Toward Evaluation of Disseminated Effects of Non-Randomized HIV Prevention Interventions Among Observed Networks of People who Inject Drugs

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Outline

Introduction

- PWIDs are embedded in social (risk) networks and exert biological and social influence on the members of these networks (Hayes et al., 2000; Ghosh et al., 2017).
- In PWID networks, interventions often have **indirect or disseminated** effects, which frequently depends on the network structure and intervention coverage levels.
- Indirect/disseminated effect could be stronger than direct/individual effects and ignoring indirect effects can under-estimate the full impact of interventions (Buchanan et al., 2018).

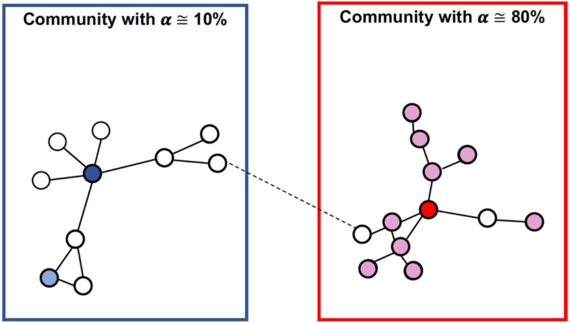
Causal Inference

- A Potential Outcome (i.e., Counterfactual)
  - $Y(0)$: Response that would have been seen if (possibly contrary to fact) the participant were not exposed.
  - $Y(1)$: Response that would have been seen if (possibly contrary to fact) the participant were exposed.
- Assumptions: Consistency, No Interference, Positivity, Exchangeability (Cole and Frangakis, 2009; Rubin, 1980)
- Relax the no interference assumption.

Two-stage Randomized Design

- One design to facilitate causal inference with interference is a **two-stage randomized design** (Halloran and Struchiner, 1991; Hudgens and Halloran, 2008).
- Clusters are randomly assigned to an allocation strategy (or coverage) of exposure at the first stage; in the second stage, individuals in a cluster are randomly exposed according to the allocation assigned in the first stage.
- **Coverage** of exposure is defined as the proportion of subject who are exposed in a certain cluster.

Interference in an Observed Network



Adapted from Benjamin-Chung, et al. (2017).

- Connections: Shared HIV risk (injection or sexual).
- Index darker shaded blue or red nodes.
- Exposed network members light blue or pink.
- Communities determined in the network.

Motivating Example

The Social Factors and HIV Risk Study (SFHR)

- Sociometric network study conducted between 1991 and 1993 in Bushwick, Brooklyn, New York among *street-recruited injection drug users*
- Investigated how HIV/AIDS infection spread through shared sexual and injection risk behaviors.
- 767 participants along with 3,162 dyadic relationships (i.e. a connection b/w two people).
- Connections were shared **risk behaviors** (i.e. inject drug together and/or having sexual intercourse) within 30 days before the interview.

full network

SFHR PWIDs Network for Analysis

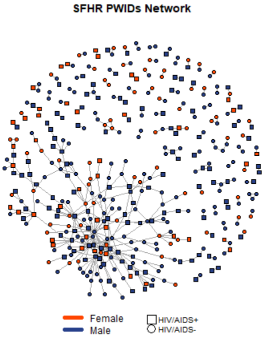


Figure 1: SFHR PWIDs Network for Analysis. There are 402 vertices and 403 edges.

Goal: To assess attitudes toward HIV/AIDS risk and their effects on health-seeking behaviors among PWIDs and their risk communities in SFHR network.

Exposures and Outcomes

Exposure

- **HIV/AIDS locus of control**: One dimension of an individual's beliefs about how much control they have about their HIV/AIDS risk.

$$A_{ij} = \begin{cases} 1, & \text{if internal} \\ 0, & \text{if external} \end{cases}$$

Outcome

- **Receipt of study-based HIV testing result**: Did the study participant receive the results of their HIV test in SFHR?

$$Y_{ij} = \begin{cases} 1, & \text{if test received} \\ 0, & \text{otherwise} \end{cases}$$

Causal Parameters

$$\textit{Direct effect}: \quad \overline{DE}(\alpha) = \overline{Y}(a=1;\alpha) - \overline{Y}(a=0;\alpha)$$

$$\textit{Indirect effect}: \quad \overline{IE}(\alpha,\alpha') = \overline{Y}(a=0;\alpha) - \overline{Y}(a=0;\alpha')$$

$$\textit{Total effect}: \quad \overline{TE}(\alpha,\alpha') = \overline{Y}(a=1;\alpha) - \overline{Y}(a=0;\alpha')$$

$$\textit{Overall effect}: \quad \overline{OE}(\alpha,\alpha') = \overline{Y}(\alpha) - \overline{Y}(\alpha')$$

coverage: $\alpha' < \alpha$

Causal Inference with Observational Network Data

- **Inverse probability weighting (IPW)** method to adjust for confounding in an observational study (Tchetgen and VanderWeele, 2012).

APPROACH

1. Determine a set of communities of PWIDs in the SFHR observed network.
2. Calculate community-level propensity score (i.e., probability of having specific attitude toward HIV/AIDS risk) for each subnetwork based on individual-level covariates of sex, race, education, age and their pairwise interactions.
3. Use the inverse of propensity scores as weights to compute IPW estimators of potential outcomes.

Assumptions

(1) **Partial interference**: Allow interference within a community, but not between communities.

(2) **Stratified interference**: Individual's potential outcome is dependent only on own exposure and the proportion exposed in their community.

(3) **Bernoulli individual group allocation strategy**: The distribution of exposure selection mechanism A is assumed to be a Bernoulli distribution and used to define the average potential outcomes Y^a.

(4) **No homophily**: Assume there is no latent variables related to health-seeking behavior with which an individual has a tie with another individual who has the similar characteristics.

Community Detection

- **Community**: A set of vertices densely connected, with only sparser tie to vertices that belong to other groups or communities.
- **Hierarchical clustering**: Common methods for community detection where the closest or most similar vertices are combined to form communities with *a measure of similarity* or *connection strength* between vertices based on the network structure.
- As the measure of similarity, we use **modularity** (Kolaczyk, 2009; Newman, 2006).

IPW estimation: Community-Level Propensity Score

Community-level propensity score can be calculated by adjusting for individual-level covariates among those in the community.

$$f_{A_i|X_i}(A_i|X_i;\theta_x,\theta_s) = \int \prod_{j=1}^{n_i} h_{ij}(b_i;\theta_x)^{A_{ij}}\{1 - h_{ij}(b_i;\theta_x)\}^{1-A_{ij}} f_b(b_i;\theta_s)db_i$$

where
$h_{ij}(b_i;\theta_x) = Pr(a_{ij} = 1|X_{ij}, b_i, \theta_x) = logit^{-1}(X_{ij}\theta_x + b_i)$ is a propensity score for jth individual in community i and $f_b(\cdot;\theta_s)$ is the density of community-specific random effect and assume $b_i \sim N(0,\theta_s)$.

IPW estimation: IPW estimator

IPW estimator for community-level potential outcome:

$$\hat{Y}_i^{ipw}(a,\alpha) = \frac{\sum_{j=1}^{n_i} \pi_i(A_{i,-j};\alpha) I(A_{ij}=a) Y_{ij}}{n_i f_{A_i|X_i}(A_i|X_i;\hat{\theta})} \tag{1}$$

Marginal community potential outcome:

$$\hat{Y}_i^{ipw}(\alpha) = \frac{\sum_{j=1}^{n_i} \pi_i(A_i;\alpha) Y_{ij}}{n_i f_{A_i|X_i}(A_i|X_i;\hat{\theta})} \tag{2}$$

Population-level IPW estimators

$$\widehat{DE}(\alpha) = \hat{Y}^{ipw}(a = 1; \alpha) - \hat{Y}^{ipw}(a = 0; \alpha)$$

$$\widehat{IE}(\alpha, \alpha') = \hat{Y}^{ipw}(a = 0; \alpha) - \hat{Y}^{ipw}(a = 0; \alpha')$$

$$\widehat{TE}(\alpha, \alpha') = \hat{Y}^{ipw}(a = 1; \alpha) - \hat{Y}^{ipw}(a = 0; \alpha')$$

$$\widehat{OE}(\alpha, \alpha') = \hat{Y}^{ipw}(\alpha) - \hat{Y}^{ipw}(\alpha')$$

coverage: $\alpha' < \alpha$

Causal Inference: IPW estimation

Table 1: Estimated risk differences (RDs) with 95% CIs of **locus of control** (internal vs. external) on likelihood of **receiving HIV test results** in SFHR (coverage of internal)

		Unadjusted		Adjusted with interactions	
Effect	Coverage (α, α')	RD	95% CI	RD	95% CI
Direct	(50%, 50%)	0.148	(0.065, 0.230)	0.160	(0.055, 0.265)
Direct	(70%, 70%)	0.142	(0.038, 0.246)	0.162	(0.055, 0.268)
Indirect	(70%, 50%)	0.041	(0.012, 0.071)	0.031	(0.008, 0.054)
Total	(70%, 50%)	0.183	(0.096, 0.271)	0.193	(0.100, 0.286)
Overall	(70%, 50%)	0.067	(0.038, 0.096)	0.065	(0.041, 0.089)

Causal Inference: IPW estimation

Table 2: Estimated risk differences (RDs) with 95% CIs of **locus of control** (internal vs. external) on likelihood of **receiving HIV test results** in SFHR (coverage of internal)

		Unadjusted		Adjusted with interactions	
Effect	Coverage (α, α')	RD	95% CI	RD	95% CI
Direct	(50%, 50%)	**0.148**	(0.065, 0.230)	**0.160**	(0.055, 0.265)
Direct	(70%, 70%)	**0.142**	(0.038, 0.246)	**0.162**	(0.055, 0.268)
Direct	(99%, 99%)	0.101	(-0.056, 0.258)	0.130	(-0.008, 0.268)
Indirect	(70%, 50%)	**0.041**	(0.012, 0.071)	**0.031**	(0.008, 0.054)
Indirect	(99%, 50%)	0.070	(-0.019, 0.156)	0.062	(-0.000, 0.123)
Indirect	(99%, 70%)	0.029	(-0.040, 0.098)	0.030	(-0.011, 0.072)
Total	(70%, 50%)	**0.183**	(0.096, 0.271)	**0.193**	(0.100, 0.286)
Total	(99%, 50%)	**0.172**	(0.066, 0.278)	**0.192**	(0.093, 0.291)
Total	(99%, 70%)	**0.130**	(0.006, 0.254)	**0.161**	(0.049, 0.272)
Overall	(70%, 50%)	**0.067**	(0.038, 0.096)	**0.065**	(0.041, 0.089)
Overall	(99%, 50%)	**0.097**	(0.010, 0.183)	**0.111**	(0.032, 0.190)
Overall	(99%, 70%)	0.030	(-0.035, 0.095)	0.046	(-0.013, 0.105)

Discussion

- Additional benefit to reporting internal locus beyond being around those who have internal for likelihood of receipt of HIV test result.
- Among those with external locus, having more community members with internal increased likelihood of receipt of HIV test.
- Attitudes are an important determinant of health-seeking behavior among PWIDs and future interventions could consider this influence in the network to increase and sustain impact.
- Communities may share edges and, if there are many edges, partial interference assumption may be dubious.
- Possibly unmeasured confounders (i.e., health insurance status) and cannot rule out homophily.

Future Research Directions

- Account for uncertainty in estimates due to community detection.
- Allow for alternative definitions of the interference set (e.g., nearest neighbor).
- Improve methods for generalizing results, particularly in the presence of dissemination.
- **New collaborations to apply these methods to important public health settings**.

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Original PWIDs Network in SFHR

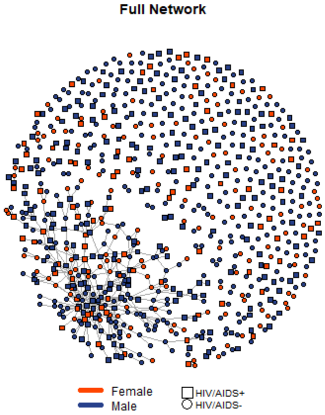
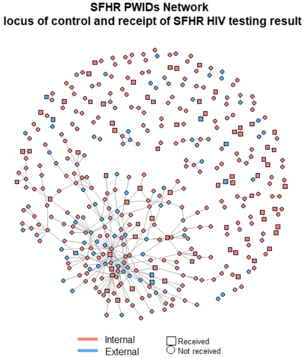


Figure 2: Full Network.

SFHR PWIDs Network for Analysis



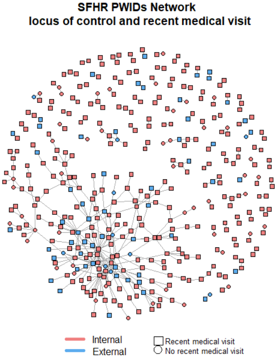


Figure 3: The Social Factors and HIV Risk Study PWIDs' network for the analysis. Locus of control and receipt of HIV testing result (Left) and recent medical encounter (Right).

Data Pre-processing

Table 3: Questions about Health Beliefs in SFHR (5-point Likert Scale)

Questions related to belief (BLF)
Q1. It is my own behavior which determines whether I get AIDS or not.
Q2. No matter what I do, if I'm going to get AIDS, I will get AIDS.
Q3. I'm in control of whether or not I get AIDS.
Q6. Getting AIDS is largely a matter of bad luck.
Q7. No matter what I do, I'm likely to get AIDS.
Q8. If I take the right actions, I can avoid getting AIDS.
Q10. No matter what I do, I'm unlikely to get AIDS.

Questions related to blame (BLM)
Q4. My family have a lot to do with whether I get AIDS.
Q5. If I get AIDS, I'm not to blame.
Q9. If I get AIDS, it is because of the society we live in.

Causal Inference: IPW estimation - Model 2

Table 4: Estimated risk differences (RDs) with 95%CIs of **blame** (others vs. self) on likelihood of **receiving HIV testing results** in SFHR (coverage of self-blame).

Effect	Coverage (α, α')	Unadjusted RD	Unadjusted 95%CI	Adjusted with interactions RD	Adjusted with interactions 95%CI
Direct	(50%, 50%)	-0.043	(-0.164, 0.079)	-0.045	(-0.159, 0.069)
Direct	(70%, 70%)	-0.035	(-0.159, 0.088)	-0.034	(-0.154, 0.085)
Direct	(99%, 99%)	-0.077	(-0.250, 0.096)	-0.065	(-0.230, 0.100)
Indirect	(50%, 70%)	-0.002	(-0.047, 0.044)	-0.001	(-0.043, 0.041)
Indirect	(50%, 99%)	0.034	(-0.077, 0.145)	0.034	(-0.066, 0.134)
Indirect	(70%, 99%)	0.036	(-0.037, 0.109)	0.035	(-0.032, 0.102)
Total	(50%, 70%)	-0.037	(-0.164, 0.090)	-0.035	(-0.154, 0.083)
Total	(50%, 99%)	-0.043	(-0.200, 0.115)	-0.031	(-0.175, 0.113)
Total	(70%, 99%)	-0.041	(-0.197, 0.115)	-0.030	(-0.176, 0.116)
Overall	(50%, 70%)	-0.005	(-0.048, 0.038)	-0.003	(-0.042, 0.036)
Overall	(50%, 99%)	-0.021	(-0.135, 0.094)	-0.008	(-0.113, 0.097)
Overall	(70%, 99%)	-0.015	(-0.095, 0.064)	-0.005	(-0.079, 0.068)

Associations with Recent Medical Visit - Model 3

Table 5: Estimated risk differences (RDs) with 95% CIs of **locus of control** (external vs. internal) on likelihood of **a recent medical visit** in SFHR (coverage of internal)

		Unadjusted		Adjusted with interactions	
Effect	Coverage (α, α')	RD	95% CI	RD	95% CI
Direct	(50%, 50%)	0.211	(-0.286, 0.708)	0.090	(-0.271, 0.451)
Direct	(70%, 70%)	0.003	(-0.296, 0.301)	-0.111	(-0.346, 0.123)
Direct	(99%, 99%)	-0.227	(-0.463, 0.009)	**-0.280**	(-0.470, -0.089)
Indirect	(50%, 70%)	-0.001	(-0.260, 0.257)	-0.008	(-0.181, 0.165)
Indirect	(50%, 99%)	0.208	(-0.298, 0.715)	0.077	(-0.311, 0.464)
Indirect	(70%, 99%)	0.210	(-0.063, 0.482)	0.085	(-0.136, 0.305)
Total	(50%, 70%)	0.001	(-0.537, 0.539)	-0.119	(-0.496, 0.258)
Total	(50%, 99%)	-0.019	(-0.491, 0.453)	-0.203	(-0.559, 0.153)
Total	(70%, 99%)	-0.017	(-0.255, 0.220)	-0.195	(-0.409, 0.018)
Overall	(50%, 70%)	-0.105	(-0.316, 0.106)	-0.131	(-0.265, 0.003)
Overall	(50%, 99%)	-0.122	(-0.358, 0.114)	**-0.246**	(-0.430, -0.061)
Overall	(70%, 99%)	-0.017	(-0.082, 0.048)	**-0.114**	(-0.181, -0.047)

Associations with Recent Medical Visit - Model 4

Table 6: Estimated risk differences (RDs) with 95%CIs of **blame** (others vs. self) on likelihood of **reporting a recent medical encounter within the past year** (coverage of self-blame)

		Unadjusted		Adjusted with interactions	
Effect	Coverage (α, α')	RD	95%CI	RD	95%CI
Direct	(50%, 50%)	0.017	(-0.141, 0.175)	0.002	(-0.156, 0.160)
Direct	(70%, 70%)	-0.054	(-0.205, 0.096)	-0.076	(-0.213, 0.060)
Direct	(99%, 99%)	-0.209	(-0.467, 0.050)	**-0.269**	(-0.527, -0.011)
Indirect	(50%, 70%)	0.076	(-0.001, 0.153)	0.086	(-0.014, 0.186)
Indirect	(50%, 99%)	**0.238**	(0.053, 0.423)	**0.272**	(0.072, 0.472)
Indirect	(70%, 99%)	**0.162**	(0.019, 0.305)	**0.186**	(0.038, 0.335)
Total	(50%, 70%)	0.022	(-0.099, 0.143)	0.009	(-0.126, 0.144)
Total	(50%, 99%)	0.029	(-0.159, 0.218)	0.003	(-0.214, 0.219)
Total	(70%, 99%)	-0.047	(-0.263, 0.170)	-0.083	(-0.299, 0.133)
Overall	(50%, 70%)	0.029	(-0.022, 0.081)	0.031	(-0.054, 0.117)
Overall	(50%, 99%)	0.023	(-0.119, 0.164)	0.005	(-0.178, 0.187)
Overall	(70%, 99%)	-0.007	(-0.148, 0.134)	-0.027	(-0.183, 0.130)

Modularity

Modularity is defined as following:

- Assume there are $C = \{C_1, C_2, \cdots, C_K\}$ candidate of K communities in an observed network G.
- We also define $f_{ij} = f_{ij}(C)$ as the fraction of edges in the original network that connect vertices in cluster i with vertices in cluster j, $i \neq j$.
- Given this,

$$mod(C) = \sum_{k=1}^{K}[f_{kk}(C) - f^*_{kk}]^2, \tag{3}$$

where f_{kk} is the fraction of edges which connect vertices within the same cluster k in G, and f^*_{kk} is the expected value of f_{kk} under some model of random edge assignment.

Modularity-Based Community Detection

85 connected components and one of them forms the giant component that include 199 participants. In total, **96 communities** in the SFHR network for analysis.