Network Bridges to Predict Emerging HIV Transmission Hotspots in North Carolina

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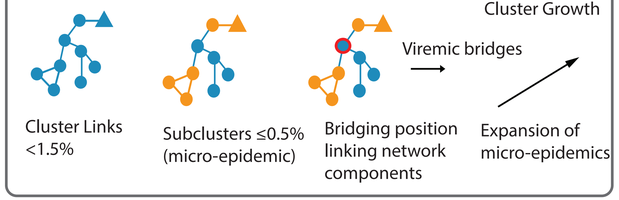
BACKGROUND

- Molecular epidemiology can be used to delineate local HIV transmission chains across time and space
- Clusters with short pairwise genetic distances (≤0.5%) with new diagnoses are prioritized in the National Cluster Detection and Response (CDR) strategy
- Growth of these "recent and rapid" clusters, often occurs within established clusters

Aims

- Characterize bridging positions to subclusters
- Hypothesize that viremic bridging positions may signal ongoing transmission

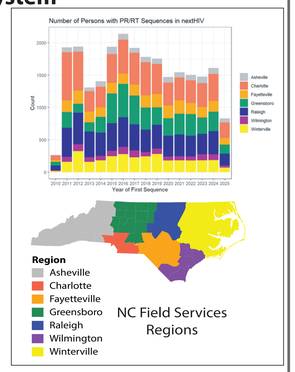
Conceptual Framework



METHODS

Statewide HIV Surveillance System

- Sequences are reported from reference laboratories (2010-2025) or de novo sequencing from remnant diagnostic specimens (2018-2022)
- In 2018 developed automated platform (nextHIV2) for monthly monitoring of NC cluster metrics
  - <1.5% -> cluster
  - ≤0.5% -> subcluster



Growing cluster

- ≥1 new diagnosis (2022–2025)

Bridging Positions

- Within 1.5% clusters
- Linked (<1.5%) to:
  - ≥2 distinct ≤0.5% subclusters or
  - subcluster and non-subcluster component

Viremic bridge

- Bridge + unsuppressed viral load (>200 last measurement)
- Sensitivity analysis at >1500 c/mL threshold

Modeling

- Baseline (pre-2022) viremic bridging in 1.5% clusters
- Outcome: 2022–2025 subcluster growth (0.5%)
- Negative binomial model with size offset
- Adjusted for structural bridging and cluster size
- IRR per +5 viremic bridges per 100 baseline members

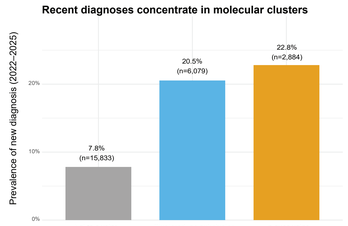
Viremic bridging positions connect growing substructures across counties and may signal early high-impact intervention points

Study Population Overview

n=24,796 persons with ≥1 PR/RT sequences

Characteristic	Growing Cluster (n=5,420)	Not Growing (n=19,387)
New HIV Dx, n (%)	1,905 (35%)	1,235 (6.4%)
Age, median (IQR)	34 (29-40)	51 (39- 61)
MSM, n (%)	3,825 (71%)	8,343 (43%)
Black/AA, n (%)	15,563 (63%)	12,174 (63%)
Deceased, n (%)	204 (3.8%)	3,068 (16%)

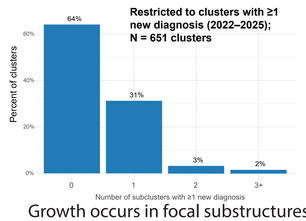
New Diagnoses Concentrate Inside Clusters



New diagnoses were nearly 3x more common inside clusters than outside (22.8% vs 7.8%).

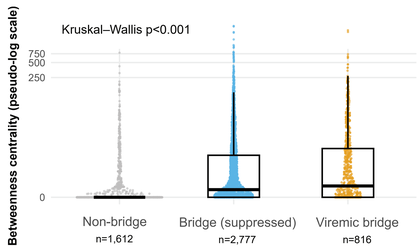
Heterogeneous Growth within Clusters

64% of clusters had no growing subclusters; 31% had one.



Growth occurs in focal substructures, not uniformly across clusters.

Viremic Bridging Positions are More Central



Subclusters within Growing Clusters

n=569 subclusters

Subcluster Characteristic	No Growth N=281	≥1 New Diagnosis N = 288
Subcluster size, Median (IQR)	2 (2-3)	2 (2- 4)
Proportion new diagnoses, Median (IQR)	0	0.67 (0.50, 1.00)
Rapid growth (5+ new diagnoses), n (%)	0	24 (8.3%)
Mean viral load, Median (IQR)	37 (20- 3,976)	162 (24-12,398)
Proportion unsuppressed, Median (IQR)	0.07 (0.00, 0.50)	0.21 (0.00-0.50)

Growing subclusters had higher viral load and more viremic bridging members

Bridging Positions within Growing Clusters

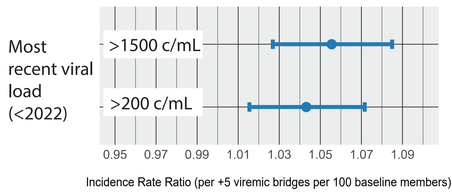
n=5,205 growing cluster members (excludes 204 deceased)

Cluster Members Characteristic	Non-Bridge N=1,612	Bridge (suppressed) N=2,777	Viremic Bridge N=816
Prior HIV Diagnosis (<2022) , n (%)	832 (52%)	1,914 (69%)	582 (71%)
Degree, median (IQR)	2 (1-3)	9 (5-18)	9 (5-16)
Betweenness, median (IQR)	0 (0-0)	1(0-7)	1(0-9)
Unsuppressed, n (%)	383 (24%)	0 (0%)	816 (100%)
Subcluster member, n (%)	175 (11%)	1,419 (51%)	411 (50%)

Bridge position members were more connected and more often previously diagnosed.

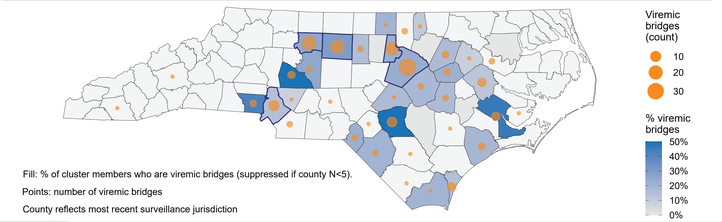
Baseline Viremic Bridging Predicts subcluster growth (2022-2025)

Adjusted for structural bridging and baseline cluster size



Viremic bridging connects counties across North Carolina

Cluster members in clusters containing ≥1 recent & rapid subcluster (≥5 new diagnoses, 2022–2025) **77.7%** of viremic-bridge ties span counties (2,749 / 3,538)



CONCLUSIONS

- New diagnoses concentrate within genetic clusters and subclusters, reflecting recent transmission
- Bridging position members link subclusters and occupy highly central network positions
- Baseline viremic bridging independently predicts future subcluster expansion, even after adjusting for structural position and cluster size
- In clusters meeting recent and rapid response thresholds, most viremic-bridge ties cross counties
- Viremic bridging within 1.5% clusters may serve as an early-warning indicator to prioritize responses before subclusters accelerate

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PLAIN LANGUAGE SUMMARY

Patterns of unsuppressed viral load among individuals linking multiple transmission groups may signal where new HIV transmission hotspots are emerging