Published in final edited form as:

J Addict Med. 2014 ; 8(1): 25–32. doi:10.1097/ADM.0000000000000001.

Characteristics and Impact of Methamphetamine Use in Patients With Chronic Hepatitis C

Dana E. Riley, BA, Lin Liu, PhD, Benjamin Cohen, MD, Shannon Robinson, MD, Erik J. Groessl, PhD, and Samuel B. Ho, MD

Departments of Medicine (DER, BC, SBH), Health Services Research and Development (LL, EJG), and Psychiatry (SR), VA San Diego Healthcare System, San Diego, CA; and Departments of Family and Preventive Medicine (LL, EJG), Medicine (BC, SBH), and Psychiatry (SR), University of California, San Diego.

Abstract

Objectives—Methamphetamine (MA) use has increased in the United States in the last 20 years and is a risk factor for hepatitis C virus(HCV) infection. The purpose of this study was to determine the characteristics and HCV infection outcomes of patients with a history of MA use.

Methods—Subjects consisted of newly entered patients in the Veterans Affairs (VA) HCV registry at a single VA medical center from January 1, 2004, to June 30, 2004, and from January 1, 2007, to June 30, 2007. Univariate and multivariate analyses related to HCV infection antiviral treatment outcomes through 2010 was performed.

Results—A total of 198 consecutive eligible HCV registry patients were analyzed, and 40% had a history of MA use. Of patients with MA use history, 46% (36/79) had active use (within 6 months) at initial contact. Active MA users were significantly younger (mean age, 45.5 years), with more concomitant drug use (86%), compared with patients without MA use (mean age, 53.5 years; 42% minority; 29% other drug use). Overall, 71% of the 198 patients reported a history of problematic alcohol use, and 47% of those reported active abuse. Logistic regression analyses indicated that MA use did not significantly adversely affect antiviral treatment initiation, completion, or sustained virological response rates compared with that in patients without MA use. Active alcohol users had lower treatment initiation than patients without alcohol use.

Conclusions—MA use is common in recent US veterans with HCV infection and occurs in younger patients with polysubstance use. Prior history or active MA use does not seem to adversely affect HCV infection clinic treatment compared with that in HCV patients without MA use.

Keywords

alcoholism; depression; hepatitis C; methamphetamine; pegylated interferon alfa; substance use disorders

Substance use and psychiatric disorders are considered to be common among patients with hepatitis C virus (HCV) infection (Yovtcheva et al., 2001; Cawthorne et al., 2002; El-Serag et al., 2002; Nguyen et al., 2002; Sylvestre et al., 2004; Bini et al., 2005). These disorders are often cited as barriers to receiving antiviral therapy and may complicate tolerance and adherence to antiviral treatments (Ho et al., 2008). Although substance use disorders (SUDs) seem to be common in this population, there has been minimal examination of the type of substance use and impact on HCV-related outcomes in the clinical setting.

Methamphetamine and amphetamine-type stimulant (MA) use has increased in the United States in the last 20 years and is a risk factor for HCV infection. Globally, North America is second to East and Southeast Asia in prevalence of amphetamine users, with an estimated 3.92 million current users in North America (United Nations Office on Drugs and Crimes [UNODC], 2012). After marijuana, amphetamine-type stimulants are the second most widely used group of illicit drugs worldwide (UNODC, 2012). In the 1980s, law enforcement patterns and the influx of Mexican criminal elements shifted the center of MA distribution to San Diego, and subsequently, the MA “epidemic” spread throughout the Western and Midwestern United States (Anglin et al., 2000). Nationwide, the number of new MA users increased by 250% between 1996 and 2001 (4.8 million to 12 million) (Rawson et al., 2002). In California, statewide admissions for MA abuse rose from 8.4% in fiscal year 1992/1993 to 34.6% in fiscal year 2004/2005, a 4-fold increase over the 13 years (Anglin et al., 2007). However, in 2008, the National Survey on Drug Use and Health documented an approximately 50% decrease in active MA users aged 12 years and older between 2006 and 2008 in the United States (National Institute on Drug Abuse, 2010).

Because of the fact that MA is often injected using unsafe methods and contributes to high-risk sexual and other behaviors, hepatitis C is frequent among MA users. Studies of MA user populations have reported that 15% to 32% have chronic HCV infection (Cherner et al., 2005; Letendre et al., 2005; Gonzales et al., 2006). MA use disorder can be particularly severe and may be expected to negatively impact on motivation and compliance with hepatitis C care. The progression from initial MA use to regular use is accelerated, particularly compared with other stimulant use (Gonzalez Castro et al., 2000; Brecht et al., 2004). This is thought to be due to the synergistic interactions of the behavioral, social, and psychological effects of the drug. Long-term MA use causes structural and functional changes in the areas of the brain associated with memory and emotion (London et al., 2004; Thompson et al., 2004; Berman et al., 2008). Furthermore, because of the unique cognitive and emotional effects of MA use disorders and the unique lifestyle and backgrounds of MA users, treatments designed for other types of substance abuse may not be particularly effective for these patients. Therefore, it may be expected that these factors may impact on MA user's ability to understand the consequences of HCV infection, accept referral for hepatitis C care, initiate hepatitis C treatment, and adequately follow through with this treatment.

In 2010, the global prevalence of HCV infection among injection drug users was 46.7%, amounting to approximately 7.4 million users infected with HCV (UNODC, 2012). Consequently, MA users are at a higher risk for contracting HCV infection, yet no data exist

regarding the potential impact of MA use or dependence on HCV patients in terms of compliance with HCV infection evaluation and treatment. The purpose of this study was to describe the prevalence of MA use in HCV clinic patients, determine the characteristics of MA users with HCV infection, and determine the HCV-related outcomes of these patients. Understanding the characteristics of HCV patients with active or previous MA use may enable targeted treatments within hepatitis clinics that take into account the special needs of these patients.

METHODS

Patients

Subjects consisted of newly entered patients in the Veterans Affairs (VA) HCV registry from January 1, 2004, to June 30, 2004, and January 1, 2007, to June 30, 2007, who were eligible for receiving antiviral therapy. The HCV registry is a record of all HCV cases in the local VA system, identified daily by new HCV antibody positivity or International Classification of Diseases, Ninth Revision, diagnosis. These 2 periods of time in 2004 and 2007 were chosen to compare whether there were any changes in practice patterns over time and also to allow for determination of treatment outcomes. Retrospective computerized record review was conducted on all patients newly identified and added to the VA HCV registry over the first, 6-month period of both 2004 and 2007. A patient was considered enrolled in the study if he was identified by the VA HCV registry and was referred to and made an appointment for an initial screening visit with the HCV clinic. Data were recorded using standardized data collection forms and indicated patient age, race, substance use history, psychiatric history, HCV clinic referral, clinic attendance, liver biopsy, and antiviral treatment outcomes through 2010. Patients who were considered ineligible for antiviral treatment were excluded and consisted of patients who had end-stage liver disease or other severe illness, died within a year of identification, were enrolled in an HCV infection treatment research protocol, had an undetectable viral load, or had previously started or were currently receiving antiviral treatment for HCV infection. An illness was considered severe if the patient died within a year of entry into the HCV registry because of this illness.

Definitions

All patients who had been enrolled in HCV clinic were routinely screened using standardized self-report questionnaires as part of standard care. Alcohol use was assessed using the Alcohol Use Disorders Identification Test–Consumption (AUDIT-C) (Bush et al., 1998). An AUDIT-C score of 4 or more points was selected to indicate a high likelihood of hazardous use or dependence and has been previously shown to have a sensitivity of 0.86 and a specificity of 0.72 for detecting medically hazardous alcohol use, and abuse and dependence, in a male VA population (Bush et al., 1998). In a general medical population, an AUDIT-C score of 4 or more points has been shown to have a sensitivity of 0.93 and a specificity of 0.66 for detecting medically hazardous use, abuse, and dependence (Rumpf et al., 2002). The AUDIT-C has been shown to be more sensitive for detecting medically hazardous drinking and active drinking than the commonly used Cut Down, Annoyed, Guilty, and Eye Opener questionnaire (Bradley et al., 1998). Alcohol use was categorized as nonproblem use versus problem use for active alcohol users. *Nonproblem use* was defined as

“no more than two drinks per day for men and one drink per day for women and no more than four drinks on any one occasion for men or three drinks on any one occasion for women,” as specified in the National Institutes of Alcohol Abuse and Alcoholism's “Physicians’ Guide to Helping Patients with Alcohol Problems,” which was in use at the time when patients were in HCV clinic and at the time of study initiation (National Institute on Alcohol Abuse and Alcoholism, 1995). Problem use was considered any use greater than these limits.

Use of illicit drugs other than alcohol was evaluated with an abbreviated version of the Drug Use Questionnaire. This questionnaire detects nonmedical drug use both in the past and within the last 6 months. The Drug Use Questionnaire is positive if the patient endorses at least 1 of the following: recent or active drug use, an item related to ever having used injection drugs, or past treatment for alcohol or chemical dependency. Any positive score resulted in examination of the medical record for additional substance use history. Data collected for substance use included marijuana, heroin, cocaine, MA, other drug use, and alcohol. Other drug use included opiates, inhalants, solvents, and sedatives. Patients were categorized as a MA user if they had any documented history of MA use in self-report questionnaires or in clinic notes. This categorization did not require a Diagnostic and Statistical Manual of Mental Disorders diagnosis in the medical record for MA use or dependence, but a record of MA use must have appeared in the clinic notes or questionnaires. Data for the other illicit substances listed earlier were categorized in the same manner. Alcohol and drug use were categorized into the following 3 categories: (1) no use reported or nonproblem use for alcohol, (2) active use included use within 6 months before initial enrollment in HCV clinic, (3) inactive use included any use greater than 6 months before enrollment. Psychiatric histories were categorized as having a documented diagnosis of either depression or “other psychiatric conditions.”

The following elements related to HCV infection evaluation and treatment outcomes were recorded: (1) recommendation for antiviral treatment, (2) initiation of antiviral treatment, (3) completion of antiviral treatment, and (4) virological outcome of treatment (sustained virological response (SVR) or no SVR). Patients were categorized as “no show” if they did not attend any HCV clinic appointments subsequent to the initial enrollment. Patients were considered “lost to follow-up” if they were initially evaluated in HCV clinic but then failed to continue with recommended appointments. Patients were considered to have “active medical conditions” if they had comorbid medical conditions at their initial HCV clinic appointment.

Statistical Analysis

Descriptive statistics were used to summarize patient characteristics by the 3 types of MA use (active use in last 6 months, inactive use, never used). Differences in patient characteristics among the 3 types of MA use were evaluated by the Kruskal-Wallis test and the Fisher exact test. If the test result was significant, pair-wise Wilcoxon rank sum test and pair-wise Fisher exact test with Hochberg adjustment for *P* values were performed. The associations between patient characteristics and treatment initiation were assessed by simple logistic regression. To study the association between MA use and treatment initiation, we

performed simple logistic regression analysis first and then multivariable logistic regression with adjustment for potential covariates. If a patient's characteristic was significantly associated with treatment initiation and also significantly different among MA use ($P < 0.10$) in univariate analysis, we included it as a covariate in the multivariable logistic regression model. Backward model selection for main effects in the final model was performed. The variable with the largest P value was removed from the model at each step and likelihood ratio test was used for model comparison. Only variables with $P < 0.10$ were kept in the final model. The Cook statistics and leverages were used to assess the influence of individual observations. The final model was rerun by excluding influential observations and compared with the final model on the basis of all data. The associations between MA use and other treatment aspects, including treatment recommendation, treatment completion, and treatment outcome SVR, were also assessed using the Fisher exact test and simple logistic regression. $P < 0.05$ indicates a statistical significance, and $P < 0.10$ indicates a marginal significance. Analyses were performed using the statistical package R (version 2.14.1).

This study was approved by the institutional review board of the University of California, San Diego, and the VA San Diego Healthcare System and the Research and Development section of the VA San Diego Healthcare System.

RESULTS

MA Patient Characteristics

From January to June of 2004, 201 consecutive new cases were entered into the local VA HCV registry. Of these, 29 were excluded on the basis of severe illness, severe end-stage liver disease, prior HCV infection treatment, or current care at an outside facility, leaving 172 new patients for further analysis. An additional 28 patients were removed from analysis because of an undetectable viral load, which made HCV infection treatment unnecessary at that time. Of the remaining 144 patients, 37% (53/144) had a history of MA use. From January through June of 2007, 91 consecutive new cases were entered into the local VA HCV registry. Of these patients, 35 were excluded because of the presence of severe illness, severe end-stage liver disease, prior HCV infection treatment, current care at an outside facility, or enrollment in a HCV research protocol. Two patients were excluded because of an undetectable viral load, leaving 54 patients for analysis in the 2007 cohort. In this cohort, 48% (26/54) of patients reported a history of MA use. In combination, 198 new HCV cases were analyzed among the 2004 and 2007 cohorts, and 40% of patients had a history of MA use. When looking at both cohorts, 46% (36/79) of patients with a history of MA use had documented active MA use at initial contact with the HCV clinic. No significant differences were observed between the 2004 and the 2007 cohorts in regard to demographic data and numbers within each substance use group, and therefore, the cohorts were analyzed together.

Significant differences were found in age, race, other psychiatric disorder, and genotype test among different MA users (Table 1). Further pair-wise comparisons showed that active MA users (45.5 years) were significantly younger than both non-MA (53.5 years; $P < 0.0001$) and inactive MA users (50.4 years; $P = 0.003$). Also, more active MA users had HCV genotype 2 or 3 (33.3%) than non-MA users (11.8%; $P = 0.03$) and inactive MA users

(16.3%; $P = 0.051$). Marginal significance was found from pair-wise comparisons in race and “other psychiatric conditions.” A greater percentage of the white patients reported active MA use (28/123 or 22.8%) than African American patients (5/41 or 12.2%) and Hispanic patients (3/26 or 11.5%). More active MA users had other psychiatric conditions than non-MA users (63.9% vs 40.3%; $P = 0.064$). There was no significant difference in distribution of sex, depression, and cohort among different groups of MA and non-MA users.

We also studied the active use of marijuana, cocaine, alcohol, and “heroin and other drugs” (any illicit drug, excluding MA, marijuana, cocaine, and alcohol) separately, and any active drug use (any illicit drug, excluding MA and alcohol). Significant differences in other types of drug use (marijuana, cocaine, alcohol, and any drug use) were found among different MA users (Table 1). Further pair-wise comparisons showed that active MA users were more likely to be active marijuana users (61.1% vs 27.9% and 9.2%; P s < 0.0001), active cocaine users (38.9% vs 11.6% and 15.1%; P s < 0.005), and any active drug users (86.1% vs 37.2% and 28.6%; P s < 0.009) than inactive MA and non-MA users. Active MA users were more likely to be active alcohol users (66.7% vs 36.1%; $P = 0.02$) than non-MA users. The association between MA use and heroin and other drugs use was marginally significant ($P = 0.07$).

Antiviral Treatment Outcomes

Antiviral treatment offer, initiation, completion, and the numbers of patients with SVR are indicated in Table 2. Overall antiviral treatment offer and initiation rates were low (25.3% referral and 17.7% initiation for total group). Active cocaine users, active heroin and other drug users, and active alcohol users had the lowest treatment initiation rates (8.1%, 11.1%, and 9.8%, respectively).

For clarity, we have presented in Table 3 the univariate analysis showing no significant difference in proportions of patients with treatment offer, treatment initiation, treatment completion, and SVR among the 3 types of MA users. Treatment initiation rates were 22.2%, 20.9%, and 15.1% ($P = 0.46$) in active, inactive, and non-MA users, respectively; and treatment completion rates were 11.1% for active, 14.3% for inactive, and 8.5% for non-MA users ($P = 0.51$). However, among those who initiated treatment, the final SVR rates were similar regardless of MA usage, with 4 of 8 (50%), 4 of 8 (50%), and 9 of 17 (53%) in active, inactive, and non-MA users, respectively (Table 3).

From simple logistic regression analysis, we found that active alcohol users were significantly less likely to have treatment initiated (odds ratio [OR] = 0.34; 95% CI, 0.14-0.85; $P = 0.02$) than nonproblem alcohol users (Table 4). Any active drug users were also significantly less likely to have treatment initiation (OR = 0.38; 95% CI, 0.14-0.99; $P = 0.048$) than nondrug users. We also found marginally significant associations of treatment initiation with cohort, cocaine use, and heroine and other drug use. Subjects registered in 2007 were more likely to have treatment initiated (OR 2.05; 95% CI, 0.95-4.04; $P = 0.07$) and active cocaine users were less likely to have treatment initiated (OR = 0.31; 95% CI, 0.09-1.08; $P = 0.07$) than noncocaine users. Active heroin and other drug users were less likely to have treatment initiation than patients with no other drug use (OR = 0.26; 95% CI, 0.06-1.18; $P = 0.08$).

From multivariable analysis, we found that overall MA use did not significantly adversely affect treatment initiation rates (Table 4). There was a trend for active MA users to be more likely to have treatment initiated than non-MA users, but it was marginally significant (OR = 2.48; 95% CI, 0.91-6.78; $P = 0.08$). In contrast, active alcohol users were significantly less likely to have treatment initiated than nonalcohol users (OR = 0.27; 95% CI, 0.10-0.70; $P = 0.01$). Excluding influential observations from the final model, results stayed similar.

Reasons for not initiating antiviral treatment in patients with history of MA and/or active MA use ($n = 62$) are listed in Figure 1. Most patients did not receive antiviral treatment because of reasons related to no show or nonattendance and lost to follow-up for scheduled HCV clinic appointments. Recent active drug and/or alcohol use were often considered cofactors in clinic nonattendance. Patient refusal or preference was also a key factor in noninitiation of antiviral treatment.

DISCUSSION

Current National Institutes of Health (2002) and professional guidelines call for increased access to antiviral therapy for HCV patients with substance use and psychiatric comorbidities (Garcia-Tsao and Lim 2009; Swan and Curry 2009). Within recent years, amphetamine-type stimulants have become the second most widely used group of illicit drugs worldwide (UNODC, 2012). To date, little is known about the characteristics of patients with MA use and chronic hepatitis C. Furthermore, there is considerable uncertainty about how best to identify, monitor, and manage patients with chronic HCV who have active substance use and MA use in particular (Davis and Rodrigue 2001; Edlin et al., 2001).

Our data indicate that MA use is common in US veterans recently diagnosed with HCV infection and tends to occur in younger patients with concomitant alcohol and marijuana use. Prior history of or recent/active MA use alone does not seem to adversely affect overall HCV clinic referral or treatment compared with that in new HCV patients without MA use and HCV patients with prior alcohol abuse. Treatment initiation rate did not change over time (2004-2007).

These data confirm that polysubstance use is exceedingly common among patients attending a long-term hepatitis clinic, and patients with a MA use history are particularly prone to polysubstance use. One characteristic of HCV patients with MA use is a relatively high marijuana use rate. Occasional marijuana use may be considered benign by many clinicians; however, abusive and dependent use of marijuana has significant adverse medical and psychiatric consequences for patients (Wu et al., 1988; Pope and Yurgelun-Todd 1996; Herning et al., 2001); (Hezode et al., 2005).

Rates of treatment initiation were low overall at 17.7% in all patients and were lowest in patients with active alcohol abuse (9.7%). The reasons for not receiving antiviral treatment were determined in MA patients and are similar to reasons found in other HCV patient cohorts (Ho et al., 2008). Notably, in our cohort of MA patients not receiving treatment, reasons related to noncompliance with scheduled clinic visits and being lost to follow-up were the most common factors. We can speculate that ongoing SUD issues may contribute

to these factors; however, the specific reasons or factors responsible for “noncompliance” or lost to follow-up remain to be determined. To address the overall low treatment rates in patients with active SUD, emerging data indicate that psychiatric and substance use comorbidities in HCV patients can be effectively managed by integrating medical and psychiatric care (Schaefer et al., 2003; Cournot et al., 2004; Sylvestre et al., 2004). Integration of substance use interventions into the HCV clinic by clinicians and/or mental health practitioners may be an effective means to increase the number of patients who receive effective HCV infection antiviral therapy (Knott et al., 2006; Ho et al., 2008). Although MA use did not seem to affect antiviral treatment initiation, recognition of MA use in patients with hepatitis C is important to provide appropriate treatment, which may improve the number that will receive appropriate HCV care. Because of the cognitive and emotional changes induced by long-term MA use and difference in background of the patients, traditional treatment strategies validated for cocaine abusing populations may be less than effective. Cognitive-behavioral interventions such as the Matrix Model, which provides behavioral and family therapy, 12-step support, and drug testing, have been shown to be effective in reducing MA use (Rawson et al., 2004). Similarly, contingency management interventions that reward abstinence with tangible incentives has been shown to be effective (Roll et al., 2006; Roll, 2007).

Interestingly, active or recent MA use per se did not seem to be more of a barrier to starting antiviral treatment compared with other types of drug and alcohol use disorders. These data suggest that long-term abstinence from MA use may not be a necessary prerequisite for initiating antiviral treatment in those who can be engaged to comply with clinic attendance, as 11.1% of patients with active MA use were able to complete treatment, whereas 8.5% of patients who never used MA completed treatment. These data also suggest that the cognitive defects that may result from MA use may not be severe enough to affect the processes involved in HCV infection treatment uptake more than in other HCV patients with SUD. To support our observations is the recent publication by Dieperink et al. (2013) that found similar findings in a group of HCV patients with a history of recent stimulant use (cocaine and/or methamphetamine), managed in an integrated care setting, in which treatment uptake and adherence were no different than in other groups of substance users.

We also note the major limitations of this study, which include the retrospective nature of data collection, which may not accurately capture drug use information or categorize patients into active and inactive groups. We were unable to analyze more heavily using patients compared with those who had occasional use. We could not analyze the specific effects of MA use per se, because non-MA users and MA users had significant overlap with other drug and alcohol use. In addition, this is a single-site study with relatively few patients examined, making it difficult to analyze patient subsets.

CONCLUSIONS

We have found that active MA use is common in our cohort of recent US veterans diagnosed with HCV infection and seems to occur in younger patients with frequent concomitant polysubstance use. Prior history or active MA use alone does not adversely affect overall HCV infection antiviral treatment and SVR rates compared with that in new

HCV patients without MA use. Although, overall rates of treatment initiation are low (17.7%) and tended to be lowest in patients with active problematic alcohol and active other drug use (6.9%-11.1%). These data indicate that facilitated access to SUD treatment in HCV clinics may be of benefit for multiple SUD issues to increase HCV infection treatment rates. Future research is required to prospectively collect accurate alcohol and drug use data to determine the relevance of specific amounts and durations of use, attitudes related to HCV infection treatment, and factors related to engagement and compliance with care.

Acknowledgments

Supported by Veterans Affairs Health Service Research and Development grant IIR 07-101-3, the VA Quality Enhancement Research Initiative, and the Research Service of the Department of Veterans Affairs. Samuel B. Ho, MD, received research and grant support from Genetech, Inc, Vital Therapies, Inc, and Aspire Bariatrics, Inc. Expert panel fees were paid by Roche Pharmaceuticals, Inc.

REFERENCES

- Anglin MD, Burke C, Perrochet B, et al. History of the methamphetamine problem. *J Psychoactive Drugs*. 2000; 32(2):137–141. [PubMed: 10908000]
- Anglin MD, Urada D, Brecht ML, et al. Criminal justice treatment admissions for methamphetamine use in California: a focus on Proposition 36. *J Psychoactive Drugs*. 2007; (suppl 4):367–381. [PubMed: 18284103]
- Berman S, O'Neill J, Fears S, et al. Abuse of amphetamines and structural abnormalities in the brain. *Ann N Y Acad Sci*. 2008; 1141:195–220. [PubMed: 18991959]
- Bini EJ, Brau N, Currie S, et al. Prospective multicenter study of eligibility for antiviral therapy among 4,084 U.S. veterans with chronic hepatitis C virus infection. *Am J Gastroenterol*. 2005; 100(8):1772–1779. [PubMed: 16086714]
- Bradley KA, Bush KR, McDonell MB, et al. Screening for problem drinking: comparison of CAGE and AUDIT. Ambulatory Care Quality Improvement Project (ACQUIP). Alcohol Use Disorders Identification Test. *J Gen Intern Med*. 1998; 13(6):379–388.
- Brecht ML, O'Brien A, von Mayrhauser C, et al. Methamphetamine use behaviors and gender differences. *Addict Behav*. 2004; 29(1):89–106. [PubMed: 14667423]
- Bush K, Kivlahan DR, McDonell MB, et al. The AUDIT alcohol consumption questions (AUDIT-C): an effective brief screening test for problem drinking. Ambulatory Care Quality Improvement Project (ACQUIP). Alcohol Use Disorders Identification Test. *Arch Intern Med*. 1998; 158(16):1789–1795. [PubMed: 9738608]
- Cawthorne CH, Rudat KR, Burton MS, et al. Limited success of HCV antiviral therapy in United States veterans. *Am J Gastroenterol*. 2002; 97(1):149–155. [PubMed: 11808940]
- Cherner M, Letendre S, Heaton RK, et al. Hepatitis C augments cognitive deficits associated with HIV infection and methamphetamine. *Neurology*. 2005; 64(8):1343–1347. [PubMed: 15851720]
- Cournot M, Glibert A, Castel F, et al. Management of hepatitis C in active drugs users: experience of an addiction care hepatology unit. *Gastroenterol Clin Biol*. 2004; 28(6–7)(pt 1):533–539. [PubMed: 15243385]
- Davis GL, Rodrique JR. Treatment of chronic hepatitis C in active drug users. *N Engl J Med*. 2001; 345:215–217. [PubMed: 11463020]
- Dieperink E, Knott A, Thuras P, et al. The effect of stimulant use on antiviral treatment in an integrated hepatitis clinic. *Gen Hosp Psychiatry*. 2013; 35(5):387–392. Available at <http://dx.doi.org/10.1016/j.genhosppsy.2013.01.007>. [PubMed: 23391612]
- Edlin BR, Seal KH, Lorrivick J, et al. Is it justifiable to withhold treatment for hepatitis C from illicit-drug users. *N Engl J Med*. 2001; 345:211–214. [PubMed: 11463019]
- El-Serag HB, Kunik M, Richardson P, et al. Psychiatric disorders among veterans with hepatitis C infection. *Gastroenterology*. 2002; 123:476–482. [PubMed: 12145801]

- Garcia-Tsao G, Lim JK. Management and treatment of patients with cirrhosis and portal hypertension: recommendations from the Department of Veterans Affairs Hepatitis C Resource Center Program and the National Hepatitis C Program. *Am J Gastroenterol*. 2009; 104(7):1802–1829. [PubMed: 19455106]
- Gonzales R, Marinelli-Casey P, Shoptaw S, et al. Hepatitis C virus infection among methamphetamine-dependent individuals in outpatient treatment. *J Subst Abuse Treat*. 2006; 31(2):195–202. [PubMed: 16919748]
- Gonzalez Castro F, Barrington EH, Walton MA, et al. Cocaine and methamphetamine: differential addiction rates. *Psychol Addict Behav*. 2000; 14(4):390–396. [PubMed: 11130157]
- Herning RI, Better WE, Tate K, et al. Marijuana abusers are at increased risk for stroke. Preliminary evidence from cerebrovascular perfusion data. *Ann N Y Acad Sci*. 2001; 939:413–415. [PubMed: 11462796]
- Hezode C, Roudot-Thoraval F, Nguyen S, et al. Daily cannabis smoking as a risk factor for progression of fibrosis in chronic hepatitis C. *Hepatology*. 2005; 42:63–71. [PubMed: 15892090]
- Ho SB, Groessl E, Dollarhide A, et al. Management of chronic hepatitis C in veterans: the potential of integrated care models. *Am J Gastroenterol*. 2008; 103(7):1810–1823. [PubMed: 18564122]
- Knott A, Dieperink E, Willenbring ML, et al. Integrated psychiatric/medical care in a chronic hepatitis C clinic: effect on antiviral treatment evaluation and outcomes. *Am J Gastroenterol*. 2006; 101:2254–2262. [PubMed: 17032190]
- Letendre SL, Cherner M, Ellis RJ, et al. The effects of hepatitis C, HIV, and methamphetamine dependence on neuropsychological performance: biological correlates of disease. *AIDS*. 2005; 19(suppl 3):S72–S78. [PubMed: 16251831]
- London ED, Simon SL, Berman SM, et al. Mood disturbances and regional cerebral metabolic abnormalities in recently abstinent methamphetamine abusers. *Arch Gen Psychiatry*. 2004; 61(1):73–84. [PubMed: 14706946]
- Nguyen HA, Miller AI, Dieperink E, et al. Spectrum of disease in U.S. veteran patients with hepatitis C. *Am J Gastroenterol*. 2002; 97:1813–1820. [PubMed: 12135041]
- National Institute on Alcohol Abuse and Alcoholism. The Physicians' Guide to Helping Patients With Alcohol Problems. National Institute on Alcohol Abuse and Alcoholism; Rockville, MD: 1995.
- National Institute on Drug Abuse. [March 14, 2011] National Institute on Drug Abuse NIDA InfoFacts: Methamphetamine. 2010. Available at <http://www.drugabuse.gov/pdf/infofacts/Methamphetamine10.pdf>.
- National Institutes of Health. National Institutes of Health consensus development conference statement: management of hepatitis C: 2002. *Hepatology*. 2002; 36:S3–S15. [PubMed: 12407572]
- Pope HG, Yurgelun-Todd D. The residual cognitive effects of heavy marijuana use in college students. *JAMA*. 1996; 275:521–527. [PubMed: 8606472]
- Rawson RA, Anglin MD, Ling W. Will the methamphetamine problem go away? *J Addict Dis*. 2002; 21(1):5–19. [PubMed: 11831500]
- Rawson RA, Marinelli-Casey P, Anglin MD, et al. A multi-site comparison of psychosocial approaches for the treatment of methamphetamine dependence. *Addiction*. 2004; 99(6):708–717. [PubMed: 15139869]
- Roll JM. Contingency management: an evidence-based component of methamphetamine use disorder treatments. *Addiction*. 2007; 102(suppl 1):114–120. [PubMed: 17493060]
- Roll JM, Petry NM, Stitzer ML, et al. Contingency management for the treatment of methamphetamine use disorders. *Am J Psychiatry*. 2006; 163(11):1993–1999. [PubMed: 17074952]
- Rumpf HJ, Hapke U, Meyer C, et al. Screening for alcohol use disorders and at-risk drinking in the general population: psychometric performance of three questionnaires. *Alcohol Alcohol*. 2002; 37(3):261–268. [PubMed: 12003915]
- Schaefer M, Schmidt F, Folwaczny C, et al. Adherence and mental side effects during hepatitis C treatment with interferon alfa and ribavirin in psychiatric risk groups. *Hepatology*. 2003; 37(2):443–451. [PubMed: 12540795]

- Swan T, Curry J. Comment on the updated AASLD practice guidelines for the diagnosis, management, and treatment of hepatitis C: treating active drug users. *Hepatology*. 2009; 50(1):323–324. author reply 324–325. [PubMed: 19554546]
- Sylvestre DL, Loftis JM, Hauser P, et al. Co-occurring hepatitis C, substance use, and psychiatric illness: treatment issues and developing integrated models of care. *J Urban Health*. 2004; 81(4): 719–734. [PubMed: 15466851]
- Thompson PM, Hayashi KM, Simon SL, et al. Structural abnormalities in the brains of human subjects who use methamphetamine. *J Neurosci*. 2004; 24(26):6028–6036. [PubMed: 15229250]
- United Nations Office on Drugs and Crimes. World Drug Report. 2012. 2012. Available at <http://www.unodc.org/unodc/en/data-and-analysis/WDR-2012.html>
- Wu TC, Tashkin DP, Djahed B, et al. Pulmonary hazards of smoking marijuana as compared with tobacco. *N Engl J Med*. 1988; 318(6):347–351. [PubMed: 3340105]
- Yovtcheva SP, Rifai MA, Moles JK, et al. Psychiatric comorbidity among hepatitis C–positive patients. *Psychosomatics*. 2001; 42(5):411–415. [PubMed: 11739908]

FIGURE 1.
Reasons for not initiating antiviral treatment in patients with history of MA and/or active MA use (n = 62). HCV indicates hepatitis C virus; MA, methamphetamine.

TABLE 1

Patient Characteristics

	Total (n = 198)	MA Use			P
		Active (n = 36)	Inactive (n = 43)	Never Used (n = 119)	
Age, yr					<0.0001
Mean (SD)	51.3 (8.11)	45.5(8.06)	50.4 (5.50)	53.5 (8.03)	
Median (25th, 75th percentiles)	51 (46.3, 55)	45 (40.8, 51.3)	50 (47.5, 55)	53 (49, 57)	
Sex					0.80
Male	189 (95.5%)	34 (94.4%)	42 (97.7%)	113 (95%)	
Female	9 (4.5%)	2 (5.6%)	1 (2.3%)	6 (5%)	
Race *					0.02
White	123 (62.8%)	28 (77.8%)	27 (64.3%)	68 (57.6%)	
African American	41 (20.9%)	5 (13.9%)	4 (9.5%)	32 (27.1%)	
Hispanic	26 (13.3%)	3 (8.3%)	7 (16.7%)	16 (13.6%)	
Others	6 (3.1%)	0 (0.0%)	4 (9.5%)	2 (1.7%)	
Depression					0.23
History of	70 (35.4%)	12 (33.3%)	20 (46.5%)	38 (31.9%)	
No history of	128 (64.6%)	24 (66.7%)	23 (53.5%)	81 (68.1%)	
Other psychiatric disorders					0.045
History of	90 (45.5%)	23 (63.9%)	19 (44.2%)	48 (40.3%)	
No history of	108 (54.5%)	13 (36.1%)	24 (55.8%)	71 (59.7%)	
Genotype					0.01
G1 or 4	132 (66.7%)	17 (47.2%)	33 (76.7%)	82 (68.9%)	
G2 or 3	33 (16.7%)	12 (33.3%)	7 (16.3%)	14 (11.8%)	
Not tested	33 (16.7%)	7 (19.4%)	3 (7%)	23 (19.3%)	
Cohort					0.105
2004	144 (72.7%)	21 (58.3%)	32 (74.4%)	91 (76.5%)	
2007	54 (27.3%)	15 (41.7%)	11 (25.6%)	28 (23.5%)	
Marijuana					<0.0001
Active use	45(22.7%)	22 (61.1%)	12 (27.9%)	11 (9.2%)	
Inactive use	43 (21.7%)	2 (5.6%)	18 (41.9%)	23 (19.3%)	
Never used	110 (55.6%)	12 (33.3%)	13 (30.2%)	85 (71.4%)	
Cocaine					<0.0001
Active use	37 (18.7%)	14 (38.9%)	5 (11.6%)	18 (15.1%)	
Inactive use	54 (27.3%)	3 (8.3%)	23 (53.5%)	28 (23.5%)	
Never used	107 (54%)	19 (52.8%)	15 (34.9%)	73 (61.3%)	
Alcohol					0.01
Active problem use	92 (46.5%)	24 (66.7%)	25 (58.1%)	43 (36.1%)	
Inactive problem use	48 (24.2%)	5 (13.9%)	9 (20.9%)	34 (28.6%)	
No history of problem use	58 (29.3%)	7 (19.4%)	9 (20.9%)	42 (35.3%)	
Heroin and other drugs [†]					0.07

	Total (n = 198)	MA Use			P
		Active (n = 36)	Inactive (n = 43)	Never Used (n = 119)	
Active use	29 (14.6%)	8 (22.2%)	5 (11.6%)	16 (13.4%)	<0.0001
Inactive use	60 (30.3%)	7 (19.4%)	20 (46.5%)	33 (27.7%)	
Never used	109 (55.1%)	21 (58.3%)	18 (41.9%)	70 (58.8%)	
Any drug [‡]					
Active use	81 (40.9%)	31 (86.1%)	16 (37.2%)	34 (28.6%)	
Inactive use	73 (36.9%)	0 (0%)	23 (53.5%)	50 (42%)	
Never used	44 (22.2%)	5 (13.9%)	4 (9.3%)	35 (29.4%)	

Active use, active use of the drug within 6 months of initial enrollment in HCV clinic; inactive use, used the drug 6 months ago or earlier; MA, methamphetamine and amphetamine-type stimulant; never used, no use of the drug reported.

* Total sample size is n = 196 for race.

[†] Any illicit drug use (opiates, inhalants, solvents, sedatives, etc) except MA, marijuana, cocaine, and alcohol.

[‡] Any illicit drug use except MA and alcohol.

TABLE 2

Antiviral Treatment Outcomes According to Group (Note Some Patients May Fall Into More Than 1 Group)

	N	Antiviral Treatment			SVR (n = 17)	SVR Rate
		Offered (n = 50)	Initiated (n = 35)	Completed (n = 20)		
Race *						
White	123	32 (26.0%)	25 (20.3%)	13 (10.6%)	11 (8.9%)	44.0%
African American	41	11 (26.8%)	5 (12.2%)	4 (9.8%)	3 (7.3%)	60.0%
Hispanic	26	5 (19.2%)	4 (15.4%)	3 (11.5%)	3 (11.5%)	75.0%
Others	6	2 (33.3%)	1 (16.7%)	0 (0.0%)	0 (0.0%)	0.0%
Depression						
History of	70	18 (25.7%)	14 (20.0%)	5 (7.1%)	5 (7.1%)	35.7%
No history of	128	32 (25.0%)	21 (16.4%)	15 (11.7%)	12 (9.4%)	57.1%
Other psychiatric disorders						
History of	90	23 (25.6%)	15 (16.7%)	7 (7.8%)	6 (6.7%)	40.0%
No history of	108	27 (25.0%)	20 (18.5%)	13 (12.0%)	11 (10.2%)	55.0%
Genotype						
G1 or 4	132	38 (28.8%)	26 (19.7%)	14 (10.6%)	11 (8.3%)	42.3%
G2 or 3	33	12 (36.4%)	9 (27.3%)	6 (18.2%)	6 (18.2%)	66.7%
Not tested	33	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0.0%
Cohort						
2004	144	31 (21.5%)	21 (14.6%)	12 (8.3%)	11 (7.6%)	52.4%
2007	54	19 (35.2%)	14 (25.9%)	8 (14.8%)	6 (11.1%)	42.9%
MA use						
Active use	36	9 (25.0%)	8 (22.2%)	4 (11.1%)	4 (11.1%)	50.0%
Inactive use	43	12 (27.9%)	9 (20.9%)	6 (14.0%)	4 (9.3%)	44.4%
Never used	119	29 (24.4%)	18 (15.1%)	10 (8.4%)	9 (7.6%)	50.0%
Marijuana						
Active use	45	9 (20.0%)	7 (15.6%)	3 (6.7%)	3 (6.7%)	42.9%
History of use	43	10 (23.3%)	7 (16.3%)	1 (2.3%)	2 (4.7%)	28.6%
Never used	110	31 (28.2%)	21 (19.1%)	16 (14.5%)	12 (10.9%)	57.1%
Cocaine						
Active use	37	6 (16.2%)	3 (8.1%)	1 (2.7%)	2 (5.4%)	66.7%
Inactive use	54	14 (25.9%)	8 (14.8%)	3 (5.6%)	1 (1.9%)	12.5%
Never used	107	30 (28.0%)	24 (22.4%)	16 (15.0%)	14 (13.1%)	58.3%
Alcohol						
Active problem use	92	17 (18.5%)	9 (9.8%)	4 (4.3%)	4 (4.3%)	44.4%
Inactive problem use	48	16 (33.3%)	12 (25.0%)	6 (12.5%)	4 (8.3%)	33.3%
No history of problem use	58	17 (29.3%)	14 (24.1%)	10 (17.2%)	9 (15.5%)	64.3%
Heroin and other drugs [†]						
Active use	29	3 (10.3%)	2 (6.9%)	0 (0.0%)	1 (3.4%)	50.0%
Inactive use	60	11 (18.3%)	9 (15.0%)	5 (8.3%)	4 (6.7%)	44.4%

	N	Antiviral Treatment			SVR (n = 17)	SVR Rate
		Offered (n = 50)	Initiated (n = 35)	Completed (n = 20)		
Never used	109	36 (33.0%)	24 (22.0%)	15 (13.8%)	12 (11.0%)	50.0%
Any drug [‡]						
Active use	81	14 (17.3%)	9 (11.1%)	4 (4.9%)	4 (4.9%)	44.4%
Inactive use	73	21 (28.8%)	15 (20.5%)	7 (9.6%)	6 (8.2%)	40.0%
Never used	44	15 (34.1%)	11 (25.0%)	9 (20.5%)	7 (15.9%)	63.6%

Active use, active use of the drug within 6 months of initial enrollment in HCV clinic; inactive use, used the drug 6 months ago or earlier; MA, methamphetamine and amphetamine-type stimulant; never used, no use of the drug reported; SVR, sustained virological response.

* Total sample size is n = 196 for race.

[†] Any illicit drug use except MA, marijuana, cocaine, and alcohol.

[‡] Any illicit drug use except MA and alcohol.

TABLE 3

Antiviral Treatment Outcomes According to MA Group

	Total (n = 198)	MA Use			P
		Active (n = 36)	Inactive (n = 43)	Never Used (n = 119)	
Treatment referral					0.87
Yes	50 (25.3%)	9 (25%)	12 (27.9%)	29 (24.4%)	
No	148 (74.7%)	27 (75%)	31 (72.1%)	90 (75.6%)	
Treatment initiation					0.46
Yes	35 (17.7%)	8 (22.2%)	9 (20.9%)	18 (15.1%)	
No	163 (82.3%)	28 (77.8%)	34 (79.1%)	101 (84.9%)	
Treatment completion*					0.51
Yes	20 (10.2%)	4 (11.1%)	6 (14.3%)	10 (8.5%)	
No	176 (89.8%)	32 (88.9%)	36 (85.7%)	108 (91.5%)	
SVR*					0.73
Yes	17 (8.7%)	4 (11.1%)	4 (9.5%)	9 (7.6%)	
No	179 (91.3%)	32 (88.9%)	38 (90.5%)	109 (92.4%)	

MA, methamphetamine and amphetamine-type stimulant.

* Total sample size is n = 196 for treatment completion and SVR; 2 subjects with unknown status after treatment initiation (1 in inactive and 1 in never used) were removed from this analysis. SVR denotes sustained virological response as a percentage of the total number of patients in each group.

TABLE 4

Logistic Regression Analysis of Association Between Patient Characteristics and Treatment Initiation

Variable	Odds Ratio	95% CI	P
<i>Simple logistic regression analysis</i>			
Age, yr	0.97	0.92-1.01	0.15
Sex			
Male	1.00		
Female	2.45	0.58-10.3	0.22
Race			
White	1.00		
African American	0.54	0.19-1.53	0.25
Hispanic	0.71	0.23-2.26	0.57
Others	0.78	0.09-7.02	0.83
Depression			
No history	1.00		
History	1.27	0.60-2.70	0.53
Other psychiatric disorders			
No history	1.00		
History	0.88	0.42-1.84	0.73
Genotype			
G1 or 4	1.00		
G2 or 3 or not tested	0.644	0.28-1.47	0.29
Cohort			
2004	1.00		
2007	2.05	0.95-4.40	0.07
MA use			
Never used	1.00		
Inactive use	1.49	0.61-3.62	0.38
Active use	1.60	0.63-4.07	0.32
Marijuana			
Never used	1.00		
Inactive use	0.82	0.32-2.11	0.69
Active use	0.78	0.31-1.99	0.60
Cocaine			
Never used	1.00		
Inactive use	0.60	0.25-1.45	0.26
Active use	0.31	0.09-1.08	0.07
Alcohol			
No history of problem use	1.00		
Inactive problem use	1.05	0.43-2.55	0.92
Active problem use	0.34	0.14-0.85	0.02
Heroin or other drug*			

Variable	Odds Ratio	95% CI	P
Never used	1.00		
Inactive use	0.63	0.27-1.45	0.27
Active use	0.26	0.06-1.18	0.08
Any drug [†]			
Never used	1.00		
Inactive use	0.78	0.32-1.89	0.58
Active use	0.38	0.14-0.99	0.05
<i>Multivariable logistic regression of association between MA use and treatment initiation</i>			
MA use			
Never used	1.00		
Inactive use	2.01	0.79-5.13	0.15
Active use	2.47	0.91-6.78	0.08
Alcohol use			
Never used	1.00	0.42-2.56	
Inactive use	1.04	0.10-0.70	0.93
Active use	0.27	0.42-2.56	0.01

Active use, active use of the drug within 6 months of initial enrollment in HCV clinic; inactive use, used the drug 6 months ago or earlier; MA, methamphetamine and amphetamine-type stimulant; never used, no use of the drug reported; SVR, sustained virological response.

* Any illicit drug use except MA, marijuana, cocaine, and alcohol.

[†] Any illicit drug use except MA and alcohol.