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Poster #00784

DEEP LEARNING APPROACHES TO INFORM NETWORK-BASED HIV INTERVENTIONS AMONG PWID

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BACKGROUND

- People who inject drugs (PWID) represent a key population with high HIV and HCV burden and account for some of the fastest growing HIV epidemics globally.
- India has a concentrated HIV epidemic, with PWID representing the population of highest burden.
- Network-based approaches represent a powerful tool for understanding and combating these epidemics; however, detailed social network studies are limited and pose analytical challenges.
- Computational advancements in deep learning, specifically Graph Neural Networks (GNNs) have made it possible to perform more powerful and complex analyses on network data, such as predicting links, network forecasting, or overlapping community detection.
- An in-depth understanding these networks and their role in transmission could play a critical role in efficiently targeting resources in program implementation and designing network-based intervention strategies.

OBJECTIVE

- Leverage network analysis and deep learning methods to identify correlates of HIV infection and optimal strategies to efficiently interrupt HIV transmission in a population of PWID in New Delhi, India.



Figure 1. Map of India with study location.

METHODS

STUDY POPULATION

Eligibility Criteria for Indexes

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

Eligibility Criteria for Recruits

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

RECRUITMENT

- PWID were recruited using name generator network referral approach between 2017-19 in New Delhi, India.
- Sampling was initiated using 10 "indexes"; these indexes were selected from participants of an RDS survey that was conducted in New Delhi in 2016-17.
- Each index was asked to recall who they injected with in the past month; for each named member, they were also asked to describe unique identifying characteristics (e.g., cell phone number, appearance, name of spouse, etc.).
- For each named individual, the index was given a referral card (egocentric network of "index").
- Similarly, each recruit named and recruited their recent injection network (egocentric network of recruit and sociometric network of "index").
- Recruitment process was continued until target sample size (~2500) was achieved.

STUDY PROCEDURES

- All participants provided written informed consent.
- Biometric registration was performed to identify duplicates and establish cross-network linkages.
- Participants completed a baseline assessment and semi-annual follow-up visits.
- An electronic interviewer-administered electronic survey that captured information on demographics, network characteristics, risk behaviors, access to HIV/HCV services, and information on injection locations was administered.
- Rapid on-site HIV (three rapid tests as per National guidelines) and HCV (anti-HCV antibody) testing was performed and results were delivered with appropriate pre- and post-testing counseling and referrals, where applicable.

LABORATORY PROCEDURES

- HIV RNA was quantified using the Abbott RealTime HIV-1 viral load assay.
- HCV RNA was quantified using the Abbott RealTime HCV viral load assay.
- All tests were performed as per manufacturers instructions.

STATISTICAL ANALYSIS

- Statistical analyses were carried out in Python (v3.7.3) and R (v3.5.1), and networks were modeled using NetworkX.
- Individual and network variables were analyzed for an association with incident HIV infection using univariable and multivariable Poisson regression.
- To determine potential points of intervention, we first identified communities in the network (i.e., groups of densely connected PWID and venues) using the Louvain method. This method computes the gain in modularity ΔQ as:

$$\Delta Q = \left[\frac{\Sigma_{in}+k_{i,in}}{2m} - \left(\frac{\Sigma_{tot}+k_i}{2m}\right)^2\right] - \left[\frac{\Sigma_{in}}{2m} - \left(\frac{\Sigma_{tot}}{2m}\right)^2 - \left(\frac{k_i}{2m}\right)^2\right]$$

where $\sum_{in}$ is the sum of the weights of the edges inside community C, $\sum_{tot}$ is the sum of the weights of the edges incident to nodes in C, k_i is the sum of the weights of the edges incident to node i, $k_{i,in}$ is the sum of the weights of the edges from i to nodes in C, and m is the sum of the weights of all the edges in the network.

- We then used the Neural Overlapping Community Detection (NOCD), which combines a graph neural network (GNN) with a Bernoulli–Poisson model to detect community overlap. The GNN architecture of NOCD uses a 2-layer Graph Convolutional Network (GCN) defined as:

$$\boldsymbol{F} := \mathrm{GCN}_{\boldsymbol{\theta}}(\boldsymbol{A}, \boldsymbol{X}) = \mathrm{ReLU}\left(\tilde{\boldsymbol{A}}\mathrm{ReLU}\left(\tilde{\boldsymbol{A}}\boldsymbol{X}\boldsymbol{W}^{(1)}\right)\boldsymbol{W}^{(2)}\right)$$

Where $\tilde{\boldsymbol{A}} = \tilde{\boldsymbol{D}}^{-1/2}\tilde{\boldsymbol{A}}\tilde{\boldsymbol{D}}^{-1/2}$ is the normalized adjacency matrix, $\tilde{\boldsymbol{A}} = \boldsymbol{A} + \boldsymbol{I}_N$ is the adjacency matrix with self-loops, and $\tilde{D}_{ii} = \sum_j \tilde{A}_{ij}$ is the diagonal degree matrix of $\tilde{\boldsymbol{A}}$.

- NOCD uses a 2-layer graph convolutional neural network, with hidden size of 128, and an output layer of size C (number of communities to detect). Batch normalization is applied after the first graph convolution layer. Dropout with 50% keep probability is applied before every layer. A weight decay is added to both weight matrices with regularization strength $\lambda = 10^{-2}$. The feature matrix $\boldsymbol{X}$ (or $\boldsymbol{A}$, in the absence of attributes) is normalized such that every row has unit L_2–norm. For training, the learning rate is set to 10^{-3} and training loss is computed every 50 epochs, optimization is halted if there is no improvement in the loss for the last 500 iterations, or after 5000 epochs.

ETHICAL CLEARANCE

- This study was approved by the Johns Hopkins Medicine and YR Gaitonde Centre for AIDS Research and Education institutional review boards.

RESULTS

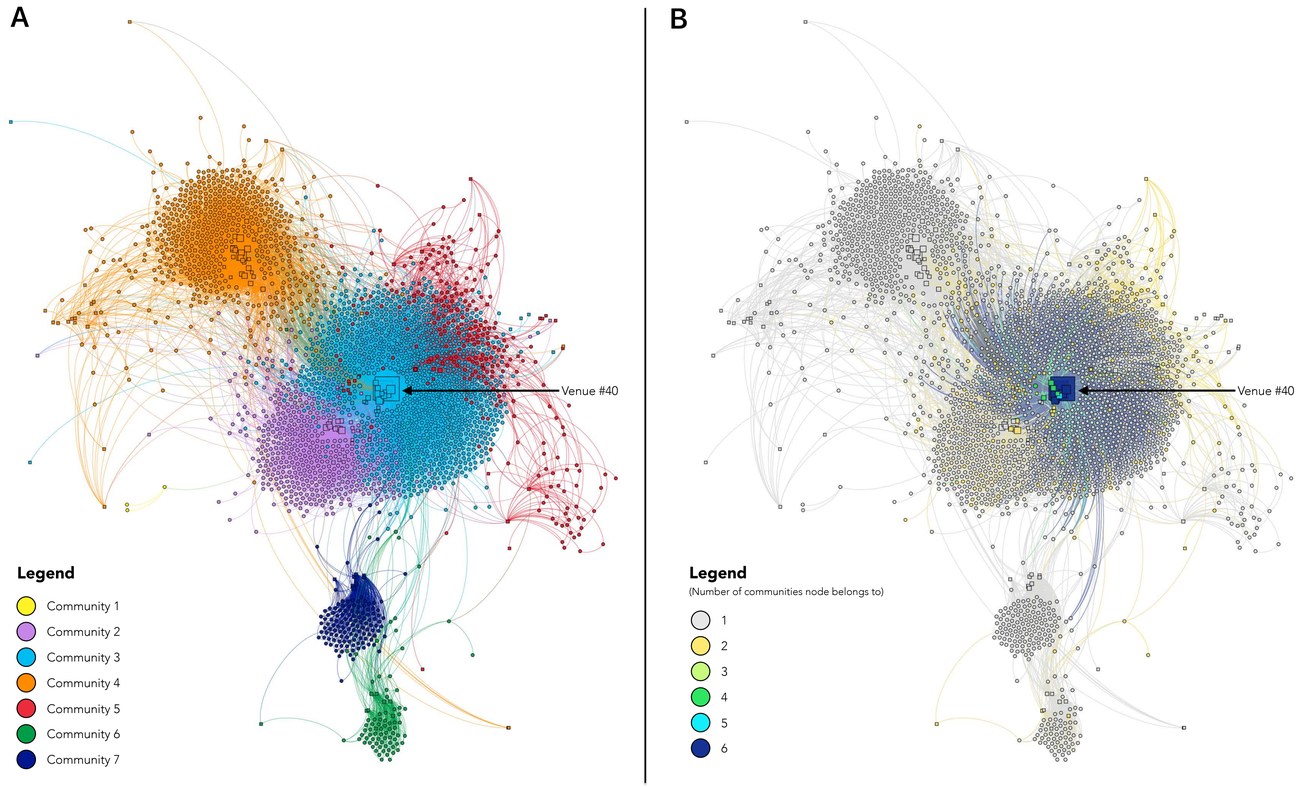


Figure 2. (A) Communities detected by modularity analysis of a sociospatial network of 2,512 people who inject drugs and 181 injection venues in New Delhi, India, and (B) the number of communities a node belongs to as identified by Neural Overlapping Community Detection. Circular nodes represent persons and square nodes represent venues. Nodes are sized by degree.

HIV INCIDENCE AND NETWORK-LEVEL RISK FACTORS FOR HIV

- Baseline HIV Prevalence: 37.0%
  - Virally Suppressed: 8.0%
- Observed 159 HIV seroconversions over 747 person-years of follow-up

  HIV Incidence: 21.3 cases per 100 person-years (Poisson exact 95% CI: 18.2, 24.9)
- HIV incidence was concentrated in community #3.
- Of the 159 incident HIV infections, 74% (117) were directly connected to at least one HIV-infected person with detectable viral load (HIV RNA > 150 copies/mL), and all 159 (100%) were within one degree of separation from an HIV-detectable participant.

Community	Number of Incident HIV Infections	Total Person Years	HIV Incidence Rate per 100 person-years (95% CI)
1	0	0	-
2	14	168.25	8.32 (4.93 – 14.1)
3	109	266.5	40.9 (33.9 – 49.4)
4	28	244	12.5 (8.60 – 18.0)
5	5	44.5	11.2 (4.68 – 27.0)
6	3	19.75	15.2 (4.90 – 47.1)
7	0	0	-

Table 2. HIV incidence by network community

Predictor	Adjusted Incidence Rate Ratio	95% CI
Number Viremic Injection Partners	1.28	1.08 – 1.50
Network Distance from an HIV Viremic Participant	0.68	0.52 – 0.89
Injecting at a Venue #40	3.11	2.19 – 4.42
Network Distance from Venue #40	0.74	0.65 – 0.84

Table 3. Network-level risk factors for HIV incidence by multivariable Poisson regression. Model was adjusted for individual-level factors including age, sexual activity, needle/syringe sharing, and injection frequency.

	Overall	HIV Negative at Baseline with Follow-up	HIV Negative at Baseline without Follow-up
Number of participants	2,512	782	797
Median Age (IQR)	26 (22 – 34)	28 (22 – 38)	26 (22 – 35)
Male Gender	99% (2489)	99% (771)	99% (789)
Self-Report of Ever Having Sex with a Man	20% (498)	20% (158)	18% (140)
Self-Identify as Gay or Bisexual	19% (479)	19% (150)	16% (130)
Highest Level of Education			
No Schooling	30% (754)	26% (200)	25% (196)
Primary School (Grades 1 – 5)	25% (618)	22% (169)	24% (190)
Secondary School (Grades 6 – 10) or above	45% (1130)	52% (409)	51% (407)
Employment			
Earn Daily Wage	62% (1545)	54% (425)	59% (465)
Earn Weekly or Monthly Wage	28% (714)	35% (275)	48% (240)
Unemployed	7% (165)	9% (67)	18% (89)
Currently Homeless	30% (754)	21% (160)	26% (210)
Median Years Injecting Drugs (IQR)	5 (2 – 10)	5 (2 – 11)	4 (2 – 8)
Median Injections in Prior 6 Mo. (IQR)	360 (180 – 540)	360 (160 – 540)	360 (144 – 360)
Mean No. Injection Partners in Prior Mo.	3.2	3.3	2.8
Ever Shared Syringes	60% (1518)	54% (421)	53% (419)
Shared Syringes in Prior 6 Mo.	51% (1284)	47% (364)	44% (349)
Type of Drug Injected (Lifetime)			
Heroin only	4% (89)	4% (29)	5% (41)
Buprenorphine only	54% (1350)	53% (413)	62% (491)
Heroin and buprenorphine	42% (1061)	43% (336)	32% (254)
Any other drug only	0% (0)	0% (0)	0% (0)
Type of Drug Injected (Prior 6 Mo.)			
Heroin only	4% (107)	4% (31)	6% (49)
Buprenorphine only	73% (1820)	72% (563)	77% (601)
Heroin and buprenorphine	22% (559)	23% (181)	17% (130)
Any other drug only	0.2% (5)	0.3% (2)	0.4% (3)
Access to Services			
Ever Tested for HIV	48% (1203)	56% (436)	40% (315)
Ever Tested for HCV	4% (104)	6% (44)	2% (17)
Ever Used Medication Assisted Therapy	36% (906)	45% (356)	31% (249)
Ever Used Syringe Service Program	17% (427)	19% (147)	11% (87)

Table 1. Participant baseline characteristics of 2,512 people who inject drugs in New Delhi, India.

NETWORK DYNAMICS

- Injection partner networks were highly dynamic.
  - Of 1,266 participants with ≥ 1 follow-up visit, 75% changed partners.
  - Average of 1.5 injection partner changes per participant per year.
- Spatial networks were more stable and 48% of participants changed venues.
  - Popular venues remained common and consistent places where participants injected.
  - The top venue saw minimal turnover with 9% of participants who reported injecting at the venue later reporting no longer injecting there.

CONCLUSIONS

- We observed explosive HIV incidence in this cohort of PWID in New Delhi, India despite over a third of the cohort being infected at baseline.
- Participants' venue ties were more stable than injection partner ties and they often reported new injection partners from spaces they commonly injected, suggesting that spaces are a more durable point of intervention.
- Deep learning community overlap detection methods further identified that venues, as opposed to individuals, tended to overlap more communities and hence, provide a better mechanism for dissemination of interventions.
- Eight nodes (all venues) overlapped six of the seven communities suggesting that these six communities could be reached by rapidly scaling-up services in just one of these eight venues (e.g., venue #40). In other words, these analyses suggest that the HIV epidemic among this entire sample of PWID in New Delhi could be mitigated by intervening at two strategic points – one venue (e.g., venue #40) that overlaps six communities, and another venue that reaches the seventh community.
- Network-based interventions that target spaces, which may represent unmeasured network connections, could be the optimal strategy to interrupt transmission among PWID while conserving resources.

ACKNOWLEDGEMENTS

This research has been supported by the National Institutes of Health, US Grants# DP2 DA040244, R01 DA041736, R01 DA032059. We thank the Office of AIDS Research, NIH, the National AIDS Control Organization (NACO), India, Division of Intramural Research, NIAID, all of our partner non-governmental organizations throughout India, and the countless participants, without whom this research would not have been possible. This work was facilitated by the Johns Hopkins Center for AIDS Research (1P30AI094189).