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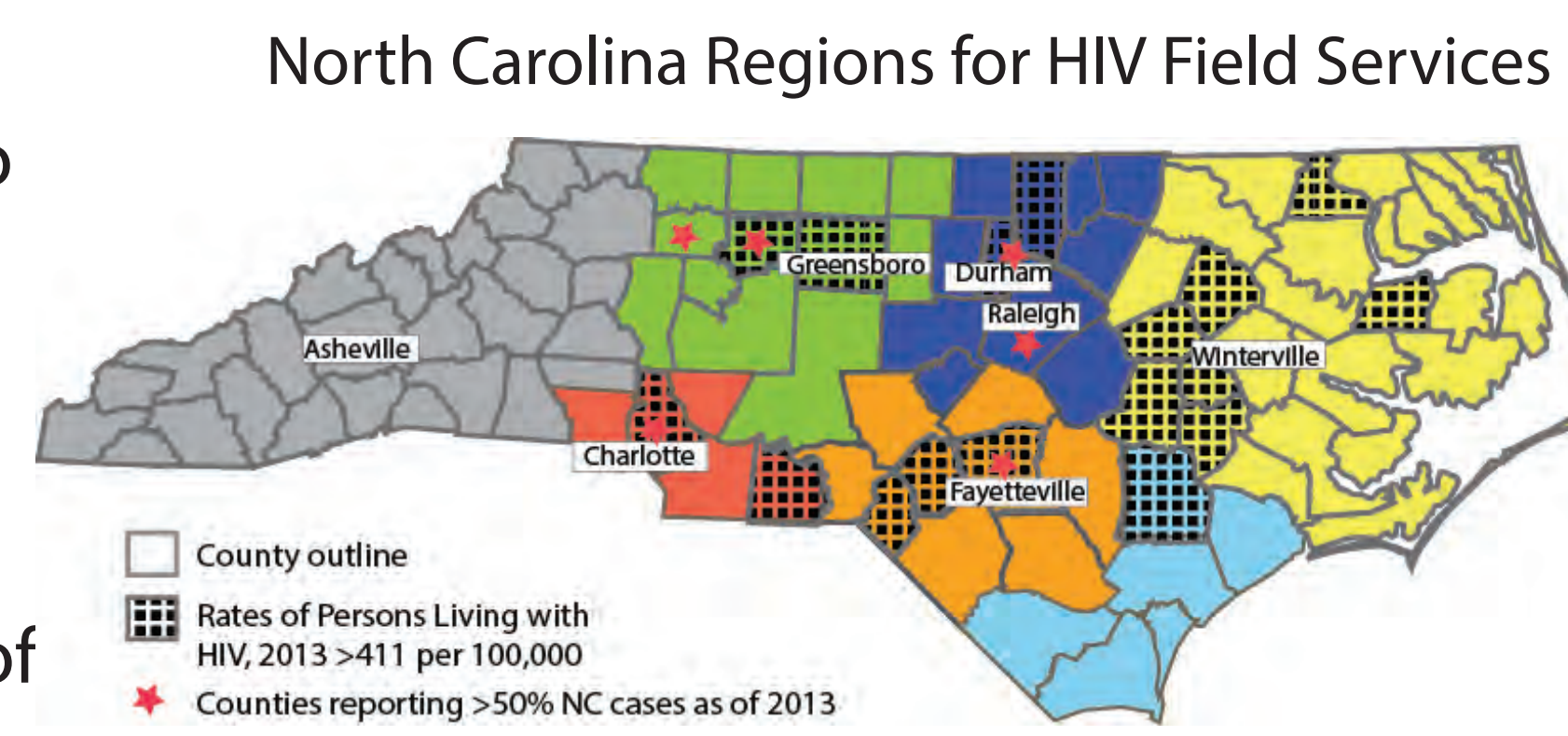
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## Background

- New HIV diagnoses continue in the Southern US despite widespread prevention efforts, underscoring the need for innovative deployment of prevention tools
- Detection and response to genetically clustered infections is a pillar to the Ending the Epidemic initiative

## Objectives

- To develop metrics to prioritize potential field service responses to genetic clusters identified during statewide surveillance using:
  - HIV RNA viral loads (VL) and surveillance data
  - Dynamic analysis and reporting of near-real time data



## Methods

### Study Population

HIV+ individuals with a sequence reported to NC surveillance through 2019. Sequences generated by:

- Drug-resistance genotypes from commercial labs (2010-2019)
- De-novo NGS with Primer-ID from diagnostic samples tested at the NC State Lab (2018-2019)

VL reported 2014-2020: estimated % time spent above 1500 c/mL using linear interpolation

### nextHIV Pipeline

- Platform for **real-time HIV surveillance** for importing sequences, generating clusters and phylogenies, and interactive reports
- Consensus sequences trimmed to overlapping regions covering PR/RT
- Clusters are constructed from pairwise genetic distances (TN-93), connecting edges <1.5% difference

### Cluster Analyses

- Clusters with  $\geq 1$  **recent diagnosis (2017-2019)** and only nodes adjacent to recent diagnoses (<1.5% distance) were analyzed
- Sub-clusters within larger clusters were identified using community edge betweenness algorithm in igraph R
- Prompt cases** were defined as members without VLs or persistent/rising viremia (VL>200 c/mL) in past 12 months (2019)

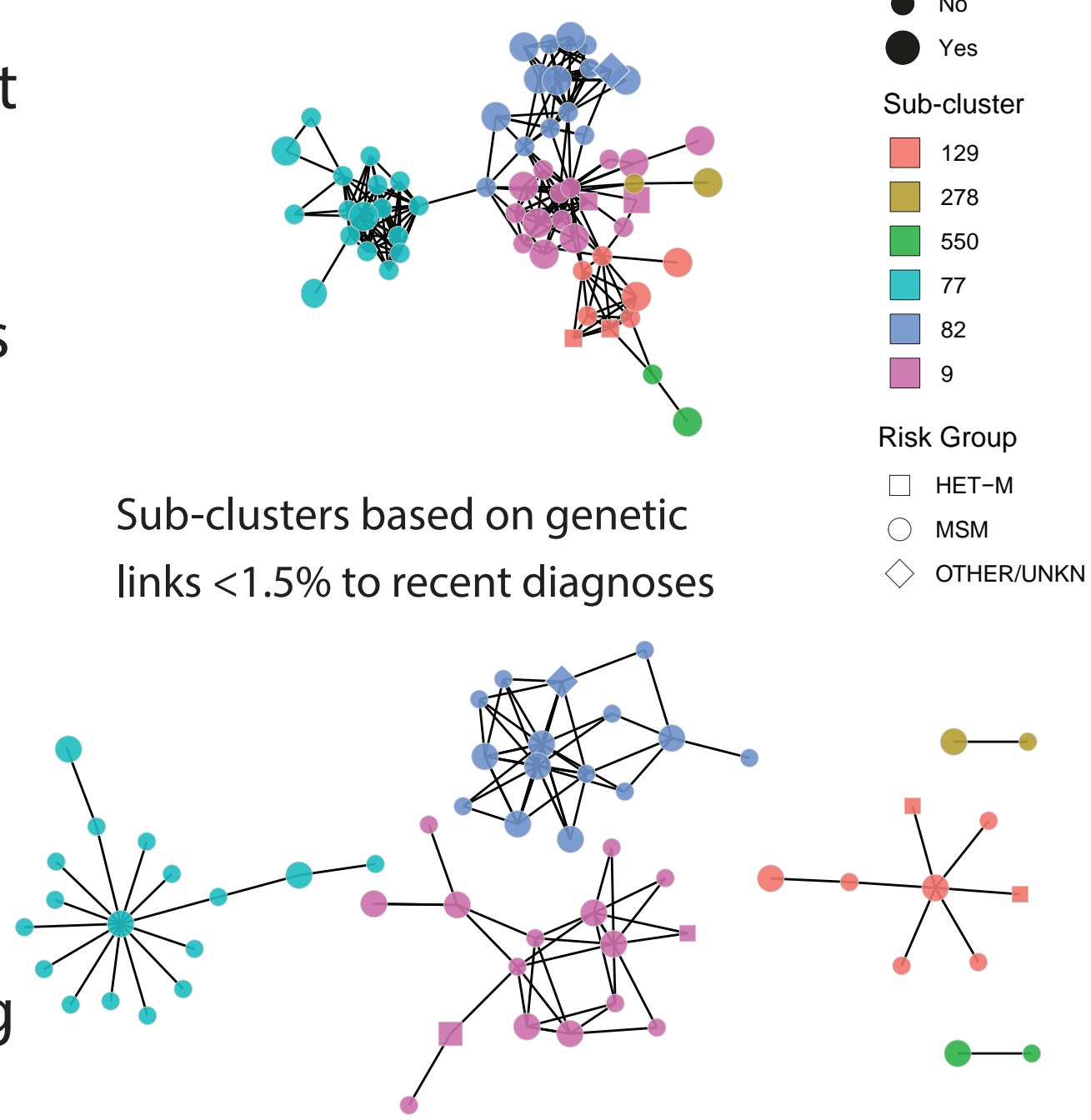
### Cluster based measures:

**Prompt Density** = average node degree among prompt cases in cluster

**Recent Density** = average node degree among all recent diagnoses in cluster

### Example Large Cluster

6 sub-clusters ("communities")



Sub-clusters based on genetic links <1.5% to recent diagnoses

## Results

### Study Population

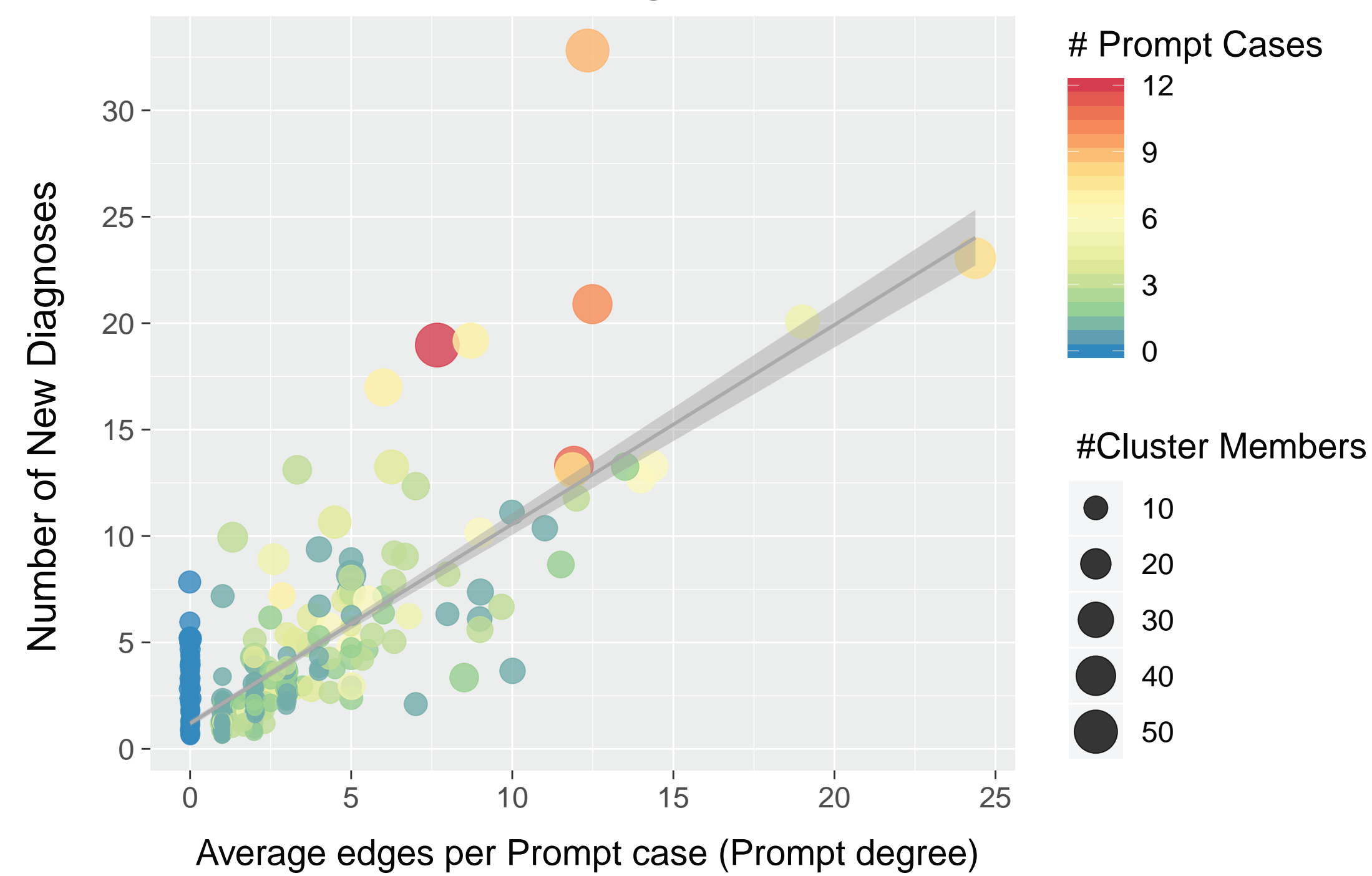
- 16,480 Persons had 24,798 PR/RT sequences
  - 2,690 were diagnosed 2017-2019
  - 13,790 were diagnosed <2017
- 2,820 Persons were cluster members
  - 1,555 Recent diagnoses (**58% of all recent**)
  - 1,265 Past diagnoses (9% of all past)
- Recent diagnoses in clusters vs. not clustered:
  - 68% vs. 47% MSM risk
  - 59% vs. 36% age <30 years at diagnosis

### Cluster members, stratified by Prompt cases

Characteristic, n (%)	PPrompt Case		Total (n=2820)
	Yes (n=632)	No (n=2188)	
Recent Diagnosis*	245 (38.8%)	1310 (59.9%)	1555 (55.1%)
Risk Group*			
MSM	416 (65.8%)	1559 (71.3%)	1975 (70.0%)
HET-Male	107 (16.9%)	264 (12.1%)	371 (13.2%)
HET-Female	66 (10.4%)	195 (8.9%)	261 (9.3%)
Black/AA Race*	479 (75.8%)	1459 (66.7%)	1938 (68.7%)
Age <30 years*	457 (72.3%)	1372 (62.7%)	1829 (64.9%)
Mean % VL >1500, median (IQR)*	68.2 (25.9, 96.6)	16.7 (6.9, 51.1)	22.9 (8.0, 69.2)

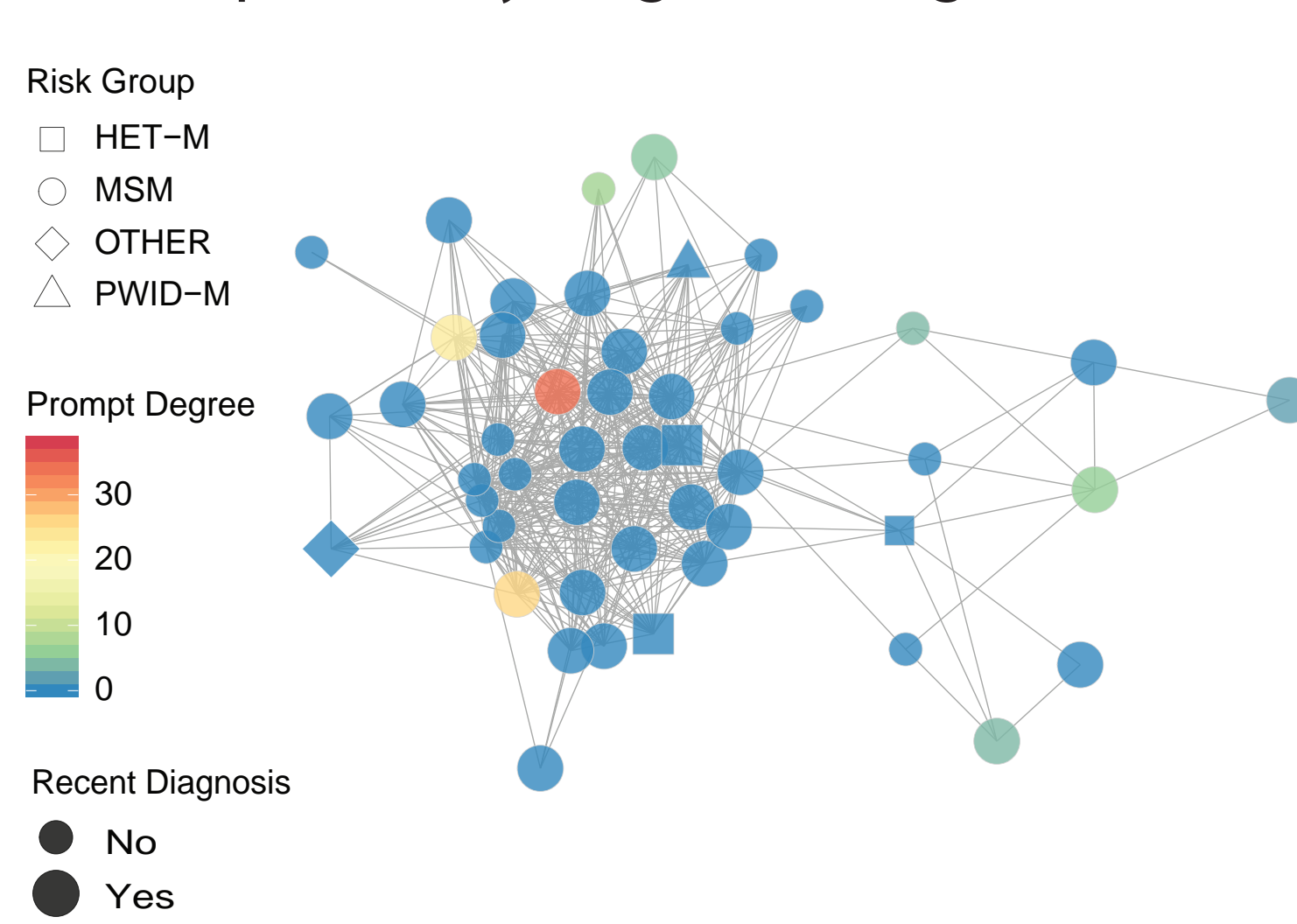
\*P<0.01

### Clusters with HIV diagnoses 2017-2019



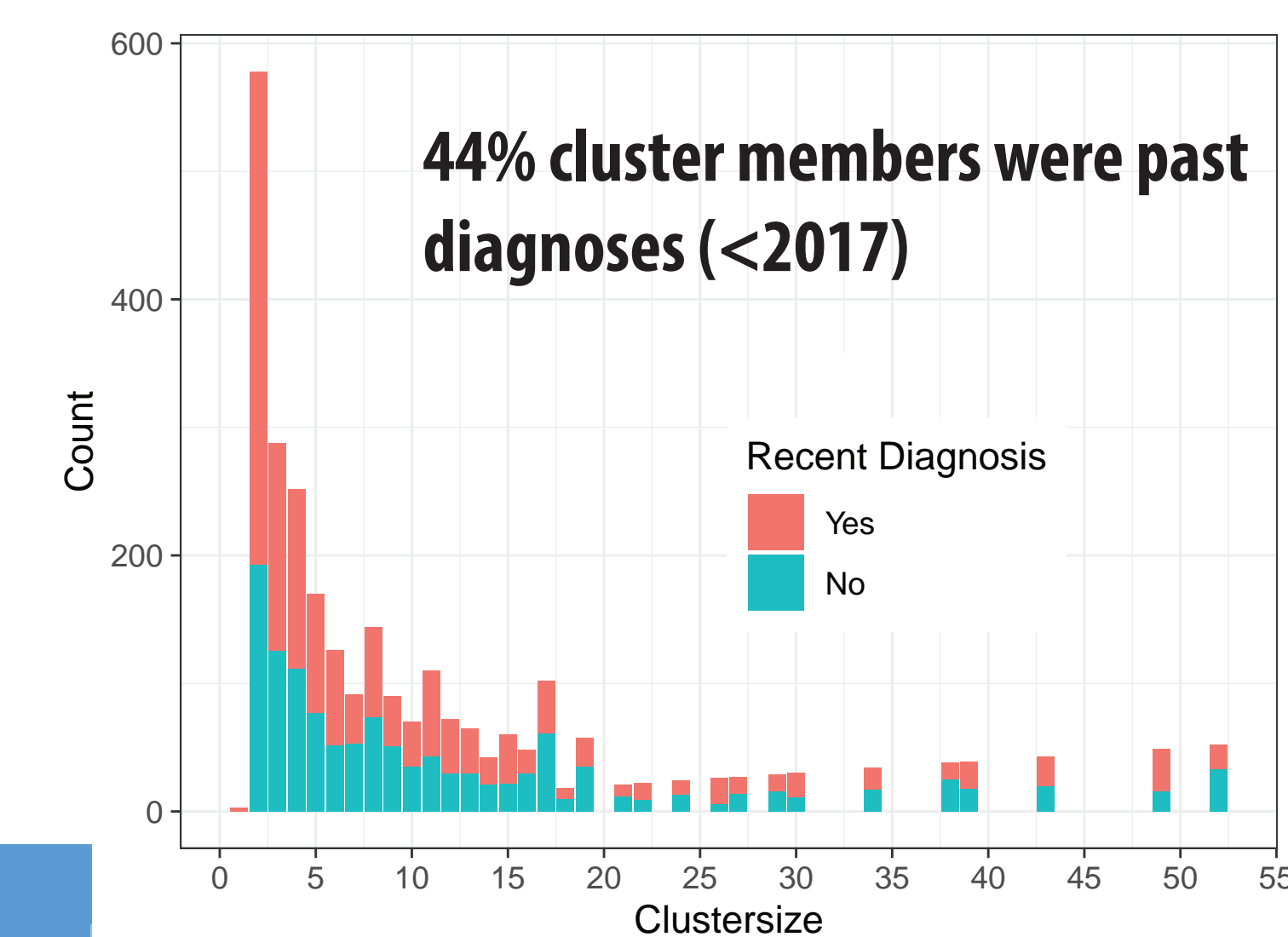
### Example Cluster 49 members

- 33 Recent Diagnoses
- 9 Prompt Cases
- Prompt Density (avg node degree) = 12



### 608 Clusters $\geq 1$ recent diagnosis

#### Distribution of Persons in Clusters



- 22% cluster members were Prompt cases** (no evidence viral suppression in 2019)

- Prompt cases have higher transmission risk potential** (time observed above 1500 c/mL): cases had a median of 68% average observed time viremic

- 53% Clusters (n=323/608) had  $\geq 1$  Prompt case**

- Number or recent diagnoses is correlated with number of prompt cases and the density of edges among prompt cases in clusters
- Clusters with  $\geq 5$  recent cases have mean **Prompt Density** of 6.2 vs. 0.8 for clusters <5 recent cases (average node degree among all Prompt cases in cluster)
- Priority clusters** defined as  $\geq 5$  recent cases and prompt density >5 yields 45 clusters

### Characteristics of Clusters by Number of Recent Diagnoses

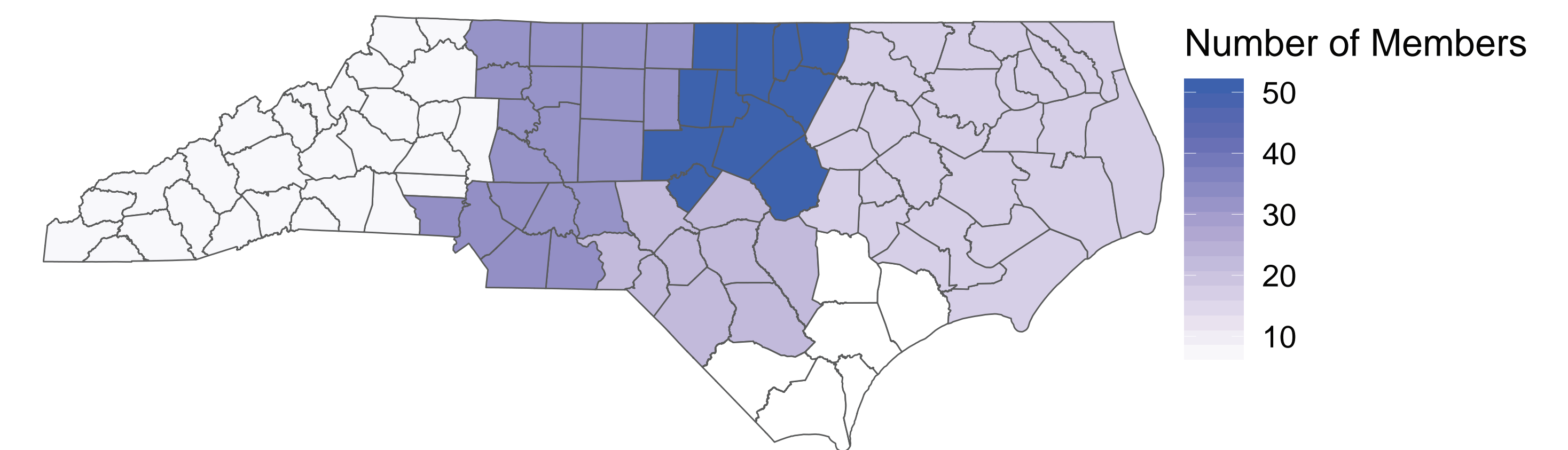
Mean (SD)	Number of Recent Diagnoses		Total (n=608)
	$\geq 5$ (n=71)	<5 (n=537)	
<b>Cluster Size</b>	18.1 (15.1)	4.2 (6.1)	5.8 (8.9)
<b>Prompt Density*</b>	6.2 (4.6)	0.8 (1.2)	1.5 (2.6)
<b>Prompt Cases*</b>	3.4 (2.8)	0.7 (1.0)	1.0 (1.6)
n (%)			
0	9 (12.7%)	274 (51.0%)	283 (46.5%)
1	12 (16.9%)	177 (33.0%)	189 (31.1%)
2-9	47 (66.2%)	86 (16.0%)	133 (21.9%)
$\geq 10$	3 (4.2%)	0 (0.0%)	3 (0.5%)
<b>Recent Density</b>	8.3 (5.0)	2.0 (1.7)	2.7 (3.1)
<b>Recent Diagnoses</b>	9.0 (5.2)	1.7 (0.9)	2.6 (3.1)

\*P<0.01

## Conclusions

- We developed a system to automate cluster detection and analysis using statewide surveillance data allowing **dynamic reporting** as new data are available
- >50% of recent diagnoses (2017-2019) were in clusters; 44% of members were **past diagnoses** with <1.5% genetic distance to recent diagnoses
- We developed **metrics to prioritize clusters** based on number of recent diagnoses and **high network connectivity** of individuals without evidence of viral suppression
- Allocation of **intensified retention support** and partner services to such prioritized clusters may be high yield for field services

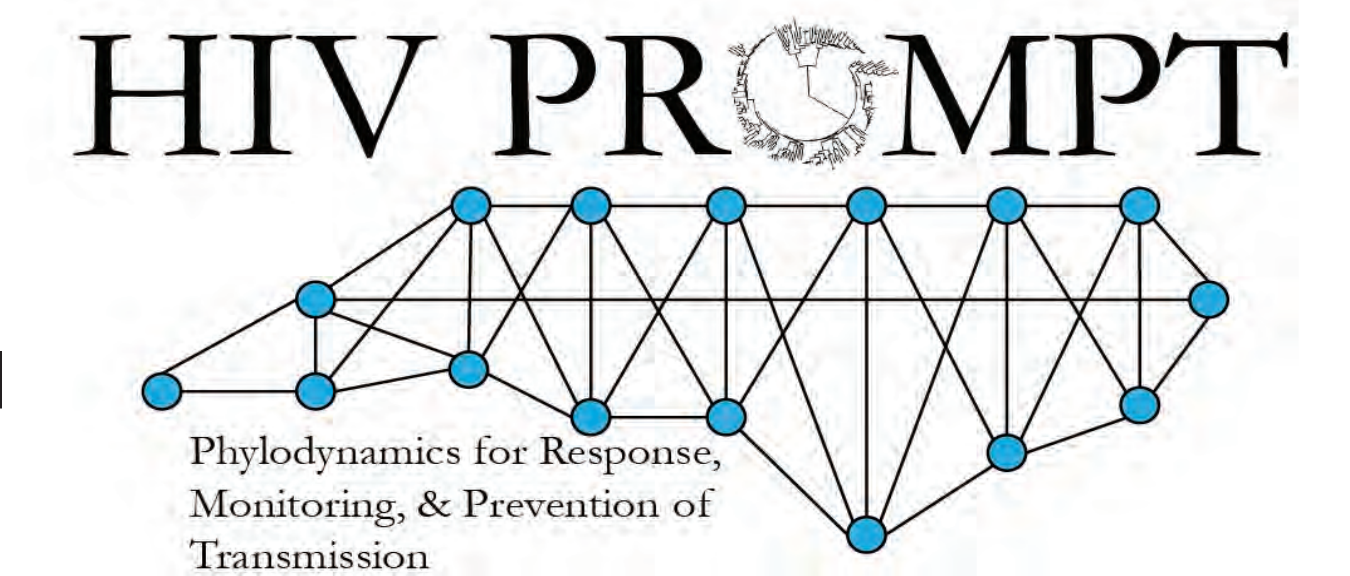
### Prompt Members in 45 Priority Clusters by Field Service Region



## Additional Information

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