



Published in final edited form as:

Int J Drug Policy. 2025 October ; 144(Pt 1): 104387. doi:10.1016/j.drugpo.2024.104387.

Hepatitis C virus infection and co-infection with HIV among persons who inject drugs in 10 U.S. cities—National HIV Behavioral Surveillance, 2018

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Abstract

Background: Characterizing acute and chronic hepatitis C virus (HCV) infection and HIV/HCV co-infection among persons who inject drugs (PWID) can inform elimination efforts.

Methods: During 2018 National HIV Behavioral Surveillance in 10 U.S. metropolitan statistical areas (MSAs), PWID were recruited using respondent-driven sampling and offered a survey, HIV testing, and HCV antibody and RNA testing. We examined prevalence and associated characteristics of HCV infection and HIV/HCV co-infection. Associations were assessed using log-linked Poisson regression models with robust standard errors accounting for clustering by recruitment chain and adjusting for MSA and network size.

Results: Overall, 44.2% had current HCV infection (RNA detected), with 3.9% classified as acute infection (HCV antibody non-reactive/RNA detected) and 40.3% as chronic (HCV antibody reactive/RNA detected). Four percent had HIV/HCV co-infection. Current HCV infection was significantly higher among PWID who were male, White, injected >1 time/day, shared syringes in past year, and shared injection equipment in past year. PWID who were transgender, injecting >5 years, and most often injected speedball (heroin and cocaine together) or stimulants alone were more likely to have HIV/HCV co-infection. Among PWID who never previously had HCV

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Conflicts of interest: All authors have no conflicts of interest.

Ethics approval: The authors declare that they have obtained ethics approval from an appropriately constituted ethics committee/institutional review board where the research entailed animal or human participation.

National HIV Behavioral Surveillance activities were approved by local institutional review boards in participating metropolitan statistical areas.

infection, 9.9% had acute HCV infection. Among PWID who started injecting ≤ 5 years ago, 41.5% had already acquired HCV infection.

Conclusions: Acute and chronic HCV infections were substantial among a sample of PWID in 10 U.S. MSAs. Accessibility to HCV RNA testing, promoting safer practices, and intervening early with harm reduction programs for recent injection initiates will be critical to disease elimination efforts for PWID.

Keywords

hepatitis C; HCV; acute HCV; HIV; persons who inject drugs; PWID

Introduction

People who inject drugs (PWID) represent less than 2% of the U.S. population yet accounted for 66% of acute hepatitis C virus (HCV) cases with available risk factor information during 2020.^{1,2} Further, by 2020 a 124% increase in cases had been observed from the 2,138 cases reported (and 29,700 estimated) during 2013.² This significant burden of HCV infection places PWID at substantial risk for liver complications, including cirrhosis and liver cancer, and extrahepatic manifestations.^{3,4} Additionally, PWID are at increased risk of other blood-borne infections including HIV, and having HCV and HIV co-infection can triple the risk of cirrhosis and liver-related death.⁵

Effective therapies that can cure HCV infection are a pillar to global and national HCV elimination plans.⁶⁻⁸ Further, effective HIV therapies are a critical component to ending the HIV epidemic.⁹ Establishing plans and setting goals for HCV and HIV elimination rely on accurate measurement of HCV and HIV prevalence among PWID. Current HCV infection prevalence estimates for PWID are limited, and many previous studies have used antibody testing without HCV ribonucleic acid (RNA) testing of positive samples.^{10,11} It has been previously estimated that a little over half of U.S. PWID are HCV antibody-positive although this has varied across geographic regions.¹¹⁻¹³ HCV antibody testing without an HCV RNA test cannot be used to measure hepatitis C infection prevalence because a reactive antibody test does not allow distinction between persons with past cleared infection, either through curative treatment or spontaneous clearance, and those with current HCV infection.^{14,15} Detection of HCV infection requires HCV RNA testing; typically a reactive HCV antibody test will trigger performance of an HCV RNA test for detection of virus (often referred to as “reflex” testing) to distinguish between current (RNA detected) or cleared infection (RNA not detected).^{10,11} With reflex testing, however, recent infection may be missed during the window period when antibodies to HCV may not be detectable (approximately 50-60 days after exposure) and therefore no RNA test is performed to assess the presence of hepatitis C viremia.¹⁶⁻¹⁹ These missed infections could be particularly important for PWID given the high risk of HCV transmission via injection practices and the need for rapid intervention to halt ongoing transmission.

Biobehavioral surveillance of populations disproportionately affected by HIV has been essential for monitoring key behaviors, access to services, and prevalence of infections to inform HIV prevention programs. In the United States, National HIV Behavioral

Surveillance (NHBS) has collected and presented HIV-related information from men who have sex with men, PWID, and heterosexually active persons at increased risk for HIV infection in annual, rotating cycles since 2003.^{20,21} PWID have been sampled from select U.S. cities approximately every 3 years, in 2005, 2009, 2012, 2015, and 2018.²⁰ Approximately 500 persons from the specific population sampled that year complete a behavioral questionnaire and HIV testing. While HIV has been the focus of NHBS, this system can be leveraged to study other important infections; in recent years, this has included expansion of biological testing activities such as testing for gonorrhea and chlamydia among MSM and HCV among PWID.^{12,20,22} Before 2018, HCV testing among PWID in NHBS had only included antibody testing, limiting understanding of current HCV infection.^{12,20}

To address the described challenges and information gaps, we performed both HCV antibody and HCV RNA testing, in addition to HIV testing, among all participants in NHBS in 10 U.S. metropolitan statistical areas (MSAs). We aimed to better understand the prevalence of acute, chronic, and cleared HCV infections as well as HIV/HCV co-infection and to identify key subgroups that may benefit from focused intervention within disease elimination efforts for U.S. PWID. This information would also provide a critical baseline for monitoring HCV and HIV outcomes to compare with future cycles of biobehavioral surveillance with PWID and assess progress towards national disease elimination goals.

Methods

In 2018, the Centers for Disease Control and Prevention (CDC)'s National HIV Behavioral Surveillance (NHBS) collected cross-sectional data on HIV prevalence, risk behaviors, and use of prevention services among PWID in 23 MSAs.²³ Since 2005, 20 of the 23 MSAs had participated in previous NHBS PWID cycles. NHBS recruited PWID using respondent-driven sampling (RDS).²¹ Initial RDS seed participants were recruited via referrals by community partners and through street outreach conducted by NHBS staff. Eligible participants were ≥ 18 years of age, currently resided in a participating MSA, did not previously participate in NHBS during the current survey cycle, were able to complete the survey in English or Spanish, reported injecting a drug that was not prescribed for them during the past 12 months, and presented with physical evidence of recent injection (e.g., track marks) or adequately described injection practices. Eligible participants completed a behavioral survey and were offered HIV testing. A rapid-rapid HIV antibody testing algorithm was implemented; for NHBS project areas that required laboratory-based HIV confirmatory testing or had participants with discordant rapid HIV results, blood specimens from participants with any reactive HIV rapid result were sent to local laboratories for HIV confirmatory testing.^{24,25} Participants were offered incentives (e.g., cash or gift cards) and provided verbal informed consent for participation. Participants received rapid test results at the end of their visit and had the option to receive results from testing at local laboratories within approximately 2 weeks of participation. NHBS activities were approved by local institutional review boards in participating MSAs.

Ten NHBS MSAs were also funded to conduct HCV antibody and RNA testing: Chicago, Illinois; Dallas, Texas; Houston, Texas; Los Angeles, California; Miami, Florida; New

York City, New York; Philadelphia, Pennsylvania; San Francisco, California; San Juan, Puerto Rico; and Washington, DC. Four of the 10 MSAs had previously conducted HCV antibody testing in the previous PWID cycle (2015); efforts were made to expand the number of cities funded to perform testing and incorporate HCV RNA testing.¹² All 10 MSAs completed rapid HCV antibody testing in the field using the OraQuick® rapid HCV antibody test (OraSure Technologies) and conducted phlebotomy for HCV RNA testing in local laboratories (nine sites) or the CDC laboratory (Miami). Both rapid HCV antibody testing and lab-based HCV RNA testing were conducted among all eligible participants consenting to hepatitis testing; RNA testing was performed regardless of antibody result. Depending on the MSA, the rapid HCV antibody test was conducted either by fingerstick or on whole blood specimens collected during phlebotomy in a separate tube with anticoagulant (e.g., separate EDTA tube). Three MSAs (Chicago, Houston, Los Angeles) also performed enzyme immunoassay (EIA) testing for HCV antibodies based on procedures and requirements of their local laboratories. HCV RNA testing was quantitative or qualitative based on local laboratory protocols.

Data for this analysis were limited to eligible participants who consented, completed, and had valid responses to the NHBS interview, and consented to hepatitis testing and HIV testing. HCV antibody results were considered 'Reactive' if either the rapid HCV antibody test or a laboratory-based HCV EIA test had a reactive test result. HCV RNA test results were categorized as 'Detected' or 'Not Detected'. Analyses of combined HCV antibody and RNA test results were limited to those with valid HCV antibody and RNA test results. These were categorized into four groups to inform on HCV infection status per the following study definitions: acute (antibody non-reactive and RNA detected), chronic (antibody reactive and RNA detected), cleared (antibody reactive and RNA not detected), and never had infection (antibody non-reactive and RNA not detected) (Table 1). Note that we did not use the conventional clinical or case surveillance definitions of acute hepatitis C as infection in either the past 12 or 6 months, respectively; rather, for this study acute hepatitis C was determined by antibody non-reactive and RNA detected results which occurs most often within the period of 50-60 days after exposure.^{19,26} HIV/HCV co-infection outcomes were: HIV/HCV co-infection (HIV-positive and HCV RNA detected), HIV infection only (HIV-positive and HCV RNA not detected), HCV infection only (HIV-negative and HCV RNA detected), neither HIV or HCV infection (HIV-negative and HCV RNA not detected).

Numbers and percentages of participants with current HCV infection and HIV/HCV co-infection were reported overall and by demographic and injection-related characteristics including gender, age, race/ethnicity, years since injection initiation, frequency of injection, most frequently injected drug, receptive syringe sharing (used a needle/syringe after prior use by someone else), distributive syringe sharing (used a needle/syringe before use by someone else), injection equipment sharing (cooker, filter, or water), and MSA.

Adjusted prevalence ratios (aPR) and their 95% confidence intervals (CI) were obtained from separate log-linked Poisson regression models that included the specific covariate of interest as well as MSA and participant's peer network size as recruitment-related fixed effects and invoked robust standard errors to account for clustering by RDS recruitment chain.²⁷⁻²⁹ Models were run for three outcomes: current HCV infection (HCV RNA detected

vs. not detected), current HIV/HCV co-infection (HIV and HCV RNA vs. HIV only or HCV RNA only or neither HIV nor HCV RNA), and acute HCV infection (HCV antibody non-reactive and HCV RNA detected vs. HCV antibody non-reactive and HCV RNA not detected). Note that models of acute HCV infection included only those with acute infection and those who never previously had HCV infection (i.e., had an HCV antibody non-reactive NHBS test result) to appropriately capture persons who would be at risk for a new acute HCV infection per our study definitions and testing algorithm. Unlike for other outcomes, models of acute HCV infection as defined for this study were not able to include the full MSA variable as a fixed effect due to lack of model convergence with small numbers; instead, a modified 3-level MSA variable (Miami, Philadelphia, all other MSAs) was used as a covariate in each model.

Finally, we assessed HCV infection prevalence by years since injection initiation and age considering two outcomes: 1) acute (typically within the prior 50-60 days), chronic, and cleared HCV infection combined among all those with valid HCV antibody and RNA results, and 2) acute HCV infection (typically within the prior 50-60 days) among those with valid HCV antibody and RNA results and who never previously had HCV infection. The prevalence at each depicted category (<1, <2, <3, <4, <5, ≤5 years) included all those who, at the time of NHBS participation, had year(s) since injection initiation up through the given category. HCV infection prevalence prior to injection initiation was assumed to be zero; we did not assess year of, or age at previous HCV diagnosis which meant we could not determine timing between previous diagnosis (if it had been diagnosed) and injection initiation to the year. All analyses were conducted in SAS version 9.3.

Results

Of 5,214 eligible participants who consented to the NHBS survey, provided complete and valid interview data, 5,198 (99.7%) consented to HCV and HIV testing. Of these, 5,190 (99.8%) received an HCV antibody test with a valid result and 3,795 (73.0%) received HCV RNA testing with a valid test result. The main reason for not receiving RNA testing was difficulty drawing blood via venipuncture from PWID participants. Overall, 62.4% (3,239/5,190) were HCV antibody reactive and 44.2% (1,678/3,795) had HCV RNA detected (Figure 1). Among those who had both valid HCV antibody and RNA results (n=3,795), 3.9% had acute HCV infection, 40.3% had chronic HCV infection, 20.0% had cleared HCV infection, and 35.8% never had HCV infection (Table 2; Figure 1).

The distribution of acute, chronic, and cleared HCV infection and those never HCV infected varied by key characteristics (Table 2). By MSA, Miami and Philadelphia had high prevalence of acute infections (17.6% and 5.3% respectively), and Philadelphia and San Juan had high prevalence of chronic infections (56.5% and 54.4%, respectively). Younger PWID <30 years old had about the same prevalence of acute or chronic infections as PWID ≥30 years, with 55% having already acquired HCV at some point (4.1% acute, 38.6% chronic, 12.7% cleared). Among those who started injecting during the past 5 years, more than one-third had ever had HCV infection (8.7% acute, 24.6% chronic, 8.2% cleared) and 1 in 12 had likely acquired HCV within the prior 50-60 days (8.7% acute).¹⁹ Those who receptively or distributively shared syringes or shared injection equipment had similar

distributions of HCV infections, with chronic infections about 10 percentage points higher among those who shared.

A few differences in the distribution of current HIV/HCV co-infections were observed (Table 3). By MSA, Miami and San Juan had the highest percentages of participants with HIV/HCV co-infection (9.5% and 6.9%, respectively). HIV prevalence was highest among transgender PWID; this group also had high HIV/HCV co-infection prevalence (15.4%). HIV/HCV co-infection prevalence was similar for younger PWID <30 years old compared with older PWID, yet those who were older had a greater percentage with HIV infection only (4.9% vs. 2.1%). As expected, those who had been injecting >5 years had higher HIV/HCV co-infection (4.4% vs. 2.4%) and HIV infection only (4.8% vs. 3.0%). HIV/HCV co-infection was highest for PWID who injected speedball (heroin and cocaine injected together; 7.4%); those who used stimulants had the largest percentage with HIV only (9.2%).

In models, current HCV infection (acute or chronic) was higher among PWID who were male (aPR(vs. female)=1.2; 95% CI, 1.1–1.3), White (aPR(vs. Black)=1.3; 95% CI, 1.1–1.5), injected >1 time/day (aPR(vs. <1 time/day)=1.5; 95% CI, 1.3–1.7), and shared syringes (aPR=1.2; 95% CI, 1.1–1.3) or injection equipment (aPR=1.3; 95% CI, 1.1–1.4) in the past year (Table 4). Current HCV infection was significantly higher in Dallas, Miami, Philadelphia, San Francisco, and San Juan (compared with Washington DC). In models of current HIV/HCV co-infection, participants who were transgender (aPR=6.3; 95% CI, 2.8–14.5) and most often injected speedballs (aPR(vs. heroin alone)=2.1; 95% CI, 1.4–3.0) or stimulants alone (aPR(vs. heroin alone)=1.8; 95% CI, 1.1–2.9) were more likely to have both HIV and HCV (Table 3). HIV/HCV co-infection was also significantly higher in Miami and substantially higher, although not significant, in San Juan (compared with Washington DC). Participants who started injecting ≤5 years were less likely to have current HCV infection (aPR(vs. >5 years)=0.7; 95% CI, 0.6–0.8) and to have current HIV/HCV co-infection (aPR(vs. >5 years)=0.5; 95% CI, 0.3–0.8).

When considering only PWID who never previously had HCV, acute HCV infection was 9.9% and was significantly greater among those who were White (aPR=1.3; 95% CI, 1.04–1.7) and who were from Miami (aPR=8.5; 95% CI, 4.9–14.9) or Philadelphia (aPR=7.1; 95% CI, 4.1–12.5) (Table 5).

We observed substantial HCV infection (acute, chronic, or cleared) among those in their first year since injection initiation for both younger (31.6%) and older PWID (30.8%) (Figure 2); this percentage increased steadily for PWID ≥30 years and more abruptly for PWID <30 years with each additional year since initiation considered. For those who never previously had HCV infection, the highest prevalence of acute HCV infection was observed among those in their first year since initiation for PWID <30 years and within 2 years for PWID ≥30 years.

Discussion

In this sample of PWID in 10 U.S. MSAs, almost two-thirds had a lifetime history of HCV infection and nearly one-half currently had HCV infection. Approximately 4% of all participants and 10% of those who never previously had HCV presented with acute HCV infection likely acquired within the 50-60 days prior to participation.¹⁹ In our study, one in 25 were currently living with HIV/HCV co-infection. The proportion of PWID with HCV and HIV/HCV co-infection differed significantly by geographic, demographic, and injection practice characteristics.

More than half of participants in Miami, Philadelphia, and San Juan were currently living with HCV infection, suggesting important geographic diversity. In Miami and San Juan, nearly 1 in 10 of participants were living with HIV/HCV co-infection. San Juan, in particular, has historically had a high HIV and HCV prevalence among PWID.³⁰⁻³² We detected acute HCV infections in nearly all MSAs, though much higher percentages were observed in Miami and Philadelphia. These two jurisdictions also experienced a marked increase in new HIV infections among PWID during 2018.^{33,34} Because injection drug use is associated with both HIV and HCV infections, our findings support evidence of new possible clusters of HIV and HCV infections that may have been occurring in local networks of PWID in these two MSAs at this time.^{33,34} In Miami, because of the very high number of acute HCV infections observed during NHBS data collection, local stakeholders advocated in real-time that local syringe services programs (SSPs) adopt a testing approach that allowed for single-visit sample collection and RNA testing without the requirement for a preceding reactive antibody result to identify even the most recent acute HCV infections occurring within the past 50-60 days.^{19,35} Local stakeholders also found that PWID with acute HCV infection in Miami were less likely to have engaged with an SSP in the past year compared with other PWID participants, suggesting a strong need for outreach of SSP services to this population.³⁵ As increases in opioid use, methamphetamine use, and injecting drugs correspond with rising acute HCV infections and outbreaks of HCV and HIV among PWID, timely identification is critical to preventing ongoing transmission and linking people to care.³⁶⁻³⁸ Engaging local stakeholders in monitoring changes in epidemiologic or behavioral characteristics of new injection initiates can prepare jurisdictions to respond quickly with intervention strategies.^{39,40} Further, PWID with acute HCV infection identified in NHBS would not have otherwise been detected had HCV RNA testing not been performed on all participants irrespective of antibody status. This underscores the importance of local capacity and flexibility in tailoring HCV testing algorithms for specific settings. These findings support single-visit sample collection for HCV antibody and RNA testing and options for point-of-care HCV RNA tests in settings where HCV transmission risk is high and opportunities for follow-up may be limited. Further, our results may suggest RNA testing regardless of antibody result could be a useful testing approach among PWID. These strategies may further serve to improve timely, low-barrier access to HCV treatment for PWID.⁴¹

Current HCV infection (acute or chronic) was greater among male PWID and White PWID in our study. Among those who never previously had HCV infection, the proportion of acute HCV infections was significantly greater for White PWID. Historically, Black or African

American persons have been disproportionately affected by HCV infection, including among those who had ever injected drugs, and it is estimated that Black or African American persons continue to have higher HCV infection prevalence compared to other races.^{42,43} In our study, we found that 1 in 3 Black or African American PWID had current HCV infection. Yet, a recent shift in demographics of PWID with new HCV infections has been observed in other studies, with White PWID predominantly affected; and this shift has been attributed, at least in part, to increasing injection of prescription opioids in this subgroup.^{36,37} Our results align with this evidence of shifting demographics in new HCV cases. Nevertheless, chronic HCV infections in an era of effective HCV treatment warrant stronger efforts for engaging all PWID in HCV care and addressing the numerous barriers to HCV treatment uptake that PWID experience, including drug abstinence requirements in some jurisdictions, provider concerns about reinfection, and drug-use related stigma.^{44,45} Furthermore, transgender PWID were more likely to have HIV/HCV co-infection likely due to a higher proportion of transgender participants with HIV (38.5%) compared with other gender categories. Because of the accelerated progression of liver disease in persons with HIV and HCV co-infection, rapid identification and treatment of HCV infection among transgender persons with HIV could greatly reduce morbidity and mortality associated with both infections.⁵

The proportions of younger PWID <30 years old with HCV infection or HIV/HCV co-infection were nearly the same as their older counterparts ≥30 years. Given opportunities for HCV and HIV exposure increase with age and duration of injection practice, this finding may indicate that both HCV and HIV infections rapidly occur among young PWID, with population-level prevalence stabilizing before the age of 30. CDC surveillance has shown young persons between 20-39 years have the highest rates of acute HCV infection, and other studies have linked increases in HCV infection to young PWID in the context of the increasing opioid crisis.^{2,36,37} We found that current HCV and HIV/HCV co-infection were significantly lower among those who started injecting ≤5 years ago, suggesting that intervention within 5 years of initiation may be important to prevention efforts. Nevertheless, over 1 in 3 PWID who started injecting ≤5 years ago had already acquired HCV at some point. When we considered HCV infection prevalence by years since injection initiation and age, we observed substantial HCV infection among those in their first year since injection initiation for both younger and older PWID; and these percentages increased with each additional year since first injection through 5 years, particularly for younger PWID. This further supports that early interventions to prevent injection initiation, implement harm reduction services, promote safer injection practices, and test and treat PWID within a short period after injection initiation will be needed to prevent HCV acquisition and ongoing transmission. Additionally, this highlights a potential need for peer-based interventions that can reach pre-initiated and newly initiated PWID quickly using existing PWID social networks.^{46 47}

More frequent injection, syringe sharing (receptive or distributive), and sharing of injection equipment were important behaviors associated with having current HCV infection. These results emphasize the need to increase access and uptake of resources that can reduce the potential for sharing syringes and injection equipment. There continues to be a critical need for improved availability, accessibility, funding, and national and local policies to

support SSPs that can provide adequate coverage of sterile syringes and equipment and access to substance use disorder treatment, including medications for opioid use disorder, to help achieve goals of the Ending the HIV Epidemic in the U.S. initiative and HCV elimination efforts.⁴⁸ Further, knowledge of HIV and HCV serostatus can reduce one's sharing behaviors to avoid transmission to others, underscoring the importance of routine periodic testing for PWID and development and approval of future options for point-of-care HCV RNA or core antigen testing in which results can be provided immediately and reflect one's infection status at that time.^{11,49}

The 2018 NHBS cycle among PWID was the first to include HCV RNA testing. Our findings serve as a baseline for understanding acute, chronic, and cleared HCV infection and HIV/HCV co-infection and for monitoring these outcomes over time in future PWID cycles. NHBS has nearly two decades of experience successfully recruiting PWID, a hard-to-reach population in the U.S.²⁰ Using NHBS as a platform for additional activities such as HCV testing both streamlines resources and underscores the comprehensive, holistic nature in which public health programs can be implemented, particularly for PWID who face syndemic conditions. Incorporation of biological markers enhances the surveillance system's ability to avoid certain biases associated with self-reported data on infection status. Further, refining these additional activities to offer the most informative best practices like HCV RNA testing for current infection can improve the impact of observed findings and present a more accurate assessment of how prevalence may change over time.

This study was subject to some limitations. First, the NHBS PWID sample is not nationally representative and therefore results are not generalizable to all U.S. PWID or all PWID in the participating MSAs. MSAs eligible to participate in NHBS are those with high prevalence of HIV; MSAs with low HIV prevalence and non-urban areas are not represented. Further, because this analysis did not use RDS sampling weights, subgroups may have been over- or underrepresented, affecting overall prevalence reported. Nevertheless, all models used generalized estimating equations clustering on RDS recruitment chain and adjusted for MSA and participant network size in an effort to account for the RDS sampling design. Second, acceptability of HCV testing among PWID in NHBS was high given 99% consented and completed an HCV antibody test. Yet, challenges with conducting phlebotomy (e.g., vein damage, staff phlebotomist availability and experience) among PWID for HCV RNA testing resulted in missing HCV RNA data for about a quarter of participants. In a sensitivity analysis, not having an HCV RNA result varied by MSA, which further supports adjustment for MSA in our models. After controlling for MSA, those who injected more than once a day were less likely to have an HCV RNA result, which would be consistent with possible vein damage impacting successful venipuncture. However, older PWID were more likely to have an RNA result and there were no significant differences in having an RNA result between participants with or without HIV; given age and HIV infection are factors for HCV infection prevalence, this could suggest minimal bias or potential slight overestimation of HCV infection prevalence due to missing HCV RNA data. Third, the cross-sectional study design and HCV testing algorithm used in NHBS allowed for detection of acute HCV infections based on HCV antibody non-reactive and RNA detected test results, which most often occurs within the period of 50-60 days after exposure, however, this definition is not the conventional clinical definition of infection in

the first six months following presumed HCV exposure and could not account for persons who previously had HCV, spontaneously cleared infection or were successfully cured, and then experienced a new reinfection; instead, these persons were classified as having chronic infection as they remained HCV antibody reactive. Lastly, our study definition of acute infection differed from both the case surveillance definition of infection within the prior 12 months and the conventional definition used in clinical care of infection in the first six months following presumed HCV exposure, both of which include seroconversions over a longer period of time, either 12 or 6 months. Our study definition for acute infection based on antibody non-reactive and RNA detected results likely underestimated prevalence of acute infection compared to data sources using the clinical definition of the first 6 months of HCV infection after exposure.²⁶

Conclusions

Acute and chronic HCV infection prevalence was substantial among a sample of PWID in 10 U.S. MSAs. Nearly half of participants had current HCV infection and 1 in 25 had HIV/HCV co-infection. Of those that started injecting drugs ≤ 5 years ago, over 1 in 3 had already acquired HCV infection. Among those who never previously had HCV infection, 1 in 10 presented with an acute HCV infection, likely acquired within the prior 50-60 days per our study definition.¹⁹ Accessibility to RNA testing, promoting safer injection practices, and intervening early with harm reduction resources for recent injection initiates will be critical to HCV elimination initiatives for PWID. Integrating HCV RNA testing in ongoing biobehavioral surveys of PWID, including NHBS, will provide the data needed for monitoring progress of national disease elimination efforts.

Funding sources

Supplemental funding for hepatitis C testing in 2018 National HIV Behavioral Surveillance was provided by the National Institute on Drug Abuse (IDDA #5610-11-21-OD).

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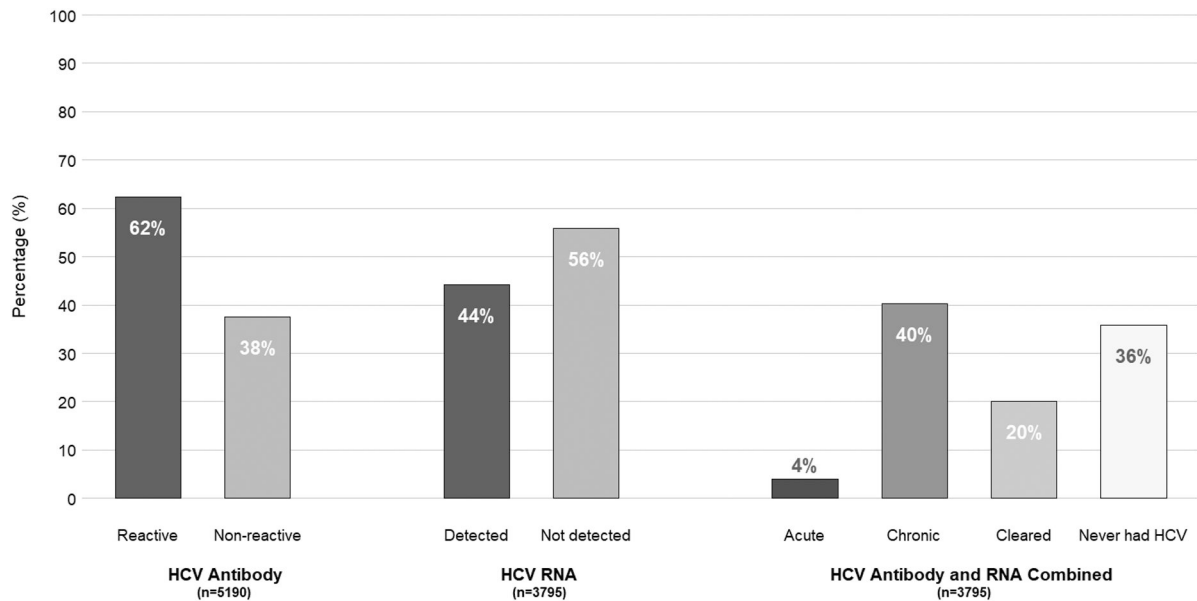


Figure 1. Hepatitis C virus antibody and RNA prevalence among persons who inject drugs – National HIV Behavioral Surveillance, 10 U.S. cities, 2018

Note: ‘Acute’ was defined for this analysis as having HCV antibody non-reactive and HCV RNA detected test results, which typically occurs within the 50-60 days after HCV exposure. ‘Chronic’ corresponds to participants with HCV antibody reactive and HCV RNA detected test results. ‘Cleared’ corresponds to participants with HCV antibody reactive and HCV RNA not detected test results. ‘Never had HCV’ corresponds to participants with HCV antibody non-reactive and HCV RNA not detected test results.

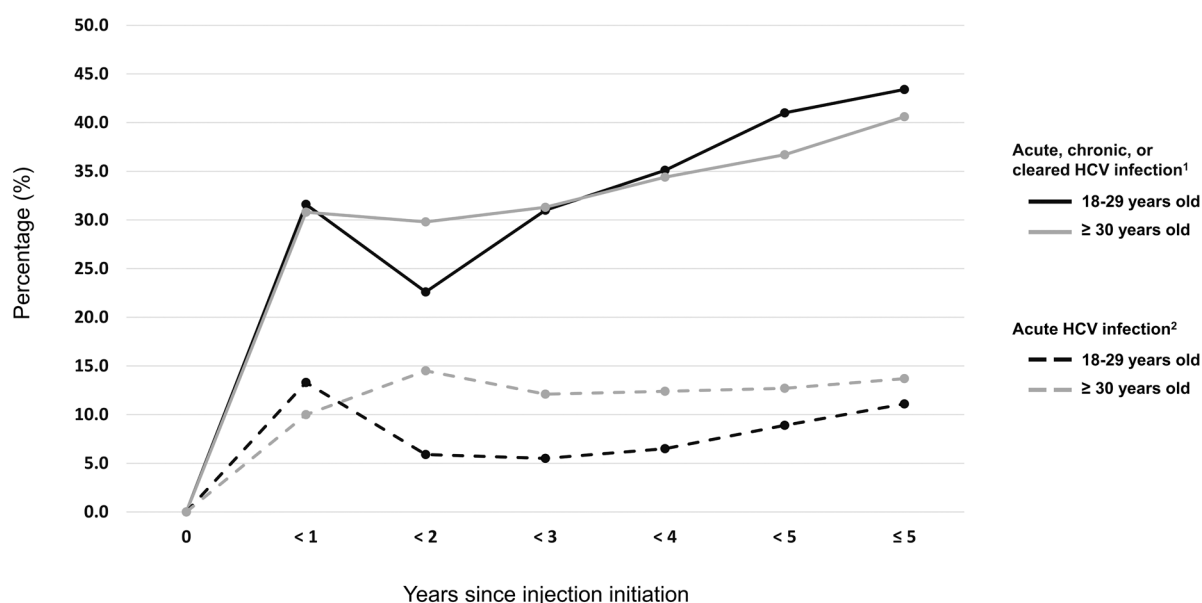


Figure 2. HCV Prevalence Among Recent Injection Initiates by Years Since Injection Initiation and Age—National HIV Behavioral Surveillance, 2018

Note: HCV prevalence prior to injection initiation was assumed to be zero.

¹Acute, chronic, or cleared HCV infection corresponds to participants with HCV antibody reactive or HCV RNA detected results among those with valid HCV antibody and RNA test results.

²Acute HCV infection corresponds to participants with HCV antibody non-reactive and HCV RNA detected test results, which typically occurs within the 50-60 days after HCV exposure. Here this denominator was limited to participants with valid HCV RNA and antibody test results and who never previously had HCV (i.e. had HCV antibody non-reactive test result).

Table 1.

Key outcomes and interpretations

TEST OUTCOMES	TEST RESULTS	INTERPRETATION
HCV antibody (rapid or lab-based EIA test)	HCV antibody reactive	Exposure to HCV infection
	HCV antibody non-reactive	No evidence of exposure to HCV infection
HCV RNA	HCV RNA detected	Current HCV infection
	HCV RNA not detected	No current HCV infection
HCV antibody and HCV RNA combined	HCV antibody non-reactive & HCV RNA detected ¹	Acute HCV infection ¹
	HCV antibody reactive & HCV RNA detected	Chronic HCV infection
	HCV antibody reactive & HCV RNA not detected	Cleared HCV infection
	HCV antibody non-reactive & HCV RNA not detected	Never had HCV infection
Current HIV and HCV co-infection	HIV-positive final test result & HCV RNA detected	HIV/HCV co-infection
	HIV-positive final test result & HCV RNA not detected	HIV infection only
	HIV-negative final test result & HCV RNA detected	HCV infection only
	HIV-negative final test result & HCV RNA not detected	Neither HIV or HCV infection
MODEL OUTCOMES	TEST RESULTS	INTERPRETATION
Current HCV infection	HCV RNA detected	Current HCV infection
	HCV RNA not detected	No current HCV infection
Current HIV and HCV co-infection	HIV-positive final test result & HCV RNA detected	HIV/HCV co-infection
	HIV-negative final test result or HCV RNA not detected (i.e., HIV infection only or HCV infection only or neither HIV or HCV infection)	No HIV/HCV co-infection
Acute HCV infection <i>Note: Among persons who never previously had HCV infection (HCV antibody non-reactive)</i>	HCV antibody non-reactive & HCV RNA detected ¹	Acute HCV infection ¹
	HCV antibody non-reactive & HCV RNA not detected	No previous or current HCV infection

¹ Acute HCV infection was defined for this analysis as having HCV antibody non-reactive and HCV RNA detected test results, which typically occurs within the 50-60 days after HCV exposure.

Table 2.

Hepatitis C virus infection among persons who inject drugs – National HIV Behavioral Surveillance, 10 U.S. cities, 2018

	Acute HCV infection ^e		Chronic HCV infection ^f		Cleared HCV infection ^g		Never had HCV infection ^h		Total
	No.	%	No.	%	No.	%	No.	%	No.
Gender									
Male	120	4.3	1156	41.5	494	17.7	1016	36.5	2786
Female	29	3.0	359	37.2	252	26.1	325	33.7	965
Transgender	0	0.0	12	30.8	12	30.8	15	38.5	39
Age (years)									
18-29	19	4.1	180	38.6	59	12.7	208	44.6	466
≥30	130	3.9	1349	40.5	700	21.0	1150	34.5	3329
Race/ethnicity									
Black/African American	48	4.5	327	30.6	181	16.9	513	48.0	1069
Hispanic/Latino ^a	53	4.0	542	41.1	285	21.6	439	33.3	1319
White	44	3.6	587	48.3	252	20.7	333	27.4	1216
Other/Multiple races	4	2.2	68	37.0	41	22.3	71	38.6	184
NHBS HIV test result									
HIV-negative	134	3.9	1381	40.0	683	19.8	1256	36.4	3454
HIV-positive ^b	15	4.6	138	42.5	73	22.5	99	30.5	325
Started injecting ≤5 yrs ago									
Yes	58	8.7	165	24.6	55	8.2	392	58.5	670
No	91	2.9	1345	43.5	699	22.6	956	30.9	3091
Injection frequency, past 12 mo									
More than once a day	122	4.2	1276	44.0	558	19.2	943	32.5	2899
Once a day	10	2.6	124	32.8	103	27.2	141	37.3	378
Less than once a day	17	3.3	128	24.9	97	18.9	272	52.9	514
Drug injected most often									
Heroin	108	4.3	1014	40.4	484	19.3	906	36.1	2512
Speedball (heroin and cocaine)	23	3.3	336	47.6	159	22.5	188	26.6	706
Stimulants (meth, cocaine)	15	3.3	119	26.1	89	19.5	233	51.1	456
Other drugs ^c	3	2.5	60	49.6	27	22.3	31	25.6	121
Receptive syringe sharing, past 12 mo									
Yes	33	3.2	489	47.2	191	18.4	323	31.2	1036
No	116	4.2	1039	37.7	567	20.6	1035	37.5	2757
Distributive syringe sharing, past 12 mo									
Yes	57	4.0	657	45.9	262	18.3	456	31.8	1432
No	92	3.9	872	36.9	497	21.0	901	38.1	2362
Shared injection equipment^d, past 12 mo									

	Acute HCV infection ^e		Chronic HCV infection ^f		Cleared HCV infection ^g		Never had HCV infection ^h		Total
	No.	%	No.	%	No.	%	No.	%	No.
Yes	67	3.5	883	46.1	398	20.8	567	29.6	1915
No	82	4.4	645	34.3	361	19.2	791	42.1	1879
MSA									
Chicago, Illinois	2	0.9	79	34.5	27	11.8	121	52.8	229
Dallas, Texas	4	1.6	106	42.1	48	19.0	94	37.3	252
Houston, Texas	5	1.3	105	26.3	79	19.8	211	52.8	400
Los Angeles, California	0	0.0	143	37.1	89	23.1	153	39.7	385
Miami, Florida	87	17.6	196	39.6	35	7.1	177	35.8	495
New York City, New York	7	1.7	134	32.1	138	33.0	139	33.3	418
Philadelphia, Pennsylvania	32	5.3	344	56.5	124	20.4	109	17.9	609
San Francisco, California	0	0	149	40.4	126	34.1	94	25.5	369
San Juan, Puerto Rico	8	2.3	193	54.4	37	10.4	117	33.0	355
Washington, DC	4	1.4	80	28.3	56	19.8	143	50.5	283
Total	149	3.9	1529	40.3	759	20.0	1358	35.8	3795

Abbreviations: HIV, human immunodeficiency virus; HCV, hepatitis C virus; mo, months; MSA, metropolitan statistical area

Note: Data include all participants with a valid HCV antibody test result (rapid or EIA test) and a valid HCV RNA test.

^aHispanics/Latinos can be of any race.

^bParticipants with a reactive rapid NHBS HIV test result supported by a second rapid HIV test or supplemental laboratory-based HIV testing.

^cIncludes prescription opioids (e.g., Oxycontin, Dilaudid, morphine, Percocet, or Demerol), fentanyl, ecstasy, and other drugs (e.g., benzodiazepine, barbiturates) or other drug combinations.

^dInjection equipment included cooker, filter, or water.

^e'Acute HCV infection' was defined for this analysis as having HCV antibody non-reactive and HCV RNA detected test results, which typically occurs within the 50-60 days after HCV exposure.

^f'Chronic HCV infection' was defined as having a reactive HCV antibody test result and a 'detected' HCV RNA test result.

^g'Cleared HCV infection' was defined as having a reactive HCV antibody test result and a 'not detected' HCV RNA test result.

^h'Never had HCV infection' was defined as having a non-reactive HCV antibody test result and a 'not detected' HCV RNA test result.

Table 3.

Current HIV and HCV co-infection among persons who inject drugs – National HIV Behavioral Surveillance, 10 U.S. cities, 2018

	HIV and HCV co-infection ^d		HIV infection only ^d		HCV infection only ^d		No HIV or HCV infection ^d		Total
	No.	%	No.	%	No.	%	No.	%	No.
Gender									
Male	118	4.3	117	4.2	1150	41.4	1390	50.1	2775
Female	29	3.0	46	4.8	357	37.2	528	55.0	960
Transgender	6	15.4	9	23.1	6	15.4	18	46.2	39
Age (years)									
18-29	19	4.1	10	2.1	180	38.6	257	55.2	466
≥30	134	4.0	162	4.9	1335	40.3	1682	50.8	3313
Race/ethnicity									
Black/African American	42	3.9	72	6.8	332	31.1	620	58.2	1066
Hispanic/Latino ^a	66	5.0	53	4.0	523	39.9	669	51.0	1311
White	38	3.1	35	2.9	591	48.7	549	45.3	1213
Other/Multiple races	7	3.8	12	6.6	64	35.2	99	54.4	182
Started injecting ≤5 yrs ago									
Yes	16	2.4	20	3.0	207	30.9	426	63.7	669
No	136	4.4	149	4.8	1291	42.0	1501	48.8	3077
Injection frequency, past 12 mo									
More than once a day	132	4.6	104	3.6	1258	43.6	1394	48.3	2888
Once a day	10	2.7	30	8.0	122	32.5	213	56.8	375
Less than once a day	11	2.2	38	7.4	134	26.2	329	64.3	512
Drug injected most often									
Heroin	78	3.1	89	3.6	1038	41.5	1296	51.8	2501
Speedball (heroin and cocaine)	52	7.4	37	5.3	304	43.3	309	44.0	702
Stimulants (meth, cocaine)	18	4.0	42	9.2	115	25.3	280	61.5	455
Other drugs ^b	5	4.1	4	3.3	58	47.9	54	44.6	121
Receptive syringe sharing, past 12 mo									
Yes	47	4.6	27	2.6	472	45.7	486	47.1	1032
No	106	3.9	145	5.3	1042	38.0	1452	52.9	2745
Distributive syringe sharing, past 12 mo									
Yes	43	3.0	21	1.5	668	46.8	696	48.7	1428
No	110	4.7	151	6.4	847	36.0	1242	52.9	2350
Shared injection equipment^c, past 12 mo									
Yes	82	4.3	49	2.6	863	45.2	914	47.9	1908
No	71	3.8	123	6.6	651	34.8	1025	54.8	1870
MSA									

	HIV and HCV co-infection ^d		HIV infection only ^d		HCV infection only ^d		No HIV or HCV infection ^d		Total
	No.	%	No.	%	No.	%	No.	%	No.
Chicago, Illinois	2	0.9	0	0.0	76	33.9	146	65.2	224
Dallas, Texas	5	2.0	5	2.0	105	41.7	137	54.4	252
Houston, Texas	10	2.5	36	9.0	100	25.0	254	63.5	400
Los Angeles, California	2	0.5	5	1.3	139	36.3	237	61.9	383
Miami, Florida	47	9.5	26	5.3	236	47.8	185	37.4	494
New York City, New York	14	3.4	29	7.0	126	30.3	247	59.4	416
Philadelphia, Pennsylvania	27	4.4	12	2.0	349	57.3	221	36.3	609
San Francisco, California	11	3.0	28	7.6	138	37.4	192	52.0	369
San Juan, Puerto Rico	24	6.9	12	3.4	173	49.4	141	40.3	350
Washington, DC	11	3.9	19	6.7	73	25.9	179	63.5	282
Total	153	4.0	172	4.6	1515	40.1	1939	51.3	3779

Abbreviations: HIV, human immunodeficiency virus; HCV, hepatitis C virus; mo, month; MSA, metropolitan statistical area

Note: Data include all participants with a valid NHBS HIV test result and a valid HCV RNA test result.

^aHispanics/Latinos can be of any race.

^bExamples of other drugs included: painkillers (Oxycontin, Dilaudid, morphine, Percocet, or Demerol), fentanyl, ecstasy, and other drugs or other drug combinations.

^cInjection equipment included cooker, filter, or water.

^d'HIV and HCV co-infection' was defined as having an HIV infection and having a detected HCV RNA test result. Participants classified as having an HIV infection had a reactive rapid NHBS HIV test result supported by a second reactive rapid HIV test or supplemental laboratory-based HIV testing that confirmed HIV infection. 'HIV infection only' referred to participants with HIV infection and HCV RNA not detected. 'HCV infection only' referred participants with no HIV infection and HCV RNA detected. 'No HIV or HCV infection' referred to participants with no HIV infection and HCV RNA not detected.

Table 4.

Factors associated with current HCV infection and HIV/HCV co-infection among persons who inject drugs – National HIV Behavioral Surveillance, 10 U.S. cities, 2018

	Current HCV infection ^{e,f} (n=3,795)					Current HIV and HCV co-infection ^{e,g} (n=3,779) ^e				
	No.	%	aPR	95% CI	p-value	No.	%	aPR	95% CI	p-value
Gender										
Male	1276	45.8	1.2	1.1–1.3	<0.01	118	4.3	1.3	0.7-2.2	0.41
Female	388	40.2	Ref			29	3.0	Ref		
Transgender	12	30.8	0.9	0.6–1.4	0.58	6	15.4	6.3	2.8-14.5	<0.01
Age (years)										
18-29	199	42.7	Ref			19	4.1	Ref		
≥30	1479	44.4	1.1	0.9-1.3	0.23	134	4.0	1.0	0.6-1.6	0.96
Race/ethnicity										
Black/African American	375	35.1	Ref			42	3.9	Ref		
Hispanic/Latino ^d	595	45.1	1.1	0.9-1.3	0.36	66	5.0	1.0	0.6-1.8	0.98
White	631	51.9	1.3	1.1-1.5	<0.01	38	3.1	0.7	0.5-1.1	0.12
Other/Multiple races	72	39.1	1.1	0.8-1.4	0.55	7	3.8	1.1	0.5-2.3	0.87
NHBS HIV test result										
HIV-negative	1515	43.9	Ref			–	–	–	–	–
HIV-positive ^b	153	47.1	1.1	0.9-1.2	0.43	–	–	–	–	–
Started injecting ≤5 yrs ago										
Yes	223	33.3	0.7	0.6-0.8	<0.01	16	2.4	0.5	0.3-0.8	<0.01
No	1436	46.5	Ref			136	4.4	Ref		
Injection frequency, past 12 mo										
More than once a day	1398	48.2	1.5	1.3-1.7	<0.01	132	4.6	1.8	0.8-3.8	0.14
Once a day	134	35.4	1.2	1.03-1.5	0.02	10	2.7	1.2	0.5-2.5	0.70
Less than once a day	145	28.2	Ref			11	2.2	Ref		
Drug injected most often										
Heroin	1122	44.7	Ref			78	3.1	Ref		
Speedball (heroin and cocaine)	359	50.8	1.1	1.0-1.2	0.13	52	7.4	2.1	1.4-3.0	<0.01
Stimulants (meth, cocaine)	134	29.4	0.7	0.6-0.9	0.02	18	4.0	1.8	1.1-2.9	0.01
Other drugs ^c	63	52.1	1.1	0.9-1.4	0.30	5	4.1	1.4	0.6-3.0	0.44
Receptive syringe sharing, past 12 mo										
Yes	522	50.4	1.2	1.1-1.3	<0.01	47	4.6	1.1	0.8-1.5	0.47
No	1155	41.9	Ref			106	3.9	Ref		
Distributive syringe sharing, past 12 mo										
Yes	714	49.9	1.2	1.1-1.3	<0.01	43	3.0	0.6	0.4-0.9	<0.01
No	964	40.8	Ref			110	4.7	Ref		

	Current HCV infection ^{e,f} (n=3,795)					Current HIV and HCV co-infection ^{e,g} (n=3,779) ^e				
	No.	%	aPR	95% CI	p-value	No.	%	aPR	95% CI	p-value
Shared injection equipment^d, past 12 mo										
Yes	950	49.6	1.3	1.1-1.4	<0.01	82	4.3	1.2	0.8-1.7	0.40
No	727	38.7	Ref			71	3.8	Ref		
MSA										
Chicago, Illinois	81	35.4	1.2	1.0-1.5	0.12	2	0.9	0.2	0.1-0.6	<0.01
Dallas, Texas	110	43.7	1.5	1.2-1.8	<0.01	5	2.0	0.5	0.3-0.98	0.04
Houston, Texas	110	27.5	0.9	0.7-1.3	0.65	10	2.5	0.6	0.3-1.2	0.18
Los Angeles, California	143	37.1	1.2	0.9-1.5	0.16	2	0.5	0.1	0.05-0.3	<0.01
Miami, Florida	283	57.2	1.9	1.5-2.3	<0.01	47	9.5	2.3	1.3-3.9	<0.01
New York City, New York	141	33.7	1.1	0.8-1.5	0.50	14	3.4	0.9	0.5-1.7	0.76
Philadelphia, Pennsylvania	376	61.7	2.1	1.8-2.5	<0.01	27	4.4	1.2	0.6-2.4	0.55
San Francisco, California	149	40.4	1.4	1.2-1.7	<0.01	11	3.0	0.8	0.5-1.3	0.31
San Juan, Puerto Rico	201	56.6	2.0	1.6-2.4	<0.01	24	6.9	1.8	1.0-3.3	0.06
Washington, DC	84	29.7	Ref			11	3.9	Ref		
Total	1678	44.2				153	4.0			

Abbreviations: HIV, human immunodeficiency virus; HCV, hepatitis C virus; mo, month; MSA, metropolitan statistical area; aPR, adjusted prevalence ratio; CI, confidence interval

Note: Data include all participants with a valid NHBS HIV test result and a valid HCV RNA test result. Numbers may not sum to total due to missing values.

^aHispanics/Latinos can be of any race.

^bParticipants with a reactive rapid NHBS HIV test result supported by a second rapid HIV test or supplemental laboratory-based HIV testing.

^cExamples of other drugs included: painkillers (Oxycontin, Dilaudid, morphine, Percocet, or Demerol), fentanyl, ecstasy, and other drugs or other drug combinations.

^dInjection equipment included cooker, filter, or water.

^eaPRs, 95%CI, and p-values were obtained from separate log-linked Poisson regression models for each independent variable and the respective outcome that adjusted for MSA and network size and accounted for clustering by recruitment chain.

^fCurrent HCV infection was defined as having a detected HCV RNA test result. This included both acute and chronic HCV infections with detectable HCV RNA.

^gHIV and HCV co-infection was defined as having an HIV infection and having a detected HCV RNA test result. Participants classified as having an HIV infection had a reactive rapid NHBS HIV test result supported by a second reactive rapid HIV test or supplemental laboratory-based HIV testing that confirmed HIV infection. Sixteen participants had valid HCV RNA test results and were included in the current HCV infection outcome but did not have valid HIV test results and therefore were not included in the HIV/HCV co-infection outcome.

Table 5.

Factors associated with acute HCV infection among persons who inject drugs who never previously had HCV^a
 – National HIV Behavioral Surveillance, 10 U.S. cities, 2018

	Acute HCV infection ^{e,f} (N=1,507)				
	No.	%	aPR	95% CI	p-value
Gender					
Male	120	10.6	1.0	0.7-1.5	0.80
Female	29	8.2	Ref		
Transgender	0	0.0	–	–	–
Age (years)					
18-29	19	8.4	Ref		
≥30	130	10.2	1.3	0.8-2.2	0.32
Race/ethnicity					
Black/African American	48	8.6	Ref		
Hispanic/Latino ^b	53	10.8	1.2	0.97-1.5	0.09
White	44	11.7	1.3	1.04-1.7	0.02
Other/Multiple races	4	5.3	0.7	0.4-1.4	0.36
NHBS HIV test result					
HIV-negative	134	9.6	Ref		
HIV-positive ^c	15	13.2	1.2	0.7-1.9	0.59
Started injecting ≤5 yrs ago					
Yes	58	12.9	1.2	0.9-1.6	0.15
No	91	8.7	Ref		
Injection frequency, past 12 mo					
More than once a day	122	11.5	1.3	0.9-1.9	0.11
Once a day	10	6.6	1.1	0.5-2.4	0.90
Less than once a day	17	5.9	Ref		
Drug injected most often					
Heroin	108	10.7	Ref		
Speedball (heroin and cocaine)	23	10.9	1.3	0.8-2.2	0.33
Stimulants (meth, cocaine)	15	6.0	1.2	0.7-2.0	0.56
Other drugs ^d	3	8.8	0.8	0.3-1.7	0.49
Receptive syringe sharing, past 12 mo					
Yes	33	9.3	0.8	0.6-1.0	0.10
No	116	10.1	Ref		
Distributive syringe sharing, past 12 mo					
Yes	57	11.1	1.1	0.8-1.5	0.65
No	92	9.3	Ref		
Shared injection equipment^e, past 12 mo					

	Acute HCV infection ^{e,f} (N=1,507)				
	No.	%	aPR	95% CI	p-value
Yes	67	10.6	1.0	0.6-1.7	0.98
No	82	9.4	Ref		
City					
Miami, Florida	87	33.0	8.5	4.9-14.9	<0.01
Philadelphia, Pennsylvania	32	22.7	7.1	4.1-12.5	<0.01
All other cities	30	2.7	Ref		
<i>Chicago, Illinois</i>	2	1.6	–	–	–
<i>Dallas, Texas</i>	4	4.1	–	–	–
<i>Houston, Texas</i>	5	2.3	–	–	–
<i>Los Angeles, California</i>	0	0.0	–	–	–
<i>New York City, New York</i>	7	4.8	–	–	–
<i>San Francisco, California</i>	0	0.0	–	–	–
<i>San Juan, Puerto Rico</i>	8	6.4	–	–	–
<i>Washington, DC</i>	4	2.7	–	–	–
Total	149	9.9			

Abbreviations: HIV, human immunodeficiency virus; HCV, hepatitis C virus; mo, months

Note: Data include all participants with a valid HCV antibody test result (rapid or EIA test) and a valid HCV RNA test.

^a PWID who never previously had HCV were defined as those who tested HCV antibody non-reactive, meaning that they were never previously exposed to HCV infection and were therefore considered at-risk for acquiring a new, acute HCV infection.

^b Hispanics/Latinos can be of any race.

^c Participants with a reactive rapid NHBS HIV test result supported by a second rapid HIV test or supplemental laboratory-based HIV testing.

^d Examples of other drugs included: painkillers (Oxycontin, Dilaudid, morphine, Percocet, or Demerol), fentanyl, ecstasy, and other drugs or other drug combinations.

^e Injection equipment included cooker, filter, or water.

^e aPRs, 95%CI, and p-values were obtained from separate log-linked Poisson regression models for each independent variable and the respective outcome that adjusted for MSA and network size and accounted for clustering by recruitment chain. A modified 3-level MSA variable (Miami, Philadelphia, all other MSAs) was used to allow for model convergence.

^f Acute HCV infection was defined for this analysis as having HCV antibody non-reactive and HCV RNA detected test results, which typically occurs within the 50-60 days after HCV exposure.