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

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Associate Professor of Medicine and Epidemiology

June 11, 2021
Disclosures

• Research grants and products from Abbott Diagnostics

• Research grants, study product and consulting from Gilead Sciences
HIV in India

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

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

HIV Prevalence

- ANC: 0.28
- Migrants: 0.51
- Truckers: 0.86
- FSW: 1.5
- TG: 3.14
- MSM: 2.69
- PWID: 6.3

Annual Report NACO 2016-17
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

World Drug Report 2016; MSJE GoI 2019
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

Solomon SS, Lancet HIV 2019
ICC: A Cluster-Randomized Trial

Baseline assessment in 27 cities to select 22

Randomization

Integrated care centers (ICC) N = 11

Usual care (UC) N = 11

Evaluation assessment in 11 ICC cities

Evaluation assessment in 11 UC cities

2012-13

2014 (Q1/2)

2014(Q3) – 2016 (Q2)

2016 (Q3) – 2017 (Q2)

Solomon SS, Lancet HIV 2019
A “single window” model

PERSON-CENTERED
Entry point for all services in a single venue with referrals as needed

STIGMA FREE
All staff undergo sensitivity training and support external referrals to reduce barriers/stigma

01 HIV testing and counseling
02 Antiretroviral therapy
03 TB screening & linkage to treatment
04 Sexually transmitted infection management
05 Viral hepatitis screening
06 Needle and syringe exchange
07 Medication for opioid use disorder
08 Condoms
09 Individual counseling
10 General medical care

Solomon SS, Lancet HIV 2019
ICCs improved testing but…

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

Solomon SS, PLoS Med 2017
Recruitment of PWID in Kanpur

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Solomon SS, PLoS Med 2017
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
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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 recruiter

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

Legend
- Negative
- Prevalent HIV mono-infection
- Prevalent HCV mono-infection
- Prevalent Co-infection
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- 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

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<thead>
<tr>
<th>HIV incidence</th>
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Clipman SJ, CROI 2020
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# HIV and HCV Incidence

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## Primary HCV incidence

(Antibody seroconversion)

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<td>364.25</td>
<td>92</td>
<td>25.3 (20.5 – 31.1)</td>
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<td><strong>Men</strong></td>
<td>404</td>
<td>359.75</td>
<td>92</td>
<td>25.6 (20.7 – 31.5)</td>
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<tr>
<td><strong>Women</strong></td>
<td>4</td>
<td>4.5</td>
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*Clipman SJ, CROI 2020*
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+

Clipman SJ, CROI 2020
# Predictors of HIV Incidence

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Clipman SJ, CROI 2020
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

<table>
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<tr>
<th>HCV</th>
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Clipman SJ, Hepatology 2021
Intercity clustering

Amritsar Cluster

Delhi Cluster

Clipman SJ, Hepatology 2021
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

• Research teams and partner organizations in India
  • Aylur K Srikrishnan and M Suresh Kumar

• National AIDS Control Organisation (NACO), India

• Funding sources:
  • Indo-US Joint Working Group (NIH/OAR)
  • NIDA (DP2DA040244, R01DA041736, R01DA018577, R01DA12568, R01DA032059), JHU CFAR (P30AI094189)
  • Abbott Diagnostics, Gilead Sciences, Elton John AIDS Foundation