

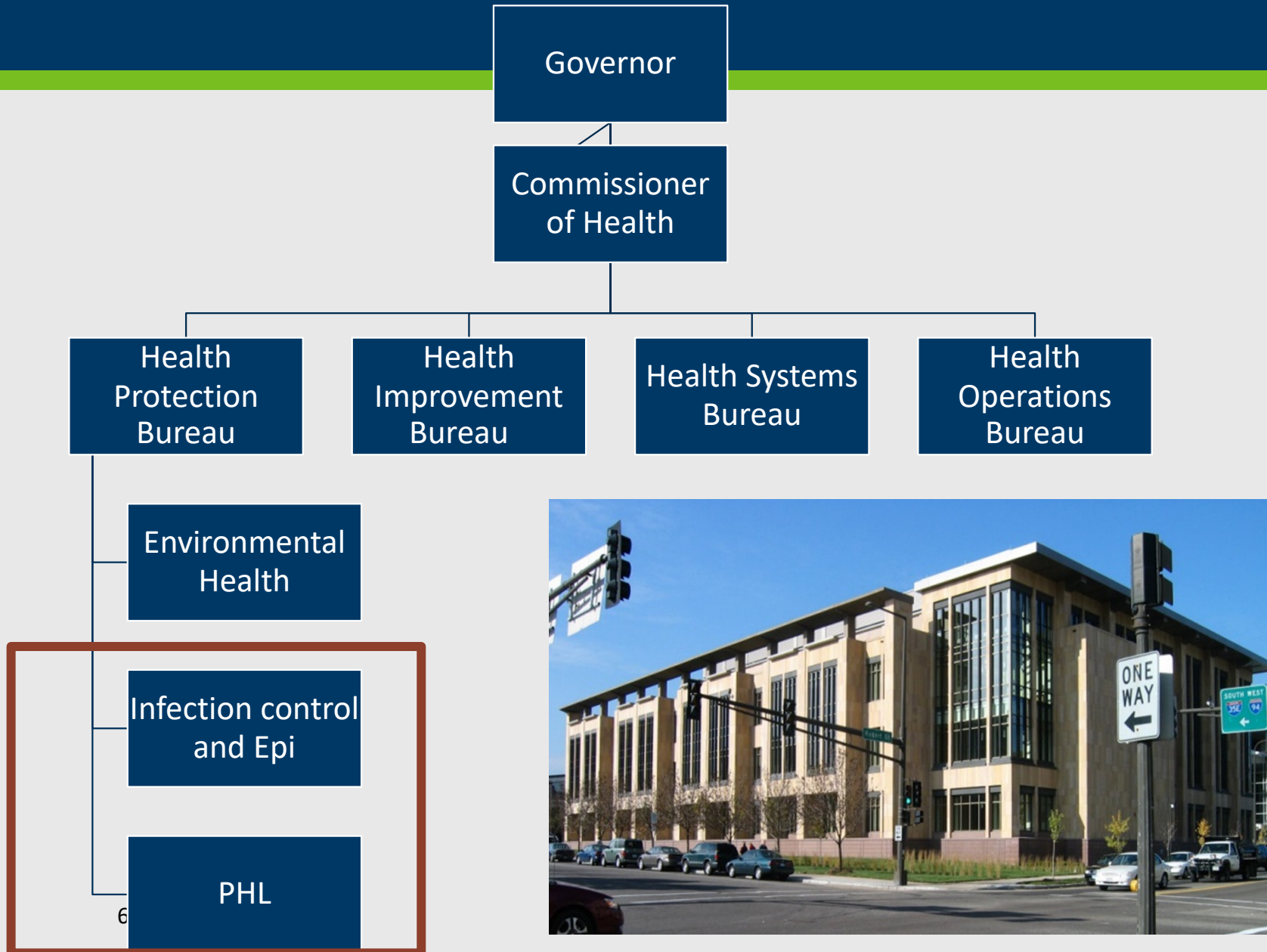


# Boots on the ground: State Public Health Laboratory's Perspective on Virus Pathogen Surveillance

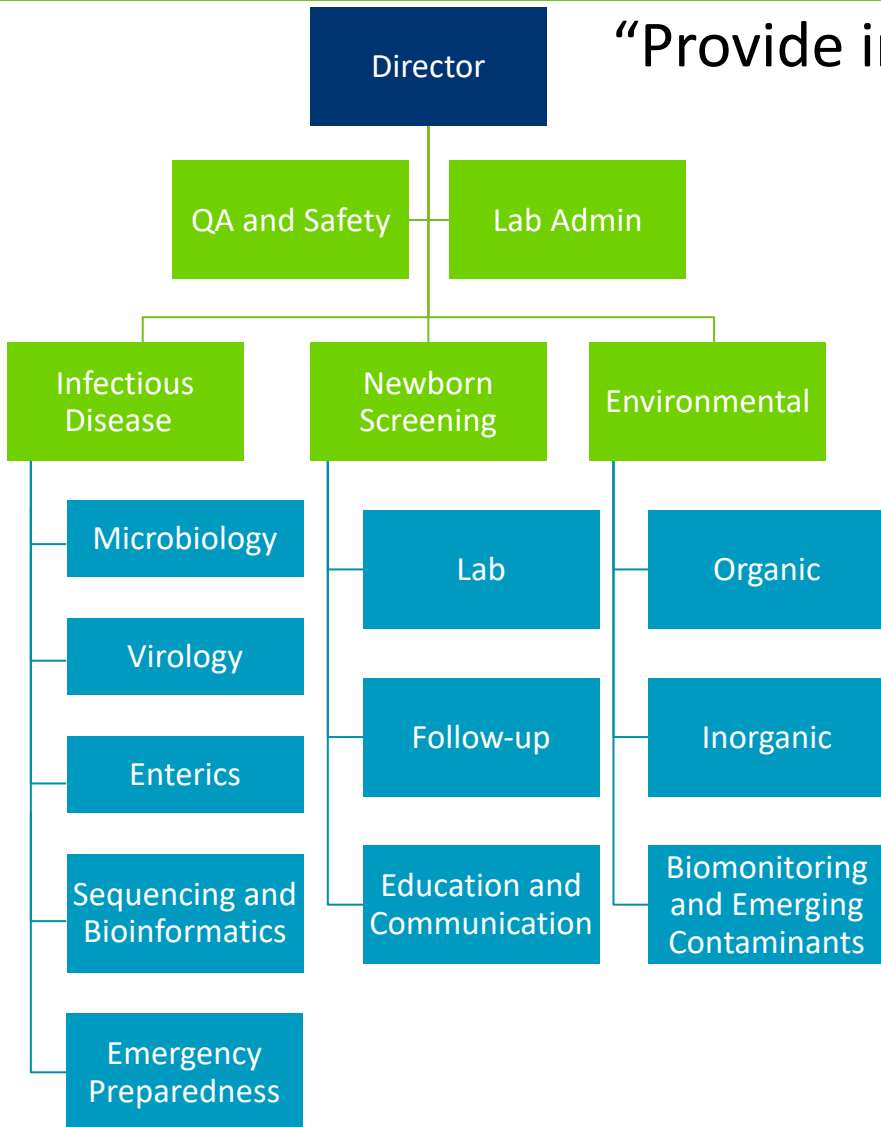
Sean Wang, Ph.D | Sequencing and Bioinformatics Supervisor | Public Health Laboratory

Viral Sub-Species Workshop, April 2024

# MN-PHL is part of state government system (not necessary the case nationwide)



# What does a public health laboratory do (or not do)?



“Provide information for decision making”

## Clinical Labs

- Diagnostic testing
- Medical management
- Focus is on individual health
- Report relevant data to public health

## Public Health Labs

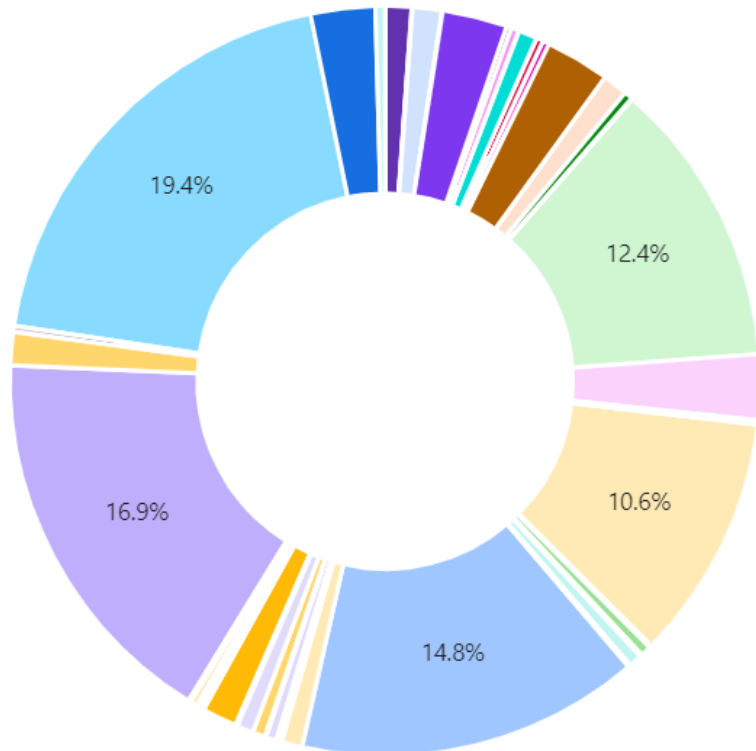
- Diagnostic testing, characterization
- Surveillance and response
- Focus is on population health
- Communicate public health needs to clinical labs

# Infectious Disease Genomic Sequencing Program at MN- PHL

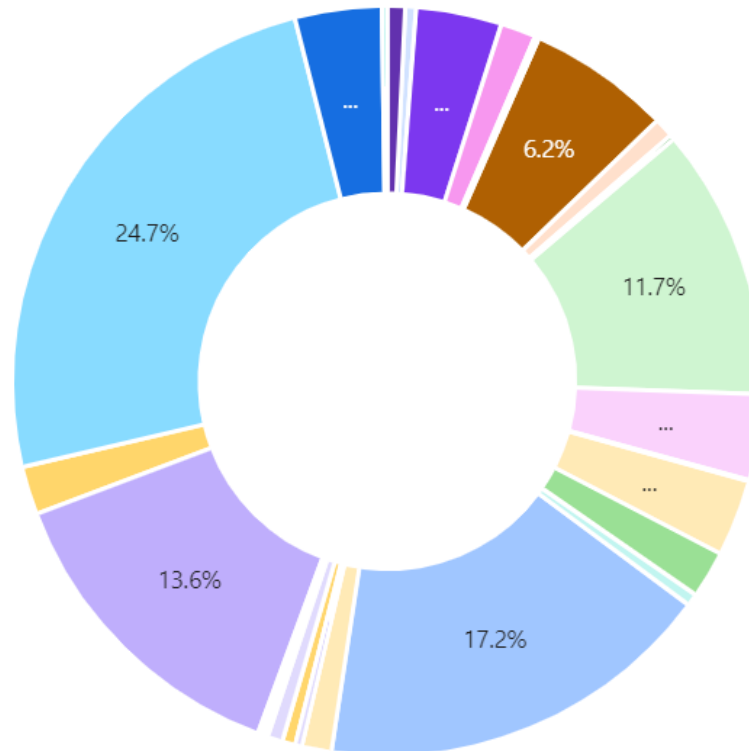
7401

2113

Organisms Sequenced in 2023



Organisms Sequenced in 2024



- Streptococcus pneumoniae
- Salmonella
- Escherichia
- Clostridium difficile
- Campylobacter
- Streptococcus pyogenes
- Candida auris

...

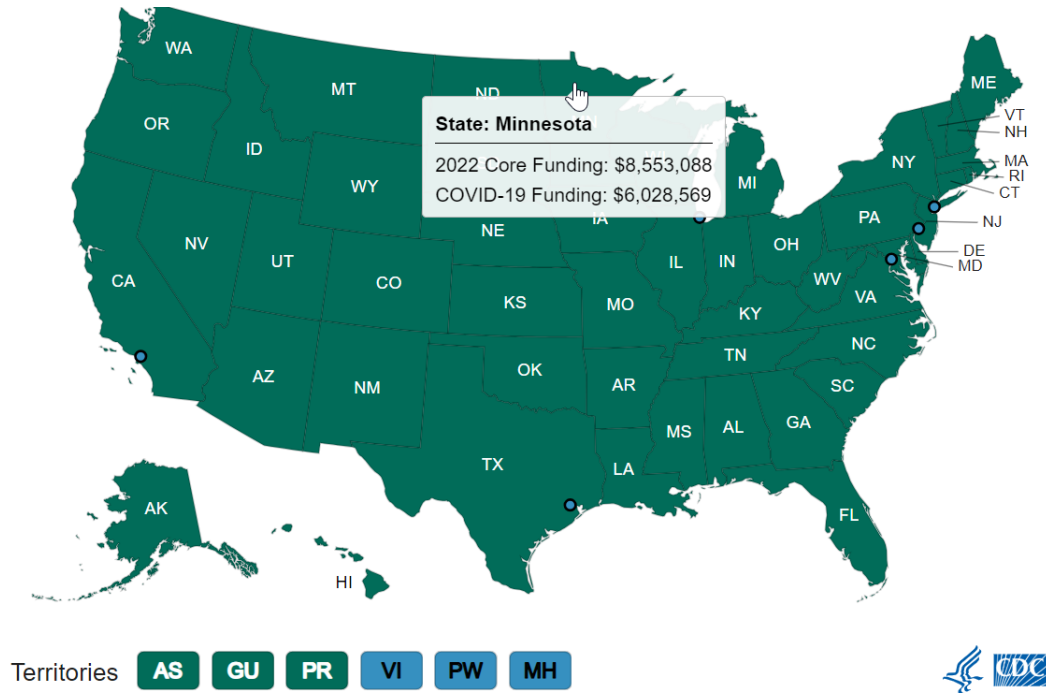


**~7,000 SARS-COV-2**

**~800-1,000 Flu**

**~800 RSV**

# State Public Health System, including the Laboratories, are at Various Stage of Pathogen Genomic Surveillance

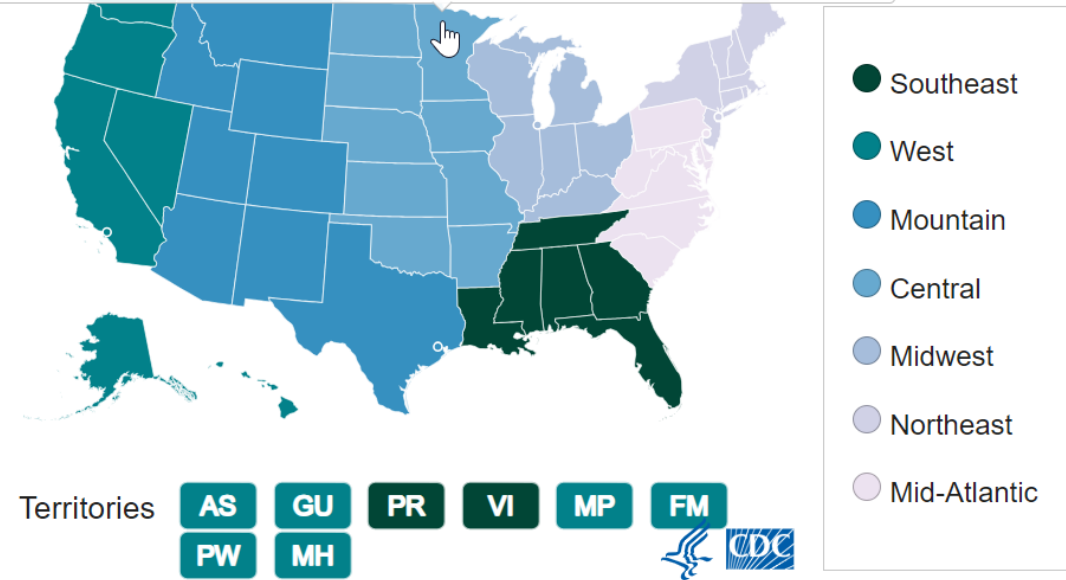


## Select to show training lead locations

State: Minnesota

Region: Central

Lead positions: AMD Training Lead & Bioinformatics Lead for the Central region

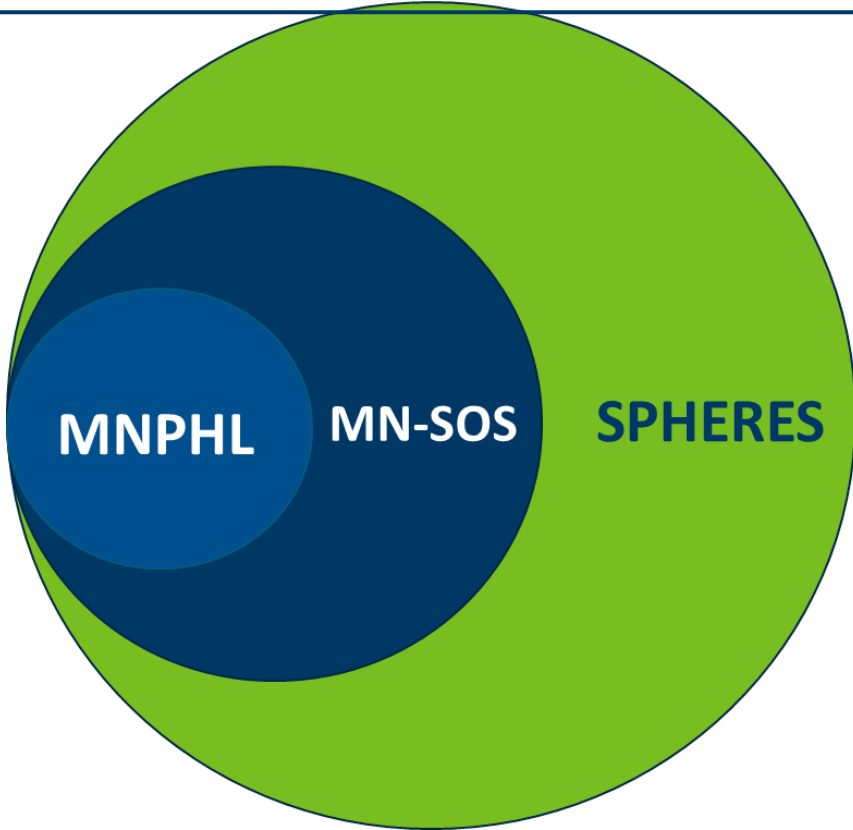




# COVID Pandemic Response is the First Time State and Local Public Health Laboratories Go Full Steam with Viral Genomic Surveillance

**SPHERES:** SARS-CoV-2 Sequencing for Public Health Emergency Response, Epidemiology, and Surveillance

**MN-SOS:** Minnesota molecular surveillance of SARS-CoV-2. Participants including Mayo and Univ. of Minnesota and all the other specimen sharing testing sites.

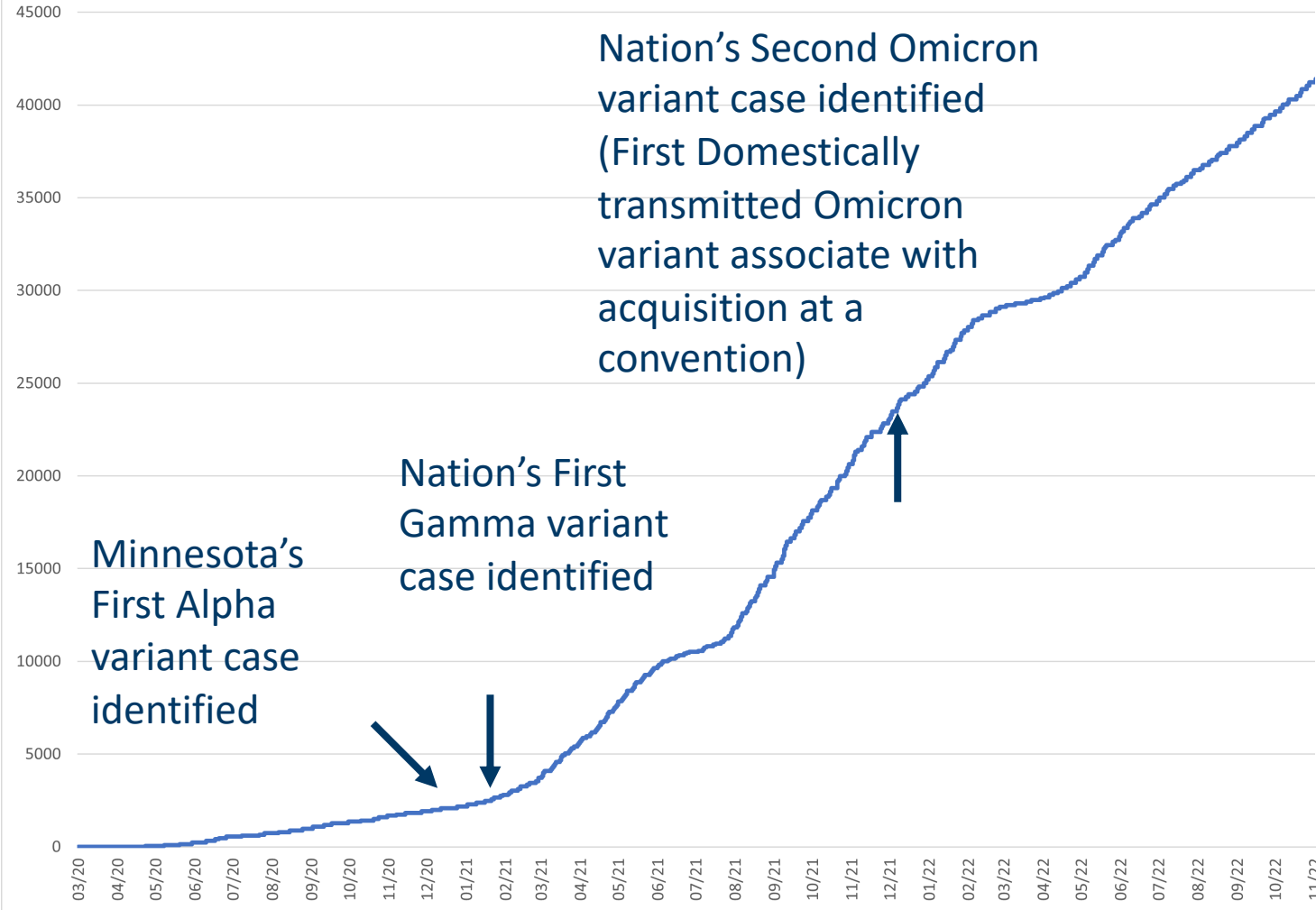


The **SPHERES** consortium brings together over **1,400** scientists from more than **200** organizations in a network of federal, state, private, academic, and non-profit organizations in the **largest public health sequencing effort** in US history.

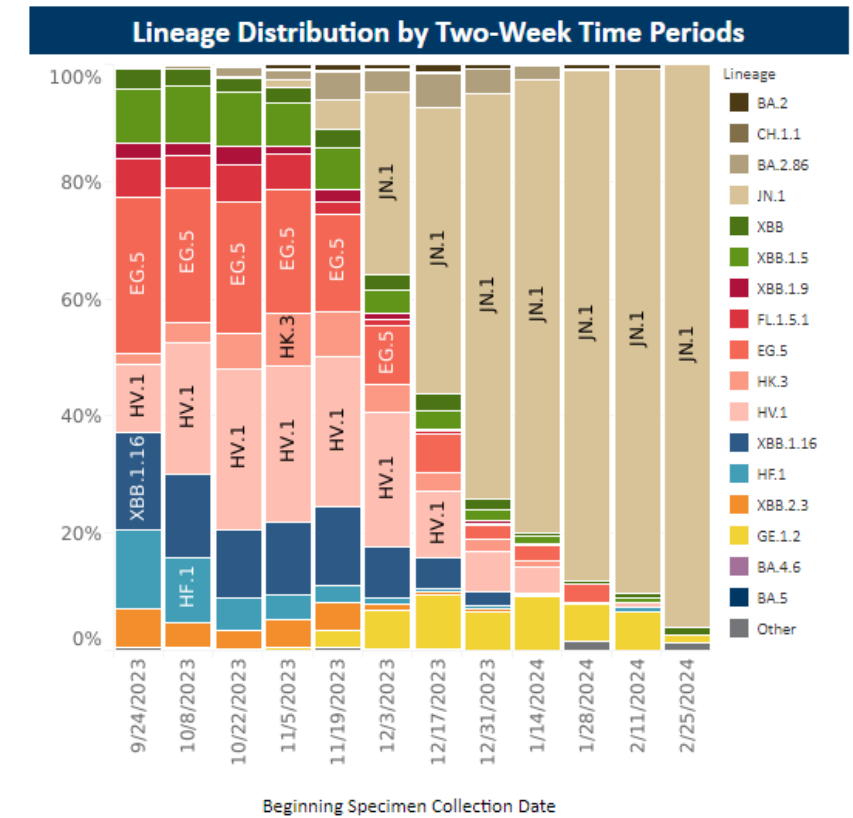
**SPHERES**  
Centers for Disease Control and Prevention

# SARS-CoV-2 genomic mutation (VOCs & VOIs) surveillance at population level

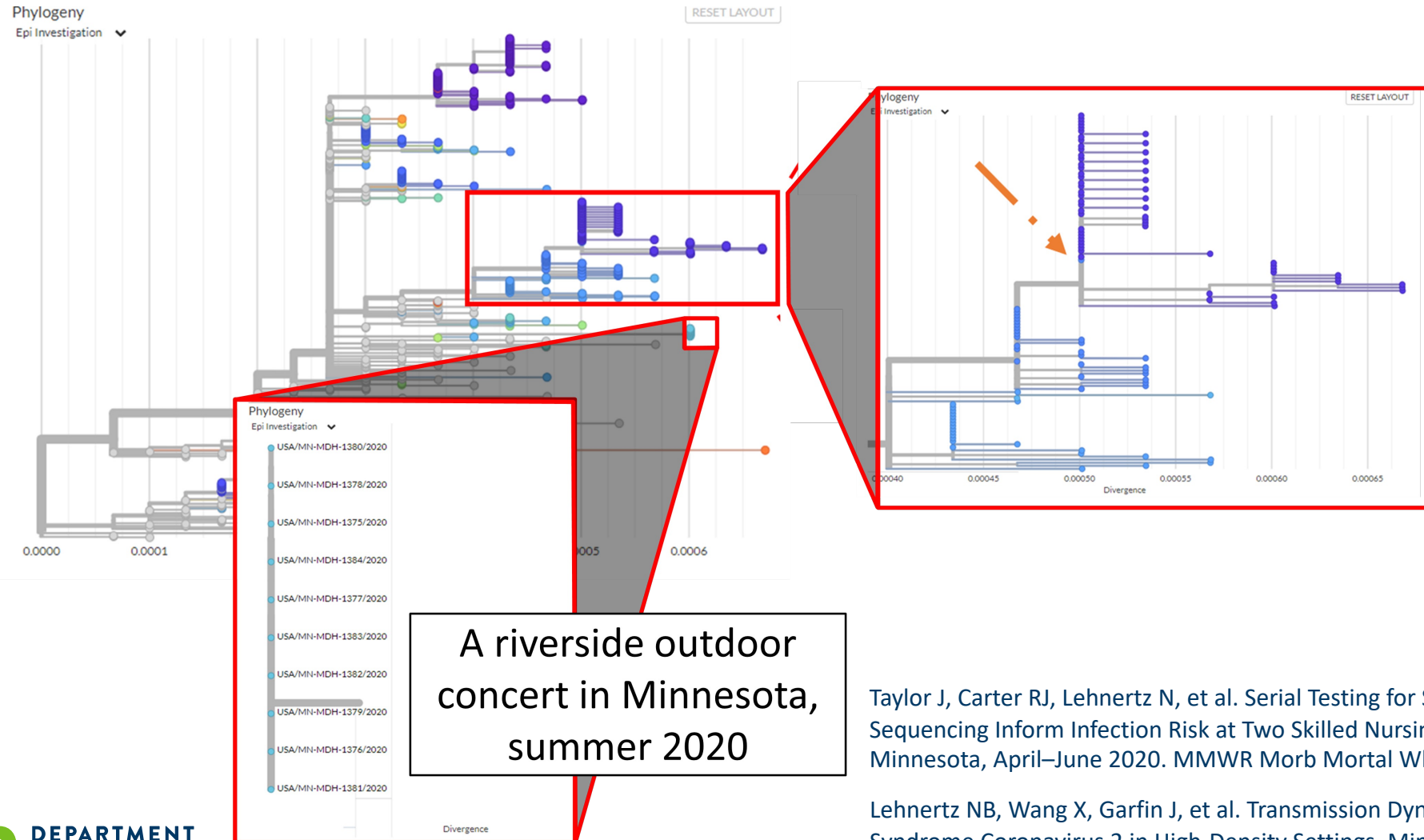
Cumulative Number of SARS-COV-2 Samples Sequenced 03/20 to 11/15/22



## Variants Circulating in Minnesota Lineage Distribution



# COVID Outbreak Detection utilizing Genomic Epidemiology at Whole Genome Level



Genomically related outbreaks in two congregate settings linked by individuals from one household who were employees at each facility

A riverside outdoor concert in Minnesota, summer 2020

Taylor J, Carter RJ, Lehnertz N, et al. Serial Testing for SARS-CoV-2 and Virus Whole Genome Sequencing Inform Infection Risk at Two Skilled Nursing Facilities with COVID-19 Outbreaks — Minnesota, April–June 2020. *MMWR Morb Mortal Wkly Rep* 2020;69:1288–1295.

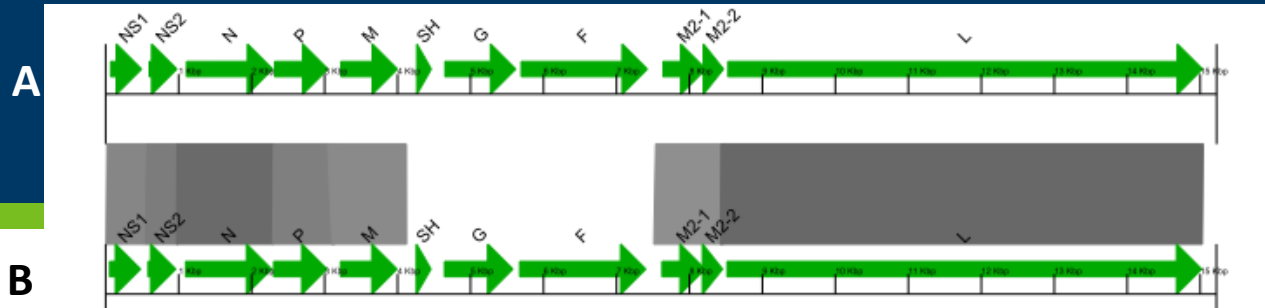
Lehnertz NB, Wang X, Garfin J, et al. Transmission Dynamics of Severe Acute Respiratory Syndrome Coronavirus 2 in High-Density Settings, Minnesota, USA, March–June 2020. *Emerg Infect Dis.* 2021;27(8):2052–2063. doi:10.3201/eid2708.204838



# “The End User Experience”

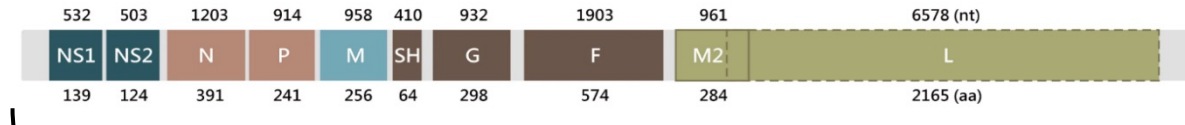
- Early pandemic response phase: “Too many cooks in the kitchen”. Public communication was challenging after “variants” concept emerged.
- Ongoing limitation of Laboratory Information Management System (LIMS) handling WGS data
- The SPHERE provided the first-ever direct communication platform among state/local public health laboratories, federal agencies and academic researchers.

# Nomenclature for RSV typing



Amino acid alignments >70%

G-protein genotype



WGS-based lineages

- Viral subtypes A and B
- G-protein based genotyping
- Whole genome-based lineage typing

Nextclade Start Dataset Results Tree Export

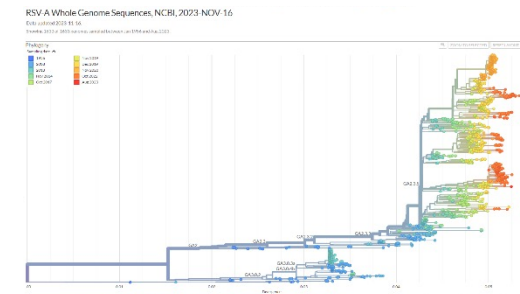
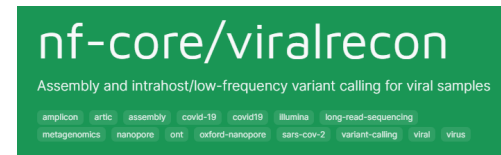
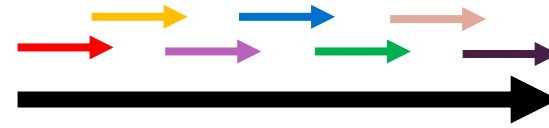
#	i	Sequence name	QC	Clade	G clades
0	0	✓ MN-MDH-RSVB-00230 [isolate=MN-M	M P F S	B.D.E.1	GB5.0.5a
1	1	✓ MN-MDH-RSVB-00235 [isolate=MN-M	M P F S	B.D.E.1	GB5.0.5a
2	2	✓ MN-MDH-RSVB-00250 [isolate=MN-M	M P F S	B.D.E.1	GB5.0.5a
3	4	✓ MN-MDH-RSVB-00227 [isolate=MN-M	M P F S	B.D.E.1	GB5.0.5a
4	3	✓ MN-MDH-RSVB-00226 [isolate=MN-M	M P F S	B.D.4.1.1	GB5.0.5a
5	5	✓ MN-MDH-RSVB-00231 [isolate=MN-M	M P F S	B.D.E.1	GB5.0.5a
6	6	✓ MN-MDH-RSVB-00232 [isolate=MN-M	M P F S	B.D.4.1.1	GB5.0.5a
7	8	✓ MN-MDH-RSVB-00237 [isolate=MN-M	M P F S	B.D.E.1	GB5.0.5a
8	7	✓ MN-MDH-RSVB-00252 [isolate=MN-M	M P F S	B.D.E.1	GB5.0.5a
9	9	✓ MN-MDH-RSVB-00238 [isolate=MN-M	M P F S	B.D.E.1	GB5.0.5a
10	10	✓ MN-MDH-RSVB-00243 [isolate=MN-M	M P F S	B.D.4.1.1	GB5.0.5a

Nextclade Start Dataset Results Tree Export

#	i	Sequence name	QC	Clade	G clades
0	0	✓ MN-MDH-RSVA-00160 [isolate=MN-M	M P F S	A.D.5.2	GA2.3.5
1	1	✓ MN-MDH-RSVA-00161 [isolate=MN-M	M P F S	A.D.5	GA2.3.5
2	2	✓ MN-MDH-RSVA-00162 [isolate=MN-M	M P F S	A.D.5.2	GA2.3.5
3	3	✓ MN-MDH-RSVA-00163 [isolate=MN-M	M P F S	A.D.5	GA2.3.5
4	5	✓ MN-MDH-RSVA-00170 [isolate=MN-M	M P F S	A.D.3	GA2.3.5
5	4	✓ MN-MDH-RSVA-00165 [isolate=MN-M	M P F S	A.D.5.2	GA2.3.5
6	6	✓ MN-MDH-RSVA-00171 [isolate=MN-M	M P F S	A.D.3	GA2.3.5
7	7	✓ MN-MDH-RSVA-00172 [isolate=MN-M	M P F S	A.D.3	GA2.3.5
8	8	✓ MN-MDH-RSVA-00174 [isolate=MN-M	M P F S	A.D.5.2	GA2.3.5
9	9	✓ MN-MDH-RSVA-00175 [isolate=MN-M	M P F S	A.D.3	GA2.3.5
10	10	✓ MN-MDH-RSVA-00180 [isolate=MN-M	M P F S	A.D.5.2	GA2.3.5

# Sequencing and bioinformatics methods

- Tiled, overlapping amplicon approach ( $n = 50 \times \sim 350\text{bp}$ )
- Sequenced on ONT GridION platform (similar to SCV2)
- QC and genome assembly using nf-core/viralrecon (modified)
- Phylogenies constructed using Nextstrain pipeline (Augur)
- Cross-reference to RSV-NET hospitalization data

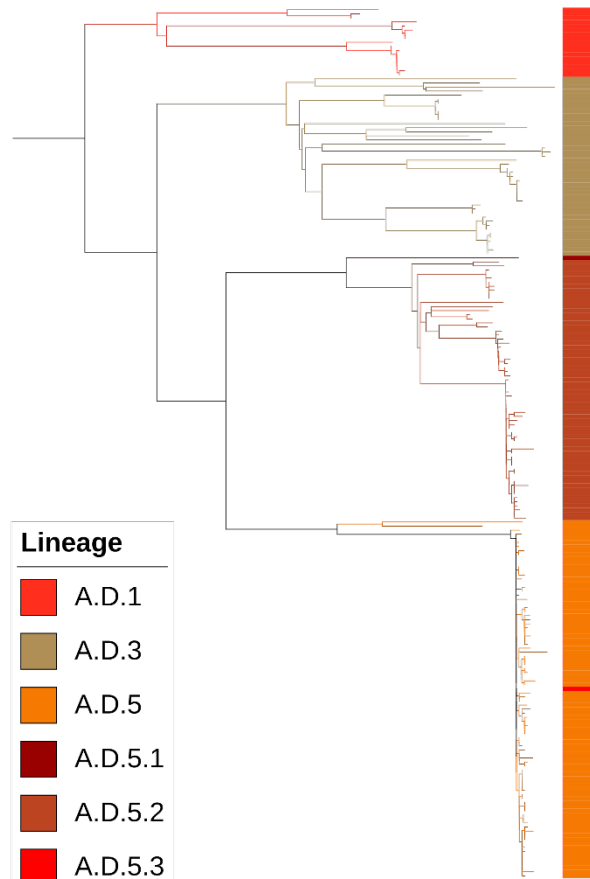


Phylogenies visualized and annotated using ITOL software

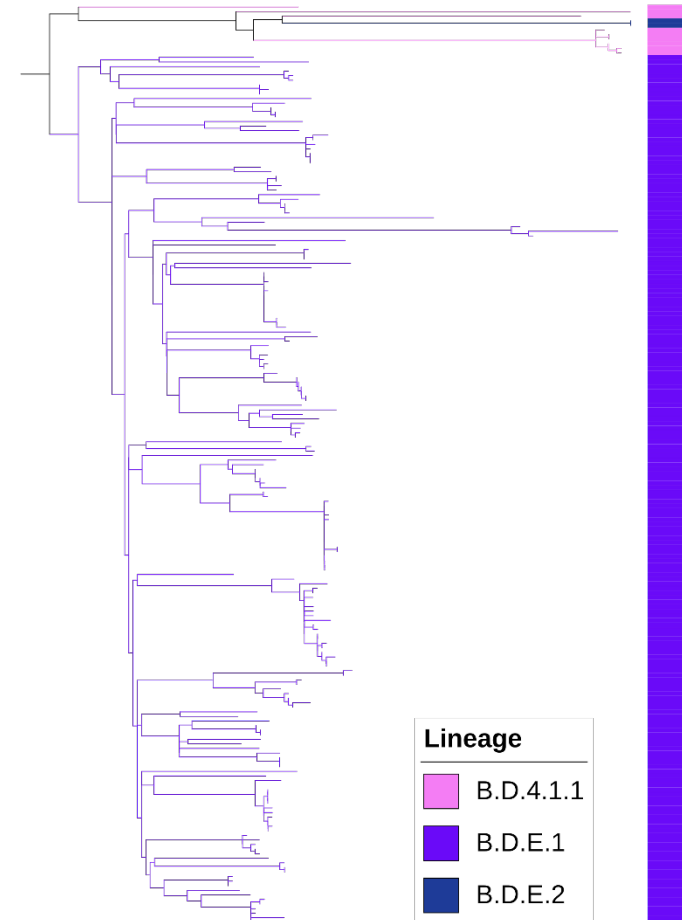
# WGS of RSV from 2023-2024 respiratory season

- Through March:
  - RSV-A: 214 sequences
  - RSV-B: 201
- Diversity of RSV-A lineages
- RSV-B dominated by B.D.E.1, but...

Tree scale: 0.001

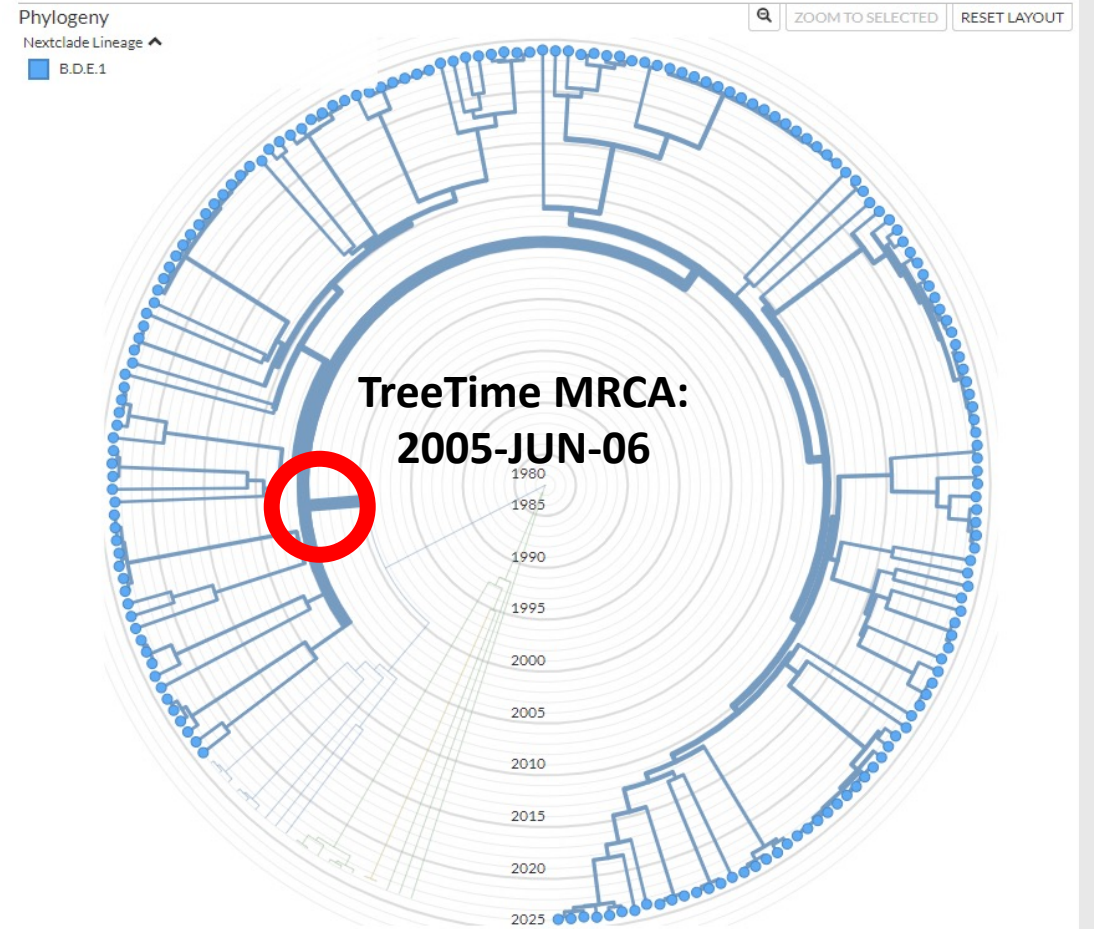
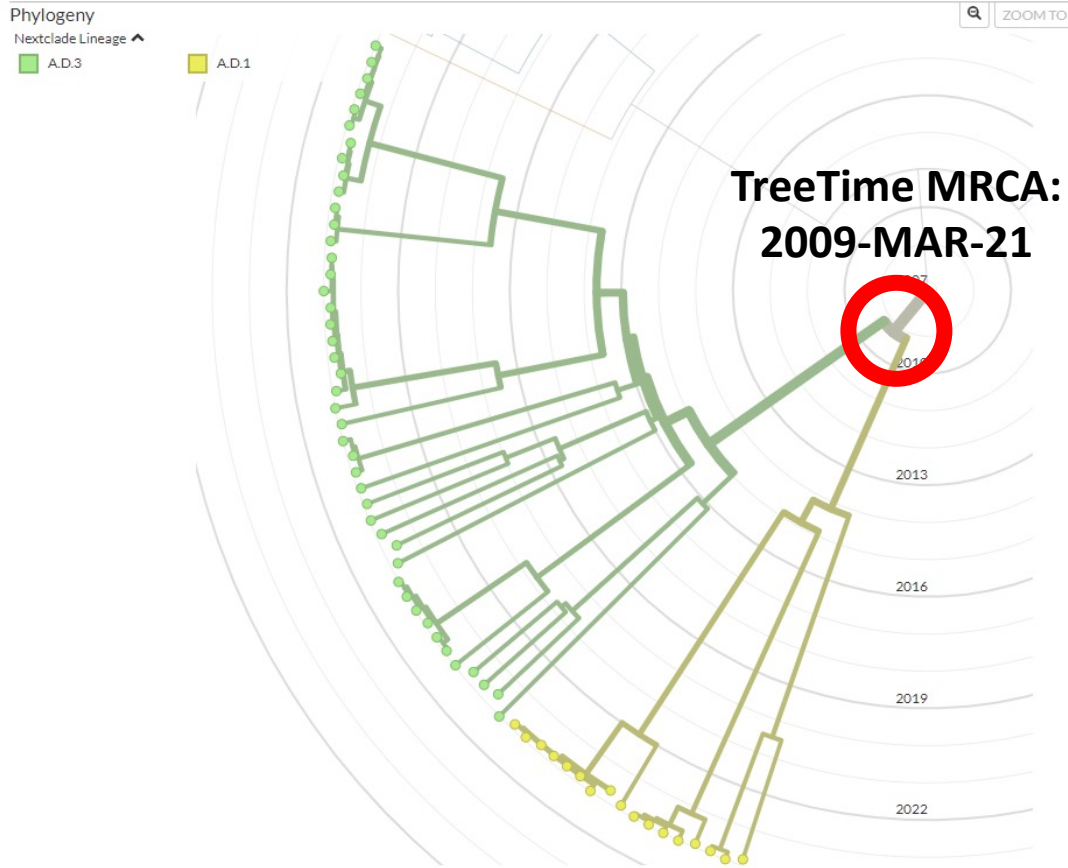


Tree scale: 0.001



Phylogenies visualized and annotated using ITOL software

# Even WGS lineage types are not specific enough



Phylogenies visualized and annotated using Nextstrain software



# General thoughts from end-user perspective

- You see one public health laboratory; you see ONE public health laboratory (Easy usage of viral sub-species classification tools, data submission tools, bioinformatic tools)
- Current limitation of Public Health Laboratory Information Management System (LIMS) and Epidemiology database handling genomic epidemiology information (i.e. phylogeny) requires reasonable viral pathogen nomenclature system(s) for different purposes (i.e. outbreak investigation, public communication etc.)
- During public health emergency, state/local public health community need faster consensus of lineage designation, followed with sustainable updates and timely communication

# Acknowledgement

- Minnesota Public Health Laboratories
  - Dan Evans
  - Matt Plumb
  - Jake Garfin
  - Henry Kunerth
  - Sarah Namugenyi
  - Bonnie Weber
  - Alyssa Mondelli
  - Kelly Pung
- CDC OAMD Office
  - State Public Health Bioinformatic (StaPh-B) group
  - BV-BRC Viral Sub-species Classification workshop Organizing committee

# Thank You!

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651-201-5050