Social networks and HCV viremia among anti-HCV positive rural drug users

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Summary

Though social networks are known to play an important role in drug-using behaviors associated with HCV infection, literature on social networks and HCV is inconsistent. This exploratory study examined HCV RNA distribution within a social network of anti-HCV positive rural Appalachia nonmedical prescription opioid users (NMPOUs). Participants were tested serologically for HCV RNA, and behavioral, demographic, and network data were collecting using interview-administered questionnaires. Multivariate analyses were performed using logistic regression. Behavioral and demographic characteristics did not differ by RNA status. In the multivariate model, recent injection drug users were more likely to be RNA-positive (OR: 4.06, 95% CI: 1.04 – 15.83), and turnover into one's drug network was significantly protective (OR: 0.15, 95% CI: 0.03-0.75). This is the first study to date to examine HCV distribution among rural NMPOUs from a network perspective and demonstrates that network characteristics significantly contribute to the epidemiology of HCV in this understudied, high-risk population.

Introduction

Hepatitis C (HCV) is the most common blood-borne infection in the US, with an estimated 3.2 million people chronically infected [1]. Injection drug use is a well-established risk factor for blood-borne infection [e.g. 2-3]. In fact, as many as 90% of injection drug users (IDUs) are infected with HCV within five years of initiating injection [4]. Injection drug use and its associated risk, however, do not occur in isolation; they are heavily influenced by the structure and composition of the social networks in which they arise [5-6].

IDUs' risk behavior and susceptibility to infection is strongly influenced by that of their network members [7-10]. For example, an individual's injection behavior is influenced by their exposure to other IDUs [11-12], particularly those who are friends [13], sex partners [14-15], or family members [16]. Previous research has also demonstrated an interrelated relationship [6] between large network size [10, 17], high network density [e.g. 10, 17-18], and high network turnover (e.g. people leaving or entering one's network) [19] and risk behavior among IDUs. The centrality of a drug user within his/her social network, as well as the types of relationships he/she has with network members can also play a role in risk behavior [5-6].

The growing recognition of social networks' contribution to IDUs' risk for HCV has led to a number of molecular epidemiological studies in which HCV RNA and genotype testing is conducted within networks [20-23]. While the literature on drug users' social networks consistently demonstrates a link between network structure and engagement in HCV risk behavior [6], such findings have yet to be consistently substantiated by molecular epidemiological research examining HCV transmission within social networks of IDUs. For example, a recent study examining HCV genotype homology between dyads and recruitment chains generated from respondent-driven sampling (RDS) of IDUs found that individuals within recruitment dyads and/or chains had no more genetic similarity in their HCV infection than did those with more distant relationships [20]. Similarly, a study involving social network analysis and HCV phylogenetic analysis of Australian IDUs found a low level of correlation between drug users' social distance and the genetic relatedness of their HCV infections [21]. On the other hand, a phylogenetic analysis of HCV-positive patients in a surveillance program in Brazil concluded that different HCV subtypes were characterized by different social networks [22]. A social network study of IDUs by Aitken and colleagues (2009) concluded that positive HCV antibody status was associated with having more network members who were age 18 or older when they initiated IDU and with having other network members who were antibody positive. Positive HCV RNA status was also associated with having network members who were HCV RNA positive [23].

Given the inconsistencies in the extant literature, more research examining the distribution of HCV infection within social networks of drug users is warranted. Previous studies have primarily focused on heroin users [21, 23], cocaine users [6], and syringe exchange program recipients [6] in urban, international settings [6, 20-23]. To our knowledge, no study has examined HCV RNA distribution in its association with social network characteristics among nonmedical prescription opioid users (NMPOU). Moreover, there is a substantial gap in previous research involving populations of rural drug users. Nonmedical prescription opioid use has become particularly problematic in the rural Appalachian region of Kentucky [e.g. 24-25], and evidence suggests that many drug users in the region are administering the prescription drugs via injection [24]. Given the increased risk of HCV transmission associated with injection drug use, a better understanding of the molecular and social epidemiology of HCV in this high-risk, understudied population of rural drug users is needed. The purpose of this exploratory study is two-fold: to examine the distribution of HCV RNA positive drug users within a network of NMPOU in rural Appalachian Kentucky, and to examine the association of their individual-level, egocentric and sociometric risk network characteristics with HCV RNA status.

Methods

Study sample

The study sample was drawn from a larger cohort of rural Appalachian nonmedical prescription opioid users (N=436). The overall purpose of the longitudinal cohort study is to determine the prevalence and incidence of HCV, HIV and herpes simplex-2 virus in the context of rural drug and sex networks. A storefront location in a rural Appalachian town of approximately 5,000 residents was used for participant recruitment and interviews. Recruitment was conducted using RDS, which is often the most feasible and appropriate sampling technique for hidden populations such as drug users [26]. Seeds for the RDS were identified through outreach workers, community informants, and through flyers posted in town and outside the study field office. Upon completion of the baseline interview, seeds were given three coupons to bring in additional network members. Individuals who redeemed the coupons were then given coupons to recruit additional members and so on until the desired sample size was achieved. The seeds were given $10 for each referred network member who redeemed their coupon and completed the baseline interview.

Study recruitment began in November, 2008 and was completed in August, 2010. Eligibility criteria for the study included those who were at least 18 years of age, were residents of an Appalachian county and had used at least one of the following drugs to get high in the prior 30-day period: prescription opioids, heroin, crack/cocaine and/or methamphetamine. An interviewer-administered questionnaire was utilized to determine self-reported behaviors. Data were entered by the interviewers directly onto a touch screen laptop loaded with computer-assisted personal interviewing (CAPI) software. Participants are compensated $50 for each study visit and the Institutional Review Board at the University of Kentucky approved the protocol.

Drug network data collection

A name-generating questionnaire (first name and last initial) was used to determine with whom individuals had used injected and non-injected drugs in the past 6 months (excluding alcohol and marijuana). For each person named, additional information about the person was gathered, including their gender, race and approximate age. Four sources of information were used to confirm network ties. The name and demographic characteristics were checked against those of other participants in the study. A match in the name and demographic information was considered a confirmed linkage. Linkages that could not be confirmed using names and demographic information were then matched against information provided by individuals screened for eligibility. Participants screened for study participation (n=939) provided detailed demographic information for the purposes of network linkage confirmation. Finally, advice from community-based research staff was sought to determine and confirm network linkages. Linkages that could not be confirmed using one of these were not included in the sociometric network. These methods are similar to that used in previous research [27]. UCInet 6.303 [28] was used for network analyses.

In addition to examining the overall drug network, participants' injection risk network was also examined. Once participants' drug network members were established, participants were asked about their injection behavior with each network neighbor. Participants were asked if in the past six months they had injected drugs with the person and/or if they had shared injection equipment (e.g. syringes, cookers, rinse water) with the person in the past six months. A sociometric network, hereinafter called "injection risk network", was constructed in which a tie constituted any relationship in which at least one person reported injecting together or sharing injection equipment.

Egocentric network variables

Four egocentric network characteristics were examined for their associations with HCV RNA status. Egocentric network size is merely a count of all the network members (alters) linked to a focal individual (ego), not including the ego themselves. For example, egocentric drug network size was determined by the number of individuals with whom the participant reported using drugs in the past six months. For analysis of egocentric drug network size was categorized into 'high' (greater than 2) and 'low' (less than or equal to 2). The density of participants' drug network was calculated as the proportion of possible connections present in one's ego network. Participants with a density of zero were classified as having low density and participants with density greater than or equal to one were classified as having 'high density'.

Turnover (both in and out) of participants' drug networks was also assessed. Network turnover in and out was defined as a gain and loss, respectively, in network members between baseline and 6-month follow-up assessments. For computation of turnover, drug network isolates were excluded (n=49). Also, participants who had not yet completed their

6-month follow-up assessment at the time of their serological testing for HCV RNA were excluded (n=6). Turnover was analyzed as continuous.

Sociometric network variables

Homophily was computed by testing if individuals who were HCV RNA positive are more likely to be tied to each other in a network of drug relations than that which would be expected at random. Homophily was also computed to test if individuals who were RNA negative were more likely to be tied to each other than would be expected at random. Homophily is computed by comparing the observed network against 20,000 permutations of random networks and the output is identical to that of a Pearson Correlation table. Homophily testing was performed with the Join-Count command in UCInet 6.30 [28].

Four measures were used to examine participants' centrality within their drug networks: degree centrality, eigenvector, betweenness, and 2-step reach. Degree centrality, the number of network members adjacent to a given participant in the network [29], was dichotomized into 'high' (centrality greater than 2) and 'low' (centrality less than or equal to 2). Eigenvector centrality [30] takes into account participants' second order connections and the interconnectedness of those connections. Considering the second-order dimension of individuals' connections is especially important in networks involving risk behaviors that facilitate the diffusion of infectious disease, as an individual whose friends are engaged in risky behaviors with multiple others are more likely to infect an individual and/or be infected than an individual whose friends do not engage in risk behaviors with other people [31]. Eigenvector values were dichotomized (0 = eigenvector of 0, 1= eigenvector greater than 0).

Betweenness served as a measure of how often the participant lies on the shortest 'path' between two nodes within the drug network. Due to the skewed distribution of the data, drug network betweenness was dichotomized according to a median split ('low': less than 17.2, 'high': greater than or equal to 17.2). Two-step reach was used to represent the number of network members who are within two network linkages from the participant. Due to distribution, drug network two-step reach was also dichotomized into 'high' and 'low' groups by a median split ('low': less than 6, 'high': greater than or equal to 6).

K-cores were used to examine sub groups within the drug network that were more connected than others. This method was originally used to assess HIV risk by Freidman and colleagues (1997) [8]. Consistent with the aforementioned study by Friedman and colleagues (1997), drug k-coreness was dichotomized into 'high' (k-coreness equal to or greater than 2) and 'low' (k-coreness equal to 0 or 1). Of note, participants with k-coreness equal to 0 were isolates in the network.

To assess participants' proximity to other actors in their risk and drug networks who engage in risk behavior (lifetime injection drug use and injection drug use within the past 6 months), as well as to actors who are anti-HCV positive, geodesic distance was computed. Geodesic distance is the length of the shortest path between a given pair of members in the network [29]. Individuals who are "unreachable", meaning they lack any connections to given individual with X characteristic, were excluded from analyses of geodesic distance. Given the risk conferred by being immediately connected to a person engaging in risk behavior or already exposed to HCV, geodesic distance variables were dichotomized, where 1=one step removed from [HCV, IDU], 0=two or more steps removed from [HCV, IDU].

Serological testing for detection of HCV RNA

During their baseline visits, all participants consented to HCV antibody testing. Testing was performed using the Home Access test for HCV antibody, a third-generation enzyme immunoassay conducted on dried blood spot specimens collected by finger-stick. The accuracy of the Home Access test has been demonstrated [32]. The baseline prevalence of anti-HCV was 45.9% (n=200). Participants were provided with post-test counseling tailored to their study result and were also provided with a list of treatment referrals in the area, where appropriate.

The sampling procedure for HCV RNA testing is described in detail elsewhere [33]. A randomly selected sample (n=81) of anti-HCV positive participants were tested for HCV RNA using COBAS® Ampliprep/COBAS® TaqMan® HCV test kit (Roche Molecular Systems, Inc), which uses real-time polymerase chain reaction (PCR), transcription-mediated amplification (TMA), and multi-probe reverse hybridization of the 5' untranslated region (5' UTR) of the HCV genome. Testing was performed by Quest Diagnostics Nichols Institute (Chantilly, VA). An IRB-approved post-test counseling protocol was administered to participants.

The randomly selected sample of participants who were tested for HCV RNA were representative of the overall pool of anti-HCV positive participants in terms of demographic characteristics (gender, age, education, insurance status), health (self-reported health status, lifetime number of hospitalizations), lifetime number of incarcerations, and HCV risk behaviors (having ever injected drugs, having ever shared equipment for snorting drugs, and having ever received a blood transfusion or tattoo).

Assessment of demographic and behavioral correlates

Participants' demographic characteristics (see Table 1) were based on their baseline assessment in the study, while behavioral characteristics were extracted from their most recently completed interview (i.e. baseline, 6-month, 12-month, or 18-month interview). The average time which had elapsed between participants' most recent interview date and the date of their blood draw was 51.7 days (SD 41.1; range: 18 – 140).

Analysis

Bivariate analyses comparing HCV RNA positive to RNA negative participants were performed using a series of chi-square tests for categorical variables and Wilcoxon sign-rank tests for continuous variables (all variables were non-normally distributed). Multivariable correlates to HCV RNA status were initially assessed using three logistic regression models. Two demographic variables (e.g. age, gender) were chosen *a priori* to be entered into the regression models based on extant literature that suggests they exert strong influences on risk behavior at the interpersonal and network level [5-6]. Similarly, one individual-level behavioral variable (injection drug use in the past 6 months) was chosen *a priori* to be included in the regression analyses due to existing evidence of its strong association with HCV transmission [e.g. 2-3]. The first model included only those three variables selected a priori for analysis. The second and third models evaluated the association between RNA status and egocentric and sociometric variables, respectively, while controlling for age, gender, and injection drug use. Egocentric and sociometric variables were chosen for inclusion in Models 2 and 3 based on their association with RNA status at p<.10 in bivariate analyses. A fourth model containing sociometric and egocentric variables as well as age, gender, and recent injection drug use was then estimated using a common backward elimination strategy [34] to produce the most parsimonious final model. At each step of the backward elimination strategy, the variable with the least significant association with RNA status was dropped and the change in the -2 log likelihood between the reduced and final

model was evaluated against a chi-square distribution with one degree of freedom. If there was no significant change in the -2 log likelihood (i.e. model fit), the variable was eliminated. This strategy was continued until the further elimination of variables would have resulted in a significant change in model fit. Collinearity was assessed at each step of the model-building process using a SAS macro which generates condition indexes and variance decomposition proportions [34].

Results

Demographic characteristics of participants by HCV RNA status are displayed in Table 1. The mean age of participants was 35 years (SD 8.3; range 21-53), the vast majority were white (95%) and nearly 60% were male. Factors which could potentially inhibit ability to seek care were common as 38% lacked access to transportation, 36% were unemployed, and 63% were uninsured. Half of the sample had graduated from high school and over one-third (36%) were unemployed. RNA positive and negative participants did not differ demographically.

Figure 1 displays the distribution of HCV RNA positive participants within the overall drug risk network and in the injection risk sub-network. The injection risk network (visualized with red ties in Figure 1) contained 40% (n=10) of the RNA negative participants and 59% (n=33) of the RNA positive participants, but the difference was not statistically significant (p=.115). The homophily value for the drug network was significant, however, indicating that individuals who are HCV RNA positive are more likely to be tied to each other in the network of drug relations than that which would be expected at random (p=.049), while RNA negative participants were no more likely to be tied to other RNA negative participants or to RNA positive participants than would be expected at random (p=.936 and p=.195, respectively).

Egocentric and sociometric drug network characteristics of participants by HCV RNA status are reported in Table 2. Participants who were HCV RNA positive had significantly higher egocentric drug network density (p=.045) and reported somewhat less turnover into their networks from baseline to six month follow-up than did RNA negative participants, though the difference was not statistically significant (p=.085). Participants did not differ by HCV RNA status on egocentric network size.

Multivariable correlates to HCV RNA status

Table 3 displays multivariable correlates to HCV RNA status. Model 1 contained only the demographic variables and recent injection drug use; none of which were significantly associated with RNA status. Models 2 and 3 extended Model 1 to include egocentric and sociometric network variables, respectively, that were significant at p<.10 in previous bivariate analyses. In Model 2, recent injection drug use and turnover into the drug network were significantly associated with RNA status (p=.016 and p=.001, respectively). In Model 3, individual-level nor sociometric-level variables were statistically significant. In estimating a final model, sociometric and egocentric variables could not be entered into the same model due to collinearity. Thus, the final comprehensive model was estimated using a backward elimination approach applied to Model 2. Age and gender were not retained in the model, leaving recent injection drug use, egocentric network density, and network turnover. Recent injection drug use was significantly associated with positive RNA status (OR: 4.06, 95% CI: 1.04 – 15.83, p=.044) and turnover into one's drug network was negatively associated with positive RNA status (OR: 0.15, 95% CI: 0.03 – 0.75, p=.020). Egocentric drug network density was not significantly associated with RNA status (OR: 3.22, 95% CI: 0.87 – 11.95, p=.081) after adjustment for the other variables in the model.

Discussion

HCV RNA positive participants in this study were demographically and behaviorally similar to participants who were HCV RNA negative. However, in models controlling for age, gender, and recent injection drug use, turnover into one's drug network had a significantly negative association with being RNA positive (OR: 0.06, 95% CI: 0.01 - 0.51). In the final model recent injection drug use was associated with four times greater odds of HCV RNA positive status (95% CI: 1.04 – 15.83), and turnover into one's drug network remained significantly protective (OR: 0.15, 95% CI: 0.03-0.75).

In this study, many egocentric and sociometric network characteristics identified in previous research to be associated with HCV risk behavior (e.g. network size, density, centrality, distance to IDUs) were not significantly associated with HCV RNA status [5-6]. However, the findings regarding recent injection drug use were consistent with the wealth of evidence that has shown it to be a strong risk factor for HCV infection [e.g. 2-3]. Notably, in the present study, injection drug use was associated with RNA status only in the models which controlled for egocentric characteristics. In the models controlling for demographic characteristics and sociometric characteristics, injection drug use was not associated with RNA status.

The negative association between positive RNA status and inward drug network turnover (e.g. a gain in network members from baseline to 6-month follow-up) is not consistent previous behavioral research which suggests that high network turnover is associated with risky injection drug use behavior among network members [6, 19]. One possibility for the association observed in this study could be that a high level of turnover into one's network is not necessarily an indication of network instability, given that network turnover-in was not correlated with network turnover-out (r=.058, p=.466). HCV RNA positive participants may be avoiding the expansion of their drug networks in an effort to avoid contact with serodiscordant partners, a phenomenon known as "serosorting" that has been observed in other research [35]. Conversely, participants who are RNA negative may be avoiding contact with those who are RNA positive, thereby decreasing the latter's opportunity for network expansion. The homophily results from this study, which found that RNA positive participants tended to 'flock together' may also provide some evidence for serosorting. More research, however, is needed to fully understand network turnover dynamics and HCV risk in this population.

These findings highlight the potential of network-based interventions for HCV prevention among IDUs. Specifically, these results indicate the importance of the participants' egocentric network in HCV transmission. Therefore, peer-driven interventions could be effective in reducing HCV risk behaviors in this population [36-38]. Though network characteristics played an important role in drug users' risk for active HCV infection, the role of better access to clean syringes cannot be ignored. Previous research has shown that after controlling for social network characteristics, syringe access/supply remains a significant predictor of risk behavior [39]. This population is in critical need of improved access to services that can reduce their long- and short-term risk for blood borne infection.

While this study provides important insight into the epidemiology of HCV infection in an understudied, high-risk population of drug users and illuminates areas for future research, it is not without limitations. For example, the study is limited by a small sample size. However, it is notable that despite the sample size, statistically significant associations between RNA status and egocentric network characteristics were observed. It is also worth noting that this sample of drug users was randomly selected from a larger cohort of HCV antibody drug users and was demographically and behaviorally representative of the larger

sample. An additional limitation is posed by the use of self-report to collect all behavioral data. However, self-reported drug and risk behaviors have been shown to be sufficiently valid and reliable [40]. Issues of temporality also present a limitation to this study, as it could not be determined if social network characteristics were a cause or consequence of drug risk behavior and HCV status. To address this limitation, longitudinal social network studies that track drug users' HCV RNA status over time are needed.

Despite limitations, this study presents important evidence that the current paradigm of understanding drug users' risk for blood borne infection only within the context of their individual-level risk factors may be inadequate for understanding HCV transmission in this sample of rural drug users. Rather, these data suggest that drug use and its associated risks are best understood within the social contexts in which they occur.

Acknowledgments

References

1. Armstrong GL, et al. The Prevalence of Hepatitis C Virus Infection in the United States, 1999 through 2002. Annals of Internal Medicine. 2006; 144:705–714. [PubMed: 16702586]

2. Xian X, et al. Epidemiology of hepatitis C virus infection among injection drug users in China: Systematic review and meta-analysis. Public Health. 2008; 122:990–1003. [PubMed: 18486955]

3. Alter MJ. Prevention of spread of hepatitis C. Hepatology. 2002; 36:S93–S98. [PubMed: 12407581]

4. Centers for Disease Control and Prevention. Recommendations for prevention and control of hepatitis C virus (HCV) infection and HCV-related chronic disease. 1998

5. Miller M, Neaigus A. Networks, resources and risk among women who use drugs. Social Science & Medicine. 2001; 52:967–978. [PubMed: 11234869]

6. De P, et al. The importance of social networks in their association to drug equipment sharing among injection drug users: a review. Addiction. 2007; 102:1730–1739. [PubMed: 17935581]

7. Neaigus A, et al. The relevance of drug injector's social and risk networks for understanding and preventing HIV infection. Social Science & Medicine. 1994; 38:67–78. [PubMed: 8146717]

8. Friedman SR, et al. Sociometric risk networks and risk for HIV infection. American Journal of Public Health. 1997; 87:1289–1296. [PubMed: 9279263]

9. Garfein RS, et al. Viral Infections in Short-Term Injection Drug Users: The Prevalence of the Hepatitis C, Hepatitis B, Human Immunodeficiency, and Human T'Lymphotrophic Viruses. American Journal of Public Health. 1996; 86:655–655. [PubMed: 8629715]

10. Rothenberg RB, et al. Social network dynamics and HIV transmission. AIDS. 1998; 12:1529–1536. [PubMed: 9727575]

11. Neaigus A, et al. Transitions to Injecting Drug Use Among Noninjecting Heroin Users. Journal of Acquired Immune Deficiency Syndromes. 2006; 41:493–503. [PubMed: 16652059]

12. Sherman SG, et al. Correlates of initiation of injection drug use among young drug users in Baltimore, Maryland: the need for early intervention. Journal of Psychoactive Drugs. 2005; 37:437–443. [PubMed: 16480171]

13. Roy E, et al. Drug injection among street youths in Montreal: predictors of initiation. Journal Of Urban Health. 2003; 80:92–105. [PubMed: 12612099]

14. Neaigus A, et al. Potential risk factors for the transition to injecting among non-injecting heroin users: a comparison of former injectors and never injectors. Addiction. 2001; 96:847–860. [PubMed: 11399216]

15. van Ameijden EJ, et al. Risk factors for the transition from noninjection to injection drug use and accompanying AIDS risk behavior in a cohort of drug users. American Journal of Epidemiology. 1994; 139:1153–1163. [PubMed: 8209874]

16. Abelson J, et al. Some characteristics of early-onset injection drug users prior to and at the time of their first injection. Addiction. 2006; 101:548–555. [PubMed: 16548934]

17. Latkin C, Mandell W. People and places: Behavioral settings and personal network characteristics as correlates of. Journal of Acquired Immune Deficiency Syndromes & Human Retrovirology. 1996; 13:273. [PubMed: 8898673]

18. Latkin C, et al. The relationships between sexual behavior, alcohol use, and personal network characteristics among injecting drug users in Baltimore, Maryland. Sexually Transmitted Diseases. 1994; 21:161–167. [PubMed: 8073344]

19. Hoffmann JP, Su SS, Pach A. Changes in network characteristics and HIV risk behavior among injection drug users. Drug and Alcohol Dependence. 1997; 46:41–51. [PubMed: 9246552]

20. Paintsil E, et al. Hepatitis C virus infection among drug injectors in St Petersburg, Russia: social and molecular epidemiology of an endemic infection. Addiction. 2009; 104:1881–1890. [PubMed: 19712125]

21. Aitken CK, et al. Molecular epidemiology of hepatitis C virus in a social network of injection drug users. Journal of Infectious Diseases. 2004; 190:1586–1595. [PubMed: 15478062]

22. Romano CM, et al. Social networks shape the transmission dynamics of hepatitis C virus. PLoS ONE. 2010; 5:1–9.

23. Aitken, et al. Does information about IDUs' injecting networks predict exposure to the hepatitis C virus? Hepatitis Monthly. 2009; 9:17–23.

24. Young AM, Havens JR, Leukefeld CG. Route of administration for illicit prescription opioids: a comparison of rural and urban drug users. Harm Reduction Journal. 2010; 7:24. [PubMed: 20950455]

25. Young AM, Havens JR. Transition from first illicit drug use to first injection drug use among rural Appalachian drug users: A cross-sectional comparison and retrospective survival analysis. Addiction. Published online: 28 August 2011. 10.1111/j.1360-0443.2011.03635.x

26. Heckathorn D. Respondent-driven sampling II: Deriving valid population estimates from chain-referral samples of hidden populations. Social Problems. 2002; 49:11–34.

27. Latkin CA, Forman V, Knowlton A, Sherman S. Norms, social networks, and HIV-related risk behaviors among urban disadvantaged drug users. Social Science and Medicine. 2003; 56:465–476. [PubMed: 12570967]

28. Borgatti, S.; Everett, M.; Freeman, L. Ucinet for Windows: Software for Social Network Analysis. Harvard, MA: Analytic Technologies; 2002.

29. Wasserman, S.; Faust, K. Social Network Analysis: Methods and Applications. Cambridge, England and New York: Cambridge University Press; 1994.

30. Bonacich P. Factoring and weighting approaches to status scores and clique identification. Journal of Mathematical Sociology. 1972; 2:113–120.

31. Borgatti SP. Centrality and AIDS. Connections. 1995; 18:112–115.

32. O'Brien J, et al. Detection of hepatitis C antibody with at-home collection kits using an innovative laboratory algorithm. Infectious Diseases in Clinical Practice. 2001; 10:474–480.

33. Young AM, Crosby R, Oser CB, Leukefeld CG, Stephens DB, Havens JR. Hepatitis C Viremia and Genotype Distribution among a sample of HCV-exposed Nonmedical Prescription Drug Users in Rural Appalachia. Journal of Medical Virology. in press.

34. Zack M, et al. Collinearity macro (SAS). Department of Epidemiology, Emory University Rollins School of Public Health. 2011 Contact dkleinb@sph.emory.edu.

35. Burt RD, Thiede H, Hagan H. Serosorting for hepatitis C status in the sharing of injection drug equipment among Seattle area injection drug users. Drug and Alcohol Dependence. 2009; 1:215–220. [PubMed: 19720473]

36. Garfein RS, et al. A peer-education intervention to reduce injection risk behaviors for HIV and hepatitis C virus infection in young injection drug users. AIDS. 2007; 21:1923–1932. [PubMed: 17721100]

37. Latka MH, et al. A randomized intervention trial to reduce the lending of used injection equipment among injection drug users infected with hepatitis C. American Journal of Public Health. 2008; 98:853–861. [PubMed: 18382005]

38. Friedman SR, et al. Harm reduction theory: users culture, micro-social indigenous harm reduction, and the self-organization and outside-organizing of users' groups. International Journal of Drug Policy. 2007; 18:107–117. [PubMed: 17689353]

39. Shaw SY, et al. Determinants of injection drug user (IDU) syringe sharing: the relationship between availability of syringes and risk network member characteristics in Winnipeg, Canada. Addiction. 2007; 102:1626–1635. [PubMed: 17854339]

40. Darke S. Self-report among injecting drug users: a review. Drug and Alcohol Dependence. 1998; 51:253. [PubMed: 9787998]
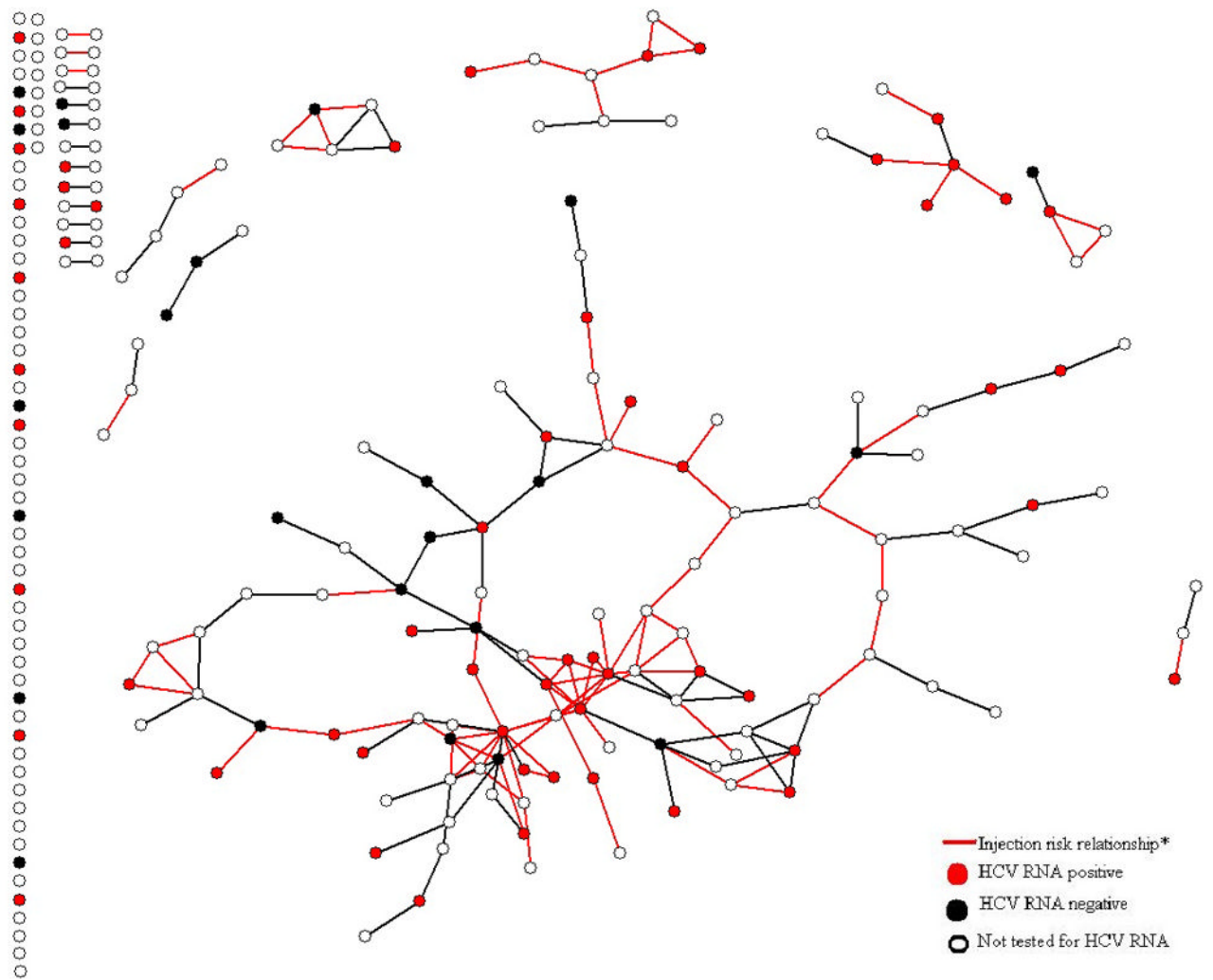
Figure 1.
HCV RNA status of randomly selected sample of anti-HCV positive drug users in a drug
risk network (n=222)
*Relationships in which network members injected together, shared needles, and/or shared
works

Table 1

Demographic and behavioral characteristics of sample (n=81)

Characteristic	Total N (%)	HCV RNA+ (n=56) n(%)	HCV RNA - (n=25) n(%)	OR (95% CI)	p-value
Male	48 (59.3)	31 (55.4)	17 (68.0)	0.58 (0.22 - 1.57)	.287
Age (years) - mean (SD)	35.0 (8.2)	34.3 (8.1)	36.5 (8.8)	0.97 (0.92 - 1.03)	.265
Caucasian	77 (95.1)	55 (98.2)	22 (88.0)	0.13 (0.01 - 1.35)	.088
Married/remarried	17 (21.0)	11 (19.6)	6 (24.0)	0.77 (0.25 - 2.40)	.657
High school graduate	42 (50.0)	27 (48.2)	13 (52.0)	0.86 (0.34 - 2.21)	.753
Unemployed	29 (35.8)	20 (35.7)	9 (36.0)	0.99 (0.37 - 2.64)	.980
Ever injected any drug in lifetime	77 (95.1)	54 (96.4)	23 (92.0)	2.35 (0.31 - 17.70)	.408
IDU in the past 6 months	45 (55.6)	35 (62.5)	10 (40.0)	2.40 (0.89 - 6.48)	.086
IDU in the past 30 days	41 (50.6)	32 (57.1)	9 (36.0)	1.19 (0.11 - 12.82)	.889

Table 2

Egocentric and sociometric drug network characteristics of HCV RNA positive/negative drug users (n=81)

Variables	RNA+ (n=56) n(%)	RNA- (n=25) n(%)	χ^2	p-value
Egocentric variables				
Network size greater than two	43 (76.8)	20 (80.0)	0.10	.748
High network density	29 (64.4)	8 (38.0)	4.04	.045[*]
Turnover (6-month)[1]				
Turnover-in	0.3 (0.0 - 0.9)	0.7 (0.2 - 1.0)	z=1.72	.085
Turnover-out	1.1 (0.3 - 1.6)	1.3 (0.7-1.8)	z=1.08	.278
Sociometric variables				
Centrality				
High degree centrality	43 (53.1)	20 (80.0)	0.10	.748
High eigenvector centrality	51 (91.1)	5 (8.9)	0.18	.669
High betweenness	36 (64.3)	16 (64.0)	0.00	.980
High 2-step reach	45 (80.4)	15 (60.0)	3.73	.054
K-core of 2 or greater	39 (69.6)	15 (60.0)	0.72	.395
Located in main component	50 (89.3)	21 (84.0)	0.45	.504
Member of injection risk network	10 (40.0)	33 (58.9)	2.49	.115
Social distance of two steps or more from a network member who is:				
Anti-HCV positive (n=76)	43 (82.7)	22 (91.7)	1.07	.301
Lifetime IDU (n=78)	51 (94.4)	23 (95.8)	0.07	.797
Recent IDU (past 6 months) (n=74)	48 (90.6)	16 (76.2)	2.66	.103

IDU: injection drug user

[*] p<.05

[1] For analysis of turnover, drug network isolates were excluded (n=155). Participants who had not yet completed their 6-month follow-up assessment at the time of substudy participation were also excluded (n=6).

Table 3

Multivariable correlates to HCV RNA status among rural Appalachian drug users

	OR (95% CI)	p-value
Model 1 (n=81)		
Age	0.99 (0.93 - 1.05)	.703
Gender	1.83 (0.65 - 5.15)	.253
IDU in past 6 months	2.49 (0.89 - 7.01)	.084
Model 2 (n=56)		
Age	1.10 (0.98 - 1.23)	.122
Gender	4.60 (1.00 - 21.27)	.051
IDU in past 6 months	8.86 (1.50 - 52.36)	.016
Egocentric variables		
Egocentric drug network density	3.96 (0.93 - 16.94)	.064
Turnover into drug network	0.06 (0.01 - 0.51)	.001
Model 3 (n=81)		
Age	0.98 (0.92 - 1.06)	.627
Gender	1.76 (0.57 - 5.43)	.328
IDU in past 6 months	2.01 (0.65 - 6.24)	.228
Sociometric variables		
Drug network 2-step reach	2.21 (0.74 – 6.64)	.156
Final Model (n=56)		
IDU in past 6 months	4.06 (1.04 – 15.83)	.044
Egocentric variables		
Egocentric drug network density	3.22 (0.87 – 11.95)	.081
Turnover into drug network	0.15 (0.03 – 0.75)	.020

OR: odds ratio, CI: confidence interval, IDU: injection drug use