Key Populations: Identification and Management of HCV in People Who Inject Drugs

Prevalence of HCV Among People Who Inject Drugs

Injection drug use (IDU) is the most common risk factor for HCV infection in North America and Europe, with an HCV seroprevalence of 18% to 88% depending on geographic location (Degenhardt, 2017) and duration of IDU exposure (Mateu-Gelabert, 2022); (Amon, 2008). In this section, the term people who inject drugs (PWID) includes individuals who are actively using drugs and those who have previously used injection drugs.

The first few years after an individual begins to inject drugs constitute a high-risk period during which the rate of HCV infection can exceed 40% (Maher, 2006). According to the National Survey on Drug Use and Health, heroin use has increased across the US among men and women, most age groups, and all income levels (Jones, 2015). IDU accounts for the majority of new HCV infections (approximately 70%) and is the driving force in the perpetuation of the epidemic. Given these facts and the absence of a vaccine against HCV, testing and linkage to care combined with antiviral treatment have the potential to decrease HCV incidence and prevalence (NAS, 2017); (Martin, 2013).

Recommendations for Screening and Treatment of HCV Infection in People Who Inject Drugs (PWID)	
RECOMMENDED	RATING
Annual HCV testing is recommended for PWID with no prior testing, or past negative testing and subsequent injection drug use. Depending on the level of risk, more frequent testing may be indicated.	IIa, C
Substance use disorder treatment programs and needle/syringe exchange programs should offer routine, opt-out HCV-antibody testing with reflexive or immediate confirmatory HCV-RNA testing and linkage to care for those who are infected.	IIa, C
PWID should be counseled about measures to reduce the risk of HCV transmission to others.	I, C
PWID should be offered linkage to harm reduction services including intranasal naloxone, needle/syringe service programs, medications for opioid use disorder, and other substance use disorder treatment programs.	I, B
Active or recent drug use or a concern for reinfection is **not** a contraindication to HCV treatment.	IIa, B

HCV Testing Among PWID

All individuals who currently inject drugs or have previously used injection drugs should be tested for HCV infection. Data

are limited regarding the optimal interval for repeat testing among individuals actively using drugs. An HCV-antibody test is recommended and if the result is positive, current infection should be confirmed by immediate HCV-RNA testing (see HCV Testing and Linkage to Care). This can be accomplished using phlebotomy for a combined reflex test performed by a laboratory, which is appropriate for clinical settings. In certain community settings, a point-of-care antibody test with an immediate blood draw or dried blood spot collection for a confirmatory HCV-RNA test may be implemented.

Among persons at risk for HCV reinfection after previous spontaneous or treatment-related viral clearance, HCV-RNA testing is recommended because an HCV-antibody test is expected to remain positive. Among persons with a negative HCV-antibody test who are at high risk for a new HCV infection due to current IDU, testing for HCV RNA or follow-up testing for HCV antibody is recommended if HCV exposure may have occurred within the past 6 months.

Integration of HCV testing services into substance use disorder treatment programs, needle/syringe service programs, and acute detoxification programs provide an opportunity for routine screening in this key population (Aronson, 2017); (Harris, 2010).

Linkage to HCV Care and Treatment Adherence

Treatment of HCV-infected PWID should ideally be delivered in a multidisciplinary care setting with services to reduce reinfection risk and manage the common social and psychiatric comorbidities in this population.

Regardless of the treatment setting, recent and active IDU are not absolute contraindications to HCV therapy. There is strong evidence from various settings in which PWID have demonstrated adherence to treatment and low rates of reinfection, countering arguments that have been commonly used to limit HCV therapy access in this patient population (Coffin, 2019); (Dore, 2016); (Hellard, 2014); (Aspinall, 2013); (Grebely, 2011). Modeling studies illustrate the high return on the modest investment of addressing this often-ignored segment of the HCV-infected population (Barbosa, 2019); (Fraser, 2018b); (Zelenev, 2018); (Martin, 2013b). Conversely, there are no data to support the utility of pretreatment screening for illicit drug or alcohol use in identifying a population more likely to successfully complete HCV therapy. These requirements should be abandoned because they create barriers to treatment, add unnecessary cost and effort, miss an opportunity to decrease HCV transmission, and potentially exclude populations that are likely to obtain substantial benefit from therapy. Instead, scaling up HCV treatment in PWID is necessary to positively impact the HCV epidemic in the US and globally.

Recent hepatitis C test-and-link programs have identified the use of patient navigators or care coordinators to be an important intervention in overcoming challenges to linkage to and retention in care (Coyle, 2019); (Ford, 2017); (Coyle, 2016); (Ramirez, 2016); (Coyle, 2015); (Trooskin, 2015). The Check Hep C program in New York City compared services delivered at 2 clinical care sites to 2 sites that linked patients to off-site care. Participants receiving clinical care co-located with testing services had higher odds of initiating treatment than those linked to off-site care (Ford, 2017). Ongoing assessment of efficacy and comparative effectiveness of this and additional strategies is a crucial area of future research for patients with chronic HCV. Replication and expansion of best practices and new models for linkage to HCV care will be essential to maximize the public health impact of newer HCV treatment paradigms.

HCV Treatment Among PWID

Clinical trials among PWID reporting current IDU at the start of HCV treatment and/or continued use during therapy demonstrate SVR12 rates approaching 95% (Grebely, 2018); (Dore, 2016). Moreover, high SVR rates among PWID are not limited to clinical trials but are also observed in clinical practice settings. A cohort study was conducted with 89 patients initiating HCV treatment between January 2014 and August 2015 at a primary care clinic in the Bronx, New York. Four patient groups were compared: no active drug use or medications for opioid use disorder (MOUDs); no active drug use with MOUDs; active drug use without MOUDs; and active drug use MOUDs. The study found that regardless of active drug or MOUD use, patients who received direct-acting antiviral (DAA) therapy at this urban primary care clinic achieved high HCV cure rates (SVR ≥95%) (Norton, 2017).

Dispensing DAA therapy within a program that provides MOUDs increases the likelihood of PWID engagement in HCV treatment (Falade-Nwulia, 2019). Importantly, MOUDs do not compromise HCV treatment outcomes. Similar SVR12 rates

are achieved by PWID engaged in MOUD use compared with individuals not engaged with such medications in clinical trials and cohort studies of various DAA regimens (Macías, 2019); (Dore, 2016); (Grebely, 2016); (Lalezari, 2015); (Zeuzem, 2015); (Feld, 2014). HCV-infected patients receiving MOUDs who were treated with elbasvir/grazoprevir had high rates of adherence to antiviral treatment and SVR12 rates >89% regardless of ongoing IDU (Dore, 2016). Similarly, an SVR12 of 97.4% was reported in a clinical trial evaluating ombitasvir/paritaprevir/ritonavir plus dasabuvir and ribavirin for 12 weeks among patients receiving MOUDs (Lalezari, 2015). Further, an analysis of a clinical trial evaluating outcomes of sofosbuvir/velpatasvir treatment in patients receiving MOUDs (n=51) compared to those not receiving these medications (n=984) demonstrated that MOUD use did not significantly reduce treatment completion, antiviral adherence, SVR12, or safety (Grebely, 2016).

Optimal models of HCV treatment among patients receiving MOUDs are still being evaluated. A recent trial conducted among PWID receiving MOUDs within 3 New York programs suggested that directly observed DAA therapy was associated with greater antiviral adherence than self-administered individual DAA treatment (86% versus 75%; p=0.001) (Akiyama, 2019). Importantly, opioid IDU and sharing has been observed to decrease following DAA HCV treatment (Artenie, 2020).

Recommendation for Testing for Reinfection in People Who Inject Drugs (PWID)

RECOMMENDED	RATING
At least annual HCV-RNA testing is recommended for PWID with recent injection drug use after they have spontaneously cleared HCV infection or have been successfully treated.	IIa, C

Reinfection

As HCV therapy is expanded to populations of PWID with high-risk behaviors for re-exposure, acknowledgement that HCV reinfection will occur in some individuals is critical, and appropriate strategies must be in place to maximize prevention of reinfection and offer retreatment for reinfection (Grebely, 2017). Importantly, the rate of HCV reinfection in the PWID population is lower (2.4/100 person-years) than the rate of incident HCV infection in the general population of PWID (6.1 to 27.2/100 person-years), although the rate of reinfection increases with active or ongoing IDU (up to 7.4/100 person-years) (Akiyama, 2019b); (Aspinall, 2013); (Grady, 2013).

Data suggest that reinfection is rare in drug users who clear HCV with therapy even if they continue to inject drugs provided steps are taken to minimize the risk. Studies of HCV reinfection in PWID have demonstrated rates of reinfection post SVR ranging from 1 to 5/100 person-years in patients who have ever injected drugs, increasing to 3 to 33/100 person-years in patients with continued injecting risk behavior (Midgard, 2016b); (Marco, 2013); (Grady, 2012); (Grebely, 2012); (Bate, 2010); (Grebely, 2010); (Currie, 2008); (Dalgard, 2002). Relapse into drug use has been associated with HCV reinfection after cure (Midgard, 2016b) while interventions that reduce drug use, such as utilization of MOUDs and mental health services, have been associated with reduced HCV reinfection risk (Islam, 2017). These services should be made available to PWID.

PWID found to be HCV reinfected should be retreated. Retreatment of a new reinfection should be as detailed in the Initial Treatment section. Increasing the HCV treatment rate among the PWID population would reduce numbers of new HCV and liver-related disease cases (Jiang, 2017). In a study that evaluated reinfection and injecting risk behavior following DAA therapy, participants on MOUDs for ≥3 months had a reinfection rate of 2.3/100 person-years, with a persistent reinfection rate of 1.6/100 person-years due to spontaneous HCV clearance in several instances. A reinfection rate of 4.2/100 person-years was found among those who reported IDU (Dore, 2017).

Harm Reduction

Harm reduction is a way of preventing disease and promoting health that meets people where they are, and provides the tools and information they need to keep themselves and those around them well (Logan, 2010). Harm reduction places drug use within the larger sociopolitical spheres of poverty, criminalization, and mental health. Accepting that not everyone is ready or able to curtail or stop high-risk behavior, harm reduction focuses on promoting a spectrum of scientifically proven, practical strategies for reducing the negative consequences of drug use and other high-risk behaviors. Harm reduction strategies include but are not limited to condom distribution; access to sterile injection equipment; utilization of MOUDs (such as methadone, buprenorphine and naltrexone); safe injection spaces; and overdose education and naloxone distribution. Heroin overdose deaths in the US increased 286% from 2002 to 2013 (Jones, 2015). Broad implementation of harm reduction strategies has the potential to significantly impact the HCV epidemic.

Medications for Opioid Use Disorder

Methadone, buprenorphine, and naltrexone are FDA-approved treatments for opioid use disorder with evidence from randomized controlled trials and real-world cohorts to support their effectiveness in reducing opioid use, improving mortality, decreasing criminal activity, and improving social functioning and retention in care (Tasillo, 2017); (Kampman 2015); (Volkow, 2014). Methadone is a long-acting opioid agonist that has the longest history in clinical use and is proven to reduce illicit drug use and improve social functioning (Mattick, 2009). Although methadone is effective, concern about diversion leads to methadone maintenance being highly regulated in the US, typically requiring daily visits to a dedicated dispensing clinic (Mattick, 2014). Buprenorphine-naloxone is a partial opioid agonist that also relieves withdrawal, and quells opioid craving. Multiple randomized trials support its effectiveness in reducing drug use and improving retention in care (Tasillo, 2017); (Volkow, 2017); (Kampman, 2015); (Volkow, 2014); (Mattick, 2014); (Moore, 2012); (Weiss, 2011); (Comer, 2010); (Jones, 2010); (Ling, 2010); (Lucas, 2010); (Mattick, 2009); (Kakko, 2007); (Fischer, 2006); (Jones, 2005); (Fudala, 2003); (Kakko, 2003); (Johnson, 2000); (Ling, 1998); (O'Connor, 1998); (Ling, 1996); (Johnson,1995). Buprenorphine-naloxone's major benefits include that it is a partial agonist which limits its overdose risk; coformulation with naloxone provides a deterrent from injecting; and it can be successfully prescribed in routine primary care settings (Korthuis, 2017); (LaBelle, 2016); (Fudala, 2003). Prescribing buprenorphine-naloxone requires 8 hours of training and registration with the US Drug Enforcement Agency and receiving a waiver from the Substance Abuse Mental Health Services Administration, which limits the number of providers (Stein, 2015). Naltrexone is an opioid antagonist that prevents the euphoric and respiratory effects of opioids, reducing cravings (SAMHSA, 2020). Naltrexone has low diversion potential and requires no special licensing for prescribers (Rudd, 2016). Further, it is available as a monthly injection. Naltrexone precipitates opioid withdrawal, however, and is therefore only initiated in opioid-abstinent patients.

Several reviews have identified MOUDs as effective in reducing illicit opioid use (Mattick, 2014); (Mattick, 2009) and opioid-related death and all-cause mortality (Sordo, 2017); (Degenhardt, 2009), and improving quality of life (Lawrinson, 2008); (Ward, 1999). Participation in methadone maintenance treatment has been shown to be protective against hepatitis C incidence among PWID, with a dose-response protective effect with increasing methadone exposure on hepatitis C incidence (Nolan, 2014).

Syringe Service Programs

Syringe service programs (SSPs) were developed to reduce the spread of bloodborne diseases among injection drug users. These programs provide PWID with sterile syringes and other equipment (cookers, filters, sterile water, alcohol swabs) to reduce the risk of bloodborne disease (eg, HIV and HCV) transmission associated with sharing injection equipment. These programs were developed in the 1980s and often include drug treatment referrals, peer education, and HIV prevention. Areas with greater syringe access through SSPs have lower rates of hepatitis C among PWID. A prospective study of PWID in New York City found a significant decline in HCV rates from 1990 to 2001, corresponding to an increase in the number of syringes distributed by SSPs during this period (Des Jarlais, 2005).

Overdose Education and Naloxone Distribution (OEND)

HCV treatment is a touchpoint with the care delivery system and should be used as an opportunity to mitigate the harms of drug use, especially overdose risk. Naloxone is a powerful opioid antagonist that reverses the respiratory depressive effects of opioids and is lifesaving to those experiencing opioid overdose (Wermeling, 2015). Expanding access to intranasal naloxone significantly decreases mortality at the community level (Walley, 2013). Many states have standing orders for intranasal naloxone, which allow providers to dispense naloxone directly to patients. When no standing order

exists or when it is not feasible to provide naloxone directly, providers should offer patients a prescription for naloxone to fill at a local pharmacy. Importantly, naloxone is not an opioid and carries no overdose risk, no dependency risk, and no risk of diversion. Naloxone is safe and effective and can be prescribed with confidence by HCV providers who do not treat addictions more generally.

Benefit of Treatment to Reduce HCV Transmission

Persons cured of chronic HCV no longer transmit the virus to others. As such, successful HCV treatment benefits public health. Several health models have shown that even modest increases in successful HCV treatment among PWID can decrease prevalence and incidence (Hellard, 2014); (Martin, 2013); (Martin, 2013b); (Durier, 2012). Models developed to estimate the impact of HCV testing and treatment on the burden of HCV at a country level reveal that large decreases in HCV prevalence and incidence are possible as more persons are successfully treated (Martin, 2015); (Wedemeyer, 2014). Elimination of HCV among PWID will also require scaling up harm reduction services (Fraser, 2018).

Last reviewed: December 19, 2023

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