TREATMENT IMPROVEMENT PROTOCOL (TIP) SERIES

Addressing Viral Hepatitis in People With Substance Use Disorders:

A Review of the Literature—Updates*

TIP 53

*This document is available online only (http://store.samhsa.gov) and supports TIP 53, *Addressing Viral Hepatitis in People With Substance Use Disorders.*

Treatment Improvement Protocol (TIP) 53,

Addressing Viral Hepatitis in People With Substance Use Disorders

Updated Findings From the Literature

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Introduction

The following updates are intended to keep current the literature review component of Treatment Improvement Protocol (TIP) 53, *Addressing Viral Hepatitis in People With Substance Use Disorders*, published in 2011. Literature searches are performed every 6 months; reviews are written every 6 to 12 months, depending on whether the search results produce relevant articles. The same search methodology used in developing the literature review for TIP 53 is used for the updates.

November 1, 2011, Through April 30, 2012

Articles that met the selection criteria for this update fall into the categories of general findings and hepatitis screening. For several categories of information covered in the TIP (chronic hepatitis evaluation, treatment, counseling for people with viral hepatitis, and adding or improving hepatitis services), no articles were published during this update period that met the selection criteria.

General Findings

Korthuis et al. (2012) surveyed 1,281 participants in the National Drug Abuse Treatment Clinical Trials Network. Researchers asked these individuals to self-report on numerous characteristics including sociodemographic status, substance use, risk behaviors, and hepatitis C virus (HCV) infection status. The investigators then used multivariable logistic regression to compare risky behaviors among those who reported being positive for HCV with those who reported being negative for HCV or who did not know their HCV status. The authors also wanted to determine if any of the characteristics related to HCV status awareness were associated with increased or decreased sharing of syringes or needles.

Of the 1,281 participants, 244 (19.0 percent) reported at baseline that they had used injection drugs in the past 6 months. Fewer than half (46.9 percent) of this subset reported that they always used a sterile syringe. In fact, 38.5 percent said they had shared syringes or needles with another person in the past 6 months.

Self-reported HCV status awareness was the independent variable of the analysis. Researchers asked participants the following question: "Have you ever been diagnosed with hepatitis C (yes, no, don't know)?" Of the 244 individuals who reported that they had used injection drugs in the past 6 months, 37.7 percent indicated they were positive for HCV. The multivariable analysis for this subset of participants revealed that those who knew they were positive for HCV more frequently practiced harm reduction behaviors such as obtaining sterile needles, cleaning needles with bleach, and avoiding alcohol intoxication compared to those who were negative for HCV or did not know their status. However, awareness of HCV positive status also was associated with increased recent sharing of syringes or needles compared to those who were negative for HCV or did not know their HCV status. The authors indicated that the latter finding has important implications for treatment programs and underscored the need for new approaches to implementing hepatitis C prevention efforts for those who use injection drugs and are seeking substance abuse treatment.

The study has some limitations. First, because all study participants were seeking or actively engaged in treatment at community-based treatment programs, these findings may not apply to the broader population of individuals who use injection drugs or those receiving treatment in other settings. Second, participants self-reported their HCV status. It is likely that more participants were positive for HCV and did not know it; however, the authors stated that a person's belief about their HCV status is, theoretically, more closely tied to injection behaviors than biologically confirmed HCV status. Third, researchers were unable to assess sero-sorting in this study. Finally, it is possible that the study's cross-sectional design limited the authors' ability

to infer causality. They admit it is possible that addiction severity rather than knowledge of HCV status may be related to increased sharing of syringes or needles; however, the authors stated that hepatitis C awareness remains an important marker for targeting harm reduction interventions.

Findings on Viral Hepatitis Screening

Between April and September 2009 Drobnik et al. (2011) recruited 503 participants from six community-based organizations in New York City to be tested with the OraQuick HCV rapid antibody test, which uses an oral swab and produces results in 20 to 40 minutes. Participants were also tested for HCV antibodies via enzyme immunoassay (EIA), the most common means of HCV screening. EIA requires a blood sample, the results take longer to obtain, and the process often poses a number of financial and logistical challenges for patients in high-risk populations. The authors also sought to assess whether using the rapid test in place of EIA would be feasible for community-based organizations that serve populations at high risk for HCV infection.

Research staff from the six community-based organizations who possessed training and experience in phlebotomy, HIV rapid testing, test counseling, and confidentiality administered the EIA tests. Study participants self-administered the oral swab rapid test after receiving pretest counseling and providing informed consent. After performing each set of tests, research personnel evaluated, via a 10-question survey, the ease of explaining the tests, administering the tests, and counseling participants for each type of test. Three weeks after specimen collection concluded, at least one research staff member from each of the six study sites participated in a focus group that was led by a city government official who had no previous involvement in the study. The focus group's discussion guide consisted of eight open-ended questions addressing:

- Their agency's HCV testing program components and resources.
- How the introduction of oral swab rapid testing might change program operations.
- The impact of rapid testing on clients.
- The types of clients for whom rapid (oral swab) testing or blood-based testing might be most appropriate.
- How the introduction of oral swab testing might create or eliminate barriers for clients, staff, and agencies.

Researchers found that OraQuick's accuracy was comparable to the EIA test. In 97.5 percent of cases, OraQuick and EIA results matched, and when the results of the two tests did not match, ribonucleic acid polymerase chain reaction (PCR) testing showed that the oral swab rapid test was more likely to yield a correct diagnosis than the EIA test.

Based on the surveys completed after the two tests were administered, research personnel preferred the rapid test over the EIA test for use in 98.5 percent of client visits over the course of the study. They found it easier to use and would be more likely to recommend rapid testing rather than EIA to clients in the future. Further, they indicated that the rapid test would be more appropriate for most clients compared to the EIA test. Focus group analysis revealed the following themes and experiences from research personnel:

- Phlebotomy constitutes a serious challenge for programs with limited resources. Such programs typically experience high staff turnover rates and a shortage of experienced phlebotomists. In addition, many clients do not like having their blood drawn, are worried that the sample may be used for unauthorized testing, or object to phlebotomy for cultural reasons.
- Many clients do not return to get phlebotomy test results. In fact, in this study only 52.4 percent of participants returned to get the results of their EIA test. (Staff did not share the results of the rapid test with clients because at the time of administration the rapid test had not yet received Food and Drug Administration approval.) Research personnel reported that they expend a great deal of time and effort to get clients to come back for test results. This challenge could be eliminated or significantly reduced by administering the test, sharing results with the client, and coordinating any necessary referrals in a single appointment.
- More clients would agree to allow rapid (oral swab) testing because they perceive it as less risky than a blood draw. Rapid testing also would make it possible to administer the test in nonclinical settings such as mobile vans and to reach more people who do not know their HCV status.
- Given that there is a 20- to 40-minute waiting period for results, the rapid test provides additional time for education and counseling, which research personnel indicated was as important as the test itself.
- The oral swab test eliminates the risk of staff exposure to blood-borne pathogens.
- It would be possible to administer HIV and HCV tests concurrently and get the results for both tests during the same client encounter.
- For some clients, the EIA test may be more appropriate, such as for immigrant populations with high rates of hepatitis B (identified through a blood test) or for clients who are convinced that the blood test is more accurate.

The authors concluded that both community-based organizations and the people they serve could benefit from the oral swab rapid test. HCV screening programs would be able to reach more individuals who are unaware of their HCV status, expand their outreach and screening efforts to other nonclinical settings such as mobile units, and facilitate client entry into mental health services, substance abuse treatment, or medical care. However, though the oral swab rapid test may allow more people to know their HCV antibody screening results more quickly than the EIA test, it will not eliminate the need for those who test positive to have followup PCR testing or medical care.

The study has some limitations. First, potential client benefits mentioned in the analysis reflect the perceptions of research staff—not the clients. Second, the experiences of participating research staff who work in New York City with a large population of individuals who use injection drugs may not be relevant to programs operating in less populated areas, to communities that have a smaller prevalence of injection drug use, or to other settings such as clinics or hospitals. Third, the authors were not able to precisely determine sensitivity of the oral swab rapid test. Finally, the study did not examine the costs of the two types of tests or the cost implications for programs that may choose to switch testing methods.

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May 1, 2012, Through October 31, 2012

Articles that met the selection criteria for this update fall into the categories of general findings, treatment services, vaccination, and coinfection with HIV. For other categories of information covered in Treatment Improvement Protocol (TIP) 53, no articles were published during this update period that met the selection criteria.

General Findings

Gelberg et al. (2012) tested 534 adults who were homeless who were either staying at shelters or attending meal programs around Los Angeles, CA. The researchers tested participants for hepatitis C virus (HCV), hepatitis B virus (HBV), and HIV infection. They found that 26.7 percent of participants were HCV positive. In addition, the predictors of infection supported the information in TIP 53—people who injected drugs had higher rates of HCV infection than those without a history of injection drug use (IDU). One-fifth of the respondents (20.4 percent) reported lifetime IDU. While the strongest predictor of infection was IDU, other predictors of HCV infection included noninjection drug use, history of incarceration, and having multiple tattoos. No rates were provided for HBV infection.

The most important finding of this study also supports the TIP—46.1 percent of those who were HCV infected were unaware of their infection. Most participants had never received counseling or education about HCV. Among participants who were aware of their HCV infection (i.e., they reported being told they had HCV and tested positive for HCV), 39.5 percent had been referred for HCV treatment, 5.2 percent had received medical care for HCV, and 3.1 percent were currently receiving medical treatment for HCV.

In another study that looked at drug use and HCV, Harrell, Mancha, Petras, Trenz, and Latimer (2012) identified subpopulations in a group of 552 people who used heroin and cocaine. The researchers attempted to identify in these populations associations among demographic characteristics, risky behaviors, hepatitis C infection, and HIV. The article focused much more on HIV than hepatitis C. The findings regarding hepatitis C follow:

- Individuals who primarily used injection routes for drug administration were more likely to have hepatitis C than those who did not inject drugs.
- People who used crack or ingested heroin nasally were less likely than those who injected heroin or used polysubstances to have hepatitis C.
- Of the 552 people in the study, 248 (50.9 percent) had HCV infection, and 43 (8.5 percent) had HIV.

Treatment Services

TIP 53 and the TIP 53 literature review discuss the lack of comprehensive testing and other health services for HBV and HCV infection in substance abuse treatment programs. A survey by Bini et al. (2012) found similar results. The researchers evaluated the continuum of viral hepatitis services offered by substance abuse treatment programs within the National Drug Abuse

Treatment Clinical Trials Network. They surveyed substance abuse treatment program administrators from around the country. Information was obtained from 269 programs; 89 of these were methadone maintenance treatment (MMT) programs. (Provision of healthcare services was done either onsite or through contractual agreement with other providers.)

Results of the survey pertinent to TIP 53 follow:

- More MMT programs (41.2 percent) tested patients for current HBV infection than non-MMT programs (10.4 percent).
- Screening patients for HCV was a service provided at 54.7 percent of MMT programs and 15.0 percent of non-MMT programs.
- Various tests for HBV were provided by 3.9 to 20.5 percent of programs.
- In addition to screening tests, various diagnostic tests for HCV (e.g., viral genotype) were provided at 4.7 to 6.2 percent of programs (both MMT and non-MMT programs).
- Hepatitis A virus (HAV) and HBV vaccination were offered to patients with HCV infection at 73.3 percent of MMT programs and at 65.9 percent of non-MMT programs.
- Slightly more than one-third of treatment programs (both MMT and non-MMT programs) ordered a complete blood count, serum chemistries, and liver function tests for new patients.

Exhibit 1 presents the survey information on HCV-related services provided by all treatment programs.

Exhibit 1 HCV-Related Healthcare Services Provided by All Treatment Programs, Onsite or by Contractual Agreement

HCV-Related Healthcare Service	**Percent (%)** ***N*=269**
Patient education	74.1
Patient risk assessment	71.9
HCV Counseling	58.9
Medical history and physical examination	50.0
HCV treatment monitoring	35.2
HCV biological testing	34.4
HCV treatment	28.9

Stein et al. (2012) performed a retrospective study that described the implementation and outcomes of a concurrent group treatment (CGT) program for HCV treatment. The CGT took place at an MMT program. The authors reviewed medical charts using a standardized review format to obtain data.

All 42 patients participating in the CGT had a history of opioid addiction, and 41 were receiving medication assisted treatment, either with methadone or buprenorphine. The participants were divided into two treatment groups according to type and duration of medication regimen, which was based on HCV genotype and HIV status. One group (*n*=27) received pegylated interferon

alpha 2a and ribavirin (Peg/RBV), and the other group (*n*=15) received Peg/RBV and a protease inhibitor (PI). Patients either received ribavirin as directly observed therapy (DOT) or took the medication on their own.

One hour of group HCV treatment was offered as an alternative to individual treatment to both groups. During the first half hour of the group session, patients completed a side effect inventory sheet. A provider conducted brief "individual visits" in a corner of the room that included:

- Taking vital signs.
- Obtaining weight.
- Discussing laboratory values, medication adherence, and new adverse effects.
- Injecting medications.
- Providing prescriptions.

The second half hour consisted of provider-led group discussions. Patients talked about their treatment experiences and side effects. Weekly discussions facilitated by medical staff during the group sessions provided basic information about HCV to participants and visitors.

The authors were encouraged by the results of the group of 27 participants and found the preliminary results for the group of 15 participants encouraging. CGT was generally acceptable to all patients, and none expressed discomfort with the group format.

The groups had high rates of patient retention and good treatment results, as measured by sustained viral response (SVR). The researchers stated that the CGT model may be effective in overcoming barriers to treatment and improving adherence and HCV treatment outcomes among patients enrolled in drug treatment programs. The researchers speculated that CGT produced promising results because it may enhance patient motivation and provide positive social peer support. This model may be particularly useful in treating people with a history of IDU or psychiatric problems or those at high risk for psychosocial instability. It may help providers closely observe patients. In addition, peers in the group are in a unique position to spot troubling behavior in other members of the group with IDU and psychiatric histories.

In another attempt at improving treatment, Bruce et al. (2012) developed a pilot program using modified-directly observed therapy (mDOT) for hepatitis C treatment in an MMT program. In this pilot program, patients were randomized to two groups. One group received HCV treatment as mDOT in the MMT program; the other group's participants were treated at a liver specialty clinic and took their medications on their own (self-administered therapy [SAT]). Randomization was based on HIV status and HCV genotype. As of publication, 21 subjects were enrolled. Of these, 10 of 12 patients participating in mDOT achieved early virologic response (EVR) measured at 12 weeks, and 6 of these 10 achieved SVR. Of the nine patients randomized to the SAT group, only four began treatment. Of these, three achieved EVR measured at 12 weeks, and one achieved SVR despite not completing the treatment. Providers also screened patients for mental disorders prior to starting and during treatment and referred them for care if needed.

The authors concluded that mDOT could be provided within an MMT program's existing staffing structure of nursing and medical staff. HCV-positive patients with co-occurring

substance use and mental disorders could be successfully treated for HCV in such recovery settings while receiving mDOT. However, considering the very small sample size, more research and replication of the intervention are needed.

Russell et al. (2012) assessed the impact of lifetime alcohol use on hepatitis C treatment outcomes in 451 privately insured members of an integrated healthcare plan who had HCV infection and no previous HCV treatment. Given the potential negative effects of alcohol use on liver function, combined with the fact that many patients with HCV have a history of moderate to heavy drinking, this line of research is an important one. The health plan's policy required a 6-month period of abstinence prior to initiation of HCV treatment. All patients were screened for substance use disorders (SUDs), and those with an active SUD were referred for treatment before being able to participate in HCV treatment. HCV treatment consisted of pegylated interferon-alpha and ribavirin (P/R).

A detailed drinking history was obtained from 259 (61.5 percent) eligible patients retrospectively using a computer-assisted personal interview. The interview obtained information on drinking patterns during four periods:

- Prior to HCV diagnosis
- Between diagnosis of HCV to initiation of HCV treatment
- During HCV treatment
- Conclusion of treatment to 6-month followup SVR test

Exhibits 2 and 3 present the pretreatment drinking histories from the interviews along with the SVR for each group.

Exhibit 2 Pretreatment Alcohol Drinking Patterns and SVR

Drinking Pattern*	***N* (%)**	**SVR (%)****
Abstaining	18 (7.1)	66.7
Moderate drinking	64 (25.0)	57.1
Heavy drinking	171 (67.9)	62.0

*National Institute on Alcohol Abuse and Alcoholism physician guidelines

**All genotypes

Exhibit 3 Pretreatment Abstinence (Excluding Lifetime Abstainers) and SVR

Time	***N* (%)**	**SVR (%)****
<6 months	70 (29.3)	57.1
6 months to 2 years	31 (13.0)	67.7
2–10 years	61 (25.5)	62.3
10 years or more	77 (32.2)	58.4

**All genotypes

Findings included:

- SVRs were obtained in 80.2 percent of patients with HCV genotypes 2 or 3 and in 45.1 percent of patients with genotypes 1, 4, or 6.
- The pattern of pretreatment drinking and total amount of alcohol intake were both unrelated to SVR rates.
- Abstaining from alcohol for less than 6 months immediately prior to treatment was related to lower SVR rates in people who drank moderately. This association was not found in individuals who drank heavily.
- HCV relapse after the end of successful treatment was unrelated to posttreatment drinking.
- More than 60 percent of patients stopped drinking when HCV was diagnosed, which could indicate one of the important health benefits of HCV screening.

A potential limitation of these findings is the accuracy of retrospective measures of patients' lifetime drinking patterns and the small sample size.

Vaccination

Ladak, Gjelsvik, Feller, Rosenthal, and Montague (2012) explored missed opportunities for vaccinating against HBV. They used data from the 2007 Behavioral Risk Factor Surveillance Survey. They culled data on adults at high risk for HBV infection and created a final study model based on data from 11,833 individuals. The researchers found that HIV testing was a predictor of receiving HBV vaccine. In addition, 121 people reported being tested for HIV at a drug treatment facility. Of these 121 people, 44 percent (n=57) received the HBV vaccine.

Coinfection With HIV

Pantalone, Hessler, Bankoff, and Shah (2012) examined health-related and psychosocial correlates of HIV/HCV coinfection in an HIV/AIDS clinic sample of men who have sex with men (MSM). The TIP and original literature review did not include extensive information regarding HIV/HCV coinfection; the summary of this article includes only information pertaining to HCV.

The researchers collected data from 171 men who were HIV positive and had a history of having sex with men. Participants provided information via a computer-assisted self-interview. Information collected included age, time since HIV diagnosis, diagnosis with or exclusion of HCV diagnosis, diagnosis with AIDS, probable transmission route, race, ethnicity, education, income, employment, relationships, disability status, psychological status (e.g., symptoms of depression, posttraumatic stress disorder [PTSD], anxiety), and health-related quality of life.

Thirty-two percent of participants were also infected with HCV—a high proportion for an outpatient clinic sample. Compared to participants infected with HIV alone (monoinfected), those coinfected with HIV/HCV were significantly more likely to report their suspected mode of

HIV transmission as IDU and were significantly less likely to mention HIV transmission via sex with men.

Both groups (monoinfected and coinfected men) had significant mental health issues, but those who were coinfected had higher rates of depression and more severe symptoms of PTSD than those who were monoinfected.

Other finding included:

- Both groups had the same perceptions of their health or physical functionality even though men who were both HIV and HCV positive had significantly lower CD4 cell counts on average.
- Self-reported adherence to HIV medications was higher in the HIV/HCV group than in the HIV-only group.
- Participants with HIV/HCV coinfection had more past-year emergency room visits than those with HIV alone.

From these results, the researchers suggested that medical and mental health providers be particularly observant to the mental health status of MSM who are HIV/HCV coinfected.

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October 31, 2012, Through April 30, 2013

Ten articles met the selection criteria for the Treatment Improvement Protocol (TIP) 53 literature review update for this period, including one meta-analysis. Review articles were not included in the text narrative; they often include articles that were reviewed in the original TIP literature review or subsequent literature review updates. A list of review articles that may be helpful to the reader are listed under "Review Articles of Interest."

Alcohol and Drug Use

Continued alcohol use can further damage a liver infected with hepatitis C virus (HCV). Hazardous drinking is a major barrier to receiving medical treatment for hepatitis C. Oser, Cucciare, McKellar, and Weingardt (2012) wanted to understand factors that may be associated with this hazardous drinking. If these factors are understood, healthcare providers may be able to modify those factors and decrease use of alcohol by people with HCV infection. The researchers used data compiled primarily from Department of Veterans Affairs outpatient mental health settings. The Alcohol Use Disorders Identification Test-Consumption (AUDIT-C) was used to assess alcohol use and typical weekly alcohol consumption. The HCV status of all veterans who reported hazardous drinking was determined. Of this group of veterans, 43 veterans were HCV positive, and 511 were HCV negative.

The researchers compared the drinking patterns of the HCV-positive and HCV-negative groups. Results are presented below.

- **Emotional or psychiatric symptoms.** Patients who were HCV positive differed significantly from patients who were HCV negative regarding use of alcohol and/or drugs to cope with emotional or psychiatric symptoms. A significantly greater proportion of HCV-positive patients used alcohol/drugs to cope with symptoms of posttraumatic stress disorder (PTSD) and depression and endorsed greater lifetime impairment associated with hazardous drinking. A significantly larger proportion of patients who were HCV positive (58.1%) reported using alcohol/drugs to cope with nightmares or flashbacks or to promote sleep compared with HCV-negative patients (40.7%). And, significantly more HCV-positive individuals reported alcohol/drug use to cope with stress or depression (83.7%) compared with HCV-negative patients (57.9%).

- **Alcohol use.** Compared with the HCV-negative group, patients who were HCV positive reported that changing their alcohol use was significantly more important, but they were significantly less confident in their ability to change their alcohol use.

- **Negative consequences.** Patients who were HCV positive reported significantly more lifetime negative consequences related to drinking than veterans without HCV. These included consequences of various types: physical (e.g., not eating properly), interpersonal (e.g., family had been hurt by the patient's drinking), social responsibility (e.g., failed to do what was expected), intrapersonal (e.g., felt guilty or ashamed), and impulse control (e.g., took foolish risks).

Reed et al. (2013) investigated injection drug use (IDU) among people with hepatitis C in an inner-city cohort. They sought to identify predictors and potential risk factors of active IDU among their target population and ran a 3-year longitudinal study, with follow-up at 12-month intervals. Participants (*N*=289) were recruited at medical clinics and were part of the Hepatitis C, HIV, and Related Morbidity study.

The researchers found that 49.1 percent (*n*=142) of the 289 participants reported active IDU at some point during the 3-year follow-up period. The researchers used both univariate and multivariate analyses. Univariate analysis showed that those slightly less likely to report IDU were male rather than female. Subjects younger than 40 years were significantly more likely to have used injection drugs. The following were associated with active IDU during the study period: history of incarceration, unmarried status, unemployment, homelessness, active hazardous alcohol use (not defined), cigarette smoking, and history of daily heroin use at baseline. A history of having received methadone treatment was related to active IDU. Although a history of mental disorders was associated with reported IDU, this association was not statistically significant. No association was found between HIV coinfection and active IDU.

After controlling for multiple factors using the multivariate model, four factors were found to be independently associated with any active IDU during the study period: unemployment, active hazardous drinking, active cigarette smoking, and a history of daily heroin use. The researchers considered three of these factors to be potentially modifiable: unemployment, active hazardous drinking, and active cigarette smoking.

At baseline, 63 percent reported at least two of these risk factors. Participants with any two of the modifiable factors were more than twice as likely to report active IDU than were those reporting one or no modifiable factor. Participants with all three modifiable predictors (15%) were more than three times as likely to report active IDU.

The researchers concluded that persons with HCV infection and a history of IDU need assistance with unemployment, alcohol use, and smoking to help them refrain from returning to IDU.

Adherence/Compliance With Hepatitis C Treatment

Dimova et al. (2013) performed a systematic review and meta-analysis of the literature on hepatitis C treatment completion and sustained viral response (SVR) rates in people who use drugs. They retrieved 36 useable studies. HCV treatment consisted of pegylated interferon and ribavirin. The studies comprised 2,866 individuals with a history of drug use; 38.2 percent were still actively using drugs. Approximately 60 percent of the patients were receiving substance use disorder (SUD) treatment during HCV medication therapy.

The authors calculated the pooled treatment completion rate as 83.4 percent. Factors affecting treatment completion rates varied by study. However, with pooled data the observations described below were made.

Some studies compared patients who received SUD treatment along with HCV treatment with groups not receiving SUD treatment during HCV therapy. These studies indicated that the higher the proportion of patients receiving SUD treatment, the higher the HCV treatment completion rate.

Factors such as HCV infection with genotype 1 or 4 and HIV coinfection were associated with a slightly lower treatment completion rate (80.0%), but genotypes 2 and 3 had higher completion rates (90.8%). For HCV monoinfection, the pooled rate was 87.0 percent, and the pooled rate for HCV/HIV coinfection was much lower at 67.9 percent. Additionally, the higher the proportion of males who were using drugs, the lower the treatment completion rate. After adjusting for HIV/HCV coinfection, gender, and SUD treatment, the reviewers found that support services (including needle exchange, counseling, educational interventions for HCV, case management, directly observed therapy, motivational interviewing, and peer support groups) during antiviral therapy increased treatment completion rates.

The authors calculated an SVR rate of 55.5 percent. Unlike treatment completion rates, there did not seem to be any differences in SVR rates between those receiving SUD treatment and those not receiving SUD treatment. SVR rate was affected by HCV genotype and HIV coinfection. For HCV genotypes 1 and 4, the SVR rate was 44.9 percent. For HCV genotypes 2 and 3, the SVR rate was 70.0 percent. For HIV coinfection, the SVR rate was 41.3 percent. The involvement of a multidisciplinary treatment team led to higher SVR rates among people who used drugs, but only after adjusting for genotype and HIV/HCV coinfection.

The authors recommended that people who are in SUD treatment be considered for HCV treatment under the same circumstances as people without histories of drug use.

Client Attributes

Cognitive Impairment

A small cross-sectional study looked at the neuropsychological (NP) performance impairments of people with HCV and/or HIV (Sun, Abadjian, Rempel, Monto, & Pulliam, 2013). The subjects were males under medical care who were not abusing drugs. The study subjects were categorized into three groups:

- HCV monoinfected (n=19)
- HCV/HIV coinfected (n=17)
- HIV monoinfected (n=14)

The study also had 28 control subjects.

The subjects were assessed for NP impairments covering seven domains:

- Attention working memory
- Executive function
- Fine motor function
- Information processing speed
- Verbal fluency

- Verbal learning/memory
- Visual learning/memory

The participants were evaluated for subclinical depression as well.

The NP test results were then converted into a global deficit score (GDS)—a single number that represented overall NP performance. Subjects coinfected with HIV/HCV had a higher mean depression score than controls and a higher mean GDS (i.e., more impairment) than people who were HCV monoinfected, HIV monoinfected, and the control subjects. Coinfection was associated with worse scores in attention working memory, executive function, fine motor function, verbal learning/memory, and visual learning/memory when compared with the control subjects. Within the monoinfected HCV group, viral load was associated with lower scores in attention working memory, executive function, and information processing speed.

The researchers wrote, "This targeted study indicates that coinfection in males is sufficient to push this group over the threshold into mild impairment and high viral load in HCV monoinfection may impact cognition" (Sun et al., 2013, p. 196). Implications for TIP readers are that counselors need to be aware of possible cognitive impairments when counseling clients with HCV/HIV coinfection or with high HCV viral loads.

Religiosity

Raghavan, Ferlic-Stark, Clarke, Rungta, and Goodgame (2013) wanted to determine the influence of patient religiosity (i.e., how religious a person is) on treatment outcomes of hepatitis C infection. The researchers wanted to know if self-reported religiosity was associated with:

- The desire for therapy.
- Completion or discontinuation of therapy.
- Frequency of SVR.

They did a prospective blinded cohort study. Participants were recruited from a gastroenterology clinic where patients were being evaluated for medication treatment for hepatitis C infection. In total, 87 patients completed questionnaires about their level or degree of religiosity. Of these, 82 provided a religious affiliation. Ten percent of the patients indicated that they had absolutely no regard for spirituality or religiosity. The researchers then categorized the patients into two cohorts according to the answers on the questionnaires: higher religiosity (n=38) and lower religiosity (n=49). The researchers compared several characteristics, including degree of depression, demographic data, pretreatment laboratory values, SVR, treatment completion, and response to treatment. The majority of patients were female (60%). Thirty-nine percent were African American, 31 percent were Hispanic, and 29 percent were Caucasian. African Americans and women had higher religiosity. The researchers followed the participants until 6 months after treatment.

The desire for treatment and completion or discontinuation of therapy were similar for both religiosity groups. SVR rates (3–6 months posttreatment) were similar for both groups, but males having higher religiosity had slightly better SVR than others with lower religiosity; however, due

to the large confidence interval, these findings should be interpreted with caution. The two groups were also similar in pretreatment liver chemistries and treatment compliance. Ethnicity did not affect response to treatment.

The only significant difference between the cohorts was in the depression category. The proportion of patients reporting depression at least once during the study period was much higher in the lower religiosity group (38.2%) than in the higher religiosity group (4.6%).

Medications

Mitchell, Memisoglu, and Silverman (2012) studied the effects of injectable extended-release naltrexone (XR-NTX) in a small cohort of patients with a high prevalence of chronic hepatitis C infection who were also receiving treatment for opioid dependence. A total of 250 patients (88.8% with a history of HCV infection) were randomized to 2 groups: monthly injections of XR-NTX or placebo. The patients were given standard liver chemistry tests at screening, baseline, and monthly for up to 6 months. For patients receiving XR-NTX who completed the 6 months of the study, any liver enzyme elevations were temporary; they returned to baseline levels despite continuing the XR-NTX. The authors concluded that XR-NTX is safe for some patients with opioid dependence who have mild to moderate chronic HCV infection.

McNicholas et al. (2012) used data from the Maternal Opioid Treatment: Human Experimental Research study. This study is a randomized clinical trial designed to examine the efficacy and safety of using methadone and buprenorphine to treat opioid dependence in pregnant women. The researchers examined the effects of both medications on liver enzymes throughout the course of pregnancy. The total number of participants was 172, and 38.4 percent (n=66) tested positive for HCV. Of the HCV-positive patients, 36 were receiving methadone, and 30 were receiving buprenorphine. The effects of the medications were assessed by using various blood chemistry tests (e.g., liver function tests, HCV tests). These tests were done every 4 weeks and once postpartum. The researchers found that women who were HCV positive had higher aspartate and alanine transaminases (two enzymes that may indicate liver inflammation) during the study compared with women who were HCV negative, regardless of which medication they were taking. All the women in the study (both HCV positive and negative) taking buprenorphine had lower levels of the liver enzyme gamma-glutamyl transferase than did women receiving methadone. The authors concluded that neither methadone nor buprenorphine seemed to have adverse effects on the liver for these study subjects.

Staff Attitudes

Talal et al. (2013) surveyed opioid treatment program (OTP) staff to assess current practices related to HCV treatment and management and staff attitudes toward onsite HCV treatment. This study was done in eight clinics in Central Harlem, NY. The majority of patients receiving methadone maintenance treatment (MMT) at these clinics were male, Hispanic, and HCV seropositive.

Eighty self-administered survey questionnaires were obtained from the 120 personnel with direct patient contact (e.g., clinic managers, counselors, nurses, physicians, physician assistants, social

workers). Of the respondents, 65 of 71[1] (92%) indicated that they discuss at least one HCV-related topic with patients at least once a year. About half the respondents stated they discuss HCV upon patient admission to the OTP. One-third indicated that they discuss HCV during monthly counseling sessions or when developing the treatment plan with the patient.

Respondents who discuss HCV at least yearly, however, stated that the follow-up by patients was generally poor. For example, the survey respondents stated that of the patients who are HCV seropositive, less than 25 percent accept referral or appear for their initial evaluation. The staff thought that the two most common reasons for the low rate of patient follow-up were fear of side effects of the HCV treatment and currently not feeling ill (due to the prolonged asymptomatic period of hepatitis C).

When asked about barriers to onsite HCV treatment, the two most frequent answers were the lack of infrastructure to support onsite treatment and patient reluctance to participate in HCV treatment. In addition, the majority of respondents wanted more HCV education to improve their skills in engaging and supporting patients in HCV treatment. Overall, respondents to this survey were supportive of providing additional treatment and support to patients in MMT who have HCV infection.

Testing and Screening for HCV

Frimpong (2013) examined data from the 2011 National Drug Abuse Treatment System Survey, in which a nationally representative sample of 200 OTPs participated. Frimpong considered these factors:

- The proportion of people with histories of IDU in an OTP
- The presence of staff who perform blood collection
- The availability of onsite testing services for HCV

Nearly 68 percent of these programs had the staff needed for HCV onsite testing, but only 34 percent offered it. If the OTP had a higher percentage of people with histories of IDU, the onsite testing percentage increased, but only slightly. These findings illustrate the gap in the availability of onsite HCV testing services and the human resources capacity of OTPs to provide that testing, even for those most at risk (e.g., people with histories of IDU).

Kim et al. (2013) devised a short questionnaire to identify acute cases of hepatitis C among newly incarcerated persons. The questionnaire took approximately 2 minutes to administer and was tested at two sites. It was used during routine intake medical evaluations (but was not administered by trained research staff). The questions were:

1. Have you ever been tested for HCV?
2. If so, what was your result?

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[1] Of the 80 respondents, not all individuals answered every question.

3. Did you ever use injection drugs?
4. If so, did you start in the last 12 months?
5. Did you ever share equipment?
6. If so, did you start in the last 12 months?

Inmates who reported a prior positive HCV test (23.2%) were referred to medical services. Inmates were considered high risk for acute HCV infection if they answered yes to questions 3 through 6. High-risk inmates received indepth medical evaluations to assess for acute HCV infection.

During the study period, 12,297 inmates were admitted to the 2 sites: 6,342 underwent health assessments within 7 days of admission, and 3,470 (55%) were screened using the questionnaire. Of the inmates who were screened, 171 (4.9%) were categorized as high risk for HCV infection. After being medically evaluated, 35 inmates were diagnosed with acute hepatitis C; the majority were female, White, and had a mean age of 29 years. The authors concluded that the questionnaire needs to be validated in other settings (e.g., detoxification centers, emergency departments, other healthcare settings, OTPs).

Review Articles of Interest

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3. Evon, D. M., Golin, C. E., Fried, M. W., & Keefe, F. J. (2013). Chronic hepatitis C and antiviral treatment regimens: Where can psychology contribute? *Journal of Consulting and Clinical Psychology, 81*(2), 361–374.

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May 1, 2013, Through October 31, 2013

Four articles met the selection criteria for the Treatment Improvement Protocol (TIP) 53 literature review update for this period. Review articles were not included in the text narrative; they often include articles that were reviewed in the original TIP literature review or subsequent literature review updates. Two review articles that may be helpful to the reader are listed under "Review Articles of Interest."

Adherence With Hepatitis Vaccination and Treatment

The TIP discusses case management, multidisciplinary teams, and using motivational approaches as means of improving hepatitis treatment outcomes. Two studies examined these strategies and provide some additional evidence that the strategies improve hepatitis prevention and treatment.

Care Coordination

Masson et al. (2013) conducted a randomized control trial of a care coordination program at methadone maintenance sites to see whether care coordination would improve adherence to hepatitis vaccination and treatment.

The researchers enrolled study volunteers at two methadone maintenance sites, one in New York City and the other in San Francisco, CA. Of the 489 people who agreed to participate, 68 percent were men. In addition, 59 percent tested positive for the presence of hepatitis C virus (HCV) antibodies, 41 percent had experienced homelessness in the past 6 months, and 47 percent were experiencing at least moderate depression.

The researchers randomized participants into two groups: the hepatitis care coordination program group (n=244) and a control group (n=245). Both groups received two sessions of individual counseling about HIV and hepatitis, one before they were tested for the diseases and one after. The counseling of those randomized to the coordination intervention included motivational interviewing techniques. The people in the care coordination group also had access to onsite vaccination for the hepatitis A and B viruses and enhanced case management for 6 months that also incorporated motivational interviewing strategies. In addition, case managers scheduled initial and follow-up appointments for HCV evaluation and helped clients get psychiatric care, alcohol treatment, legal assistance, and social service entitlements. The people in the control group were referred to offsite hepatitis A and B vaccination and HCV evaluation services.

When the care coordination and the control groups were compared, the participants in the care coordination program were far more likely to have received the first dose of the three-dose series vaccine against the hepatitis A and B viruses 30 days after being referred for vaccination than were those in the control group (77% vs. 12%). The participants in the care coordination program were also more likely to get an HCV evaluation within the 6-month period of active case management (65% vs. 37%).

This study was conducted at methadone maintenance programs linked to academic medical centers, so the results may not be generalizable to other treatment settings. The authors also

noted that further studies need to be done to see how this case coordination program would affect HCV care beyond the initial evaluation.

Multidisciplinary Group Visits

Ho et al. (2013) conducted a pilot study to see how multidisciplinary group visits would affect adherence to treatment for HCV infection among people with mental illnesses, substance use disorders, and housing instability.

The study was conducted at a clinic in San Jose, CA, that serves several thousand people, most of whom have histories of homelessness, substance abuse, or mental illness, or various combinations of the three. People who receive primary care at the clinic are routinely screened for HCV; those who had a detectable HCV viral load and were willing to be treated for HCV infection were invited to participate in the study. Of those who started treatment, all had a history of a substance use disorder, most (77%) had a mental illness, and a sizable minority (40%) had a history of homelessness. Two-thirds of the participants were men, and their average age was 49.

The weekly group visits were an hour long and were conducted jointly by a primary care physician, a psychologist, and a registered nurse. Before HCV treatment, patients were assessed for mental health, substance abuse, housing, and social support. If a patient was considered unstable in any of those areas, a treatment plan was drawn up to address the problem. Once the area of concern was stabilized, the patient could become eligible for HCV treatment. Prior to treatment, patients were also required to attend 75 percent of their group visits for approximately 2 months. Thirty of the 76 people who participated in the group visits started HCV treatment. Patients were assigned to standard courses of pegylated interferon and ribavirin (48 weeks for those with genotype 1 infections and 24 weeks for those with genotypes 2 and 3).

Medication adherence and virologic response were the two primary outcomes measured. Medication adherence was measured by attendance at group meetings, self-report, and review of refill history in pharmacy records. Measurements of virologic response included end-of-treatment response (absence of HCV ribonucleic acid by qualitative analysis) and sustained virologic response (undetectable viral load 6 months after treatment end date).

The adherence outcomes showed that 77 percent of the patients attended more than 80 percent of the recommended group visits, and 80 percent reported taking at least 80 percent of their prescribed doses. Twenty-four patients in the study completed a full course of HCV treatment.

This study was a pilot study and has the limitations typical of such studies, including a small number of participants and no comparison group.

Hepatitis E Virus Prevalence

Mahajan et al. (2013) assessed the prevalence of the hepatitis E virus (HEV) among San Diego County, CA, residents, ages 18–40, who inject drugs. This study used data collected from a study of HCV infection prevalence among San Diego County residents who had injected drugs in the previous 6 months. Of the 508 people in the study, most were men (72%), White (55%),

experiencing homelessness (59%), and had a history of incarceration (76%). Many tested positive for antibodies to hepatitis A (38%), hepatitis B (40%), and hepatitis C (26%).

The test for Immunoglobulin G (IgG) antibodies to HEV was positive for 14 (2.7%) of the study volunteers. Other studies of similar populations have found an HEV prevalence of between 5 and 23 percent. However, as the authors explained, data from previous research suggest that older age is a risk factor for HEV infection among people who inject drugs in countries where the background rate of infection is relatively low. The average age of the volunteers for this study was 29, and when the authors used bivariate logistic regression to identify risk factors associated with HEV infection, the only associated factor was being 30 or older.

This study has several limitations. Most of the comparisons between the study participants who tested positive for HEV and those who tested negative did not reach statistical significance, so aside from age, no risk factors for HEV infection could be identified. The researchers did not have access to information about important exposures, such as travel to areas where HEV infection is common, and HEV genotype, which can be an important clue to how the virus was contracted.

Educational Sessions

Dunn et al. (2013) tested whether a 1-hour educational session improved the understanding of HIV and HCV transmission, prevention, and treatment among people who abuse prescription opioids. The researchers also assessed changes in self-reported risk behaviors.

The study was conducted as part of a randomized clinical trial of buprenorphine tapering as a detoxification strategy for adults dependent on prescription opioids. The trial was conducted at an outpatient research clinic in Burlington, VT, and volunteers were recruited through newspaper ads and fliers. The eligibility requirements included being 18 or older, meeting the diagnostic criteria for opioid dependence, providing an opioid-positive urine sample, and being willing to undergo detoxification. Of the 54 people included in the study, 70 percent were men, and 98 percent were White. Most (70%) indicated that oxycodone was their primary drug of abuse, and most (70%) reported that intranasal was their primary route of opioid administration.

The education session, conducted by a master's level therapist, consisted of feedback on questionnaires the study participants had completed before the session, a short video on HIV/AIDS, and pamphlets, including three on hepatitis. Before and immediately after the education session, the study participants filled out a standard 50-item questionnaire on HIV/AIDS and a 15-item questionnaire on HCV developed by the researchers. The questions could be answered true, false, or don't know. (The "don't know" option has been shown to reduce guessing.)

The study participants answered, on average, 47 percent of the HCV questions correctly before the educational session. Afterward, they answered 84 percent correctly. The percentage of correct answers to HIV/AIDS questions also increased after the educational session but not by as much. The authors noted that the HIV/AIDS scores before the educational session were already high, so there wasn't as much room for improvement.

The risky behavior aspect of the study included four sets of questions delivered before and after the education session. Before the education session, 54 percent of the study participants indicated they were likely to use a condom the next time they had sex. Afterward, 62 percent said they would. No other changes to answers to the questions about risky behavior reached statistical significance.

The limitations of this study include the lack of a control group, the small sample size, and the homogeneity of study volunteers. People were asked their HIV status but not their HCV status, and no testing was done, so the study could not address whether knowledge or risk behaviors changed depending on disease status. The researchers noted that the knowledge questionnaires have not been statistically validated. Finally, the study was not designed to track whether people retained the knowledge they gained in the educational session.

Review Articles of Interest

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