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Drug use stigma and its association with active hepatitis C virus infection and injection drug use behaviors among community-based people who inject drugs in India

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Abstract

Background: Although drug use stigma is globally pervasive, quantitative evidence of its role in hepatitis C virus (HCV) transmission is limited. We evaluated the psychometric properties of a drug use stigma scale and examined the association between drug use stigma and active HCV infection among a community-based sample of people who inject drugs (PWID) in India.

Methods: Between 8/2016 and 5/2017, a cross-sectional sample of PWID was recruited from 12 Indian cities (~1000/city) using respondent-driven sampling. Participants were ≥18 years old and reported injection drug use (IDU) in the past 2 years. Multivariable logistic regression with

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Competing interests

The authors declare no potential conflicts of interest.

Declaration of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Ethical approval

This study was approved by the institutional review boards at the Johns Hopkins University School of Medicine and the Y.R. Gaitonde Centre for AIDS Research and Education in 2012.

a random-intercept for each city was used to estimate adjusted odds ratios (aOR) of active HCV infection (RNA>30 IU/mL). Analyses incorporated RDS-II weights.

Results: Of 11,663 participants, 73.1% reported IDU in the past 6 months and 33.8% had active HCV infection. Exploratory factor analysis yielded a four-factor solution of enacted, vicarious, felt normative and internalized drug use stigma with high internal consistency (Cronbach's α: 0.85–0.92). In analyses adjusted for age, gender, northeast region, education, homelessness, incarceration, alcohol dependence, HIV status, frequency of IDU, and ever sharing needles/syringes, PWID reporting any enacted stigma had greater odds of active HCV infection (aOR=1.27 [95%CI=1.13–1.43]) as did PWID with internalized stigma scores in the highest quartile (vs. lowest quartile; aOR=1.69 [95%CI=1.11–2.56]). Among PWID who reported IDU in the past 6 months, multiple forms of stigma were associated with higher frequency of IDU, sharing needles/syringes, having multiple injection partners, and IDU in public spaces.

Conclusion: Using a multidimensional drug use stigma scale, various forms of stigma were significantly associated with active HCV infection and injection drug use-related risk behaviors. Collectively, these data suggest that drug use stigma may play a role in HCV transmission and impede efforts to achieve HCV elimination. Strategies to diminish drug use stigma are warranted.

Keywords

Stigma; discrimination; persons who inject drugs; addiction; substance use; hepatitis

Introduction

Globally, in 2015, there were an estimated 71 million people living with chronic hepatitis C virus (HCV) infection, including 6.1 million people who injected drugs in the past year (Grebely et al., 2019; Polaris Observatory HCV Collaborators, 2017). People who inject drugs (PWID) remain at increased risk of HCV infection and lag behind other populations for all indicators of the HCV care continuum in most settings (World Health Organization, 2017). Achieving the World Health Organization's (WHO) ambitious global target to eliminate HCV by 2030 (i.e., a reduction of 90% in HCV incidence and 65% in mortality) will require increased efforts to scale-up access and uptake of direct prevention strategies, including behavioral risk-reduction counseling and harm reduction services (i.e., needle/syringe exchange programs and medication for opioid use disorder), as well as indirect prevention strategies, including HCV testing and treatment, among PWID (World Health Organization, 2016a). Many individual and structural barriers to HCV elimination among PWID, including stigma, have been well described (Day et al., 2019; World Health Organization, 2016b); however, there are limited empirical data quantifying the direct impacts of stigma in the context of HCV elimination. More broadly, stigma is considered a fundamental cause of population health inequalities (Hatzenbuehler, Phelan, & Link, 2013).

Stigma is a multi-dimensional social construct and its definition is continually evolving. In his seminal work, Goffman (1963) defined stigma as "an attribute that is deeply discrediting" such that it reduces an individual "from a whole and usual person to a tainted, discounted one" (p.3). Link & Phelan (2001) conceptualized stigma as a social process that consists of co-occurring components, including labeling, stereotyping, separation, status loss

and discrimination, in the context of a social, economic, and political power imbalance that permits these stigmatization processes to transpire. In addition to macro-level manifestations of stigma such as structural stigma, contemporary stigma frameworks have outlined distinct types of individual-level stigma manifestations or processes (i.e., mechanisms), including *enacted* (or experienced) stigma, *vicarious* stigma, *felt normative* (or perceived community) stigma, and *internalized* (or self) stigma (Earnshaw & Chaudoir, 2009; Nyblade, Mingkwan, & Stockton, 2021; Stangl et al., 2019; Steward et al., 2008). These individual-level manifestations of stigma can be further classified as being interpersonal processes (e.g., enacted and vicarious stigma) or intrapersonal processes (e.g., felt normative and internalized stigma) (Steward et al., 2008). Enacted stigma reflects explicit actions of discrimination directed at an individual because of their stigmatized status, vicarious stigma reflects hearing stories about persons being mistreated because of their stigmatized status, felt normative stigma reflects the perceived prevalence of stigmatizing attitudes about persons with their stigmatized status in the community, and internalized stigma reflects the degree to which a person accepts their stigmatized status as being valid or deserved. While all of these manifestations of stigma can be interdependent, they are distinct mechanisms that can have unique health-related impacts (Earnshaw, Smith, Chaudoir, Amico, & Copenhaver, 2013). Moreover, intersectionality theory suggests that an individual can experience intersecting stigmas through multiple interconnected statuses (e.g., race, drug use, mental health illnesses, HIV, and HCV) that contribute to the overall stigmatization process (Turan et al., 2019).

Drug use stigma in particular is globally pervasive, but it remains understudied using quantitative approaches compared to other stigmas (e.g., HIV). In most settings, there is a substantial degree of structural drug use stigma that manifests through the criminalization of drug use and related punitive policies, which are often harsher for intravenous drugs (Csete et al., 2016; DeBeck et al., 2017). There is also evidence of widespread public drug use stigma, including general populations having negative (stereotyped and prejudiced) attitudes about injection drug use (Broady, Brener, Cama, Hopwood, & Treloar, 2020; Ezell et al., 2021; Ha, Liu, Li, Nield, & Lu, 2012). Experiences of drug use stigma can vary by the type of drug used and the route of administration; injection drug use has typically been associated with greater drug use stigma, which may partly be because it is associated with the use of “hard drugs”, is less concealable (i.e., visibility of stigmata or track marks), and is linked to HIV and HCV transmission (Brown, 2015; Crawford, Rudolph, Jones, & Fuller, 2012; Etesam, Assarian, Hosseini, & Ghoreishi, 2014; Ezell et al., 2021; Luoma et al., 2007). Drug use stigma can also persist despite cessation of injection drug use. There are limited validated multidimensional scales that measure distinct types of individual-level manifestations of drug use stigma among PWID, thus hindering our ability to effectively study the impacts of drug use stigma in this key population.

Drug use stigma has been associated with increased frequency of drug use and severity of drug dependence, including among PWID (Cama, Brener, Wilson, & von Hippel, 2016; Latkin et al., 2010; von Hippel, Brener, & Horwitz, 2018). Based on other stigmas and substance use research and theory, it is plausible that drug use stigma leads to increased drug use through psychological responses to stigma (e.g., increased anxiety and depressive symptoms), social isolation (e.g., social rejection from friends and family), and lower

availability of, access to and uptake of health-related resources (e.g., medication for opioid use disorder) (Earnshaw, 2020; Hatzenbuehler et al., 2013). In a few relatively small studies of PWID, greater perceived drug use stigma and discrimination have also been associated with increased likelihood of sharing needles/syringes and other injection-related equipment as well as a greater number of actively injecting partners (Crawford et al., 2013; Latkin et al., 2010; Wilson, Brener, Mao, & Treloar, 2014). Additionally, greater enacted drug use stigma has been linked to increased odds of non-fatal overdose (Latkin et al., 2019). In a recent study of 279 young suburban PWID in Chicago, IL, greater drug use stigma was associated with increased odds of having ever been infected with HCV (i.e., HCV antibody positive); notably, the study did not examine the individual effects of different types of drug use stigma mechanisms (Williams, Mackesy-Amiti, Latkin, & Boodram, 2021). Importantly, drug use stigma may facilitate HCV transmission by driving riskier injection drug use behaviors. Studies examining the impact of different types of drug use stigma mechanisms on high-risk injection drug use behaviors and HCV infection within the same population remain limited.

The negative effects of drug use stigma may be more pronounced in low- and middle-income countries (LMIC), especially in South Asia where cultural norms are particularly more conservative (Bose & Jalal, 2017; Lasco, 2020; Yang et al., 2007). India has a remarkable history of drug use given its proximity to the Golden Triangle (Thailand, Laos, and Myanmar) on the east and the Golden Crescent (Afghanistan, Iran and Pakistan) on the west (Dorabjee & Samson, 2000; Mehta et al., 2014). Accordingly, in 2018, approximately 23 million people used opioids in the past year and approximately 7.7 million had an opioid use disorder in India (Ambekar et al., 2019). Use of narcotic and psychotropic substances is heavily criminalized in India with extremely harsh punishments (Tandon & Collective, 2015). One single-site survey and a few qualitative studies suggest PWID in India experience intense levels of drug use stigma (Chakrapani, Velayudham, Shunmugam, Newman, & Dubrow, 2014; Kumar, Gupte, Isaakidis, Mishra, & Munjattu, 2018; Latkin et al., 2010; Solomon, Mehta, Latimore, Srikrishnan, & Celentano, 2010). In a cross-sectional survey of PWID conducted in 2016–2017, we previously reported prevalence of active HCV infection ranged from 4.1% to 66.4% across 12 cities in northern, northeastern, and central India (Solomon et al., 2020). There remains limited coverage of HCV testing among PWID in India, as well as poor access to HCV treatment, despite increasing availability of generic direct acting antiviral therapies (Patel et al., 2018; Solomon et al., 2015, 2020). Like many countries, India has a national action plan to eliminate viral hepatitis, but to date, fewer than 5% of all PWID have been treated for HCV (Solomon et al., 2020).

The primary aim of this study was to examine the association between individual-level manifestations of drug use stigma and active HCV infection (HCV RNA+) among community-based PWID in India. While active HCV infection represents the primary indicator for monitoring HCV elimination as a composite biomarker of primary infection, reinfection and treatment-associated cure, we also examined associations between drug use stigma and high-risk injection drug use behaviors that can facilitate HCV transmission. Additionally, we describe the psychometric properties of a brief multidimensional drug use stigma scale used in this study.

Methods

Study design and participants

Data were obtained from the National Collaboration on AIDS (NCA) study, which was a cluster-randomized trial designed to assess the effectiveness of integrated HIV prevention and treatment service delivery on HIV testing among men who have sex with men (MSM) and PWID strata across 21 cities (22 sites) in India (Solomon et al., 2019). The integrated care intervention also provided HCV testing in the PWID stratum and was associated with a significant increase in population-level awareness of HCV infection among HCV antibody positive PWID and population-level (self-reported) initiation of HCV treatment among HCV RNA-positive PWID (Solomon et al., 2020). However, even in the intervention sites, awareness of HCV infection status among HCV antibody positive PWID was <20% and treatment uptake was <5%. The present study was restricted to data obtained from the cross-sectional evaluation survey conducted among PWID in 12 Indian cities between August 2016 and May 2017. There were five cities in the northeast with historical epidemics of injection drug use (Dimapur, Imphal, Churchandpur, Aizawl, and Lunglei), five cities in north and central India with emerging epidemics of injection drug use (Amritsar, Bilaspur, Chandigarh, Kanpur and Ludhiana), and 2 megacities (Mumbai and New Delhi) (Supplemental Figure 1).

The study protocol is publicly available and study procedures have been previously described (Solomon et al., 2016; Solomon et al., 2019; Solomon et al., 2020). In brief, PWID were recruited using respondent-driven sampling (RDS)—a peer chain-referral strategy that is typically used for “hidden” populations that do not have a sampling frame (Heckathorn, 1997; Volz & Heckathorn, 2008). Two individuals (“seeds”) considered to be highly influential PWID in the local city were given two bar-coded hologram-labeled referral coupons to recruit other PWID in their peer network. Each eligible recruit that enrolled was given two coupons to recruit other PWID. Recruitment was continued until an enrollment target of approximately 1000 PWID was reached within each city. Eligible participants self-reported injection drug use in the previous two years; were aged ≥18 years; spoke Hindi, English, or the local language; provided informed oral consent; and possessed a valid RDS referral coupon. Across the 12 sites, the median number of RDS recruitment waves was 16 (range: 9 to 27 waves) and the median time to complete recruitment was 149 days (range: 95 to 269 days). Of note, one site (Mumbai) did not meet the enrollment target and was stopped early due to slow recruitment.

After providing verbal consent, participants provided a fingerprint image that was converted to a unique hexadecimal code to allow biometric tracking and prevent duplicate enrollment; fingerprint images were not stored. Participants were reimbursed with 250 Indian rupees (INR) for completing the study visit and 50 INR per eligible participant they recruited (maximum of two other participants). Trained interviewers administered face-to-face structured surveys using an electronic tablet. The survey collected data on demographics, risk behaviors including substance use, access to HIV and HCV testing and services, and other modules including on drug use stigma. All surveys were translated into the local language for each site. To minimize response bias due to social desirability, interviewers

were unaffiliated with any local health care centers or organizations that serve PWID. All participants received on-site rapid HIV testing and counseling per Indian guidelines, and HIV-positive participants were referred to government-sponsored antiretroviral therapy centers. A blood sample was also collected from each participant. Blood samples were shipped to a laboratory in Chennai, India for further processing, storage at −80°C, and additional laboratory testing.

Laboratory methods

Stored serum samples were assessed for the detection of anti-HCV antibody (i.e., prior exposure to HCV) using the Murex anti-HCV ELISA version 4.0 (Murex Biotech, South Africa). Specimens that were positive for anti-HCV antibody were subsequently assessed for HCV RNA using the quantitative RealTime HCV assay (Abbott Molecular, Des Plaines, IL, USA), which had a lower limit of quantification of 30 IU/mL.

Drug use stigma measures

We aimed to design a multidimensional scale that would be an appropriate measure of individual-level manifestations of drug use stigma in India while remaining cross-culturally relevant for potential use in similar settings. The survey included 22 items on drug use stigma that were adapted from a scale that was previously developed and validated to measure HIV-related stigma in India, including four types of stigma mechanisms (i.e., enacted, vicarious, felt normative, and internalized) (Steward, Bharat, Ramakrishna, Heylen, & Ekstrand, 2013; Steward et al., 2008). The English version of the survey questions are provided in Supplemental Material. Items for this study were selected to reflect the four types of stigma mechanisms, diverse sources of stigma (e.g., healthcare workers, family members, and community members), and mild to severe forms of stigma (e.g., being asked to stay away from children vs. receiving physical threats of harm). Some of the selected items were also chosen because they reflected forms of stigma reported by PWID in prior work (Latkin et al., 2010). To further ensure content validity, the final selected items were reviewed and approved by a multidisciplinary research team of social scientists, epidemiologists and clinicians—all of whom have extensive experience conducting interdisciplinary research among PWID in India and other settings.

The survey collected data on 6 enacted stigma items that reflected explicit actions of discrimination directed at an individual because of their drug use (e.g., “How often has a hospital worker mistreated you because of your drug use?”) and 6 vicarious stigma items that reflected hearing stories about persons being mistreated because of their drug use (e.g., “How often have you heard stories about someone being forced by family members to leave their home because they used drugs?”). Responses for both enacted and vicarious stigma items ranged from 0 (never) to 3 (frequently). The survey also included 5 felt normative items that reflected the perceived prevalence of stigmatizing attitudes in the community towards people who use drugs (e.g., “In your community, how many people avoid visiting homes of people who use drugs?”); responses ranged from 0 (no one) to 3 (most people). There were also 5 internalized stigma items that reflected the degree to which a person accepts drug use stigma to be valid or deserved (e.g., “How much do you feel disgusting

because of your drug use?"); responses ranged from 0 (not at all) to 3 (a great deal). The felt normative and internalized stigma items paralleled each other.

Outcome measures

The primary outcome was the prevalence of active HCV infection (HCV RNA>30 IU/mL) in the overall population; given the cross-sectional study design, we could not establish chronicity. Secondary outcomes included injection drug use risk behaviors in the past 6 months among participants who reported any injection drug use in the past 6 months (i.e., active PWID). Risk behaviors of interest included daily injection drug use (no vs. yes), sharing needles/syringes (no vs. yes), having multiple injection partners (no vs. yes), and injection drug use in public spaces (no vs. yes). Public spaces included public parks, public toilets, shooting galleries, and/or graveyards.

Statistical analysis

Seed participants were excluded from all analyses. The analytic sample additionally excluded participants missing data on active HCV infection status (n=53) for a total sample size of 11,663.

The measurement model for drug use stigma was first examined using exploratory factor analysis (EFA) among participants with complete data on all 22 stigma items. A polychoric correlation matrix was used in the EFA given categorical item responses. The decision on the number of factors extracted was based on results from a principal components analysis including the percentage of variance explained and the number of eigenvalues >1.0 (Kaiser-Guttman Criterion), visualization of Cattell's screeplot, Horn's parallel analysis with 1,000 bootstrap iterations, and comprehensibility. Iterated principal factor estimation was used and an oblique (promax) factor rotation was performed with Kaiser normalization to facilitate interpretation of factor loadings. Promax rotation was selected based on an a priori expectation of interdependent factors. Items were retained based on high factor loadings (>0.4) and high communality estimates (>0.4). Based on a final measurement model, four subscales were developed, including enacted, vicarious, felt normative, and internalized stigma. Cronbach's alpha coefficient (α) was used to assess the internal consistency of each subscale in the overall study sample and within each site using an available-case approach. Final subscale stigma scores were standardized to range from 0–3 (i.e., for each subscale, we summed the responses of each item and divided by the total number of items). Higher subscale scores reflect a greater degree of stigma experienced.

For the remainder of the analysis, the RDS-II estimator was used to account for non-random sampling (Volz & Heckathorn, 2008). RDS-II weights were calculated using the peer network size (i.e., the number of PWID seen in the previous 30 days). To calculate population-level estimates with data from all cities combined, we used a composite weight which accounts for the RDS-II weight and the relative population size of PWID in each city that was derived from state-level data (National Institute of Medical Statistics and National AIDS Control Organization (NACO), 2010). The composite weight was used to examine the population-level frequency and distribution of variables (e.g., summary statistics), including

the drug use stigma subscale scores, in the overall study population and by active HCV infection status.

To assess the association between each drug use stigma mechanism and active HCV infection, we used multi-level logistic regression models with a random intercept for city and scaled RDS-II weights as sampling weights. For each drug use stigma domain, we performed univariable analysis and examined two multivariable models. The first multivariable model included adjustment for age group, gender, northeast region, educational attainment, experiencing homelessness, history of incarceration in the past 6 months, alcohol use/dependence (i.e., AUDIT), and HIV status. The second multivariable model was an extension of the primary model that additionally included adjustment for frequency of injection drug use in the past 6 months (none, less than daily, or daily) and a history of ever sharing needles/syringes (never vs. ever). While many of these covariates can be considered either confounders or mediators of the potential association between drug use stigma and active HCV infection, we included adjustment for these covariates given the lack of temporal ordering in this analysis. Each stigma subscale score was modeled as a categorical variable based on the overall population-level distribution. Enacted and vicarious stigma scores were dichotomized as ever vs. never experienced (i.e., >0 vs. 0). Felt normative and internalized stigma scores were categorized as $<25^{th}$ percentile, $25–75^{th}$ percentile, and $>75^{th}$ percentile. We also modeled each stigma subscale score continuously. Given that the drug use stigma subscales captured different sources of stigma, we also examined the association of each individual stigma item and active HCV infection using similar approaches. For this analysis, enacted and vicarious item responses were dichotomized as never (0) vs. ever (1–3), while felt normative and internalized item responses were dichotomized as low (0–1) vs. high (2–3).

Additionally, we examined associations between each drug use stigma mechanism and injection drug use risk behaviors in the past 6 months among participants who reported any injection drug use in the past 6 months. Each stigma subscale and risk behavior was separately examined using multi-level logistic regression models with a random intercept for city and scaled RDS-II weights. For these analyses, adjusted odds ratios (aOR) and corresponding 95% confidence intervals (CI) were estimated from a multivariable model that included adjustment for age group, gender, northeast region, educational attainment, experiencing homelessness, history of incarceration in the past 6 months, alcohol use/dependence, and HIV status.

All statistical analyses were conducted using Stata/MP, version 15.2 (Statacorp, College Station, TX). An available-case approach was used to handle missing data, with the exception of the complete-case EFA, given that missing data were rare. All reported sample sizes were unweighted. All reported summary statistics (e.g., percentages and medians) and measures of association (e.g., aORs) in the main analysis were weighted, unless stated otherwise.

To test the sensitivity of results to the RDS-II estimator, we repeated analyses without RDS-II weights (Avery et al., 2019; White et al., 2015); the corresponding unweighted estimates are provided in Supplemental Material. We also conducted a sensitivity analysis

to examine the association of drug use stigma with HCV antibody serostatus in the overall study population.

Ethical oversight

This study was approved by institutional review boards at the Johns Hopkins University School of Medicine and the Y.R. Gaitonde Centre for AIDS Research and Education.

Results

1. Characteristics of the study population

In the overall study population (n=11,663), the median age was 30 (interquartile range [IQR], 24–37) and the majority of participants were male (n=11,165; 94.1%) (Table 1). Most participants reported active injection drug use in the past 6 months (n=9,309; 73.1%). Among those who reported active injection drug use in the past 6 months, 60.5% (n=6,102) reported injecting daily, 38.4% (n=3,869) reported sharing needles/syringes, 62.8% (n=6,560) reported having multiple injection partners, and 74.0% (n=7,021) reported engaging in injection drug use in public spaces in the past 6 months. Overall, there was high prevalence of HIV infection (n = 2,480; 20.3%) and active HCV infection (n=5,046; 33.8%) (Table 1). The distribution of demographic, sociostructural, and behavioral characteristics of the study population are also shown stratified by active HCV infection status in Table 1. Of note, only 11.0% (n=684) of participants with active HCV infection were aware of their HCV infection status.

2. Measurement of drug use stigma

2.1 Exploratory factor analysis—The unweighted distribution of responses for each stigma item are shown in Supplemental Table 1; the percentage of participants that refused to answer each item was low (<1.5% per item). In a complete-case sample (n=11,213), principal components analysis yielded four factors with eigenvalues >1.0 that explained 78.7% of the total variance (Supplemental Figure 2). Cattell's scree plot and Horn's parallel analysis also suggested there were four common factors. Factor 1 had six items with high factor loadings (range: 0.70–0.89), factor 2 had six items with high factor loadings (range: 0.57–0.98), factor 3 had five items with high factor loadings (range: 0.57–0.95), and factor 4 had five items with high factor loadings (range: 0.64–0.91) (Supplemental Table 2). All communality (h^2) estimates were >0.45 and none of the items loaded strongly on multiple factors, providing evidence of good divergent validity. The four-factor solution fit the theoretical conceptualization of the four different stigma constructs. Accordingly, factor 1 reflected enacted stigma, factor 2 reflected vicarious stigma, factor 3 reflected felt normative stigma, and factor 4 reflected internalized stigma.

Correlations between each item and common factor are provided in Supplemental Table 3. Factor 1 (enacted stigma) correlated with factor 2 (vicarious stigma) (0.61), consistent with both constructs being interpersonal processes (Supplemental Table 4). Factor 3 (felt normative stigma) correlated with factor 4 (internalized stigma) (0.59), consistent with both constructs being intrapersonal processes and felt stigmas. To a lesser degree, factor 1 also

correlated with factors 3 (0.29) and 4 (0.34), and factor 2 also correlated with factors 3 (0.33) and 4 (0.33).

2.2 Scale reliability—Overall, the enacted (α=0.85), vicarious (α=0.86), felt normative (α=0.92), and the internalized (α=0.90) stigma subscales all had good to excellent internal consistency (Supplemental Table 5). The internal consistency of each subscale ranged from acceptable to excellent within each of the 12 cities (α≥0.70), with the exception of the enacted stigma subscale in Aizawl (α=0.53) (Supplemental Table 6).

2.3 Population-level distribution of drug use stigma levels—Overall, there were 5,130 (39.3%) participants who reported ever experiencing enacted stigma (i.e., score >0), and the median enacted stigma score was 0.0 (IQR, 0.0–0.5) (Table 2). There were 7,901 (69.1%) participants who reported ever experiencing vicarious stigma (i.e., score >0) and the median vicarious stigma score was 0.5 (IQR=0.0–1.2). The overall median felt normative stigma score was 1.8 (IQR=1.0–2.4) and median internalized stigma score was 1.8 (IQR, 1.0–2.6). There was substantial variability in the distribution of stigma subscale scores by city (Supplemental Table 6).

3. Association of drug use stigma with HCV infection

In univariable analysis, ever experiencing enacted stigma was associated with higher odds of active HCV infection (vs. never; odds ratio=1.35 [95% CI: 1.22, 1.50]) (Table 3). This association between enacted stigma and active HCV infection remained after adjustment for age group, gender, northeast region, educational attainment, experiencing homelessness, history of incarceration in the past 6 months, alcohol use/dependence, and HIV status (aOR=1.36 [95% CI: 1.22, 1.52]) and additional adjustment for frequency of injection drug use in the past 6 months and a history of ever sharing needles/syringes (aOR=1.27 [95% CI: 1.13, 1.43]). Each individual enacted stigma item was associated with higher odds of active HCV infection in fully adjusted multivariable models (Table 4), including having ever been told to stay away from children due to drug use, having ever been denied housing due to drug use, and having ever been threatened with physical harm due to drug use.

There was also a positive association between internalized stigma and active HCV infection in univariable and multivariable analyses (Table 3). In the fully adjusted multivariable model, persons with internalized stigma scores in the 25–75th percentile (aOR=1.42 [95% CI: 1.07, 1.88) and >75th percentile (aOR=1.69 [95% CI: 1.11, 2.56]) had higher odds of active HCV infection as compared to persons with internalized stigma scores in the lowest quartile. Additionally, all internalized stigma items were positively associated with active HCV infection (Table 4).

There were no associations of vicarious and felt normative stigma with active HCV infection in either univariable or multivariable analyses (Table 3).

4. Association of drug use stigma with injection drug use behaviors

Univariable and multivariable associations with injection drug use behaviors in the past 6 months among participants who reported any injection drug use in the past 6 months are

shown in Table 5. After adjustment for age group, gender, northeast region, educational attainment, experiencing homelessness, history of incarceration in the past 6 months, alcohol use/dependence, and HIV status, ever experiencing enacted drug use stigma was associated with 1.30 (95% CI: 0.96, 1.74) greater odds of daily injection drug use, 1.34 (95% CI: 1.16, 1.55) greater odds of sharing needles/syringes, 1.46 (95% CI: 1.15, 1.85) greater odds of having multiple injection partners, and 1.24 (95% CI: 1.01, 1.53) greater odds of injection drug use in public spaces. Ever experiencing vicarious drug use stigma was associated with 1.28 (95% CI: 1.05, 1.56) greater adjusted odds of having multiple injection partners and 1.46 (95% CI: 1.17, 1.81) greater adjusted odds of injection drug use in public spaces. Compared to people with felt normative stigma scores in the lowest quartile, those with felt normative stigma scores in the highest quartile had 1.52 (95% CI: 0.99, 2.33) greater adjusted odds of having multiple injection partners and 2.31 (95% CI: 1.49, 3.59) greater adjusted odds of injection drug use in public spaces. Compared to people with internalized stigma scores in the lowest quartile, those with internalized stigma scores in the highest quartile had 1.92 (95% CI: 1.33, 2.79) greater adjusted odds of injection drug use in public spaces. Additionally, those with internalized stigma scores in the 25^{th}–75^{th} percentile had 1.37 (95% CI: 1.14, 1.64) greater adjusted odds of sharing needles/syringes and 1.31 (95% CI: 1.07, 1.59) greater adjusted odds of having multiple injection partners, as compared to people with internalized stigma scores in the lowest quartile.

5. Sensitivity analyses

Results on the association of drug use stigma with active HCV infection were insensitive to the RDS-II estimator, as similar findings were obtained in unweighted analyses (Supplemental Tables 7–8). Interestingly, in unweighted analyses of PWID who engaged in injection drug use in the past 6 months, all four drug use stigma mechanisms were associated with all four of the injection drug use behaviors that were examined (Supplemental Table 9). In addition, the associations were generally stronger than those reported using the RDS-II estimator. Finally, similar to what was observed with active HCV infection in the primary analysis, both enacted and internalized drug use stigma were associated with HCV seropositivity (Supplemental Table 10).

Discussion

We observed a high burden of enacted, vicarious, felt normative, and internalized drug use stigma in a large, community-based sample of PWID in India with considerable heterogeneity across 12 cities. Across the entire population, experiences of enacted and internalized drug use stigma were strongly associated with a higher prevalence of active HCV infection (HCV RNA+). Moreover, strong associations were observed between multiple mechanisms of drug use stigma and high-risk injection drug use behaviors that can facilitate HCV transmission. Overall, this study provides quantitative evidence that drug use stigma may serve as a critical barrier to achieving HCV elimination. The multidimensional drug use stigma scale developed for this study can be used to further study drug use stigma and accelerate progress toward diminishing it.

There is a dearth of quantitative and theory-driven multidimensional drug use stigma data among PWID in LMIC, which is in part due to a lack of a standardized tool to appropriately measure it. This population-based study provides a critical step in developing a measurement model for drug use stigma among PWID. Specifically, the drug stigma scale used in this study had a factor structure congruent with distinct theory-based constructs (Steward et al., 2008), strong evidence of construct validity given the associations with drug use behaviors and active HCV infection (i.e., bio-validation), and high internal consistency for each subscale across multiple settings. Interestingly, correlations observed between stigma subscales were not as strong as expected. That combined with the observed differential associations of drug use stigma subscales with active HCV infection together provide evidence of divergent validity and the need to separately measure and examine the distinct stigma processes. These strong psychometric properties of the scale suggest it could be useful in quantifying drug use stigma, examining the impacts of drug use stigma, and assessing the effects of public health interventions on drug use stigma. Indeed, this scale requires external validation and can potentially be further refined. The relatively lower reports of enacted drug use stigma, as compared to the other types of stigma examined, suggests the potential need to consider additional sources of drug use-related discrimination for the enacted stigma subscale. Lower reporting of enacted stigma as compared to felt normative stigma is consistent with prior work on HIV-related stigma in India (Steward et al., 2008). There are also other types of individual-level stigma manifestations that should be further explored, such as anticipated drug use stigma (Biancarelli et al., 2019; Burke et al., 2015).

This study demonstrates that enacted and internalized drug use stigma mechanisms are associated with active HCV infection—a biomarker of sustained parenteral risk behavior. This finding is consistent with a smaller recent study that found an association between drug use stigma and HCV seropositivity among young PWID in the U.S. (Williams et al., 2021). Active HCV infection represents a composite measurement of primary HCV infection, HCV reinfection, spontaneous viral clearance and HCV treatment uptake (and associated clearance/cure). While we cannot definitively deduce from these data whether drug use stigma was associated with more HCV transmission or reduced HCV clearance, given the near negligible uptake of treatment at this time and constant rate of spontaneous clearance, it seems more likely that the association is with transmission, either primary or reinfection, through the influence of stigma on the risk environment of PWID. This is further supported by the strong positive associations observed between drug use stigma and high-risk individual-level injection drug use behaviors, including sharing needles/syringes and having multiple injection partners, as has been seen in prior studies (Crawford et al., 2013; Latkin et al., 2010; Wilson, Brener, Mao, & Treloar, 2014). We also uniquely demonstrate a strong relationship between drug use stigma and injection drug use in public spaces, which may promote interactions with unknown injection partners and other high-risk behaviors (Mazhnaya, Tobin, & Owczarzak, 2018; Trayner et al., 2020). Collectively, these data suggest the need to de-stigmatize drug use to achieve HCV elimination.

The widespread and multifaceted nature of drug use stigma, as described in this study, will be challenging to combat and will require intervening at multiple levels. The association between enacted stigma and active HCV infection suggest that it is not just about stigma

in one type of setting (e.g., health care settings) but rather pervasive stigma across multiple venues and facets of life. Specifically, we observed strong associations with experiences of discrimination within the community, including restrictions on interactions with children, access to housing and threats of general physical harm. Many public health interventions, including the trial that these data derive from (Solomon et al., 2019), have focused on establishing PWID enabling environments for health care. While this might be an important first step to intervene on stigma (Nyblade et al., 2019), these data suggest that such efforts may not be sufficient and that broad, social and structural interventions are needed, including removing punitive policies, introducing anti-discrimination laws, and broad interventions that change cultural and social attitudes towards drug use—as is recommended for HIV stigma (Andersson et al., 2020; Nyblade et al., 2021). The extremely high levels of internalized drug use stigma observed in this population and the association of internalized drug use stigma with active HCV infection and injection drug use risk behaviors is also particularly concerning. Although not assessed in this study, internalized drug use stigma has also been associated with low self-esteem and depressive symptoms among PWID (Burke et al., 2015; Cama et al., 2016). Stigma-reduction interventions at the individual-level, such as those that provide mental health and social support to PWID may prove useful in addressing internalized stigma among PWID.

This study was conducted using data from a large community-based sample of well-characterized PWID from several cities across India that have diverse drug use and HCV epidemics. However, this study has several limitations owing to its cross-sectional design. We are unable to draw causal inferences and results may be subject to unmeasured and residual confounding, despite the observed effect estimates being fairly robust to adjustment for a comprehensive set of covariates. Indeed, the directionality and mechanism of the association of drug use stigma with active HCV infection and injection drug use behaviors remains unknown. While we cannot definitively draw conclusions about the mechanism of the observed associations, several explanations are plausible and require further study. First, greater experience of drug use stigma may lead to increased frequency of injection drug use as a means of coping with the stigma and its mental health impacts (Couto E Cruz, Salom, Dietze, Burns, & Alati, 2019; Couto E Cruz, Salom, Maravilla, & Alati, 2018; Earnshaw et al., 2020). Second, it is possible that a greater experience of drug use stigma and social rejection from family and the broader community may lead PWID to turn to other PWID for social support, which may facilitate sharing syringes/needles and other risk behaviors (Morris et al., 2019, 2015; Rhodes, Rance, Fraser, & Treloar, 2017). Third, internalized drug use stigma may serve as a barrier to the use of needle/syringe exchange programs and treatment of substance use disorders (Biancarelli et al., 2019; Paquette, Syvertsen, & Pollini, 2018; Rivera, DeCuir, Crawford, Amesty, & Lewis, 2014), both of which have consistently been associated with reductions in transmission-related risk behaviors (Platt et al., 2017; Reddon, Marshall, & Milloy, 2019; Sawangjit, Khan, & Chaiyakunapruk, 2017). Finally, it should also be noted that these increased injection drug use behaviors may also contribute to drug use stigma, perhaps creating an unrelenting cyclical process between stigma and its harms. Longitudinal studies are needed to explore the temporal relationships between drug use stigma, risk behaviors, service utilization and HCV infection.

This study has other limitations that warrant consideration. There may have been response biases, such as acquiescence, social desirability, and recall biases, particularly in the measurement of drug use stigma and injection drug use risk behaviors (Latkin, Edwards, Davey-Rothwell, & Tobin, 2017; Latkin et al., 2010; Napper, Fisher, Reynolds, & Johnson, 2010). While it is possible that PWID who experienced the greatest amount of stigma were less likely to participate in a study among PWID, this potential bias was mitigated by using RDS to recruit participants. Furthermore, our study was limited to the measurement of drug use stigma and did not consider the effects of intersecting stigmas (e.g., drug use and HIV/HCV). Additional research is needed to characterize the role of interesecting stigmas on the health and well-being of PWID.

High levels of stigma are known to be associated with a myriad of negative physical and mental health outcomes (Hatzenbuehler et al., 2013). In this study, several types of individual-level drug use stigma manifestations were associated with active HCV infection and high-risk injection drug use behaviors that can facilitate HCV transmission. This study provides empirical quantitative evidence to support calls for the reduction of stigma to promote an enabling environment to achieve HCV elimination among PWID.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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HIGHLIGHTS

- A multidimensional drug use stigma scale had excellent psychometric properties.
- High levels of drug use stigma were observed among people who inject drugs.
- Greater drug use stigma was associated with active hepatitis C virus infection.
- Greater drug use stigma was associated with high-risk injection practices.
- Achieving HCV elimination will require addressing drug use stigma.

Table 1.

Characteristics of the study population overall and by active hepatitis C virus (HCV) infection status.

Characteristic	No. of Participants (Weighted %)		
	Overall (n=11,663)	HCV RNA negative (n=6,617)	HCV RNA positive (n=5,046)
Age group, y			
18–24	3255 (26.7%)	1897 (26.2%)	1358 (27.6%)
25–29	2580 (21.5%)	1383 (20.1%)	1197 (24.1%)
30–39	3739 (31.2%)	2051 (31.4%)	1688 (30.8%)
40–49	1589 (15.0%)	915 (15.6%)	674 (13.7%)
≥50	500 (5.7%)	371 (6.6%)	129 (3.8%)
Male	11165 (94.1%)	6238 (92.5%)	4927 (97.5%)
Northeast region	4989 (44.3%)	2943 (50.9%)	2046 (31.4%)
Educational attainment			
Primary school or less	3599 (36.5%)	2143 (37.2%)	1456 (35.3%)
Some secondary education	5538 (44.2%)	3061 (43.0%)	2477 (46.4%)
High school graduate or more	2525 (19.3%)	1412 (19.8%)	1113 (18.4%)
Experiencing homelessness	987 (9.2%)	574 (8.3%)	413 (11.1%)
Incarceration in the past 6 mo.	1075 (7.0%)	515 (6.0%)	560 (9.0%)
Alcohol use (AUDIT score)			
None/mild/moderate (0–7)	7502 (61.5%)	4136 (57.8%)	3366 (68.7%)
Harmful/hazardous (8–14)	2006 (19.4%)	1135 (20.4%)	871 (17.3%)
Dependence (15–40)	2155 (19.2%)	1346 (21.8%)	809 (14.0%)
Non-injection drug use in past 6 mo.	7578 (64.0%)	4152 (62.3%)	3426 (67.3%)
IDU in the past 6 mo.	9309 (73.1%)	4766 (64.8%)	4543 (89.1%)
Frequency of IDU in the past 6 mo.			
None	2354 (26.9%)	1851 (35.2%)	503 (10.9%)
Less than daily	3207 (28.9%)	2113 (31.4%)	1094 (24.0%)
Daily	6102 (44.2%)	2653 (33.5%)	3449 (65.2%)
Ever shared a needle/syringe	6296 (47.4%)	2814 (39.2%)	3482 (63.6%)
HIV antibody positive	2480 (20.3%)	845 (12.3%)	1635 (36.0%)
HCV antibody positive	6455 (43.4%)	1409 (14.4%)	5046 (100%)
HCV RNA positive	5046 (33.8%)	-	5046 (100%)
Aware of HCV infection	-	-	684 (11.0%)
Intervention arm	5961 (48.1%)	3310 (51.0%)	2651 (42.4%)

Note: Data are unweighted sample sizes (no.) and *weighted* column percentages (%) calculated using a composite weight including relative city size and RDS-II weights. There were 34 participants missing data on incarceration status; all other variables had <5 participants with missing data.

Table 2.

Distribution of drug use stigma subscale scores overall and by active hepatitis C virus (HCV) infection status.

Drug use stigma subscale	Overall		HCV RNA negative		HCV RNA positive	
	n	Median (IQR)	n	Median (IQR)	n	Median (IQR)
Enacted	11,502	0.0 (0.0–0.5)	6,490	0.0 (0.0–0.5)	5,012	0.2 (0.0–0.7)
Vicarious	11,503	0.5 (0.0–1.2)	6,488	0.5 (0.0–1.2)	5,015	0.7 (0.0–1.2)
Felt normative	11,351	1.8 (1.0–2.4)	6,411	1.8 (1.0–2.4)	4,940	2.0 (0.8–2.6)
Internalized	11,510	1.8 (1.0–2.6)	6,490	1.6 (0.8–2.4)	5,020	1.8 (1.0–2.6)

Note: Data are unweighted sample sizes (n) and *weighted* medians and corresponding interquartile ranges (IQR) calculated using a composite weight including relative city size and RDS-II weights.

Table 3.

Association of drug use stigma with hepatitis C virus (HCV) infection.

Drug use stigma subscale	n	Outcome: HCV RNA positive			
		%[a]	Univariable OR (95% CI) [b]	Multivariable Model 1: aOR (95% CI) [b,c]	Multivariable Model 2: aOR (95% CI) [b,d]
Categorical variables					
Enacted stigma					
Never	6,372	28.0	Ref.	Ref.	Ref.
Ever	5,130	43.0	1.35 (1.22–1.50)	1.36 (1.22–1.52)	1.27 (1.13–1.43)
Vicarious stigma					
Never	3,602	32.2	Ref.	Ref.	Ref.
Ever	7,901	34.6	0.99 (0.86–1.15)	1.02 (0.92–1.13)	0.97 (0.86–1.10)
Felt/normative stigma					
< 25th percentile	2,862	36.1	Ref.	Ref.	Ref.
25–75th percentile	5,889	29.8	1.04 (0.89–1.21)	1.02 (0.86–1.21)	0.97 (0.83–1.13)
> 75th percentile	2,600	41.5	1.01 (0.78–1.30)	0.95 (0.71–1.27)	0.92 (0.68–1.23)
Internalized stigma					
< 25th percentile	2,850	21.3	Ref.	Ref.	Ref.
25–75th percentile	6,338	35.6	1.52 (1.12–2.06)	1.49 (1.13–1.98)	1.42 (1.07–1.88)
> 75th percentile	2,322	44.4	1.84 (1.26–2.68)	1.73 (1.14–2.63)	1.69 (1.11–2.56)
Continuous variables					
Enacted stigma	11,502	-	1.21 (1.10–1.34)	1.26 (1.16–1.35)	1.20 (1.11–1.30)
Vicarious stigma	11,503	-	1.09 (0.94–1.27)	1.09 (0.97–1.24)	1.07 (0.93–1.23)
Felt/normative stigma	11,351	-	1.02 (0.94–1.12)	1.00 (0.91–1.10)	0.98 (0.89–1.08)
Internalized stigma	11,510	-	1.22 (1.09–1.37)	1.20 (1.07–1.35)	1.16 (1.04–1.30)

[a] Prevalence of HCV RNA (>30 IU/mL) was estimated using a composite weight of the relative city size and RDS-II weights.

[b] Separately for each stigma subscale, odds ratios (OR) of hepatitis C virus infection were estimated from a multilevel logistic regression model with a random-intercept for each site and scaled RDS-II weights.

[c] Multivariable model 1 included adjustment for age group, gender, northeast region, educational attainment, homelessness, history of incarceration in the past 6 months, alcohol use (AUDIT), and HIV status.

[d] Multivariable model 2 included adjustment for age group, gender, northeast region, educational attainment, homelessness, history of incarceration in the past 6 months, alcohol use (AUDIT), HIV status, frequency of injection in the past 6 months and a history of ever sharing needles/syringes.

Table 4.

Association of individual drug use stigma items with hepatitis C virus (HCV) infection.

Drug use stigma items	Outcome: HCV RNA positive (*weighted*)		
	Univariable OR (95% CI) [a]	Multivariable Model 1: aOR (95% CI) [a,b]	Multivariable Model 2: aOR (95% CI) [a,c]
Enacted stigma items (Ref: never)			
1. Mistreated by hospital worker	1.20 (1.03–1.41)	1.19 (1.00–1.40)	1.17 (1.01–1.35)
2. Denied medical care or hospital services	1.21 (1.01–1.44)	1.21 (1.01–1.45)	1.21 (0.99–1.49)
3. Told to stay away from children	1.24 (1.02–1.50)	1.32 (1.15–1.51)	1.25 (1.07–1.45)
4. Forced to move out of home by family	1.14 (0.98–1.34)	1.21 (1.05–1.39)	1.16 (1.01–1.33)
5. Received threat of physical harm	1.22 (1.06–1.40)	1.24 (1.12–1.38)	1.17 (1.06–1.30)
6. Denied housing	1.23 (1.04–1.47)	1.27 (1.09–1.49)	1.26 (1.08–1.46)
Vicarious stigma items (Ref: never)			
7. Mistreated by hospital workers	1.17 (0.96–1.44)	1.19 (1.00–1.41)	1.15 (0.96–1.38)
8. Mistreated when getting HIV testing	1.18 (0.95–1.47)	1.17 (0.96–1.43)	1.19 (0.95–1.48)
9. Mistreated when getting HIV treatment	1.16 (0.97–1.40)	1.17 (0.97–1.40)	1.17 (0.95–1.43)
10. Refused care from family when sick	1.08 (0.83–1.40)	1.13 (0.92–1.37)	1.07 (0.86–1.33)
11. Forced to move out of home by family	1.05 (0.84–1.30)	1.07 (0.91–1.26)	1.02 (0.85–1.22)
12. Ostracized by community or village	1.12 (0.97–1.30)	1.12 (0.97–1.28)	1.07 (0.92–1.25)
Felt normative stigma items (Ref: no one/very few people)			
13. Avoid visiting homes of PWUD	1.01 (0.87–1.17)	0.99 (0.84–1.17)	0.97 (0.82–1.15)
14. PWUD bring shame to their families	1.04 (0.87–1.24)	1.00 (0.83–1.21)	0.96 (0.81–1.15)
15. PWUD should feel guilty	1.06 (0.92–1.21)	1.03 (0.91–1.16)	1.00 (0.88–1.13)
16. PWUD are disgusting	1.01 (0.87–1.18)	0.99 (0.85–1.15)	0.96 (0.83–1.12)
17. PWUD are paying for their karma or sins	1.04 (0.89–1.22)	1.00 (0.85–1.17)	0.98 (0.84–1.16)
Internalized stigma items (Ref: not at all/a little)			
18. Feels need to avoid visiting people due to drug use	1.29 (1.12–1.49)	1.25 (1.06–1.48)	1.19 (1.01–1.40)
19. Feels shame brought to family due to drug use	1.45 (1.24–1.70)	1.40 (1.20–1.63)	1.32 (1.14–1.54)
20. Feels guilty about drug use	1.31 (1.04–1.67)	1.29 (1.02–1.64)	1.24 (0.99–1.55)
21. Feels disgusting about drug use	1.29 (1.06–1.57)	1.24 (1.03–1.49)	1.19 (1.01–1.41)
22. Uses drugs as a payment for karma or sins	1.24 (1.02–1.49)	1.22 (1.02–1.46)	1.19 (1.00–1.42)

[a]Separately for each stigma item, odds ratios (OR) of active hepatitis C virus infection were estimated from multilevel logistic regression models with a random-intercept for each site and scaled RDS-II weights.

[b] Multivariable model 1 included adjustment for age group, gender, northeast region, educational attainment, experiencing homelessness, history of incarceration in the past 6 months, alcohol use/dependence (AUDIT), and HIV status.

[c] Multivariable model 2 included adjustment for age group, gender, northeast region, educational attainment, experiencing homelessness, history of incarceration in the past 6 months, alcohol use/dependence (AUDIT), HIV status, frequency of injection in the past 6 months and a history of ever sharing needles/syringes.

Table 5

Association of drug use stigma with injection drug use behaviors among active people who inject drugs in the past 6 months.

Drug use stigma subscale	Daily injection drug use			Shared needles/syringes			Multiple injection partners			Injection drug use in public spaces		
	%[a]	OR (95% CI)[b]	aOR (95% CI)[b,c]	%[a]	OR (95% CI)[b]	aOR (95% CI)[b,c]	%[a]	OR (95% CI)[b]	aOR (95%CI)[b,c]	%[a]	OR (95% CI)[b,c]	aOR (95% CI)[b,c]
Enacted stigma												
Never	53.9	Ref.	Ref.	33.4	Ref.	Ref.	60.1	Ref.	Ref.	70.0	Ref.	Ref.
Ever	68.3	1.27 (1.00–1.61)	1.30 (0.96–1.74)	44.2	1.38 (1.17–1.62)	1.34 (1.16–1.55)	60.8	1.52 (1.21–1.92)	1.46 (1.15–1.85)	79.0	1.31 (1.09–1.57)	1.24 (1.01–1.53)
Vicarious stigma												
Never	57.5	Ref.	Ref.	36.7	Ref.	Ref.	63.6	Ref.	Ref.	64.0	Ref.	Ref.
Ever	61.6	1.04 (0.77–1.41)	1.17 (0.82–1.65)	39.0	1.06 (0.86–1.30)	1.10 (0.84–1.44)	62.5	1.30 (1.06–1.59)	1.28 (1.05–1.56)	77.5	1.46 (1.20–1.76)	1.46 (1.17–1.81)
Felt normative stigma [d]												
<25th	58.8	Ref.	Ref.	35.4	Ref.	Ref.	60.0	Ref.	Ref.	68.6	Ref.	Ref.
25–75th	58.1	0.96 (0.70–1.33)	1.08 (0.80–1.47)	36.9	1.20 (0.92–1.57)	1.22 (0.89–1.67)	60.5	1.14 (0.80–1.62)	1.16 (0.81–1.66)	74.1	1.17 (0.89–1.56)	1.22 (0.93–1.61)
>75th	69.1	1.00 (0.69–1.45)	0.99 (0.71–1.36)	44.0	1.22 (0.88–1.67)	1.18 (0.87–1.60)	73.2	1.53 (1.00–2.33)	1.52 (0.99–2.33)	80.5	2.29 (1.52–3.47)	2.31 (1.49–3.59)
Internalized stigma [e]												
<25th	49.4	Ref.	Ref.	27.4	Ref.	Ref.	62.8	Ref.	Ref.	68.8	Ref.	Ref.
25–75th	61.7	0.98 (0.63–1.53)	1.10 (0.82–1.48)	41.0	1.32 (1.07–1.63)	1.37 (1.14–1.64)	62.9	1.28 (1.04–1.58)	1.31 (1.07–1.59)	73.6	1.03 (0.73–1.46)	1.07 (0.77–1.47)
>75th	67.2	0.90 (0.53–1.54)	0.99 (0.64–1.52)	41.6	1.12 (0.69–1.83)	1.20 (0.80–1.78)	62.6	1.03 (0.73–1.46)	1.05 (0.74–1.48)	79.4	1.83 (1.22–2.74)	1.92 (1.33–2.79)

Note: This analysis was restricted to participants who reported injection drug use in the past 6 mo. ($n = 9309$).

[a] Prevalence of each behavior was estimated using a composite weight of the relative city size and RDS-II weights.

[b] Odds ratios were estimated from multilevel logistic regression models with a random-intercept for each city and scaled RDS-II weights.

[c] A separate multivariable model was used for each stigma-behavior relationship shown and included adjustment for age group, gender, northeast region, educational attainment, homelessness, history of incarceration in the past 6 mo., alcohol use/dependence (AUDIT), and HIV status.

[d] Cut-offs are based on the population-level distribution in the overall study population (i.e.. 25th–75th percentile: 1.0–2.4).

[e] Cut-offs are based on the population-level distribution in the overall study population (i.e., 25th–75th percentile: 1.0–2.6).