



Disentangling networks and their role in transmission of HIV and HCV among PWID

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Disclosures

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- Research grants, study product and consulting from Gilead Sciences

HIV in India

“Evidence for HTLV-III Infection in prostitutes in Tamil Nadu (India)”

Simoes et al. Indian J Med Res 1987; 85:335-8

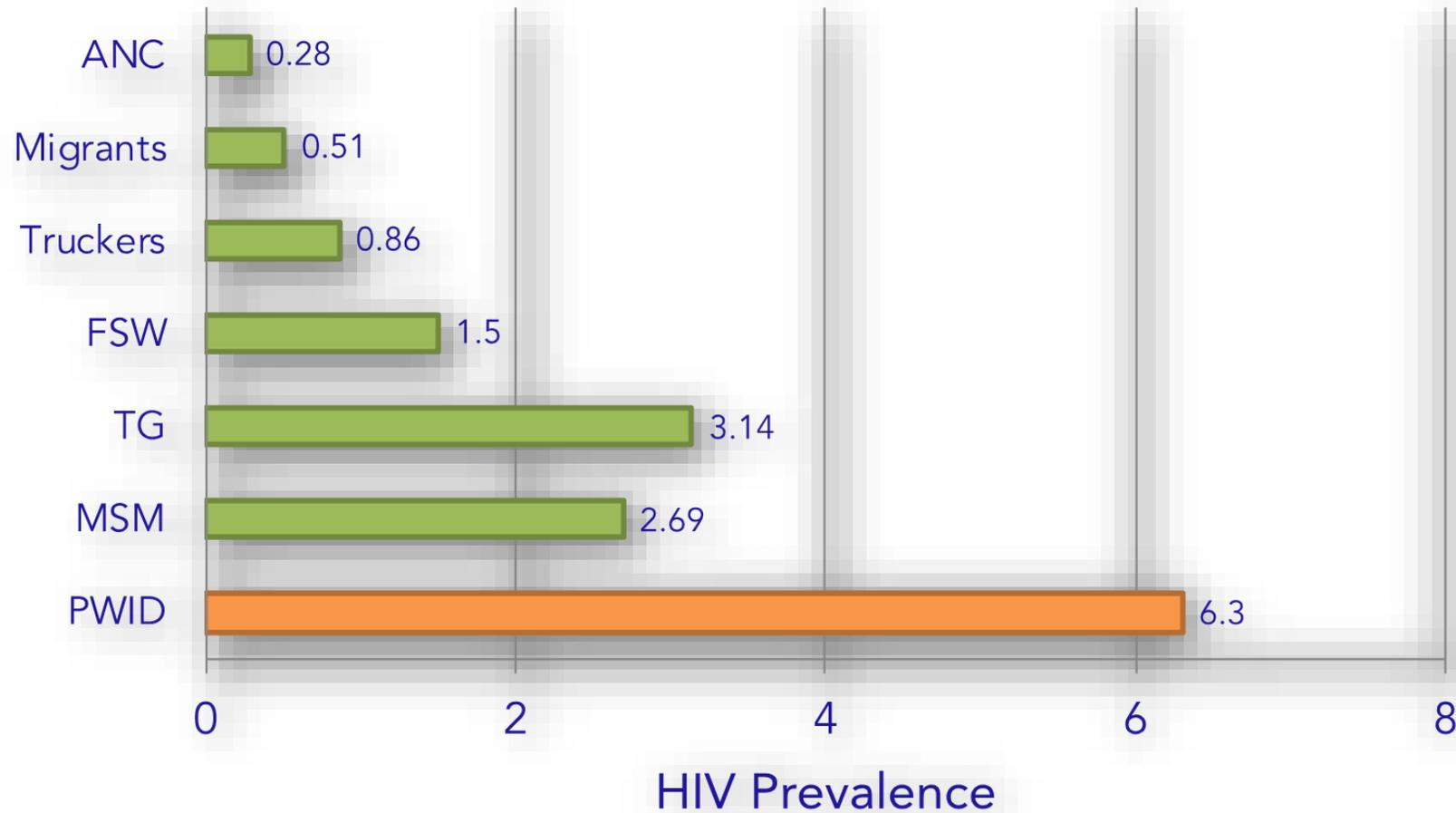


“Marriage, monogamy and HIV: a profile of HIV-infected women in south India”

Newmann et al. Int J STD AIDS 2000; 11:250-3



India: A concentrated HIV epidemic

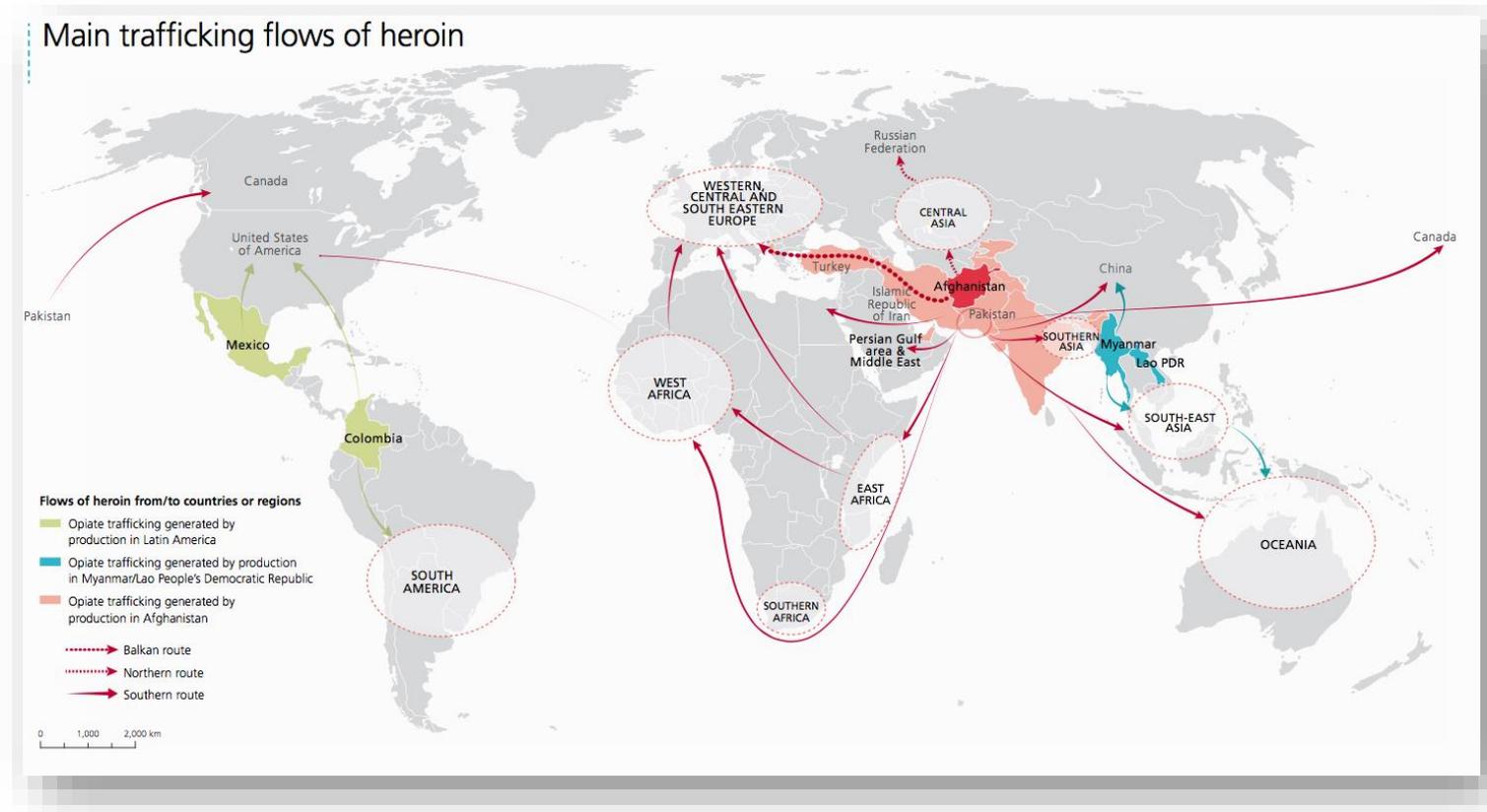


The beginning...

- It all started with one NIH supplement!
- Established one of the first longitudinal cohorts of PWID in Chennai, India (n=1,100)
 - Characterized HIV/HCV incidence and prevalence, natural history of HIV, natural history of drug use, liver disease and impact on families
- Demonstrated via a RCT that non-monetary vouchers incentives to improve linkage to care and ART initiation among PWID



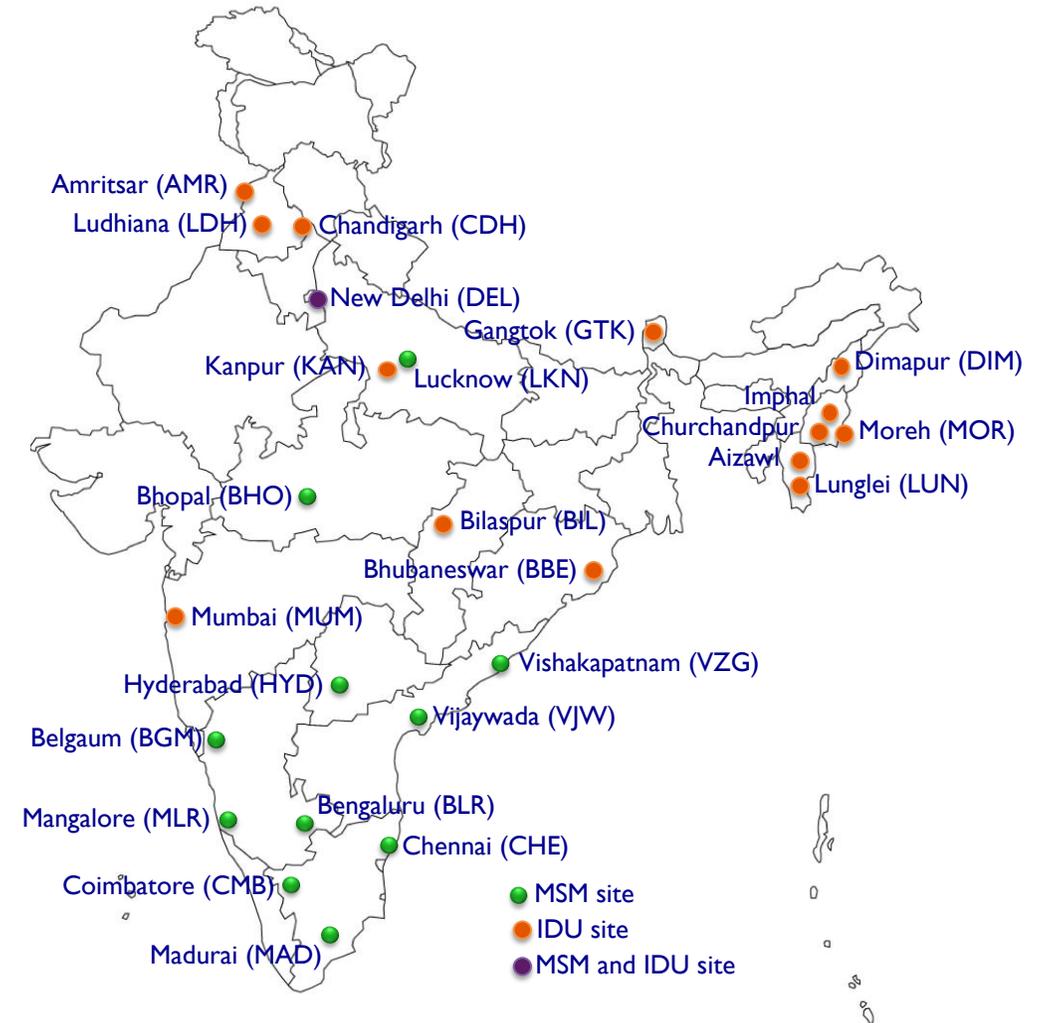
India's strategic location



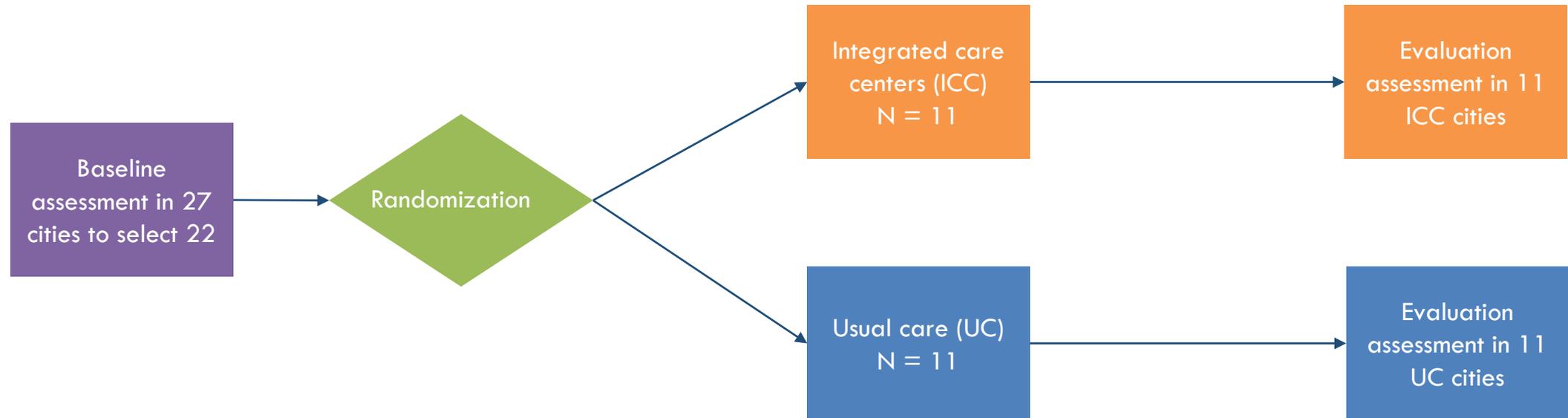
- Home to approximately 6 million opioid users
- Recent estimates suggest as many as 850,000 people who inject drugs

From Chennai to India....

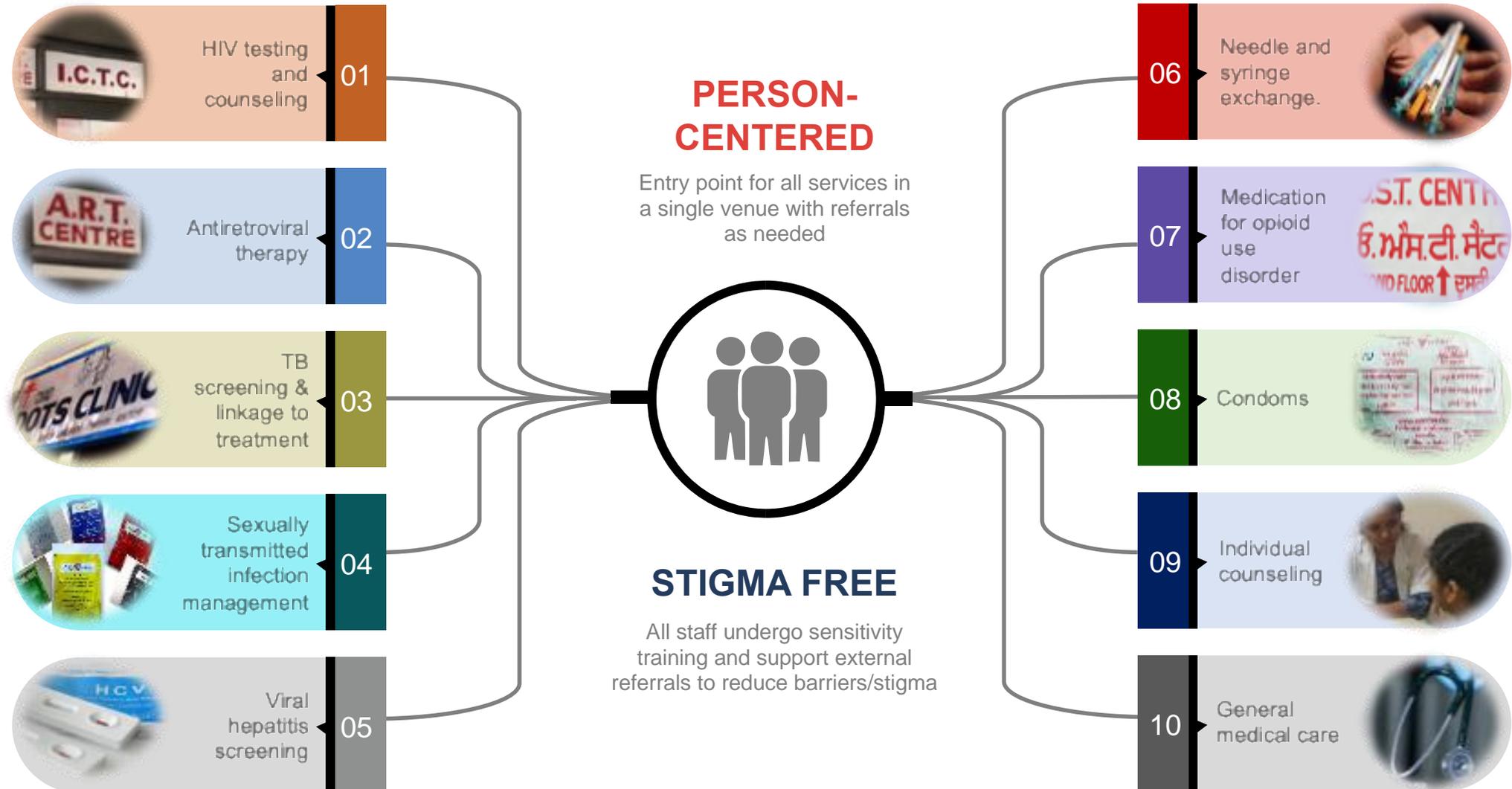
- Cluster randomized trial
 - ClinicalTrials.gov identifier:
NCT01686750
- Primary objective of trial:
Impact of integrated delivery of HIV prevention and treatment services in a non-discriminatory setting on uptake of HIV testing among PWID and MSM in India



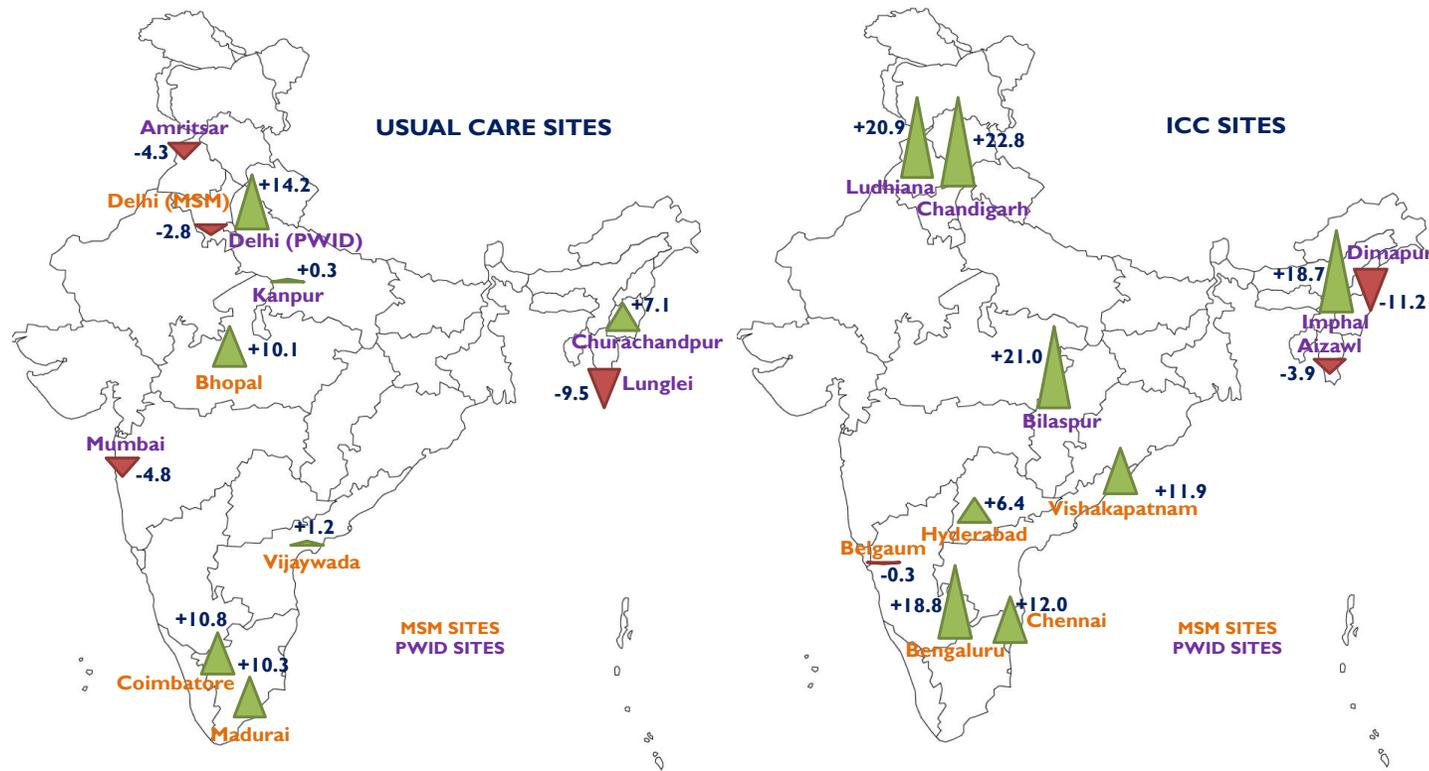
ICC: A Cluster-Randomized Trial



A “single window” model



ICCs improved testing but...



Recent HIV testing was 31% higher in intervention (ICC) vs. control sites ($p=0.09$)

A SINGLE WINDOW COMPREHENSIVE HIV PREVENTION AND CARE FACILITY: THE NEXT STEP IN HIV PROGRAMMING

EXECUTIVE SUMMARY

The National AIDS Control Programme (NACP) envisages ending AIDS as a public health threat by 2030 and has adopted the Fast Track targets of 90-90-90 to be achieved by 2020 that is 90% of People Living with HIV (PLHIV) who know their status; 90% of PLHIV who know their status on Antiretroviral Therapy (ART) and 90% of PLHIV on ART with suppressed viral load. Despite significant progress in the coverage of the HIV programme in India over the past two decades, there are still a considerable number of people who are left behind i.e they are not yet reached by the national programme efforts. Today, the ART centres are thought to be overburdened, and the NACP proposes models of ART decentralization and ART incorporation with other essential services for PLHIV and other at-risk/vulnerable populations.

The National Collaboration on AIDS (NCA) study was conducted by Johns Hopkins University, USA, Yeshwanth Raghunath Gaitonde Centre for AIDS Research and Education (YRGCARE), and the National AIDS Control Organisation (NACO), India in order to test the feasibility and acceptability of a single window approach to improve HIV service delivery for Men Who have Sex with Men (MSM) and Injecting Drug Users (IDU). The NCA study was implemented across 22 Indian cities where Integrated Care Centres (ICCs) were established.

The study validated the feasibility of setting up a single window comprehensive health care model in both public sector and private sector venues. The ICs provided a bouquet of HIV prevention and treatment services under a single roof and catered to a large number of clients, about a third of whom had not been reached through the traditional Targeted Intervention (TI) programmes. In conclusion, community-based care models that are non-Key Population (non-KP)-identified but in KP-enabling environments, delivering essential HIV prevention, treatment and other support services (e.g., mental health, non-communicable diseases) may potentially play a key role in ensuring India meets the 90-90-90 targets particularly for communities left behind, such as IDU, MSM and other Key Population (KP).

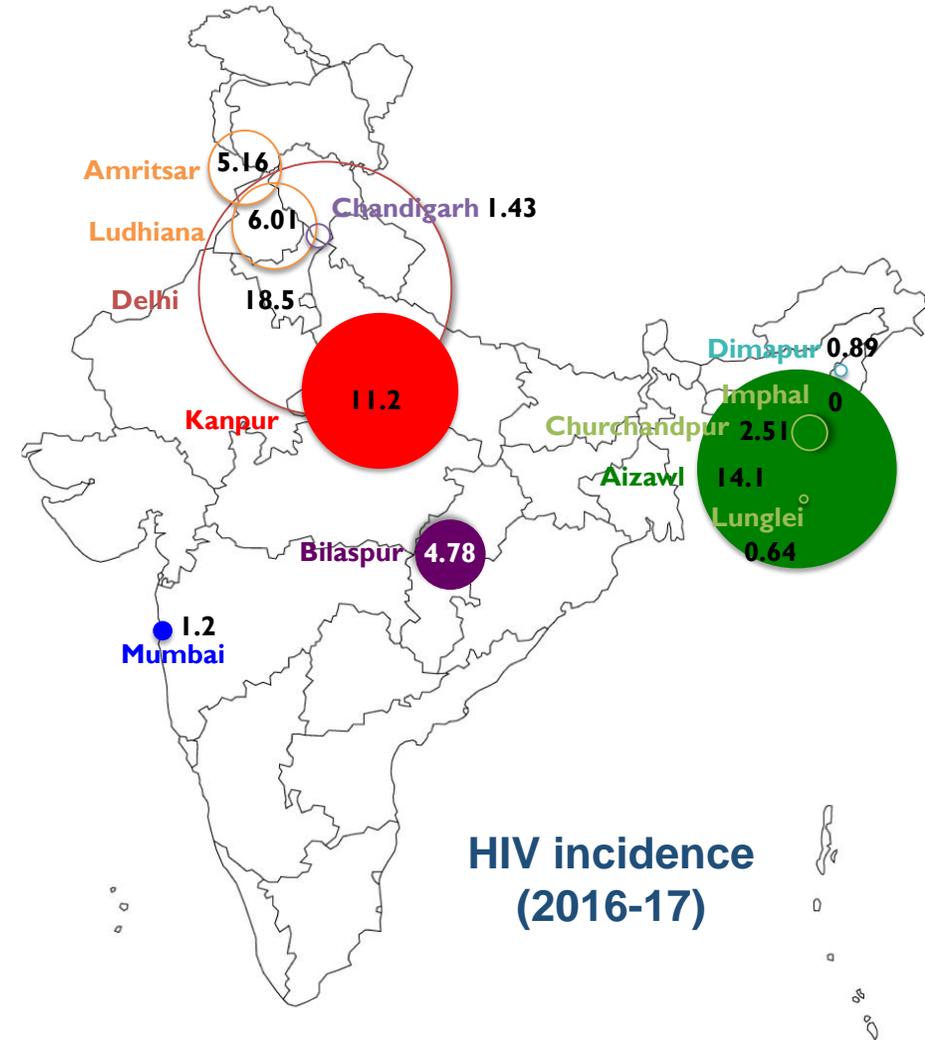
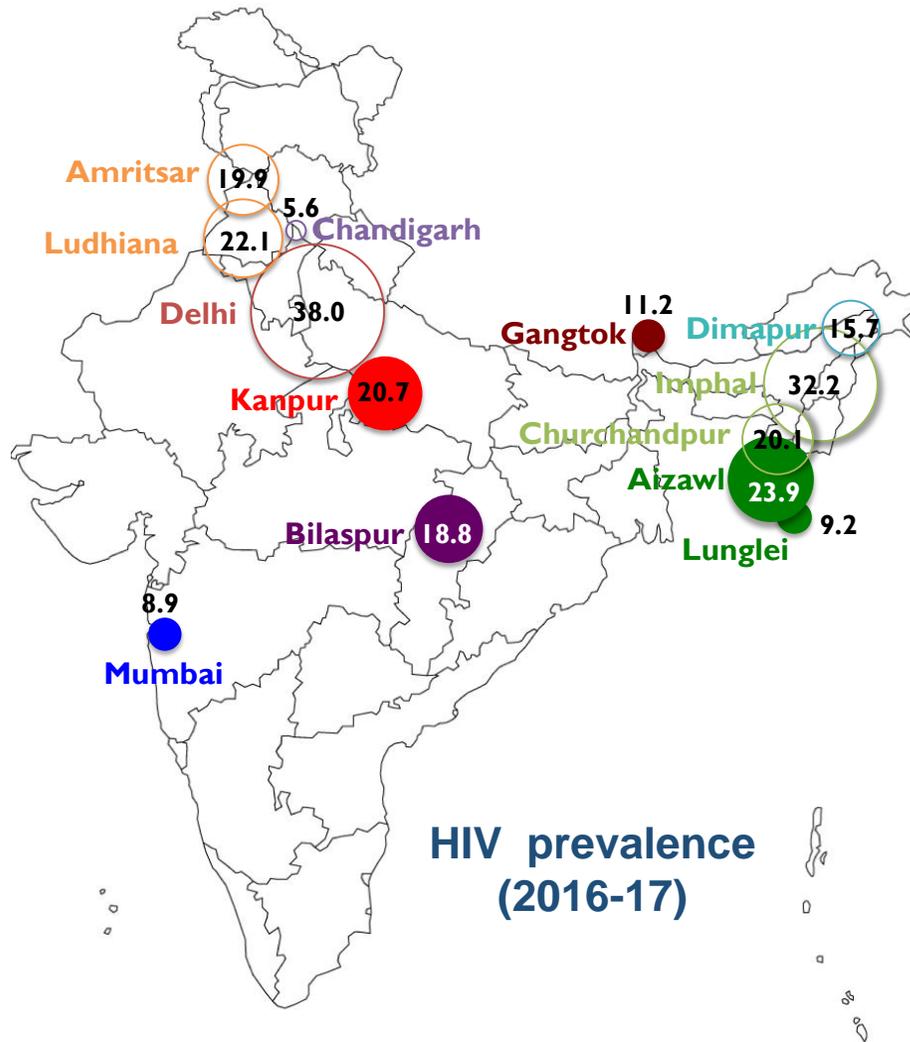
Sunil S Solomon^{1,2}, Prof Suniti Solomon¹, Allison M McFall², Aylur K Srikrishnan¹, Santhanam Anand¹, Shobini Rajan³, Vinita Verma³, Canjeevaram K Vasudevan¹, Pachamuthu Balakrishnan¹, Elizabeth L Ogburn², Prof Lawrence H Moulton², Muniratnam S Kumar¹, Kuldeep Singh Sachdeva¹, Oliver Laeyendecker², Prof David D Celentano², Prof Gregory M Lucas², Prof Shruti H Mehta²

The NCA study was **implemented across 22 Indian cities** where Integrated Care Centres (ICCs) were established.

Learnings from ICC

1. PWID continued to have a high burden of HIV

High burden of HIV...



Learnings from ICC

1. PWID continued to have a high burden of HIV
2. PWID networks highly interconnected

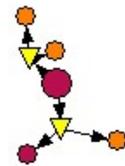
Interconnectedness of PWID...



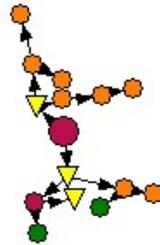
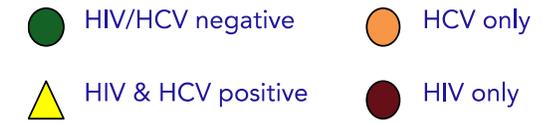
Recruitment of PWID in Kanpur



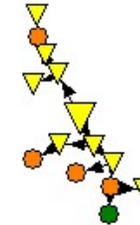
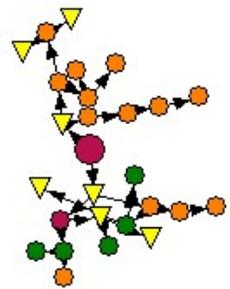
Recruitment of PWID in Kanpur



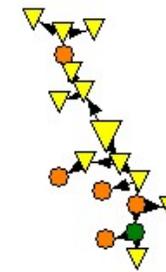
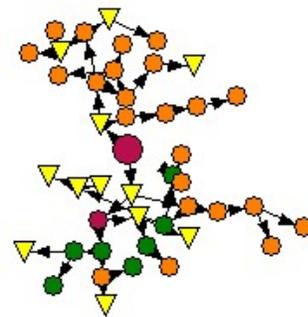
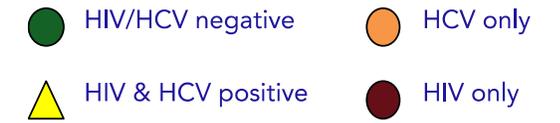
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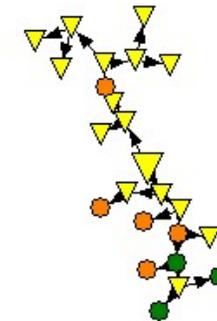
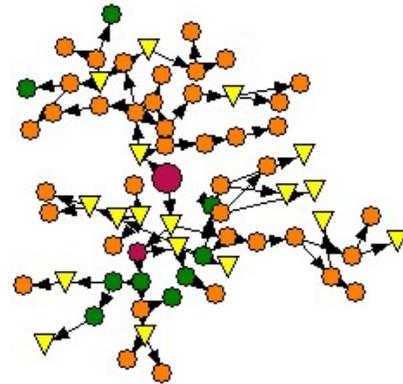
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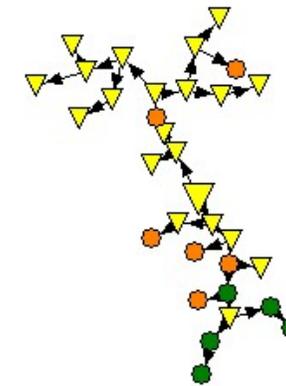
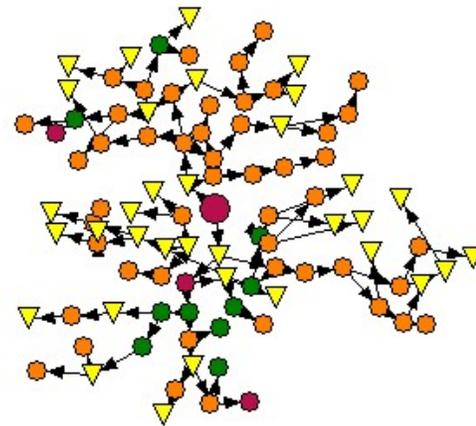
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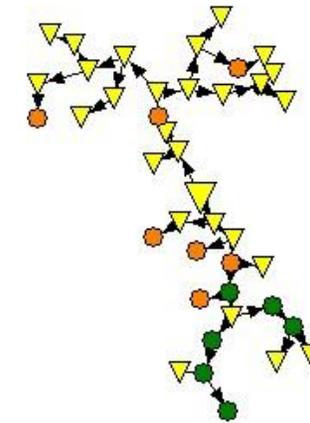
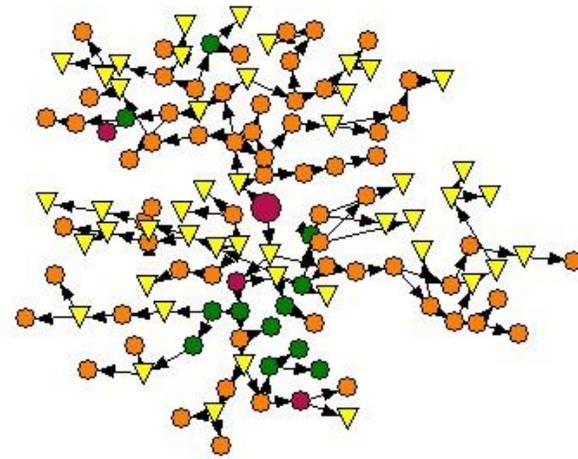
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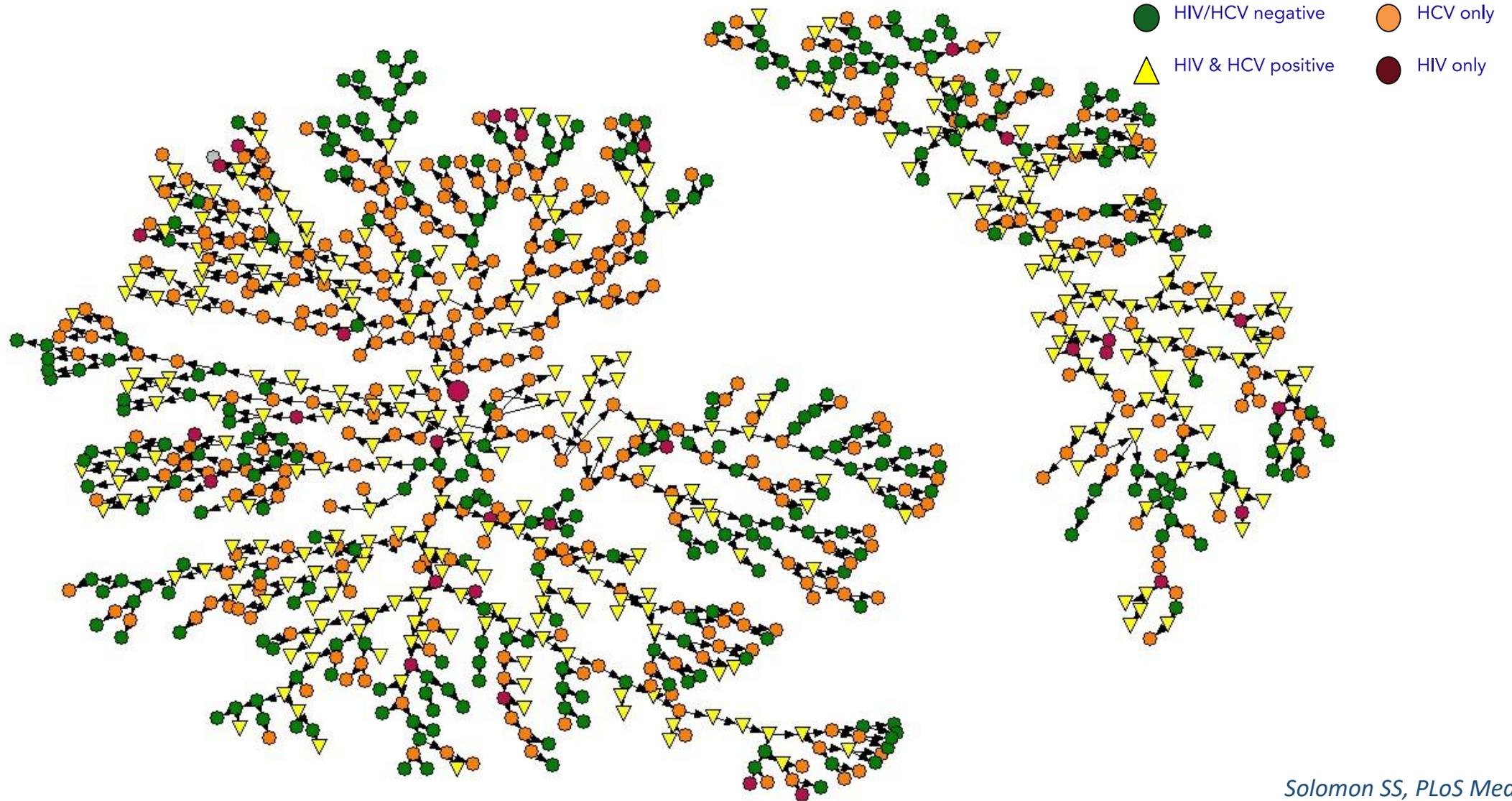
Recruitment of PWID in Kanpur



Recruitment of PWID in Kanpur



Recruitment of PWID in Kanpur



What we *didn't learn* from RDS...

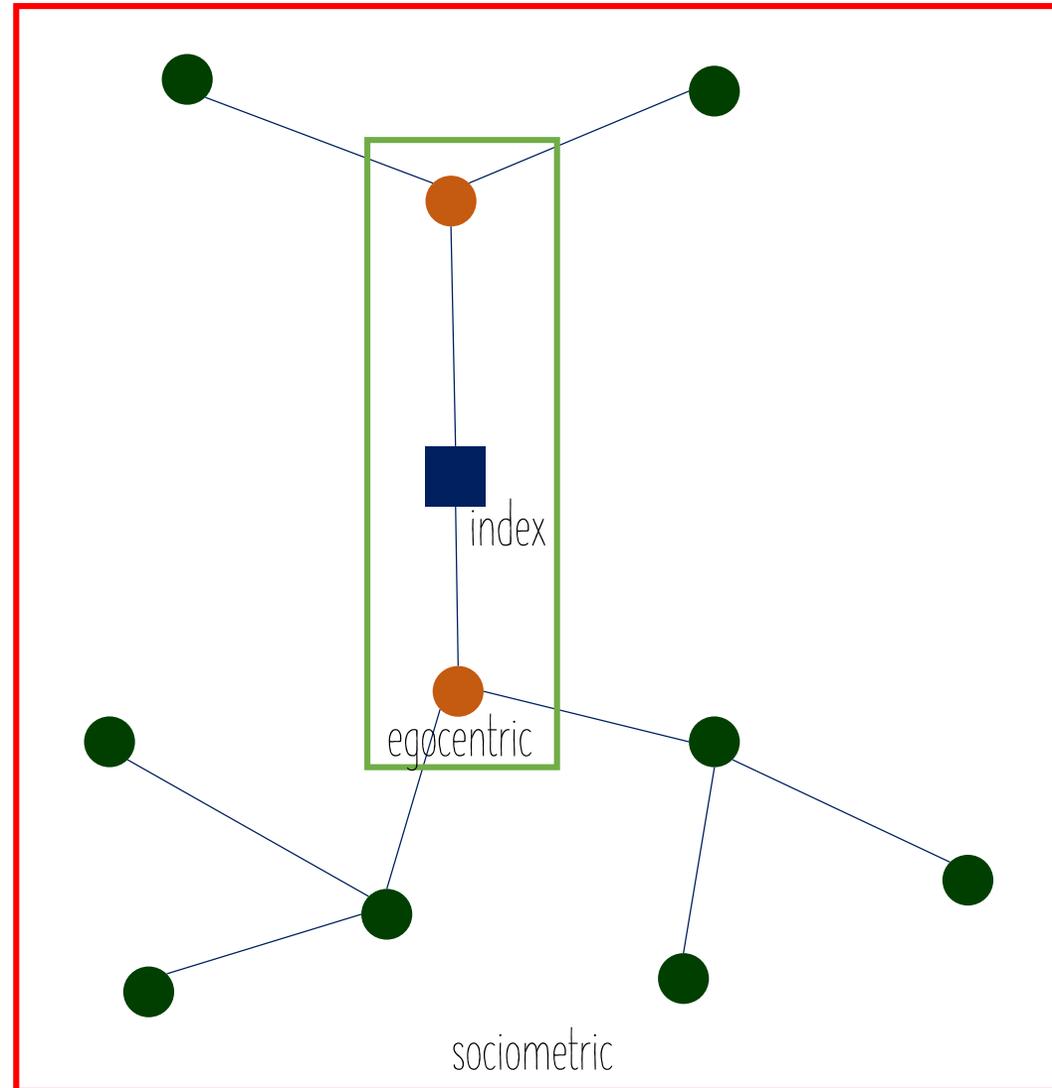
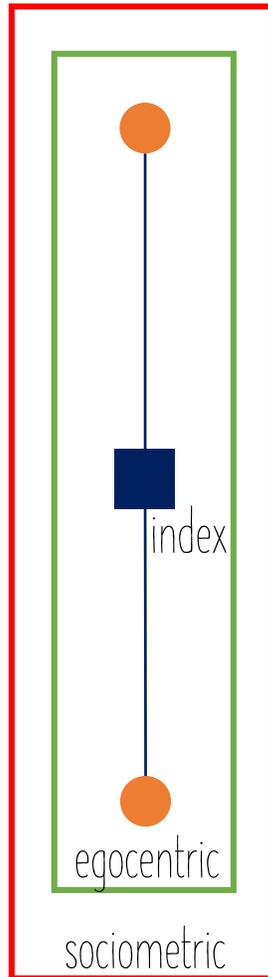
- In RDS, PWID recruit randomly from networks (not transmission networks)
- RDS does not capture complete network information (connections between participants recruited by different recruiters)
- Role of spaces in transmission not clearly understood

In order to prevent onward HIV/HCV transmission, need to know more about underlying network structure, overlap with space and time....

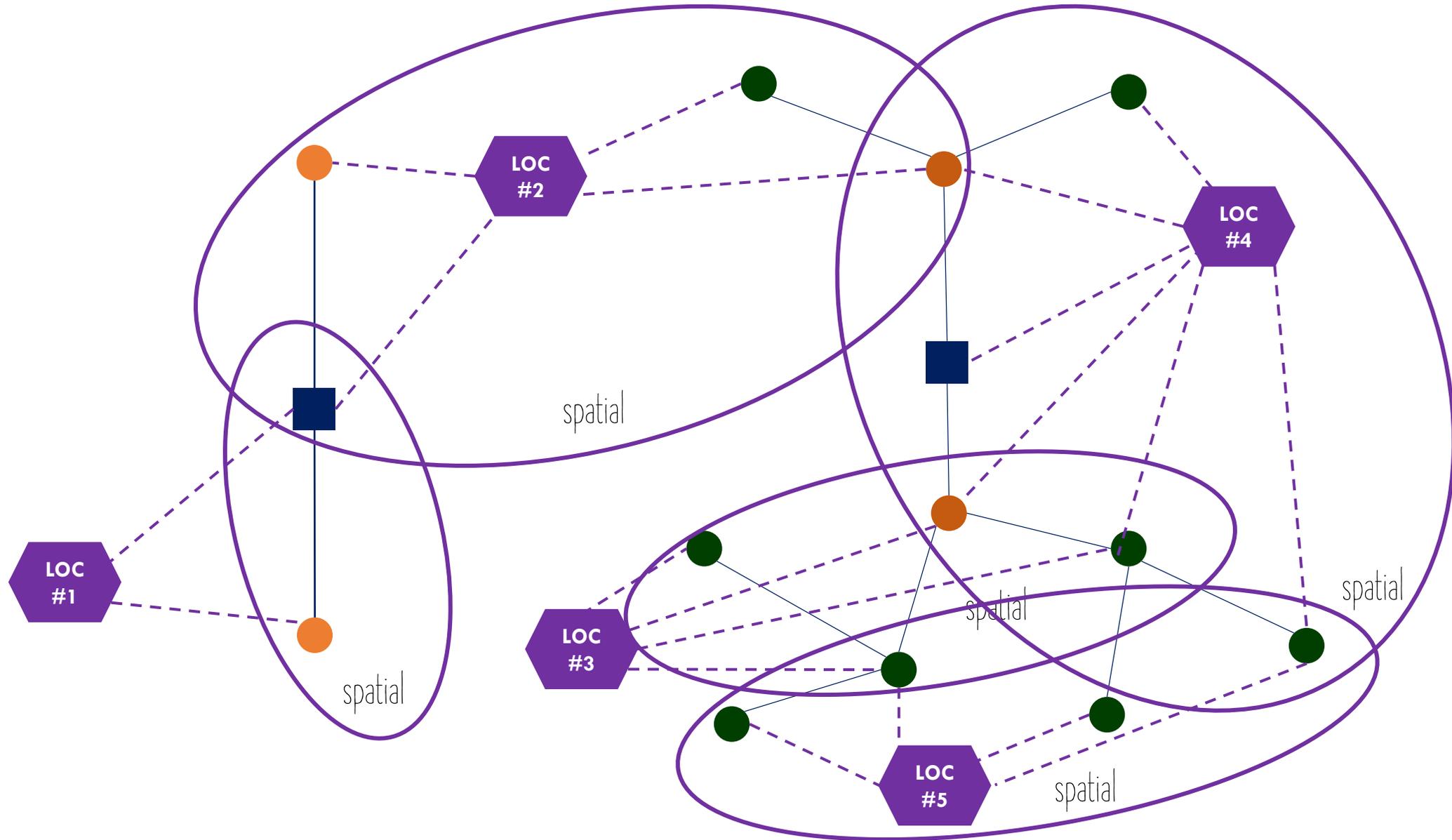
Spatial Network

- Longitudinal cohort of PWID in New Delhi, India
- **Objective:** To characterize the role of egocentric, sociometric, spatial and sociospatial networks on HIV and HCV transmission among people who inject drugs (PWID) in New Delhi, India
- Networks of PWID recruited
 - Recruitment initiated with “index” participants
 - “Index” participants recruited their active injection “network” members (injected with in prior month)
 - “Network” members served as next wave of “index” participants

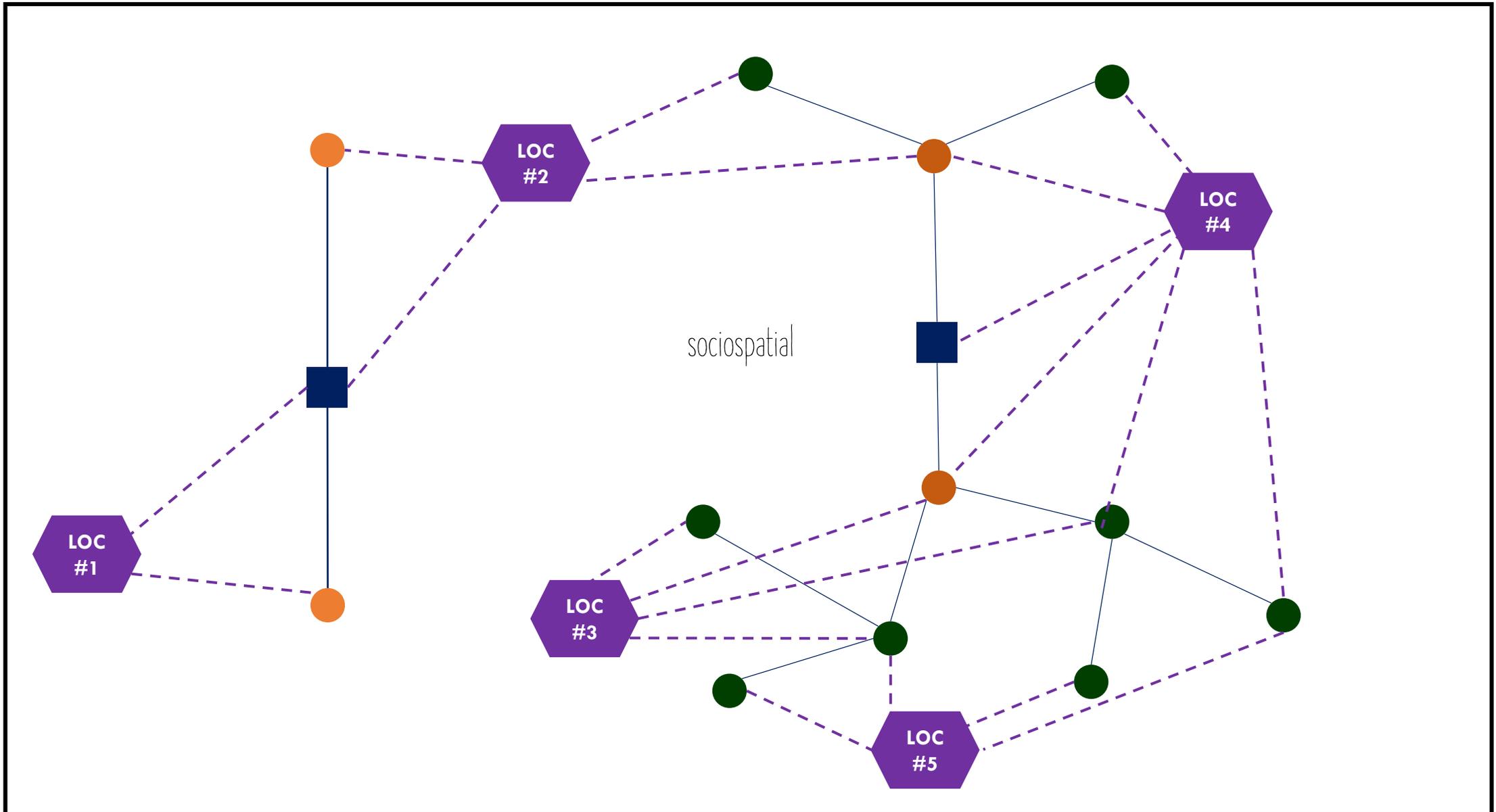
Recruitment and networks



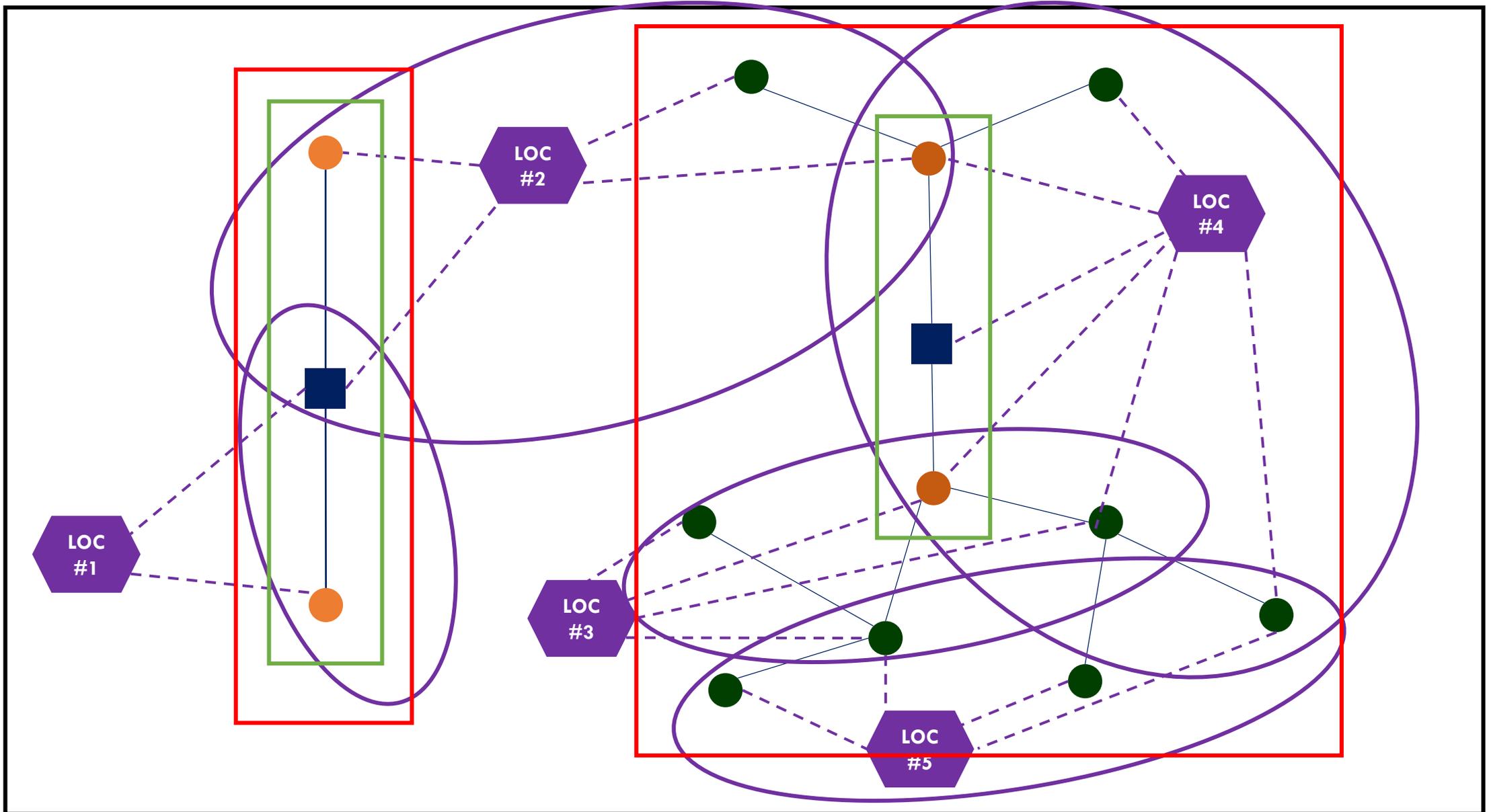
Recruitment and networks



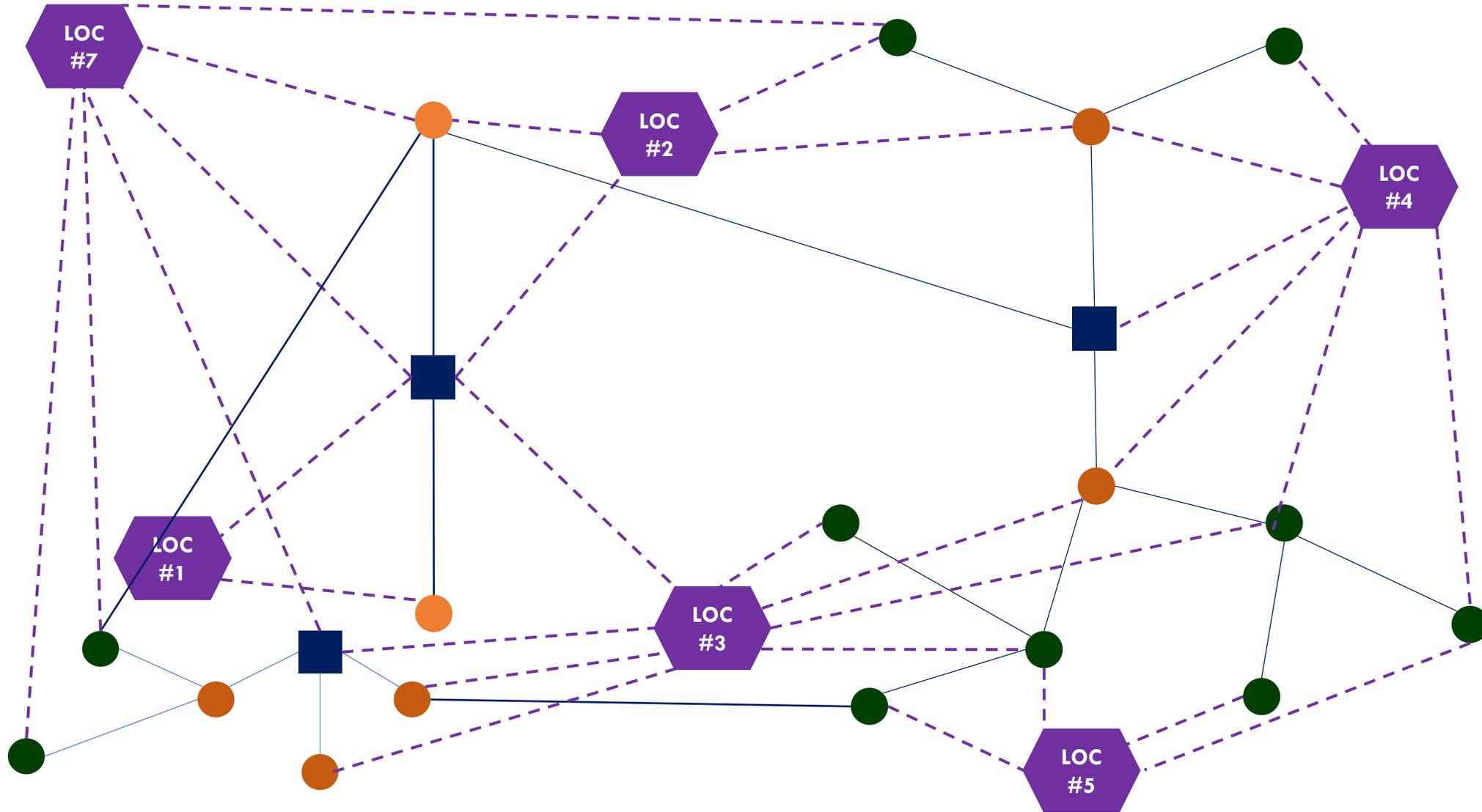
Recruitment and networks



Recruitment and networks



Recruitment and networks



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
4. Unique identifier listed by

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

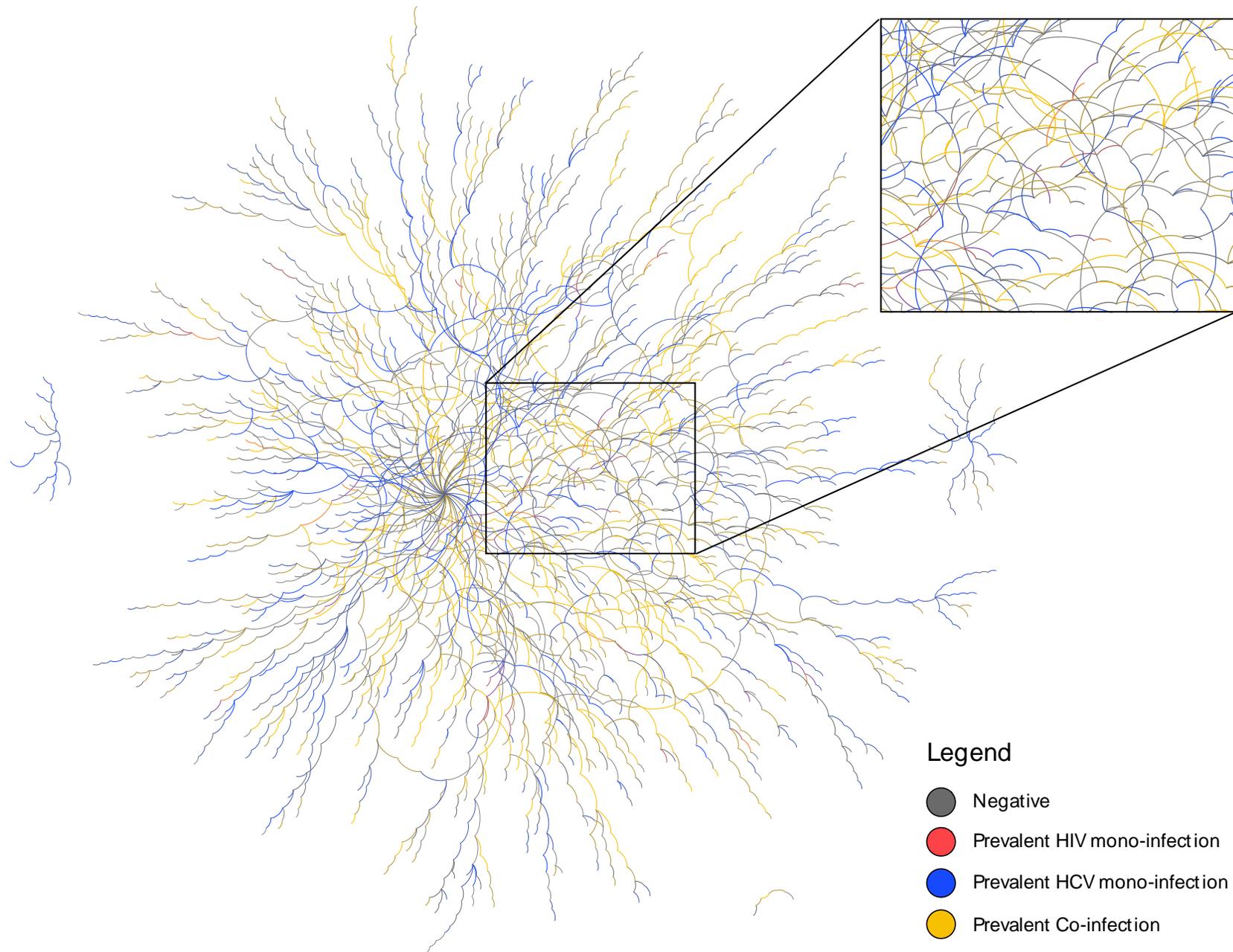
Study Procedures

- Informed consent
- Electronic interviewer administered survey
 - Demographics, risk behaviors, access to HIV services
 - Network information:
 - Partners (injection and social support)
 - Places (injection locations, residence, travel)
 - Referral coupons for active injection network partners
- Blood specimen
 - Rapid on-site HIV/HCV testing (referrals, where applicable)
 - HIV and HCV RNA
 - Specimen Storage
- Compensation for time/incentives for referrals

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 network structure

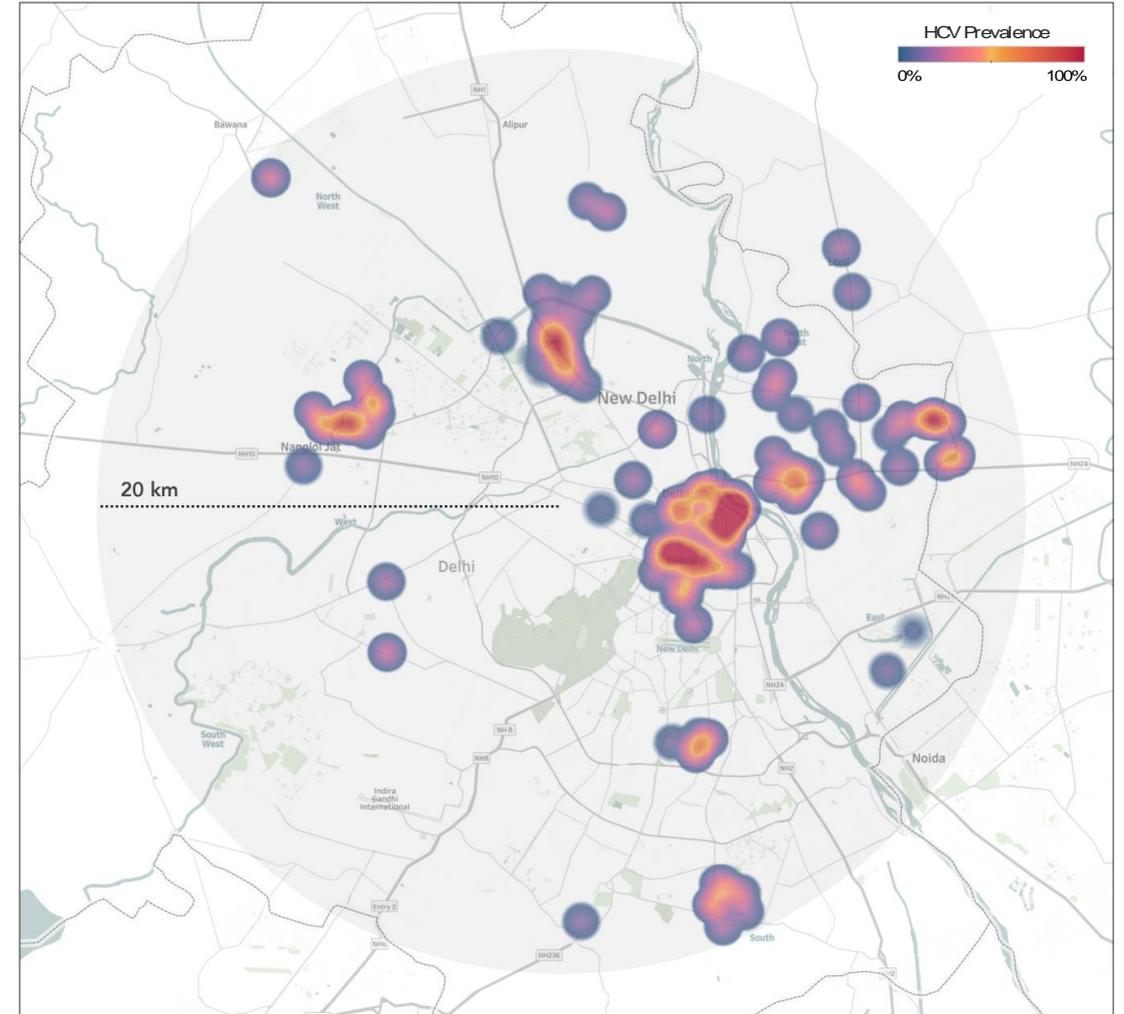
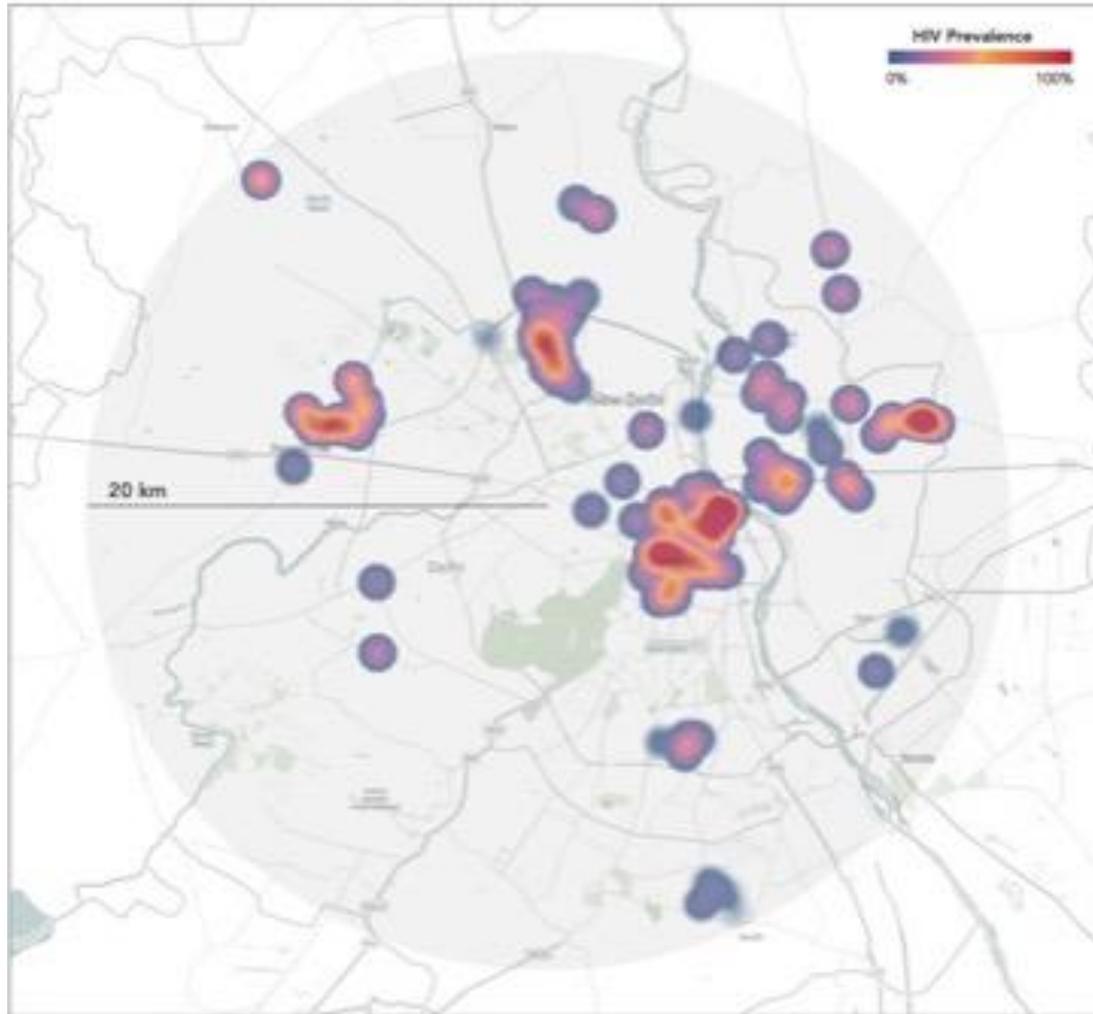




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 - 75% (2437/3244) of coupons were returned
- Baseline disease prevalence:
 - Number HIV-infected (prevalence): 37.0% (928/2506)
 - Proportion with detectable HIV RNA: 92.6%
 - Number anti-HCV antibody positive (prevalence): 65.1% (1634/2512)
 - Proportion with chronic HCV (HCV RNA+): 79.6%

Distribution of HIV and HCV



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)

HIV and HCV Incidence

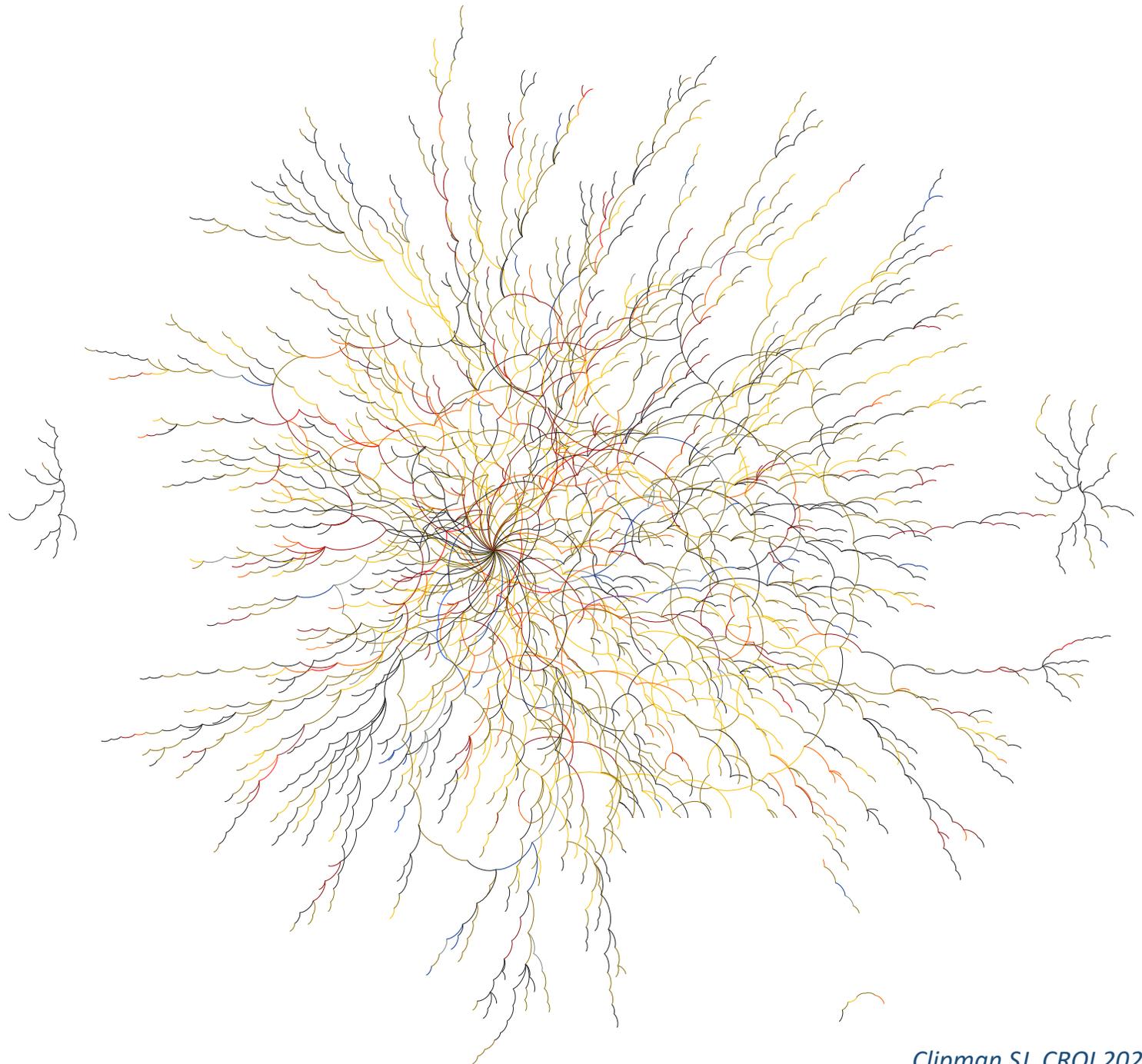
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Men	772	700.25	158	24.1 (20.5 – 28.3)
Women	15	11.75	1	8.51 (1.2 – 60.4)

HIV and HCV Incidence

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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

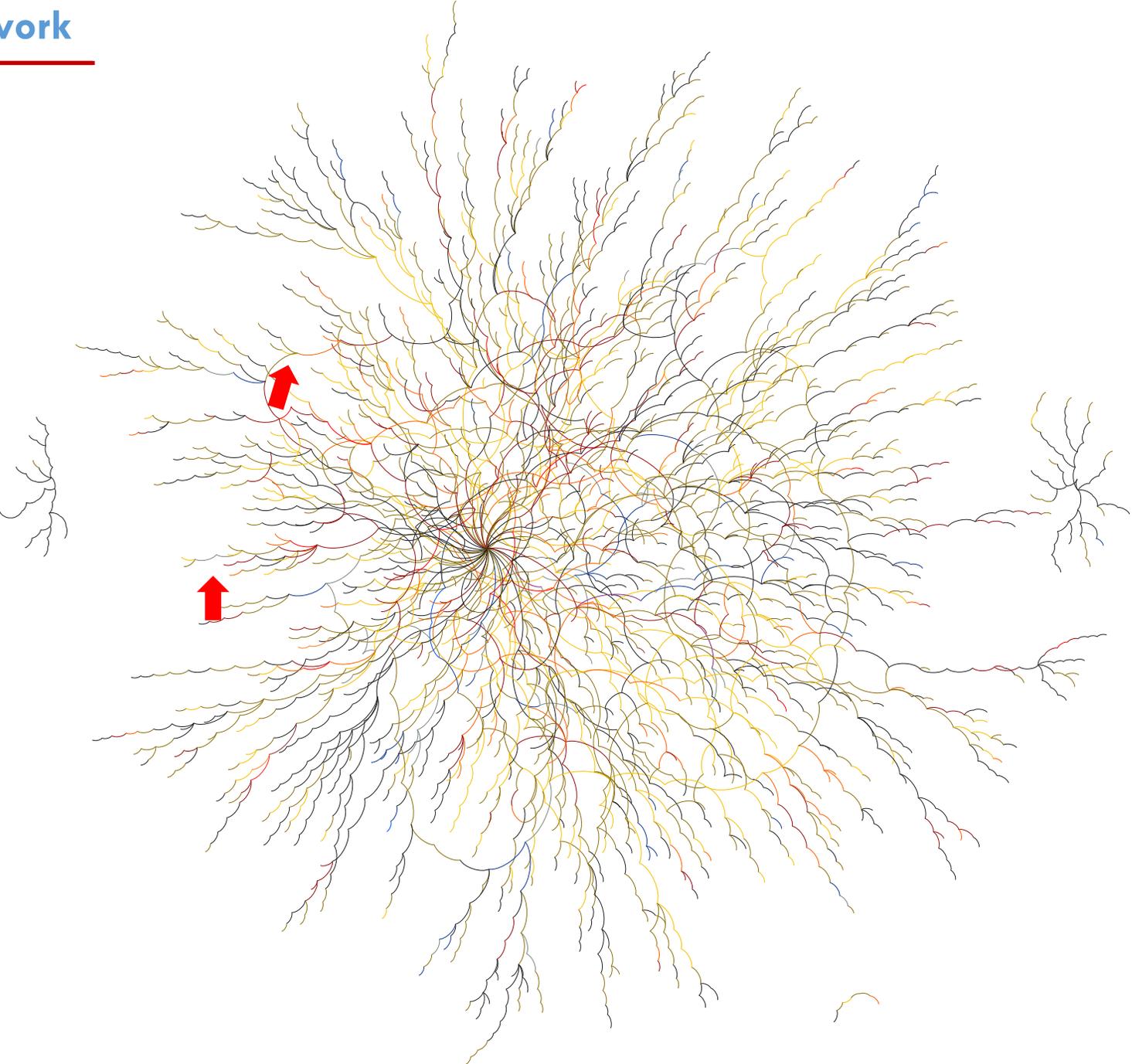
HIV incidence



Legend

- Negative
- Prevalent HIV+ (Undetectable VL)
- Prevalent HIV+ (Detectable VL)
- Incident HIV+

Sociometric Network



Legend

- Negative
- Prevalent HIV+ (Undetectable VL)
- Prevalent HIV+ (Detectable VL)
- Incident HIV+

Predictors of HIV incidence

Characteristic	aIRR (95% CI)
Age (per 5-year increase)	0.82 (0.75 - 0.91)**
Recent injection/needle sharing (Shared syringes in prior 6 months)	2.70 (1.81 - 4.0)**
Injection frequency in past 6 months (per 50 injections)	1.05 (1.05 - 1.10)**
Network viremia (egocentric) (per unit increase in egocentric network members with HIV RNA >150 copies/mL)	—
Path Distance (sociometric) (per unit increase in the shortest path length from index to a member with HIV RNA>150 copies/ml)	—

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

Predictors of HIV incidence

Characteristic	aIRR (95% CI)	aIRR (95% CI)
Age (per 5-year increase)	0.82 (0.75 - 0.91)**	0.82 (0.75 - 0.90)**
Recent injection/needle sharing (Shared syringes in prior 6 months)	2.70 (1.81 - 4.0)**	2.58 (1.75 - 3.80)**
Injection frequency in past 6 months (per 50 injections)	1.05 (1.05 - 1.10)**	1.05 (1.05 - 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)	—	—

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Predictors of HIV incidence

Characteristic	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)**
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)**
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)**
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)**

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Predictors of HIV incidence

Characteristic	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)*
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)**
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)*
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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)**	—
Injecting at Spatial Hotspot #40 (spatial)	—	—	—	3.40 (2.38 - 4.84)**

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

Predictors of HIV incidence

Characteristic	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 (spatial)	—	—	—	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](https://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)

Next steps in spatial...

- Whole genome sequencing of HIV and HCV to examine linked transmissions (U=U in PWID)
 - Re-create networks using phylogenetic data
 - Simplifying data needs to identify transmission clusters
- Study visits have resumed post-COVID pause
 - 24 seroconversions in 239 unique HIV negative participants
 - SARS-CoV-2 transmission across networks
- “Spatial Network” is being studied in one city
 - How does this fit in to the larger elimination agenda?

How does Delhi fit into India?

Cities:

1. Amritsar (AM)
2. New Delhi (DH)
3. Kanpur (KA)
4. Imphal (IM)

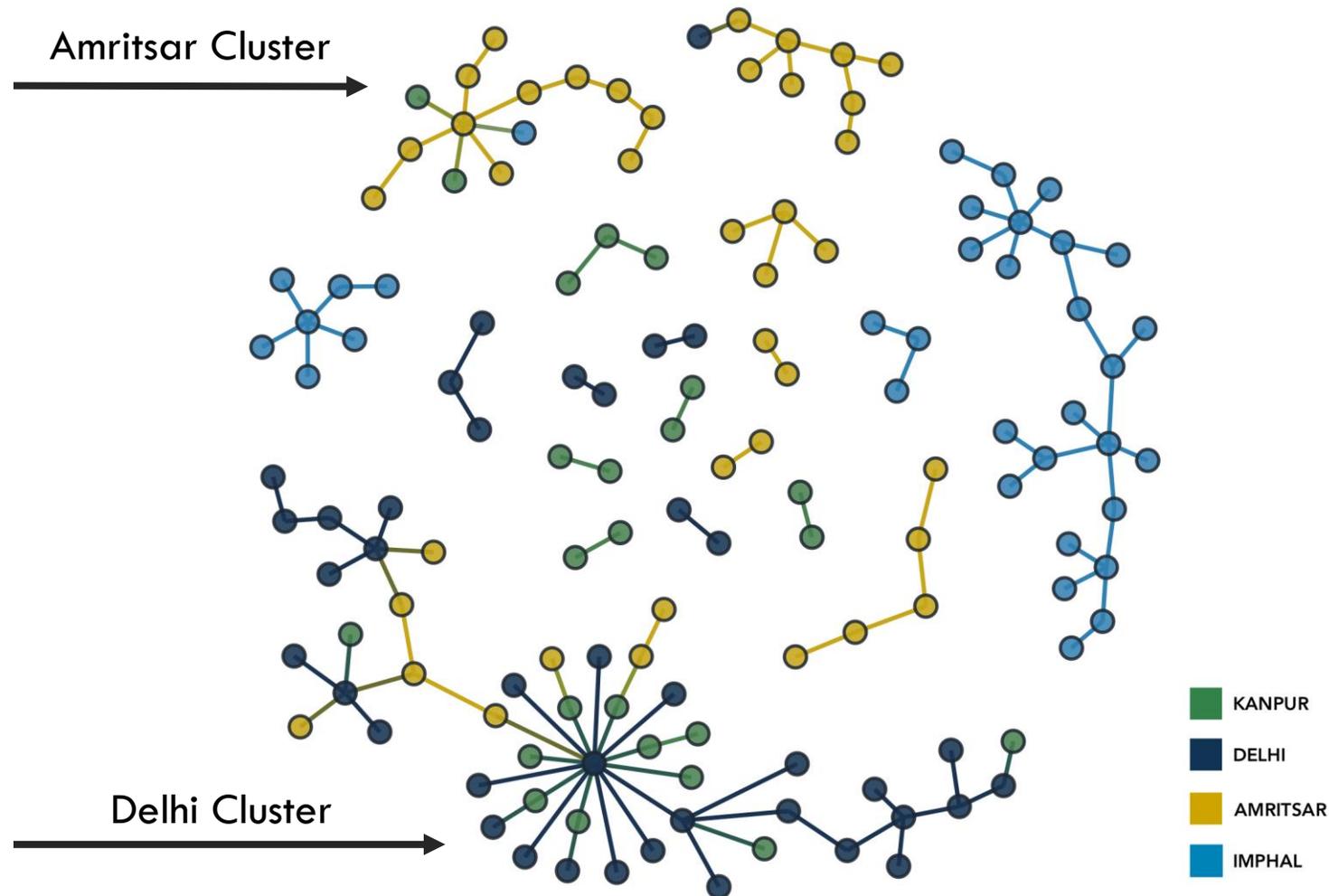
Viral Region:

HCV: Core 5' UTR



HCV	Total	AM	DH	KA	IM
Sample Size	483	123	128	138	94

Intercity clustering



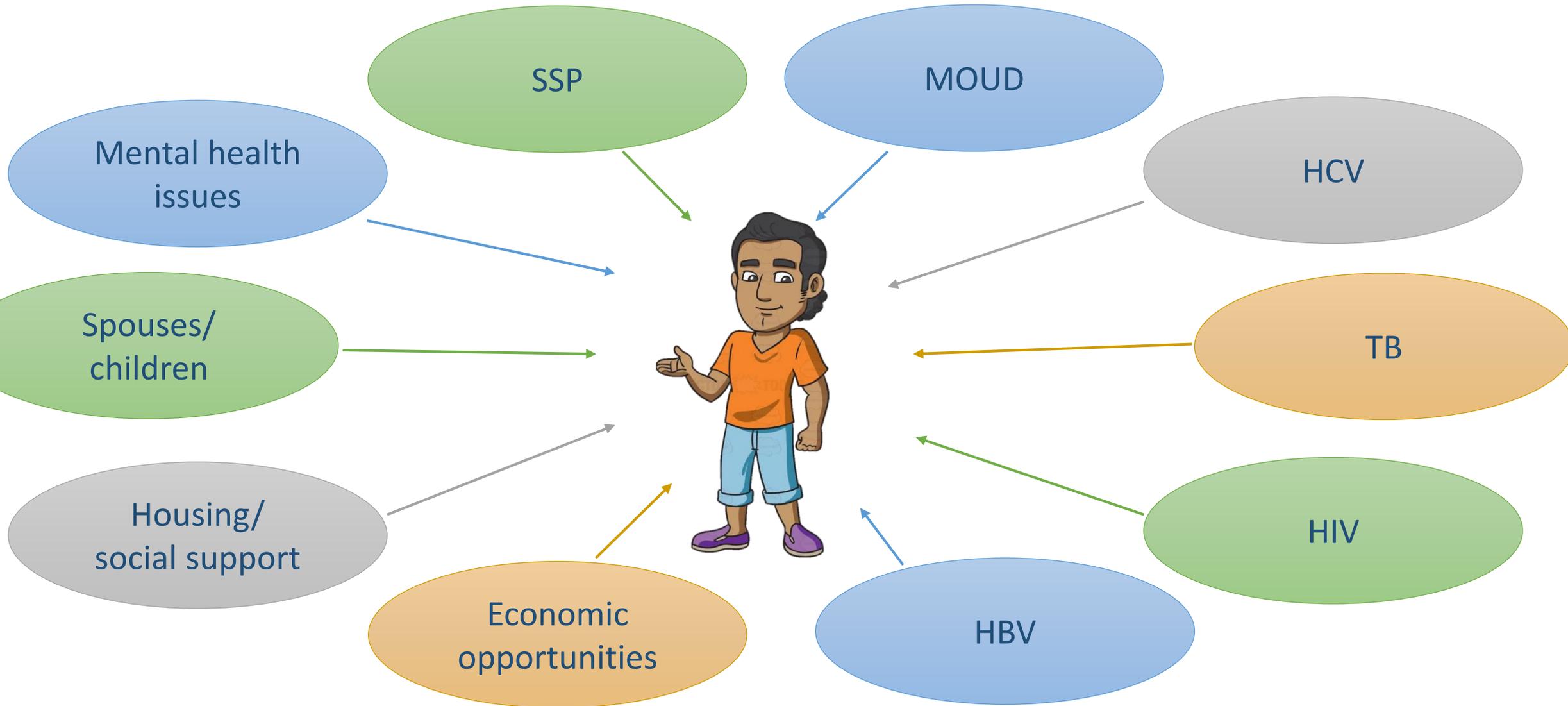
Geospatial diffusion of HCV



Conclusions

- To interrupt transmission, need to recognize multiple layers of network connections across individuals, space, time and cities!
- Spatially focused service interventions may be more effective than those that simply target individuals or egocentric networks
- Interventions are urgently needed for PWID (particularly in Delhi) to engage in HIV/HCV treatment, harm reduction and interrupt transmission
- And....

...the goal of every program should be to improve survival and quality of life!



Acknowledgements

- Participants who graciously participate in research studies globally
- Johns Hopkins University
 - Steven Clipman, Gregory Lucas, Shruti Mehta, David Celentano, Carl Latkin, Dave Thomas, Mark Sulkowski, Tom Quinn, Allison McFall, Katie Zook, Elizabeth Ogburn, Stuart Ray
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 - Aylur K Srikrishnan and M Suresh Kumar
- National AIDS Control Organisation (NACO), India
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 - NIDA (DP2DA040244, R01DA041736, R01DA018577, R01DA12568, R01DA032059), JHU CFAR (P30AI094189)
 - Abbott Diagnostics, Gilead Sciences, Elton John AIDS Foundation

