

Clinical Characteristics of Neuroinvasive Arbovirus Infections Detected by Metagenomic Next-Generation Sequencing

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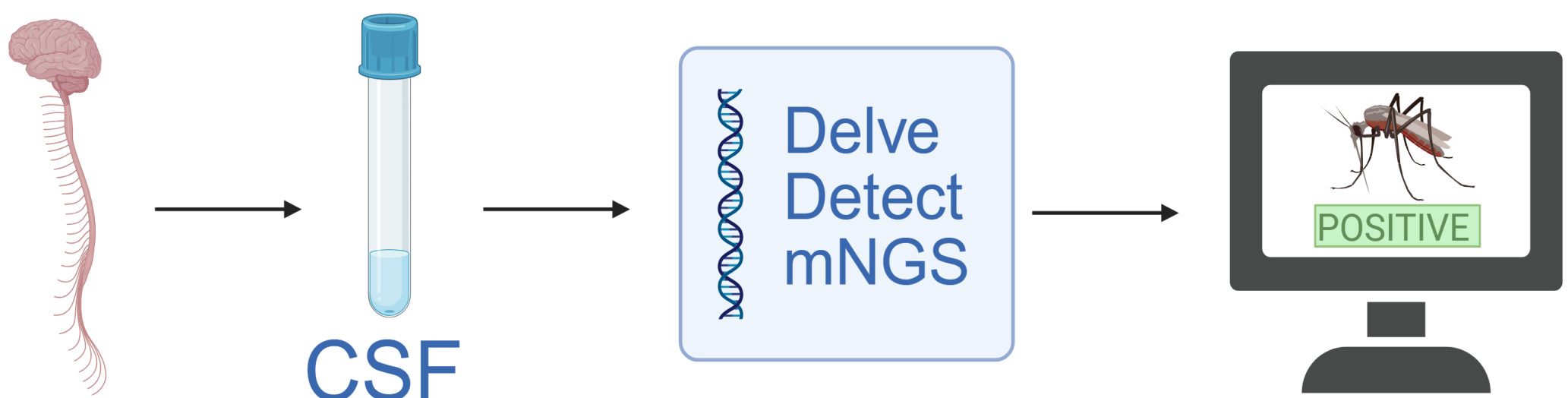


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INTRODUCTION

- Arbovirus infections in the United States can cause neuroinvasive disease (NID) with high mortality rates¹.
- Serology-based diagnostics may be falsely negative early in disease course² and are insensitive in immunocompromised patients³.
- PCR often fails to detect viral RNA in immunocompetent patients⁴.
- This study describes the clinical and epidemiological features of arboviral infections detected in cerebrospinal fluid (CSF) by metagenomic next-generation sequencing (mNGS) in patients with NID.

METHODS



- mNGS is an unbiased sequencing method that detects pathogen genetic material.
- 11 cases of arboviral infection with neuroinvasive presentations were detected by Delve Detect mNGS of CSF in 2025.

RESULTS

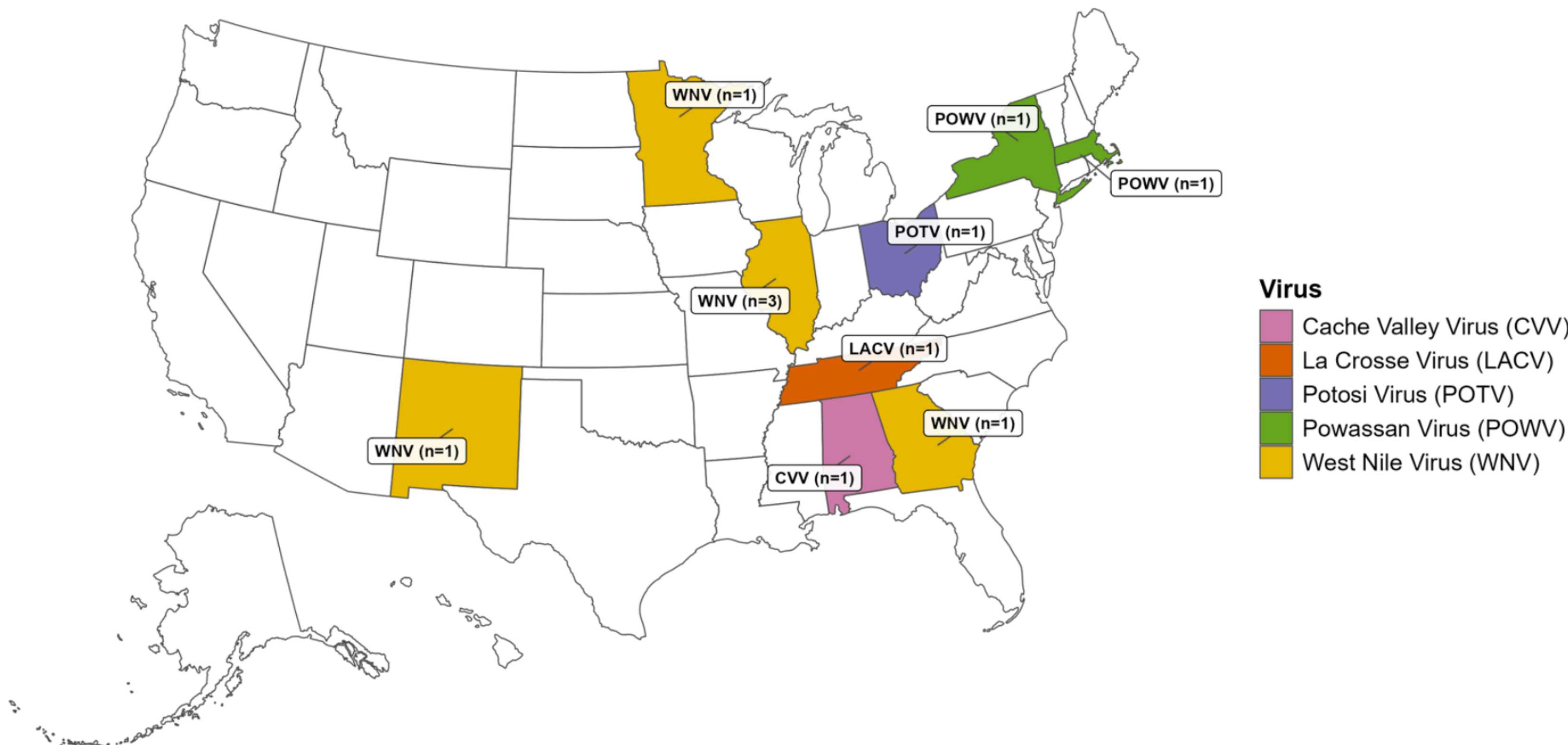
Cohort demographics

- Arboviruses included West Nile (n=6), Powassan (n=2), La Crosse (n=1), Cache Valley (n=1), and Potosi (n=1).
- Of 10 patients with demographic information available, 9 were immunocompromised (90%). Reasons for immunocompromised status were leukemia/lymphoma (n=3), CD20-inhibitor (n=3), solid-organ transplant (n=2), and solid tumor on chemotherapy (n=1).

Virus	Mean Age (SD)	Male/Female	Patient immunocompromised		
			Yes	No	Unknown
West Nile (n=6)	55.0 (24.5)	5/1	6	0	0
Powassan (n=2)	70.5 (7.8)	2/0	0	1	1
Cache Valley (n=1)	18	1/0	1	0	0
La Crosse (n=1)	37	0/1	1	0	0
Potosi (n=1)	37	0/1	1	0	0

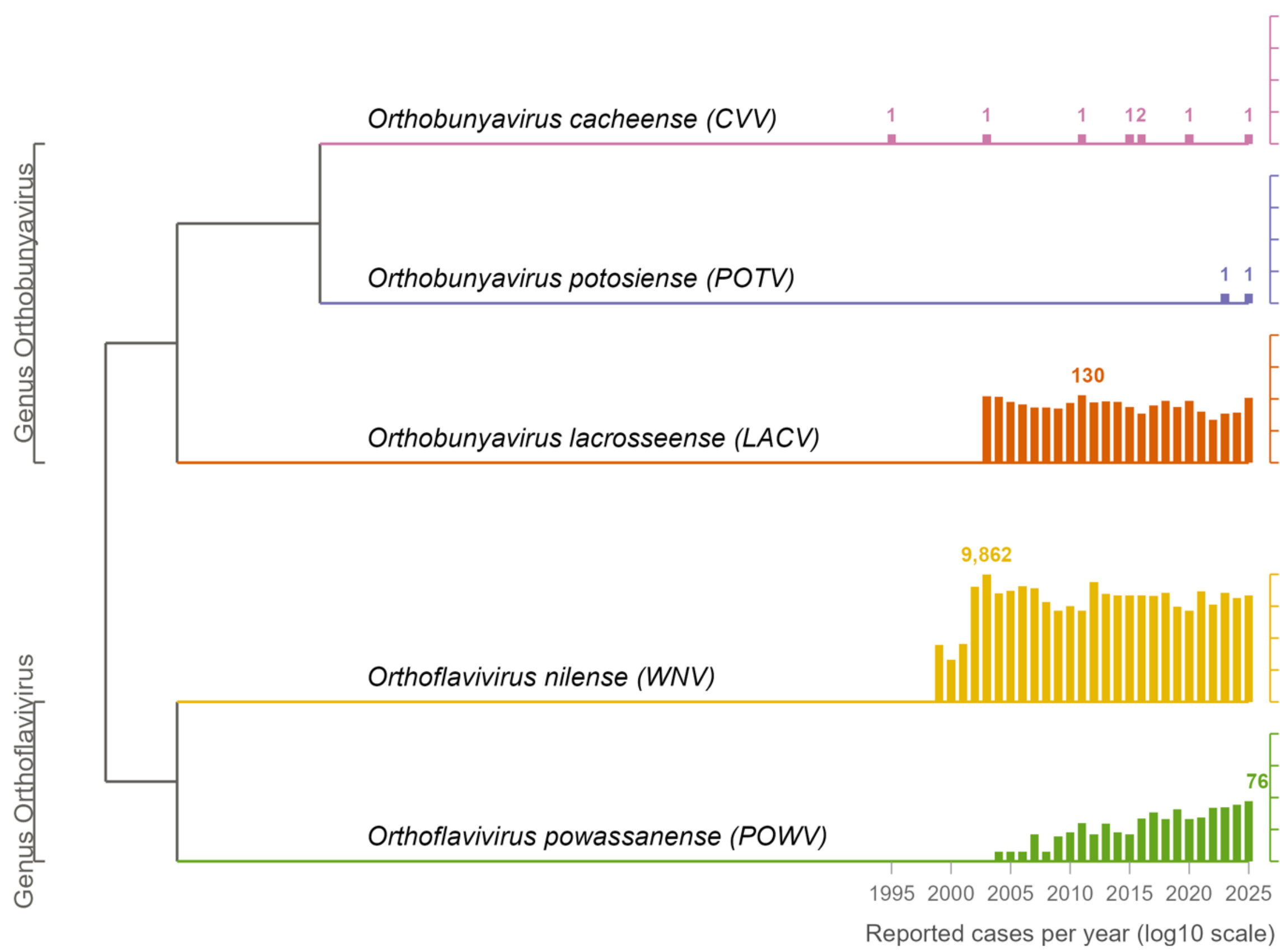
- Two patients received directed antiviral therapy: the patient with CVV received molnupiravir for a total of 10 months and monthly IVIG⁵, and one patient with POWV received ribavirin for 21 days. Additionally, 3 patients received IVIG.
- 3 of 8 (37.5%) patients with available outcome data survived.

Geographic location of arbovirus detections



- The institutions from where patients had samples collected for mNGS analysis were primarily located in the South, East, and Southeast United States.

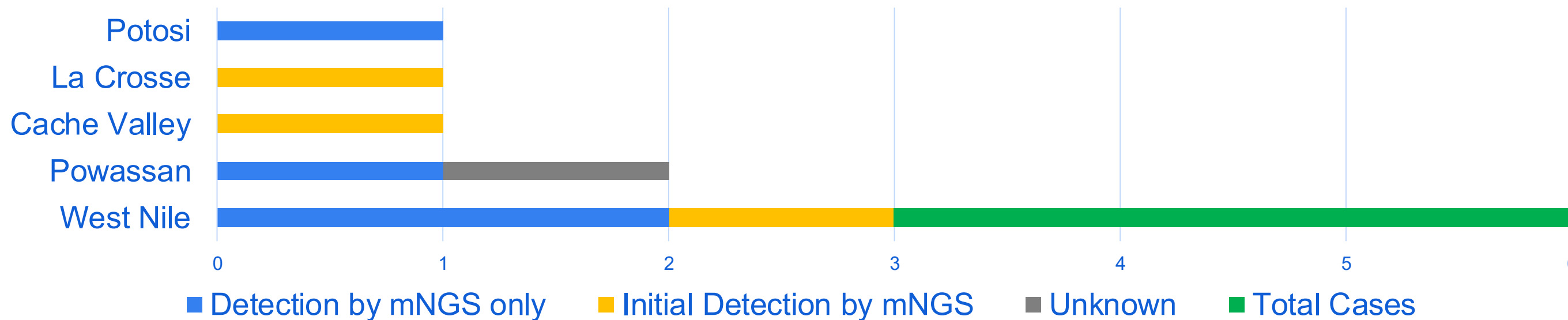
Increasing diversity of arbovirus disease diagnoses over time



Data sources: CDC ArboNET (LACV, WNV, POWV) and literature / this case series (CVV, POTV).

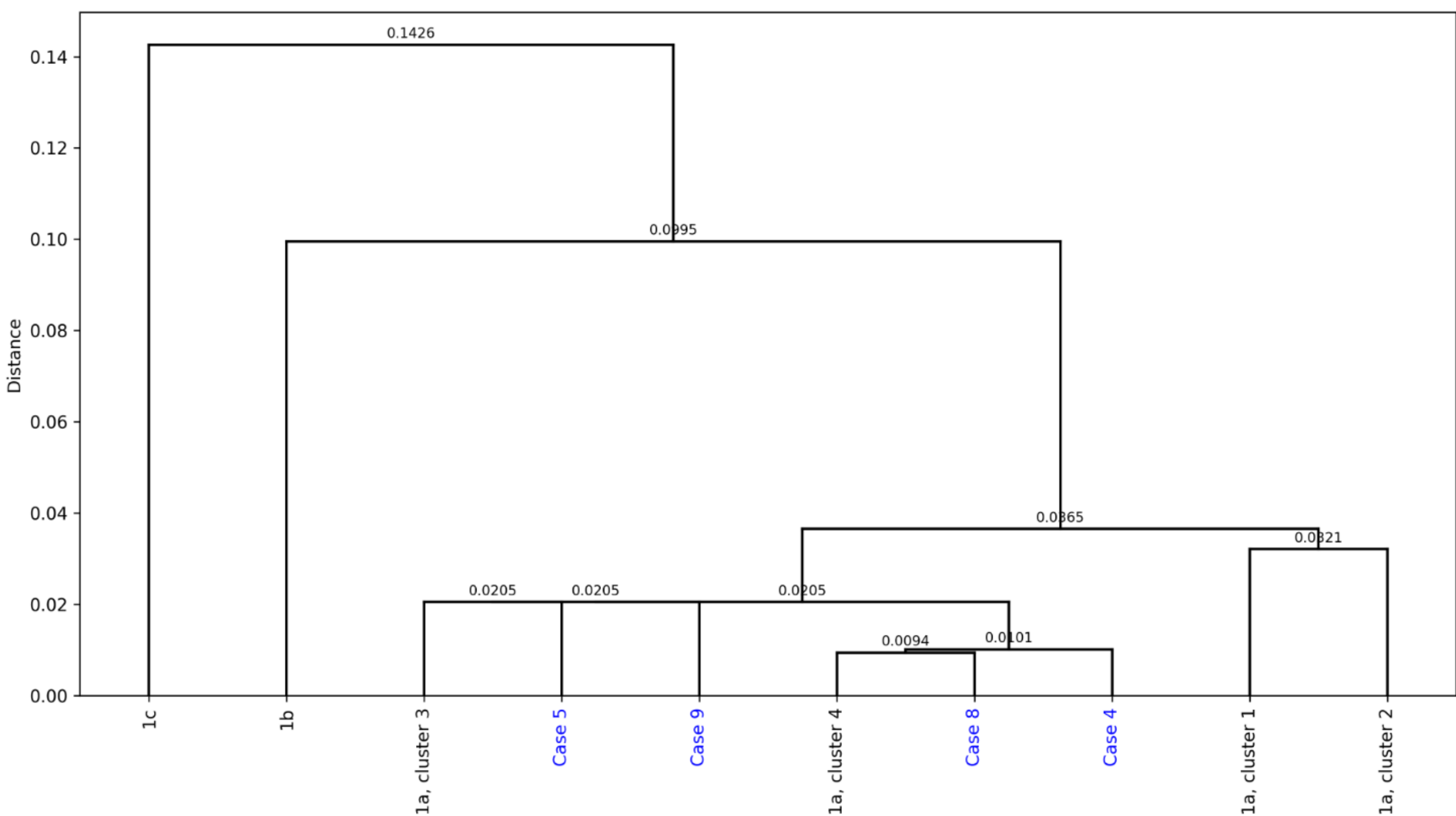
- Reported arboviral infections remain rare, but show increasing frequency for some agents (POWV).
- Human infection with novel arboviruses is being increasingly reported (CVV, POTV).
- Reported cases are likely to represent a small fraction of actual infections in the community.

Comparison of mNGS against standard diagnostics



- mNGS was the first or only test to identify the causative arbovirus in 7 of 10 patients (70%).
- Of 6 patients with serology testing from initial presentation, 1/6 (16.7%) were positive.
- Serum PCR testing was performed in 4 patients (3 of whom had WNV) and was positive in 3 (75% of total, but 100% for WNV); dedicated PCR testing is rarely performed or not available for other viruses.

mNGS sequencing can drive epidemiologic insights



- Reference-constrained subtype dendrogram of 6 patients with WNV showed that all sequences aligned to clade 1a, the most common WNV clade.
- 2 patient sequences aligned more specifically to cluster 3 (common in Russia)⁶, while 2 patients' sequences aligned to cluster 4 (common in the Americas, Africa, and Europe)⁶.

CONCLUSIONS

- mNGS has the potential to detect rare and emerging arboviruses.
- mNGS may detect arboviral NID more rapidly than conventional PCR or serology tests, which can fail to identify the causative agent.
- Epidemiologic insights can be obtained using sequences obtained in mNGS testing.
- Many patients with arboviral diagnosed NID have similar immunocompromised state risk factors.
- None of these arboviruses have approved treatment; prompt diagnosis will be key to exploring potential therapeutics (i.e. IVIG, ribavirin, molnupiravir) and improving survival.

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