HPTN 078: High Prevalence of HCV Antibodies Among Urban U.S. Men Who Have Sex with Men (MSM) Independent of HIV Status

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Summary: Nearly 1 in 5 MSM screened for HPTN 078 have been infected with HCV. The prevalence is high regardless of HIV status. In HIV burden networks, high HCV infection prevalence may occur in MSM without HIV.

Abstract

Background: Sexual transmission of hepatitis C virus (HCV) is uncommon, yet documented among men who have sex with men (MSM), primarily among those with HIV.

Me**thods:** In HPTN 078, which assessed an integrated strategy to achieve HIV viral suppression, 1305 MSM were screened across four geographically diverse US cities. At screening, demographic/behavioral/psychosocial questionnaires were completed, along with HIV and HCV testing. Multivariable logistic regression was used to evaluate associations with HCV antibody positivity.

Results: Of the 1287 (99%) MSM with HCV antibody results, median age was 41, 69% were Black, 85% had a high school diploma or more, 35% were employed, 70% had HIV, and 21% had undergone substance use counseling. The median lifetime number of male sexual partners was 17 (IQR: 6, 50) and 246 (19%) were HCV antibody positive. HCV antibody positivity was high in MSM with HIV (20%) and MSM without HIV (17%) (P=0.12) and was higher in those receiving substance use counseling (36%) than those that had not (15%)(P=<0.01). Substance use counseling [OR 2.51, 95% CI 1.80-3.51] and unstable housing [OR 2.16, 95% CI 1.40-3.33] were associated with HCV antibody positivity.

Conclusion: Nearly 1 in 5 MSM screened for HPTN 078 have been infected with HCV. The prevalence is high regardless of HIV status and is high even in those who did not undergo substance use counseling. In HIV burden networks, high HCV infection prevalence may occur in MSM without HIV. As PrEP implementation expands and condom use declines, routine HCV counseling and screening among MSM is important.

Key words: hepatitis C; HIV; men who have sex with men

Introduction

In the United States, approximately 4.3 million individuals have been exposed to hepatitis C virus (HCV), and 2.7 million individuals are currently viremic.[1] HCV infection places these individuals at elevated risk of liver cancer and liver failure.[2] Notably, mortality linked to HCV infection has surpassed that of 60 other reportable infectious diseases including HIV.[3] HCV coinfection with HIV is particularly common with approximately 25% of people living with HIV also coinfected with HCV.[4] HIV/HCV coinfection is of particular concern as HIV coinfection increases liver related mortality from HCV.[5] However, with the emergence of short duration, all oral regimens for the treatment and cure of HCV infection, there is hope that HCV elimination can be achieved.[6] Yet, HCV elimination will be dependent on widespread HCV testing, targeted elimination focusing on populations at elevated risk of HCV infection (including men who have sex with men, MSM), and broad access to curative therapies.[7]

The most common route of HCV transmission remains injection drug use.[8] While sexual transmission of HCV is uncommon, it has been documented among MSM, particularly among those with HIV.[9] Several studies have reported sexually transmitted HCV infection outbreaks among MSM with HIV thought to be related to rectal mucosa trauma, decreased condom use, group sex practices, bacterial sexually transmitted infections, HCV shedding in semen, and chemsex, drug use during sex, which may lower inhibition and increase duration of sex.[10-16] However, it has been unclear why lower rates of HCV infection were being seen in MSM without HIV in the early 2000s but it was thought that this could be potentially related to serosorting and decreased condom use in MSM with HIV.[17] Recent phylogenetic analyses reveal that some MSM without HIV are infected with HCV strains circulating in transmission networks of MSM with HIV.[18] Thus, there has been heightened interest in obtaining additional data on HCV infection among MSM with and without HIV to refine current guidelines on HCV testing. Current HCV guidelines in the United States (US) recommend one-time testing for all individuals 18 years of age and older along with annual HCV testing in sexually active MSM with HIV.[19] For MSM without HIV, HCV testing is only

recommended at initiation of pre-exposure prophylaxis (PrEP) and annually thereafter while on PrEP.[19] All MSM, irrespective of HIV status, may be tested more frequently for HCV infection if high-risk sexual or drug use practices are occurring.[19]

In this study, we determined the prevalence of HCV antibodies among MSM with and without HIV and evaluated factors associated with HCV antibody positivity among MSM screened for HPTN (HIV Prevention Trials Network) 078. HCV antibodies reliably reflect the sum of all infection (past and current) and therefore provide information on the level of risk of HCV acquisition in MSM.

Materials and Methods

HPTN 078 was designed to develop and assess the efficacy of an integrated case manager intervention strategy to identify, recruit, link to care, retain in care, and attain and maintain viral suppression among MSM with HIV in the US as previously described.[20] The study was developed in response to the sustained and even growing HIV epidemics among gay men and other MSM given complex interactions of individual, network level, and structural HIV risks.[21, 22] The study used deep-chain respondent driven sampling (DC-RDS) and direct recruitment to identify and recruit MSM with HIV who were not virally suppressed (>1,000 copies/ml) across four geographically diverse US cities (Atlanta, GA; Baltimore, MD; Birmingham, AL; Boston, MA).[23] DC-RDS has been a sampling method widely used in HIV surveillance and research to identify and recruit marginalized populations (including MSM, transgender women, or people who inject drugs), often in challenging contexts for these communities.[24, 25] RDS relies on the identification and enumeration of a discrete number of “seed” participants who are incentivized to refer members of their social or sexual networks. Deep chain RDS (DC-RDS) allows for referral chains to be maintained over longer waves of recruitment. DC-RDS has shown the potential to reach the most marginalized subsets of study participants.[26] The study sites in HPTN 078 included Ponce de Leon Center Clinical Research Site, Johns Hopkins University Clinical Research Site (JHU), University of Alabama at Birmingham Clinical Research Site (UAB), and Fenway Health Clinical Research Site. Three sites were university-

affiliated and two were community-based organization (the UAB site worked in two distinct institutions, one university-affiliated and one community-based).

Participants were eligible for screening if they were at least 16 years of age (for Birmingham and Boston) or at least 18 years of age (for Atlanta and Baltimore), assigned male sex at birth, and reported having anal sex with another man in past six months. Screening began in March 2016 and ended in December 2017. Out of the 1305 participants screened, 154 had HIV and were virally unsuppressed, 710 had HIV and were virally suppressed, 38 had HIV and did not have a viral load performed, 392 did not have HIV, and 11 had unknown HIV status. The local institutional review board for each study site approved the protocol prior to study implementation.

Within HPTN 078, we focused this investigation on the prevalence of HCV antibodies to document the sum of all infection (past and current) and to evaluate factors associated with HCV antibody positivity among MSM with and without HIV infection screened for HPTN 078. Demographic, behavioral, and psychosocial characteristics were collected at the screening visit through audio computer-assisted self-interview (ACASI) and included a sexual activity matrix to document numbers of partners and sexual behaviors that was adapted from other HPTN studies and the National HIV Behavioral Surveillance MSM cycle questionnaire.[21, 27] However, detailed data on sexual practices and injection drug use history were not obtained in HPTN 078 since it was focused on linkage to care for MSM. Participants were tested for HIV infection at study sites prior to enrollment using HIV rapid testing or a 4th generation assay. Additional testing was performed retrospectively at the HPTN Laboratory Center (Baltimore, MD). Participants were also tested at study sites for HCV antibody through a Quest Diagnostics Immunoassay except for UAB where the Abbott Architect anti-HCV Assay was used. Syphilis testing was performed using treponemal and non-treponemal tests with locally determined test algorithms based on CDC guidance.

Statistical Analysis

Baseline demographic, behavioral, psychosocial, and clinical characteristics of the study population were compared by HCV antibody status using chi-square tests for categorical variables and Wilcoxon rank sum tests for continuous variables. Multivariable logistic regression was used to evaluate correlates of HCV antibody positivity. Baseline covariates with a p-value <0.1 were included in a multivariable model. An additional model where HIV was forced into the model was also completed. Odds ratios (OR) and 95% confidence intervals (CI) are reported. All analyses were performed using STATA version 16 (StataCorp LLC., College Station, Texas).

Results

Of 1305 MSM screened for HPTN 078, 1287 (99%) had HCV antibody results available. For the 1287 MSM, median age was 41, 69% were Black, 85% had a high school diploma or more, 35% were employed, 84% had insurance, and 70% had HIV (Table 1). The median lifetime number of male sexual partners was 17 (Interquartile range, IQR: 6, 50) while the median number of receptive anal sex partners with no condom in the last six months was 1 (IQR: 0, 2). One-fifth of the participants reported that they had undergone substance (drug or alcohol) use counseling or treatment in the past six months and 11% reported that they currently had unstable housing.

Of the 1287 participants with HCV antibody data, 246 (19%) were HCV antibody positive. Notably, HCV antibody positivity was similarly high in both MSM with HIV (20%) and without HIV (17%) (P=0.12). HCV antibody positivity was higher in individuals reporting substance use counseling or treatment (36%) than those that did not (15%) (P<0.0001). The number of lifetime male sexual partners was similar between those with a positive HCV antibody (20, IQR: 7, 50) and those that were HCV antibody negative (16, IQR: 6, 50) (P=0.54). With respect to median number of receptive anal sex partners without a condom in the last six months, no difference was seen by HCV antibody status.

Screening covariates with a p-value <0.1 in univariate analysis were included in the multivariable model (Table 1). Univariate covariates that met this threshold included older age, Black race, less than a high school education, employed, insured, substance use counseling or treatment, and unstable housing. In the multivariable model, older age (OR 1.07, 95% CI 1.05-1.08), less than a high school diploma (OR 1.67, 95% CI 1.13-2.48), substance use counseling or treatment (OR 2.51, 95% CI 1.80-3.51), and unstable housing (OR 2.16, 95% CI 1.40-3.33) were associated with HCV antibody positivity (Table 2). Individuals of Black race were less likely to be HCV antibody positive (OR 0.71, 95% CI 0.51-0.98). When HIV was introduced into the model with the co-variates in Table 2, it was not associated with HCV antibody positivity (OR 0.89, 95% CI 0.61, 1.31).

Discussion

In this high HIV burden network recruited through DC-RDS and direct recruitment, nearly 1 in 5 MSM screened for HPTN 078 had been infected with HCV as documented by HCV antibody positivity. Notably, high rates of HCV antibody positivity were seen in both MSM with HIV (20%) and MSM without HIV (17%). While several studies have documented sexually transmitted HCV infection outbreaks among MSM with HIV since the early 2000s, research data and phylogenetic studies have only recently revealed higher rates of HCV infection among MSM without HIV. Further, these studies also demonstrate that the HCV strains in MSM without HIV also circulate in transmission networks of MSM with HIV.[10-18, 28] The data from our study again raise concern that HCV may be broadly spreading in MSM networks, irrespective of HIV status.

A systematic review of HCV infection from 38 cross-sectional studies of MSM in industrialized countries and published in English from 2000 to 2015 reported that pooled HCV prevalence was substantially higher in MSM with HIV (8.3%, 95% CI 6.7-9.9) than in MSM without HIV (1.5%, 95% CI 0.8-2.1).[9] While our study also revealed a higher rate of HCV antibody positivity in MSM with HIV (20%) versus MSM without HIV (17%), this was not statistically significant and the rates were high in both groups. This is consistent with an increasing incidence of HCV infection among MSM without HIV in the era of PrEP and U=U (Undetectable=Untransmittable) perhaps due

to higher risk sexual practices in overlapping networks of MSM with HIV and MSM without HIV.[18, 28, 29] This concern for higher rates of HCV prevalence among MSM without HIV supports HCV testing among MSM without HIV with higher frequency. Current HCV guidelines in the US developed by the America Association for the Study of Liver Diseases and the Infectious Diseases Society of America recommend annual HCV testing in all sexually active MSM living with HIV and in MSM without HIV on PrEP.[19] However, for MSM without HIV not on PrEP, there are no recommendations beyond the standard one-time test although HCV guidelines do note that MSM may be tested more frequently for HCV infection if high-risk sexual or drug use practices are occurring.[19] This is in contrast to European guidelines that recommend HCV testing every 3-6 months in MSM engaging in high risk activities regardless of HIV status.[30] While data have suggested that MSM without HIV being screened for PrEP are at higher risk of HCV infection than MSM without HIV in the community not on PrEP, it may also be true that there are populations of HCV-uninfected MSM that are being missed in standard HCV screening or who may be apprehensive about sharing their sexual or drug use practices with healthcare professionals.[28, 29] In an era where HCV treatment is oral, safe, and has the ability to cure, screening to identify unknown HCV infection may be an important part of an elimination strategy in HCV-uninfected MSM as it is possible that HCV transmission risk could increase as PrEP implementation expands and condom use declines among MSM.

Our study also revealed that HCV antibody positivity was higher in those receiving substance use (drug or alcohol) counseling or treatment (36%) than those that had not (15%)(P=<0.01). This is consistent with other studies, which have revealed that injection drug use, nasal drug use, and alcohol use disorder are risk factors for HCV acquisition.[31, 32] These data suggest the need to co-locate HCV screening and treatment, alcohol, and other drug treatment in order to make care easily accessible.[33, 34] MSM-IDU cohorts have higher rates of HCV infection than MSM cohorts that fully exclude IDU.[35, 36] Notably, in some states, drug and alcohol use may also pose barriers to accessing HCV treatment although studies have shown that individuals with substance use disorders

can complete HCV treatment with adherence support.[37] However, if substance use counseling or treatment is used as a proxy for injection drug use, the most common route of HCV transmission, HCV antibody prevalence is still notably higher than other MSM cohorts.[35, 38] Finally, no statistically significant differences were seen by HCV antibody status in lifetime male sexual partners and number of receptive anal sex partners without a condom, which is surprising due to proposed sexual transmission of HCV in MSM. However, the failure to see an association between receptive anal sex without a condom and HCV antibody positivity may be due to the sexual activity matrix being limited to six months and the MSM screened may have had different sexual activity patterns throughout their lifetimes. The multivariable model revealed that having less than a high school education, being older, reporting substance use counseling or treatment, and/or unstable housing were associated with HCV antibody positivity. These factors are consistent with other research data.[39-42] This may suggest that HCV education should be focused on individuals with lower education levels and that outreach to venues focused on substance use and homeless services are important as we try to reach HCV elimination goals. Black MSM in this cohort were less likely to have a positive HCV antibody than those of non-black race which is different from what has been documented in many previous studies; however, recent data have also revealed rising rates of HCV infection in young, white injection drug users which may play a role in these network characteristics.[43, 44] Moreover, this study focused on MSM who were not fully engaged in care, so may represent a subgroup of MSM at particularly high risk for HCV, independent of race.

This study revealed that approximately 1 in 5 MSM screened for HPTN 078 have been infected with HCV; however, the study has limitations. First, HPTN 078 was a study focused on HIV viral suppression, so questionnaires in the screening period were not designed to specifically evaluate HCV infection risk. Unfortunately, we do not know the full overlap of sexual risk and injection drug use as it relates to HCV risk and we had to use substance use counseling or treatment as a proxy. Second, HCV antibody testing was conducted at all sites, but HCV RNA testing was not standard across all sites. Although HCV RNA testing was done when samples were available, the data

were not informative for this analysis since information was not collected that would allow differentiation between spontaneous and therapeutic clearance of HCV. Yet, for this study, HCV antibody status was paramount since we wanted to document current and past HCV infection in order to assess the overall risk of HCV acquisition in MSM with and without HIV.

In this study of a high HIV burden MSM network recruited through DC-RDS and direct recruitment, we found high HCV antibody positivity irrespective of HIV status. DC-RDS has been documented as a method to recruit marginalized populations such as MSM cohorts in the US but was supplemented in this study with direct recruitment to reach study target goals. The MSM with and without HIV included in this sample are very representative of high burden HIV networks throughout the US but particularly among Black MSM who have been disproportionately impacted by HIV and HCV infection. This work is in line with a growing body of evidence that HCV is circulating in MSM networks broadly due to the overlapping nature of the networks of MSM with and without HIV. This is especially concerning as HCV transmission could increase as therapeutic optimism grows (i.e. the perception that HIV is highly manageable), PrEP expands and condom use declines. The further introduction of HCV into networks could increase rates of HCV in a wider array of MSM subgroups and supports aggressive HCV screening and counseling among MSM regardless of HIV infection status. Further research is needed to more fully explore sexual risk in MSM without HIV.

NOTES

Acknowledgements: The authors would like to thank the participants and study staff of the HIV Prevention Trials Network (HPTN) 078 study.

Funding: The HIV Prevention Trials Network is funded by the National Institute of Allergy and Infectious Diseases (UM1AI068619, UM1AI068613, UM1AI1068617), with co-funding from the National Institute of Mental Health, and the National Institute on Drug Abuse, all components of the U.S. National Institutes of Health. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. The primary author also received support from the National Institute on Drug Abuse [R37DA013806] and the National Institute of Allergy and Infectious Diseases (Johns Hopkins University Center for AIDS Research [P30AI094189]). JM was supported by the National Institute of Allergy and Infectious Diseases (Johns Hopkins Center for Health and Human Rights [2T32AI102623-06]).

Conflicts of Interest: JM, ZW, EW, JF, KHM, VC, RHR, and CB have no conflicts to report. RI reports grants from the NIH during the conduct of the study; grants from the CDC, outside the submitted work. TG and DSB report grants from FHI 360 (NIH cooperative agreement UM1AI068619), during the conduct of the study. JPH reports grants from NIH, during the conduct of the study; grants from NIH, outside the submitted work. CDR reports grants from NIH/NIAID (Emory-CDC HIV Clinical Trials Unit and Emory Center for AIDS Research), and grants from NIH/NCATS (Emory CTSA (UL1TR002378)), during the conduct of the study.CLT reports grants from NIH, during the conduct of the study; grants from NIH, outside the submitted work.

References

1. Chhatwal J, Chen Q, Bethea ED, Hur C, Spaulding AC, Kanwal F. The impact of direct-acting anti-virals on the hepatitis C care cascade: identifying progress and gaps towards hepatitis C elimination in the United States. Alimentary pharmacology & therapeutics **2019**; 50(1): 66-74.
2. Thomas DL, Astemborski J, Rai RM, et al. The natural history of hepatitis C virus infection: host, viral, and environmental factors. Jama **2000**; 284(4): 450-6.
3. Ly KN, Hughes EM, Jiles RB, Holmberg SD. Rising Mortality Associated With Hepatitis C Virus in the United States, 2003-2013. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America **2016**; 62(10): 1287-8.
4. The Centers for Disease Control and Prevention. HIV and Viral Hepatitis. Available at: http://www.cdc.gov/hiv/pdf/library_factsheets_hiv_and_viral_hepatitis.pdf. Accessed August 11, 2016.
5. Sulkowski MS, Mehta SH, Torbenson MS, et al. Rapid fibrosis progression among HIV/hepatitis C virus-co-infected adults. AIDS (London, England) **2007**; 21(16): 2209-16.
6. Thomas DL. Global Elimination of Chronic Hepatitis. The New England journal of medicine **2019**; 380(21): 2041-50.
7. Lazarus JV, Wiktor S, Colombo M, Thursz M. Micro-elimination - A path to global elimination of hepatitis C. Journal of hepatology **2017**; 67(4): 665-6.
8. The Centers for Disease Control and Prevention. Hepatitis C Virus Overview and Statistics. Available at: http://www.cdc.gov/hepatitis/hcv/hcvfaq.htm#section1 Accessed June 6, 2016.
9. Jin F, Matthews GV, Grulich AE. Sexual transmission of hepatitis C virus among gay and bisexual men: a systematic review. Sexual health **2017**; 14(1): 28-41.
10. Witt MD, Seaberg EC, Darilay A, et al. Incident hepatitis C virus infection in men who have sex with men: a prospective cohort analysis, 1984-2011. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America **2013**; 57(1): 77-84.
11. Daskalopoulou M, Rodger AJ, Phillips AN, et al. Condomless sex in HIV-diagnosed men who have sex with men in the UK: prevalence, correlates, and implications for HIV transmission. Sexually transmitted infections **2017**; 93(8): 590-8.
12. Sexual transmission of hepatitis C virus among HIV-infected men who have sex with men--New York City, 2005-2010. MMWR Morbidity and mortality weekly report **2011**; 60(28): 945-50.
13. Wandeler G, Gsponer T, Bregenzer A, et al. Hepatitis C virus infections in the Swiss HIV Cohort Study: a rapidly evolving epidemic. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America **2012**; 55(10): 1408-16.
14. Pufall EL, Kall M, Shahmanesh M, et al. Sexualized drug use ('chemsex') and high-risk sexual behaviours in HIV-positive men who have sex with men. HIV medicine **2018**; 19(4): 261-70.
15. van de Laar TJ, van der Bij AK, Prins M, et al. Increase in HCV incidence among men who have sex with men in Amsterdam most likely caused by sexual transmission. The Journal of infectious diseases **2007**; 196(2): 230-8.
16. Turner SS, Gianella S, Yip MJ, et al. Shedding of Hepatitis C Virus in Semen of Human Immunodeficiency Virus-Infected Men. Open forum infectious diseases **2016**; 3(2): ofw057.
17. Mao L, Kippax SC, Holt M, Prestage GP, Zablotska IB, de Wit JB. Rates of condom and non-condom-based anal intercourse practices among homosexually active men in Australia: deliberate HIV risk reduction? Sexually transmitted infections **2011**; 87(6): 489-93.
18. Hoornenborg E, Coyer L, Boyd A, et al. High incidence of HCV in HIV-negative men who have sex with men using pre-exposure prophylaxis. Journal of hepatology **2020**; 72(5): 855-64.
19. American Association for the Study of Liver Diseases, The Infectious Diseases Society of America. HCV Guidance: Recommendations for Testing, Managing, and Treating Hepatitis C. Available at: http://hcvguidelines.org/. Accessed August 26, 2016.

20. Fogel JM, Sivay MV, Cummings V, et al. HIV drug resistance in a cohort of HIV-infected MSM in the United States. AIDS (London, England) **2020**; 34(1): 91-101.
21. Koblin BA, Mayer KH, Eshleman SH, et al. Correlates of HIV acquisition in a cohort of Black men who have sex with men in the United States: HIV prevention trials network (HPTN) 061. PloS one **2013**; 8(7): e70413.
22. Irvin R, Vallabhaneni S, Scott H, et al. Examining levels of risk behaviors among black men who have sex with Men (MSM) and the association with HIV acquisition. PloS one **2015**; 10(2): e0118281.
23. Rao A, Stahlman S, Hargreaves J, et al. Sampling Key Populations for HIV Surveillance: Results From Eight Cross-Sectional Studies Using Respondent-Driven Sampling and Venue-Based Snowball Sampling. JMIR public health and surveillance **2017**; 3(4): e72.
24. Franks J, Mannheimer SB, Hirsch-Moverman Y, et al. Multiple strategies to identify HIV-positive black men who have sex with men and transgender women in New York City: a cross-sectional analysis of recruitment results. Journal of the International AIDS Society **2018**; 21(3): e25091.
25. Wei C, McFarland W, Colfax GN, Fuqua V, Raymond HF. Reaching black men who have sex with men: a comparison between respondent-driven sampling and time-location sampling. Sex Transm Infect **2012**; 88(8): 622-6.
26. Baral SD, Ketende S, Schwartz S, et al. Evaluating respondent-driven sampling as an implementation tool for universal coverage of antiretroviral studies among men who have sex with men living with HIV. Journal of acquired immune deficiency syndromes (1999) **2015**; 68(0 2): S107.
27. Chapin-Bardales J, Rosenberg ES, Sullivan PS, Jenness SM, Paz-Bailey G. Trends in Number and Composition of Sex Partners Among Men Who Have Sex With Men in the United States, National HIV Behavioral Surveillance, 2008-2014. Journal of acquired immune deficiency syndromes (1999) **2019**; 81(3): 257-65.
28. Hoornenborg E, Achterbergh RCA, Schim van der Loeff MF, et al. MSM starting preexposure prophylaxis are at risk of hepatitis C virus infection. AIDS (London, England) **2017**; 31(11): 1603-10.
29. Charre C, Cotte L, Kramer R, et al. Hepatitis C virus spread from HIV-positive to HIV-negative men who have sex with men. PloS one **2018**; 13(1): e0190340.
30. Recently acquired and early chronic hepatitis C in MSM: Recommendations from the European treatment network for HIV, hepatitis and global infectious diseases consensus panel. AIDS (London, England) **2020**; 34(12): 1699-711.
31. McMahon JM, Simm M, Milano D, Clatts M. Detection of hepatitis C virus in the nasal secretions of an intranasal drug-user. Annals of clinical microbiology and antimicrobials **2004**; 3: 6.
32. Schmidt CS, Schön D, Schulte B, Lüth S, Polywka S, Reimer J. Viral hepatitis in alcohol-dependent inpatients: prevalence, risk factors, and treatment uptake. Journal of addiction medicine **2013**; 7(6): 417-21.
33. Day E, Broder T, Bruneau J, et al. Priorities and recommended actions for how researchers, practitioners, policy makers, and the affected community can work together to improve access to hepatitis C care for people who use drugs. The International journal on drug policy **2019**; 66: 87-93.
34. Csete J, Kamarulzaman A, Kazatchkine M, et al. Public health and international drug policy. Lancet (London, England) **2016**; 387(10026): 1427-80.
35. Tieu HV, Laeyendecker O, Nandi V, et al. Prevalence and mapping of hepatitis C infections among men who have sex with men in New York City. PloS one **2018**; 13(7): e0200269.
36. Beyrer C, Sripaipan T, Tovanabutra S, et al. High HIV, hepatitis C and sexual risks among drug-using men who have sex with men in northern Thailand. AIDS (London, England) **2005**; 19(14): 1535-40.

37. Irvin R, Chander G, Ward KM, et al. Unreported Alcohol Use Was Common But Did Not Impact Hepatitis C Cure in HIV-Infected Persons Who Use Drugs. Journal of viral hepatitis **2019**.
38. Seaberg EC, Witt MD, Jacobson LP, et al. Differences in hepatitis C virus prevalence and clearance by mode of acquisition among men who have sex with men. Journal of viral hepatitis **2014**; 21(10): 696-705.
39. Irvin R, Chander G, Falade-Nwulia O, et al. Overlapping epidemics of alcohol and illicit drug use among HCV-infected persons who inject drugs. Addictive behaviors **2019**.
40. Noska AJ, Belperio PS, Loomis TP, O'Toole TP, Backus LI. Prevalence of Human Immunodeficiency Virus, Hepatitis C Virus, and Hepatitis B Virus Among Homeless and Nonhomeless United States Veterans. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America **2017**; 65(2): 252-8.
41. Mehta SH, McFall AM, Srikrishnan AK, et al. Morbidity and Mortality Among Community-Based People Who Inject Drugs With a High Hepatitis C and Human Immunodeficiency Virus Burden in Chennai, India. Open forum infectious diseases **2016**; 3(3): ofw121.
42. Akiyama MJ, Kaba F, Rosner Z, et al. Correlates of Hepatitis C Virus Infection in the Targeted Testing Program of the New York City Jail System. Public health reports (Washington, DC : 1974) **2017**; 132(1): 41-7.
43. Thomas DL, Vlahov D, Solomon L, et al. Correlates of hepatitis C virus infections among injection drug users. Medicine **1995**; 74(4): 212-20.
44. Suryaprasad AG, White JZ, Xu F, et al. Emerging epidemic of hepatitis C virus infections among young nonurban persons who inject drugs in the United States, 2006-2012. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America **2014**; 59(10): 1411-9.

TABLE 1. DEMOGRAPHIC, BEHAVIORAL, AND CLINICAL CHARACTERISTICS BY HCV ANTIBODY STATUS AMONG MEN WHO HAVE SEX WITH MEN AT SCREENING VISIT (HPTN 078)

Characteristic	Total N=1287* (%)	HCV Ab Positive N=246 (%)	HCV Ab Negative N=1041 (%)	p-value
Age, median years (IQR)	41 (30, 52)	51 (42, 56)	38 (29,50)	<0.01
Race (Black)	893 (69)	159 (65)	734 (71)	0.07
Education (<High School Diploma)	190 (15)	56 (23)	134 (13)	<0.01
DC-RDS	711 (55)	147 (60)	564 (54)	0.11
Employed	453 (35)	55 (22)	398 (38)	<0.01
Insured (Public, Private)	1083 (84)	222 (90)	861 (83)	<0.01
Income (<$5,000)	344 (27)	64 (26)	280 (27)	0.79
Lifetime Male Sexual Partners (IQR)	17 (6,50)	20 (7, 50)	16 (6, 50)	0.54
Number of Receptive Anal Sex Partners (No Condom) in 6 Months (IQR)	1 (0,2)	1 (0,2)	1 (0,2)	0.81
MSM with HIV	900 (70)	182 (74)	718 (69)	0.12
Syphilis (Active)	276 (22)	50 (20)	226 (22)	0.65
Substance Use Counseling/Treatment	262 (21)	95 (40)	167 (17)	<0.01
Unstable Housing	147 (11)	51 (21)	96 (9)	<0.01

*18 individuals missing HCV antibody data from total HPTN 078 screening cohort of 1305
HCV: Hepatitis C virus
Ab: Antibody
DC-RDS: Deep-chain respondent driven sampling
IQR: Interquartile range
HIV: Human immunodeficiency virus

TABLE 2. MULTIVARIABLE ANALYSIS OF FACTORS ASSOCIATED WITH HCV ANTIBODY POSITIVITY AMONG MEN WHO HAVE SEX WITH MEN AT SCREENING VISIT (HPTN 078)

Characteristic	Odds Ratio	Odds Ratio 95% Confidence Interval	Adjusted Odds Ratio	Adjusted Odds Ratio 95% Confidence Interval
Age, median years (IQR)	1.06	(1.05, 1.08)	1.07	(1.05, 1.08)
Black race (ref: Non-black)	0.76	(0.57, 1.03)	0.71	(0.51, 0.98)
Education (ref: high school or more)	1.99	(1.41, 2.83)	1.67	(1.13, 2.48)
Employed (ref: unemployed)	0.47	(0.35, 0.64)	1.02	(0.70, 1.48)
Insured (Public, Private) (ref: not insured)	1.93	(1.23, 3.04)	1.35	(0.80, 2.26)
Substance Use Counseling/Treatment (ref: no treatment)	3.35	(2.46, 4.55)	2.51	(1.80, 3.51)
Unstable Housing (ref: stable home)	2.57	(1.77, 3.74)	2.16	(1.40, 3.33)

HCV: Hepatitis C virus
Ab: Antibody
DC-RDS: Deep-chain respondent driven sampling
IQR: Interquartile range