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ABSTRACT

Background: The prevalence of hepatitis C (HCV) and HIV among persons who inject drugs (PWID) and the ability of these diseases to spread through injection networks are well documented in urban areas. However, less is known about injection behaviors in rural areas. *Objectives*: This study focuses on the association between the number of self-reported injection partners with the PWID's self-reported HCV and HIV status. Injection networks provide paths for infection and information to flow, and are important to consider when developing prevention and intervention strategies. *Methods*: Respondent driven sampling was used to conduct 315 interviews with PWID in rural Puerto Rico during 2015. Negative binomial regression was used to test for associations between the number of self-reported injection partners and self-reported HCV and HIV statuses. Multinomial logistic regression was used to test for associations with the participant's self-reported HCV and HIV statuses. *Results*: Self-reported HCV status is significantly associated with injection risk network size. Injection partner networks of self-reported HCV− respondents are half what is reported by those with a positive or unknown status. Self-reported HIV statuses are not associated with different numbers of injection partners. *Conclusions*: Smaller injection networks among those who self-report a HCV− status suggests that those who believe their status to be negative may take protective action by reducing their injection network compared to those have a self-reported HCV+ or an unknown status. Although the cross-sectional design of the study makes it difficult verify, such behavior has implications for prevention programs attempting to prevent HCV transmission.

The high prevalence of the hepatitis C virus (HCV) among people who inject drugs (PWID) has been well documented, with estimates ranging from 60% to 80% globally (Nelson et al., 2011), 50% to 60% in the United States mainland (Lansky et al., 2014) and up to 89% in Puerto Rico (Reyes et al., 2006). HCV spreads through unsafe injection practices (Hagan et al., 2001), can be symptomless for many years (D. J. Smith, Combellick, Jordan, & Hagan, 2015), and has been linked to social network characteristics of injectors (Brewer et al., 2006; Sacks-Davis et al., 2012). HCV testing and counseling has become a readily accepted aspect of interventions for PWID (CDC, 2013; WHO, n.d.). Such strategies assume that awareness of a HCV status will influence injection risk behavior in a positive manner, reducing the spread of the HCV virus (Aspinall et al., 2014; Cox et al., 2009). This assumption is based on proven HIV intervention strategies which contain strong elements of testing information, education, and counseling (MacArthur et al., 2014) to reduce risky behavior and further disease transmission.

Social networks among PWID provide paths for infections and information to spread across. In recent years studies have traced different viral genotypes of HCV across networks, demonstrating how the spread of specific types of HCV are associated with network characteristics (Pilon et al., 2011; Romano et al., 2010; Sacks-Davis et al., 2012). Here, clusters of related HCV genotypes have been found within groups of injection partners (Sacks-Davis et al., 2012) and also associated with disparate social networks of injection partners in Brazil (Romano et al., 2010) and Canada (Pilon et al., 2011). Other studies focused on the risk of HCV spread found that over 78% of injection partnerships (network connections) involved behavior that could transmit HCV (Brewer et al., 2006); even knowing someone else who injected increased a PWID's odds of contracting HIV or HCV (Latkin et al., 2011). Overall, networks seem to matter, but it remains largely unknown how PWID injection risk network interactions may reflect local understandings and self-perceptions of one's HCV status.

There is a lack of clear evidence on whether individual PWID risk network behavior may reflect or respond to self-reported HCV status. Smith and colleagues (B. D. Smith et al., 2013) found that PWID had higher odds of

sharing injection materials when they shared the same self-reported HCV status and other studies have found a variety of behavioral changes associated with learning actual HCV status (Hahn, Evans, Davidson, Lum, & Page, 2010; Kwiatkowski, Fortuin Corsi, & Booth, 2002; Vidal-Trécan, Coste, Varescon-Pousson, Christoforov, & Boissonnas, 2000). In each of these studies the emphasis was on changes in risk network behavior that accompanied a transition from self-reported to known HCV status. However, these changes are not confined to learning about either a negative (Hagan et al., 2006) or positive HCV result (Bruneau et al., 2014; Spelman et al., 2015; Vidal-Trécan et al., 2000), and do not always reduce risk. Several studies have also found that moving from self-reported to known HCV status was not associated with any changes in PWID risk behavior (Miller, Mella, Moi, & Eskild, 2003; Ompad, Fuller, Vlahov, Thomas, & Strathdee, 2002). Further, there is some suggestion that important differences may exist between the behavior of rural versus urban PWID with respect to self-reported HCV status and risk partner selection (Duncan et al., 2017).

Ambivalent reactions on the part of PWID to their HCV infection status are perhaps not surprising. Given high HCV prevalence rates within the community, many PWID see the acquisition of HCV as an inevitable side-effect of injecting drugs (Norden et al., 2009; Nordén & Lidman, 2005; Rhodes & Treloar, 2008). Furthermore, considering that the disease itself remains asymptomatic for many years, it is not unreasonable that PWID would have different attitudes towards HCV than towards faster acting diseases such as HIV (Lansky et al., 2014; Rhodes & Treloar, 2008). However, this difference in attitude remains speculative without more evidence, leaving assumptions about the effectiveness of testing as intervention unchallenged. Moving forward, it remains important to examine how current risk network size may reflect past perceptions of one's own HCV status.

In Puerto Rico, rural rather than urban communities seem to contribute disproportionately to overall HIV infection rates (Colón-López, Ortiz, Banerjee, Gertz, & García, 2013; Norman, Dévieux, Rosenberg, & Malow, 2011; Pérez et al., 2010). Furthermore, over 20% of new HIV diagnoses in Puerto Rico listed injection drug use as their cause, compared to 8.3% in the continental United States (CDC, 2010). While similar surveillance data for HCV is not available from this area, related transmission scenarios indicate equivalent (or greater) risk for disparities in hepatitis (Abadie, Welch-Lazoritz, Gelpi-Acosta, Reyes, & Dombrowski, 2016). Given the recent rise of HCV in rural mainland United States (Suryaprasad et al., 2014), a recent HIV outbreak in the Midwest (Peters et al., 2016), and a continuing increase in rural drug use in general (Cicero, Ellis, Surratt, & Kurtz, 2014; Dombrowski, Crawford, Khan, & Tyler, 2016), the experiences of PWID in rural Puerto Rico provide timely insight into the trajectory of rural injection use in the contiguous United States.

The number of people a participant reports injecting with is an important aspect of an injection network. It is an indicator of potential exposure and transmission of HCV and HIV for both individuals and the larger network. Knowing the extent to which PWID are exposed to injection network risk is critical to understanding disease spread within this community (Dombrowski et al., 2013b, 2016b; Dombrowski, Curtis, Friedman, & Khan, 2013; Friedman et al., 1997; Khan, Dombrowski, Saad, McLean, & Friedman, 2013; Neaigus, Friedman, Kottiri, & Des Jarlais, 2001). We hypothesize that there will be a relationship between a participant's HCV or HIV status and their injection network size, and that this relationship may not be the same for similar statuses—e.g., that HIV+ status will not necessarily reflect the same association with risk network degree that an HCV+ status will. Indeed, it is possible that, given documented expectations of HCV acquisition among PWID, self-reported HCV+ status may be associated with higher network degree (rather than the lower degree often seen among self-reported HIV+ PWID). While the studies cited above have established the importance of the relationship between HIV status and risk network size/degree, the same is not true for HCV status. Further, there is reason to believe that there are significant differences in PWID response to self-reported HCV status when compared with HIV (Abadie et al., 2016).

In what follows we use negative binomial regression to test whether self-reported HCV status predicts larger risk network sizes for active injectors in rural Puerto Rico. While the cross section nature of the data prevents us from examining how rural Puerto Rican PWID react to a change in self-reported status (as a result of a recent test, for example), these data do allow us to investigate the association between self-reported status based on prior testing and current overall risk network size. Where prior research in the area has pointed to importance of self-reported HCV status on equipment sharing (Abadie et al., 2016), risk partner selection (Duncan et al., 2017) and overall risk network topology (Coronado-García et al., 2017); this analysis extends these investigations to the critical issue of overall risk network size.

Methods

Sample recruitment

Interviews with 315 participants were completed between April 2015 and June 2015 in the mountainous interior of Puerto Rico, 15–30 miles south of San Juan. Eligible

participants were alert, 18 years of age or older, and had injected drugs within the last 30 days. Female injectors comprise 10% of the final analytical sample and the average age of participants was 42, ranging between 18 and 70. Interviews were conducted by a postdoctoral ethnographer alongside Puerto Rican staff working out of a storefront in one of the towns in the region while working in close association with the region's only syringe exchange program. Transportation for participants from neighboring communities was facilitated by a regular pattern of van pick-up/drop-off. Continuing relationships were maintained with respondents in anticipation of planned additional rounds of data collection, including in situ ethnographic research. After completing the questionnaire, participants were compensated with $25. The study received IRB approval through the University of Nebraska-Lincoln (IRB# 20131113844FB) and the University of Puerto Rico (IRB# A8480115).

Respondent driven sampling was used to recruit participants, starting with two interviews (seeds) in each of the four focal towns. Seeds were recruited through collaboration with the only needle exchange in the area. Participants who completed the survey were given three referral coupons to pass out to other qualified individuals who had not previously participated in the project. For every referral that completed the survey, the referee could earn an additional $10. Respondent driven sampling differs from other methods in that the researcher never knows the number of people who may have been given a coupon and refused an interview. As such, traditional response rates are not applicable. Respondent driven sampling is often preferred for hidden and hard-to-reach populations (Johnston, Chen, Silva-Santisteban, & Raymond, 2013; Paquette, Bryant, & De Wit, 2011).

There is some risk of using a network based recruitment strategy to assess a network outcome. However, standard methods of RDS analysis (Gile & Handcock, 2010; Spiller, Cameron, & Heckathorn, 2012) were employed to control for network size in sample correction. Furthermore, a range of individual risk network size measures were collected from the sample and tested for the effects of "degree homophily" across a range of participant attributes on sample recruitment bias. These were shown to be nonsignificant for the variables used in this analysis, suggesting that the network size of the recruiter and the recruit did not influence recruitment patterns in the data considered here.

Measures

The questionnaire was interviewer-administered and based on the CDC National HIV and Behavioral Surveillance (NHBS) of Injection Drug Users Round 3 Questionnaire version 13. The NHBS is designed to produce regular estimates of the number and behavior of PWID in 23 urban areas in the United States; one of which is San Juan, Puerto Rico, an urban area north of this project's target rural area. The instrument asked questions about injection behavior, prior HCV and HIV status and testing, and several other topics related to drug use and HIV/HCV risk.

In addition, the project provided rapid testing for both HIV and HCV using INSTI Rapid HIV antibody tests (Biolytical Laboratories) and OraQuick HCV Rapid antibody tests (OraSure Technologies). Participants were compensated an additional $5 for each test. The OraQuick HCV Rapid test is FDA approved and has demonstrated an accuracy rate greater than 98% (FDA, 2011). The test is not confirmatory evidence of a current HCV infection, as it cannot distinguish between antibodies which are present from a current or prior HCV infection. Participants who tested positive for HCV or HIV antibodies were offered referral and transportation to a primary care doctor for confirmatory testing and link-to-care.

The focal dependent variable for this article is the *number of injection partners* reported by participants in the study's four focal towns. These towns are located in a contiguous region in the mountainous interior of Puerto Rico, 15–30 miles south of San Juan. Understanding that PWID in the area are often highly mobile (due to uneven supply, local enforcement trends, and financial reasons), participants were asked to estimate how many injection partners they currently have in each of these towns (i.e., "How many injecting partners do you have in town X"). Responses were summed to provide an overall number of injection partners in the region.

The primary focal independent variables are *self-reported HCV* and *self-reported HIV* status of the participant. These categories are defined by the participant's report of having a prior positive HCV or HIV test, a prior negative HIV or HCV test, or having never been tested for either HIV or HCV. These results are classified as three categories for both HIV and HCV: a self-reported positive, a self-reported negative, or an unknown status. During the current survey, rapid antibody tests for HCV and HIV were administered to each participant in order to provide a current antibody status for HIV and HCV, providing comparisons between self-reported and current status.

Other independent variables control for external factors, which may influence individual numbers of risk partners, including *number of towns lived in* and *number of towns injected in* within the region. These measure if the participant has ever lived or injected in any of the four communities with possible values ranging from zero to four. In addition, measures of the number of *main sex*

partners and *casual sex partners* (as defined by NHBS) were collected and summed across each location. *Frequency of injection* is measured as 1–3 times per month (0), 1–6 times per week (1), 1–3 times per day (2), and 4 or more times per day (3). *Years injecting* is measured by subtracting the participant's age when they first report injecting from their current age. *Income* is a dichotomous measure where (0) indicates having earned or received less than $5,000 in the past year and (1) is earnings above $5,000. *Education* has three categories which are used as dummy variables: less than high school (1), completed high school (2), and any further education past high school (3). *Marital status* also has three categories: married or cohabiting (1); separated, divorced, or widowed (2); and single (3). Additionally, *sex* (female = 1), *age* (mean centered in models), and *born in Puerto Rico* (1) are used as controls in the models.

Data analysis

This article uses a two-pronged analytical strategy. Negative binomial regressions test the associations of controls and independent variables with the number of injection partners. This method is appropriate for dependent variables which are counts, over dispersed, and do not have an overabundance of zeros (Long, 1997). Models progress in a stepwise fashion as first controls and then possible explanatory variables are added in successive models. Results from the negative binomial models are presented and discussed in terms of percent change of the expected number of injection partners (i.e., incident rate ratios (Long & Freese, 2006)). Multinomial logistic regression is then used to examine other possible associations between self-reported HCV and HIV statuses and the focal independent and control variables. These models are used for dependent variables which are categorical and nominal (Long, 1997). Results from the multinomial logistic regression models are presented and discussed in terms of percent change of the relative risk of reporting a self-reported HCV or HIV status (i.e., relative risk ratios (Long & Freese, 2006)). Due to limited missing data, the final sample is 297 out of the original 315 (listwise deletion).

Results

In the final sample 90% of the participants are male and are on average 42 years old (Table 1). On average, participants reported 16 current injection partners across the focal locations, had been injecting for almost 20 years, and currently inject 1–3 times per day. A majority of the participants were born in Puerto Rico and reported receiving less than $5,000 in income and assistance in the previous year. The unbalanced sex distribution of the

sample is unlikely to be an artifact of the RDS recruitment. Sample weighting from a range of RDS estimators (Gile & Handcock, 2010; Spiller et al., 2012; Wejnert, 2009) showed low levels of both degree and affiliation homophily by gender. The sampled distribution of gender is expected to be within 2–3 percentage points of the region's PWID population proportion.

Almost 80% of the participants tested HCV+ according to the rapid antibody tests conducted at the end of the interview, but only 50% self-reported themselves as HCV positive before the test (Table 2). Approximately half those with an unknown HCV status had a positive HCV antibody test result. For those who reported a negative HCV result on their last test, 65% tested positive through the antibody test during the interview. Six percent of the sample tested HIV+ in the rapid test and 4% knew they were HIV+ when they started. Two percent of those who reported a self-reported HIV− status tested HIV+, and 6% of those who reported an unknown status tested HIV+. Few participants with a self-reported positive status received a negative antibody test (0% of HIV+ participants and 3% of HCV+ participants).

Table 3 shows a series of negative binomial regression models that explore the association between several factors and the expected number of injection partners. Models 1–3 show simplified models where the association between self-reported HCV and HIV status are examined individually and then in tandem with the expected number of injection partners. In Model 1 the expected number of injection partners is higher for those with a self-reported HCV unknown status (+88%, $p < 0.01$) and for those with a self-reported HCV+ status (+146%, $p < 0.001$) compared to those with a self-reported HCV− status. Model 2 shows that there is no significant association between self-reported HIV status and the expected number of injection partners. In Model 3, which tests self-reported HCV and HIV status we see a similar pattern from Model 1. Self-reported Unknown HCV and self-reported HCV+ status are associated with greater expected counts of injection partners (+106%, $p < 0.01$; +156%, $p < 0.001$) compared to those with a self-reported HCV− status. Unlike prior models, Model 3 shows a negative association between self-reported HIV+ (−54%, $p < 0.05$) and the expected count of injection partners when compared to those with a self-reported HIV− status.

Models 4 and 5 then test the association between self-reported HCV and HIV statuses and the number of injection partners independently with controls. Here, reporting a self-reported unknown HCV status is associated with a higher expected number of injection partners (+82%, $p < 0.01$) than those reporting a self-reported HCV− status. Similarly, a self-reported

Table 1. Descriptive statistics ($n = 297$).

Variables	Mean/%	Std. D.	Min	Max
Number of injection partners (current)	15.72	22.20	0	159
Female	10%	0.30	0	1
Age	41.89	10.17	18	70
Income: greater than or equal to $5,000	20%	0.40	0	1
Born in Puerto Rico	93%	0.26	0	1
Education				
Less than high school	47%	0.50	0	1
High school	35%	0.48	0	1
More than high school	18%	0.39	0	1
Marital status				
Together (married/cohabiting)	22%	0.41	0	1
Previously married (divorced/widowed/separated)	31%	0.46	0	1
single	47%	0.50	0	1
Employed FT/PT/retired/student (ref = unemployed)	11%	0.31	0	1
Number of years injecting	19.97	10.71	0	52
Frequency of injection	2.19	0.83	0	3
Number of focal towns lived in (ever)	1.20	0.59	0	4
Number of focal towns injected in (ever)	1.63	0.86	0	4
Number of main sex partners (current)	1.87	3.70	0	32
Number of casual sex partners (current)	2.69	5.23	0	41
Self-reported HIV status				
HIV unknown	10%	0.30	0	1
Self-Reported Negative Status	86%	0.35	0	1
Self-reported positive status	4%	0.20	0	1
HIV+ antibody post survey test	6%	0.25	0	1
Self-reported HCV status				
HCV unknown	23%	0.42	0	1
Self-reported negative status	27%	0.45	0	1
Self-reported positive status	49%	0.50	0	1
HCV+ antibody post survey test	78%	0.41	0	1
N	297			

HCV+ status is associated with a much higher expected number of injection partners ($+117\%$, $p < 0.001$) than a HCV− status. There are no statistically significant associations between self-reported HIV status and the expected number of injection partners found.

Model 6 of Table 3 includes all controls and predictors and shows that the expected number of injection partners is significantly associated with being single compared to being married or cohabiting ($+46\%$ $p < 0.05$). The expected number of injection partners also increases for every year a participant has been injecting ($+2\%$, $p < 0.05$) and for every additional focal town ever injected in ($+84\%$, $p < 0.001$). The expected number is higher for HCV unknown ($+102\%$, $p < 0.001$) and HCV+ self-reported statuses ($+124\%$, $p < 0.001$) than for a self-reported HCV− status. The association between

a self-reported HIV+ status and the expected number of injection partners is only marginally significant in a full model with controls compared to a self-reported unknown HIV status. The final model thus shows that even under considerable controls, reported unknown and positive HCV statuses are significantly associated with approximately double the expected injection network size than those with a self-reported negative HCV status.

Although the differences in injection network size are clear, it is possible that there is a common factor associated with these differences that then influences a participant's self-reported HCV or HIV status. A multinomial logistic regression model tests the differences between reporting self-reported HCV and HIV statuses (Table 4). For HCV, the only significant association is that the relative risk of a participant reporting a self-reported HCV

Table 2. Percent distribution of antibody test results by participant's self-reported HCV or HIV status prior to the antibody test ($n = 297$).

	Negative	Positive	Total
Self-reported HCV status		HCV antibody test result	
Unknown Status	46% (32)	54% (37)	23% (69)
Self-reported negative	34% (28)	66% (54)	27% (82)
Self-reported positive	3% (2)	97% (148)	50% (152)
Total	21% (64)	79% (239)	
Self-reported HIV status		HIV antibody test result	
Unknown status	93% (41)	7% (3)	14% (44)
Self-reported negative	98% (254)	2% (4)	82% (258)
Self-reported positive	7% (1)	92% (12)	4% (13)
Total	94% (296)	6% (19)	

Table 3. Negative binomial regression predicting the number of injector partners by self-reported HCV and HIV status with controls ($n = 297$).

Variables	(1)	(2)	(3)	(4)	(5)	(6)
Female				0.924	0.858	0.924
				[0.58, 1.48]	[0.52, 1.37]	[0.57, 1.45]
Age (mean centered)				0.985	0.984	0.984
				[0.96, 1.01]	[0.96, 1.01]	[0.96, 1.00]
Together: Married or Cohabiting (reference)				Reference	Reference	Reference
Previously Married				1.066	1.009	1.133
				[0.72, 1.57]	[0.68, 1.49]	[0.76, 1.66]
Single				1.405[+]	1.319	1.457[*]
				[0.99, 1.99]	[0.93, 1.90]	[1.04, 2.08]
# of Years Injecting				1.022[*]	1.028[**]	1.024[*]
				[1.00, 1.04]	[1.01, 1.05]	[1.00, 1.05]
Frequency of Injection				1.057	1.050	1.055
				[0.91, 1.23]	[0.90, 1.22]	[0.90, 1.22]
# of Focal Towns Lived In (ever)				1.078	1.079	1.113
				[0.81, 1.43]	[0.81, 1.44]	[0.84, 1.47]
# of Focal Towns Injected In (ever)				1.892[***]	1.833[***]	1.847[***]
				[1.55, 2.32]	[1.49, 2.24]	[1.50, 2.24]
# of Main Sex Partners (current)				0.997	1.000	0.997
				[0.95, 1.05]	[0.95, 1.05]	[0.95, 1.05]
# of Casual Sex Partners (current)				1.031[+]	1.038[*]	1.033[+]
				[0.99, 1.07]	[1.00, 1.08]	[0.99, 1.07]
HCV Unknown Status	1.879[**]		2.063[**]	1.817[**]		2.023[***]
	[1.25, 2.82]		[1.33, 3.21]	[1.24, 2.67]		[1.36, 3.04]
HCV Self-Reported Positive Status	2.458[***]		2.559[***]	2.168[***]		2.235[***]
	[1.74, 3.47]		[1.81, 3.61]	[1.57, 2.99]		[1.62, 3.09]
HCV Self-Reported Negative Status (reference)	Reference		Reference	Reference		Reference
HIV Unknown Status		0.798	0.764		0.751	0.684
		[0.52, 1.22]	[0.48, 1.21]		[0.48, 1.05]	[0.45, 0.99]
HIV Self-Reported Positive Status		0.561	0.456[*]		0.621	0.533[+]
		[0.26, 1.20]	[0.22, 0.96]		[0.30, 1.22]	[0.26, 1.03]
HIV Self-Reported Negative Status (reference)		Reference	Reference		Reference	Reference
Intercept	8.161	16.492	8.298	1.417	2.967[*]	1.377
N	297	297	297	297	297	297
Pseudo R^2	0.01	0.001	0.01	0.05	0.04	0.05

Coefficients are presented as incident rate ratios and 95% confidence intervals are presented below:
[+]$p < 0.10$, [*]$p < 0.05$, [**]$p < 0.01$, [***]$p < 0.001$ Not shown are non-significant coefficients for being born in Puerto Rico, income, education, and current employment status.

unknown status rather than a HCV− status is 8.498 times greater when the participant reports an HIV unknown status rather than a HIV− status. For self-reported HIV status, a one year increase in the participant's age is associated with an 8.4% ($p < 0.05$) lower relative risk of that participant reporting a self-reported HIV unknown status than a HIV− status. Participants who are single compared to those who are currently together have a greater relative risk (+231%, $p < 0.05$) of self-reporting an unknown HIV status compared to a HIV− status. Those who self-reported an unknown HCV status have a greater relative risk (+740%, $p < 0.001$) of reporting an unknown HIV status as well. Finally, participants who inject more frequently are associated with a lower relative risk (−54%, $p < 0.05$) of reporting a self-reported HIV+ status than a HIV− status. The majority of the controls and possible other explanations for the relationships in Table 3 remain non-significant for both models.

Discussion

There are clear associations between the number of injection partners and self-reported HCV status among rural PWID in Puerto Rico. On average, those who think that they are HCV negative have half the expected number of current injection partners than those who are either HCV positive or do not know their HCV status. These associations are different for HIV, where there are no significant associations. Multinomial logistic regressions reveal few differences associated with self-reported HCV status. Therefore, it is likely that the observed differences in injection network sizes among these participants are associated with how they view HCV and HIV.

In other settings, HCV is seen as omnipresent and an inevitable consequence of injecting drugs by users themselves (Norden et al., 2009; Nordén & Lidman, 2005; Rhodes & Treloar, 2008), and PWID in rural Puerto Rico are unlikely to be an exception. In this context, it is perhaps unsurprising that those who do not know their status have similar behavior to those who self-report a HCV+ status. Many of those who do not know their status may assume they are infected, and similarly, may assume that their potential risk partners are the same. A lack of perceived risk may determine many interactions, especially when one considers that HCV is perceived as a far less threatening infection than HIV (Rhodes & Treloar, 2008).

Table 4. Multinomial logistic regression models predicting perceived HCV and HIV status ($n = 297$).

Variables	HVC self-reported status (ref: Negative)		HIV self-reported status (ref: Negative)	
	Unknown	Positive	Unknown	Positive
Female	0.876	1.104	0.386	2.254
	[0.24, 3.15]	[0.43, 2.85]	[0.07, 2.18]	[0.27, 18.9]
Age (mean centered)	0.973	0.994	0.916[*]	1.063
	[0.92, 1.03]	[0.96, 1.03]	[0.85, 0.99]	[0.96, 1.18]
Together: Married or Cohabiting (reference)	*Reference*	*Reference*	*Reference*	*Reference*
Previously Married	0.577	0.789	3.111[+]	0.349
	[0.20, 1.67]	[0.34, 1.81]	[0.86, 11.3]	[0.05, 2.35]
Single	0.794	1.141	3.308[*]	0.552
	[0.30, 2.07]	[0.52, 2.48]	[1.02, 10.7]	[0.09, 3.25]
# of Years Injecting	1.024	1.027	1.041	1.047
	[0.97, 1.08]	[0.99, 1.07]	[0.98, 1.12]	[0.96, 1.14]
# of Focal Towns Lived In (ever)	1.044	0.919	1.180	0.805
	[0.53. 2.07]	[0.54, 1.55]	[0.57, 2.45]	[0.22, 2.96]
# of Focal Towns Injected In (ever)	1.028	1.394[+]	0.781	0.752
	[0.62, 1.70]	[0.99, 2.07]	[0.46, 1.33]	[0.29, 1.97]
Frequency of Injection	1.280	1.067	1.047	0.460[*]
	[0.81, 2.03]	[0.76, 1.50]	[0.64, 1.71]	[0.21, 0.99]
# of Main Sex Partners (current)	0.981	1.064	0.895	0.746
	[0.84, 1.15]	[0.95, 1.20]	[0.64, 1.71]	[0.43, 1.29]
# of Casual Sex Partners (current)	1.053	0.990	1.056	1.100
	[0.95, 1.16]	[0.91, 1.08]	[0.97, 1.15]	[0.90, 1.34]
HIV: Unknown Status	8.498[***]	1.578		
	[2.82, 25.6]	[0.51, 4.90]		
HIV: Self-Reported Positive Status	0.000	1.916		
	[0.00, 0.00]	[0.46, 7.96]		
HIV: Self-Reported Negative Status (reference)	*Reference*	*Reference*		
HCV: Unknown Status			8.397[***]	0.000
			[2.77, 25.5]	[0.00, 0.00]
HCV: Self-Reported Positive Status			1.596	3.152
			[0.51, 5.01]	[0.57, 17.6]
HCV: Self-Reported Negative Status (reference)			*Reference*	*Reference*
Intercept	0.085[+]	0.413	0.075	2.824
N	297		297	
Pseudo R^2	0.11		0.25	

Coefficients are presented as relative risk ratios and 95% confidence intervals are presented below:
[+]$p < 0.10$, [*]$p < 0.05$, [**]$p < 0.01$, [***]$p < 0.001$. Not shown are non-significant coefficients for being born in Puerto Rico, income, education, and current employment status.

Under these conditions, a negative HCV status may motivate greater risk avoidance than a positive or unknown one, and may prompt some self-protective action.

Though it's limited, evidence for this has been discussed for other locations (Norden et al., 2009; Vidal-Trécan et al., 2000). In their qualitative synthesis of the literature on HCV, Rhodes and Treloar (2008) found a trend toward the individualization of responsibility as a major theme raised by injectors when discussing their attitudes toward risk of HCV infection. Such considerations were paramount in balancing health risk and drug intake to avoid withdrawal while maintaining social ties critical to future drug access (Samuel R. Friedman, Sandoval, Mateu-Gelabert, Meylakhs, & Jarlais, 2011). The situation is clearly complex, but a simple solution for PWID who perceive their HCV status as negative may be reducing the number of people they inject with. As smaller personal injection networks entail less exposure risk.

Among injectors in rural Puerto Rican, self-reported HIV status was not associated with the expected number of injection partners in models with controls. This stands against what would be anticipated given evidence from other settings, that HIV positive PWID would be more likely to disclose their status to injection partners (Nordén & Lidman, 2005), which would in turn potentially reduce the number of possible injection partners. The absence of similar findings here may be due to the small number of people in the sample who reported themselves to be HIV positive (4%), or it may reflect an artificial situation where HIV positive PWIDs are, at times unwillingly, sent to the mainland United States for treatment programs by local municipalities, and are thus removed from the environment of this study (Perez Torruella, 2010).

In addition to self-reported HCV status, the expected number of injection partners was also associated with the number of towns in the region a participant injected in, single participants compared to married or cohabiting participants, and those who have been injecting for a longer period of time. These associations collectively indicate that participants with the largest injection networks

would be those who are single, have injection partners in multiple towns, have been injecting for many years, and who have a self-reported HCV positive or unknown status.

Although many of these associations are quite substantial in size, they offer complex guidance for the development of policy. Marital status or the ability of individuals to move freely in their own country are not attributes which are easily modified through policy, nor should they be. Furthermore, in places where most or even all PWID expect to already be (or become) HCV positive and social pressure to truthfully disclose HCV status is low, "testing-as-intervention" strategies like those found to reduce risk among HIV positive PWID may not be as effective in rural Puerto Rico.

Considering HCV to be a routine consequence of injecting among rural PWID may seem unreasonable in many places given the seriousness of HCV infection, but in Puerto Rico, where state provided insurance does not cover HCV care for HIV negative patients, these expectations may reflect larger social disconcern. Here, we speculate that greater expectations of engaging risk partners who are HCV negative could potentially change these results, but this may require a larger change in the social value placed in HCV prevention. The extent to which a lack of services contributes to this pattern of behavior and risk assessments goes beyond the data available to us at this stage of the research, but we note that syringe exchange access in the region is limited to a single mobile operation covering a large rural area while attempting to serve a highly mobile population (López et al., 2015).

Limitations

Although we have outlined scenarios where injection network size is associated with health statuses, injection frequency is not associated with either the size of injection networks or the participant's self-reported HCV or HIV status. A smaller injection network may reduce the reach of a disease spreading within the larger network, but the frequency of injection sets the pace for a disease to jump between two individuals (Mackesy-Amiti et al., 2011). Limiting the size of an individual's personal injection risk network may, therefore, not influence the risk of transmission for a given dyad when injection frequency remains the same.

These findings are also limited by the cross-sectional nature of the study. The lack of time depth is, to some extent, addressed by looking at how self-reported disease status (which is based on past HCV/HIV testing) is associated with differences in current behavior, thereby associating prior attitudes with current practice.

However, there is no substitute for a longitudinal study. This limitation is compounded by evidence that HCV diagnoses in particular can be highly variable in terms of quality, information, and empathy (Treloar, Newland, Harris, Deacon, & Maher, 2010).

Another limitation is that the number of HIV+ participants is low and likely causing cell size problems in Table 4. Our understanding, informed by research elsewhere in the United States, is that low HIV prevalence levels are not simply a reflection of low HIV incidence in Puerto Rico. As noted above, HIV+ PWID in rural Puerto Rico have reportedly been sent to the mainland United States for treatment by local municipalities and may therefore be uniquely underrepresented in this data (Perez Torruella, 2010).

Conclusion

Despite these limitations, the results presented here provide a clear view of how the number of injection partners varies in association with knowledge of HCV status. In an environment with high levels of HCV, it is the minority group, the ones who have not acquired HCV and are aware of that status, that have the lowest number of injection partners. Those who are HCV positive or unaware of their status have twice as many injection partners. Several alternative explanations for larger injection networks such as age, years of injecting, the number of towns a person has lived or injected in, and their number of sexual partners have been included and the focal relationship persists. We view this as evidence that the knowledge of a previous HCV− test (which defines an unknown from a negative status) is associated with a decision to reduce injection network sizes, and a self-reported HCV+ or unknown status does not.

If our desire is to reduce the spread of HCV (of which injection network size is a component) then we suggest that practitioners attempt to confirm HCV− status when possible and helping users develop safe injection practice before HCV is acquired. Although this may appear similar to those involving outreach HIV testing, the latter is frequently focused on identifying individuals with a positive status and helping them to minimize the risk of HIV spread while managing the health consequences of their new diagnoses (MacArthur et al., 2014).

The time frame during which a HCV− intervention can be staged is limited however, especially among active injectors in HCV saturated environments such as that found in rural PR. Similarly, a focus on locating PWID who have negative status later in their injection careers (either due to clears, long-term behavior, or recent developments in HCV cures) would require very active

surveillance. The result, however, could help establish different expectations toward the likelihood of future HCV infection. This in turn could potentially lower the overall level of network risk through reducing the average number of network injection partners throughout the network. Such a change can have implications for disease transmission across a range of pathogens. Furthermore, as novel HCV treatment protocols increase the number of mid-career HCV negatives, efforts to prevent reinfection grow more important.

Reaching injectors early and consistently can be challenging. Research has found that 78% of injection partnerships involve behaviors with a high risk of HCV transmission (Brewer et al., 2006) and that newer injectors quickly acquire HCV (E. R. Miller, Hellard, Bowden, Bharadwaj, & Aitken, 2009). This provides a short window of time to deliver a HCV test. Here, work with existing prevention programs such as syringe exchange programs (SEPs) is likely to be critical to prevention success. SEPs are likely to recognize new injectors, but seldom have available the means for field-testing for HCV due to financial limits or lack of facilities. The results discussed here, however, indicate that for rural Puerto Rico, and perhaps other rural locations as well, attempting to confirm HCV— statues alongside harm reduction interventions already aimed at reaching rural populations may be effective for HCV prevention.

Acknowledgments

Conflict of interests

The authors declare that they have no conflict of interests.

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