Network Systems Science & Advanced Computing

Biocomplexity Institute & Initiative

University of Virginia

Estimation of COVID-19 Impact in Virginia

February 23rd, 2022

(data current to Feb 19th – 22nd)

Biocomplexity Institute Technical report: TR 2022-015

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biocomplexity.virginia.edu

About Us

- Biocomplexity Institute at the University of Virginia
  - Using big data and simulations to understand massively interactive systems and solve societal problems
- Over 20 years of crafting and analyzing infectious disease models
  - Pandemic response for Influenza, Ebola, Zika, and others

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Overview

- **Goal**: Understand impact of 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:

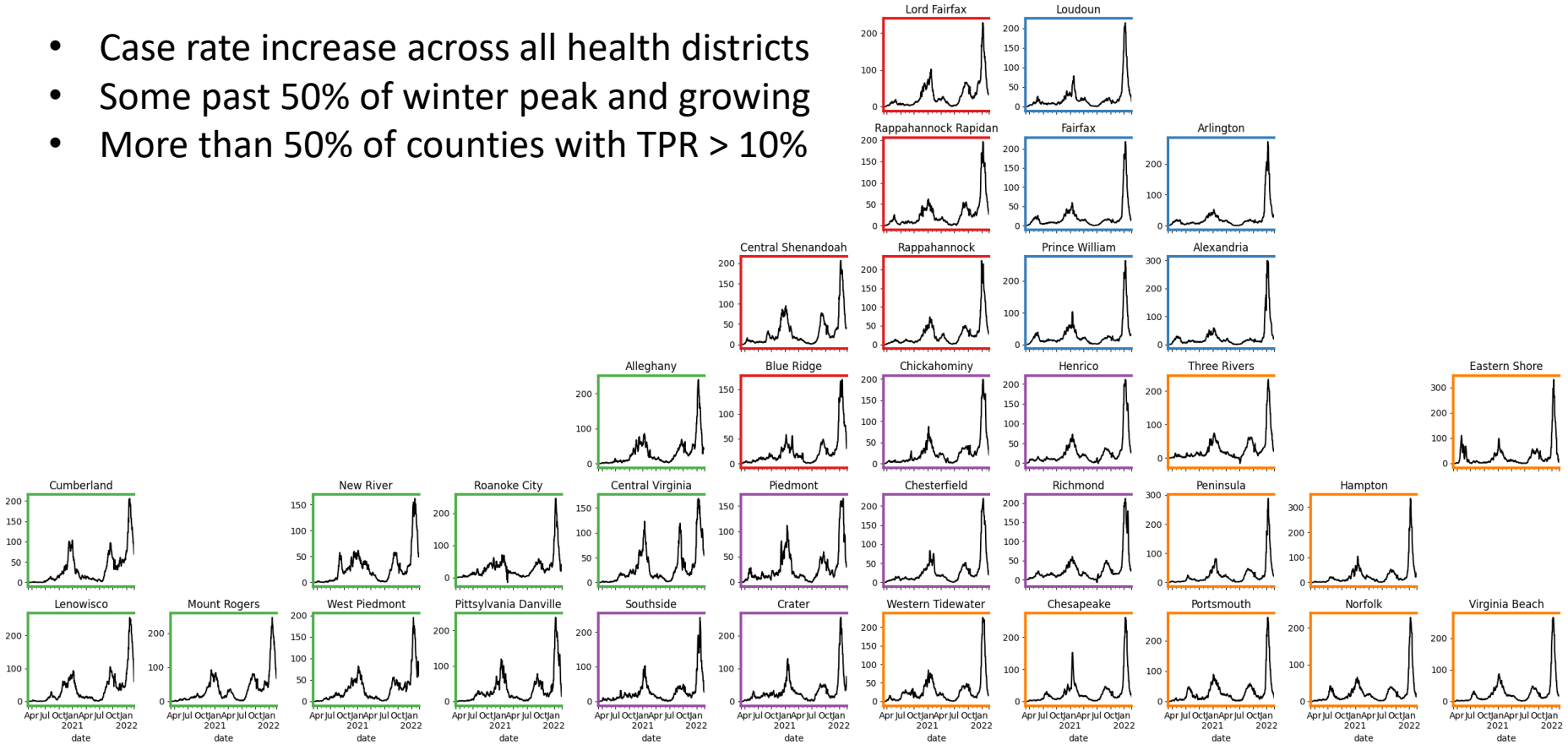
- **Case rates and hospitalizations continue to dramatic decline**
- VA 7-day mean daily case rate is sharply down to 30/100K from 44/100K
  - US is also considerably down to 26/100K (from 46/100K)
- BA.2 subvariant growth is slowed by the drastic declines, likely to take longer to reach predominance than initial trends suggested

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

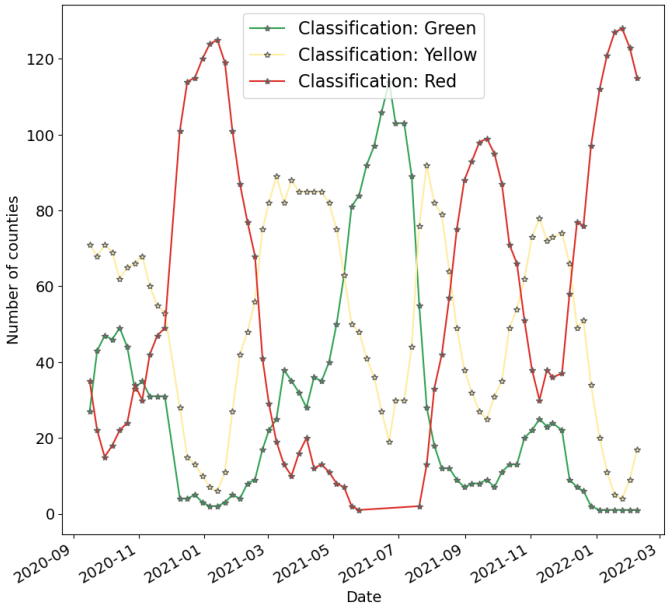
Situation Assessment

Case Rates (per 100k) and Test Positivity

- Case rate increase across all health districts
- Some past 50% of winter peak and growing
- More than 50% of counties with TPR > 10%



Data source: https://data.cms.gov/covid-19/covid-19-nursing-home-data



County level RT-PCR test positivity

Green: <5.0% (or <20 tests in past 14 days)

Yellow: 5.0%-10.0% (or <500 tests and <2000 tests/100k and >10% positivity over 14 days)

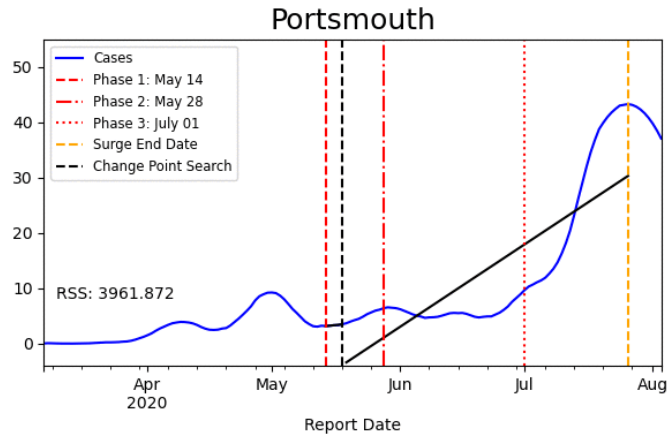
Red: >10.0% (and not "Green" or "Yellow")

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

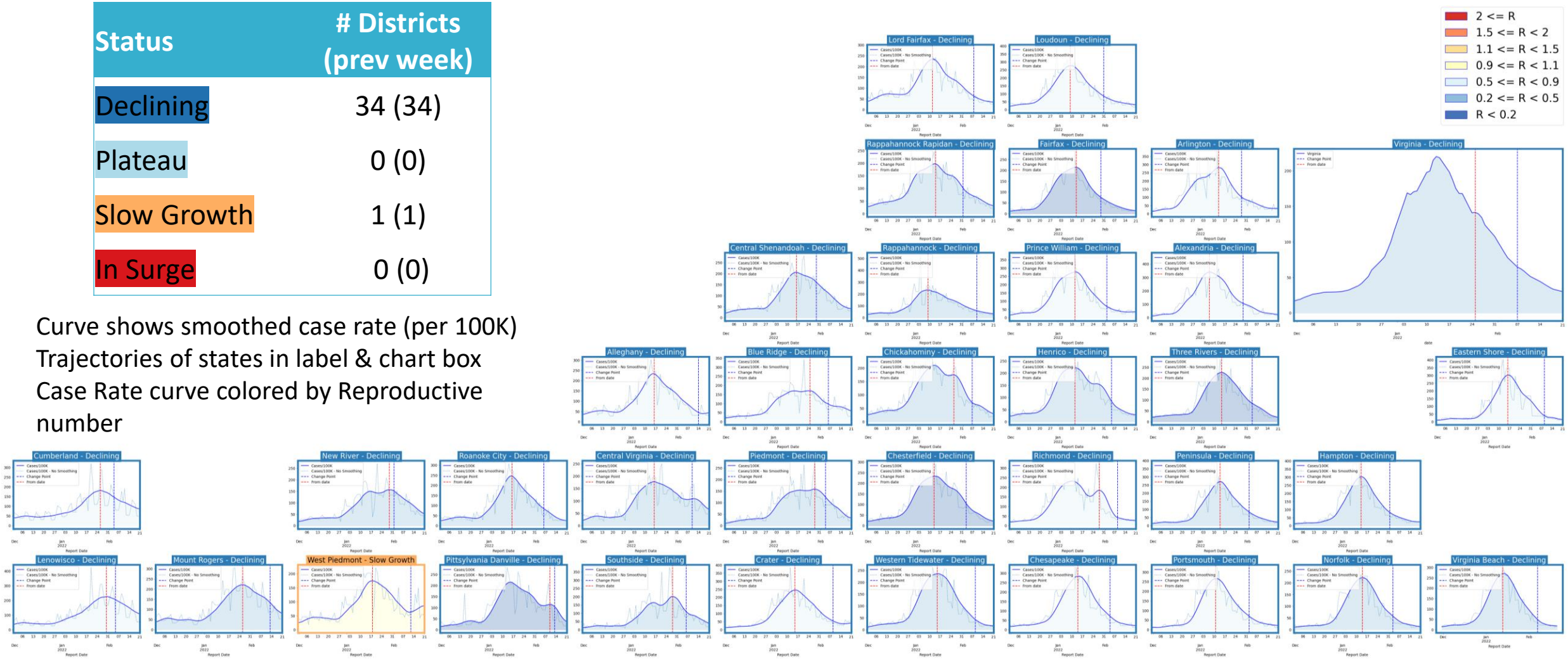


Trajectory	Description	Weekly Case Rate (per 100K) bounds	# Districts (prev week)
Declining	Sustained decreases following a recent peak	below -0.9	34 (34)
Plateau	Steady level with minimal trend up or down	above -0.9 and below 0.5	0 (0)
Slow Growth	Sustained growth not rapid enough to be considered a Surge	above 0.5 and below 2.5	1 (1)
In Surge	Currently experiencing sustained rapid and significant growth	2.5 or greater	0 (0)

District Trajectories – last 10 weeks

Status	# Districts (prev week)
Declining	34 (34)
Plateau	0 (0)
Slow Growth	1 (1)
In Surge	0 (0)

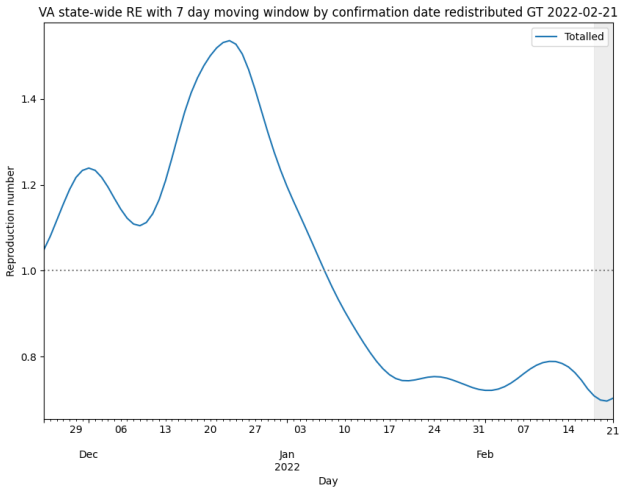
Curve shows smoothed case rate (per 100K)
Trajectories of states in label & chart box
Case Rate curve colored by Reproductive number

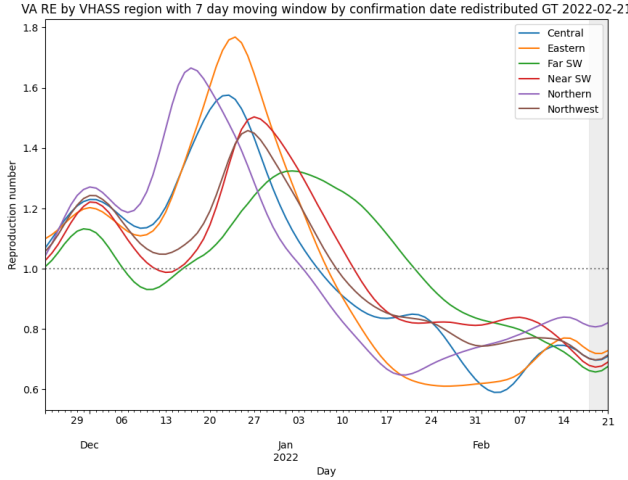


Estimating Daily Reproductive Number – Redistributed gap

Feb 21st Estimates

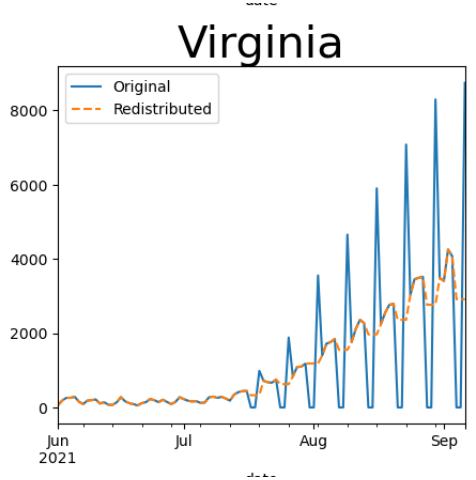
Region	Date Confirmed R_e	Date Confirmed Diff Last Week
State-wide	0.705	0.038
Central	0.710	0.093
Eastern	0.734	0.261
Far SW	0.674	-0.090
Near SW	0.693	-0.132
Northern	0.824	0.183
Northwest	0.716	-0.028





Skipping Weekend Reports & holidays biases estimates

Redistributed "big" report day to fill in gaps, and then estimate R from "smoothed" time series



Methodology

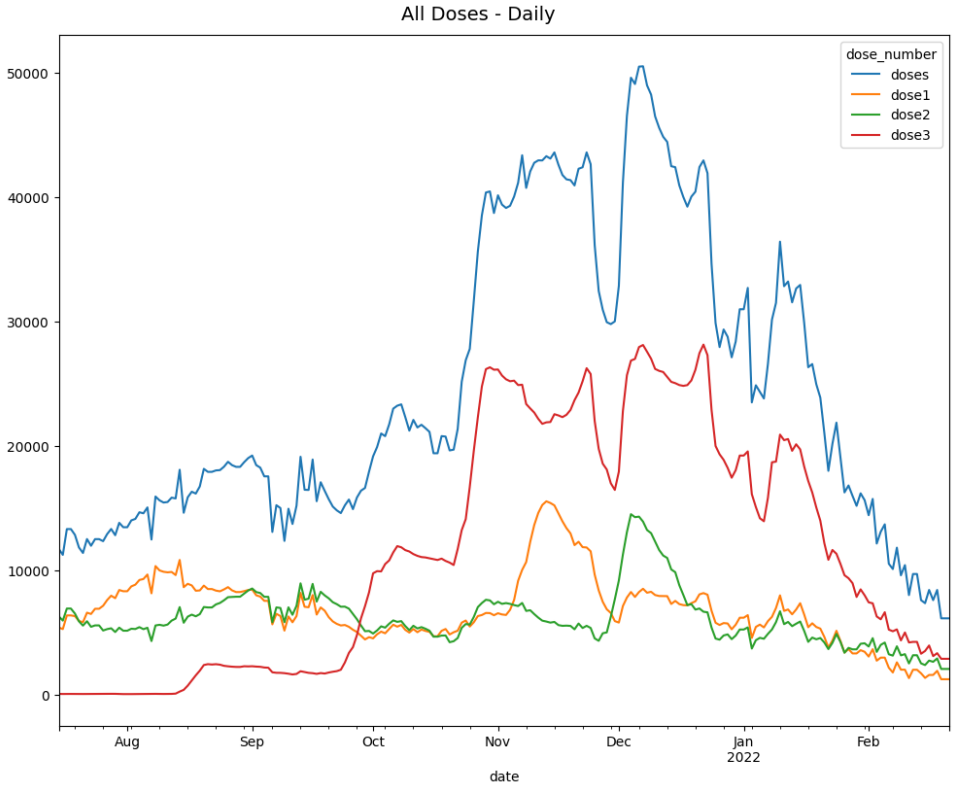
- Wallinga-Teunis method (EpiEstim[1]) for cases by **confirmation date**
- Serial interval: Discrete distribution from observations (mean=4.3, Flaxman et al, Nature 2020)
- Using Confirmation date since due to increasingly unstable estimates from onset date due to backfill

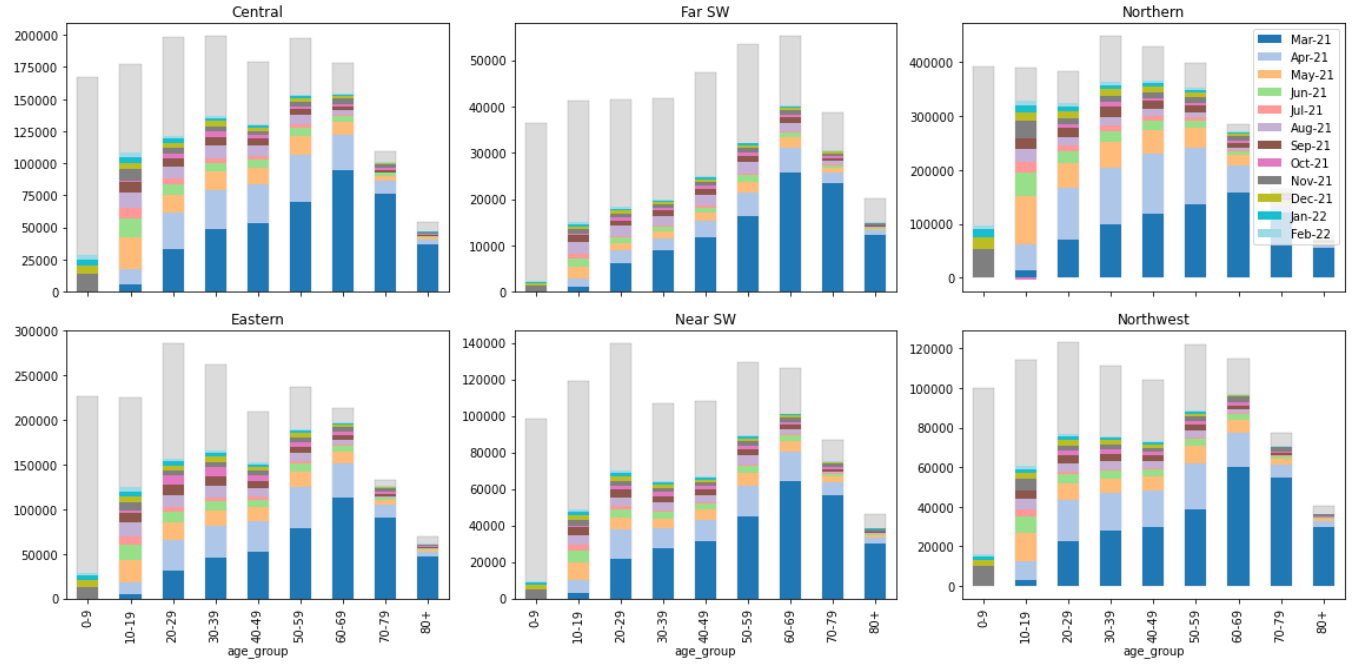
1. Anne Cori, Neil M. Ferguson, Christophe Fraser, Simon Cauchemez. A New Framework and Software to Estimate Time-Varying Reproduction Numbers During Epidemics. American Journal of Epidemiology, Volume 178, Issue 9, 1 November 2013, Pages 1505–1512, https://doi.org/10.1093/aje/kwt133

Vaccination Administration in Virginia

Vaccine Doses administered:

- Doses administered rates approach levels first experienced when vaccines were first available
- Considerable reduction in vaccination rate experienced since mid-January
- Third dose administration outpaces 1st dose

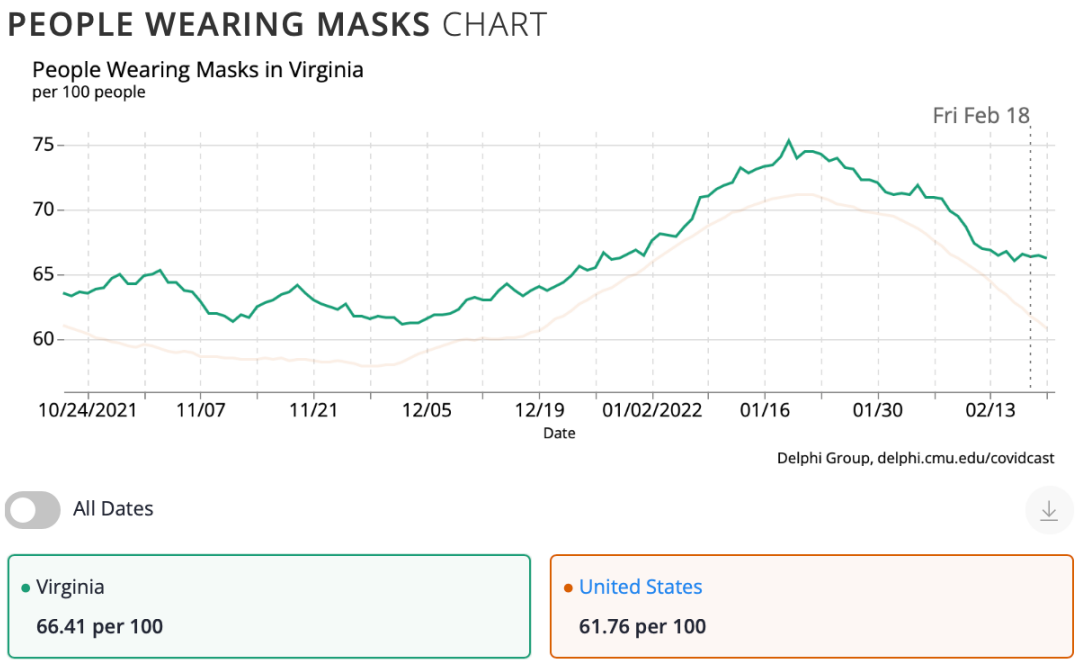


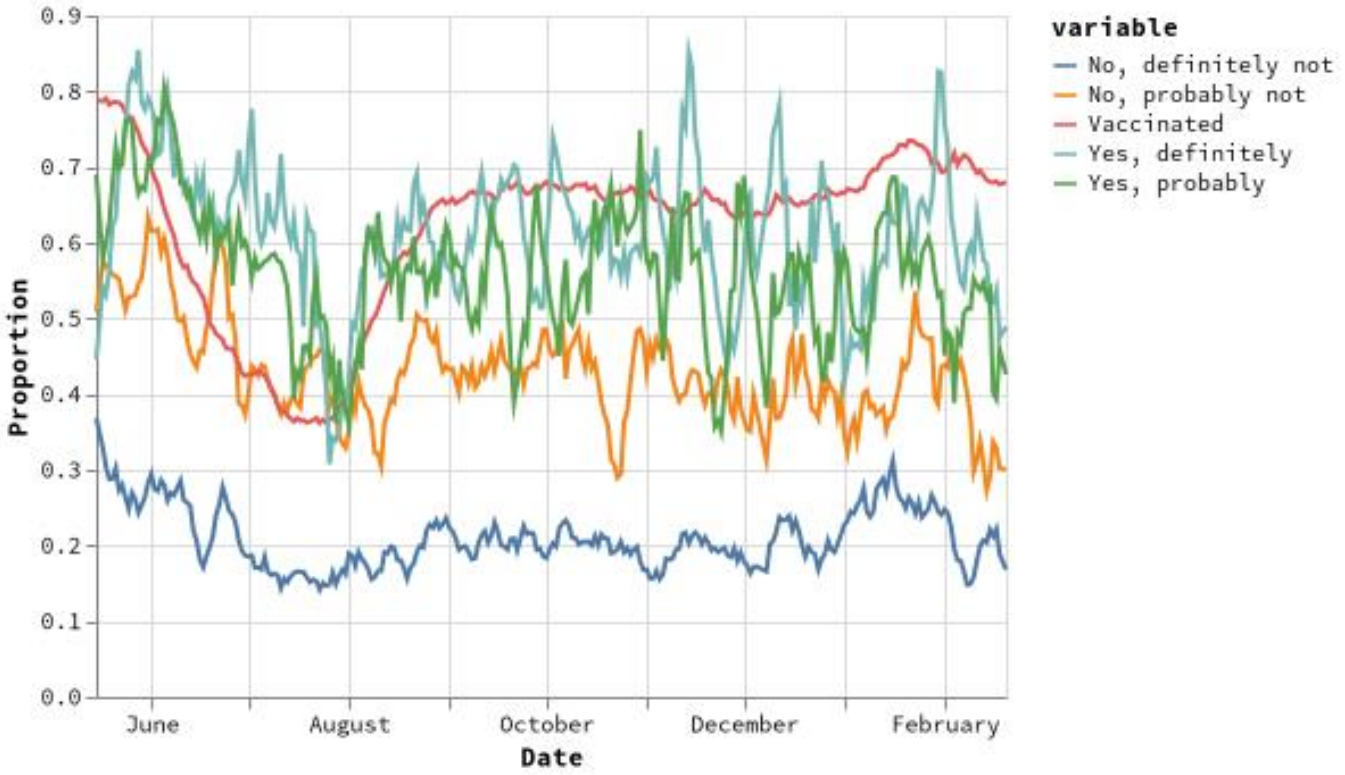


Mask Usage

Self-reported mask usage seems to be leveling off at ~65% after a month of slow decline

- US and VA experienced similar increases
- Mask wearing remains lower amongst unvaccinated especially among least willing to be vaccinated



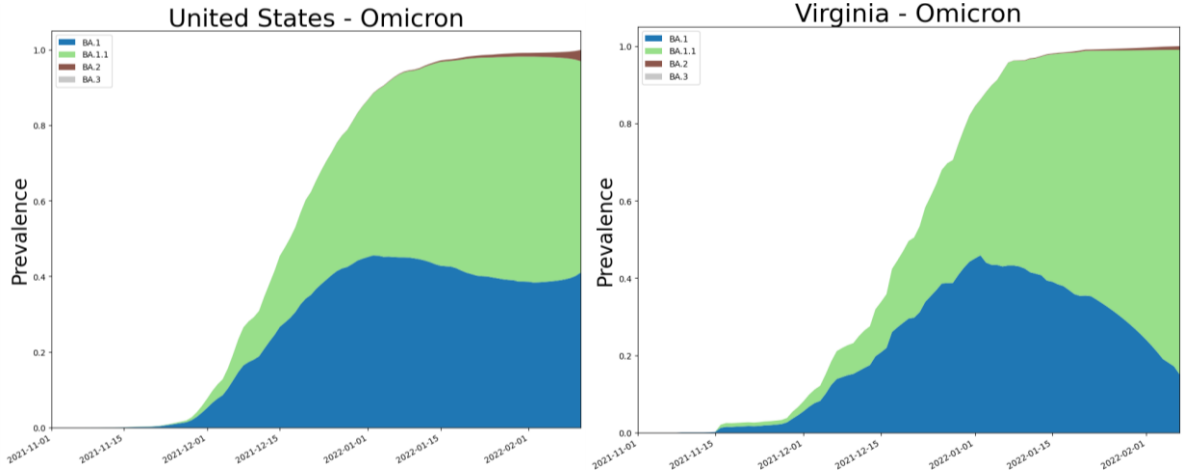


Data Source: https://covidcast.cmu.edu

SARS-CoV2 Variants of Concern

Emerging new variants will alter the future trajectories of pandemic and have implications for future control

- Emerging variants can:
  - Increase transmissibility
  - Increase severity (more hospitalizations and/or deaths)
  - Limit immunity provided by prior infection and vaccinations
- Genomic surveillance remains very limited
  - Challenges ability to estimate impact in US to date and estimation of arrival and potential impact in future



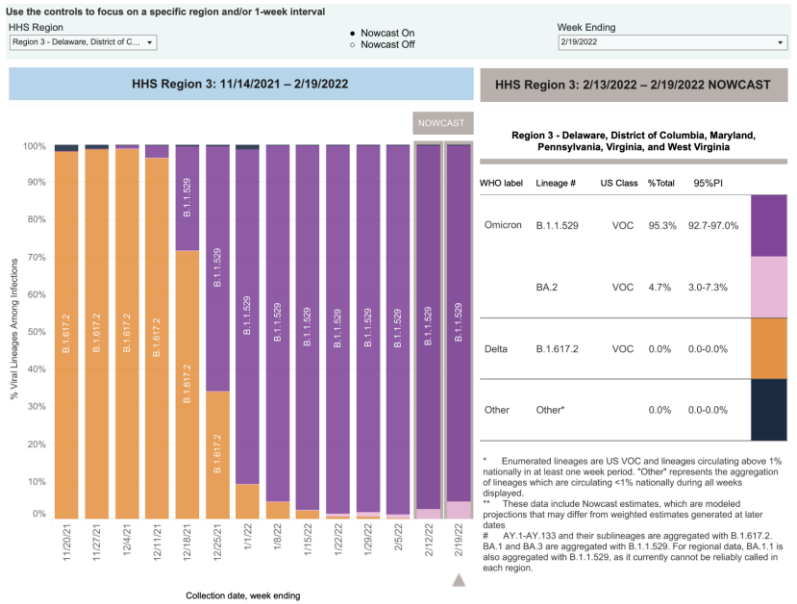
WHO label	Pango lineage*	GISAID clade	Nextstrain clade	Additional amino acid changes monitored*	Earliest documented samples	Date of designation
Alpha	B.1.1.7	GRY	20I (V1)	+S:484K +S:452R	United Kingdom, Sep-2020	18-Dec-2020
Beta	B.1.351	GH/501Y.V2	20H (V2)	+S:L18F	South Africa, May-2020	18-Dec-2020
Gamma	P.1	GR/501Y.V3	20J (V3)	+S:681H	Brazil, Nov-2020	11-Jan-2021
Delta	B.1.617.2	G/478K.V1	21A, 21I, 21J	+S:417N +S:484K	India, Oct-2020	VOI: 4-Apr-2021 VOC: 11-May-2021
Omicron*	B.1.1.529	GRA	21K, 21L	+R346K	Multiple countries, Nov-2021	VUM: 24-Nov-2021 VOC: 26-Nov-2021

World Health Organization [WHO]

Omicron Prevalence

CDC nowcast for week ending Feb 19th shows 4.6% BA2 in Region 3 (3.8% BA2 for USA)

Pace of growth faltering significantly



CDC [CDC Variant Tracking]

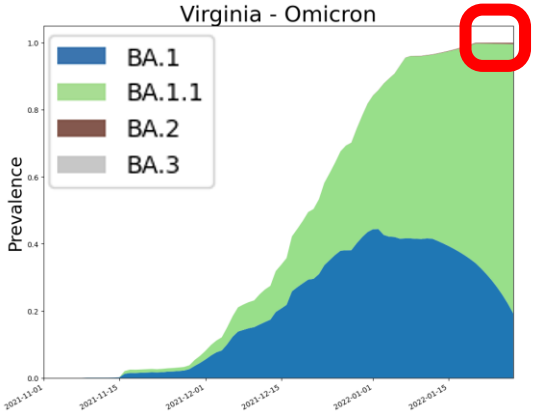
SARS-CoV2 BA.2 subvariant Tracking

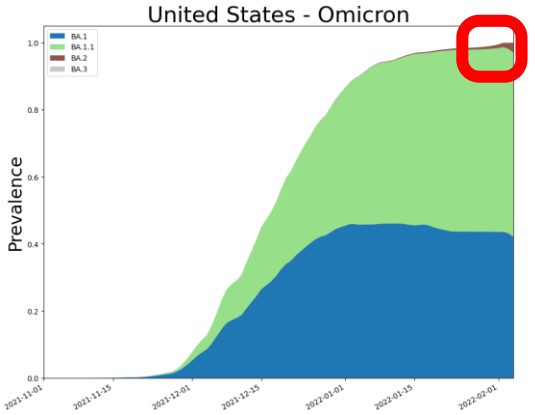
BA.2 subvariant growing rapidly in some European countries

- Both Delta and the Omicron BA.2 subvariant don't have the SGTF signal with PCR tests, so the reduction caused by Omicron BA.1 SGTF can be an imperfect signal for increased BA.2
- Subvariant BA.2 in all HHS regions of USA, Region 3 (includes VA) has highest estimated prevalence
- BA.2 is now majority subvariant in most northern European countries and India and some neighbors

CoVariants.org

Whole Genomes in public repositories

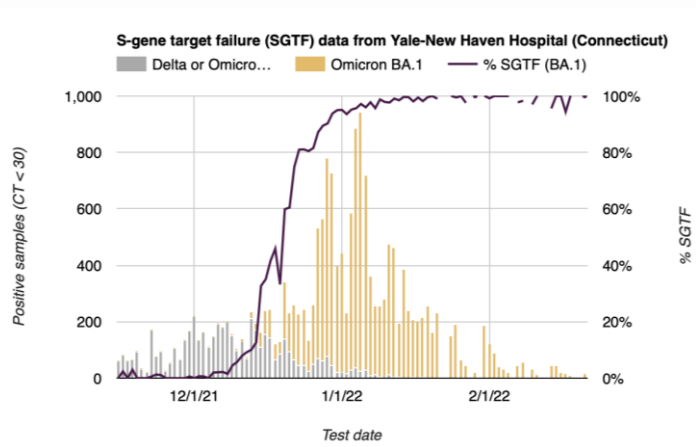




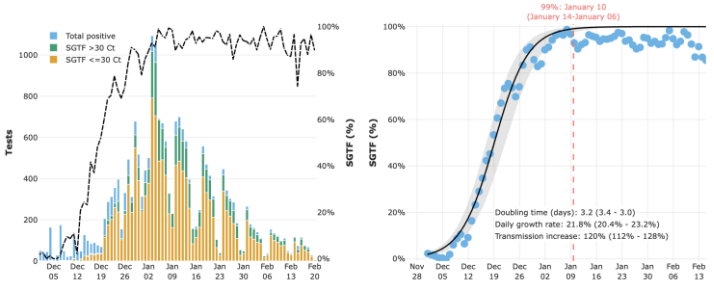
GISAID outbreak.info

SGTF proxy in US

Yale- New Haven



San Diego



Some drops in SGTF in CT and CA

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Pandemic Pubs

1. Danish scientists identified 47 instances of BA.2 reinfections shortly after a BA.1 infection, mostly in young unvaccinated individuals with mild disease not resulting in hospitalization or death.
2. National Estonia study shows increased risk of death from COVI 19 is not limited to the acute illness. Any COVID-19 infection carries substantially increased risk of death in mainly older people under an array of causes.
3-4. Israeli study shows 4th COVID-19 mRNA dose restores antibody titers to third dose peak. Both Israeli and Kaiser Permanente study shows 3rd/4th dose has low efficacy in preventing mild or symptomatic Omicron infections but excellent VE against hospitalization.
5. Sanofi & GSK announce another vaccine with high efficacies against severe and modete COVID (100% and 75%) but limited in prevention of symptomatic infection (58%)

1

First infection	Second infection			
	BA.1	BA.2	Delta	Total
BA.1	17	47	0	64
BA.2	0	3	0	3
Delta	26	140	30	196
Total	33	190	30	263

		Vaccination status		
Age groups	N (%)	Not vaccinated (N= 42; 89%)	Started primary vaccination program (N=2; 4%)	Full effect after primary vaccination program (N=3; 6%)
0-5 years	3 (6%)	3	0	0
6-9 years	9 (19%)	8	1	0
10-14 years	11 (23%)	10	1	0
15-19 years	10 (21%)	9	0	1
20-29 years	10 (21%)	8	0	2
30-39 years	4 (9%)	4	0	0

Denmark: Selected from more than 1.8 million cases of infections in the period from November 22, 2021, until February 11, 2022. Top: Overview over all SARS-CoV-2 cases in Denmark with >1 positive sample collected 20 to 60 days apart where lineage information from WGS data were available Bottom: Age groups and vaccination status of the 47 cases with Omicron BA.2 reinfection
https://www.medrxiv.org/content/10.1101/2022.02.19.22271112v1

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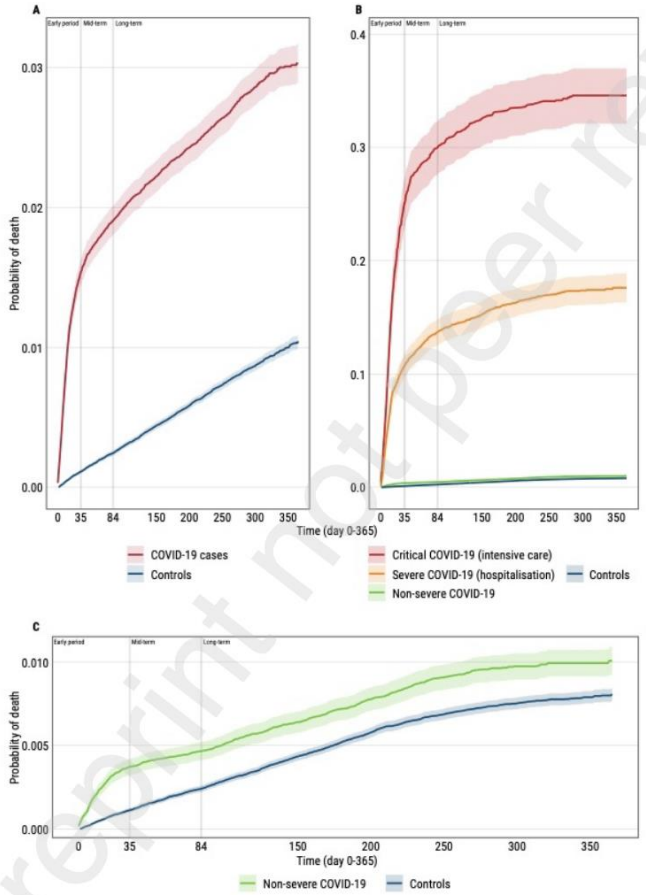

OVERALL MORTALITY

	Age <60		Age 60+	
	Adjusted hazard ratio * (95% CI)	p-value	Adjusted hazard ratio (95% CI)	p-value
Early, acute period	4·7 (3·7-5·)	<0·0001		
1-10 days			20·1 (15·5-26·1)	<0·0001
11-20 days			15·5 (12·1-19·7)	<0·0001
21-35 days			7·9 (6·2-9·9)	<0·0001
Mid- and long-term	0·9 (0·7-1·2)	0·5360		
36-50 days			3·9 (2·9-5·1)	<0·0001
51-84 days			2·8 (2·2-3·5)	<0·0001
85-365 days			1·7 (1·5-1·8)	<0·0001

From 66k confirmed Covid-19 cases (>90% mild cases), time matched on a 1:4 ratio with randomly selected to get 254k controls. People infected with COVID-19 had more than three times the risk of dying over the following year compared with those who remained uninfected. For COVID-19 cases over 60 years old, increased risk for cardiovascular (aHR 2·1, 95%CI 1·8-2·3), cancer (aHR 1·5, 95%CI 1·2-1·9), respiratory system diseases (aHR 1·9, 95%CI 1·2-3·0), and other causes of death (aHR 1·8, 95%CI 1·4-2·2)
https://papers.ssrn.com/sol3/papers.cfm?abstract_id=4028547
https://twitter.com/jsm2334/status/1495723919826948098

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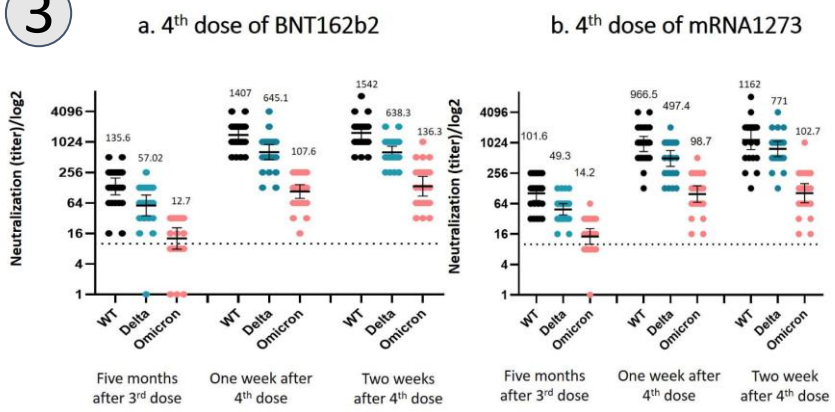


Eligible participants were **healthcare-workers (HCW) vaccinated with three BNT162b2 doses**, and whose IgG antibody levels were ≤700 BAU (40-percentile). Of 1050 eligible HCW, 154 and 120 were enrolled to receive BNT162b2 and mRNA1273, respectively, and compared to 426 age-matched controls. **Vaccine efficacy against infection was 30% (95%CI:-9% to 55%) and 11% (95%CI:-43% to +43%) for BNT162b2 and mRNA1273, respectively.**
https://www.medrxiv.org/content/10.1101/2022.02.15.22270948v1

4

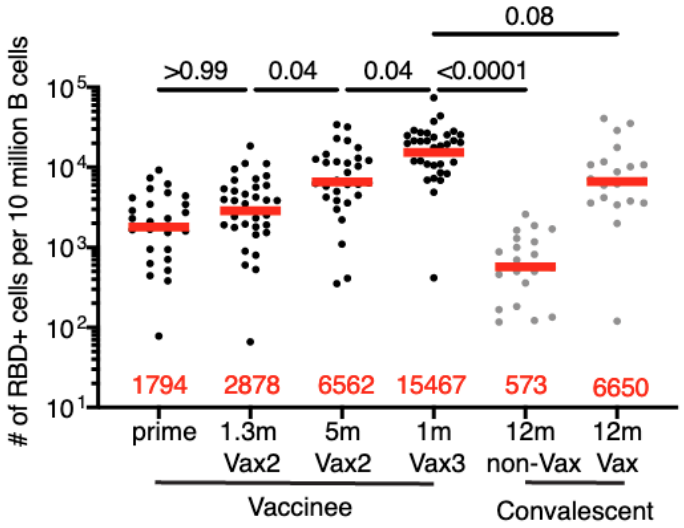
		VE (95% CI)[a]	
		Unadjusted	Adjusted
3-dose excluding immunocompromised patients	Delta	89.6% (87.4%, 91.4%)	93.7% (92.2%, 94.9%)
	14-60 days	90.6% (88.4%, 92.3%)	94.2% (92.7%, 95.3%)
	>60 days	77.6% (64.0%, 86.0%)	88.1% (80.2%, 92.9%)
	Omicron	64.2% (62.3%, 66.0%)	70.5% (68.6%, 72.4%)
	14-60 days	67.1% (65.2%, 68.9%)	72.1% (70.2%, 73.9%)
	>60 days	34.8% (26.4%, 42.3%)	51.2% (44.2%, 57.3%)
Hospitalization[b,d]			
1-dose	Delta[e]	82.2% (-31.4%, 97.8%)	71.2% (-68.7%, 97.4%)
	Omicron	100.0% (N/A)	N/A
2-dose	Delta[e]	95.9% (86.9%, 98.7%)	99.0% (93.3%, 99.9%)
	Omicron[f]	81.1% (29.8%, 94.9%)	84.5% (23.0%, 96.9%)
3-dose	Delta[e]	98.3% (87.7%, 99.8%)	99.7% (96.5%, 100.0%)
	Omicron[g]	89.0% (58.5%, 97.1%)	99.2% (76.3%, 100.0%)

In recent Kaiser Permanente study large, diverse study population included 26,683 positive individuals using SGTF as Omicron indication. **mRNA-1273 3-dose** VE was 93.7% (92.2–94.9%) and 86.0% (78.1–91.1%) against Delta infection and **71.6% (69.7–73.4%) and 47.4% (40.5–53.5%) against Omicron infection at 14–60 days and >60 days, respectively.** The 3-dose VE was 29.4% (0.3–50.0%) against Omicron infection in immunocompromised individuals. The 3-dose VE against hospitalization with Delta or Omicron was >99% across the entire study population.
https://www.nature.com/articles/s41591-022-01753-y#Sec13

Pandemic Pubs

1. A 3rd mRNA vaccine is shown to cause rapid recall and expanded/diversified memory B cell repertoire. A key mechanism that contributes to the enhanced protection against severe disease by boosters even when neutralizing antibody isn't sufficient to prevent infection.
2. Tokyo experiments indicate BA.2 is more pathogenic than BA.1 in animal model and BA.2 is more replicative in human nasal epithelial cells.
3. UKHSA estimates shorter serial interval for BA.2. Possible contribution to growth advantage and increasing prevalence.
4. MMWR study looks at the Omicron wave's impact on children, demonstrating that this "more mild" disease caused significant morbidity in children, especially the 0-4 year olds

1



For n=43 individuals Individuals that received a 3rd vaccine dose developed significantly increased numbers of RBD-binding memory cells compared to the 2nd dose or naturally infected individuals
https://www.biorxiv.org/content/10.1101/2022.02.14.480394v1

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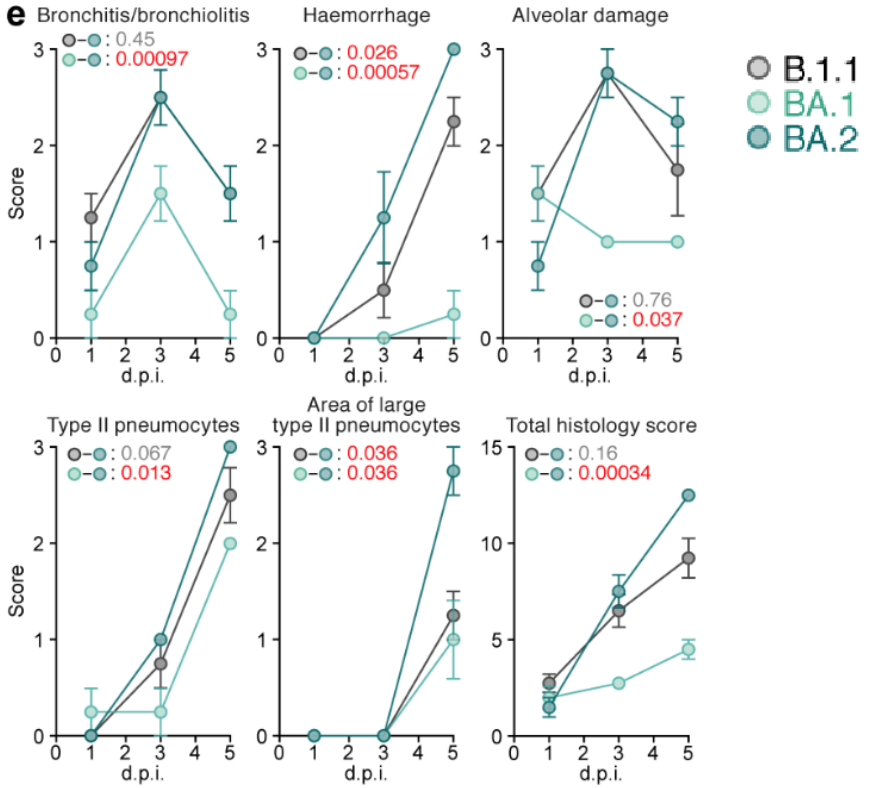

Researchers in Tokyo investigated the dynamics of viral replication of BA.2 in vivo through hamster infection experiments. All histopathological parameters including bronchitis/bronchiolitis, haemorrhage, alveolar damage, and the levels of type II pneumocytes, of BA.2-infected hamsters were significantly higher than those in BA.1
https://www.biorxiv.org/content/10.1101/2022.02.14.480335v1

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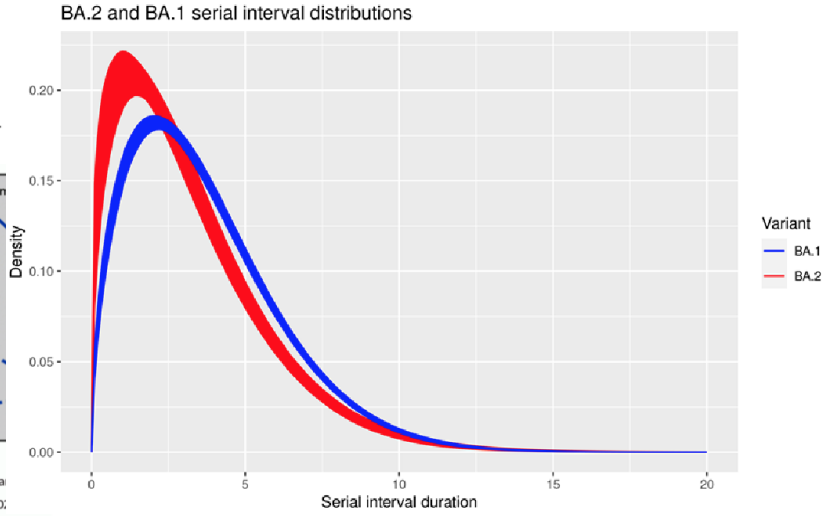

UKHSA estimates that the mean serial interval for BA.2 is 3.27 days compared to BA.1 3.72 days. The serial interval suggests the time between primary and secondary infections is shorter.
https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1054357/Technical-Briefing-36-11February2022_v2.pdf
https://twitter.com/corneliusroemer/status/1492434232664375304

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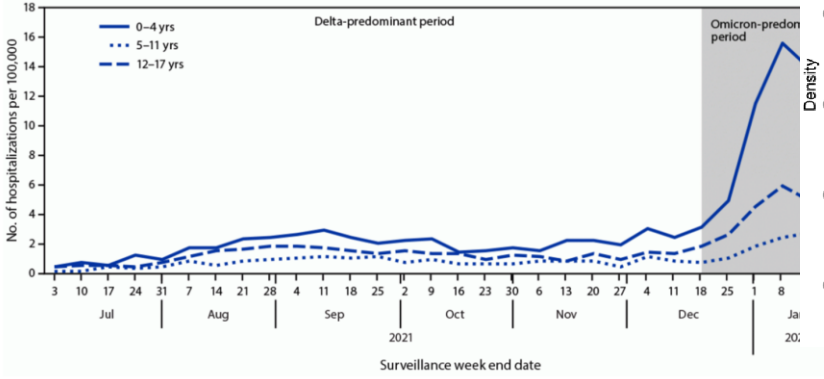
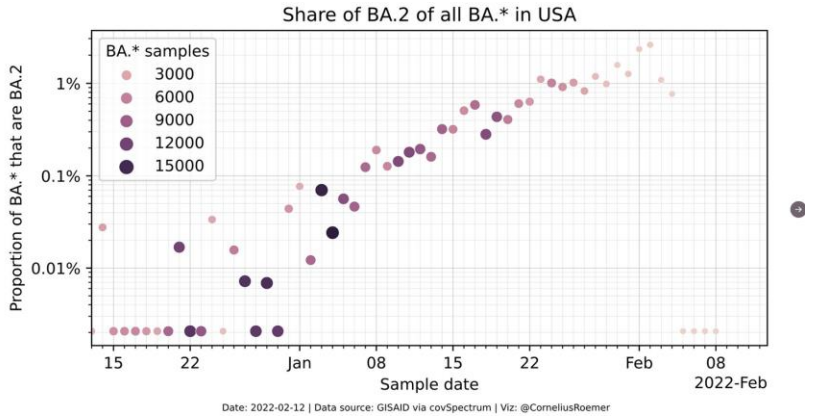
FIGURE. Weekly COVID-19–associated hospitalization rates* among children and adolescents aged 0–17 years, by age group — COVID-NET, 14 states,† July 3, 2021–January 22, 2022



MMWR study from CDC illustrates the burden of increased transmission on children, especially the very young who are ineligible for vaccination.
https://www.cdc.gov/mmwr/volumes/71/wr/mm7107e4.htm?s_cid=mm7107e4_w

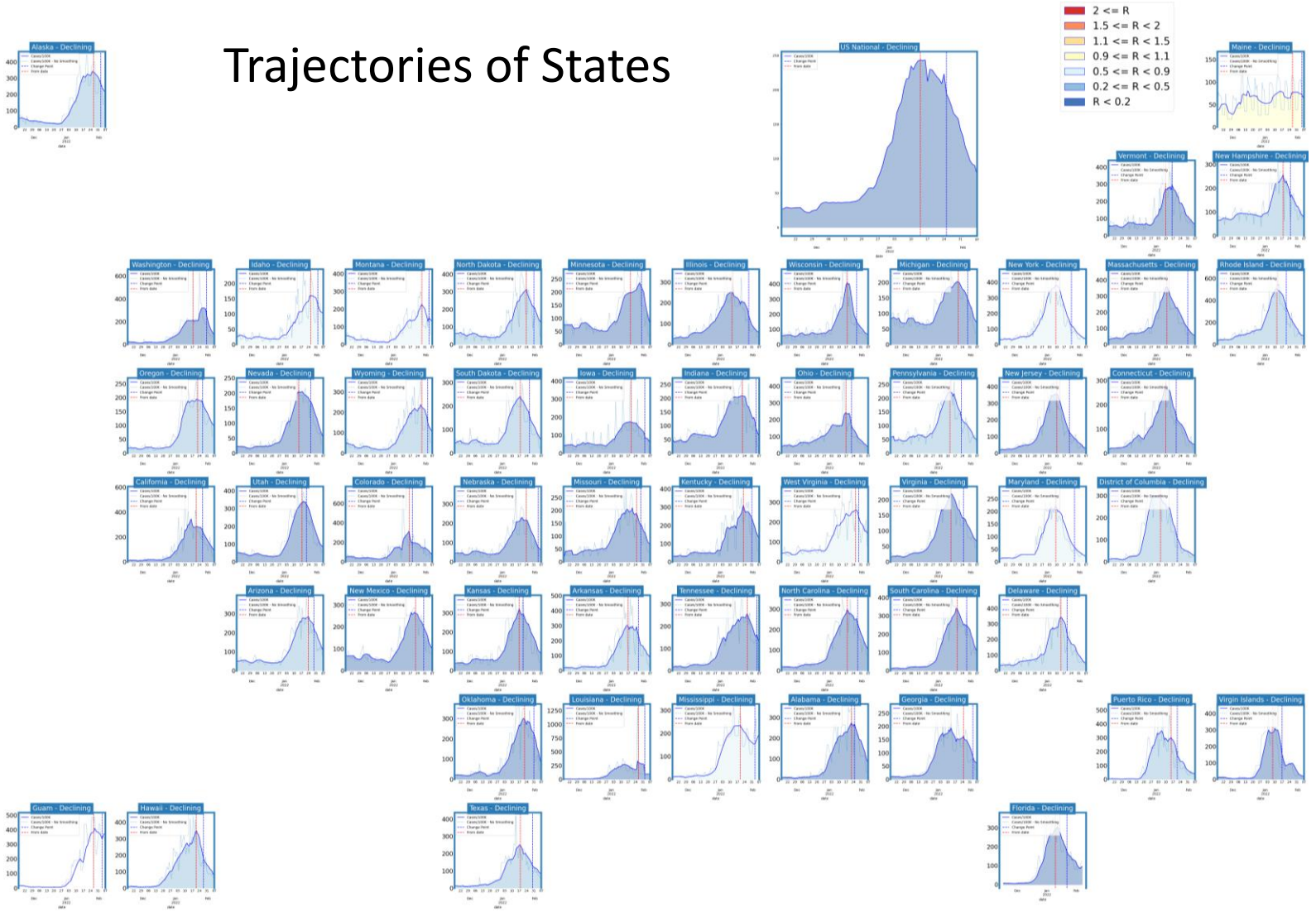


United States Overall

- Nation completely declining
- Most are sustained declines

Status	# States
Declining	54 (46)
Plateau	0 (1)
Slow Growth	0 (4)
In Surge	0 (3)

Trajectories of States



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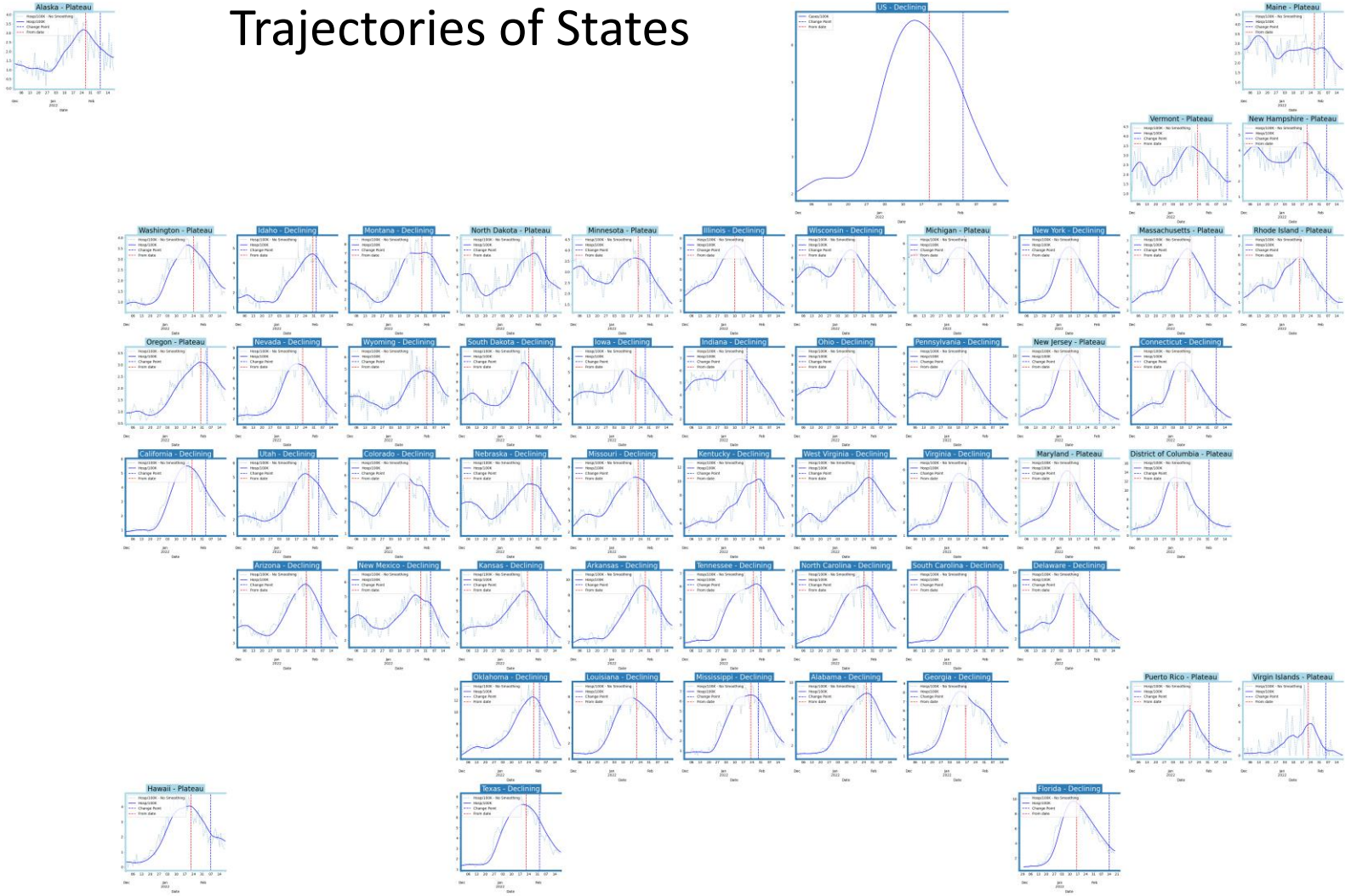
United States Hospitalizations

- Hospital admissions are lagging case rates, and are declining

Status	# States (prev week)
Declining	30 (38)
Plateau	16 (15)
Slow Growth	0 (6)
In Surge	0 (1)

Trajectories of States



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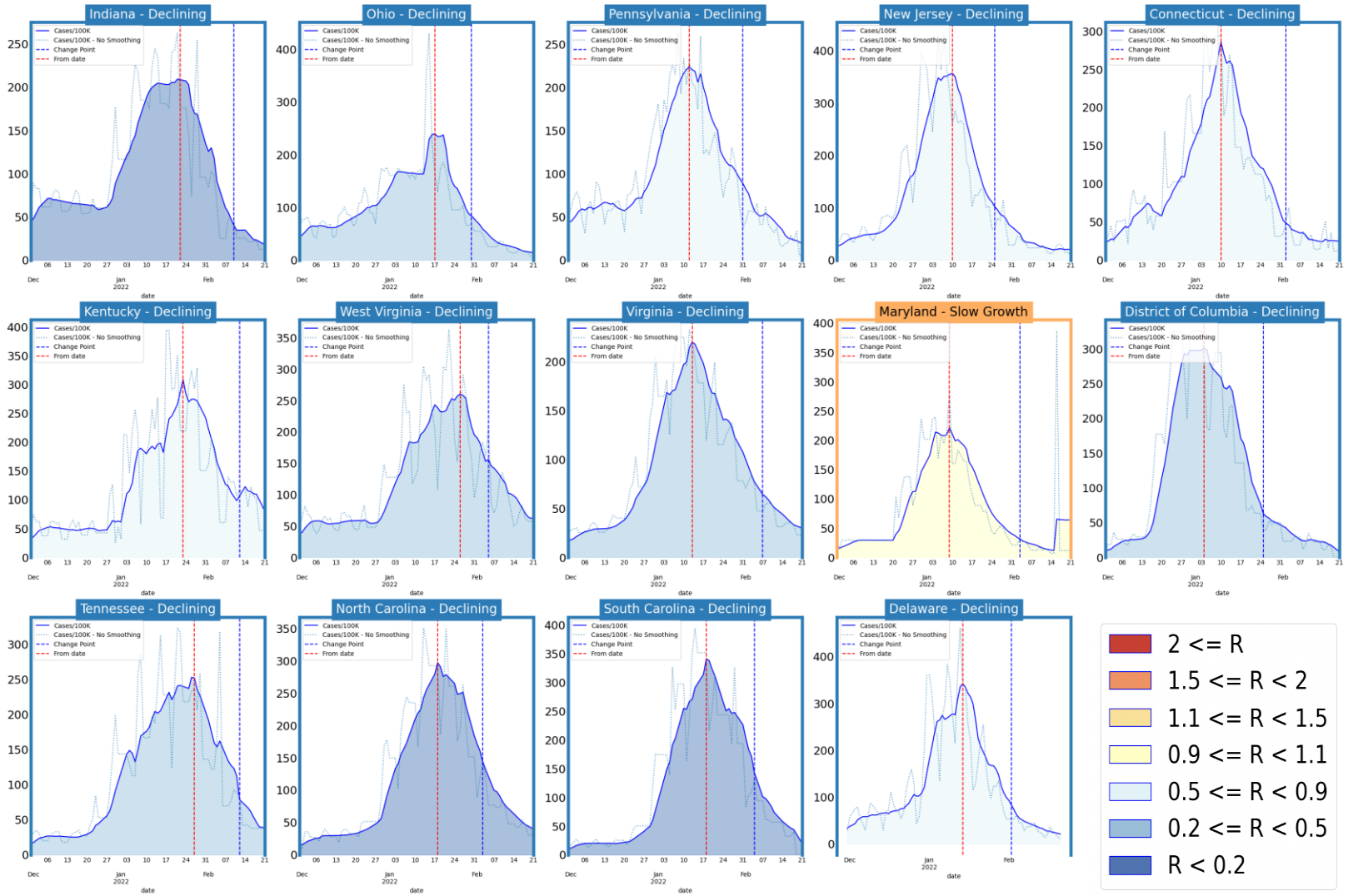
Virginia and Her Neighbors

- Case rates are much lower and dipping into the moderate range
- All experiencing around or below 50/100K daily incident case rates
- Some states in North east showing a plateauing



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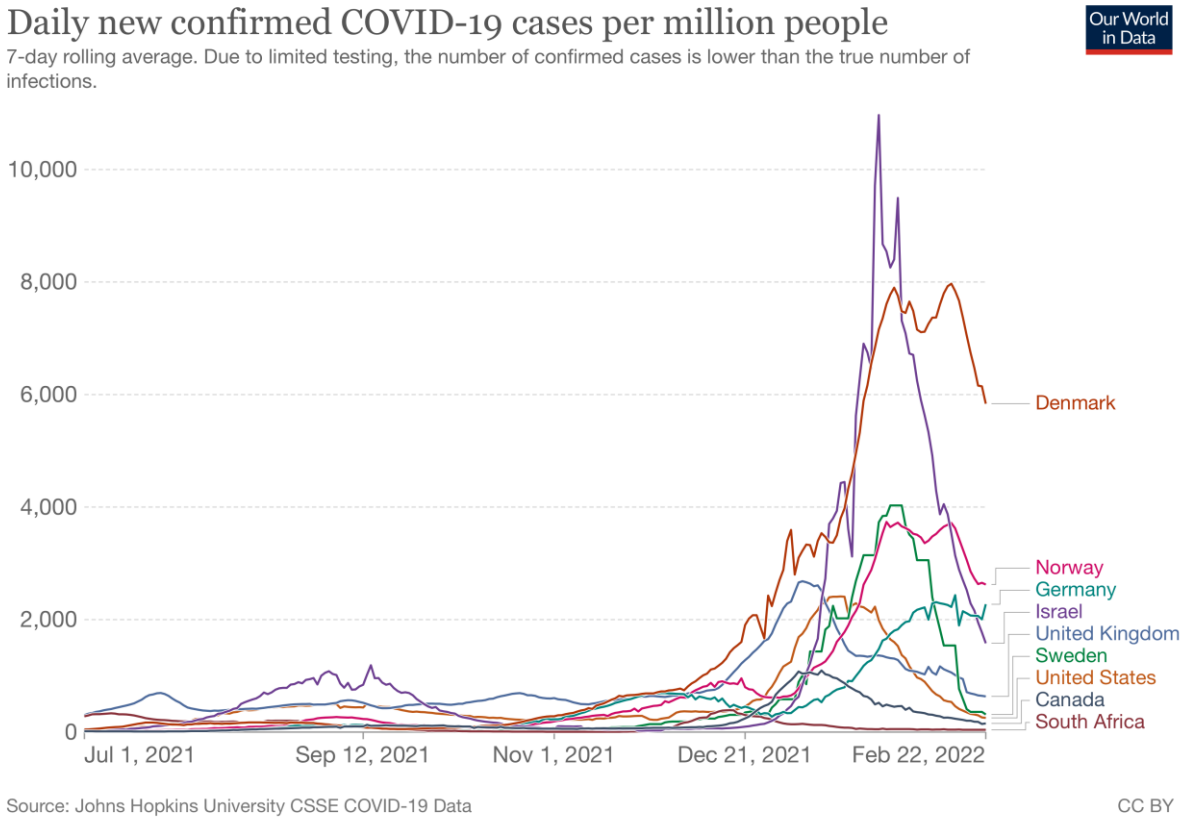
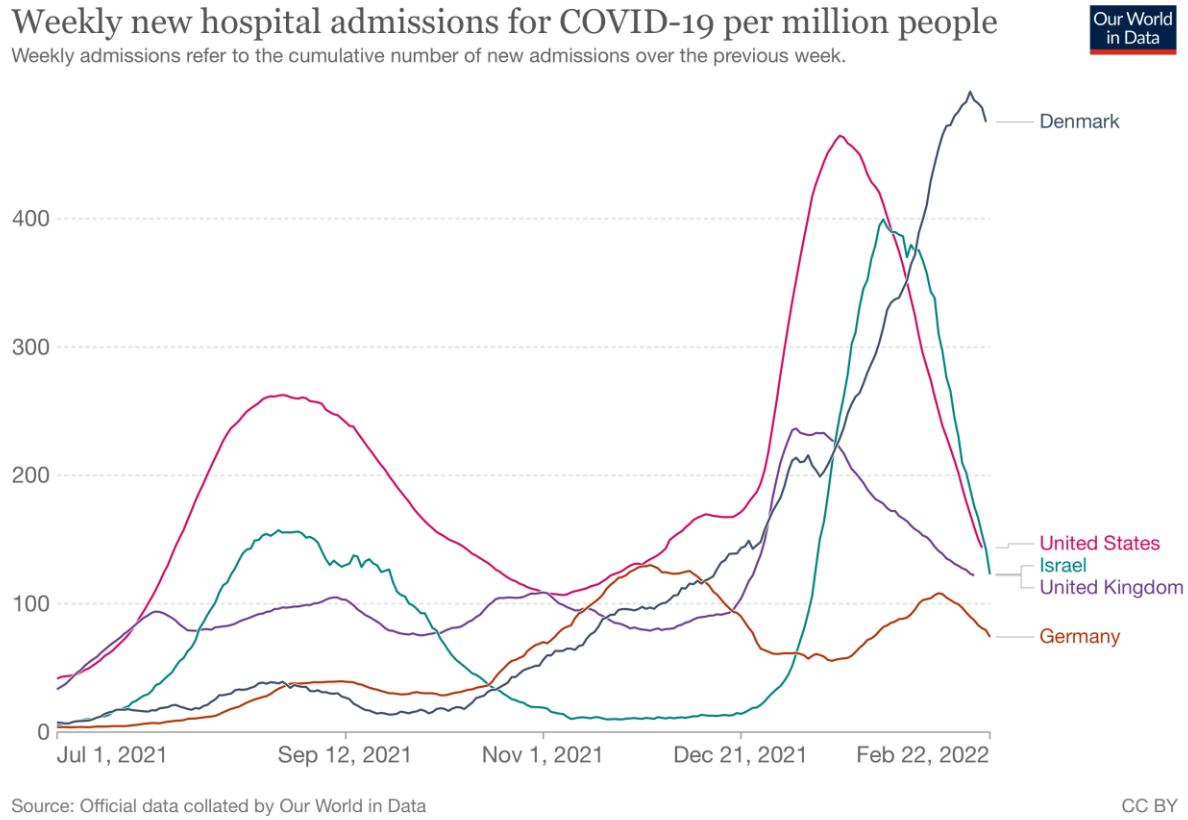
Other Countries

- UK continues to see case rates flattening out, and case rates are very high but flat in Denmark
- US, Israel, Sweden have continued declines start to slow
- US continues per capita hospitalization rates have declined dramatically

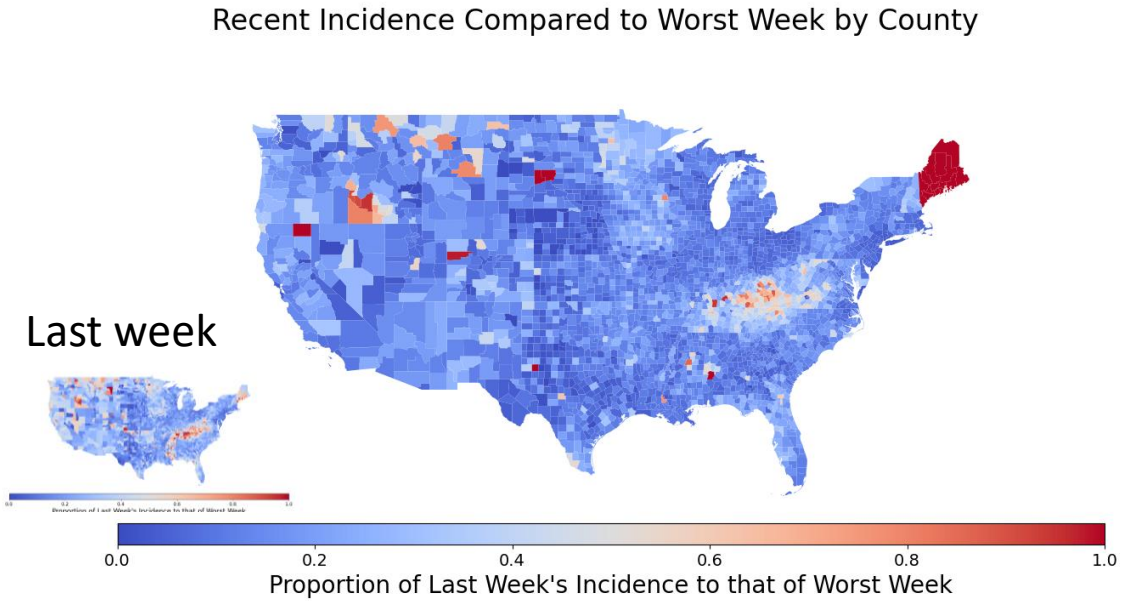


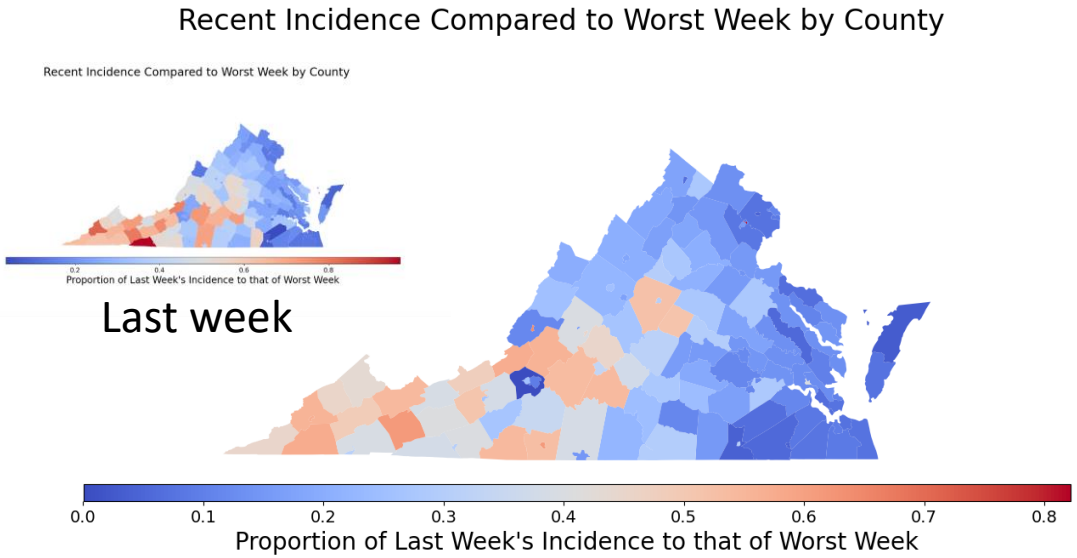


Our World in Data

County-level comparison to previous highest peak

- Most counties in VA have had the highest case rate of the pandemic in the last week
- Nationally the number of counties at their highest rate has expanded considerably





Additional Analyses

Overview of relevant on-going studies

Other projects coordinated with CDC and VDH:

- **Scenario Modeling Hub:** Consortium of academic teams coordinated via MIDAS / CDC to that provides regular national projections based on timely scenarios
- **Genomic Surveillance:** Analyses of genomic sequencing data, VA surveillance data, and collaboration with VA DCLS to identify sample sizes needed to detect and track outbreaks driven by introduction of new variants etc.
- **Mobility Data driven Mobile Vaccine Clinic Site Selection:** Collaboration with VDH state and local, Stanford, and SafeGraph to leverage anonymized cell data to help identify

COVID-19 Scenario Modeling Hub

Collaboration of multiple academic teams to provide national and state-by-state level projections for 4 aligned scenarios that vary vaccine rates (high – low) and impact of the Delta variant (high and low)

- Round 12 underway to update 11
- Round 11 recently released to assist in federal response to Omicron wave
- Only national consortium tracking Omicron wave well
- Rounds 4-11 now available

Round 4 results were published May 5th, 2021 in MMWR

https://covid19scenariomodelinghub.org/viz.html