EXPLOSIVE HIV AND HCV EPIDEMICS DRIVEN BY NETWORK VIREMIA

Steven J. Clipman,[1] Shruti H. Mehta,[1] Aylur K. Srikrishnan,[2] Katie JC. Zook,[3] Shobha Mohapatra,[2] Priya Duggal,[1] Saravanan Shanmugam,[2] Paneerselvam Nandagopal,[2] Muniratnam Suresh Kumar,[2] Elizabeth Ogburn,[1] Allison M. McFall,[1] Carl Latkin,[1] Gregory M. Lucas,[3] **Sunil S. Solomon**[1,3]

1 – Johns Hopkins Bloomberg School of Public Health, Baltimore, MD;
2 – YR Gaitonde Centre for AIDS Research and Education, Chennai, India;
3 – Johns Hopkins University School of Medicine, Baltimore, MD

2020 Conference on Retroviruses and Opportunistic Infections (CROI), Boston, USA; Abstract# 147
March 11, 2020

Background

- Misuse of opioids rapidly growing outside of the US
- India home to the largest number of opioid users globally
- India has an estimated 2.14 million PLHIV (Prevalence: 0.22%)[1]
- Dramatic variability exists among key populations:
  - PWID have the highest prevalence (6.3%) of all key populations
  - HIV incidence among PWID in India in 2016-17 as high as 18.5%[2,3]
- Gaps in understanding the role of networks on HIV/HCV transmission:
  - Limited network data from LMICs
  - Limited data on complete networks (sociometric) vs. immediate contacts (egocentric)
  - Nearly no data on behavior of networks over time and space and their influence on transmission

[1]NACO, India HIV Estimations 2017; Solomon SS, Lancet HIV 2019; [3]McFall AM, CROI 2020 Abstract# 00889

Objective

To characterize the role of egocentric, sociometric and sociospatial networks on HIV and HCV transmission among people who inject drugs (PWID) in New Delhi, India

METHODS

Study Design and Setting

- Spatial Network: a longitudinal cohort of PWID in New Delhi, India
  - Semi-annual follow-up visits
- Networks of PWID recruited
  - Recruitment initiated with 10 "index" participants

Study Population

Index participants:

1. 18 years of age or older
2. Provide written informed consent
3. History of injecting drugs for non-medicinal purposes in the prior 24 months
4. Part of evaluation RDS assessment of a cluster-randomized trial

Study Design and Setting

- Spatial Network: a longitudinal cohort of PWID in New Delhi, India
  - Semi-annual follow-up visits
- Networks of PWID recruited
  - Recruitment initiated with 10 "index" participants
  - "Index" participants recruited their injection network members who were the next wave of "index" participants

Study Population

Index participants:

1. 18 years of age or older
2. Provide written informed consent
3. History of injecting drugs for non-medicinal purposes in the prior 24 months
4. Part of evaluation RDS assessment of a cluster-randomized trial

Network members:

1. 18 years of age or older
2. Provide written informed consent
3. Recruited to participate in the study via network referral card
4. Unique identifier listed by recruiter matches participant (fun fact)

Study Population

Index participants:

1. 18 years of age or older
2. Provide written informed consent
3. History of injecting drugs for non-medicinal purposes in the prior 24 months

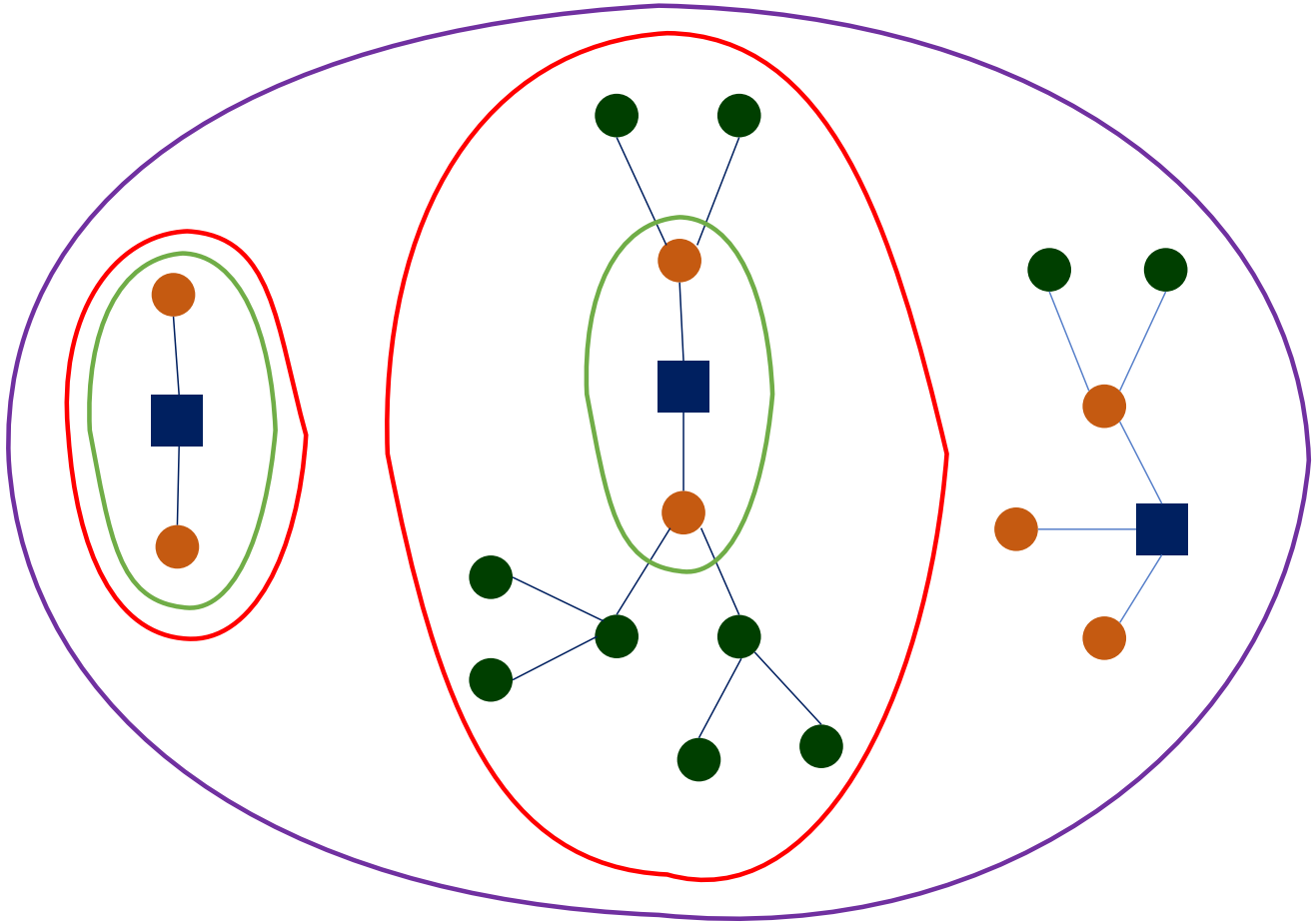
Network members:

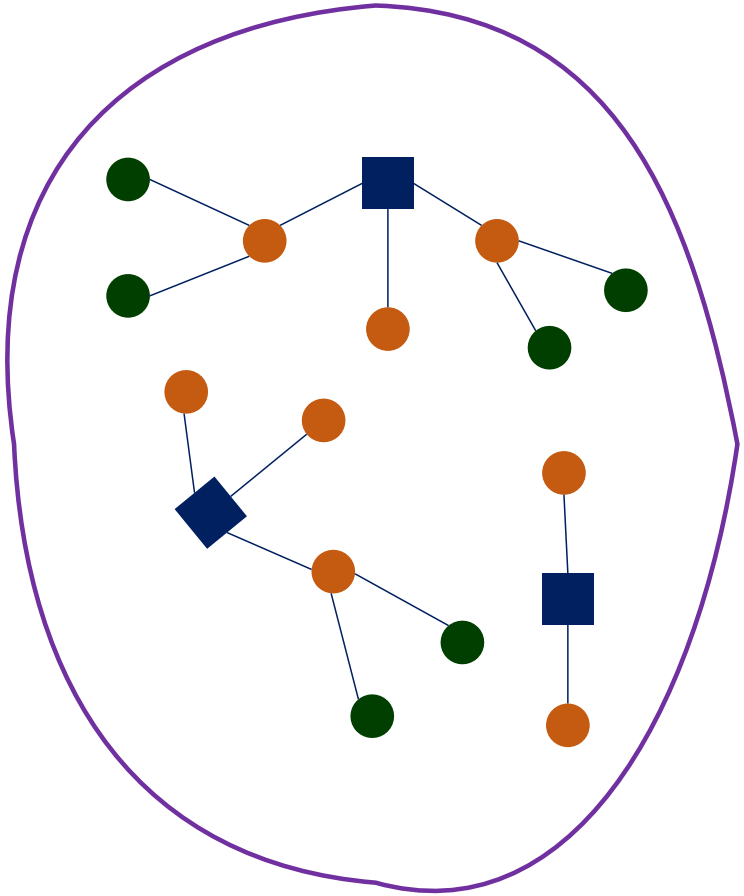
1. 18 years of age or older
2. Provide written informed consent
3. Recruited to participate in the study via network referral card

Duplicate participants (verified by biometric) were registered a second-time to establish cross-network linkages

Recruitment

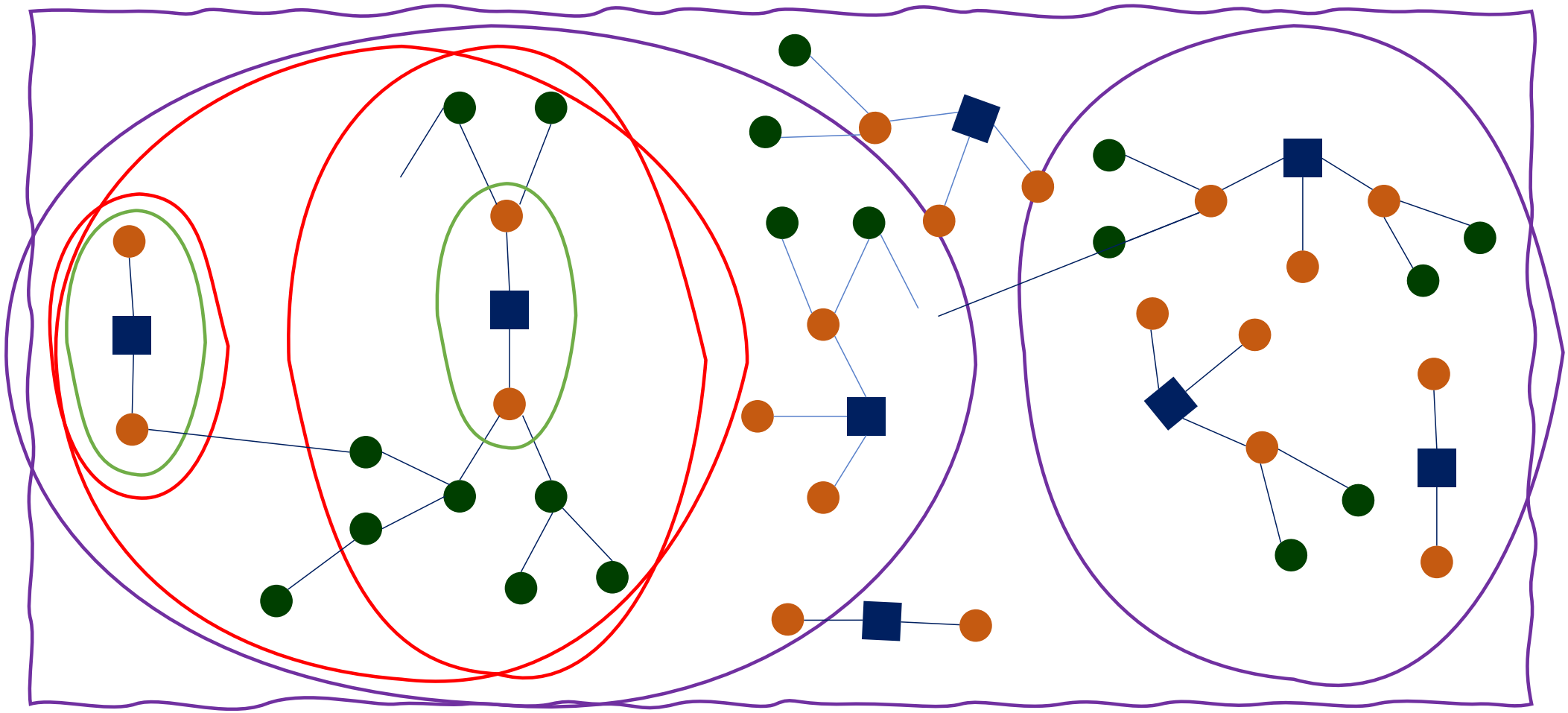
egocentric network
sociometric network
sociospatial network





Recruitment & Follow-up

egocentric network
sociometric network
sociospatial network



Data Collection

- Electronic interviewer-administered survey:
  - Egocentric network data
  - Spatial data (injection location, residence, travel)
  - Risk behavior
  - Access to HIV and HCV services
- Blood draw:
  - Rapid on-site HIV and HCV testing (with appropriate counseling and referrals as applicable)
  - HIV RNA and HCV RNA at central lab in Chennai
  - Specimen storage (HIV and HCV whole genome sequencing)

Statistical Methods

- Dynamic network structures were constructed and analyzed using custom Python code and visualized with JavaScript and Gephi
  - Person-nodes placed using a degree-dependent force-directed algorithm
  - Spatial nodes placed using GPS coordinates
- Network measures and path lengths were calculated using Python
  - Path length was defined as the number of steps between an index and a network member with the detectable HIV RNA (>150 copies/mL)
- Random forest machine learning feature selection algorithms were used to nominate candidate risk factors
  - Z-scores were calculated using randomly permuted shadow attributes for each feature
- Poisson regression was used to identify predictors of incident HIV

RESULTS

Recruitment Characteristics

- Recruitment was initiated with 10 indexes (all were male)
- 2512 PWID were recruited between November 2017 – July 2019
  - 20 cisgender women and 3 transgender women were recruited
- Median number of coupons handed out: 1 (Range: 0 – 6)
  - 75% (2437/3244) of coupons were returned
- Baseline disease prevalence:
  - Number HIV-infected (prevalence): 37.0% (928/2506)
    - Proportion with detectable HIV RNA: 92.6%
  - Number anti-HCV antibody positive (prevalence): 65.1% (1634/2512)
    - Proportion with chronic HCV (HCV RNA+): 79.6%

Follow-up Experience

- 787 of 1578 HIV negative at baseline had at least one follow-up visit
  - 14 were confirmed dead
  - 15/20 cisgender women had at least one follow-up visit
  - None of the three transgender women have had any follow-up to date

Participant Characteristics

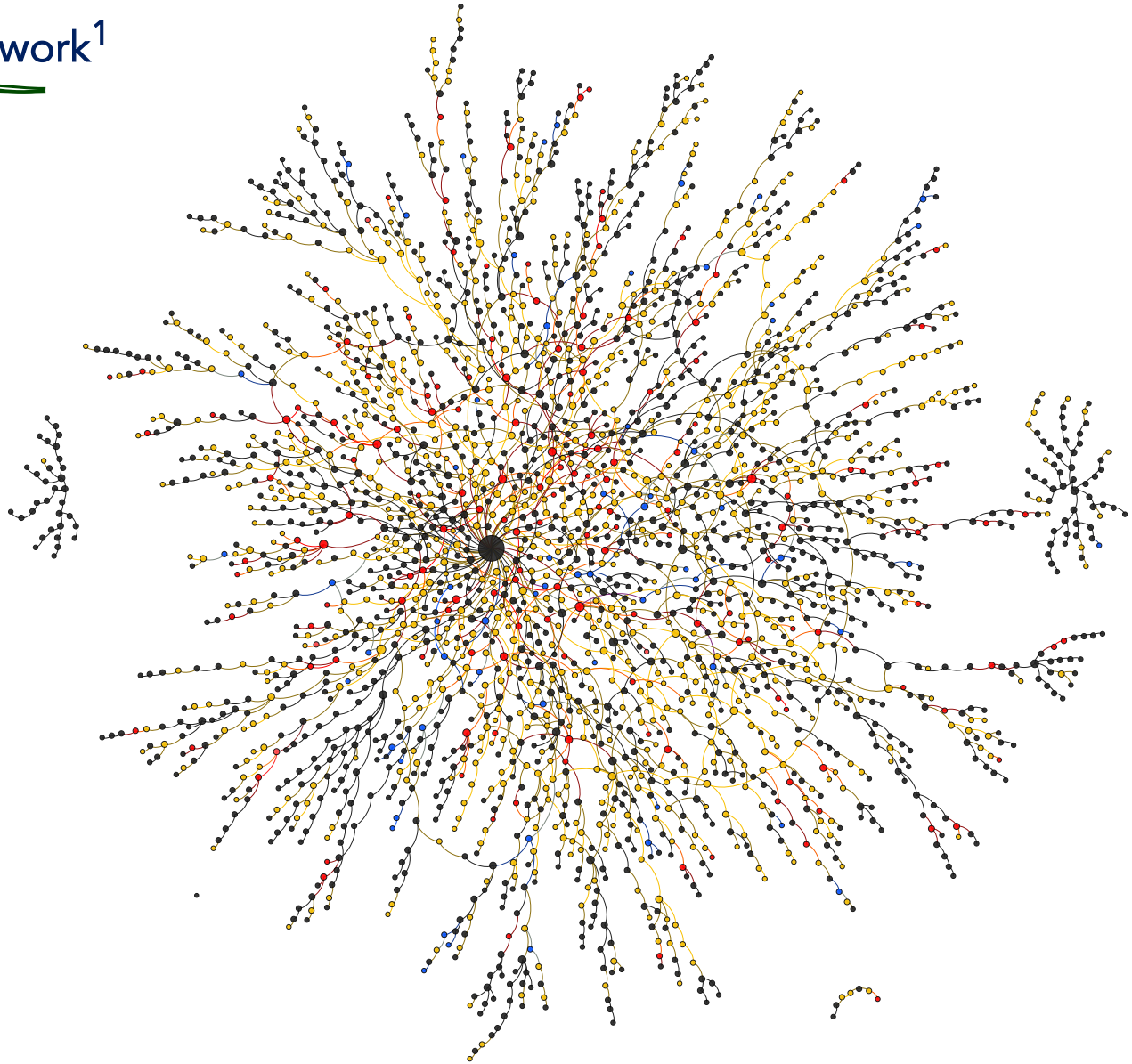
	HIV-negative at baseline with follow-up data (n=787)
Median age in years (IQR)	28 (IQR: 22 – 38)
Proportion male, n(%)	772 (98%)
Type of drug injected in prior 6 months, n (%) • Heroin • Pharmaceutical opioid	 213 (27%) 748 (95%)
Median number of times injected in prior 6 months (IQR)	360 (160 – 540)
Shared syringes in the prior 6 months, n (%)	333 (42%)

HIV and HCV Incidence

HIV incidence				
	Number HIV negative at baseline with follow-up	Person years of follow-up	Number of incident infections	Incidence rate (95% CI)
Overall	787	712	159	22.3 (19.1 – 26.2)
Men	772	700.25	158	24.1 (20.5 – 28.3)
Women	15	11.75	1	8.51 (1.2 – 60.4)

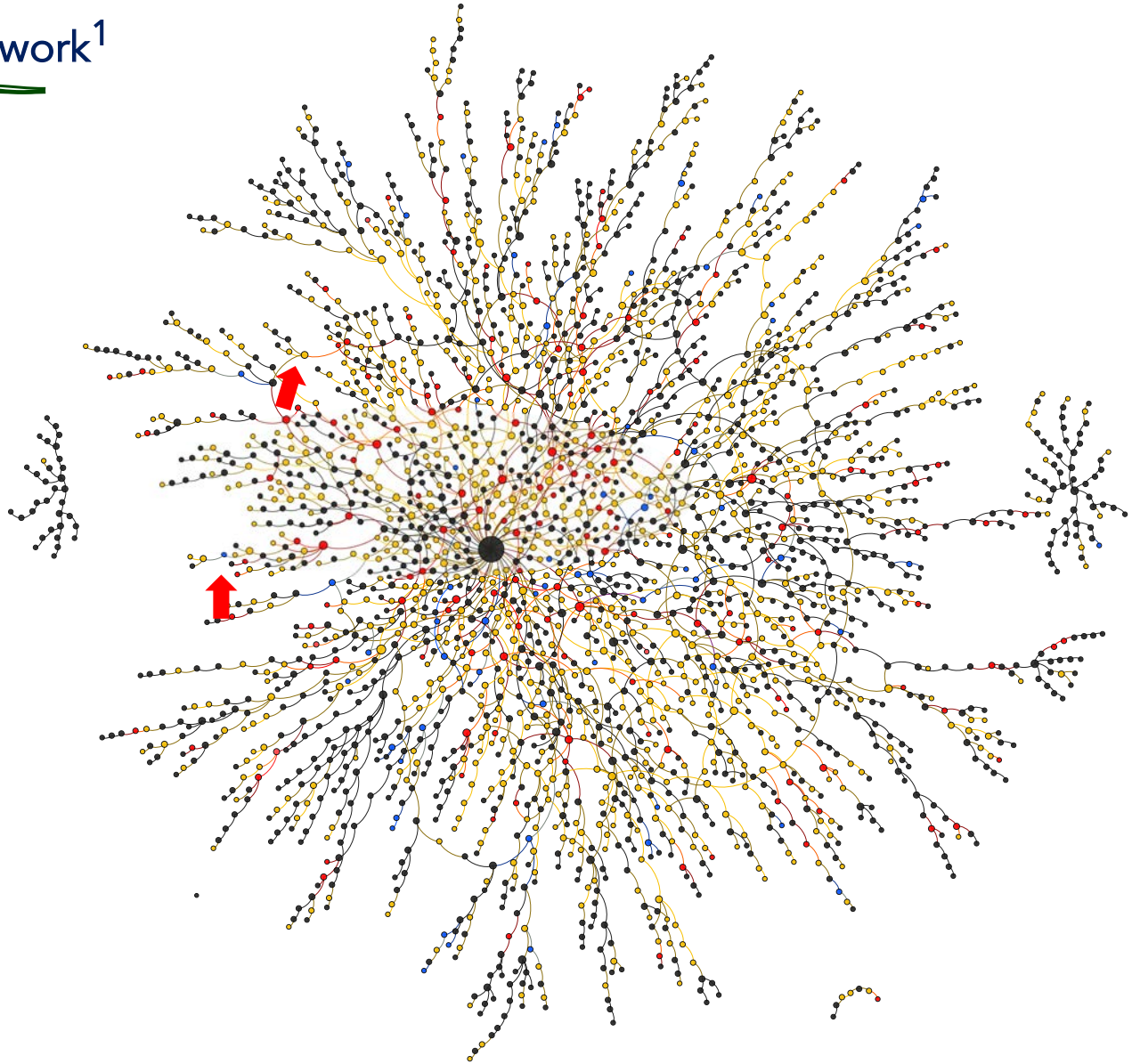
Primary HCV incidence (Antibody seroconversion)				
	Number anti-HCV negative at baseline with follow up	Person years of follow-up	Number of incident infections	Incidence rate (95% CI)
Overall	408	364.25	92	25.3 (20.5 – 31.1)
Men	404	359.75	92	25.6 (20.7 – 31.5)
Women	4	4.5	0	0

Sociometric Network[1]



[1]*Clipman SJ, CROI 2020 Abstract# 913*

Sociometric Network[1]



[1]*Clipman SJ, CROI 2020 Abstract# 00913*

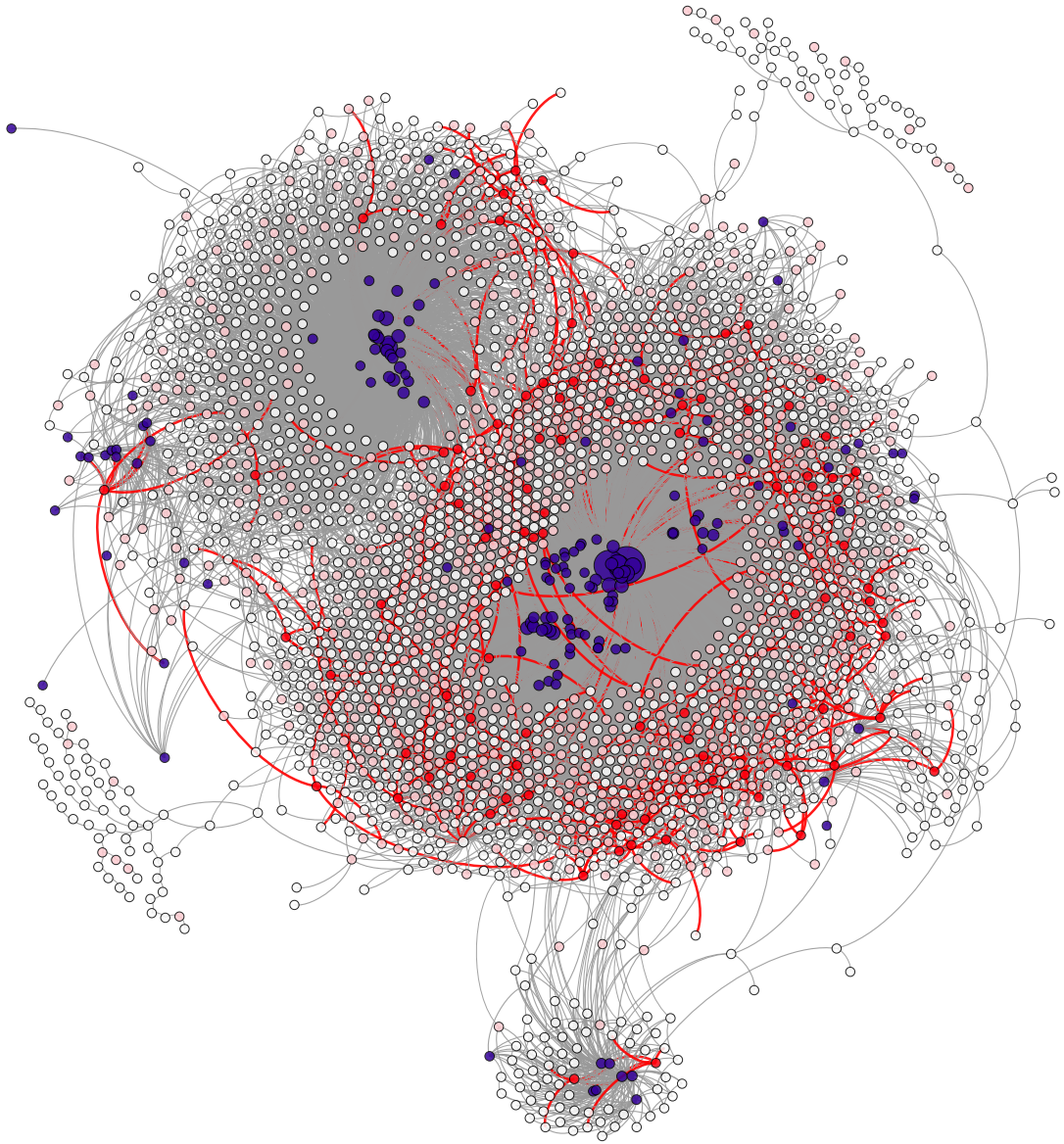
Predictors of HIV incidence

Characteristic	aIRR (95% CI)	aIRR (95% CI)	aIRR (95% CI)	aIRR (95% CI)	aIRR (95% CI)
Age (per 5-year increase)	0.82 (0.75 - 0.91)**	0.82 (0.75 – 0.90)**	0.81 (0.74 – 0.90)**	0.84 (0.75 - 0.95)*	0.81 (0.74 - 0.89)*
Recent injection/needle sharing (Shared syringes in prior 6 months)	2.70 (1.81 - 4.0)**	2.58 (1.75 – 3.80)**	2.47 (1.68 – 3.63)**	2.28 (1.55 - 3.34)**	2.16 (1.47 - 3.17)**
Injection frequency in past 6 months (per 50 injections)	1.05 (1.05 - 1.10)**	1.05 (1.05 – 1.10)**	1.05 (1.00 – 1.10)**	1.05 (1.00 - 1.10)*	1.05 (1.0 - 1.10)*
Network viremia (egocentric) (per unit increase in egocentric network members with HIV RNA >150 copies/mL)	–	1.31 (1.10 – 1.55)*	–	–	–
Path Distance (sociometric) (per unit increase in the shortest path length from index to a member with HIV RNA>150 copies/ml)	–	–	0.61 (0.47 – 0.81)**	–	0.69 (0.53 – 0.90)*
Injecting at Spatial Hotspot #40 (sociospatial)	–	–	–	3.40 (2.38 – 4.84)**	3.14 (2.20 – 4.49)**

* P-value < 0.05; ** P-value < 0.001

Sociospatial Network

Interact with this figure online:
Tiny.cc/sociospatial

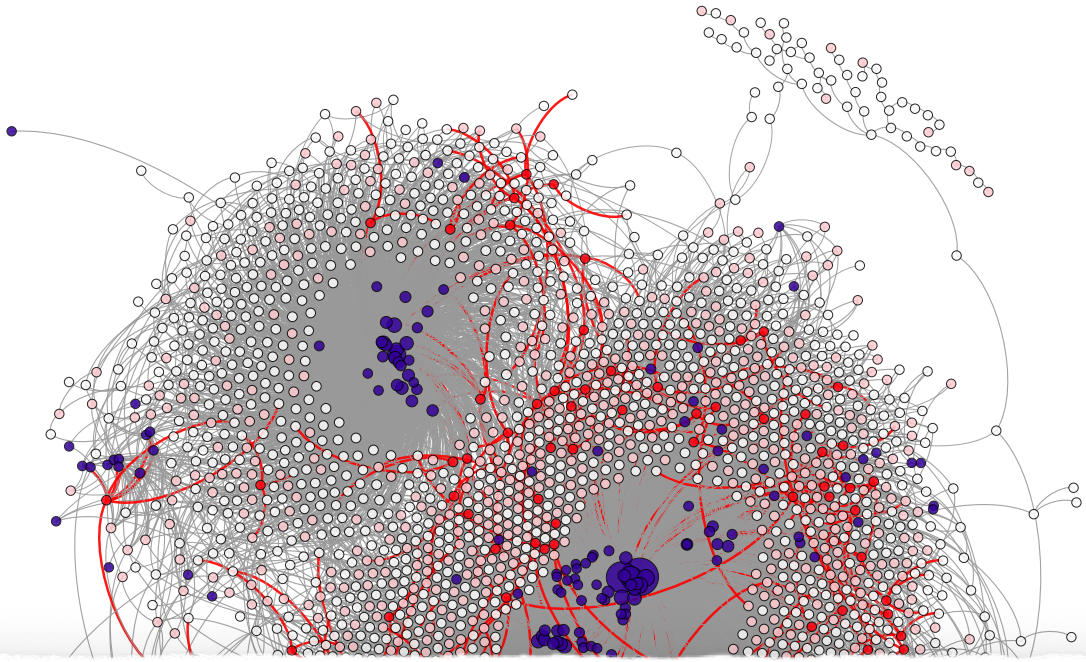


Legend

- Negative & Undetectable Prevalent HIV+
- Spatial Hotspot
- Prevalent HIV+ (Detectable VL)
- Incident HIV+

Sociospatial Network

Interact with this figure online:
Tiny.cc/sociospatial



Legend

- Negative & Undetectable Prevalent HIV+
- Spatial Hotspot
- Prevalent HIV+ (Detectable VL)
- Incident HIV+

113 (71%) incident infections reported injecting at Spatial Hotspot #40

For every increased step in the path to Hotspot #40, risk of incident HIV infection reduced by 23% (IRR: 0.77; 95%CI: 0.66, 0.90)

Limitations

- Incomplete network structure
  - 25% of coupons were not returned
  - Could be missing additional network connections
- Ongoing cohort study
  - Participants can transition status between HIV negative to positive, undetectable to detectable, etc.
- HCV incidence likely higher if we include re-infection
  - HCV RNA quantification of prospective samples planned
- Sequence data not available
  - HIV and HCV whole genome sequencing underway

Conclusions

- Extremely high-incidence of HIV and HCV in this cohort of PWID in India
  - Epidemic control not achievable without addressing growing burden of PWID in LIMCs
- Egocentric viremia and path distance support prior data from MSM/heterosexual populations on role of viral load in transmission
  - Sequence data required to support U=U among PWID
- Networks are dynamic and complicated
  - Spatial network was the strongest predictor of incidence in this cohort
- Incorporating the sociospatial dynamics of underlying networks into programming will be critical to "EHE"

Acknowledgements

- People who inject drugs who generously participate in research studies globally
- Research teams based in Baltimore, New Delhi and Chennai
- National AIDS Control Organisation (NACO), India
- Funding sources:
  - NIDA (R01DA041736, DP2DA040244)
  - JHU CFAR (P30AI094189)


LABORATORY
JACK&
Happy
Birthday