Incident HIV Infection Drives Community HIV Cluster Growth

1064

Antoine Chaillon[1], Tom Chen[2], Alan Wells[1], Ravi Goyal[1], Samantha Tweeten[3], Sanjay R. Mehta[1,4], **Susan J. Little[1]**

[1]University of California San Diego, San Diego, CA, USA , [2]Harvard Pilgrim Health Care Institute, Boston, MA, USA, [3]Public Health Services, County of San Diego, San Diego, CA, USA, [4]VA Medical Center San Diego, San Diego, CA, USA

BACKGROUND

- Molecular HIV surveillance (MHS) is routinely used by U.S. public health departments to monitor HIV transmission dynamics within populations and regions.
- We analyzed MHS data to identify potential drivers of ongoing community transmission.

METHODS

- De-identified data from the Health and Human Services Agency (HHSA) of San Diego County were analyzed.
- A baseline HIV genetic network was inferred using a genetic distance of 0.5% (proxy for recent linkage) for all HIV diagnoses (2006-2016).
- Analysis performed using the Andersen-Gill model, a recurrent events extension of the traditional Cox proportional hazards model.
- Analyses focused on determining the influence of predefined covariates (**Table 1**) on rate of cluster growth.
- Putative transmission 'events' represent addition of a new genetically linked person with HIV (PWH) to a cluster (2017-2023).
- Time-varying covariates were imputed using the next-observation-carried-backward (NOCB).
  - Incident HIV was defined using the CD4 depletion model[1] to estimate duration of infection <6 months.
  - 'Local' infection refers to PWH diagnosed in San Diego County.

Table 1. Cluster properties associated with future cluster growth

Variable	log(rate)	rate	SE log(rate)	z	Pr(>|z|)
Cluster Size	0.760	2.140	0.040	**19.100**	**0.000**
Prop. Acute/Early HIV	0.882	2.420	0.235	**3.750**	**0.000**
Prop. Hispanic	0.199	1.220	0.154	1.290	0.198
Prop. Local	1.040	2.840	0.257	**4.050**	**0.000**
Prop. IDU	0.181	1.200	0.273	0.664	0.507
Prop. MSM	0.155	1.170	0.166	0.936	0.349
Prop. Unsuppressed	0.105	1.110	0.186	0.564	0.573

Abbreviations: IDU=injection drug use, MSM=men who have sex with men, Unsuppressed=VL>200 copies/ml

Incident HIV infection is significantly associated with future community level HIV transmissions.

RESULTS

- 2,088 PWH with at least one HIV sequence were included in the analysis (**Table 2**).
- Among the 2,088 PWH, the HIV sequence was collected a mean of 117 days following the date of HIV diagnosis (IQR 41).
- Among the 2,088 PWH, 1,153 (55%) had prevalent infection and 683 (33%) had incident infection.
- Overall, 16% of sequences were linked in 128 clusters (median size 2; range 2-9).
- **Cluster growth (≥3 nodes) rate was significantly associated with:**
  - Larger cluster size (Z score 19.1; p<0.05)
  - Proportion of PWH in the cluster with incident infection (Z score 3.8; p<0.05)
  - Proportion local (Z score 4.1; p<0.05)
- Cluster growth rate was not significantly associated with:
  - Proportion of Hispanic PWH in the cluster (Z score 1.3; p>0.05
  - Proportion of a) PWH and IDU (Z score 0.66; p>0.05), b) MSM with HIV (Z score 0.94; p>0.05), and c) PWH and unsuppressed viremia (Z score 0.56; p>0.05)

LIMITATION

Sensitivity of the CD4 depletion model to estimate incident infection is poor (55%[2]) and may also overestimate the proportion of PWH with incident infection[2].

CONCLUSIONS

This is the first study to utilize routinely collected public health data to demonstrate that incident infection is significantly associated with an increased rate of community-level HIV transmissions. Incident HIV infection has been shown by our group[3,4] and others[5] to be associated with HIV transmission, but not using routinely collected County-wide public health data. Cluster size has previously been associated with cluster growth.

The lack of association between viral suppression and recent bacterial STI and cluster growth may be related to suboptimal laboratory reporting of clinical data to the public health department, occurrence of unsuppressed VL **prior** to documentation of a new PWH joining a cluster, or incomplete sampling of the HIV network.

These findings support the importance of incident HIV infection as a driver of community level HIV transmissions. These findings also support widespread rapid initiation of antiretroviral therapy (ART) to limit transmission among PWH, particularly those with incident HIV infection.

Table 2	Clustering (N=344)	Not clustering (N=1744)	Overall (N=2088)
Sex at Birth			
F	41 (11.9%)	203 (11.6%)	244 (11.7%)
M	284 (82.6%)	1431 (82.1%)	1715 (82.1%)
Missing	19 (5.5%)	110 (6.3%)	129 (6.2%)
Age at Diagnosis			
Mean (SD)	34.2 (11.7)	36.6 (12.3)	36.2 (12.2)
Race			
Hispanic, any race	188 (54.7%)	881 (50.5%)	1069 (51.2%)
Not Hispanic, Asian	6 (1.7%)	78 (4.5%)	84 (4.0%)
Not Hispanic, Black	26 (7.6%)	224 (12.8%)	250 (12.0%)
Not Hispanic, Multi-race	15 (4.4%)	52 (3.0%)	67 (3.2%)
Not Hispanic, White	88 (25.6%)	403 (23.1%)	491 (23.5%)
Not Hispanic, American Indian/Alaska Native	0 (0%)	5 (0.3%)	5 (0.2%)
Not Hispanic, Native Hawaiian/Pacific Islander	0 (0%)	3 (0.2%)	3 (0.1%)
Missing	21 (6.1%)	98 (5.6%)	119 (5.7%)
Locality at Diagnosis			
Outside SD County	34 (9.9%)	428 (24.5%)	462 (22.1%)
SD County	283 (82.3%)	1155 (66.2%)	1438 (68.9%)
Missing	27 (7.8%)	161 (9.2%)	188 (9.0%)
Stage of HIV infection			
Incident	141 (41.0%)	542 (31.1%)	683 (32.7%)
Prevalent	166 (48.3%)	987 (56.6%)	1153 (55.2%)
Missing	37 (10.8%)	215 (12.3%)	252 (12.1%)
Viral suppression (baseline)"			
Suppressed	15 (4.4%)	74 (4.2%)	89 (4.3%)
Unsuppressed	299 (86.9%)	1539 (88.2%)	1838 (88.0%)
Missing	30 (8.7%)	131 (7.5%)	161 (7.7%)
HIV RNA level (baseline)			
Mean (SD)	520000 (1610000)	556000 (1710000)	550000 (1690000)
Missing	30 (8.7%)	131 (7.5%)	161 (7.7%)
CD4 T cell count (baseline)			
Mean (SD)	470 (274)	401 (292)	412 (290)
Missing	4 (1.2%)	18 (1.0%)	22 (1.1%)

ACKNOWLEDGEMENTS

Funding provided by the Health Resources and Services Administration (HRSA)

References:

1. Song R, et al. (2017). *JAIDS;* 74(1):3-9.
2. Tang ME, et al. (2023). AIDS; 37(10): 1617-1624.
3. Little SJ, et al. (2021). *Clin Infect Dis;* 73:842-49.
4. Little SJ, et al. (2014). *PLoS One* 9(6): e98443.
5. Li Z, et al. (2019). *MMWR Rep*. 68:267-93.

AUTHOR CONTACT INFORMATION

Susan J. Little, MD
slittle@health.ucsd.edu