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Hepatitis C Care Cascades for 3 Populations at High Risk: Low-income Trans Women, Young People Who Inject Drugs, and Men Who Have Sex With Men and Inject Drugs

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Background. To achieve elimination of hepatitis C virus (HCV) infection, limited resources can be best allocated through estimation of "care cascades" among groups disproportionately affected. In San Francisco and elsewhere, these groups include young (age ≤ 30 years) people who inject drugs (YPWID), men who have sex with men who inject drugs (MSM-IDU), and low-income trans women.

Methods. We developed cross-sectional HCV care cascades for YPWID, MSM-IDU, and trans women using diverse data sources. Population sizes were estimated using an inverse variance-weighted average of estimates from the peer-reviewed literature between 2013 and 2019. Proportions of past/current HCV infection, diagnosed infection, treatment initiation, and evidence of cure (sustained virologic response at 12 weeks posttreatment) were estimated from the literature using data from 7 programs and studies in San Francisco between 2015 and 2020.

Results. The estimated number of YPWID in San Francisco was 3748; 58.4% had past/current HCV infection, of whom 66.4% were diagnosed with current infection, 9.1% had initiated treatment, and 50% had confirmed cure. The corresponding figures for the 8135 estimated MSM-IDU were: 29.4% with past/current HCV infection, 70.3% diagnosed with current infection, 28.4% initiated treatment, and 38.9% with confirmed cure. For the estimated 951 low-income trans women, 24.8% had past/current HCV infection, 68.9% were diagnosed with current infection, 56.5% initiated treatment, and 75.5% had confirmed cure.

Conclusions. In all 3 populations, diagnosis rates were relatively high; however, attention is needed to urgently increase treatment initiation in all groups, with a particular unmet need among YPWID.

Keywords. hepatitis C; care cascade; MSM; PWID; transgender women.

Availability of hepatitis C virus (HCV) therapies known as direct-acting antivirals (DAAs) represented a turning point for the HCV epidemic, resulting in cure for > 95% of those treated [1]. However, prior studies have shown that DAA availability is not translating to treatment initiation among the most marginalized groups [2], particularly those engaged in illicit drug use [3]. New HCV elimination strategies aimed at reducing incidence by 90% from 2015 levels by 2030 are being established nationally and internationally [4–7], but these strategies will not succeed unless the groups at highest risk for HCV transmission receive curative treatment.

We set out to support San Francisco's HCV elimination initiative, End Hep C SF, by gaining a better understanding of engagement in testing and treatment for some of the most highly affected subgroups in the local HCV epidemic. An estimated 2.5% of people in San Francisco are HCV seropositive, with approximately 12 000 people having untreated HCV infection in 2015 [8]. Of those with chronic HCV infection, 67.9% are people who inject drugs (PWID) and 13.8% are men who have sex with men (MSM). One in 6 trans women are living with HCV [8]. However, more information is needed regarding the care cascades for 3 highly affected subgroups within these larger categories: young adult PWID aged ≤ 30 years (YPWID), MSM who inject drugs (MSM-IDU), and trans women who are low income. Among PWID, YPWID are an expanding high-risk group [9, 10] with unique needs related to engagement in healthcare, who have been largely overlooked in prior research. Compared with MSM as a whole, MSM-IDU are a distinct group with a high burden of HCV infection who face unique challenges [11], including poor access to MSM-friendly substance use programs [12] and increased stigma and social isolation [13]. Trans women have a high prevalence of human immunodeficiency virus (HIV) infection (39%) and HCV seroprevalence (24%) in San Francisco, as well as a high frequency of historical injection drug use (36%).

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Health departments use what is commonly known as a "care cascade" to estimate the number of individuals at various stages from HCV diagnosis through treatment and cure (sustained viral response [SVR]). Care cascades provide baseline information regarding engagement at each stage, serving as a powerful tool for informing and evaluating elimination strategies [14, 15]. However, cascades are typically created using a single large clinical or surveillance data source that is inherently biased by including only those reached for testing and treatment; further, many datasets have substantial limitations related to accuracy and completeness of variables identifying more marginalized subsets of people [16], thereby hindering the use of most cascades for evaluation of key subgroup needs. To address these challenges, we identified multiple data sources focused on the 3 subgroups of interest and triangulated them to estimate the number of people in each subgroup at each stage of a local HCV cascade.

METHODS

To better understand the continuum of HCV infection and treatment among these 3 subgroups, we used a collection of data from 7 different programmatic sources and epidemiological studies collected between 2015 and 2020 (Supplemental Table 1). We developed care cascades with measures for the following stages for each subgroup from 2015 through 2020 (Figure 1). Stage 1: Evidence of past or current HCV infection, defined as reporting having ever had any positive HCV test, or testing positive for anti-HCV antibodies through study-based serological testing. Stage 2: Diagnosed current HCV infection, defined by self-report of a positive result on an HCV RNA test, or having a reactive confirmatory RNA test through study-based testing. Stage 3: Initiation of HCV treatment, defined through self-report of having begun treatment for HCV infection. Stage 4: Confirmation of HCV cure (SVR 12 weeks posttreatment) via medical record documentation or self-report.

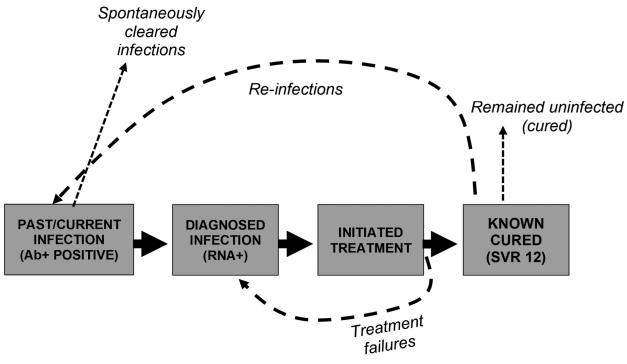

Figure 1. Continuum of infection and treatment (cascade of care) for hepatitis C virus. Abbreviations: Ab+, anti-HCV (antibody) positive; HCV, hepatitis C virus; RNA+, HCV RNA detected in a blood specimen to confirm infection; SVR 12, sustained virologic response was found at 12 weeks posttreatment, indicated successful cure.

Analytic Methods: Population Size Estimation

Population size estimates (PSEs) and 95% credible intervals for each of the 3 subgroups served as the denominator for the first stage of each cascade. There are a number of commonly accepted, advanced methods for estimating population sizes of so-called "hidden" populations, including capture-recapture [17, 18], network scale-up methods [19, 20], Bayesian model averaging [21], and multiplier methods [22, 23], often based in respondent-driven sampling (RDS) studies [24]. Rather than attempting to recreate any of these methods and directly estimate the population size of each group, we used a meta-analysis approach, incorporating estimates using these methods that were already in published literature using an inverse variance-weighted average and fixed effects model, as follows.

Young People Who Inject Drugs

After a search for all publications with data from the past decade (2010–2019) estimating the size of the PWID population in San Francisco, 2 publications were identified (Supplemental Table 2). Tempalski et al [25] used multiplier methods to estimate the number of PWID ≤ 30 years of age in San Francisco. The other 5 measures came from a study by Chen et al that estimated the number of PWID in San Francisco by triangulating estimates generated using multiple methods [26]. We used each of the original data sources cited in this paper but excluded: (1) a multiplier estimate based on obtaining sexually transmitted disease (STD) testing from the municipal STD clinic, which appeared biased because of underreporting of injection drug use, and (2) the successive-sampling method, which used a median of estimates that were strongly influenced by the assumptions used in the scenarios for each Bayesian model, rather than the source data. For the 5 PWID PSEs included from Chen et al, we multiplied each point estimate by an estimated proportion of PWID in San Francisco who are ≤ 30 years of age, which was calculated by averaging the proportion of PWID ≤ 30 years of age in 4 unpublished SF datasets: (1) the 2018 PWID HIV National Behavioral Surveillance (NHBS) wave; (2) individuals seen at the San Francisco AIDS Foundation in 2019 for clinical or syringe access services; (3) patients seen in 2019 at San Francisco's municipal STD clinic; and (4) people tested for HCV in 2019 by a set of community-based organizations funded by the San Francisco Department of Public Health.

Men Who Have Sex With Men Who Inject Drugs

After a search of publications with data from the past decade estimating the size of the MSM population in San Francisco, 4 publications were identified (Supplemental Table 2). We used PSEs from Grey et al [27] and Hughes et al [28], each of which included an MSM-IDU–specific estimate. We also

used a PSE for MSM-IDU from Raymond et al [29] that was updated per the authors' 2019 commentary suggesting a 19.4% increase in the size of the MSM population in San Francisco from 2013 to 2017 [30]. Last, we included a PSE for the total MSM population by Wesson et al [21], generated by multiplying the total number of MSM derived from a Bayesian successive-sampling model by the proportion of MSM who reported injecting drugs in the prior 12 months during the 2018 MSM wave of NHBS.

Trans Women Who Are Low Income

Only 1 publication was identified with a PSE for trans women in San Francisco: Wesson et al [23] incorporated estimates from 9 multiplier-based estimates produced from service-utilization data within the Transfemales Empowered to Advance Community Health 2 study (TEACH2, 2013) as the recapture phase (Supplemental Table 2). We excluded the successive sampling method for consistency with our PWID PSE. The PSE produced using this method likely captures almost exclusively low-income trans women, who are those most likely to be identified as trans women in HIV- or HCV-related services or studies, and may represent only 49% of all trans women in San Francisco [31].

Analytic Methods: Cascade Stage Estimation

We estimated cross-sectional, denominator-numerator prevalence cascades [32] for each subgroup. Denominator-numerator prevalence cascades use the total PSE as the denominator of the first stage of the cascade and use the numerator from each stage as the denominator for the subsequent stage. To calculate the numerators of each cascade stage, we first calculated the proportion of participants in each cascade stage in multiple individual observational cohorts and studies. Once proportions had been calculated for each stage for each individual study (Supplemental Table 1), we then calculated an inverse-variance–weighted average of proportions for each cascade stage overall and applied that proportion to the denominator from the prior stage to calculate a count of people in that stage (eg, an average proportion of 0.584 for stage 1, applied to a PSE of 3748, results in a numerator count of 2188 for that stage). The studies and data incorporated into these estimates are detailed next.

Young People Who Inject Drugs

(1) The U-Find-Out (UFO) study, a prospective observational cohort of HCV-negative PWID age ≤ 30 years [33]. We included behavioral and serological data collected at quarterly intervals between 2015 and 2019 (n = 293), including results of HCV antibody (anti-HCV) and RNA testing, and self-report of HCV treatment initiation. (2) The most recent PWID wave from San Francisco's NHBS, a serial cross-sectional study conducted every 3 years using RDS to recruit and survey approximately 500 anonymous participants per cycle. In the 2018 wave, rapid anti-HCV testing was conducted as part of the study, with RNA confirmation when possible. We used data from the 2018 wave restricted to respondents aged ≤ 30 years who self-reported any lifetime injection drug use. Analysis included anti-HCV and RNA testing data, self-reported data about having previously been told they were anti-HCV positive or were infected with HCV, as well as self-reported data about HCV treatment and cure.

Men Who Have Sex With Men and Inject Drugs

(1) The 2017 MSM wave from San Francisco's NHBS, restricted to those who had reported any history of injection drug use. In this wave, no HCV testing was conducted; therefore, data included self-report of having been previously told they were anti-HCV positive, previously told they were HCV infected, or having initiated treatment for HCV. (2) The UFO study, restricted to men who reported ever having had sex with men. These data included study-performed anti-HCV and RNA testing, as well as self-report of HCV treatment initiation and cure. (3) STOP AIDS street intercept surveys, which are annual cross-sectional surveys of MSM in San Francisco using venue-based sampling. Data were used from participants in the 2019 survey (n = 800) who reported both injection drug use in the prior year and having ever had a test for HCV. We included self-report of anti-HCV test results, RNA test results, treatment initiation, and cure. (4) Electronic health record data from February 2017 through June 2019 from Strut, a health center designed to support gay men's sexual and substance health, for all MSM patients who reported injection drug use in the prior year and received at least 1 HCV test during that period (n = 47). We included anti-HCV test results, RNA test results, evidence of treatment initiation, and SVR results or self-report of having been cured.

Low-income Trans Women

(1) The TEACH study from 2018 (TEACH3), an RDS study of trans women in San Francisco. We included only participants who reported ever being tested for HCV, prior to or during the study (N = 250/318), and for this analysis used results of study-based anti-HCV testing from 2016 to 2018, results of RNA confirmation via external referral for participants testing anti-HCV positive, and self-report of HCV treatment initiation and cure. (2) Data from TEACH4, the 2019 trans-focused supplemental wave of NHBS, restricted to participants who did not also report participation in TEACH3 (n = 112). Included data variables were results of study-based anti-HCV and RNA testing, and self-report of HCV treatment initiation and cure.

All estimates were conducted using R statistical software [34]. This research was approved by the University of California San Francisco institutional review board, Protocol #18-26975.

RESULTS

The estimated number of YPWID in San Francisco from 2015 to 2019 was 3748 (95% confidence interval [CI], 2516–4979). The estimated number of MSM-IDU was 8135 (95% CI, 7704–8567). The estimated number of trans women was 951 (95% CI, 889–1013).

We estimated that 58.4% (95% CI, 53.4–63.4) of YPWID in San Francisco have evidence of past or current HCV infection (ie, HCV antibodies are present) (Figure 2). Of these, 66.4% (95% CI, 60.6–72.3) have been diagnosed. Only 9.1% (95% CI, 5.0–13.2) of those diagnosed have engaged in HCV treatment, of whom 50% (95% CI, 10.0–90.0) had confirmed cure.

For MSM-IDU, 29.4% (95% CI, 23.6–35.3) of the population were estimated to have past/current HCV infection (Figure 3), and 70.3% (95% CI, 60.0–80.7) of those have been diagnosed. The proportion diagnosed who have initiated treatment was estimated at 28.4% (95% CI, 18.4–38.4), with 38.9% (95% CI, 14.8–63.0) of those having confirmed cure.

We estimated that 24.8% (95% CI, 20.4–29.2) of trans women in SF have past/current HCV infection (Figure 4), with 68.9% (95% CI, 59.3–78.5) of those having been diagnosed. More than one-half (56.5%; 95% CI, 44.3–68.8) of those diagnosed have initiated HCV treatment; of those, 75.5% (95% CI, 47.4–83.6) had confirmed cure.

DISCUSSION

A central finding in our study is the distressingly low proportion of YPWID (9.1%), MSM-IDU (28.4%), and low-income trans women (56.5%) in San Francisco with diagnosed HCV infection who have initiated treatment. Untreated HCV infection can result in onward transmission [35] and leads to cirrhosis in approximately 20% of patients and hepatocellular carcinoma in 3%–8% of people with HCV cirrhosis each year, outcomes that are frequently fatal [36].

Treatment was particularly low among YPWID, in whom fewer than 1 in 10 of those with chronic HCV infection have been treated. These low treatment levels persist despite changes in policies and programs over the past 5 years to expand eligibility and access to HCV treatment through End Hep C SF. Today, HCV treatment is available in San Francisco through

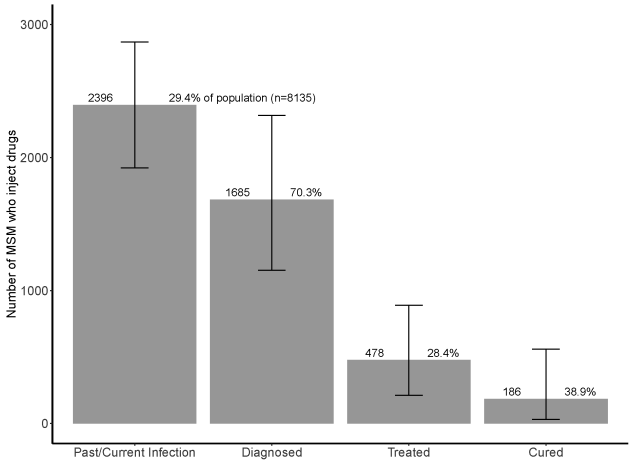

Figure 3. Cascade of HCV care for men who have sex with men and inject drugs in San Francisco, 2016–2020. Abbreviations: Cured, demonstrated HCV cure via sustained virologic response at 12 weeks posttreatment; diagnosed, active infection confirmed via RNA testing; HCV, hepatitis C virus; MSM, men who have sex with men; past/current infection, anti-HCV (antibody) positive; treated, self-reported initiating HCV treatment.

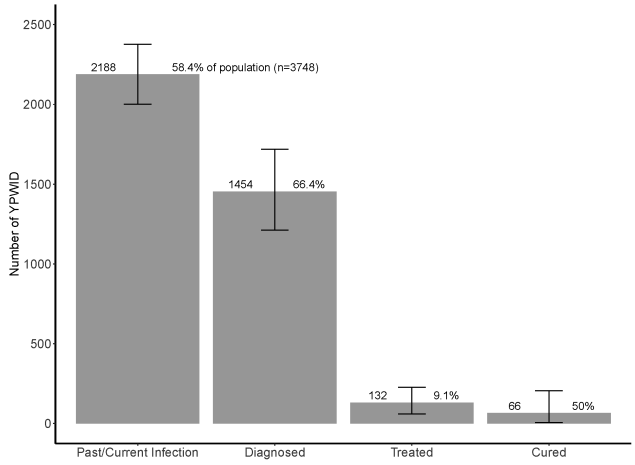

Figure 2. Cascade of HCV care for people age ≤ 30 years who inject drugs in San Francisco, 2016–2020. Abbreviations: Cured, demonstrated HCV cure via sustained virologic response at 12 weeks posttreatment; diagnosed, active infection confirmed via RNA testing; HCV, hepatitis C virus; past/current infection, anti-HCV (antibody) positive; treated, self-reported initiating HCV treatment; YPWID, young people aged 30 years or younger who inject drugs.

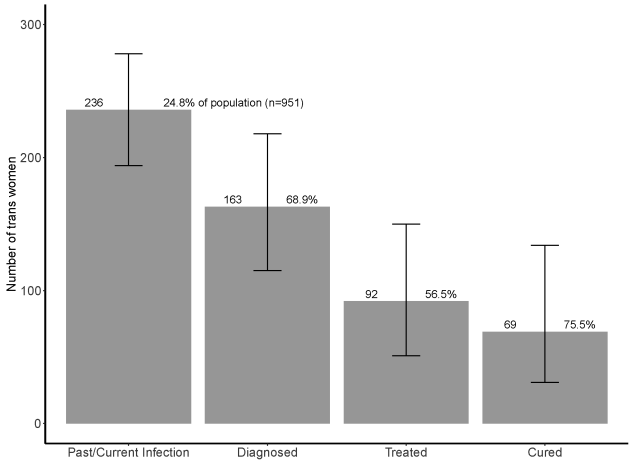

Figure 4. Cascade of HCV care for low-income trans women in San Francisco, 2016–2020. Abbreviations: Cured, demonstrated HCV cure via sustained virologic response at 12 weeks posttreatment; diagnosed, active infection confirmed via RNA testing; HCV, hepatitis C virus; past/current infection, anti-HCV (antibody) positive; treated, self-reported initiating HCV treatment.

most primary care physicians [37], and at syringe services programs, homeless shelters and navigation centers, and single residence occupancy hotels [38], yet this continued low level of treatment initiation highlights ongoing major systemic failures.

We found the proportion of treatment initiation to be moderately higher among trans women (56.5%). It is possible that a number of recent longitudinal and cross-sectional studies of trans women in the city, many providing HCV testing with referral or direct treatment, could have resulted in increased treatment rates. Similarly, many trans women use gender-affirming hormones obtained in trans-focused primary care clinics where HCV testing may be offered during routine care. Treatment among MSM-IDU diagnosed with HCV (28.4%) was lower than for trans women but higher than for YPWID. It is possible that estimates are biased by the inclusion of clinical data from Strut, where mostly MSM patients with chronic HCV infection have ready access to in-house HCV treatment services. MSM-IDU may also be more likely to be served by programs aimed at HIV prevention and care tailored to MSM, with many such programs incorporating HCV testing and care into their routine services.

Our estimates of the drop-off from the number of people who are anti-HCV positive to the number of people with diagnosed infection are in line with published estimates of the rate of spontaneous clearance of HCV [39–41]. Our estimates of the fourth cascade stage involve "known cure" via receipt of SVR results at 12 weeks posttreatment. Notably, prior research has demonstrated that the vast majority of people who initiate DAA treatment are likely cured of infection [42–44], and therefore the proportion of people cured of HCV is likely far higher than these cascades estimate. Improving the number of people returning for cure confirmation will improve population estimates of disease burden.

Our analysis is subject to a number of limitations. First, we have calculated cross-sectional HCV care cascades using multiple deidentified data sources, and not all data sources contribute to each stage within the same cascade. These estimates may differ from those derived from cohort studies, where linking of individual records is possible and a single person can be followed throughout each stage of the cascade. Where possible, we included patients or study participants in each stage based on their survey answers at a prior stage (ie, we followed individuals through the cascade). Second, our data sources represent timepoints from 2015 to 2020, and population size estimates were created from studies ranging from 2010 to 2019. Some evidence suggests that both population sizes and rates of HCV treatment have increased over the study period [28, 30, 37]; therefore, a weighted average of all studies during the entire period may have led us to underestimate the number of people in each stage (ie, the denominator) and the proportion of people in each stage for each subgroup in 2019. Third, because some of the same data sources are used in more than 1 cascade, bias or measurement error in 1 data source could affect more than 1 subgroup cascade. Fourth, the MSM-IDU category used here is broadly defined to include any men who have had sex with a man or injected drugs in their lifetime; this is an overrepresentation of the actual group of men who concurrently have sex with men and inject drugs. Finally, our analysis was designed to estimate the care cascades in these subgroups before coronavirus disease 2019, and the proportions of people in each of these cascade stages in early 2021 may already have substantially changed.

Although we used data sources specific to the 3 subgroups of interest within San Francisco, the methods we used could be applied by other areas with local data sufficient for triangulation. Other cities, including New York [45], Philadelphia [46], and Vancouver [47] have already developed local HCV cascades, including cascades for PWID. However, our results underscore the need for an expansion of these efforts to include estimates of cascades for highly affected subpopulations within these larger groups, which may require using a combination of data sources rather than a single clinical program or study. Subgroup estimates also provide better parameters for infectious disease models to inform guidelines for viral hepatitis elimination, such as those released by the World Health Organization [7] and National Academies of Sciences, Engineering, and Medicine [6].

These findings highlight the need for San Francisco to focus on efforts to diagnose and treat HCV infections among YPWID, MSM-IDU, and trans women. To eliminate HCV, we must improve our focus on interventions that are appropriately tailored to those at the highest risk for HCV infection. This tailoring will require understanding the epidemic among subgroups typically aggregated within broad population categories during data analyses to effectively drive public health response.

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

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