

# Hepatitis C Screening and Treatment Outcomes in Patients With Substance Use/Dependence Disorders

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*The authors evaluated the association between hepatitis C virus (HCV) seropositivity status and substance use treatment outcomes in an alcohol- and substance-dependent population undergoing rehabilitation. The second aim was to assess the impact of early screening for HCV infection and substance use treatment on HCV treatment outcomes. HCV-antibody testing of 338 patients attending a substance-use residential program was performed. HCV antibody status, lifetime comorbid psychiatric diagnoses, program completion rates, and 6-month abstinence rates after program discharge were assessed. HCV treatment outcomes were followed in patients who remained abstinent 6 months after completion of substance-use treatment. Almost one-fourth (23.1%) of patients were HCV antibody-positive. HCV-seropositive patients were more likely to complete the 28-day program and more likely to remain abstinent at 6 months after program discharge. HCV seropositive status was the strongest predictor for the likelihood of completing the program, and remaining abstinent for 6 months afterward. Patients with HCV who completed a substance-use treatment program were more likely to receive HCV treatment than substance-dependent patients with HCV who never attended a substance-use treatment program. Detecting HCV infection in the structured setting of substance-use treatment is ideal to initiate management of this infection, and it has a positive influence on the outcomes of both substance-use treatment and HCV treatment.*

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Chronic hepatitis C virus (HCV) infection is a major public health problem in the United States, with approximately 2% of the population having been exposed.<sup>1,2</sup> Untreated HCV infection may result in cirrhosis, end-stage liver disease, and hepatocellular carcinoma.<sup>3</sup> The use of interferon-alpha-based therapies (interferon) in combination with ribavirin have resulted in sustained virologic response rates (i.e., complete eradication of HCV; absent

HCV viral load 6 months after interferon treatment is completed, “cure from HCV”) of 30%–59% for patients with HCV Genotype 1 (70% of U.S. patients with HCV) and 60%–90% for patients with HCV Genotypes 2 or 3 (15%–25% of U.S. patients with HCV).<sup>4–7</sup>

Targeted screening for HCV infection in patients with well-established risk factors (intravenous [IV] drug use, blood or blood-product transfusions, hemodialysis, and multiple sexual partners) is clearly indicated.<sup>8,9</sup> However, evidence is beginning to emerge that patients with alcohol- and substance use other than IV drug use may also be at higher risk for HCV infection.<sup>10–13</sup> Several researchers reported that IV drug use was absent in at least 50% of their HCV-seropositive substance-dependent patients.<sup>10–15</sup> Marsano et al.<sup>16</sup> found that patients with alcohol use disorders had an HCV-seropositive rate that was more than double

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that of the general population, even when individuals with other HCV risk factors were excluded (4.8% versus 2%, respectively).<sup>16</sup>

Despite the intuitive value of screening for HCV in alcohol- and substance-dependent populations (without history of IV drug use), screening for HCV has not been a routine practice in these populations. In fact, the United States Preventive Services Task Force recently recommended against routine screening for HCV in asymptomatic high-risk individuals because of the lack of data on the efficacy of HCV treatment in reducing morbidity and mortality.<sup>17</sup> Although it is well known that continued alcohol and substance use can accelerate HCV-induced liver disease and reduce the likelihood of viral clearance with interferon treatment,<sup>18-20</sup> it remains to be demonstrated that screening for HCV in alcohol- and substance-dependent populations reduces substance use and that interferon treatment will result in a reduction in morbidity and mortality from HCV infection.<sup>21</sup>

Since HCV infection is a disease in its infancy,<sup>21</sup> it seemed impractical to wait decades for evidence that HCV screening and treatment will reduce morbidity and mortality.<sup>22</sup> In 2000, we initiated routine screening for HCV in all new admissions to our substance-use residential and rehabilitation treatment program (the Program) and provided counseling and education about HCV infection.<sup>12</sup> This report is, in part, a retrospective analysis of the outcome of this screening.<sup>23</sup>

Several studies have shown that patients with HCV and active substance use have inferior sustained virologic response rates in response to interferon, as compared with sustained virologic response rates of patients with HCV who are abstinent from substance use.<sup>20,24</sup> However, there have been no studies of the impact of early identification of HCV infection on substance-use treatment outcomes or HCV treatment outcomes. We designed our project to explore two aims:<sup>23</sup> 1) To evaluate the possible impact of education and early screening for HCV on substance-use treatment outcomes, since abstinence from alcohol and substance use has been a requirement to receive HCV treatment. We assessed the rates of program completion and abstinence rates 6 months after program completion as measures of the success of this early screening and education in increasing the eligibility for interferon treatment. We hypothesized that early screening for HCV and education about the HCV disease process might improve rates of program completion and abstinence rates and thus increase eligibility for interferon treatment. 2) To assess the impact of early screening for HCV and substance-use treat-

ment on HCV treatment outcomes. We tracked HCV treatment outcomes in those patients who remained abstinent 6 months after program completion. We hypothesized that they might not be able to achieve the optimum HCV clearance rates reported in the literature because of noncompliance and comorbid psychiatric illness.

## METHOD

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### Subjects

All patients admitted to the program at a rural Veterans Affairs (VA) Medical Center in Virginia from January 2000 to October 2001 were included in this analysis. The majority of patients were motivated toward sobriety and requested referral through their primary-care providers or psychiatrists. Patients with pending legal problems or in court-mandated treatment were not accepted.

HCV treatment outcomes were tracked in a sample of patients with HCV and alcohol- or substance-use disorder who have never been enrolled in a substance-use treatment program. This control group was derived from a sample described in a previous report<sup>25,26</sup> and was matched with the study group (program attendees) for age, race, marital status, psychiatric disorder, IV drug use, and substances used.

### The Program

This 28-day inpatient substance-use treatment program focuses primarily on alcohol- and substance- (cocaine, marijuana, benzodiazepines, LSD, phencyclidine, oxycodone) use disorders. Patients with primary IV drug use disorders are referred to other centers for treatment. All new admissions to the program received a psychiatric history and mental status examination performed in typical clinical fashion by the admitting psychiatrist, and psychiatric diagnoses were established on the basis of this interview. Patients also received the Addiction Severity Index (ASI),<sup>27,28</sup> administered by trained substance-abuse counselors.<sup>29</sup> For the 12 months after program completion, patients attended weekly group meetings and bimonthly individual substance-abuse counseling sessions. Abstinence determinations were based on clinical observations documented in the medical records by substance-abuse counselors, psychiatrists, or medical providers. Random urine drug and alcohol testing helped confirm observations of sobriety for most patients.

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### HCV Screening, Education, and Evaluation

HCV-antibody testing was performed on admission to the program by use of anti-HCV enzyme immunoassay and was confirmed by Hepatitis C Quantitative RNA Polymerase Chain Reaction (PCR). HCV-seropositive patients were informed of their HCV-positive status and had post-test counseling (offered HIV testing, vaccinations against hepatitis A and B initiated, informed how to limit the exposure of others to their blood).<sup>1</sup> HCV-seropositive patients viewed a 1-hour patient-education slide presentation (the VA National Hepatitis C Program, available at [www.hepatitis.va.gov/vahep?page=tm-ce-00](http://www.hepatitis.va.gov/vahep?page=tm-ce-00)) about HCV infection and had the opportunity to ask questions. HCV-seropositive patients were advised to eliminate alcohol and drug use so as to minimize liver damage and were informed about the current recommendations of 6 months of abstinence to qualify for HCV treatment.

A nurse-practitioner from the gastroenterology (GI) service evaluated HCV-seropositive patients during their program stay. This practitioner provided additional education about HCV disease process and treatment options. HCV-seropositive patients received a follow-up appointment with GI approximately 1 month after program completion. A medical evaluation was initiated for those patients who completed the program and remained abstinent (HCV genotype, laboratory work-up). A liver biopsy was performed within 2–3 months of program completion for all patients who remained abstinent and agreed to undergo HCV treatment. Patients treated before January 2002 received regular interferon- $\alpha$  and ribavirin combination, and those treated after January 2002 received pegylated-interferon and ribavirin combination. Patients continued with program attendance every 2 weeks during HCV treatment in addition to mood-rating and follow-up with a psychiatrist.

### Data Collection

After obtaining approval from the local institutional review board, the electronic and paper medical records of all patients admitted to the program over the study period were reviewed by one of two clinicians. Demographic information (age, race, marital status), substances used, methods of use, and lifetime comorbid DSM-IV-based psychiatric disorders were obtained from the record. Program completion rates (defined as attendance for the full 28 days) were assessed. Abstinence at 6 months after program discharge was determined for all patients who had clinical follow-up visits 6 months or longer after discharge

from this program. Patients were classified as Abstinent, Not Abstinent, or Indeterminate (medical record documentation of follow-up was insufficient or absent).

HCV treatment outcomes were tracked for those patients abstinent 6 months after program completion, as well as for the control group. Patients with HCV Genotype 1 received interferon and ribavirin treatment for 12 months, whereas patients with HCV Genotypes 2 or 3 received interferon and ribavirin treatment for 6 months. Those who failed to achieve sustained virologic response or had a relapse of viremia were classified as Nonresponders. Patient who had to discontinue HCV treatment were classified as either stopping treatment for neuropsychiatric adverse effects (severe depression unresponsive to treatment, suicidal ideation) or medical complications (neutropenia, anemia, thrombocytopenia).

### Statistical Analysis

Differences in the frequencies of categorical data were compared by means of two-tailed chi-square or Fisher's exact test, as appropriate. Differences between the means for continuous data were compared by use of the *t*-test or the Mann-Whitney *U* test, respectively. A *p* value of less than 0.05 was considered to indicate statistical significance.

We used a multivariate logistic-regression analysis to identify the strongest predictors of program completion, 6-month abstinence rates, and the likelihood of receiving HCV treatment. Covariates that were found significant on univariate analysis (age, psychiatric diagnoses, HCV-positive status, IV drug use, type of substance used) were fitted into stepwise logistic-regression models with backward elimination. Goodness-of-fit testing, with likelihood ratio and chi-square, revealed that all models accounted for the outcome better than chance alone (for the 28-day program-completion model:  $\chi^2 = 62.67$ ,  $p < 0.001$ ,  $N = 338$ ; for the 6-month abstinence model:  $\chi^2 = 59.78$ ,  $p < 0.001$ ,  $N = 244$ ; for HCV treatment:  $\chi^2 = 8.19$ ,  $p < 0.01$ ,  $N = 30$ ). The final models were obtained by fitting only the main effect terms. Statistical analyses were performed with SAS 8.2 (SAS Institute; Cary, NC).

## RESULTS

Over 99% of these patients (338/340; 99.41%) received testing for HCV antibody, and approximately 23% (78/338; 23.1%) were HCV-seropositive (Table 1). In 98% of the HCV-seropositive sample, the diagnosis of hepatitis C was a de-novo diagnosis, and only two patients already knew

about their HCV status. HIV-antibody screening was negative in all of those who agreed to undergo testing (64/78; 82%).

What demographic, diagnostic, or risk factors would explain this high prevalence of HCV infection in a sample with low admitted IV drug use? As illustrated in Table 1, the HCV-seropositive patient group was younger than the HCV-seronegative group. Poly-substance use was not statistically different across the two groups. The percentage of HCV-seropositive patients with a history of cocaine use (smoking, snorting) was higher than that for HCV-seronegative patients, and this difference was statistically significant. None of the HCV-seropositive patients reported any other risk factors for HCV infection. The frequencies of lifetime comorbid, DSM-IV-based psychiatric disorders were similar when comparing HCV-seropositive and HCV-seronegative patients (data not shown). Antisocial personality disorder was the only psychiatric diagnosis that differed significantly across the two groups (15/78 versus 24/260;  $\chi^2 = 4.49$ ,  $df = 1$ ,  $p < 0.05$ ).

What was the impact of early HCV identification on substance-abuse treatment outcomes? As shown in Figure 1, almost 90% of HCV-seropositive patients completed the program and had a planned discharge, versus 67% of HCV-seronegative patients, and 49% of HCV-seropositive patients were abstinent from alcohol and other drugs 6 months after program completion, versus 31% of HCV-seronegative patients. The association between HCV-seropositive status, program completion, and sobriety at 6 months was statistically significant. Abstinence status could be determined in approximately 80% of HCV-seropositive patients, versus 75% of HCV-seronegative individuals. Abstinence was assessed by substance-abuse counselors, supported by random alcohol- and drug-testing in 74% (46/62) of HCV-seropositive patients and 76% (149/195) of HCV-seronegative patients. Sobriety assessments were based on psychiatrists' observations in 16% (10/62) of the HCV-seropositive group and 18% (35/195) of the HCV-seronegative group. Primary-care physicians' observations were utilized to determine abstinence in 10%

**TABLE 1. Demographics, Substances Used, and Substance-Use Treatment Outcomes in Patients Attending a Substance-Use Treatment Program, Comparing HCV-Seropositive With HCV-Seronegative Patients**

Demographic Variables	Hepatitis C-Positive	Hepatitis C-Negative	Statistical Analysis				
	(N = 78) Mean (SD)	(N = 260) Mean (SD)	U	df	p	Odds Ratio	95% Confidence Interval
Age, years	46 (4.2)	52 (5.5)	3.12	≅300	0.002		
Race	N (%)	N (%)	$\chi^2$	df	p		
White	41 (52.5)	137 (52.6)	0.0120	1	0.91		
Black	37 (47.5)	123 (47.4)					
Marital status			0.17	2	0.91		
Single	15 (19.2)	45 (17.3)					
Married	15 (19.2)	49 (18.8)					
Divorced/separated/widowed	48 (62.6)	166 (63.9)					
Substances used							
Alcohol	74 (94.8)	244 (93.8)	0.004	1	0.94		
Cocaine	42 (53.8)	104 (40.0)	4.14	1	0.041	1.70	1.67–1.83
Marijuana	31 (39.7)	104 (40.0)	0.0083	1	0.92		
Other	20 (25.6)	91 (35.0)	1.97	1	0.15		
Polysubstance use	45 (57.6)	178 (68.5)	2.63	1	0.1		
Intravenous drug use	28 (35.8)	11 (4.2)	58.93	1	$p < 0.0001$	12.6	10.2–14.8
Substance-abuse treatment outcomes							
Type of discharge			15.43	1	$p < 0.001$	4.3	3.5–5.1
Planned	70.0 (89.7)	174.0 (66.9)					
Unplanned	8.0 (10.2)	86.0 (33.1)					
Six-month abstinence			8.68	2	0.013	2.1	1.8–2.4
Abstinent	38.0 (48.7)	80.0 (30.8)					
Not abstinent	24.0 (30.7)	115.0 (44.2)					
Indeterminate	16.0 (20.5)	65.0 (25.0)					

Note: SD: standard deviation.

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(6/62) of HCV-seropositive patients, versus 6% (10/195) of HCV-seronegative individuals. There were no statistically significant differences in the methods of sobriety assessment between HCV-seropositive and HCV-seronegative groups ( $\chi^2 = 1.67$ ,  $df = 2$ ,  $p = 0.43$ ).

What are the variables or diagnostic factors that would account for the rates of program completion and 6-month abstinence? As illustrated in Table 2, a younger age (age in increments of 1 year) and HCV-seropositive status were the strongest predictors of completing the 28-day program and remaining abstinent for 6 months after program completion. The comorbid psychiatric diagnoses in patients undergoing substance-abuse treatment did not predict program completion or the 6-month abstinence rate after program completion.

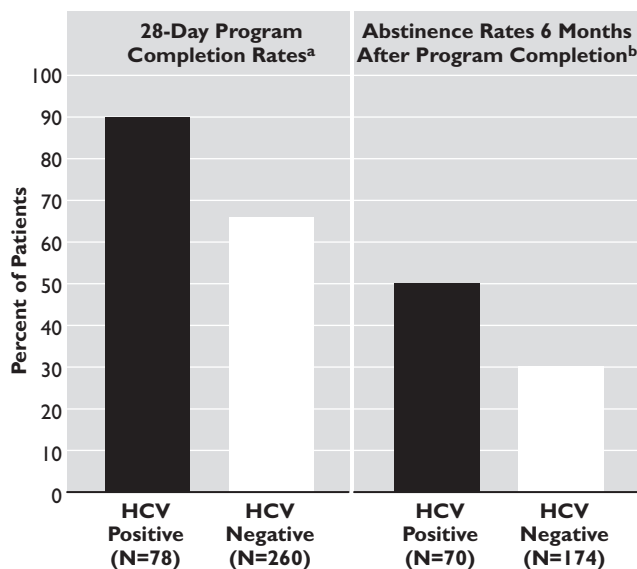
What were HCV treatment outcomes in patients remaining abstinent for 6 months? As illustrated in Figure 2, 30 patients received HCV treatment with interferons/ribavirin. Almost 74% (22/30) of patients treated with interferon regimens were infected with HCV Genotype 1, and the remainder, 26% (8/30), were infected with HCV Genotypes 2 or 3. Sustained virologic response (i.e., eradication of HCV) was achieved in 46% (14/30), whereas 33% (10/30) were Nonresponders, and the HCV treatment regimen had to be stopped in 20% (6/30) of patients because of medical (2/30) or neuropsychiatric side effects

(4/30). In patients with Genotypes 2 or 3, sustained virologic response was achieved in 75% (6/8), but only 36% (8/22) of patients with Genotype 1 were able to achieve sustained virologic response. Across genotypes and between the groups treated with interferon or pegylated interferons, there were no significant differences in viral load or liver biopsy findings, when comparing patients with different HCV genotypes (Genotype 1 versus Genotypes 2 or 3), as well as patients who were treated with regular interferon or pegylated interferons. Patients who achieved sustained virologic response had lower HCV viral loads than those who did not achieve sustained virologic response (32.5 [standard deviation {SD}: 15.6] versus 78.2 [SD: 23.5] iU/ml  $\times 10^5$ ;  $t = 25.4$ ;  $p = 0.02$ ) and were less likely to have cirrhosis on liver biopsy (2/14 versus 8/16;  $\chi^2 = 4.28$ ,  $df = 1$ ,  $p = 0.03$ ). Psychiatric side effects from interferon use led to discontinuation of treatment in 27% (5/22) of those with Genotype 1 and 12% (1/8) in those with Genotypes 2 or 3; however, this tendency did not have statistical significance ( $\chi^2 = 0.55$ ,  $df = 1$ ,  $p = 0.45$ ).

How did treatment results for HCV patients who remained abstinent for 6 months compare with patients with HCV and substance-use disorders who never attended a substance-abuse treatment program? As illustrated in Figure 2, patients with HCV infection and substance use disorders who attended a substance-abuse treatment program were more likely to receive HCV treatment when compared with patients who never attended a substance-abuse treatment program (30/78 versus 18/80;  $\chi^2 = 4.03$ ,  $df = 1$ ,  $p = 0.04$ ).

Multivariate logistic-regression analysis (Table 2) indicates that a younger age and the absence of psychotic or anxiety disorders were associated with an increased likelihood of receiving HCV treatment. Patients who were married and had significant social support were also more likely to receive HCV treatment after completing a treatment program and remaining abstinent for 6 months after program completion. A direct comparison of sustained virologic response rates between program attendees and nonprogram attendees was not possible (because some program attendees received treatment with regular interferon). However, on the basis of an intention-to-treat analysis, program attendees were more likely to achieve a sustained virological response, as compared with substance-dependent patients who never attended a treatment program (8/76 versus 12/38;  $\chi^2[1] = 13.35$ ;  $p = 0.0003$ ).

**FIGURE 1. Substance-Use Treatment Outcomes in Patients Attending Substance-Use Treatment Program Comparing HCV-Seropositive (N = 78) With HCV-Seronegative (N = 260) Patients**



Note: <sup>a</sup>  $p < 0.001$ . <sup>b</sup>  $p < 0.01$ .

## DISCUSSION

Our study has two important findings: first, early HCV identification resulted in improved compliance with

substance-abuse treatment, and abstinence rates of HCV-seropositive patients were significantly better than those of HCV-seronegative patients 6 months after treatment completion. Second, patients with histories of alcohol- and substance-dependence can complete HCV treatment and have viral clearance rates that are better than alcohol- and substance-dependent patients who never attended a treatment program.

Almost one-fourth of new admissions to our program were HCV-seropositive. These rates are in line with those from other studies in predominantly alcohol-dependent populations (rates of 10% to 36%).<sup>10-16</sup> These rates, however, are substantially higher than those in the general U.S. population (2%),<sup>1</sup> or the general U.S. veteran population (5.5%) visiting VA Medical Centers.<sup>30,31</sup> The finding that almost one-fourth of substance-dependent patients in this study were HCV-seropositive is particularly interesting, given the relatively low lifetime prevalence of reported IV drug use and the fact that alcohol dependence was the primary diagnosis in a large majority of our patients. Our findings, coupled with those from other researchers,<sup>11,14</sup> suggest that alcohol use may promote HCV infection, independent of an association with IV drug exposure.

The mechanisms of HCV transmission in substance-dependent patients who do not report other established HCV risk factors are not well understood.<sup>32</sup> Certainly, patients may not recall or be forthcoming in reporting their exposure to IV drugs or other HCV risk factors. Alcohol intoxication may also promote high-risk behaviors for further HCV transmission.<sup>33</sup> Alternatively, substance-induced behavioral disinhibition may result in high-risk behaviors, and alcohol-induced immunosuppression may stimulate

HCV replication and also contribute to the chronicity of HCV infection.<sup>34</sup> Furthermore, the recreational use of intranasal cocaine may account for HCV transmission in our sample and may play a role in HCV transmission in other substance-dependent patients. Recent studies have been highly suggestive of a role for intranasal drug use in HCV transmission in substance-dependent populations with no IV drug use.<sup>10,32</sup>

In contrast to our results about improved rates of program-completion in HCV-seropositive patients, Martinez-Raga *et al.*<sup>13,35</sup> found that patients who failed to complete a substance-abuse treatment program were more likely to be HCV-seropositive. However, logistic-regression analysis did not show the HCV seropositive status to be a predictor of unplanned discharges from their program.<sup>13,35</sup> Differences in study populations, methodology, and rehabilitation programs may account for the disparity in the findings of these two studies. Martinez-Raga *et al.*<sup>13,35</sup> evaluated patients from a large metropolitan center (London), and the prevalence of IV heroin, cocaine, and amphetamine use was higher among HCV-seropositive patients than in the current study.

Patients in this study were informed about their HCV-antibody status and the requirement for 6 months of sobriety to be considered for HCV treatment while they were still undergoing substance-abuse rehabilitation. Early notification and the education provided to HCV-seropositive patients, as well as the evaluation by the GI may have increased their motivation toward program completion and sobriety. In support of this notion, several studies have also found that a diagnosis of HCV infection may precipitate positive healthy transitions in lifestyle and promote absti-

**TABLE 2. Best-Fitting Logistic-Regression Models Indicating Variables That Are the Best Predictors of 28-Day Program Completion, Abstinence Rates 6 Months After Program Completion, and Likelihood of Receiving HCV (Hepatitis C) Treatment**

Model	Odds Ratio	95% Confidence Interval	p
Predictors of 28-day program completion			
Age	1.56	1.30-1.82	<0.001
Psychiatric diagnoses <sup>a</sup>	1.26	0.89-1.63	0.07
HCV seropositive status	3.08	2.6-3.56	<0.001
Predictors of abstinence 6 months after program completion			
Age	1.82	1.60-2.04	<0.002
Psychiatric diagnoses <sup>a</sup>	0.90	0.82-0.98	0.79
HCV seropositive status	2.16	1.92-2.40	<0.01
Likelihood of receiving HCV treatment			
Age	1.73	1.50-1.96	0.01
Absence of psychotic and anxiety disorders	2.64	2.51-2.77	0.004
Marital status <sup>b</sup>	1.89	1.77-2.01	0.03

<sup>a</sup>Included psychotic and anxiety disorders versus affective and personality disorders.

<sup>b</sup>Marital status (married versus single, separated).

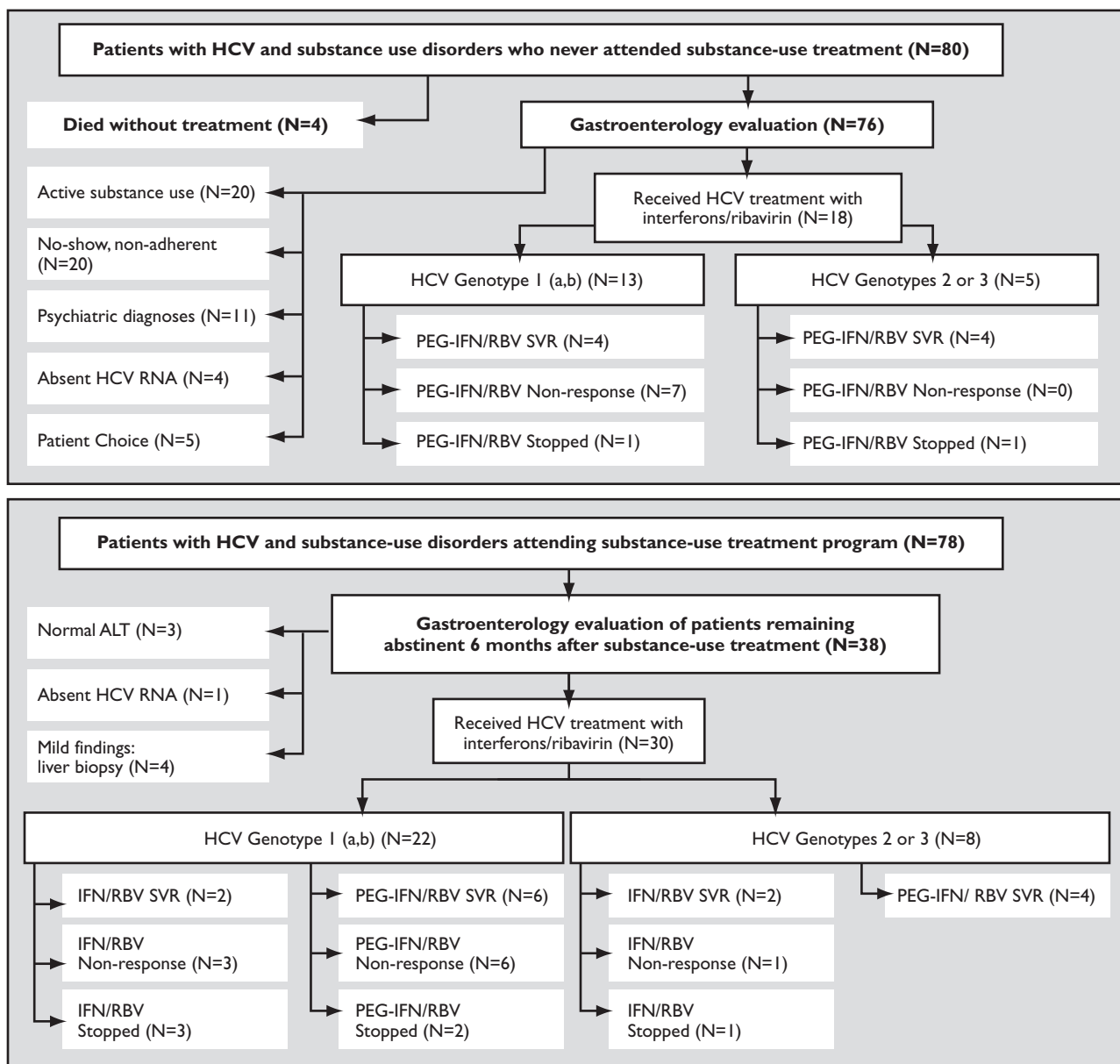
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nence from substances as well as compliance with treatment.<sup>36,37</sup>

To our knowledge, this is the first study to compare 6-month abstinence rates between HCV-seropositive and HCV-seronegative patients after discharge from a substance-use rehabilitation program. Six months of abstinence is a particularly important goal for HCV-seropositive

patients, and current recommendations for HCV treatment suggest withholding interferon therapy from patients with HCV who are actively drinking or using substances.<sup>38,39</sup> HCV infection was the strongest predictor of program completion and remaining abstinent 6 months after program completion. To our knowledge, our study is the first to show that the specific interventions of substance-use treatment and

**FIGURE 2. Hepatitis C Treatment Outcomes in Patients With HCV Infection and Substance-Use Disorders, Comparing Those Who Attended a Substance-Use Rehabilitation and Treatment Program and Those Patients Who Never Attended a Program**



*Note:* HCV: hepatitis C virus; ALT: alanine aminotransferase; IFN: interferon; PEG-IFN: pegylated interferons; RBV: ribavirin; SVR: sustained virological response.

rehabilitation and education about HCV infection may lead to improved eligibility for HCV treatment.

Interferon treatment and ribavirin were effective in eradicating HCV infection in almost half of those treated patients who were abstinent from substances for 6 months. These results are similar to those reported in a similar recently-abstinent HCV population.<sup>40,41</sup> It has been proposed that sustained virologic response rates in the literature may not be applicable to the HCV-infected population with histories of alcohol- or substance-dependence because those rates were derived from large HCV-treatment clinical trials that focused on highly-selected populations and excluded patients with a preexisting history of substance use during the previous year. In contrast to large HCV-treatment trials, reports detailing clinical experience with interferon use indicate that histories of alcohol- and substance-use are barriers to engaging patients in treatment.<sup>42,43</sup> Furthermore, these reports describe little success in eradicating HCV infection in their patient population (sustained virologic response rates: 10%–15%).<sup>42,43</sup> However, our results are in line with previously reported treatment results from large HCV clinical trials that have excluded patients with psychiatric and substance-use disorders.<sup>5,6</sup>

Our sustained virologic response rates were unexpected and contrary to our hypothesis, which was based on the published experience of several liver clinics in Cleveland<sup>42</sup> and St. Louis (VA Medical Center),<sup>43</sup> reporting little practical success in eradicating HCV infection. Compared with patients in those liver clinics, the percentage of treated patients (38%) and sustained virologic response rates (46%) is significantly higher in our patient sample. Other researchers who were primarily treating abstinent patients with HCV and histories of IV-drug use had similar unexpected outcomes, as they anticipated that their patients would not be able to achieve sustained virologic response rates comparable to non-IV-using HCV populations.<sup>41</sup>

Several well-established factors have been associated with reduced sustained virologic response rates in patients receiving interferon-based therapies with ribavirin; these include: male gender; African American race; increased body mass index; advanced age (>40); higher HCV viral load; the presence of cirrhosis, and HCV Genotype 1.<sup>1–4</sup> In our sample, those who achieved sustained virologic response had one or several favorable prognostic indicators (i.e., younger age, lower viral loads, absence of cirrhosis). Our results suggest that substance-abuse treatment and early screening for HCV had an additive value to these more-favorable prognostic indicators. This means that in order to maximize viral response rates to interferon in an alcohol-

and non-IV drug-dependent population, such treatment should be initiated during substance-abuse treatment and at a younger age, before the development of cirrhosis.

Our report highlights the improvement in our ability to engage and administer HCV therapy to patients with comorbid substance use and affective and personality disorders. However, patients with severe psychiatric illness (psychotic and anxiety disorders) were excluded from treatment. In fact, the absence of severe mental illness (a diagnosis of psychotic or posttraumatic stress disorder) was a predictor for receiving interferon treatment, and this underlines the need to develop better management approaches to engage and safely administer HCV treatment in patients with severe mental illness.

Our study has some important limitations. Our base population consisted entirely of male veterans receiving substance-abuse rehabilitation at a VA Medical Center. This population has a high prevalence of psychopathology and a higher prevalence of HCV infection than that of the general U.S. population. Another important limitation of this study was that, other than the Addiction Severity Index, standardized assessments were not utilized. A more rigorous, structured clinical interview might have yielded different prevalence rates of comorbid psychopathology, and more rigorous standardized assessments of sobriety may have yielded different 6-month abstinence rates. However, psychopathology and abstinence rates were assessed in similar fashion across the two study groups.

Although it is plausible that our sample could have achieved the same HCV treatment outcomes without undergoing substance-abuse treatment, the most probable cause for this improved outcome of both substance-abuse treatment and HCV outcome is the early screening and engagement in HCV treatment that this patient sample received. Last, the number of patients who received interferon treatment was small (N = 30), yet our results are consistent with previously published reports about similar population with histories of IV drug use.<sup>40,41</sup>

## CONCLUSIONS

Our results strongly suggest that routine HCV antibody screening is warranted in alcohol-dependent patients and those in substance-abuse rehabilitation programs. Identifying patients infected with HCV while they are involved in the structured setting of a substance-abuse rehabilitation program would afford a prime opportunity to receive education about HCV and establish gastrointestinal follow-up at a time when motivation for lifestyle change and medical

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treatment is high. Furthermore, detecting HCV infection early and providing education about this illness has a positive influence on both HCV and substance-abuse outcomes, and affords HCV-seropositive patients the best possible chance to be engaged in HCV treatment and achieve clearance of HCV infection.

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