HHS Public Access

Author manuscript

AIDS Behav. Author manuscript; available in PMC 2020 January 01.

Published in final edited form as:

AIDS Behav. 2019 January ; 23(1): 15–20. doi:10.1007/s10461-018-2202-6.

A network intervention to locate newly HIV infected persons within MSM networks in Chicago

Ethan Morgan[1], **Britt Skaathun**[1], **Georgios K. Nikolopoulos**[2], **Dimitrios Paraskevis**[3], **Leslie D. Williams**[4], **Pavlo Smyrnov**[5], **Samuel R. Friedman**[4], **John A. Schneider**[1]

[1]Department of Public Health Sciences, University of Chicago, Chicago, IL, USA

[2]Medical School, University of Cyprus, Cyprus

[3]Department of Hygiene and Epidemiology, University of Athens, Athens, Greece

[4]National Development and Research Institutes, New York, NY, USA

[5]Alliance for Public Health, Kyiv, Ukraine

Abstract

Individuals with recent/acute HIV-infection have an increased likelihood of disease transmission. To evaluate effectiveness of identifying recent infections, we compared networks of recently and long-term HIV-infected individuals.

The Transmission Reduction Intervention Project included two separate arms of recruitment, networks of recently HIV-infected individuals and networks of long-term HIV-infected individuals. Networks of each were recruited and tested for HIV and syphilis infection. The per-seed yield ratios of recruitment were compared between arms.

Overall, 84 (41.6%) of 202 participants were identified as HIV-positive. HIV prevalence was higher (p<0.001) among networks of recent seeds (33/96, 34.4%) compared to long-term seeds (6/31, 19.4%). More individuals were identified with active syphilis infection (p=0.007) among networks of recent seeds (15/96, 15.6%), compared to networks of long-term seeds (3/31, 9.7%).

Network-based recruitment of recently HIV-infected individuals was more effective at identifying HIV and syphilis infection. Allocating public health resources may be improved by targeting interventions toward networks of recently HIV-infected individuals.

Keywords

HIV; network; syphilis; intervention

Corresponding author: Ethan Morgan, PhD, 625 N Michigan Ave, Ste 14-044A, Chicago, IL 60625, ethan.morgan@northwestern.edu, 312/503-5426.

Disclosures: The authors declare that they have no conflicts of interest.

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent: Informed consent was obtained from all individual participants included in the study.

Introduction

Treatment as prevention (TasP) relies on the successful implementation of the HIV continuum of care – HIV testing, linkage to care, retention in care, adherence to antiretroviral medication, and viral suppression.[1] HIV testing and the early identification of individuals who are recently or acutely infected with HIV are of critical importance to the continuum of care. Some estimates suggest that up to 43% of transmissions occur during the first ten weeks of infection[2] with the increased risk of transmission being attributed to acutely/recently HIV-infected individuals having higher viral loads,[2,3] being less likely to be aware of their status,[4,5] and a continued participation in risk-related behaviors.[6,7] Past research has also shown that early treatment with ART has the potential to reduce transmission of HIV between sexual partners.[8] One recent intervention study in Thailand found that, when diagnosing individuals with HIV early, viral loads decreased dramatically and up to 78% of onward transmission may be avoided during the first six months following infection.[9]

Recent work has shown that network interventions may play a critical role in preventing ongoing HIV-infection.[10] An early example of this is contact tracing wherein Disease Intervention Specialists (DIS) trace sexual partner histories through known sexual contacts provided by a newly diagnosed individual. These methods, however, are limited as they rely solely on the ability of the individual to recall, and be willing to provide, information regarding their sexual history. Sociometric networks, meanwhile, have been shown to be pathways along which HIV travels, suggesting that novel network interventions may play a key role in preventing the spread of HIV.[11] This is further supported by work in Denmark suggesting that, among HIV transmission networks, recent HIV infections are largely responsible for sustaining the local epidemic.[12] Results such as these suggest that identifying recent or acute HIV infections in an individual's network may provide a new standard for HIV prevention.

Past research has shown that individuals who are members of the same network are more likely to have similar HIV risk behaviors.[13] We hypothesized that individuals who are recently infected with HIV are located within networks which are composed of other recently HIV-infected individuals.[14–16] Therefore, recruiting and testing individuals from these networks into a network-based intervention is more likely to identify those who have been recently infected with HIV, compared to networks of individuals who have long-term HIV infections. In this study, we evaluated a network-based intervention which was aimed at identifying individuals undiagnosed with HIV, and individuals actively infected with syphilis. Our intervention had a particular focus on examining network members connected to acutely or recently infected persons and comparing those yields to those connected to long-term infected individuals.

Methods

The Transmission Reduction Intervention Project (TRIP) is a an induction type network-based intervention (e.g. respondent-driven sampling, snowball, etc)[14] whose primary goal is to increase early detection of recently HIV-infected individuals. A secondary goal, at the

Chicago site only, is to increase the yield of individuals with active syphilis infection.[17] A two-step approach was utilized where network chain recruitment started with "seeds" – either recently or long-term infected - and continued no further than two steps from an HIV positive individual; repeating the process if another HIV positive individual was identified at either the first or second step in the process. The two-step approach was utilized in order to remain within that individuals risk-network environment; anything beyond this was considered as too far removed from the immediate risk network.

Laboratory methods

Blood samples were tested by 4th generation HIV immunoassay (Abbott ARCHITECT HIV Ag/Ab Combo assay), HIV-1/−2 Ab differentiation (Bio-Rad Multispot HIV-1/−2 Rapid Test) and viral load testing (Abbott ReaLTime HIV-1 assay). All HIV+ participants were tested using the Limiting Antigen Avidity (LAg) assay (Sedia™ Biosciences Corportation).[11] Time from test to determination of new infection occurred within 7–10 days based on test results. Samples were also tested for syphilis using Treponemal enzyme immunoassay and immunochemoluminescence (EIA) followed by quantitative RPR; if these results did not match testing was followed up via *T pallidum* particle agglutination (TTPA) or fluorescent treponemal antibody-absorption (TPA) test.

Eligibility criteria and TRIP arms

Eligibility criteria included: 1) 18 years or older, 2) completed informed consent, and 3) for seeds, were either acutely/recently or long-term infected as described below. The intervention arm consisted of Recent Seeds (RS) - where "Seed" refers to a primary participant recruited by the study team. RS were newly HIV-diagnosed MSM or transgender women identified from community-based testing programs or other collaborating testing facilities who had laboratory evidence of acute infection or documented seroconversion in the previous 9 months. Following release of information signed by study participants, department of public health surveillance data was also used to confirm that previous HIV seropositive testing was not evident in the previous 9 months for clients classified as recent.

The comparison arm consisted of participants who were newly HIV diagnosed, but did not fit criteria above (Control Seeds with "Long-term" HIV infection or LCS) *and* their network members. LCS were newly HIV *diagnosed* but not recently *infected* MSM or transgender women who were referred from the same testing programs as described. LCS were matched to RS on age (± 5 years) and gender. LCS were not excluded from this arm if a previous seropositive test was discovered through Department of Public Health surveillance data.

Questionnaire

All TRIP participants were interviewed using a questionnaire which included items on sex and injection practices for themselves and their network members, including demographic information on network members. TRIP staff also asked participants to indicate venues they usually visit to have sex, use drugs or to meet new sex partners. Participants were given $50 for the baseline interview and $20 for each named risk network member who enrolled in TRIP. The project staff educated affected communities about recent/acute HIV infection, and

about the importance of avoiding stigma. Participants were provided with standard counseling and were actively linked to care as appropriate.

Network tracing

Network members of RS and LCS were tested for HIV and syphilis using the same methods as the seeds. Network members were individuals within the "risk environment"[16] and could include individuals who were sex or drug-using partners or individuals from venues where partners are met: these groups were not necessarily mutually exclusive. Newly HIV diagnosed individuals were defined as recently infected if they had a documented testing history of recent infection (last negative – first positive test < 9 months). Antibody negative samples of network members were tested for HIV-RNA to identify acute infections who were classified as recents for the analyses. Long-term infected network members were those newly diagnosed HIV seropositive not classified as recents in seeds' networks. If a recent was found in networks of seeds, the network members of the newly identified recents (referred to as "recents" throughout) were recruited for 2 additional steps. Unless stated otherwise, recent and acute infections were analyzed together, and they would be referred to hereafter simply as "recents".

Statistical methods

The following yield metrics (Table 2) were compared between the RS and LCS groups: total number of HIV-diagnosed individuals; individuals who were diagnosed as HIV-positive and previously unaware of their status (HIV-diagnosed unaware); those with active syphilis infection (titer ≥1:8); and a combined analysis of HIV-diagnosed unaware individuals or those with active syphilis infection. The yield ratio was calculated as the number of network individuals identified per seed (e.g. 15 network members of recent seeds identified with active syphilis and 23 recent seeds: 15/23 = 0.65). Yield ratios for recent and long-term networks were utilized to account for the differences in size between the networks and were treated as incidence rates for purposes of comparison and determining significance.

Chi-square and Student's t-tests were used to determine whether or not demographic and risk characteristics were associated with the type of network. All statistical tests were two-sided and conducted in STATA 14.

Results

Table 1 presents characteristics of TRIP participants. Study participants had a mean age of 29.1 (SD = 9.7). The majority of study participants were cis-male (176, 87.1%), had at least some college education or greater (112, 55.4%), and identified as gay (106, 52.5%). Overall, 84 (41.6%) participants were HIV positive. All network members were sex network members, no injection network members were observed. HIV prevalence was significantly higher ($p < 0.001$) among the networks of recent seeds (33/96, 34.4%) than among the networks of long-term seeds (6/31, 19.4%). There were also significantly more ($p = 0.007$) individuals identified with active syphilis infection among the networks of recent seeds (15/96, 15.6%), compared to the networks of long-term seeds (3/31, 9.7%). There were significantly more participants who identified as gay ($p = 0.001$) and cis-male ($p < 0.001$) in

the networks of recent seeds. There were no significant differences between the intervention and control arms across other sociodemographic categories – including education and housing instability. Nor were there any significant difference among those who did or did not use pre-exposure prophylaxis (PrEP).

There were 23 recent seeds and 19 long-term seeds with 96 and 31 network members, respectively, and a total of 202 total network members (the remaining participants were HIV-negative). Seeds named an average of 20.6 (SD=87.99; median=3) partners and recruited an average of 1.8 (SD=1.91; median=1) partners. The networks of recent seeds resulted in a higher rate of identifying HIV-diagnosed individuals, HIV-diagnosed unaware individuals, and active syphilis infections (Table 2). Recent seeds recruited a total of 33 HIV-diagnosed individuals per seed (per-seed ratio = 1.43), compared to 6 (per-seed ratio = 0.32) among the long-term infected long-term seeds. The per-seed ratio of recruitment of HIV-diagnosed individuals, comparing recent to long-term seeds, was 4.54 (95% Confidence Interval [CI]: 2.34–8.72). Recent seeds also identified 8 HIV-diagnosed unaware individuals per seed (per-seed ratio = 0.35), compared to none among the long-term seeds (per-seed ratio = 0). Further, recent seeds recruited more individuals with active syphilis infection (n = 15; per-seed ratio = 0.65), compared to the long-term seeds (n = 3; per-seed ratio = 0.16). Finally, in separate analyses removing the two transgender HIV-diagnosed individuals, we saw no change to our findings (data not shown).

Discussion

In this work, we described and tested a new network intervention for identifying persons with infectious HIV and syphilis. We found that networks of recent seeds compared to networks of long-term seeds were more likely to include HIV positive individuals, HIV positive unaware individuals, and persons with active syphilis infection. Specifically, we found higher yield ratios among each of the aforementioned categories when comparing recent to long-term infected seeds, however, we did not identify many recent HIV infections in either arm of the study.

A two-step network-based approach is effective at identifying both HIV-diagnosed and diagnosed-unaware individuals as well as active syphilis infections, particularly when using focused recruitment with recent seeds. Our findings are similar to those of the TRIP team in another site (Athens, Greece) who recently found that public health network tracing efforts would best be supported by utilizing recently infected individuals as seeds[10,18] and that network-based interventions have the potential to reduce risk of HIV acquisition.[19,20] Past research has also found a large amount of episodic clustering and a high rate of transmission among recent HIV infections.[11,21] We may have identified more recently infected individuals if we had more, or better, access to individual testing history, some of these individuals may have been classified into the unaware with long-term HIV infection category. Additionally, we chose to include transgender individuals in our analyses given that their removal did not change our results, however, future work should take care to separately analyze these individuals as their network dynamics are unlikely to be identical to those among MSM. What we do find is that the networks of those who are recently infected represent a network risk environment,[22] for both HIV diagnosis and syphilis infection. In

combination with past work, our results suggest that allocation of public health resources can be optimized by specifically targeting interventions toward networks of recently HIV-infected individuals.

Compared to the current standard of contract tracing undertaken by DIS officers, tracing networks of recently-diagnosed individuals may have a positive impact on reducing the rate of future community HIV transmission. For example, DIS officers could potentially transition to a two-degree contract tracing method where they ask the partners of those recently/acutely diagnosed with HIV to also name their recent partners, encouraging this second wave of partners to get tested as well. Given the work presented in this analysis and the limits of government funding, this type of two-degree tracing may not be warranted for those identified with a long-term infection. One concern with this approach, however, would be the limited incentive for individuals to name their partners. Certainly, providing a pay structure is feasible for a study such as this, but might not be feasible at the city or state level. Future work should aim to work with departments of public health in order to develop novel methods of incorporating these findings into the daily work of DIS officers.

Primary and secondary syphilis infection rates among MSM in the United States, including Chicago,[23,24] have been on the rise, making network interventions a potentially useful tool in interrupting transmission.[25] In this study, we had no *a priori* hypothesis regarding syphilis, however, we noted high rates during data collection and chose to analyze the data in a similar way to HIV, particularly given the high rate of co-infection these diseases. We identified many more syphilis infections in the networks of recent seeds, compared to the networks of long-term seeds. The networks of recent seeds had much higher yields. Contrary to our findings, past research has found social and sexual networks of those infected with syphilis to be largely unconnected, but that the sex partners of those infected with syphilis were often connected with core transmitters, putting the entire network at risk of infection.[26] In the context of this past work, perhaps our method of recruitment is better at identifying core transmitters which, if true, would potentially make this a useful tool in preventing further syphilis infections. Further, more recent research has suggested that venue based interventions may serve as a suitable proxy for network membership and may aid in curbing the syphilis epidemic experienced in many cities.[14,16] Further work should be conducted to ascertain the network positions of individuals identified with this recruitment method and assess whether venue based recruitment would be comparable to the methods presented here.

Our data and analyses should be viewed in the context of their limitations. As with all network studies, our networks are incomplete and thus we have substantial missing information. Second, given the nature of the study design, our recruitment methods were neither random nor independent. Newly diagnosed long-term controls may be susceptible to reporting bias of their HIV negative status given the stigma of HIV in these settings. It is also possible that, given their limited size, the networks recruited by long-term HIV-diagnosed individuals are not representative of the population. It is unclear whether the differing network sizes were: 1) of a statistically different size; 2) whether this was the nature of these networks by chance; or perhaps interestingly 3) recents were more effective

at recruiting their network members or staff were more diligent given that they were not blinded to the recent or long-ter status of study participants.

Even in the context of these limitation, we found meaningful results. Namely, the networks of recently HIV-infected individuals all-around yielded individuals with undiagnosed HIV infections or syphilis infections, compared to LCS networks. It is possible that these individuals are less likely to use condoms or other antiretroviral forms of prevention, although future research would be needed to address this hypothesis. Overall, our findings suggest that the targeted allocation of public health resources to these networks may potentially be improved by working with networks of recently HIV-infected individuals.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

This intervention was supported by the United States (US) National Institute on Drug Abuse (NIDA) (DP1DA034989). This work was also supported by grants R01DA033875, R21 AI118998 and the FOCUS 801266112, Gilead Sciences.

The funding source had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

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Table 1.

Characteristics of Transmission Reduction Intervention Project (TRIP) participants in Chicago, IL (N = 218), 2013–2016

Characteristic	Total	Recent seeds	Network of Recent Seeds	Long-term Seeds	Network of Long-term Seeds	p-value[2]
Total, n (%)	202[1]	23	96	19	31	
HIV diagnoses, n (%)	84 (41.6)	23 (100)	33 (34.4)	19 (100)	6 (19.4)	<0.001
Syphilis infection[3]	36 (17.8)	5 (21.7)	15 (15.6)	9 (47.4)	3 (9.7)	0.007
Mean age, SD	29.1 (9.7)	25.9 (9.5)	29.5 (9.6)	26.5 (6.6)	33.4 (12.3)	<0.001
Gender, n (%)						<0.001
Cis-male	176 (87.1)	21 (91.3)	87 (90.6)	18 (94.7)	18 (58.1)	
Cis-female	22 (10.9)	1 (4.3)	6 (6.3)	1 (5.3)	12 (38.7)	
Trans-female	5 (2.5)	2 (8.7)	2 (2.1)	0 (0.0)	0 (0.0)	
Trans-male	1 (0.5)	1 (4.3)	0 (0.0)	0 (0.0)	0 (0.0)	
Education, n (%)						0.673
<High school	20 (9.9)	1 (4.3)	7 (7.3)	2 (10.5)	2 (6.5)	
High school	71 (35.1)	7 (30.4)	36 (37.5)	6 (31.6)	10 (32.3)	
Some college	96 (47.5)	15 (65.2)	44 (45.8)	10 (52.6)	16 (51.6)	
≥Bachelors	16 (7.9)	1 (4.3)	8 (8.3)	3 (15.8)	2 (6.5)	
Housing instability,[4] n (%)	3 (1.0)	0 (0.0)	2 (2.1)	0 (0.0)	0 (0.0)	0.673
Unemployed, n (%)	62 (30.7)	9 (39.1)	32 (33.3)	7 (36.8)	5 (16.1)	0.373
Sexual orientation, n (%)						0.001
Gay	106 (52.5)	13 (56.5)	58 (60.4)	12 (63.2)	11 (35.5)	
Bisexual	54 (26.7)	5 (21.7)	27 (28.1)	7 (36.8)	3 (9.7)	
Other	44 (21.8)	6 (26.1)	11 (11.5)	2 (10.5)	16 (51.6)	
Ever used PrEP	11 (5.4)	2 (8.7)	6 (6.3)	1 (5.3)	2 (6.5)	0.582

[1] Does not total to 202, remaining individuals were HIV-negative

[2] Comparing characteristics in networks of recent vs long-term seeds

[3] Defined as titer ≥1:8

[4] Over the past six months

Table 2.

Yield ratios for identification of recents in the Transmission Reduction Intervention Project (TRIP) in Chicago, IL, 2013–2016

Network Contact Tracing Yield	Network of Recent Seeds (NRS)	Recent Seeds (RS)	NRS / RS	Network of Long-term Seeds (NLCS)	Long-term Seeds (LCS)	NLCS / LCS	(NRS / RS) / (NLCS / LCS)
HIV-diagnosed	33	23	1.43	6	19	0.32	4.54 (2.34−8.72) *
HIV-diagnosed unaware	8	23	0.35	0	19	0.00	-[2]
Active syphilis infection[1]	15	23	0.65	3	19	0.16	4.13 (2.13−7.93) *
HIV diagnosed unaware or Active syphilis infection	23	23	1.00	3	19	0.16	6.33 (3.26−12.16) *

[1] Defined as titer ≥1:8

[2] Undefined

* $p < 0.05$