Estimation of COVID-19 Impact in Virginia

August 4th, 2021
(data current to July 25th – 27th)

Biocomplexity Institute Technical report: TR 2021-086
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 in Virginia continue to rise quickly amidst a background of surges across the nation**

  • VA mean weekly incidence up to 14/100K from 7.8/100K, US up to 25/100K (from 15.6/100K)

  • Vaccination rates continue rebound while acceptance among the unvaccinated ticks up and mask usage also increases slightly

  • Uncertainty around severity of Delta variant remains, however, the experience of other states / countries suggest potential for higher severity

  • Recent updates:
    • Analysis of mask use, reasons by vax acceptance level
    • Deeper dive on Delta variant severity

The situation continues to change. Models continue to be updated regularly.
Situation Assessment
Case Rates (per 100k) and Test Positivity

County level test positivity from RT-PCR tests.

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

Yellow: 5.0%-10.0%
(or with <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

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### Trajectory Descriptions

<table>
<thead>
<tr>
<th>Trajectory</th>
<th>Description</th>
<th>Weekly Case Rate (per 100K) bounds</th>
<th># Districts (prev week)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Declining</strong></td>
<td>Sustained decreases following a recent peak</td>
<td>below -0.9</td>
<td>0 (1)</td>
</tr>
<tr>
<td><strong>Plateau</strong></td>
<td>Steady level with minimal trend up or down</td>
<td>above -0.9 and below 0.5</td>
<td>0 (1)</td>
</tr>
<tr>
<td><strong>Slow Growth</strong></td>
<td>Sustained growth not rapid enough to be considered a Surge</td>
<td>above 0.5 and below 2.5</td>
<td>10 (23)</td>
</tr>
<tr>
<td><strong>In Surge</strong></td>
<td>Currently experiencing sustained rapid and significant growth</td>
<td>2.5 or greater</td>
<td>25 (10)</td>
</tr>
</tbody>
</table>
District Trajectories – last 10 weeks

<table>
<thead>
<tr>
<th>Status</th>
<th># Districts (prev week)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Declining</td>
<td>0 (1)</td>
</tr>
<tr>
<td>Plateau</td>
<td>0 (1)</td>
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<tr>
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Curve shows smoothed case rate (per 100K)
Trajectories of states in label & chart box
Case Rate curve colored by Reproductive
Estimating Daily Reproductive Number

August 2\textsuperscript{nd} Estimates

<table>
<thead>
<tr>
<th>Region</th>
<th>Date Confirmed $R_e$</th>
<th>Date Confirmed Diff Last Week</th>
</tr>
</thead>
<tbody>
<tr>
<td>State-wide</td>
<td>1.202</td>
<td>0.009</td>
</tr>
<tr>
<td>Central</td>
<td>1.216</td>
<td>-0.015</td>
</tr>
<tr>
<td>Eastern</td>
<td>1.206</td>
<td>0.016</td>
</tr>
<tr>
<td>Far SW</td>
<td>1.237</td>
<td>0.027</td>
</tr>
<tr>
<td>Near SW</td>
<td>1.179</td>
<td>-0.002</td>
</tr>
<tr>
<td>Northern</td>
<td>1.196</td>
<td>0.002</td>
</tr>
<tr>
<td>Northwest</td>
<td>1.184</td>
<td>0.058</td>
</tr>
</tbody>
</table>

Methodology

- Wallinga-Teunis method (EpiEstim\textsuperscript{1}) 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

Vaccination Administration Continues Slow Rise

Regional Vaccine courses initiated per day per capita:
• Total counts of first dose of vaccines across regions
• Very slight rise across all regions
• Reflected in 1st dose of Pfizer and Moderna uptick

[Graph showing the daily % of eligible population vaccinated from Jan 2021 to Jul 2021 across different regions.

[Graph showing the administered doses of different vaccines from Jun 2021 to Aug 2021.]
Vaccinations Shift to Younger Populations
Vaccination Acceptance by Region

Corrections to surveys:
• Facebook administered survey is timely and broad, but biased by who accesses Facebook and answers the survey
• Correction approach:
  • Calculate an over-reporting fraction based on reported vaccinations compared to VDH administration data
  • Cross-validate coarse corrections against HPS survey at the state level and corrected in same manner

<table>
<thead>
<tr>
<th>Region</th>
<th>COVIDcast accepting corrected</th>
<th>VDH proportion eligible vaccinated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central</td>
<td>77%</td>
<td>64%</td>
</tr>
<tr>
<td>Eastern</td>
<td>74%</td>
<td>60%</td>
</tr>
<tr>
<td>Far SW</td>
<td>62%</td>
<td>50%</td>
</tr>
<tr>
<td>Near SW</td>
<td>69%</td>
<td>56%</td>
</tr>
<tr>
<td>Northern</td>
<td>100%</td>
<td>75%</td>
</tr>
<tr>
<td>Northwest</td>
<td>73%</td>
<td>64%</td>
</tr>
<tr>
<td>Virginia</td>
<td>80%</td>
<td>65%</td>
</tr>
</tbody>
</table>

Grey Bar: Survey measured and corrected acceptance  
Green Bar: Proportion of eligible population administered a vaccine  
Dots: Proportion administered at least one dose for each county
Vaccine Acceptance has risen as vaccination rates have climbed

- Corrected Acceptance reflects the daily measured overall acceptance and has risen in the past couple days
- Unvaccinated Acceptance shows still ~10% of those who are unvaccinated are definitely or probably willing to be vaccinated
- Unvax acceptance has declined a bit and leveled off in last couple of weeks, final 10% may be waiting for FDA approval

Data Source: https://covidcast.cmu.edu
Levels of Acceptance and potential acceptance in flux:

- Nearly all the “definitely yes” have been vaccinated, yet there are 10-15% remaining across the regions.
- Northwest and Southwest (to lesser degree) see growth in “probably not”, seemingly from “definitely not”.

Data Source: [https://covidcast.cmu.edu](https://covidcast.cmu.edu)
Reasons for Hesitancy vary across tiers of likeliness to accept the vaccine

• Probably Yes and Probably No most concerned about side effects & are waiting to see
• Definitely No are concerned about side effects but also don’t think they need the vaccine and don’t trust the government
• Most other reasons are below 30% within these tiers of likeliness

Data Source: https://covidcast.cmu.edu
Reasons for Hesitancy vary across Regions

- Side Effects and waiting to see safety are primary
- Far SW and Near SW concerned for others and have more reasons
- Central and Eastern show larger gap

Data Source: [https://covidcast.cmu.edu](https://covidcast.cmu.edu)
Mask Usage Increases Slightly

Self-reported mask usage has declined for months, but rebounded
- State-wide up to 43% from low 37%, similar to US overall
- Uptick experienced in most counties across VA

Data Source: https://covidcast.cmu.edu
Vax Acceptance is High among Mask Wearers

Self-reported mask usage in Virginia

- Of those who do wear a mask most of the time, 90% are vaccine accepting

Data Source: [https://covidcast.cmu.edu](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

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**New WHO Name | Transmissibility | Immune Evasiveness | Vaccine Effectiveness**

| Ancestral | —— | —— | ✓ |
| D614G | + | — | ✓ |
| B.1.1.7 | Alpha | +++ | — | ✓ |
| B.1.351 | Beta | + | ++++ | ✓ |
| P1 | Gamma | ++ | ++ | ✓ |
| B.1.429 | Epsilon | + | + | ✓ |
| B.1.526 | Iota | + | + | ✓ |
| B.1.617.2 | Delta | ++++* | ++# | ✓ |

*Relative transmissibility to B.1.1.7 yet to be fully defined

†Effectiveness from real world evidence vs. severe illness, not all vaccines are effective vs all variants, and importance of 2 doses, especially for B.1.617.2 for which 1 dose of mRNA or A2 is only ~30% effective * May carry more immune escape than P1, to be determined

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World Health Organization [WHO] and [Eric Topol]

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CDC Variant Tracking

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6-Aug-21
SARS-CoV2 Variants of Concern

**Alpha α - Lineage B.1.1.7**

**Prevalence:** Levels have stalled and are now dropping in most states; flat in VA

**Transmissibility:** Estimated increase of 50% compared to previous variants. B.1.1.7’s mutations boost its overall levels of viremia; study from Public Health England shows contacts of B.1.1.7 cases are more likely (50%) to test positive

**Severity:** Increased risk of hospitalization (60%) and mortality (60%). Danish study shows B.1.1.7 to have a 64% higher risk of hospitalization, while Public Health Scotland studies showed a range of 40% to 60%; Study in Nature estimates 60% higher mortality

**Beta β - Lineage B.1.351**

**Prevalence:** Levels have remained low, as this variant’s transmissibility can’t compete with B.1.1.7, however, as more of the population becomes immune it may gain an advantage

**Immune Escape:** Many studies show that convalescent sera from previously infected individuals does not neutralize B.1.351 virus well which is predictive of protection, however, vaccine induced immunity shows signs of effectiveness

**Gamma γ - Lineage P.1**

**Prevalence:** Nationally at 10%, slow increase in VA at 9%

Study estimates 17-32% of all infections in Manaus in 2021 were reinfections, which helps explain data from Brazil demonstrating P.1’s continued dominance in Rio despite presence of B.1.1.7
SARS-CoV2 Variants of Concern

Delta \( \delta \) - Lineage B.1.617.2 and related subvariants

- Delta plus \( \delta^+ \) lineage which contains the K417N mutation is emerging as a sub-variant that is even more transmissible; declared a VoC in India
- Delta variant now dominates most of Europe and US
- CDC recommends resumption of mask wearing indoors due to reports of breakthrough infections of the vaccinated possibly being transmissible
- More reports describe time Delta variant escapes vaccine immunity, with recent Israeli study showing a 64% efficacy against infection, however, remains highly effective against hospitalization and death
- Public Health Scotland study in Lancet suggests Delta is 2x more likely to cause hospitalization than Alpha
- Subvariant AY.3 of Delta is increasingly prevalent and arose in US, may be more transmissible than Delta itself, though some fitting studies suggest otherwise

Fully vaccinated breakthrough cluster in Barnstable County, Massachusetts, July 2021. Ct values only marginally higher in vaccinated individuals

CDC MMWR

Recent multinomial fits appear to show no growth advantage of AY.3 over other Delta substrains

Twitter
Among 1497 fully vaccinated health care workers for whom RT-PCR data were available, 39 SARS-CoV-2 breakthrough infections were documented. Neutralizing antibody titers in vaccinated breakthrough infections during the peri-infection period were lower than those in matched uninfected controls (case-to-control ratio, 0.361; 95% confidence interval, 0.165 to 0.787). Higher peri-infection neutralizing antibody titers were associated with lower infectivity (higher Ct values).

Supplemental mRNA vaccines for those who originally got J&J offered in San Francisco

https://sfist.com/2021/08/03/if-you-got-the-johnson-johnson-shot-sf-general-will-give-you-a-supplemental/

Potential for universal betacoronavirus vaccine

https://science.sciencemag.org/content/early/2021/08/03/science.abj3321
Other State Comparisons

Trajectories of States

- Surges expand further
- Some limited signs of slowing in Missouri and Arkansas
- Nearly half of jurisdictions in Surge (26) with Slow Growth (15) and Plateau (13) nearly evenly split

Virginia and her neighbors

- All neighbors show upward trends
- Many neighbors are in surge and/or now have case rates above 20/100K
Hospitalizations across the US

Hospitalization rates remain low in VA but rapid change is possible as seen in other states

- Hotspot states see rapid rise in hospitalizations especially among the younger age groups
- Hospitalization data is lagged and is current as of July 23

- Virginia
- Louisiana
- Arkansas
- Nevada
Recent Cases Correlate with Vax Coverage

United States

Mean cases per 100K vs. vaccination coverage
- Reasonable correlation at state level but quite a few outliers at sub-state level

Virginia in the middle of the pack
Recent Cases Correlate Low Vax in VA counties

Mean cases per 100K vs. vaccinations for Virginia Counties

- Counties with higher vax coverage are maintaining lower case rates
- Many counties with low vax coverage continue to enjoy low case rates as well, though this may not hold
Model Update – Adaptive Fitting
Using Ensemble Model to Guide Projections

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

- Autoregressive (AR, ARIMA)
- Neural networks (LSTM)
- Kalman filtering (EnKF)

Weekly forecasts done at county level.

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

Ensemble forecast provides additional ‘surveillance’ for making scenario-based projections.

Also submitted to CDC Forecast Hub.
Model Assessment

Spot check of last week’s projection

• This week’s projection doesn’t change much compared to last week’s
• Last week’s projection aligned well with
Delta Severity Suggestive Evidence

Table S1: Numbers of individuals testing positive (1 April to 6 June 2021) and number admitted to hospital from the community within 14 days of testing positive from the EAVE II cohort

<table>
<thead>
<tr>
<th>S Gene</th>
<th>Person Years Exposure</th>
<th>N</th>
<th>Number Admitted to Hospital</th>
<th>Rate per 100 person years</th>
</tr>
</thead>
<tbody>
<tr>
<td>S Gene Negative</td>
<td>615.2</td>
<td>9996</td>
<td>223</td>
<td>36.2</td>
</tr>
<tr>
<td>S Gene Positive</td>
<td>214.7</td>
<td>7723</td>
<td>134</td>
<td>62.4</td>
</tr>
<tr>
<td>Weak S Positive</td>
<td>97.6</td>
<td>1824</td>
<td>20</td>
<td>20.5</td>
</tr>
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</table>

S Gene Negative are mostly Alpha
S Gene Positive are mostly Delta

N = Number of individuals testing positive

In a recent study 97% of S gene positive cases sequenced in Scotland were the Delta variant and that 99% of Delta variants were S gene positive. Found that S gene-positive cases were associated with an increased risk of COVID-19 hospital admission: hazard ratio (HR) 1·85 (95% CI 1·39–2·47) when compared to S gene-negative cases

https://www.thelancet.com/action/showPdf?pii=S0140-6736%2821%2901358-1

Study of infections in Ontario Feb. to June 2021 showed increases with Delta variant were more pronounced:
120% (93-153%) for hospitalization; 287% (198-399%) for ICU admission; and 137% (50-230%) for death.

https://www.medrxiv.org/content/10.1101/2021.07.05.21260050v2

838 VOC infections in Singapore in the study period. After adjusting for age and gender, B.1.617.2 infection was associated with higher odds of oxygen requirement, ICU admission, or death (adjusted odds ratio (aOR) 4·90, [95% CI 1·43-30·78]) B.1.617.2 was associated with significantly lower PCR Ct values and significantly longer duration of Ct value ≤30 (estimated median duration 18 days for B.1.617.2, 13 days for wild-type).


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Similar to trend seen in Scotland, more severe outcomes in unvaccinated youth

https://twitter.com/cmyeaton/status/1422624128918556684

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S Gene Positive are mostly Delta
Key Takeaways

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- Vaccination rates continue rebound while acceptance among the unvaccinated ticks up and mask usage also increases slightly
- Uncertainty around severity of Delta variant remains, however, the experience of other states / countries suggest potential for higher severity
- Recent updates:
  - Analysis of mask use, reasons by vax acceptance level
  - Deeper dive on Delta variant severity
- The situation continues to change. Models continue to be updated regularly.
Questions?

Biocomplexity COVID-19 Response Team

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Supplemental Slides
Agent-based Model (ABM)

EpiHiper: Distributed network-based stochastic disease transmission simulations

• Assess the impact on transmission under different conditions
• Assess the impacts of contact tracing

Synthetic Population
• Census derived age and household structure
• Time-Use survey driven activities at appropriate locations

Detailed Disease Course of COVID-19
• Literature based probabilities of outcomes with appropriate delays
• Varying levels of infectiousness
• Hypothetical treatments for future developments