

# Identifying the key nodes of HIV molecular transmission network among men who have sex with men in Guangzhou, China: A cross-sectional study

**Juan Yang**

National Center for AIDS STD Control and Prevention

**Zhigang Han**

Guangzhou Center for Disease Control and Prevention

**Huifang Xu**

Guangzhou Center for Disease Control and Prevention

**Hui Xing**

National Center for AIDS STD Control and Prevention

**Weibin Cheng**

Guangzhou Center for Disease Control and Prevention

**Yuzhou Gu**

Guangzhou Center for Disease Control and Prevention

**Peng Xu**

National Center for AIDS STD Control and Prevention

**Fan Lv** (✉ [fanlv0925@163.com](mailto:fanlv0925@163.com))

China CDC <https://orcid.org/0000-0003-3294-4754>

---

## Research article

**Keywords:** key nodes, HIV molecular transmission network, MSM

**Posted Date:** September 17th, 2020

**DOI:** <https://doi.org/10.21203/rs.3.rs-47539/v1>

**License:**   This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

---

# Abstract

## Background

Identifying the most influential spreaders in HIV transmission networks is crucial to develop effective prevention strategies. The purpose of this study is to identify the key nodes of the molecular transmission network among MSM, which has significant insight into developing effective HIV prevention strategies.

## Methods

We analyzed HIV-1 pol sequences provided through the Center for Disease Control and Prevention, Guangzhou, China. Sequences were obtained from newly-HIV diagnosed MSM during 2015–2017. We calculated pairwise genetic distance, identified linked pairs of sequences (those with distance  $\leq 1.5\%$ ), and examined key nodes of these potential transmission partners.

## Results

Of 184 HIV recently diagnosed men who have sex with men (MSM), 40.76% were linked to other MSM. Social network analysis demonstrated that there were 9 key nodes were detected. From the results of multivariate logistic regression model, young MSM born in the 1990s and 1980s was 0.06 and 0.12 times as likely to be a key node as was the older MSM born in the 1970s and before.

## Conclusions

There were a lot of subgroups connected by sharing comembers in HIV molecular transmission network among MSM in Guangzhou. Some HIV-infected MSM called as key nodes mediated the transmission of HIV among different subpopulations. Young MSM were less likely to promote HIV transmission than older MSM.

## Background

HIV/AIDS has been a major public health concern for a long time, the model of HIV transmission has been changed in recent years in China. Based on the report of AIDS epidemic in China in December 2017[1], sexual transmission accounts for more than 90% infections. And 26.86% of the sexual transmission infections were the men who have sex with men (MSM). A report from UNAIDS pointed out that MSM has 24 times higher risk of HIV infection than heterosexual men[2].

Several social factors contribute to the high incidence of HIV among MSM according to prior studies[3, 4]. According to the research conducted by Ethan Morgan and his colleagues, it is necessary to conduct some investigations which focus on networks of targeted population rather than traditional epidemiologic

factors such as geographic areas of high incidence[5]. Social networks are conceived as stable patterns of interactions among people. Social network analysis allows for the assessment of the perceived relationships of individuals[6]. The Transmission Reduction Intervention Project (TRIP) used a network-based contact tracing intervention proved it was more effective and economical[7] in detecting undiagnosed HIV-positive people[8] as well as to find and treat people early in their HIV infection[9].

From an epidemiological perspective, an intervention changing or removing the small number of individuals from target population is the most cost-effective means of constraining disease transmission. Therefore, it is absolutely essential to identify the small key population who has been playing important role in causing HIV transmission.

*Samuel R Friedman* and their colleagues mentioned in a review article that a person's position within the network can have an important impact on HIV transmission and the social network research has potential in interventions[10]. *Yuri A Amirkhanian* et al. conducted several two-arm randomized trials found that interventions that engage the identified influence leaders of target MSM social networks to communicate theory-based counseling and advice can reduce significantly sexual risk behavior [11, 12]. The process of identification of network leaders was classic siometric method which belongs to a sort of network structure analysis.

The analysis of structure of networks provides the optimal way to confirm the location and its role of the members which can be helpful to identify the key nodes. *Sté phane Helleringer* and *Hans-Peter Kohler* revealed important differences in the structural position of HIV-positive individuals when analyzed sexual network structure and the spread of HIV in Africa in a cross-sectional sociocentric survey[13]. Given the hidden nature of the MSM population, it is difficult to confirm the relationship ties between any two members of the communities which is the first step to analyze network structure during traditional fielding epidemiologic investigations. Phylogenetics provides the probability for network structure analysis in HIV research. Inferring putative transmission is the process of utilizing molecular phylogenetics analyzed by using HIV sequence to identify the transmission events in groups of individuals[14]. The large HIV clinical trials of HIV antiretroviral therapy (Hp052) was an example of this application[15]. Thus, we can use the linkage between sequences to reconstruction of HIV transmission network on the level of molecular. For example, *Ethan Morgan* et al. utilized the data of molecular genetic network combining with social, sexual and Facebook network data from the same cohort to examine potential overlap between the networks[16].

However, most studies on HIV transmission networks concerned about HIV molecular clusters, as well as the associated factors[17–19] rather than network structure analysis such as cohesive subgroup method which are more helpful for us to identify one or more specific key nodes in the networks. The purpose of this analysis is to identify key nodes of the molecular transmission network among MSM, which has significant potential in developing effective HIV prevention strategies.

## Methods

## Sources of Sequence Data and Inclusion Criteria

In this study, the boundary of network which is important for whole-network analysis was newly diagnosed as HIV-positive men who were transmitted through having had sex with men in the HIV voluntary counseling and testing clinics (VCT) in Guangzhou during 2015-2017. Our research included as many MSMs as possible who were willing to participate in the network interview and provide blood samples. Due to the concealment of MSM population, the participants included in this study is only the tip of the iceberg of new diagnosed as HIV-positive MSMs in Guangzhou in 2015-2017.

The sequences were collected from two processes. 100 HIV-1 pol sequences were reported through the Center for Disease Control and Prevention(CDC), Guangzhou, China. These sequences were collected from those who were newly diagnosed as HIV-positive in one of the National HIV sentinel Surveillance of MSM during 2015–2016 in Guangzhou. Others were collected from our fielding survey targeting MSM conducted in 2016-2017 in HIV VCT clinics[20]. Most of the samples collected at two different times came from the same VCT. A total of 184 sequences were assessed and stratified over two-time eras based on the year of sample collection (2015-2016, 2016-2017). Each of the HIV sequences has a unique identification number, the information of the year the sequence was performed, the age, education and marital status of the patient at the time of diagnosed.

## Sequence analysis

All of 184 sequences were aligned with all known sequences in the HIV database by a Basic Local Alignment Search Tool (BLAST) search (<http://hiv-web.lanl.gov/content/index>) before analysis. The sequences were edited with software Sequencher 5.0. The reference sequences which were available on HIV Databases(<http://hiv-web.lanl.gov/content/index>) covered the major HIV-1 subtypes/CRFs.

## Identification of HIV molecular transmission networks

HIV molecular transmission network was identified on the base of genetic distance[21]. Putative transmission ties of the network were identified by dichotomized data, which is determined by whether the pairwise genetic distance is less than 0.015 substitutions per site within all sequences[22, 23] . In our study, the Tamura-Nei 93 pairwise genetic distances were calculated by Mega V.7.0[24].

## Cohesive subgroups analysis

All social network analysis was conducted by UCINET6.0.

Cohesive subgroups analysis is a powerful and mathematically rigorous method to characterize network robustness. The strength lies in the capability to detect strong connections among nodes that not only have no neighbors in common, but that may be distantly separated in the graph[25].

## 2-cliques

A clique is a subgroup of actors in which each actor is adjacent to any other actors in it, and it is impossible to add any other actors to the clique without violation of this condition[26]. In our study, we constrain the minimum size of any clique is three.

### **clique co-membership**

When there are a large number of cliques, it is difficult to interpret the result of cohesive subgroups for the overlap between cliques can hide features of the structure. An optimal way would be to try to remove or reduce the overlap by performing additional analysis such as clique co-membership[26]. The first step is to combine the cliques who share the same actors more than 2/3 of the members. After the first step, we can merge again the cliques who share the same actors more than 1/3 of the members if there remain a lot of cliques[27]. From the small number of cliques, we can detect a set of key nodes acting as bridge between Subgroups.

### **Lambda sets**

lambda sets, based on the property that members of the set have greater edge connectivity with other members than with non-members, is shown to correspond to a particular hierarchical clustering of the nodes in a network. It is a maximal subset of actors who have more edge-independent paths connecting them to each other than to outsiders. Since Actors in lambda sets with connectivity  $\lambda$  have a minimum of  $\lambda$  independent paths linking any one to any other. When  $\lambda$  is large, a lambda set describes a subset that is relatively difficult to disconnect by means of edge removals[28]. In infectious disease research, we can detect who are the most active in the subgroup which is most important for disease control.

### **Statistical analysis**

All statistical analyses were conducted by SAS V.9.4. Multivariate logistic regression model was used to analyze the demographic characteristics of these key nodes.

### **Network visualization**

The network data were visualized and analyzed using UCINET 6.0.

## **Results**

Of the 184 HIV-1 sequences which were recently HIV diagnosed in 2015–2017, 75 sequences at least had one relationship tie with another (Fig. 1: Network diagram of 75 nodes who at least had one relationship tie with another among 184 sequences). The characteristics of the participants are presented in Table 1.

Table 1  
 Characteristics of the study population according to categories of number of connections

Characteristics	respondents,no. %	Number of connections			P-value*
		0	1	≥ 2	
Total	184(100.00)	109(59.24)	36(19.57)	39(21.20)	
Age(years)					0.21
18–25	69(37.50)	47(68.12)	10(14.49)	12(17.39)	
26–35	71(38.59)	37(52.11)	19(26.76)	15(21.13)	
≥ 36	44(23.91)	25(56.82)	7(15.91)	12(27.27)	
Educational level					0.53
Primary school	44(23.91)	27(61.36)	6(13.64)	11(25.00)	
High school	44(23.91)	29(65.91)	7(15.91)	8(18.18)	
University and above	96(52.17)	53(55.21)	23(23.96)	20(20.83)	
Marital status					0.26**
Married	29(15.76)	13(44.83)	7(24.14)	9(31.03)	
Unmarried	143(77.72)	89(62.24)	28(19.58)	26(18.18)	
Divorced	12	7(58.33)	1(8.33)	4(33.33)	
Diagnose time					0.007
2015	100	53 (53.00)	28 (28.00)	19 (19.00)	
2016	84	56 (66.67)	8 (9.52)	20 (23.81)	
Note: * p value for chi-square test for categorical variables.					
** Fisher exact test for marital status.					
All percentages are line percentages.					

## Cohesive Subgroup Analysis

### 2-cliques

Social network analysis demonstrated that there were 14 cliques which at least include 3 nodes. The biggest clique includes 24 members, and there were some cliques sharing the same member. The clique 1 through 8 shared a lot of same members, and clique 9 which only includes 4 members did not share any member with others (Table 2).

Table 2  
clique analysis in HIV transmission network with 184 nodes

cliques	Number of nodes	ID
1	24	10 14 15 20 26 27 34 37 4 41 62 80 R10 R3 M003 M004 M010 M011 M050 M057 M060 M064 M100 M107
2	22	14 15 20 26 27 34 37 4 59 62 80 R3 M003 M004 M010 M011 M050 M057 M060 M064M100M107
3	22	14 15 20 26 27 34 37 4 47 59 80 9 M003 M004 M010 M011 M050 M057 M060 M064M100M107
4	24	10 14 15 20 26 27 34 37 4 41 62 80 R10 R3 M003 M004 M010 M011 M013 M050 M057 M060 M064 M100
5	22	14 15 20 26 27 34 37 4 59 62 80 R3 M003 M004 M010 M011 M013 M050 M057 M060 M064 M100
6	17	10 20 26 27 34 4 41 62 R10 R3 M003 M010 M017M050 M057 M060 M107
7	12	2 20 26 27 4 59 62 R3 M013 M050 M057 M060
8	5	34 4 41 M057 M073
9	4	25 M101 M103 M104
10	6	30 75 R12 M026 M048 M056
11	4	30 M026 M037 M065
12	5	75 R12 M026 M056 M108
13	5	8 R12 M026 M056 M109
14	3	M026 M048 M068

The clique co-membership method yields a large subgroups consisting of several cliques {1-8}, with a median subgroup of cliques {10,12} four small groups of clique {9},{11},{13} and {14}, and the outsiders. We denote the six subgroups as A, B, C, D, E and F. M026 acted as a broker between subgroup B and F, E and F, D and F, as well as D and E. Subgroup B and D shared two actors{30&M026}acting as brokers between them. There were three shared members between groups B and E, respectively:{R12, M026, M056}.

### Lambda set

From the result of Lambda analysis (Table 3), There were 17 lambda sets with  $\lambda = 1$  which have a minimum of 1 independent path linking for any two actors. The largest number of members in lambda sets with connectivity 1 was 31. The largest  $\lambda$  was 19, it include 2 actors {27, M057}. A little bit smaller  $\lambda$  were 15 and 10, the actors in the lambda sets were {4, 27, M057} and {26, M050, 4, 27, M057} respectively. All of

the above 5 nodes were nested hierarchically in the set with  $\lambda = 1$  which has the largest number of members. These five nodes have the most relationship ties in the set and were in the most active central position. Furthermore, there were 3 lambda sets with  $\lambda$  value of 3, at least three independent paths were connected between any two nodes in the set.

Interestingly, no matter we analyzed the 2-cliques or the Lambda set, we always found that there was a small group composed of four members independent of any other group, the set composed of 25, M101, M103 and M104 shows relatively independent and stable characteristics. Of the four members, aged under 30, were born in the late 1980s and 1990s., and each member maintains a communication relationship with the other three members.

Table 3. Lambda sets in HIV transmission network with 184 nodes

$\lambda$	The number of sets	actors
1	17	1 (3,13) 2 (44, M009) 3 (R11, M016) 4 (M024, M025) 5 (M045, M046) 6 (M034, M051) 7 (6, M069) 8 (M019, M083) 9 (M078, M086) 10 (M079, M087) 11 (M080, M088) 12 (M028, M090) 13 (M084, M092) 14 (M098, M099) 15 (25, M101, M103, M104) 16 (47, 9, M017, M073, 14, 2, 37, 41, 59, 80, M003, M004, M011, M013, 15, 34, M010, 10, R10, 20, 62, R3, 26, M050, 4, 27, M057, M060, M064, M100, M107) 17 (8, M048, 75, R12, M026, M056, 30, M037, M065, M068, M108, M109, M110, M111)
2	4	1 (25, M101, M103, M104) 2 (14, 2, 37, 41, 59, 80, M003, M004, M011, M013, 15, 34, M010, 10, R10, 20, 62, R3, 26, M050, 4, 27, M057, M060, M064, M100, M107) 3 (75, R12, M026, M056) 4 (30, M037, M065)
3	3	1 (25, M101, M103, M104) 2 (41, 59, 80, M003, M004, M011, M013, 15, 34, M010, 10, R10, 20, 62, R3, 26, M050, 4, 27, M057, M060) 3 (M026, M056)
4	1	1 (15, 34, M010, 10, R10, 20, 62, R3, 26, M050, 4, 27, M057, M060)
5	1	1 (M010, 10, R10, 20, 62, R3, 26, M050, 4, 27, M057, M060)
6	1	1 (10, R10, 20, 62, R3, 26, M050, 4, 27, M057, M060)
8	1	1 (20, 62, R3, 26, M050, 4, 27, M057)
10	1	1 (26, M050, 4, 27, M057)
15	1	1 (4, 27, M057)
19	1	1 (27, M057)

## Key nodes

We identified 9 key nodes by using cohesive subgroup analysis in the HIV molecular transmission network finally. {30, M026, R12, M056} acted as brokers between subgroup, and {26, M050, 4, 27, M057} were confirmed as the most active nodes in one subgroups. We analyzed the demographic characteristics of these key nodes. From the results of multivariate logistic regression model, young MSM born in the 1990s and 1980s was 0.06 and 0.12 times as likely to be a key node as was the older MSM born in the

1970s and before, given that they were the same for educational level, marital status and diagnose year (Table 4).

Table 4  
The demographic characteristics of the key nodes in HIV transmission network

Characteristics	key nodes N(%)	Others N(%)	Adjusted OR 95% CI	P value
Total	9 (4.89)	175 (95.11)		
Age(years)				
18–25*	1 (1.45)	68 (98.55)	0.06 (0.01–0.74)	0.03
26–35 <sup>#</sup>	2 (2.82)	69 (97.18)	0.12 (0.02–0.84)	0.03
≥ 36 <sup>□</sup>	6 (13.64)	38 (86.36)	1.00	
Educational level				
Primary school	3 (6.82)	41 (93.19)	0.42 (0.06–2.95)	0.38
High school	1 (2.27)	43 (97.73)	0.28 (0.03–3.07)	0.29
University and above	5 (5.21)	91 (94.79)	1.00	
Marital status				
Married	3 (10.34)	26 (89.66)	1.35 (0.11–16.12)	0.81
Unmarried	5 (3.50)	138 (96.50)	1.40 (0.09–22.93)	0.81
Divorced	1 (8.33)	11 (91.67)	1.00	
Diagnose time				
2015	4 (4.00)	96 (96.00)	0.61 (0.14–2.75)	0.52
2016	5 (5.95)	79 (94.05)	1.00	
*were born in the 1990s; # were born in the 1980s; □ were born in the 1970s and before;				
All percentages are line percentages.				

## Discussion

To response the high HIV prevalence among MSM in China, it is necessary to analysis the characteristics of the transmission network.

One study conducted in San Diego, California identified that 54% were connected by at least one putative transmission link to others in the network of HIV infected MSM[22]. Our study showed that the actor had

at least one transmission relationship tie with another were 40.76% in the network of HIV newly diagnosed in 2015-2017 among MSM in Guangzhou. The transmission network clustering degree was lower than the result of previous research in San Diego, the limit sample size and different areas could be part of the reason, however, to a certain extent, it also showed that there was a widespread transmission relationship among HIV-infected MSM in Guangzhou.

One of the key features of a network which are more important for controlling infection disease is the location and its role of the members which is detected by network structure analysis. The network structure analysis has potential ability to detect a set of specific key nodes which has a significant influence on [disease transmission](#) dynamics by exploring centrality or cohesive subgroup.

Based on accessibility cohesive subgroup analysis called as 2-clique method we detected 14 cliques. Furthermore, By using clique co-membership method there were four key nodes {30, M026, R12, M056} acting as brokers between Subgroups. The four nodes which occupied important bridge locations were critical in controlling and understanding the spread processes as well as to develop effective prevention strategies. A HIV Prevention Network Approach research has proved it: to select candidates who connect across groups of otherwise disconnected individuals (such individuals are known as "bridging actors") based on their network positions were more likely to enhance the diffusion of innovative HIV prevention interventions when compared to other centrally-located popular opinion leader [29]. The difference was that we used different approach to identify bridging actors. John A. Schneider and his colleagues identified bridging actors by calculating the bridging scores using betweenness centrality. Betweenness centrality is a measure of how often a given node falls along the shortest path between two other nodes. The score is a single value for each node in the network. In our study, the top three nodes with the highest score were 27, M057 and 4. M026, R12, 30 and M056 were only in 4th, 7th, 8th and 9th place. In this study, we thought the node has power because it can threaten to stop transmitting. But this threat only works if the other nodes cannot easily create new ties to simply go around the recalcitrant node. From figure 1, we can see that 27, M057 and 4 did not have this threat capability. Moreover, Betweenness centrality method did not successfully identify actor M026 and 30 who played an important potential role in mediating HIV transmission between different subgroups. Therefore, we used cohesive subgroup analysis method which apply subgroup concepts to identify bridging actors. From our results, we can infer that there were a lot of subgroups connected by sharing comembers in HIV transmission network among MSM in Guangzhou. It is essential to recognize the bridging population who mediated the transmission of HIV between different subpopulations among MSM.

Based on connectivity cohesive subgroup analysis called lambda sets method we detected 17 lambda sets. The fact that lambda sets generate a series of groups that are nested hierarchically within each other means that the data analyst is able to choose the level of detail to analyze [28]. There were 5 nodes {26, M050, 4, 27, M057} have a minimum of 10 independent paths linking for any two of them. That means all 5 of them are difficult to disconnected by means of edge removals. They were in eight different sets together, indicating that these nodes were important within the group and were possibly taking on some kind of leadership role, we can use degree centrality to measure this. Actually, the 5 nodes {26,

M050, 4, 27, M057} were the top five nodes with the highest degree centrality in the HIV transmission network with 184 nodes in our research, but we can get a clearer understanding of the position and role of these five nodes through lambda sets analysis. In fact, they were active only in a larger subgroup of the transmission network in this study, rather than participating in the whole network of HIV transmission. So that the effect of intervention may be limited to small groups if the intervention program identifies the peer leaders by calculating degree centrality in the target network. In our study, there were at least three independent subgroups with members closely connected with each other within them. Therefore, it is immensely vital for HIV prevention and control to determine the subgroups with different characteristics in HIV transmission network among MSM.

Centrality which is defined as the number of connections with the other nodes in the network were widely proved to be associated with the dynamics of transmission of infectious diseases[30, 31]. However, centrality measures are simple but maybe less effective for they neglect the whole structure of the network [32, 33]. From our analysis above, we can see that it is easy to ignore some important nodes and subgroups by calculating centrality to identify key nodes. Therefore, we used more stable cohesive subgroup method basing on accessibility and connectivity among its members to detect a collection of key nodes.

Recently years, the HIV incidence in Chinese younger MSM was significantly higher than that in older MSM[34]. However, based on our results, young MSM were less likely to promote the wide spread of HIV than older MSM. The point of intervention activities should be to improve the self-protection awareness of young MSM. On the other hand, the result of a Large-Scale Systematic Analysis in China showed that HIV prevalence was the highest in those aged 50 years and older among MSM[35]. Accordingly, the focus of intervention should be to promote HIV testing and antiretroviral therapy in older MSM.

At first sight, it appears easy to identify cohesive subgroups in the network just by looking at the visualizable network. However, it must be a problem for some group members or subgroups would be missed by simply visualizing it if the number of members in the network is too large.

The main limitation of this study was the small sample size. The network used to analyze structure characteristics in this paper was partial network, so that the number and scale of the subgroups may be underestimated, and some key nodes were not successfully identified. Because of the limit sample size, we did not get enough information about key nodes except age. Large sample size research is needed to explore the demographic and behavioral characteristics of key nodes. Besides, HIV molecular transmission network can't completely represent social network. However, molecular procedures can distinguish HIV-infected individuals socially linked with another person in about half of the phylogenetic transmission clusters [36].

## Conclusions

There were a lot of subgroups connected by sharing members in HIV molecular transmission network among MSM in Guangzhou. Some HIV-infected MSM called as key nodes mediated the transmission of

HIV among different subpopulations. Young MSM were less likely to promote HIV transmission than older MSM.

## **Abbreviations**

HIV

Human Immunodeficiency Virus;

AIDS

Acquired Immune Deficiency Syndrome;

MSM

Men who have Sex with Men;

UNAIDS

The Joint United Nations Programme on HIV/AIDS;

VCT

HIV voluntary counseling and testing clinics;

CDC

the Center for Disease Control and Prevention.

## **Declarations**

### **Ethics approval and consent to participate**

The research protocol and informed consent form received ethical approval from the Institutional Review Board of the National Center for AIDS/STD Control and Prevention, China CDC.

### **Consent for publication**

Not applicable.

### **Availability of data and materials**

All data generated or analysed during this study are included in this published article.

### **Competing interests**

The authors declare that they have no competing interests.

### **Funding**

This work was supported by the National Natural Science Foundation of China (NSFC) (No. 71473234 and 71573239).

### **Authors' contributions**

FL and JY collaborated in drafting the article and revising it critically for important intellectual content; FL, JY and PX conducted the conception and design of the study;

ZGH, HFX, EBC and YZG contributed on acquisition of data; FL, JY and HX accounted for analysis and interpretation of data; All authors reviewed, read and approved the final version before submission.

## Acknowledgements

We would like to thank Yali Zhang and Qiuyan Yu, a graduate student and a Ph. D student, for assisting with the data collation.

## References

- 1) NCAIDS, NCSTD, China CDC. Update on the AIDS/STD epidemic in China in December 2017. *Chin J AIDS STD* 2018;24(2). doi:10.13419/j.cnki.aids.2018.02.01. in Chinese.
- 2) UNAIDS, Blind spot: reaching out to men and boys. 2017, UNAIDS.
- 3) Nelsensius KF, Maria SM, Mitra AS, Sukma P, Lillian M. Culture, social networks and HIV vulnerability among men who have sex with men in Indonesia. *PLoS One*. 2017;12(6): e0178736. Published 2017 Jun 5. doi:10.1371/journal.pone.0178736
- 4) Glenn JW, Matthew H, Harold G, Johnny T, Jacques M. Social, Relational and Network Determinants of Unprotected Anal Sex and HIV Testing Among Men Who Have Sex with Men in Beirut, Lebanon. *Int J Sex Health*. 2015;27(3):264–275. doi:10.1080/19317611.2014.969467.
- 5) Ethan M, Alexandra MO, Stephanie T, Donna P, Nanette B, John AS. HIV-1 Infection and Transmission Networks of Younger People in Chicago, Illinois, 2005-2011. *Public Health Rep* 2017; 132(1):48-55. DOI: 10.1177/0033354916679988.
- 6) Latkin C, Mandell W, Oziemkowska M, Celentano D, Vlahov D, Ensminger M, et al. Using social network analysis to study patterns of drug use among urban drug users at high risk for HIV/AIDS. *Drug Alcohol Depend*. 1995;38(1):1–9. DOI:10.1016/0376-8716(94)01082-v.
- 7) Leslie DW, Ania K, Pavlo S, Yana S, Georgios KN, Britt S, et al. Social network approaches to locating people recently infected with HIV in Odessa, Ukraine. *J Int AIDS Soc*. 2019; 22(6): e25330. DOI: 10.1002/jia2.25330.
- 8) Pavlo S, Leslie DW, Ania K, Yana S, Georgios KN, Britt S, et al. Risk network approaches to locating undiagnosed HIV cases in Odessa, Ukraine. *J Int AIDS Soc*. 2018; 21(1): e25040. doi: 10.1002/jia2.25040.
- 9) Georgios KN, Eirini P, Stephen QM, John S, Mina P, Leslie DW, et al. A network intervention that locates and intervenes with recently HIV-infected persons: The Transmission Reduction Intervention Project (TRIP). *Sci Rep*. 2016; 6:38100. doi: 10.1038/srep38100.

- 10) Samuel RF, Leslie W, April MY, Jennifer T, Dimitretios P, Evangelia K, et al. Network Research Experiences in New York and Eastern Europe: Lessons for the Southern US in Understanding HIV Transmission Dynamics. *Curr HIV/AIDS Rep.* 2018;15(3):283-292. doi: 10.1007/s11904-018-0403-2.
- 11) Amirkhanian YA, Kelly JA, Kabakchieva E, Kirsanova AV, Vassileva S, Takacs J, et al. A randomized social network HIV prevention trial with young men who have sex with men in Russia and Bulgaria. *AIDS.* 2005;19(16):1897–1905. doi:10.1097/01.aids.0000189867.74806.fb
- 12) Amirkhanian YA, Kelly JA, Takacs J, McAuliffe TL, Kuznetsova AV, Toth TP, et al. Effects of a social network HIV/STD prevention intervention for MSM in Russia and Hungary: a randomized controlled trial. *AIDS.* 2015;29(5):583–593. doi:10.1097/QAD.0000000000000558
- 13) Stéphane HELLERINGER, Hans-Peter Kohler. Sexual network structure and the spread of HIV in Africa: evidence from Likoma Island, Malawi. *AIDS.* 2007;21(17):2323-2332. doi:10.1097/QAD.0b013e328285df98.
- 14) Mary KG, Andrew DR. Molecular tools for studying HIV transmission in sexual networks. *Curr Opin HIV AIDS* 2014; 9(2):126-133. doi:10.1097/COH.0000000000000040.
- 15) Eshleman SH, Hudelson SE, Redd AD, Wang L, Debes R, Chen TQ, et al. Analysis of genetic linkage of HIV from couples enrolled in the HIV Prevention Trials Network 052 trial. *J Infect Dis* 2011; 204(12):1918-1926. doi: 10.1093/infdis/jir651.
- 16) Morgan E, Skaathun B, Schneider JA. Sexual, Social, and Genetic Network Overlap: A Socio-Molecular Approach Toward Public Health Intervention of HIV. *Am J Public Health.* 2018; 108(11):1528-1534. doi: 10.2105/AJPH.2018.304438.
- 17) Lubelchek RJ, Hoehnen SC, Hotton AL, Kincaid SL, Barker DE, French AL. Transmission clustering among newly diagnosed HIV patients in Chicago, 2008 to 2011: using phylogenetics to expand knowledge of regional HIV transmission patterns. *J Acquir Immune Defic Syndr.* 2015; 68(1):46-54. doi:10.1097/QAI.0000000000000404.
- 18) Oster AM, Pieniazek D, Zhang X, Switzer WM, Ziebell RA, Mena LA, et al. Demographic but not geographic insularity in HIV transmission among young black MSM. *AIDS.* 2011; 25(17):2157-2165. doi: 10.1097/QAD.0b013e32834bfde9.
- 19) Castley A, Sawleshwarkar S, Varma R, Herring B, Thapa K, Dwyer D, et al. A national study of the molecular epidemiology of HIV-1 in Australia 2005-2012. *PLoS One.* 2017;12(5):e0170601. doi: 10.1371/journal.pone.0170601.
- 20) Yang J, Xu H, Li S, Cheng W, Gu Y, Xu P, et al. The characteristics of mixing patterns of sexual dyads and factors correlated with condomless anal intercourse among men who have sex with men in Guangzhou, China. *BMC Public Health.* 2019;19(1):722. doi:10.1186/s12889-019-7082-9.

- 21) Oster AM, Wertheim JO, Hernandez AL, Ocfemia MC, Saduvala N, Hall HI. Using Molecular HIV Surveillance Data to Understand Transmission Between Subpopulations in the United States. *J Acquir Immune Defic Syndr*. 2015;70(4):444–451. doi:10.1097/QAI.0000000000000809.
- 22) Pines HA, Wertheim JO, Liu L, Garfein RS, Little SJ, Karris MY. Concurrency and HIV transmission network characteristics among MSM with recent HIV infection. *AIDS*, 2016. 30(18): p. 2875–2883. doi:10.1097/QAD.0000000000001256.
- 23) Little SJ, Kosakovsky Pond SL, Anderson CM, Young JA, Wertheim JO, Mehta SR, et al. Using HIV networks to inform real time prevention interventions. *PLoS One*. 2014;9(6):e98443. Published 2014 Jun 5. doi:10.1371/journal.pone.0098443.
- 24) Li X, Gao R, Zhu K, Wei F, Fang K, Li W, et al. Genetic transmission networks reveal the transmission patterns of HIV-1 CRF01\_AE in China. *Sex Transm Infect*. 2018;94(2):111–116. doi:10.1136/sextrans-2016-053085.
- 25) Sinkovits RS, Moody J, Oztan BT, White DR. Fast determination of structurally cohesive subgroups in large networks. *J Comput Sci*, 2016. 17(Pt 1): p. 62-72. doi: 10.1016/j.jocs.2016.10.005.
- 26) Borgatti SP, Everett MG, Johnson JC. *Analyzing Social Networks*[J]. 2013.
- 27) Liu J. *Analysis of whole network*. [M]. 2014. Century Publishing Co., Ltd press. in Chinese.
- 28) Stephen P. Borgatti, Martin G. Everett, Paul R. Shirey. LS Sets, Lambda Sets and Other Cohesive Subsets[J]. *Social Networks*, 1990, 12(4):337-357. Doi:[10.1016/0378-8733\(90\)90014-Z](https://doi.org/10.1016/0378-8733(90)90014-Z)
- 29) Schneider JA, Zhou AN, Laumann EO. A new HIV prevention network approach: sociometric peer change agent selection. *Soc Sci Med*. 2015; 125:192-202. doi: 10.1016/j.socscimed.2013.12.034.
- 30) Gómez JM, Verdú M. Network theory may explain the vulnerability of medieval human settlements to the Black Death pandemic. *Sci Rep*. 2017;7:43467. Published 2017 Mar 6. doi:10.1038/srep43467.
- 31) de Arruda GF, Barbieri AL, Rodríguez PM, Rodrigues FA, Moreno Y, Costa Lda F. Role of centrality for the identification of influential spreaders in complex networks. *Phys Rev E Stat Nonlin Soft Matter Phys*. 2014;90(3):032812. doi:10.1103/PhysRevE.90.032812.
- 32) [Mark E. J. Newman](#). *Networks: An Introduction*. 2010: Oxford University Press, Inc.
- 33) Ahajjam S, Badir H. Identification of influential spreaders in complex networks using HybridRank algorithm. *Sci Rep*. 2018;8(1):11932. doi:10.1038/s41598-018-30310-2
- 34) Mao X, Wang Z, Hu Q, Huang C, Yan H, Wang Z, et al. HIV incidence is rapidly increasing with age among young men who have sex with men in China: a multicentre cross-sectional survey. *HIV Med*. 2018; 19(8):513-522. doi: 10.1111/hiv.12623.

