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### Authors

Morris, Meghan D  
Mirzazadeh, Ali  
Evans, Jennifer L  
[et al.](#)

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## Treatment cascade for hepatitis C virus in young adult people who inject drugs in San Francisco: Low number treated

Meghan D. Morris<sup>1,2</sup>, Ali Mirzazadeh<sup>1,2</sup>, Jennifer L. Evans<sup>2</sup>, Alya Briceno<sup>2</sup>, Phillip Coffin<sup>3,4</sup>, Judith A. Hahn<sup>1,4</sup>, and Kimberly A. Page<sup>5</sup>

<sup>1</sup>Department of Epidemiology and Biostatistics, University of California, San Francisco, San Francisco, CA, USA

<sup>2</sup>Institute for Global Health Sciences, University of California, San Francisco, San Francisco, CA, USA

<sup>3</sup>San Francisco Department of Public Health, San Francisco, CA, USA

<sup>4</sup>Department of Medicine, University of California, San Francisco, San Francisco, CA, USA

<sup>5</sup>Department of Internal Medicine, University of New Mexico Health Sciences Center, Albuquerque, NM, USA

### Abstract

**Objective:** To understand the number of young adult people who inject drugs (PWID) with hepatitis C virus (HCV) infection accessing direct-acting antiviral (DAA) treatment and their barriers and facilitators to treatment uptake.

**Methods:** Using prospective cohort data from young adult PWID in San Francisco with newly identified HCV infection, we calculated the number who: (i) accepted referral to DAA therapy, (ii) initiated DAA therapy, (iii) completed DAA therapy, and (iv) achieved sustained virologic response (SVR) or cure. Behavioral survey data identified possible barriers and facilitators to DAA therapy.

**Results:** Of 60 young adult PWID with new HCV infection identified between February 2015 and January 2018, thirty accepted a referral to HCV care; five initiated and completed HCV treatment and achieved cure. Barriers to DAA uptake included fear of medical establishments, competing basic needs, and delaying care because they were feeling well.

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**Correspondence:** Meghan D. Morris, 550 16<sup>th</sup> Street, Box 1224, San Francisco, CA, 94153, Phone: +1 415-476-5822, Meghan.Morris@ucsf.edu.

#### Contributors

MDM, AM and KP designed the study. JE and AB oversaw the collection and management of data. MDM and JE conducted the data analysis. MDM wrote the first draft of the manuscript. All authors contributed to the interpretation of the results, provided critical revisions to the manuscript, and read and approved the final version of the manuscript.

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#### Conflict of Interest

The authors have declared that no competing interests exist. PC has previously directed National Institutes of Health-funded trials, unrelated to this study, that have received donated study medications from Alkermes (2014–2015) and Gilead (2015–2017).

**Conclusion:** While few HCV-positive young adult PWID engaged in DAA therapy, all those who did achieved cure. Youth-tailored services that overcome the stigma and marginalization related to injection drug use are needed to improve treatment uptake.

## Keywords

Hepatitis C Virus (HCV); HCV Treatment; Injection Drug Use

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## 1. Introduction

Successful hepatitis C treatment (HCV) results in sustained virologic response (SVR), achieving cure for >95% of people who complete an 8-12 week treatment course of direct-acting antiviral (DAA) therapies (Pawlotsky et al., 2015). People who inject drugs (PWID), notably young adults, represent the group at highest risk for acquiring and transmitting HCV (Hagan et al., 2010; Morris et al., 2017). Intravenous drug use is responsible for most HCV infections in high- and middle-income countries due to the sharing of injecting equipment (Hagan et al., 2001). The US and the World Health Organization have set parallel goals of reducing HCV incidence by 90% by 2030 (Buckley and Strom, 2017; Organization, 2016); key to this target is treating 80% of infected persons with DAAs (Martin et al., 2013). Expanding DAA treatment uptake among young PWID is a key step in reducing the HCV epidemic (Panel et al., 2015).

The “cascade of care” model provides a framework to monitor population-level clinical and public health outcomes, identify leakages in the care continuum, and offer insight into opportunities for intervention. The few studies that provide information about screening, treatment engagement, and treatment response for PWID focus on substance use treatment (hence, not all are actively injecting) or older PWID (Grebely et al., 2017). Thus we sought to characterize the cascade of care (CoC): HCV testing, diagnosis, treatment, and achievement of SVR. We used data from a prospective community-based longitudinal study of young adult PWID in San Francisco, CA (The UFO Study). We further explored reasons for drop-off in the CoC through survey data.

## 2. Methods

We analyzed behavioral and HCV testing data from participants enrolled through community recruitment strategies into an ongoing prospective study of acute HCV in young adult (age <30 years) PWID (injected drugs in past month) in San Francisco between February 1, 2015 and January 31, 2018 (Page et al., 2009). Of the 258 persons screened for HCV (anti-HCV and HCV RNA), 130 (51%) were anti-HCV and RNA positive at baseline and ineligible for prospective follow-up. Among those testing RNA-negative at baseline (n=173), follow-up, including study interview and serology, occurred quarterly, and those with newly detected HCV RNA (i.e. recently infected at follow-up) were followed monthly. Participants were remunerated for all study visits (20-30 USD per visit). All participants provided written informed consent. The Committee for Human Research Institutional Review Board at the University of California San Francisco approved the study (CHR # 10-00063).

We restricted the analytic sample to participants with new HCV infection detected after February 1, 2015, when DAA therapy became widely available locally through expanded MediCal eligibility, and to those who had completed at least one follow-up study visit. We examined participant sociodemographic characteristics, and calculated the cumulative proportion for participants with newly identified HCV infection across the following HCV CoC stage outcomes: (i) accepted direct referral, (ii) initiated DAA therapy, (iii) completed DAA therapy, and (iv) achieved SVR. Survey data collected starting in February 2017 were reviewed for information regarding barriers to accessing medical care and HCV treatment. During the study period, treatment was available at no cost via two research studies (NCT02609893, NCT02824640) and several local medical providers.

### 3. Results

Between February 1, 2015 and January 31, 2018, sixty persons were identified as newly infected at baseline or follow-up; among whom 37 were identified during the acute phase of infection (HCV RNA positive, anti-HCV negative). Overall, most (73%) were male and recently homeless (88%), and had injected for a median of 4 years (Interquartile Range (IQR): 1, 6), shared injecting equipment in the past three-months (65%) and reported heroin (74%) as the drug injected most often in the past month. Of the sixty with new infection, 7 (12%) spontaneously cleared within 6 months, and 4 were lost to follow-up and therefore were not referred to treatment. Of the 49 persons who remained viremic and retained in follow-up, thirty (60%) accepted referral to HCV care. Five (17%) initiated HCV treatment, and of those, 100% completed treatment and achieved SVR at 12-weeks (Figure 1). All five accessed HCV treatment via another research study that offered no-cost HCV treatment and monetary compensation. Four of the five were male, four reported heroin as their main drug. Three reported having >30 injecting partners in the past 30 days; the other two reported having two or three recent injecting partners. All five reported to research staff they were “feeling better” and “happy to have received treatment.”

Among those with newly identified infection, starting in February 2017 were administered survey questions about perceived barriers to receiving medical care (n=30). The primary circumstances cited included: lack of transportation (50%), community stigma against persons living with HCV (50%), lack of financial resources (65%) and lack of adequate/affordable housing (65%). A few noted lack of supportive and understanding work environments for people living with HCV (15%) as a barrier to medical care. When asked what the main reason for not accessing HCV care (among those who did not n=25), 40% reported feeling good, and 25% wanted to see if their infection spontaneously cleared.

### 4. Discussion

Although only half of the study sample of young adult PWID with acute HCV infection accepted a referral to DAA treatment and five (17%) started treatment, all five that completed treatment cleared their HCV infection. The five who engaged in treatment may represent a subgroup highly motivated to start HCV treatment. Our findings derive from a small sample but suggest that young adult PWID engaged in HCV treatment can achieve similar outcomes when compared with other populations (Christensen et al., 2018; Martin et

al., 2018). Additional research, especially in rural and suburban contexts, are needed to expand the field's understanding of HCV treatment experiences and associated needs for young adult PWID.

Even in a context with high access to HCV treatment through community-based opportunities targeting people who currently inject drugs, most did not engage. Conversations between individual research interviewers and the twenty-five who accepted referral but did not initiate HCV treatment signaled additional barriers, including the desire for youth-friendly community based clinical care. Notably, there are opportunities for improved linkage services for young adult PWID appropriate, which likely need to take into account the competing needs and priorities of transportation and housing. Further, discussion of the impact of HCV on health despite being asymptomatic or "feeling good" is needed. Better messaging to communicate how HCV infection affects one's health despite being asymptomatic delivered in a manner that is appropriate for youth is needed. If we are going to pursue a treatment as prevention approach to HCV elimination then innovative strategies to overcome barriers specific to young adult PWID are urgently needed (Zelenev et al., 2018).

Further, barriers to medical engagement reported in this study included the social stigmatization that people who inject drugs experience daily, as well as unstable housing, including homelessness, which San Francisco's young adult PWID experience disproportionately. On-site testing and treatment integrated into existing programs catering to PWID, including lockers for secure medication storage, have helped older PWID be cured through HCV therapy (Gray and Crouch, 2018) and could be replicated in youth focused settings. It is difficult to discern the influence financial compensation offered via the two research studies played for the five participants who accessed treatment. Additional research is needed to understand how to appropriately engage this population and others with unstable social environment in medical care.

#### 4.1 Public Health Implications

Our study provides preliminary evidence of successful HCV treatment among young adults who initiate treatment, but also identifies missed opportunities for linking young adult PWID to therapy. To put our results into context, of an estimated 16,393 people with HCV infection in San Francisco, 11,147 (68%) are PWID; an estimated 847 are under the age of 30 years (Facente et al., 2018). Nationally, young adult PWID are the fastest growing population infected with HCV (Zibbell et al., 2018). Collectively these findings signal an urgent need to address the competing needs of young adult PWID when delivering linkage services. Longitudinal studies, through consistent interaction with PWID, may offer another opportunity for early HCV diagnosis, transmission prevention, treatment linkage, and post-care follow-up.

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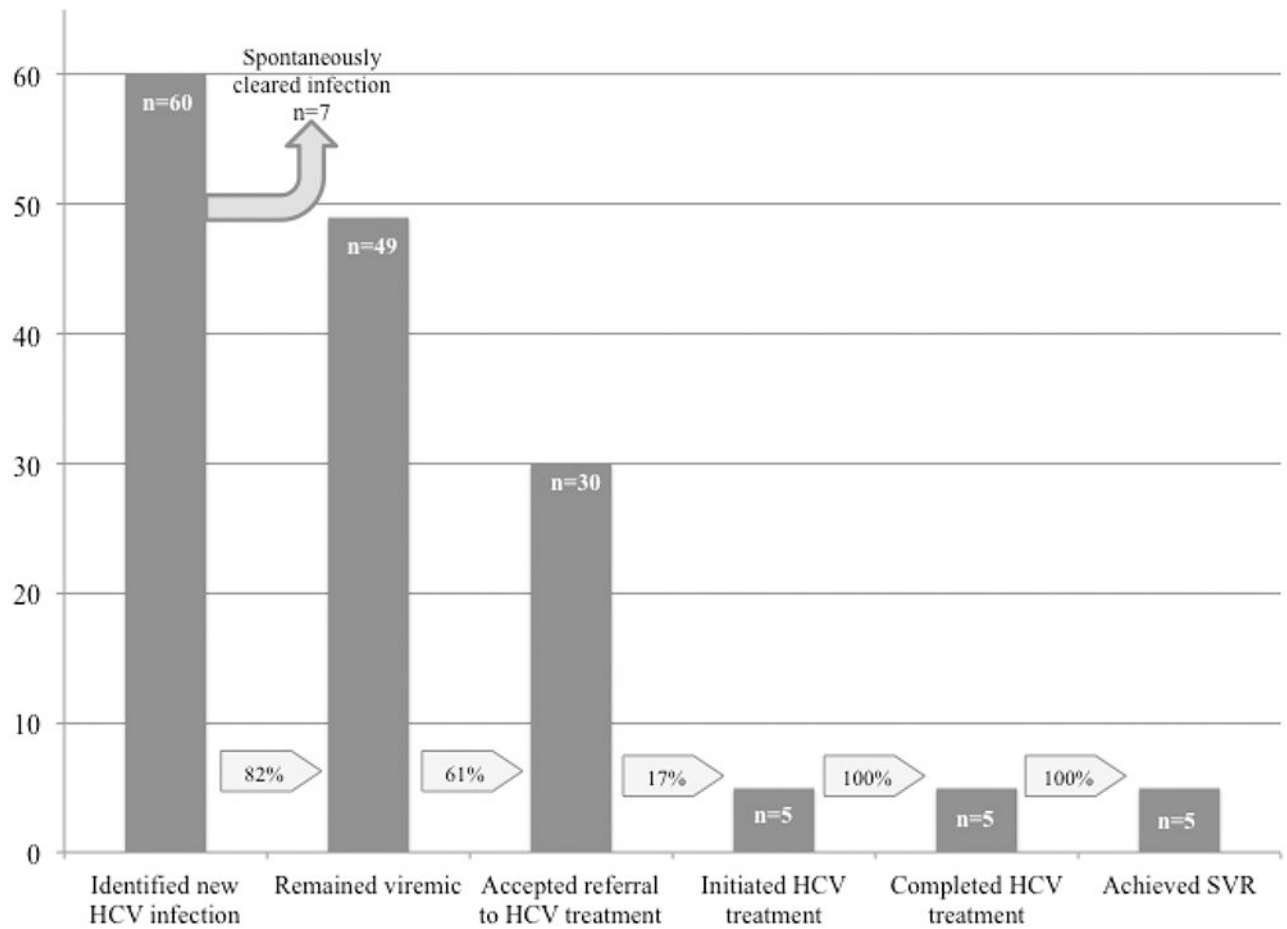
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### Highlights

- While only half accepted a treatment referral, all 5 who started therapy achieved SVR.





**Figure 1:** HCV cascade of care for young adult PWID between 2015 and 2018 in San Francisco, USA. Arrows between bars represents the proportion of persons in each step of the cascade from the persons in the preceding step. In addition to the 7 persons who spontaneously cleared infection, another 4 were lost to follow up after test disclosure.