



Regular article

Successful treatment of chronic hepatitis C with pegylated interferon in combination with ribavirin in a methadone maintenance treatment program

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Abstract

Injection drug users constitute 60% of the more than 4 million people in the United States with hepatitis C virus (HCV), including many methadone maintenance patients. Few data exist describing clinical outcomes for patients receiving HCV treatment on-site in methadone maintenance settings. In this retrospective study, we describe clinical outcomes for 73 patients receiving HCV treatment on-site in a methadone maintenance treatment program. Fifty-five percent of patients achieved end-of-treatment response, and 45% achieved sustained viral response. These treatment response rates are nearly equivalent to previously published HCV treatment response rates, despite high prevalences of ongoing drug use (49%), psychiatric comorbidity (67%), and HIV coinfection (32%). These data show that on-site HCV treatment with pegylated interferon and ribavirin is effective in methadone-maintained patients, many of whom are active drug users, psychiatrically ill, or HIV coinfecting, and that methadone maintenance treatment programs represent an opportunity to safely treat chronic hepatitis C. © 2009 Elsevier Inc. All rights reserved.

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1. Introduction

Hepatitis C virus (HCV) infection affects more than 4 million people in the United States and is a major cause of morbidity, mortality, and health care expenditure (Armstrong et al., 2006; Wong et al., 2000). Although injection drug users (IDUs) have high HCV infection rates and may

transmit HCV by sharing drug paraphernalia, few active or recent IDUs have received treatment for HCV (Davis & Rodrigue, 2001; Stephenson, 2001). Physician reluctance to treat HCV in IDUs has been attributed to concerns about poor treatment adherence associated with ongoing drug abuse or comorbid psychiatric disorders, lack of urgency by providers regarding the initiation of HCV treatment, or pessimism regarding HCV treatment tolerability or effectiveness (Davis & Rodrigue, 2001; Edlin et al., 2001). Despite these concerns, a growing number of studies now provide support for using interferon and ribavirin to treat HCV in patients with active substance abuse disorders or psychiatric illnesses (Backmund et al., 2001; Cournot et al., 2004; Dalgard et al., 2002; Grebely et al., 2007; Huber et al.,

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2005; Jeffrey et al., 2007; Mauss, Berger, Goelz, Jacob, & Schmutz, 2004; Sylvestre, Litwin, Clements, & Gourevitch, 2005; Robaey et al., 2006; Van Thiel, Anantharaju, & Creech, 2003). These studies show that IDUs respond to HCV treatment nearly as well as non-drug-using patients. One randomized study of HCV treatment in 27 HCV-monoinfected drug users delivered on-site in a methadone maintenance treatment program in Switzerland demonstrated a sustained viral response (SVR) rate of 48% (Huber et al., 2005). Another observational study of directly observed HCV treatment in 40 drug users (55% with genotype 2 or 3; 52% methadone maintained; and 8% HIV/HCV coinfecting) delivered on-site within a community clinic in Canada demonstrated a SVR rate of 55% (Grebely et al., 2007).

The need for alternative models of HCV-related treatment is supported by retrospective studies that show that most HCV-infected drug users referred to specialized liver clinics do not have satisfactory outcomes (Falck-Ytter et al., 2002; Fishbein, Lo, Reinus, Gourevitch, & Klein, 2004; Walley, White, Kushel, Song, & Tulskey, 2005). In addition, prior studies have shown that linking drug abuse treatment with on-site primary medical care has improved outcomes for both tuberculosis and HIV (Batki, Gruber, Moon Bradley, Bradley, & Delucchi, 2002; Gourevitch, Wasserman, Panero, & Selwyn, 1996; Selwyn et al., 1989), but this model has only been recently tested for HCV. We now describe the implementation of a model of colocated opioid agonist (methadone) and HCV-related treatment and report clinical outcomes among the first 73 HCV-infected patients undergoing treatment in this model.

2. Methods

2.1. Treatment setting

The Division of Substance Abuse (DoSA) of the Department of Psychiatry and Behavioral Sciences at Albert Einstein College of Medicine operates nine methadone maintenance treatment clinics in four Bronx, NY, communities, serving approximately 3,400 adults with opioid dependence. In addition to comprehensive substance abuse treatment, clinics offer medical and psychiatric care to Medicaid-insured patients choosing on-site care. Approximately 80% of DoSA patients are Medicaid insured.

2.2. HCV-related training

In eight of our nine DoSA clinics, HCV evaluation and treatment are provided by internists and physician assistants with expertise in both HIV and addiction medicine, using a standardized protocol, available upon request. One internist and physician assistant met monthly with an experienced hepatologist for 18 months and subsequently developed a standardized HCV evaluation and treatment protocol. The other internists received several formal training sessions and

ongoing mentoring in person, by phone, or by email. In two clinics, the standardized HCV evaluation and treatment protocol (described below) was systematically applied to all Medicaid-insured HCV-infected patients. In six clinics, medical providers were just beginning to implement this protocol at the time of this study, with few patients initiating treatment. In one of the nine DoSA clinics, on-site HCV treatment was not offered during this time.

2.3. Hepatitis screening and evaluation

All DoSA patients are routinely screened for hepatitis A, B, and C on admission to methadone maintenance treatment. Treatment of all anti-HCV-positive patients includes vaccination against hepatitis A and B (if lacking immunity) and counseling regarding abstinence from alcohol. Medicaid-insured patients testing positive for HCV antibody are offered further evaluation and treatment, beginning with viral load testing to diagnose chronic HCV infection. We estimate that 65% of all DoSA patients are anti-HCV positive and that 75% of anti-HCV-positive patients have chronic hepatitis C (active viremia). HCV genotype is most often performed at the same time as HCV viral load but is sometimes determined after active viremia has been established.

Patients with chronic hepatitis C undergo additional blood tests and evaluation prior to HCV treatment, including (but not limited to) liver panel (aspartate aminotransferase, alanine aminotransferase, total bilirubin, direct bilirubin, alkaline phosphatase, albumin, and prothrombin time), serum chemistries, and complete blood counts. HIV/HCV-coinfecting patients undergo regular CD4 cell count and HIV viral load monitoring as part of on-site HIV-related primary care. Liver biopsy is recommended for all patients without a contraindication (except HCV monoinfected patients with genotypes 2 or 3), and ultrasound-guided liver biopsies are performed off-site at affiliated hospitals. Liver biopsy staging is used to guide HCV treatment decisions in accord with current standards of care (Bedossa & Poynard, 1996; Ishak et al., 1995). HCV treatment recommendations are individualized for patients unwilling to undergo liver biopsy.

Prior to treatment for HCV, ophthalmologic examinations are performed on all patients by internists (and by an ophthalmologist for all patients with diabetes or hypertension). Finally, electrocardiograms (EKGs) are performed in all patients older than 40 years and in all patients with diabetes or hypertension. Patients with abnormal EKGs or cardiac risk factors may also undergo cardiac stress testing. All tests are performed on-site in DoSA clinics, except ophthalmologist examinations and stress tests.

HCV treatment candidates are screened for psychiatric disease by an internist and referred to a psychiatrist for formal psychiatric evaluation and management if indicated. This HCV treatment screening and evaluation program has been previously described (Litwin, Soloway, & Gourevitch, 2005).

2.4. HCV treatment eligibility criteria

Eligibility for HCV treatment is based on liver biopsy results, contraindications to HCV treatment, psychiatric stability, and judgment of patients' medical providers. Patients with moderate fibrosis by liver biopsy (Metavir score of ≥ 2 or Ishak score of ≥ 3) are eligible for HCV treatment. Patients with mild fibrosis (Metavir score of < 2 or Ishak score of < 3) are eligible for HCV treatment if they are HIV infected, have HCV genotype 2 or 3, have steatosis on liver biopsy, were HCV infected within the last 10 years, or are relatively young (generally less than 40 years of age).

Patients with the following medical conditions are ineligible for HCV treatment: poorly controlled diabetes, severe cardiovascular disease, severe chronic pulmonary disease, poorly controlled seizure disorder, immunologically mediated disease, hemoglobinopathy, hemochromatosis, alpha 1-antitrypsin deficiency, Wilson's disease, previous organ transplant, or decompensated liver disease. Patients with poor prognosis from HIV disease are ineligible for HCV treatment; these include HIV/HCV-coinfected patients who have had any AIDS-defining opportunistic infection within the past year or who have a CD4 count less than $200/\text{mm}^3$ in combination with either an HIV viral load greater than 20,000 copies/ml, or a negative slope for their three most recent CD4 cell counts.

Patients with current unstable psychiatric disorders are also ineligible for HCV treatment. Such instability is defined by active suicidal ideation or a suicide attempt within the last 12 months, active homicidal ideation, or new auditory or visual hallucinations within the past 3 months. In addition, patients with psychiatric illness for whom psychotropic medications have changed within the last 3 months or for whom the psychiatric condition significantly disrupts activities of daily living may be excluded from HCV treatment. Finally, patients with demonstrated nonadherence to psychotropic medications or absence of any social support may be excluded from HCV treatment. Psychiatric assessment before and during HCV treatment is discussed in detail below.

Active or recent drug use is not a contraindication to HCV treatment. In these cases, treatment eligibility is determined on an individualized basis, taking into account adherence to medical visits, commitment to behavior that prevents reinfection with HCV (e.g., not sharing syringes or other drug paraphernalia), stable activities of daily living, and intact social support.

In sum, patients with active drug or alcohol use, HIV coinfection, current stable psychiatric illness, and compensated cirrhosis (Child-Turcotte-Pugh Class A) are all eligible for HCV treatment according to this protocol.

2.5. Psychiatric assessment before and during HCV treatment

DoSA medical providers perform psychiatric assessments on all HCV-infected patients during evaluation for

HCV treatment and regularly during HCV treatment. Pretreatment assessments include history of previous psychiatric diagnoses, psychiatric medications, psychiatric hospitalizations, and any previous suicide attempts, as well as a mental status examination including current suicidal or homicidal ideation, auditory or visual hallucinations, mood, affect, grooming, and adherence to psychiatric visits and medications. In some cases, providers administer Beck Depression Inventory prior to initiating HCV treatment.

During the pretreatment evaluation and at each HCV intratreatment visit, patients are screened for depression, including bipolar disorder. Patients with mild or moderate depression are generally managed by DoSA internists, whereas patients with severe depression, bipolar disorder, or psychotic disorders are referred to psychiatrists for stabilization prior to initiating or continuing HCV treatment. During HCV treatment, patients are monitored for psychiatric symptoms as often as is clinically indicated (at least monthly and as often as weekly). Psychiatric symptoms that emerge during HCV treatment are treated by HCV medication dosage adjustments or by increasing the frequency and/or intensity of psychiatric care. If psychiatric symptoms during HCV treatment become severe, interferon doses for HCV may be reduced, or HCV treatment may be discontinued completely. In such cases, HCV therapy may be reinstated if psychiatric symptoms are stabilized and/or stronger social supports are established. During the course of HCV treatment, patients with preexisting or new severe psychiatric diagnoses are closely followed by psychiatrists. Medical providers, psychiatrists, substance abuse counselors, nurses, and social workers participate in regular interdisciplinary team meetings, which serve as venues for assessing patient progress and fostering an inclusive treatment plan.

Prompt consideration for withdrawal from HCV treatment may be considered in cases of severe psychiatric instability. These include active suicidal or homicidal ideation, behavioral changes that jeopardize continued enrollment in methadone maintenance treatment, and other unstable psychiatric symptoms or conditions serious enough to warrant discontinuation. Decisions for HCV treatment discontinuation are made on an individualized basis.

2.6. HCV treatment

Our standardized protocol calls for treatment with once-weekly pegylated interferon in combination with twice daily ribavirin for either 24 or 48 weeks. Pegylated interferon alfa-2a and alfa-2b are dosed according to established guidelines (Strader, Wright, Thomas, & Seeff, 2004). The dose of ribavirin is weight-based for patients with genotypes 1 or 4 (1,000 mg if ≤ 75 kg or 1,200 mg if > 75 kg) and fixed (800 mg) for patients with genotypes 2 or 3. HCV-monoinfected patients with genotypes 2 or 3 are treated for 24 weeks; all others are treated for 48 weeks.

Patients generally discontinue HCV treatment at 12 weeks if an early viral response (EVR; defined below) is not achieved. Treatment and monitoring are by standardized protocols. On-site programs available to minimize treatment discontinuations include expert HCV mentoring and consultation if needed (by experienced internists and hepatologists), medical interventions (hematologic growth factors and directly administered interferon injections), and intratreatment social support (HCV support groups, peer educators, and substance abuse counselors; Litwin et al., 2005).

2.7. Data collection and analysis

We conducted a retrospective review of medical charts using a standardized chart review instrument for all patients undergoing on-site HCV treatment (received at least one dose of interferon) between January 1, 2003, and December 15, 2005. All charts were reviewed systematically for laboratory and urine toxicology results. Additional factors hypothesized to be associated with viral response, including sociodemographic and clinical characteristics, psychiatric diagnoses, and recent and active drug use (Table 1), were also obtained by chart review. Associations between these factors and both end-of-treatment response (ETR) and SVR were then identified using chi-square and Fisher exact tests. This study was approved by the Albert Einstein College of Medicine Committee on Clinical Investigations.

2.8. Definitions of key outcome and independent variables

The main outcome variables were ETR and SVR.

EVR: 2 log decrease in HCV viral load or undetectable viral load 12 weeks into treatment.

ETR: undetectable viral load at the end of treatment.

SVR: undetectable viral load 6 months after the end of treatment.

Psychiatric diagnoses: Psychiatric diagnoses were determined through review of admission history and physical, most recent annual history and physical, progress notes, and problem list.

Recent drug use was defined as at least one positive monthly urine toxicology result (opioid, cocaine, or benzodiazepine) in the 6 months preceding HCV treatment initiation. Patients who had been prescribed either opioids or benzodiazepines during this time period were not considered to have recent drug use.

Active drug use was defined as any positive urine toxicology result within 1 month of HCV treatment initiation.

Drug use during treatment was defined as any positive urine toxicology result during the period of HCV treatment.

Years of HCV infection was estimated by the following equation: [(age at HCV treatment initiation) – (age at first

injection drug use) – (1 year)] (Garfein, Vlahov, Galai, Doherty, & Nelson, 1996).

3. Results

3.1. Sociodemographic and clinical characteristics

Seventy-three current or former drug users initiated on-site treatment for HCV during this 3-year period (Fig. 1). At the two DoSA clinics in which the HCV evaluation and treatment protocol was systematically applied, 37 patients were treated. This is estimated to be 15% of the 252 Medicaid-insured patients with chronic hepatitis C in these two clinics. At the six other clinics in which the protocol was recently initiated, fewer patients were treated: a median of 6.5 patients per clinic were treated. This is estimated to be between 1% and 8% of all potentially eligible patients with chronic hepatitis C in each of these six clinics.

Patient characteristics are summarized in Table 1. At the time of HCV treatment initiation, patients had been enrolled in methadone maintenance for a median of 3.3 years (interquartile range, 1.2–8.8 years) and were taking a mean methadone dose of 114 mg ($SD = 67$ mg). The mean estimated duration of HCV infection was 26 years ($SD = 9$ years). Almost all (97%) had Medicaid insurance. Two thirds of patients were Latinos, had current psychiatric illness, and had genotype 1 infection. Seventy-six percent of patients with current psychiatric illnesses were receiving care from a psychiatrist at the time of HCV treatment initiation. Fifty percent of the 30 patients who were administered the Beck Depression Inventory had evidence of depression. Sixty-eight percent of all patients were taking psychiatric medications at the time of HCV treatment initiation, including selective serotonin reuptake inhibitors (67%), antipsychotics (38%), benzodiazepines (23%), or other antidepressants (18%). Nearly one third (32%) were HIV infected, and one patient was infected with HBV, HCV, and HIV. Almost all (98%) were administered either pegylated interferon alfa-2a in combination with ribavirin (66%, 48) or pegylated interferon alfa-2b in combination with ribavirin (32%, 23). One patient received thrice weekly consensus interferon in combination with ribavirin, and another received thrice weekly interferon alfa-2b without ribavirin. Seven patients had been previously treated for HCV unsuccessfully by an off-site medical provider.

3.2. HCV treatment results

Eighty-six percent of patients completed at least 12 weeks of treatment. Twenty-three percent discontinued treatment early (<80% expected duration) due to virological failure ($n = 17$); 21% discontinued treatment early due to adverse medication effects ($n = 15$), most often psychiatric symptoms ($n = 6$) or anemia ($n = 5$). Nineteen percent of patients required a decrease in ribavirin dose, and 8% a

Table 1
 Characteristics of 73 methadone-maintained patients treated on-site for HCV and factors associated with ETR and SVR

Characteristic	<i>n</i> (%) or <i>M</i> ± <i>SD</i>	ETR (<i>n</i> = 73)	SVR (<i>n</i> = 73)
Age (years)	46 ± 8		
≥40	59 (81)	33/59 (56)	27/59 (46)
<40	14 (19)	7/14 (50)	6/14 (43)
Sex			
Male	52 (71)	32/52 (62)	27/52 (52)
Female	21 (29)	8/21 (38)	6/21 (29)
Race/Ethnicity			
Latino	49 (67)	28/49 (57)	22/49 (45)
African American	9 (12)	2/9 (22)	2/9 (22)
Caucasian	15 (21)	10/15 (67)	9/15 (60)
Route of drug use			
IDU	66 (90)	36/66 (55)	30/66 (45)
Intranasal drug use	7 (10)	4/7 (57)	3/7 (43)
Recent illicit drug use			
Used within 6 months	36 (49)	19/36 (53)	15/36 (42)
Used more than 6 months ago	37 (51)	21/37 (57)	18/37 (49)
Active illicit drug use			
Used within 1 month	27 (37)	14/27 (52)	13/27 (48)
Used more than 1 month ago	46 (63)	26/46 (55)	20/46 (43)
Alcohol			
History of alcohol dependence/abuse (<i>DSM-IV</i> criteria)	24 (33)	13/24 (54)	10/24 (42)
No history	49 (67)	27/49 (57)	23/49 (47)
Tobacco			
Current smoker	58 (79)	28/58 (48)*	22/58 (38)*
Not current smoker	15 (21)	12/15 (80)	11/15 (73)
Psychiatric illness			
Current psychiatric illness	49 (67)	23/49 (47)	19/49 (39)
No current psychiatric illness	24 (33)	17/24 (71)	14/24 (58)
Depression	45 (62)		
Anxiety disorder	21 (29)		
Psychosis	15 (21)		
Posttraumatic stress disorder	8 (11)		
Bipolar disorder	4 (5)		
Patients with current psychiatric illness (<i>n</i> = 49) prior to HCV treatment initiation			
Followed by psychiatrist and internist	37/49 (76)	16/37 (43)	13/37 (35)
Followed by internist only	12/49 (24)	7/12 (58)	6/12 (50)
Currently taking psychiatric medications			
Yes	50 (68)	24/50 (48)	20/50 (40)
No	23 (32)	16/23 (70)	13/23 (57)
Employment			
Employed	11 (15)	9/11 (82)	8/11 (73)*
Unemployed	62 (85)	31/62 (50)	25/62 (40)
Ever attended HCV support group			
Yes	28 (38)	14/28 (50)	11/28 (39)
No	45 (62)	26/45 (58)	22/45 (49)
BMI	29 ± 6		
Overweight (BMI between 25 and 29.9)	31 (42)	12/23 (52)	11/23 (48)
Obese (BMI ≥30)	23 (32)	28/50 (56)	22/50 (44)
HIV status			
HIV–	50 (68)	29/50 (58)	23/50 (46)
HIV+	23 (32)	11/23 (48)	10/23 (43)
CD4 (cells/mm ³)	534 ± 288		
Taking HAART	12/23 (52)		
HCV genotype			
1 or 4	50 (68)	24/50 (48)	20/50 (40) [†]
2	12 (16)	9/12 (75)	9/12 (75)
3	11 (15)	7/11 (64)	4/11 (36)
HCV viral load (4 patients listed as >700,000 or >750,000)			
≥800,000 IU/ml*	35/69 (51)	20/35 (57)	15/35 (43)
<800,000 IU/ml	34/69 (49)	18/34 (53)	16/34 (47)

(continued on next page)

Table 1 (continued)

Characteristic	n (%) or M ± SD	ETR (n = 73)	SVR (n = 73)
Liver biopsy performed (n = 48)			
Advanced stage (Metavir ≥3; Ishak ≥4)	19/48 (40)	7/19 (37)	4/19 (21)*
Mild to moderate stage (Metavir ≤2; Ishak ≤3)	29/48 (60)	17/29 (59)	15/29 (52)
Completed at least 80% of planned duration of treatment (among those who achieved EVR—51 of 69)			
≥80% of planned duration of treatment	38/51 (75)	33/38 (87)**	26/38 (68)**
<80% of planned duration of treatment	13/51 (25)	3/13 (23)	3/13 (23)

Note. BMI = body mass index; DSM-IV = Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition; HAART = highly active antiretroviral therapy.

* $p < .05$.

** $p < .01$.

† Genotype 2 versus nongenotype 2 (ETR, $p = .12$; SVR, $p = .02$).

decrease in interferon dose. Most patients were administered growth factors during treatment, either erythropoietin (74%) or filgrastim (18%). Fifty patients (68%) received at least 80% of all interferon injections directly administered in the methadone clinic.

Most (74%) of the patients achieved EVR, including three patients who had a rapid viral response at 4 weeks but discontinued HCV treatment prior to 12 weeks. More than half (55%) achieved ETR, and 45% achieved SVR. Surprisingly, HIV/HCV-coinfected patients achieved an equivalent SVR rate (43%) as HCV-monoinfected patients (46%), although 87% (20/23) of HIV/HCV-coinfected patients were taking erythropoietin compared with 68% (34/50) of HCV-monoinfected patients ($p = .09$).

Thirty percent of patients used illicit substances during HCV treatment, but there was no association between illicit drug use and virological outcomes. Thirty-three percent (24/73) of patients required a methadone dose increase during HCV treatment. Two thirds of patients (8/12) who used heroin during HCV treatment received a methadone increase, compared with 20% of patients (12/61) who did not use heroin during HCV treatment.

Three patients without preexisting psychiatric diagnoses developed new onset depression (3) or anxiety (2) during treatment, and all three achieved SVR. Two of these patients were referred to an on-site psychiatrist and were able to complete HCV treatment; the third wanted to discontinue HCV treatment early and refused referral to a psychiatrist.

3.3. Factors associated with HCV treatment response

Patients who were nonsmokers, employed, infected with genotype 2 (vs. all other genotypes), who had mild or moderate liver disease on liver biopsy (Metavir ≤2; Ishak ≤3), or who completed at least 80% of planned duration of treatment (among those who achieved EVR) were significantly more likely to achieve SVR (Table 1). Treatment response rates did not differ based on the type of pegylated interferon used or prior HCV treatment. Treatment response rates did not differ between patients treated in the two clinics where HCV evaluation and treatment was systematically applied and patients treated in the six clinics where the protocol was less frequently

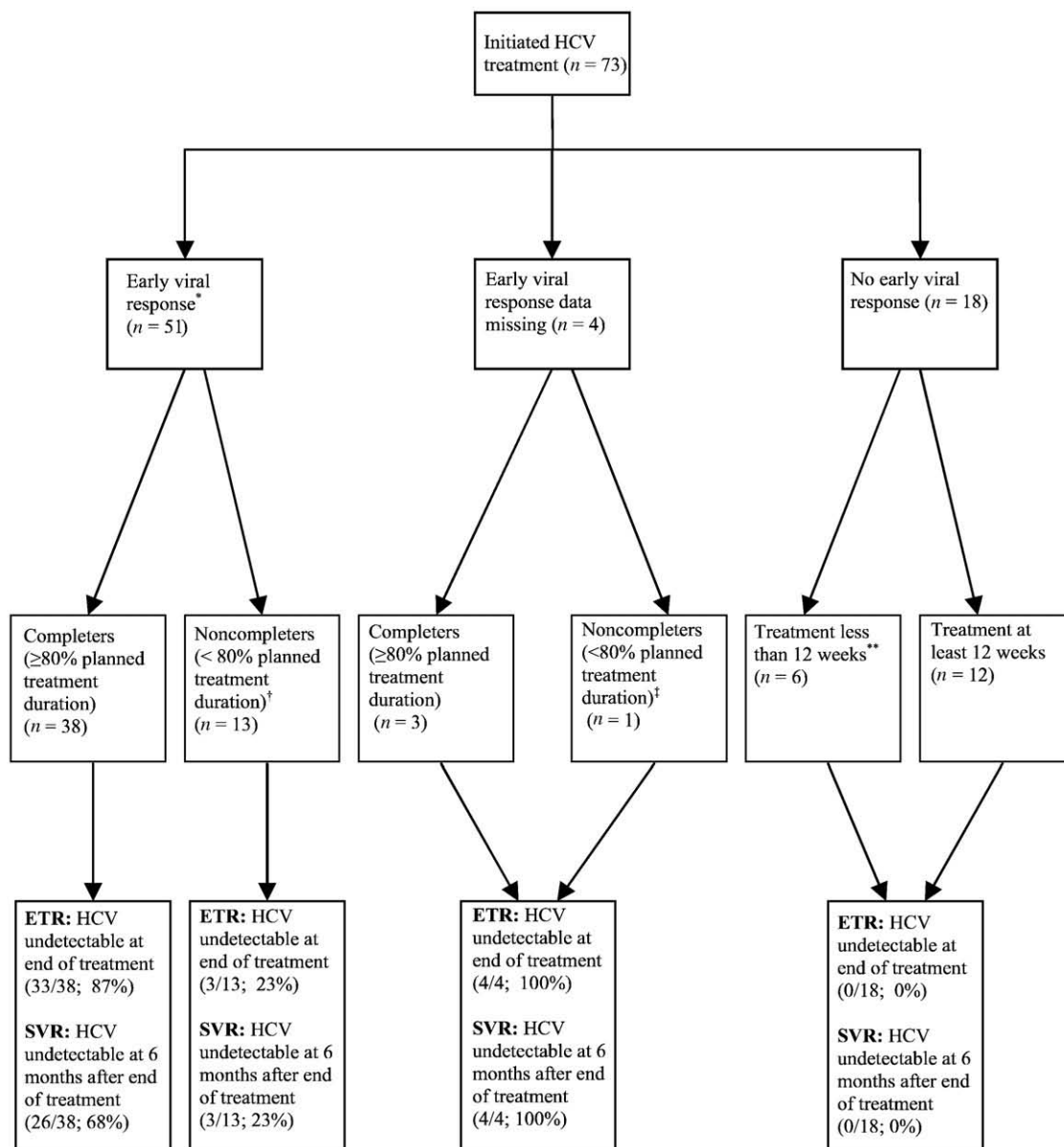
utilized. There was no association between recent or active drug use and virologic outcomes.

4. Discussion

To our knowledge, this is the first comprehensive description of hepatitis C treatment with pegylated interferon and ribavirin delivered on-site in a methadone maintenance treatment program in the United States. Treatment success rates were nearly equivalent to outcomes in other published studies for HCV-monoinfected and HCV/HIV-coinfected patients (Carrat et al., 2004; Chung et al., 2004; Fried et al., 2002; Mann et al., 2001; Torriani et al., 2004), and with international studies of HCV treatment delivered on-site within a methadone maintenance treatment program or community clinic (Grebely et al., 2007; Huber et al., 2005). Successful treatment of HIV-coinfected patients may have been facilitated by the foundation of our existing HIV primary care program. Our results demonstrate that IDUs with complex medical and psychiatric comorbidities can be effectively treated for HCV with a model of colocated substance abuse and primary medical care. Primary care providers knowledgeable in the treatment of HCV and HIV infections, substance abuse, and working in tandem with psychiatrists and HCV support groups may mitigate the potentially negative effects on treatment outcomes of active psychiatric illness and substance abuse.

Methadone maintenance treatment programs, which require regular contact with patients, may promote adherence to antiviral treatment. Completion of at least 80% of planned treatment is associated with improved virological outcomes (McHutchison et al., 2002). As in the correctional setting (Allen et al., 2003; Farley et al., 2005; Sterling et al., 2004), methadone treatment programs may also facilitate directly administered once-weekly interferon injections (Grebely et al., 2007).

In the two clinics in our system in which systematic HCV evaluation and treatment programs were in place, 15% of Medicaid-insured patients with chronic hepatitis C initiated HCV treatment. This estimate compares favorably to other cohorts of drug users. In three other cohorts of community-based IDUs, only 6% to 7% initiated HCV treatment (Fishbein et al., 2004; Mehta et al., 2008; Schackman et al.,



Overall end of treatment response ETR: 40/73; 55%

Overall sustained viral response SVR: 33/73; 45%

*Undetectable viral load or at least 2 log decrease in viral load at 12 weeks - 3 patients had rapid viral response at 4 weeks, but discontinued prior to 12 weeks due to anemia (3) and renal failure (2)

†Reasons for noncompletion: virological failure at 24 weeks (5); anemia (4); acute renal failure (2); psychiatric side effects (1); anorexia (1); weight loss (1); domestic violence victim (1); unstable drug use (1); loss of insurance (1)

‡Reason for noncompletion: psychiatric side effects (1)

**Reasons for early treatment discontinuation (<12 weeks): psychiatric side effects (4); unstable alcohol use (2); anorexia/nausea (2); anemia (1); unstable HIV (1)

Fig. 1. Outcomes in 73 patients treated for hepatitis C on-site at Albert Einstein College of Medicine methadone maintenance treatment program.

2007). Further, the rate of SVR rate we observed (45%) also compares favorably to a retrospective study of antiviral therapy in a metropolitan clinic population, in which only 13% of 83 patients (none active alcohol or drug users) initiating HCV treatment had an SVR. Although our rates of

treatment initiation and success are encouraging, we cannot conclude that on-site treatment is associated with greater proportions of patients evaluated or treated than off-site care, nor can we conclude that there improved virological outcomes for patients treated on-site versus off-site.

There are many reasons patients may not initiate on-site treatment for HCV in a methadone clinic, including receiving off-site medical care, previous HCV treatment, mild liver disease on biopsy, patient fear of biopsy and interferon-based treatment, treatment contraindications (medical, psychiatric, psychosocial, or addiction related), discontinuation of methadone, loss of medical insurance, lack of patient interest, or limited provider time. The relative contributions of these are beyond the scope of this study.

This study is limited because it is from a single institution, retrospective, and has a modest sample size. There was also a potential for selection bias given the small percentage of infected patients treated. It was beyond the scope of this study to review every chart to determine what percentage of all DoSA patients with chronic hepatitis C were evaluated for and offered HCV treatment. Rather, our goal was to demonstrate the feasibility and treatment outcomes of an on-site integrated model of care delivered by internists with expertise in both HCV and addiction treatments. In this model, HCV treatment is integrated within a substance abuse treatment program and is addressed concurrently with addiction and comorbid medical and psychiatric disorders. Still, provider time for initiating HCV treatment remains limited by competing priorities, including addiction treatment, primary medical care, and HIV-related care.

Despite its limitations, our study has several strengths. Generalizability is increased because medical providers and patients came from eight different clinics, treatment was highly standardized and provided by internists, and the patients had many complicating factors that may be associated with decreased virologic response.

Additional resources are urgently needed to expand the capacity of existing programs and to develop new on-site treatment programs because a significant proportion of addiction treatment physicians are willing to treat HCV on-site if given the appropriate training and resources (Litwin et al., 2007). Integration of on-site viral hepatitis treatment programs within existing HIV treatment programs is also promising strategy. Future studies should evaluate interventions such as directly administered treatment (both interferon and ribavirin) designed to improve HCV treatment adherence in methadone-maintained patients and compare outcomes of on-site versus off-site HCV treatment. Our study shows that models of integration of tuberculosis and HIV-related care with drug abuse treatment can be successfully extended to HCV-related care. Such an integrated approach holds promise to significantly increase access to care for real-world patients, who are all too often excluded in clinical trials and practice (Hagan et al., 2006).

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