90%
- XBB.1.5.1 steady at 3%
- XBB.1.9 now at 3.7% up from 1% last week
- All other XBB strains (including XBB.1.16.1) increasing to 2.2%
- BQ.1.1, CH.1.1, and BQ.1 are all below 1% but remain in the population



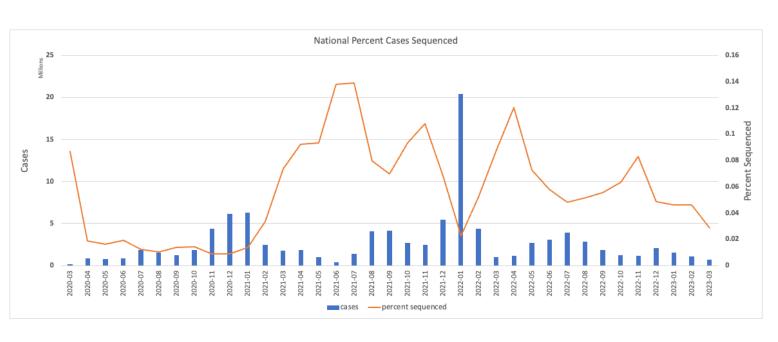
[#] BA.1, BA.3 and their sublineages (except BA.1.1 and its sublineages) are aggregated with B.1.1.529, Except BA.2.12.1, BA.2.75, XBB and their sublineages, BA.2 sublineages are aggregated with BA.2.75 except BA.2.75.2, CH.1.1 and BN.1, BA.2.75 sublineages are aggregated with BA.2.75. Except BA.4.6, sublineages of BA.5 are aggregated to BA.4. Except BF.7, BF.11, BA.5.25, BQ.1 and BQ.1.1, sublineages of BA.5 are aggregated to BA.5. Except XBB.1.9.1, XBB.1.5 and its sublineages, sublineages of XBB are aggregated to XBB. Except XBB.1.5. For all the other lineages isted, their sublineages are aggregated to the lineages isted, their sublineages are aggregated to the lineages respectively. Previously, XBB.1.9.1 was aggregated to XBB. Lineages BA.2.75.2, XBB.1.5, 1XBB.1.5, 1XBB.1.5,

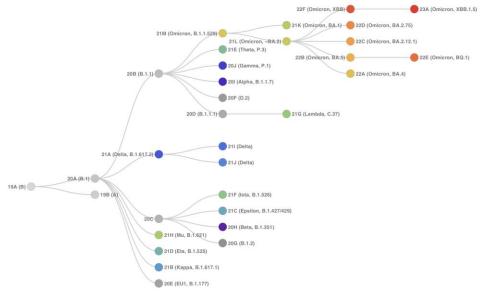
^{*}percentages are CDC NowCast Estimates

SARS-CoV2 Sequencing

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

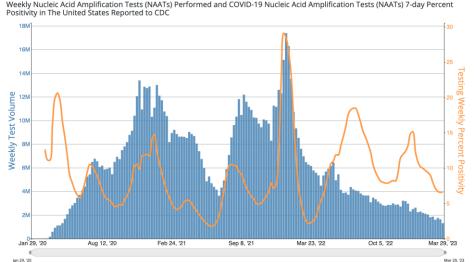
- Current proportion of cases being sequenced is on a downward trend nationally.
- Leveraging additional resources such as wastewater sequencing and adopting into existing infrastructure will be an important supplement





United States

https://clades.nextstrain.org

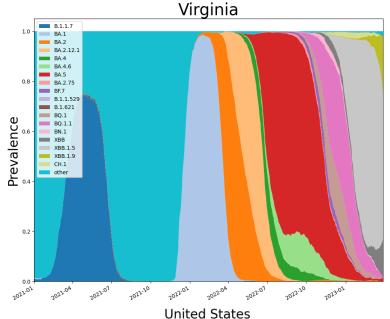


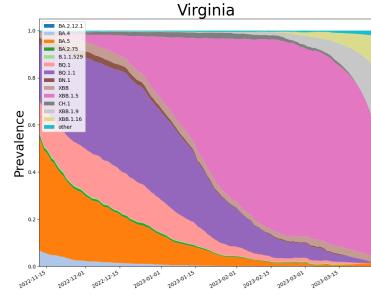
https://covid.cdc.gov/covid-datatracker/#trends 7daytestresultsreported 7daytestingpositive 00

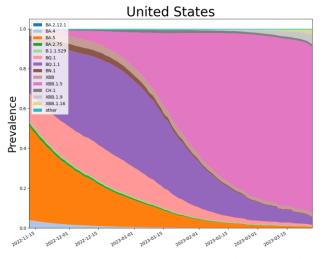


Enabled by data from **GISAID**

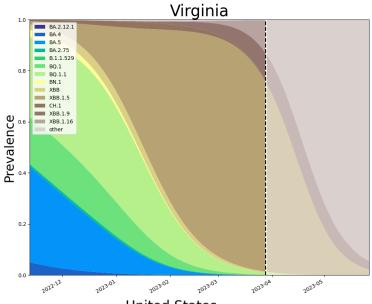
As detected in whole Genomes in public repositories

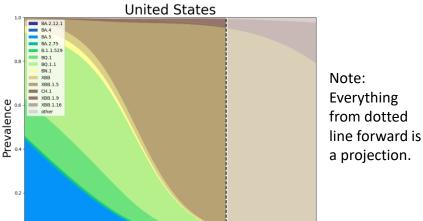






VoC Polynomial Fit Projections





32

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B.1.1.7

BA.2 BA.2.12.

BA.4.6

B.1.1.52

B.1.621

BO.1.1

XBB.1.5

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COV-spectrum

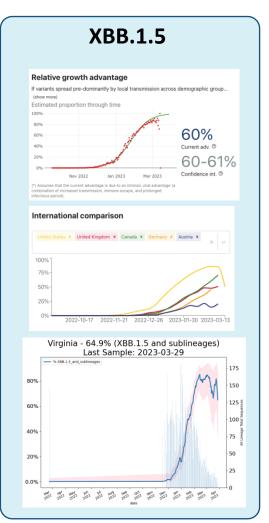
"Editor's choice" Variants to watch

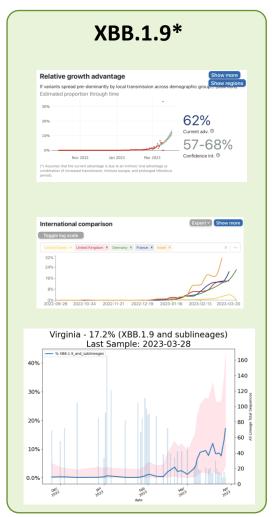
Known variants

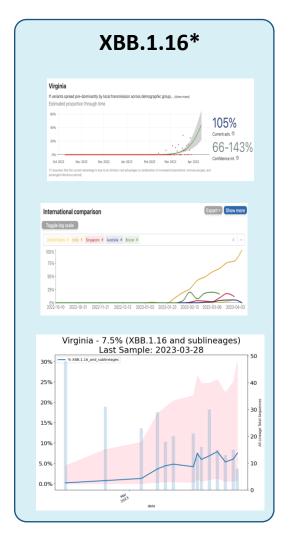


COVSPECTRUM

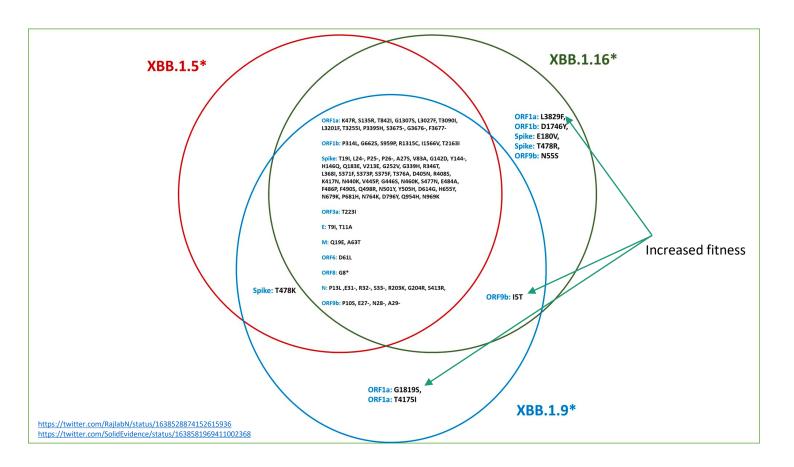
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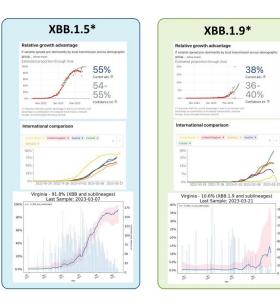


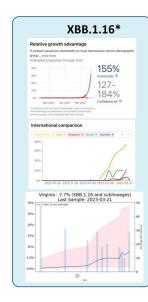








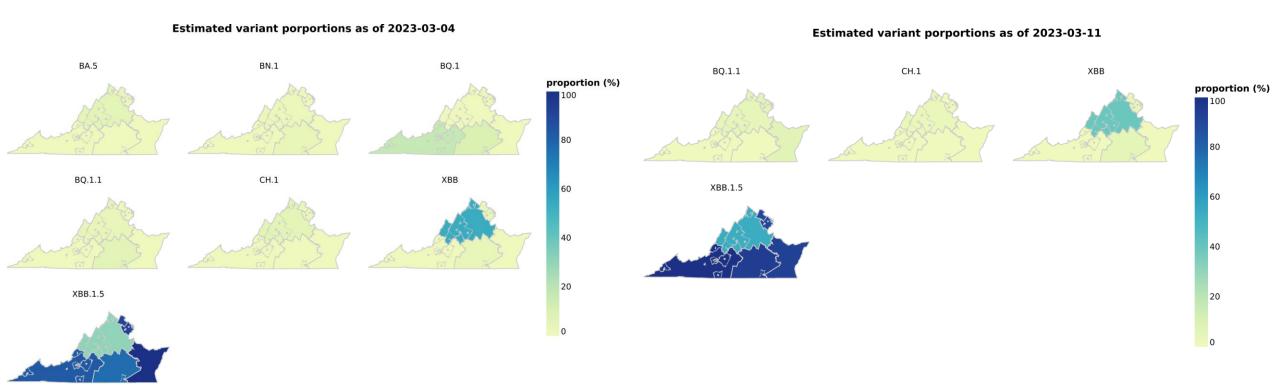




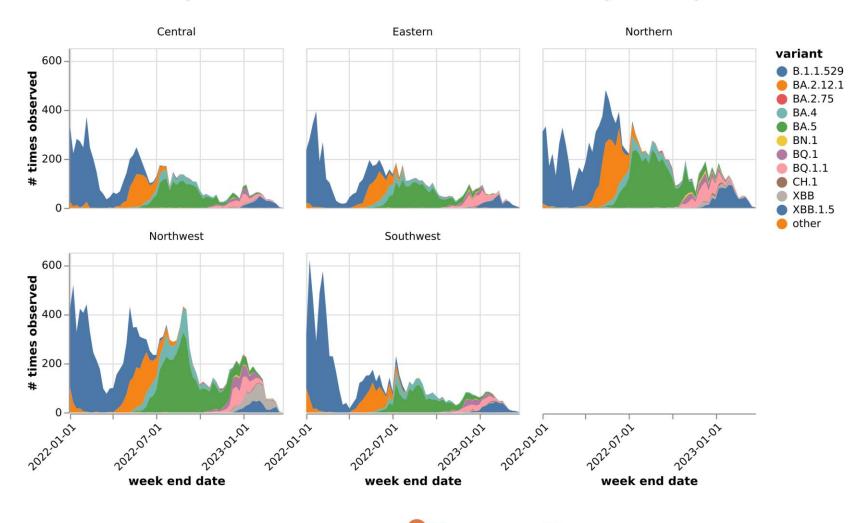


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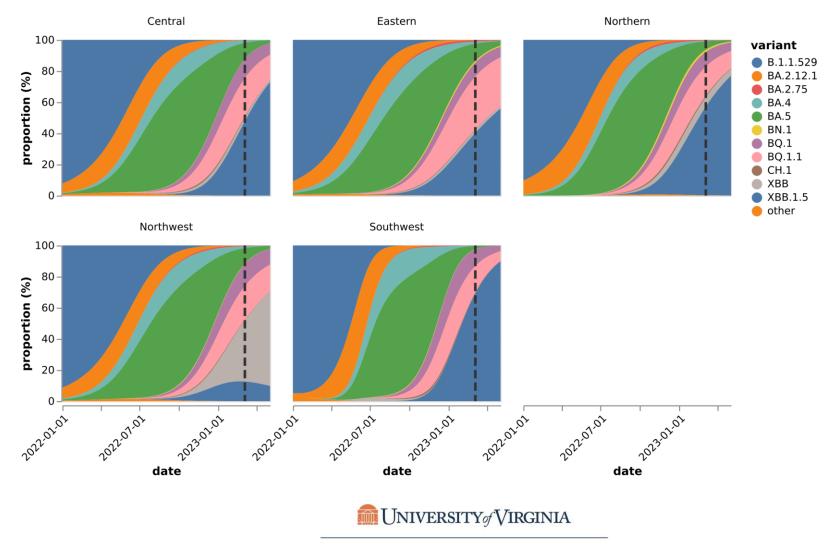


Weekly variant count observations over time in different regions of Virginia

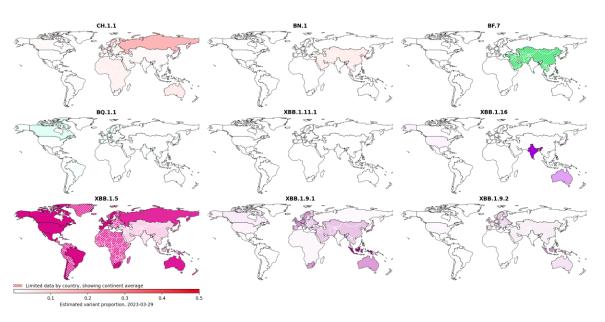


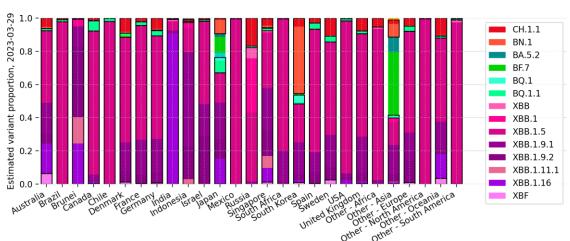
SARS-CoV2 Omicron Sub-Variants

Daily variant prevalance over time in different regions of Virginia (predicted)

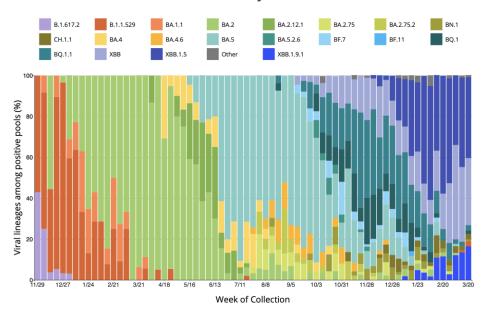


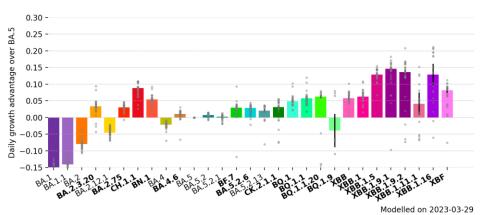
Global SARS-CoV2 Variant Status





Variants Detected, by Collection Week



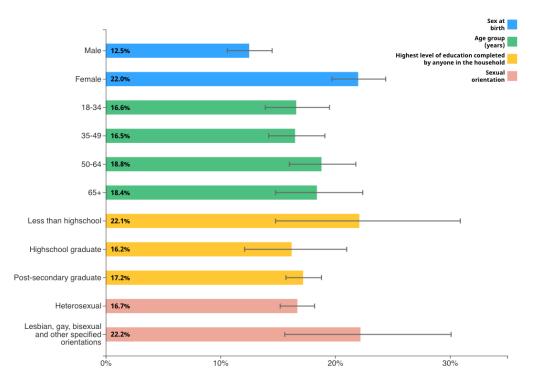


https://covid.cdc.gov/covid-data-tracker/#traveler-genomic-surveillancehttps://github.com/gerstung-lab/SARS-CoV-2-International (03/29/23)

Pandemic Pubs (April 05th, 2023)

1. Canadian national survey indicates that female sex, pre-existing comorbidities, more severe initial SARS-CoV-2 infection symptoms, obesity, identifying as a person with a disability, and being infected earlier in the COVID-19 pandemic were all associated with an increased risk of reporting longer-term symptoms, while having received more vaccine doses prior to infection was associated with a reduced risk of longer-term symptoms.

Figure 2: Percent of adults (aged 18+) self-reporting longer-term symptoms after a positive COVID-19 test or suspected infection by sociodemographics, Canada, January 2020 to August 2022



The Public Health Agency of Canada partnered with Statistics Canada to conduct the 2nd Canadian COVID-19 Antibody and Health Survey (CCAHS-2). The survey aimed to identify population subgroups disproportionately affected by longer-term symptoms and the risk and protective factors associated with experiencing longer-term symptoms. Respondents completed an electronic questionnaire between April 1, 2022 and August 31, 2022. Longer-term symptoms are defined as self-reported persistent, recurring, or new symptoms 3 or more months after a confirmed (via PCR or RAT) or suspected SARS-CoV-2 infection.

https://health-infobase.canada.ca/covid-19/post-covid-condition/spring-2023-report.html

Figure 7: Percent of adults (aged 18+) self-reporting longer-term symptoms after a positive COVID-19 test or suspected infection by time period of infection, Canada, January 2020 to August 2022

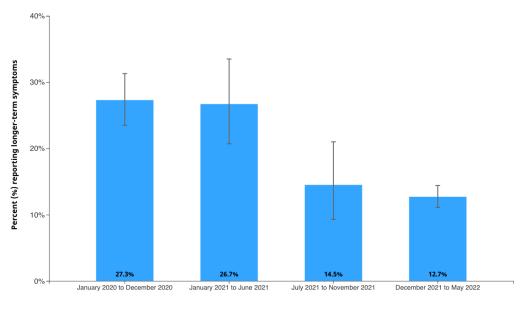
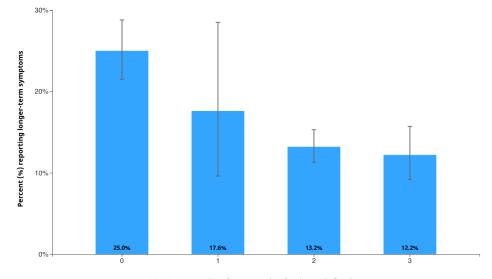


Figure 8: Percent of adults (aged 18+) self-reporting longer-term symptoms after a positive COVID-19 test or suspected infection by number of COVID-19 vaccine doses received prior to infection, Canada, January 2020 to August 2022

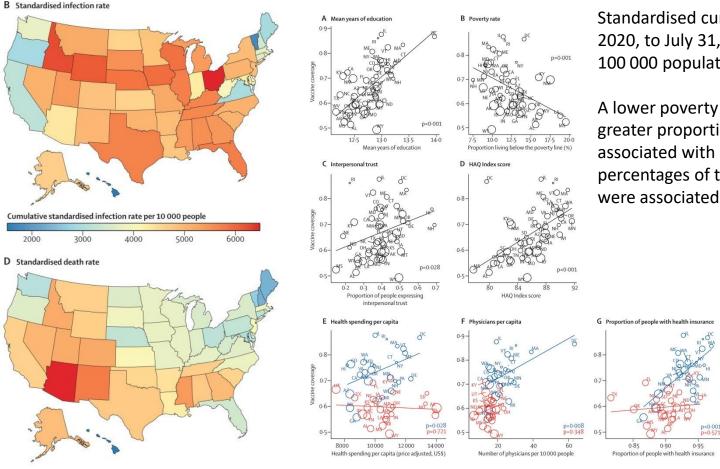


COVID-19 vaccine doses received prior to infection

Pandemic Pubs (March 30th, 2023)

ulative standardised death rate per 100 000 people

1. A comprehensive assessment of factors associated with standardized infection, hospitalization, and death rates were performed, including healthcare, social, and political factors that vary by state. Virginia's standardized death rate was lower than the national average. Many other outcomes and factors were assessed. <u>Lancet</u>



Standardised cumulative COVID-19 death rates for the period from Jan 1, 2020, to July 31, 2022 varied across the USA (national rate 372 deaths per 100 000 population [95% uncertainty interval [UI] 364–379]),

A lower poverty rate, higher mean number of years of education, and a greater proportion of people expressing interpersonal trust were statistically associated with lower infection and death rates, and states where larger percentages of the population identify as Black (non-Hispanic) or Hispanic were associated with higher cumulative death rates.

Access to quality health care (measured by the IHME's Healthcare Access and Quality Index) was associated with fewer total COVID-19 deaths and SARS-CoV-2 infections, but higher public health spending and more public health personnel per capita were not, at the state level. The political affiliation of the state governor was not associated with lower SARS-CoV-2 infection or COVID-19 death rates, but worse COVID-19 outcomes were associated with the proportion of a state's voters who voted for the 2020 Republican presidential candidate. State governments' uses of protective mandates were associated with lower infection rates, as were mask use, lower mobility, and higher vaccination rate, while vaccination rates were associated with lower death rates. State GDP and student reading test scores were not associated with state COVD-19 policy responses, infection rates, or death rates.

Influenza Update

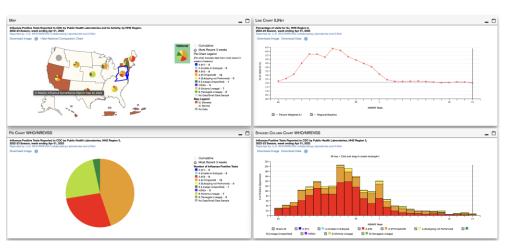


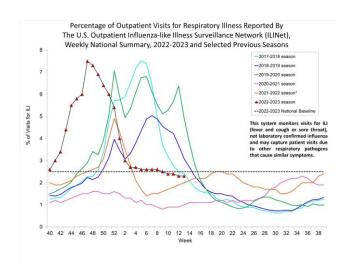
Current Influenza Situation — ILI Activity

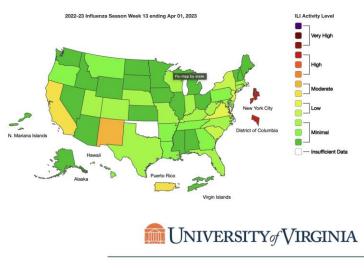
Influenza Activity remains below threshold

- Virginia remains at a "Low" level as is most of the nation
- National ILI activity has also consistently declined since a peak in late November, and remains below threshold
- Most regions and the nation are now below the seasonal threshold for ILI activity, though a couple regions have ticked above threshold in recent weeks

Region 3

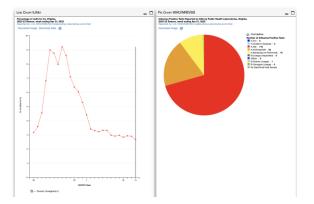






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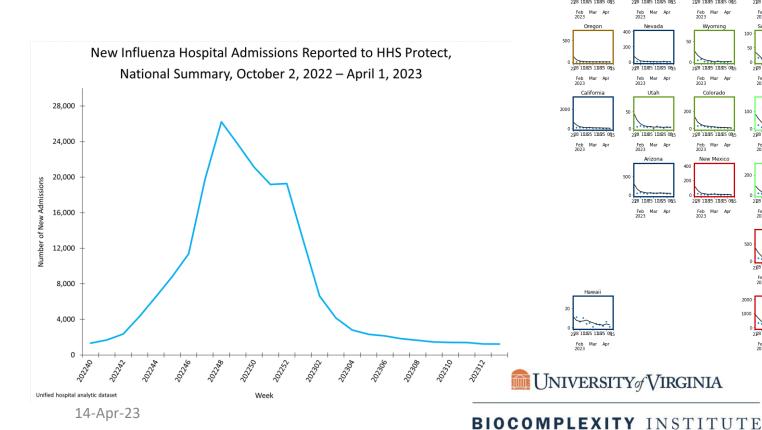
Virginia



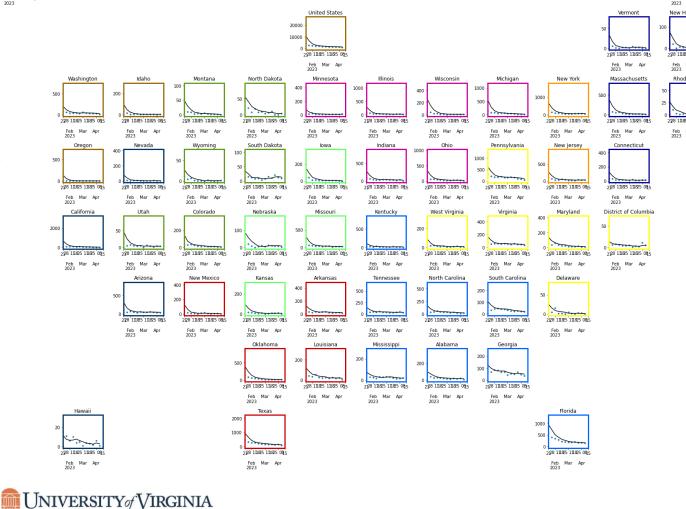
Current Influenza Situation - Hospitalizations

Influenza A hospitalizations continue decline

 National level of influenza hospitalizations have dropped to pre-season levels

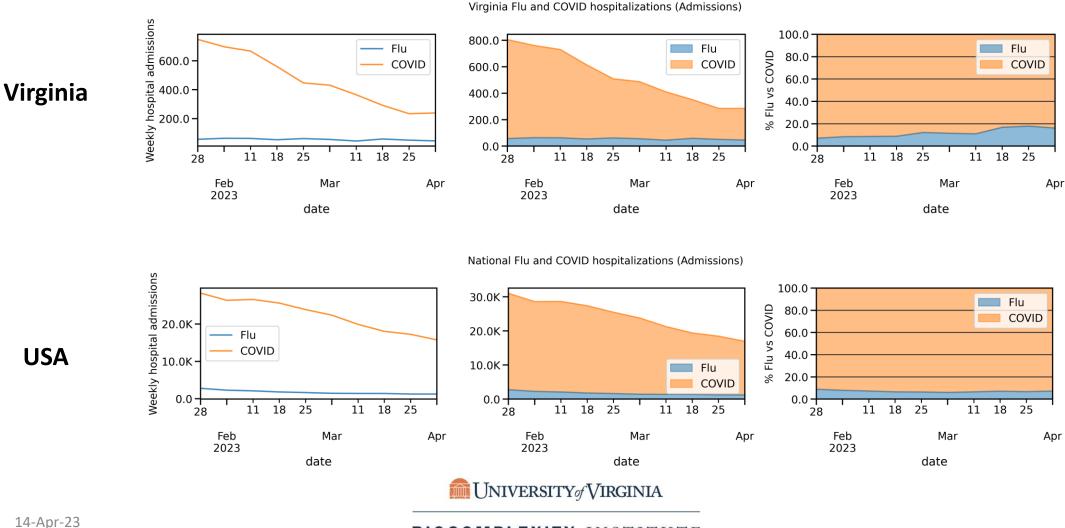






Current Combined Hospitalizations (COVID-19 & Influenza)

COVID-19 and Influenza Weekly Hospitalizations (HHS Protect)



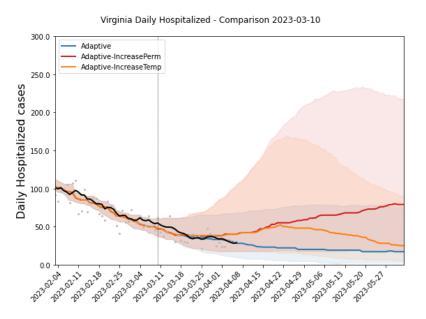
Model Results



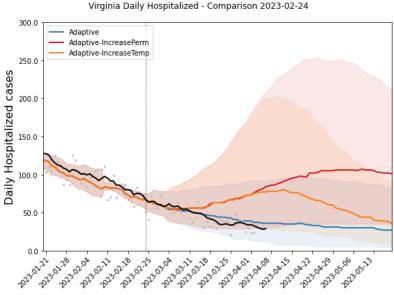
Previous projections comparison - Hospitalizations

- Previous projections have tracked observed hospitalizations well
- Past 8 weeks have stayed steady and indicate no increases in transmissions

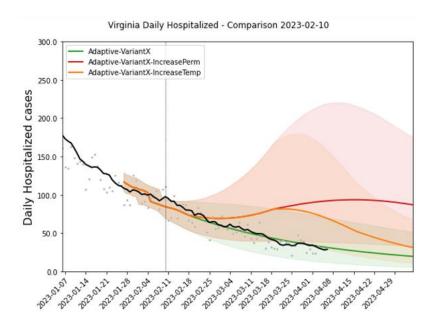
Previous round – 4 weeks ago



Previous round – 6 weeks ago



Previous round – 8 weeks ago



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National Modeling Hub Updates

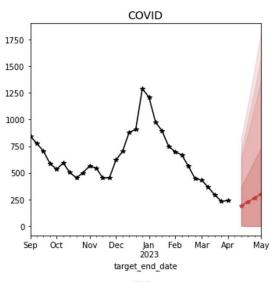


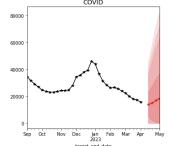
Current COVID-19 Hospitalization Forecast

Statistical models for submitting to CDC FluSight forecasting challenge

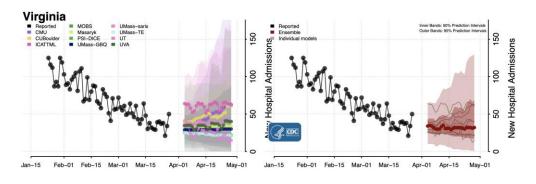
• Uses a variety of statistical and ML approaches to forecast weekly hospital admissions for the next 4 weeks for all states in the US

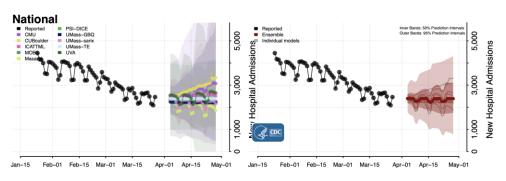
Hospital Admissions for COVID-19 and Forecast for next 4 weeks (UVA ensemble)





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









Combined ILI and COVID-19 Hospitalizations

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

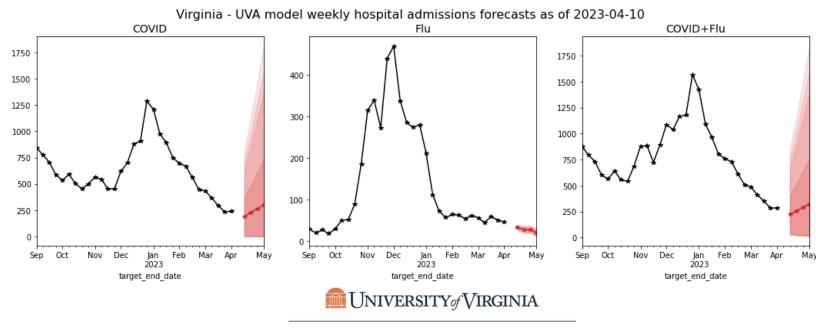
• Autoregressive (AR, ARIMA), Neural networks (LSTM), Kalman filtering (EnKF), G-model (phase), Holt-Winters

Weekly forecasts of hospitalizations 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

Weekly Hospitalizations Short-term COVID-19 and Influenza Forecasts



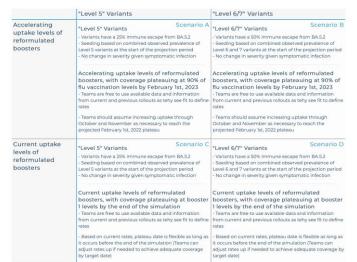
Scenario Modeling Hub - COVID-19 (Round 16)

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

- Round 16 results published
- Moderate escape scenarios tracking best

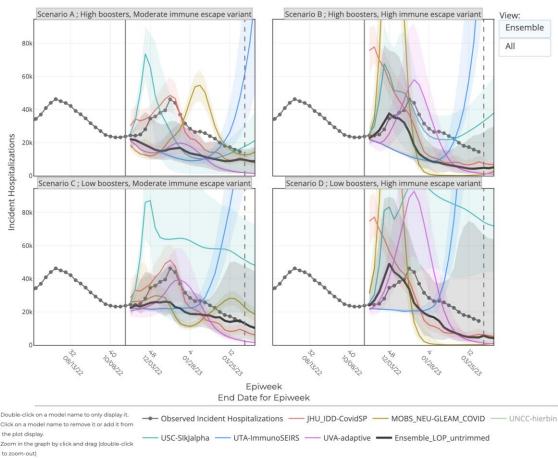
• Round 17 is underway, prelim results in

coming weeks



https://covid19scenariomodelinghub.org/viz.html

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



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Scenario Modeling Hub – Influenza (Round 3)

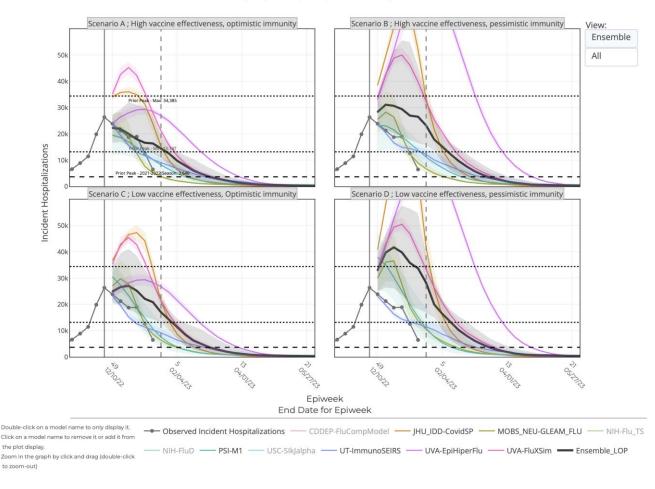
Collaboration of multiple academic teams to provide national and state-by-state level projections for 4 aligned scenarios

- All rounds so far have explored the combination of a prior immunity axis and a vaccine effectiveness axis
- Round 2 and 3 are identical in design (Round 3 cutoff December 3rd)

	Optimistic flu prior immunity	Pessimistic flu prior immunity
High Vaccine Effectiveness	Scenario A Optimistic flu prior immunity	Scenario B 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 influenza illnesses and hospitalizations (comparable to 2015-16 season).	High Vaccine Effectiveness - VE = 50% against medically attended influenza illnesses and hospitalizations (comparable to 2015-16 season).
Low Vaccine Effectiveness	Scenario C Optimistic flu prior immunity - No 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.	Scenario D Pessimistic flu prior immunity 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

Projected Incident Hospitalizations by Epidemiological Week and by Scenario for Round 3 - US (- Projection Epiweek; -- Current Week)



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Key Takeaways

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

- Case rates and hospitalizations from COVID-19 continue declines but rate has slowed and have seemingly entered a plateau
 - Hospital occupancy down to levels last seen in early May of 2022
- Nearly all indicators point to this trend continuing in near term
- Influenza hospitalizations remain very low and ILI activity remains below seasonal threshold

Model Updates

• Projected Trajectories from previous rounds remain on target, no new projections made this round



Questions?

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