

TRAINING AND IMPLEMENTATION GUIDE



Delivering Hepatitis C Treatment in an HIV Care Setting

September 2014



U.S. Department of Health and Human Services
Health Resources and Services Administration
HIV/AIDS Bureau
Special Projects of National Significance Program



Training and Implementation Guide: Delivering Hepatitis C Treatment in an HIV Care Setting

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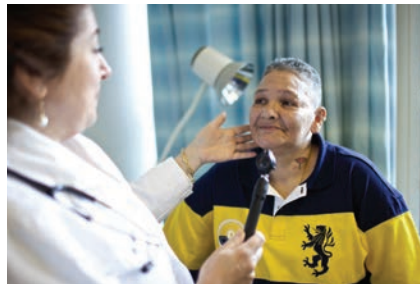
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The Health Resources and Services Administration (HRSA), HIV/AIDS Bureau (HAB) has developed the Integrating HIV Innovative Practices (IHIP) manuals, curricula, and trainings to assist health care providers and others delivering HIV care in communities heavily impacted by HIV/AIDS. This IHIP guide is part of that effort. Additional IHIP materials can be found at www.careacttarget.org/ihip.



OVERVIEW

While antiretroviral therapy (ART) has significantly improved health outcomes and longevity among people living with HIV (PLWH), hepatitis C (HCV) has emerged as a major contributing factor of morbidity and mortality among PLWH who are coinfectd. Complications from chronic HCV, such as end-stage liver disease and liver cancer, are among leading causes of death among PLWH, despite HIV treatment.¹⁻³ HIV accelerates HCV progression.^{4,5}

Chronic HCV is often called a “silent killer” because it slowly damages the liver over many years and without noticeable symptoms.⁶ An estimated 75 to 85% of acute HCV infections become chronic, and approximately 75% of individuals with chronic HCV are unaware of their infection.⁷ In addition, HCV is a common, and serious, coinfection among PLWH. In the United States, an estimated 25% of all PLWH are HCV coinfectd.⁸

HCV treatment is available and is a lifesaving intervention for coinfectd people. Curing HCV—an outcome called sustained virologic response, or SVR—lowers AIDS-related, liver-related, and non-AIDS-related death rates among coinfectd people, even if they are cirrhotic.⁹⁻¹¹

However, many coinfectd patients are poor and come from underserved and marginalized communities where they may face significant barriers to entry into the health care system and to accessing services. Ryan

White HIV/AIDS Program grantees are familiar with the numerous barriers facing PLWH. For people with HIV/HCV coinfection, there are additional barriers, however, such as low referral rates and exclusion criteria,

ADDRESSING HEPATITIS: A FEDERAL PRIORITY

In January 2010, the Institute of Medicine (IOM) issued “Hepatitis and Liver Cancer: A National Strategy for Prevention and Control of Hepatitis B and C.” The report called for increased funding, research, and awareness around viral hepatitis.

In March 2010, the SPNS Hepatitis C Treatment Expansion Initiative Funding Opportunity Announcement was released.

In May 2011, the “Action Plan for the Prevention, Care and Treatment of Viral Hepatitis” was rolled out, and in February 2014 the plan was updated.

Together, these efforts help shine a light on hepatitis infection, its severity, and its treatment. Given high rates of coinfection among PLWH, these efforts concurrently support the National HIV/AIDS Strategy.

including psychiatric illness, ongoing drug or alcohol use, and medical contraindications, which have traditionally limited access to HCV treatment.^{12,13}

The prevalence and severity of HCV coinfection among PLWH—combined with the known benefits of being cured from HCV—call for expanding HCV care and treatment to PLWH.

In recognition of the need to focus on HCV coinfection, the Health Resources and Services Administration's (HRSA's), HIV/AIDS Bureau's (HAB's) Special Projects of National Significance (SPNS) Program launched the *Hepatitis C Treatment Expansion Initiative* (SPNS Hepatitis C Initiative). The Initiative, funded from 2010 to 2014 in two separate cohorts, sought to develop innovative, replicable, and sustainable models for delivering HCV care and treatment in the context of HIV primary care. The Initiative funded grantee sites and a central Evaluation and Technical Assistance Center (ETAC), and compared four different models of care:

1. Integrated HCV treatment without a designated HCV clinic
2. Integrated HCV treatment with a designated clinic
3. Primary care with expert backup
4. Co-located care with a specialist.

Although treatment for HCV virus has become simpler, safer, and more effective since the SPNS Hepatitis C Initiative began, the lessons learned and tools and

processes developed by grantees remain relevant to and highly valuable for implementing and scaling up HCV care and treatment in HIV primary care.

The target audience for this guide includes health care provider sites and community partners with an interest in treating HCV among their HIV-positive coinfecting patients.

The following chapters include:

- An overview of HCV infection and specific considerations for HCV/HIV coinfecting people;
- A discussion of the HCV treatment barriers that coinfecting people face;
- A synopsis of key details of the SPNS Hepatitis C Initiative, its grantees, and the models of care studied;
- A summary of the best practices gained from the SPNS Hepatitis C Initiative, and the potential benefits and challenges associated with each model of care discussed (along with logistics, sustainability, and other considerations); and
- A list of additional resources to assist grantees in the delivery of high-quality HCV treatment to PLWH.

This training and implementation guide is part of the Integrating HIV Innovative Practices (IHIP) project, which promotes dissemination and replication of successful SPNS models of care. IHIP materials can be found at: <https://careacttarget.org/ihip>.



UNDERSTANDING THE NEED FOR HEPATITIS C TREATMENT EXPANSION

WHAT IS HEPATITIS C?

HCV is a blood-borne virus that enters, and infects, liver cells. There are five known hepatitis viruses, named alphabetically in the order of their discovery: hepatitis A, B, C, D, and E.

The HCV virus has at least six different strains, called *genotypes*, numbered in the order of their discovery. Each HCV genotype has subtypes, which are lettered (1a, 1b, 1c, 2a, etc.) It is possible to be infected with more than one HCV genotype (called *mixed infections*; these usually occur in people with multiple exposures, including injection drug users, dialysis patients, and recipients of blood or blood products).^{14–17}

Currently, HCV treatment is tailored according to a person's HCV genotype, and sometimes even the subtype; pan-genotypic (“one size fits all”) regimens are in clinical trials and will be available in the coming years.

HCV does not always become chronic; 20% to 40% of infected people have a strong immune response that rids them of the virus (an outcome called *spontaneous viral clearance*).¹⁸ For the other 60% to 80%, hepatitis C is a lifelong infection, unless it is cured with treatment (an outcome called *sustained virologic response*).

Untreated HCV can lead to liver cirrhosis. People with cirrhosis are at risk for liver cancer and liver failure (called *hepatic decompensation*). In the United States, these hepatitis C complications are the reason for most liver transplants.¹⁹ From 1999 to 2007, more people in the United States died from HCV-related liver disease than AIDS, and in 2010, the death toll from HCV was over 16,500.^{20,21}

HOW MANY PEOPLE HAVE HEPATITIS C?

Worldwide, an estimated 185 million people have been infected with the HCV virus, and at least 2 million more people are newly infected annually.²² Each year, almost

DID YOU KNOW?

From 1999 to 2007, more people in the United States died from HCV-associated complications than from AIDS.

Source: Ly KN, Xing J, Kleven RM, Jiles RB, Ward JW, Holmberg SD. The increasing burden of mortality from viral hepatitis in the United States between 1999 and 2007. *Ann Intern Med*. 2012 Feb 21;156(4):271–8.

THE U.S. HCV EPIDEMIC

Of the estimated 2.7 million chronically infected people in the United States,

- 81% are 40 to 59 years old — prevalence in this group is 3.5%.
- Most are male.
- Most are low-income (less than twice the poverty level in 2010, which was \$22,050 for a four-person family).
- Most have a high school education — or less.
- Blacks have the highest HCV prevalence (2% versus 1.3% among Whites and 1% among Hispanics).
- HCV prevalence is higher among black males (2.9%) than black females (1.7%).

Sources:

Denniston MM, Jiles RB, Drobeniuc J, et al. Chronic hepatitis C virus infection in the United States, National Health and Nutrition Examination Survey 2003 to 2010. *Ann Intern Med.* 2014 Mar 4;160(5):293–300.

Department of Health and Human Services. Office of the Assistant Secretary for Planning and Evaluation. Prior HHS Poverty Guidelines and Federal Register. Available at: <http://aspe.hhs.gov/poverty/figures-fed-reg.cfm>. Accessed on August 7, 2014.

500,000 people die worldwide from HCV-associated liver disease.²³

In the United States, the Centers for Disease Control and Prevention (CDC) estimated that 7,200 to 43,400 people were newly infected with HCV in 2011.²⁴ According to the National Health and Nutrition Examination Survey (NHANES), 1% of the population—or 2.7 million people—are chronically infected with HCV.²⁵ It is likely that HCV prevalence is actually even higher, since NHANES did not include high-prevalence groups such as homeless and incarcerated people in its count. In fact, researchers who included these high-prevalence groups have estimated that almost a million more people are infected with HCV.²⁶

HCV is the most common blood-borne infection in the United States, where almost 3 million people are chronically infected with HCV; most of them born between 1945 and 1965 (“baby boomers”).^{27–29} Many baby boomers are unaware that they have been infected, which is why the CDC and the U.S. Preventive Services Task Force (USPSTF) recommend one-time screening for people in this birth cohort.

But HCV screening should not be limited to the baby boomer birth cohort. HCV screening is also recommended for all people at high risk for infection.³⁰ HCV is particularly prevalent among African-Americans,*

prisoners, current and former injection drug users (IDUs), and homeless people.³¹

Nonmedical use of prescription opioids is rampant among young people, and the plentiful supply of cheap heroin has led many of them to transition from oral opioids to heroin injecting.^{32,33} HCV infections among young IDUs are being reported across the country; lack of access to sterile injection equipment also puts them at risk for HIV.³⁴

As with HIV, African-Americans bear a disproportionate burden of HCV. In the United States, 22% of people with HCV are African-American, although they comprise only 13% of the population.^{35,36}

African-Americans are almost four times more likely to develop chronic HCV than Caucasians or Hispanics, and interferon-based treatment is less effective for African-Americans, in part because of genetic factors.³⁷ [Fortunately, new HCV direct-acting antivirals (DAAs) appear to be highly effective regardless of race or genetics]. Survival rates after liver transplantation are also lowest in African-Americans.³⁸

HOW IS HCV TRANSMITTED?

As a blood-borne virus, HCV is transmitted when blood from an infected person enters another person’s bloodstream. HCV is a small virus; therefore, it is highly concentrated in blood. Unlike HIV, which is fragile, HCV is tough—it can survive in dried blood for weeks at room

*African-American and black are used interchangeably, to be consistent with source material.

temperature.³⁹ For these reasons, HCV is considered to be 10 times more infectious than HIV.⁴⁰

HCV prevention is important, even for people who already have chronic HCV, since a person can become infected with HCV more than once (called reinfection). Sometimes a person can be infected with more than one HCV genotype. Reinfection can occur in people who have spontaneously cleared their HCV, or been cured by treatment.⁴¹ There is no HCV vaccine.

Because HCV is blood-borne, it is especially common among current and former IDUs. Sharing injection equipment can increase risk for HIV, hepatitis B (HBV), and especially HCV, since it is present even in tiny amounts of blood. It is therefore essential to provide patients who are injecting drugs with information on safer injection practices and referral to syringe exchange programs (in states where this is permissible), so they can avoid other blood-borne viruses and avoid becoming infected—or reinfected—with HCV.

HCV is prevalent among people with bleeding disorders who were treated with blood products before 1988 (when viral inactivation was instituted), and people who were transfused before 1992, when more thorough blood screening was introduced.⁴² People have also acquired HCV from transplantation with infected tissue or organs (in 2011, the U.S. Public Health Service recommended that donors undergo HCV ribonucleic acid (RNA) testing to reduce risk); invasive medical and dental procedures or dialysis under inadequate infection control; tattooing with shared needles, ink, and inkwells; needlestick injuries (health care workers); sharing razors, toothbrushes, manicuring equipment, and other personal care items that may have another person's blood on them; and vertical transmission (risk ranges from 4% to 7% from an HIV-negative mother; it increases to 7% to 15% if the mother is HIV/HCV coinfectd).⁴³

HCV can be transmitted sexually, and is especially common among HIV-positive men who have sex with men (MSM). Since 2000, outbreaks of sexually transmitted HCV have been reported among HIV-positive MSM in Asia, Australia, Canada, Europe, and the United States.^{44–46} Researchers have identified a cluster of risk factors associated with sexual transmission of HCV, including condomless receptive anal intercourse, fisting, use of noninjection recreational drugs, group sex, rectal bleeding, and other sexually transmitted infections, including HIV.^{47–49} Many of these HCV infections were detected by vigilant clinicians who noticed abnormally

elevated liver enzyme levels during routine monitoring of people on antiretroviral therapy (ART).^{50,51}

HCV sexual transmission between monogamous, HIV-negative heterosexual partners is rare. The risk increases for people who have multiple partners, and people with sexually transmitted infections, including HIV.⁵²

HIV AND HCV

HCV is prevalent among, and can be deadly for, PLWH. In the United States, an estimated 25% of PLWH—more than 287,000 people—are HCV coinfectd.^{53,54} Over 90% of people who acquired HIV from injection drug use are HCV coinfectd.⁵⁵

- HCV screening is one of HAB's clinical HIV Performance Measures for adults and adolescents. It is considered a critical part of care and treatment for PLWH.⁵⁶
- The *HAB Guide for HIV/AIDS Clinical Care* recommends initial HCV screening for all HIV-positive adults and adolescents, and additional screening at regular intervals for people at ongoing risk of HCV coinfection.⁵⁷
- The U.S. Department of Health and Human Services (HHS) *Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents* recommends HCV screening for all HIV-positive patients, preferably before starting HIV treatment.⁵⁸
- The American Association for the Study of Liver Diseases (AASLD), and the Infectious Diseases Society of America (IDSA)/International Antiviral Society (IAS)-USA recommend initial HCV screening for all HIV-positive patients, and annual HCV screening for HIV-positive MSM who engage in condomless sex.⁵⁹

WHAT HAPPENS TO PEOPLE WITH HCV?

HCV becomes chronic in 60% to 80% of people; others, who have a strong immune response spontaneously clear the virus, usually within six months.^{60,61} Young people (especially female), people with the IL28B CC genotype (a genetic factor associated with strong immune responses to HCV, most common among people of European and Asian ancestry), and HIV-negative people are most likely to spontaneously clear HCV.^{62–65} In

HIV-positive people, rates of spontaneous HCV clearance range from 15% to 33%.^{66,67}

Acute HCV infection often goes undiagnosed because it is frequently asymptomatic. Symptoms of acute HCV—among the 25% of patients who experience them—include yellowed skin and eyes (called *jaundice*), fatigue, nausea, abdominal pain, and appetite loss.^{68,69} People with chronic HCV may experience nonspecific symptoms such as fatigue, depression, and “brain fog” (difficulty with memory and concentration).^{70–72}

Chronic HCV infection may significantly shorten lifespan. Non-liver-related deaths (substance-related psychiatric disorder, cardiovascular disease, diabetes, hypertension, respiratory or renal failure) occur two decades earlier in people with chronic HCV than people who do not have HCV.⁷³

During chronic HCV infection, the immune system tries to prevent HCV from spreading, by surrounding and walling off infected liver cells. Over time—usually decades—this immune response creates liver scarring (called *fibrosis*; serious liver scarring is called *cirrhosis*). Up to 40% of people with chronic hepatitis develop cirrhosis, and are then at risk for liver failure and liver cancer.⁷⁴ Each year, 1% to 4% of people with cirrhosis develop liver cancer.⁷⁵ Although HCV is curable, it can be deadly.

HCV AND HIV COINFECTION: COMPLEX COMORBIDITIES

In recognition of the morbidity and mortality associated with HIV/HCV coinfection, the AASLD/IDSA/IAS-USA *Recommendations for Testing, Managing and Treating Hepatitis C* consider treating HCV as a high priority in people coinfecting with HIV, and recommend treatment at any fibrosis stage.⁷⁶

HCV does not appear to worsen HIV. Nonetheless, all-cause and non-AIDS-related hospitalization rates are higher among HIV/HCV coinfecting patients than those with HIV alone.⁷⁷

Some of the same comorbidities—or a higher risk of developing them—are prevalent among both PLWH and people with chronic HCV. For example, antiretroviral therapy is associated with type 2 diabetes, which also increases the risk for cirrhosis in people with HCV.^{78,79} As with HIV, HCV is a risk factor for cardiovascular disease, kidney disease, and stroke.^{80–82} Each virus can cause bone loss, but people who are HIV/HCV coinfecting are at higher risk.⁸³ Similarly, both HIV and HCV have

been associated with neurocognitive impairment, but coinfection can worsen it.^{84–86} HIV-associated neuroretinal disorder (HIV-NRD), which impairs vision, is more common among people who are HCV-coinfecting than those with HCV alone.⁸⁷

HCV is associated with other conditions that occur outside of the liver (known as *extrahepatic manifestations*), including Sjögren syndrome (dry mouth and eyes), lichen planus (an itchy skin or mouth rash), cryoglobulinemia (damage to and inflammation of blood vessels), and non-Hodgkin’s lymphoma.^{88–90}

HCV: WORSE FOR PEOPLE LIVING WITH HIV

- HCV is a common and serious coinfection among PLWH. In the United States, an estimated 25% of all PLWH are HCV coinfecting.⁹¹
- HIV/HCV coinfection increases the risk for non-AIDS-related, liver-related, and all-cause hospitalizations among PLWH.⁹²
- HIV increases both the risk for, and the rate of liver damage from, HCV.^{93–95}
- HCV worsens neurocognitive impairment in PLWH.^{96,97}
- HCV coinfection increases the risk of cardiovascular disease, kidney disease, and bone loss.^{98–101}
- Complications from chronic HCV—such as end-stage liver disease and liver cancer—have become a leading cause of death among PLWH, despite treatment with ART.^{102–104}
- In the ART era, AIDS-related, non-AIDS-related, and liver-related mortality rates are higher in people with HIV/HCV than people with HIV alone.^{105–107}
- HCV coinfection doubles the risk of death among PLWH.¹⁰⁸
- Among people with AIDS, overall mortality rates are 50% higher in people with HIV/HCV versus those who do not have HCV.¹⁰⁹
- HCV treatment is a lifesaving intervention for coinfecting people. Curing HCV lowers AIDS-related, liver-related and non-AIDS-related death rates among coinfecting people, even if they are already cirrhotic.^{110–112}

According to the AASLD/IDSA/IAS-USA *Recommendations for Testing, Managing and Treating Hepatitis C*, HCV treatment is a high priority for people with HIV/HCV, due to their rapid liver disease progression, shortened survival after liver failure, and limited access to and poor outcomes after liver transplantation.¹¹³

HIV worsens HCV. Rapid HCV progression—defined as worsening by at least one stage (by the METAVIR system; F0 [no liver scarring] to F4 [cirrhosis] within 2.5 years)—occurs in a third of HIV/HCV coinfecting people. In particular, rapid fibrosis progression is most likely to occur in people with a low CD4 cell nadir (<200 cells/mL).¹¹⁴

Liver damage is more likely to occur in coinfecting people than in those with HCV monoinfection. HIV coinfection doubles the risk of HCV-associated cirrhosis.^{115,116} Although ART may delay fibrosis progression, coinfecting people remain at risk for liver failure (called hepatic decompensation) especially if they have advanced fibrosis or cirrhosis, severe anemia, or diabetes.¹¹⁷ HIV coinfection significantly shortens survival in people who have developed hepatic decompensation.¹¹⁸ (See text box “The Liver and HCV” for more.)

In the ART era, complications from HCV coinfection have become a leading cause of death among HIV-positive

people.^{125–127} HIV/HCV coinfection also increases the rate of AIDS-related death.¹²⁸ HCV coinfection worsens overall survival; rates of AIDS-related, liver-related, and non-AIDS-related mortality are higher in people with HIV/HCV than people with HIV alone.¹²⁹

HCV TREATMENT

The difficulty of undergoing HCV treatment adds to the known barriers faced by HIV/HCV coinfecting patients (including stigma, incarceration, homelessness, poverty, addiction, psychiatric illness, and other comorbidities).

In 2009, when the SPNS Hepatitis C Initiative began, the standard of care for HIV/HCV coinfection was weekly injections of pegylated interferon (PEG-IFN), plus twice-daily ribavirin (RBV) tablets or capsules, for 48 weeks. These drugs cause a range of side effects, including flu-like symptoms, depression, and anemia; some have been treatment-limiting and led to high dropout rates in clinical trials. Side effects from PEG-IFN and RBV tend to be more severe in people with HIV/HCV than HCV alone, especially weight loss and certain laboratory abnormalities, called cytopenias (anemia [low red blood cells], neutropenia [low bacterial infection-fighting white blood cells], and thrombocytopenia [low platelets]).^{130,131}

PEG-IFN and RBV are less effective for people with HIV/HCV coinfection than for individuals with HCV monoinfection. In clinical trials of PEG-IFN and RBV in HIV/HCV, cure rates in genotype 1 ranged from 17–35%.^{132–136} In real-life studies of PEG-IFN and RBV in HIV/HCV, the overall cure rate was 24% in genotypes 1 and 4 and 59% in genotypes 2 and 3.¹³⁷ In HCV monoinfection, PEG-IFN and RBV cures approximately 50% of people; also genotypes 2 and 3 are more likely to be cured than people with genotype 1 (which is most common in the United States).^{138–140}

In genotype 1, adding an HCV protease inhibitor (Incivek or Victrelis) has increased cure rates among HCV monoinfected and HIV/HCV coinfecting people—in fact, cure rates from clinical trials in HIV/HCV were similar to those reported in HCV monoinfection.^{141,142} In phase 2 clinical trials, 48 weeks of triple therapy with Victrelis or Incivek boosted the cure rate to 63% and 74%, respectively (versus 29% and 45% for peginterferon and ribavirin).^{143,144}

Although these drugs significantly increase cure rates among HIV/HCV coinfecting people, adding them made HCV treatment much more complicated for

THE LIVER AND HCV

The liver is the largest internal organ, located on the right, under the rib cage over the gallbladder, pancreas, and intestines—organs that work with the liver to help digest and process food. The liver works as a filter, storage unit, and processing plant for the body. It removes toxins and bacteria, breaking down drugs, alcohol, and other toxins, making proteins that help blood to clot, and metabolizing carbohydrates, regulating sugar and hormone levels, producing bile, and storing energy.

Viruses, infections, toxic fumes, and alcohol can cause liver damage. HCV, a blood-borne virus, was first identified in 1989. HCV can become chronic and lead to liver cirrhosis. People with cirrhosis are at risk for liver failure and liver cancer.

Chronic HCV can damage the liver, especially in HIV/HCV coinfecting people, because HIV accelerates HCV disease progression and increases the risk for several HIV-associated comorbidities (e.g., cardiovascular and kidney disease, neurocognitive impairment, and bone loss).^{119–124}

patients and their providers. HCV protease inhibitors worsen side effects, require frequent monitoring, and cannot be used with some HIV antiretrovirals and other commonly used drugs.

EXPERIENCE WITH HIV CAN BE A CHALLENGE—AND AN ADVANTAGE—FOR HCV TREATMENT

For people with HIV/HCV coinfection, low referral rates coupled with exclusion criteria that include psychiatric illness, ongoing drug or alcohol use, and medical contraindications have limited their access to HCV treatment with PEG-IFN and RBV.^{145,146} Socioeconomic factors, including poverty, homelessness, intermittent incarceration, fear of side effects, and limited access to specialists, are additional obstacles for HIV/HCV coinfecting people.^{147,148}

Bias against active drug users presents unnecessary barriers to HCV treatment for coinfecting people. A survey of physicians reported that they often made inaccurate judgments about which patients were likely to adhere to ART.¹⁴⁹ The HIV experience has demonstrated that people with ongoing drug and alcohol use can engage in HIV treatment, which is lifelong. In fact, researchers in France found that treating coinfecting people for HCV often increased their adherence to ART, even if they were drinking or using drugs during treatment.¹⁵⁰ Adherence to HCV treatment can be high, regardless of ongoing injection drug use.¹⁵¹

People with chronic HCV face some of the same socioeconomic challenges as PLWH, but they are without a medical home—or a dedicated infrastructure to diagnose, care for, and treat HCV. Ryan White HIV/AIDS Program clinics are natural settings for administering HCV treatment. For more than two decades, Ryan White HIV/AIDS Program grantees have been working to break down the barriers to HIV care and treatment by providing HIV primary care and other services. Grantees work within a strong infrastructure and have expertise in screening, monitoring, and counseling PLWH struggling with substance use, illness, incarceration, and homelessness. They have demonstrated that integrating medical and mental health care increases retention in care, improves HIV treatment outcomes, and reduces hospitalization.^{152–54}

Ryan White HIV/AIDS Program grantees have years of experience with providing HIV treatment and support

services, and are therefore well suited to integrate HCV treatment. They are accustomed to making complex treatment decisions, managing drug-drug interactions, and providing adherence education and support. Years of adherence education, interventions, and support are paying off for PLWH. In some HCV treatment trials, and in clinical practice, sustained virologic response rates have been higher in HIV/HCV coinfection than those with HCV monoinfection; this has been attributed to better adherence based on years of experience with ART.^{155–159}

Grantees have a wealth of experience in providing multidisciplinary patient care, which is essential for coinfecting patients.

Psychiatric comorbidities (especially substance use disorders, depression, and anxiety) are more common among PLWH and people with chronic HCV than the general population.^{160,161} Coinfecting patients are more likely to be hospitalized for psychiatric disorders than people with HIV monoinfection.¹⁶²

Depression has been linked with poorer ART adherence.¹⁶³ Patients with untreated psychiatric disorders are more likely to experience slower virologic response to ART.¹⁶⁴ Patients with a co-occurring psychiatric disorder initiate ART later, at lower CD4 cell counts and higher HIV RNA; they are also more likely to be considered ineligible for interferon-based HCV treatment.^{165,166}

Treating depression, anxiety disorders, and substance abuse improves engagement in and outcomes of HIV and HCV treatment. PLWH treated for depression were more likely to initiate and adhere to ART, and had improved virologic and immunologic response to treatment than patients with untreated depression.^{167–170} Delivering medication-assisted treatment (MAT) for opioid addiction in the context of HIV primary care is feasible, increases health-related quality of life and engagement in care, and can improve HIV treatment outcomes.^{171–175} (To learn more about delivering buprenorphine within HIV primary care clinics to treat opioid addiction, visit <https://careacttarget.org/ihp/buprenorphine>.) Note that a side effect of interferon is depression and so patients should be thoroughly screened. Although they are often considered ineligible for HCV treatment with interferon-based therapy, people with co-existing substance use and psychiatric disorders can be safely and effectively treated using multidisciplinary care; their outcomes are similar to those of other patients.^{176–178}



THE SPNS HEPATITIS C TREATMENT EXPANSION INITIATIVE

This chapter provides a summary of the Hepatitis C Initiative, the overall outcomes of the project, and the four models studied. Clinics considering HCV treatment should examine these models to determine which might be the best fit for their particular organizations and review useful tips for rollout.

BACKGROUND

SPNS funded the Hepatitis C Initiative from 2010 to 2014 to expand HCV treatment in Ryan White HIV/AIDS Program-funded clinics. SPNS grantees implement and evaluate innovative models of care and develop evidence of best practice to be shared with the broader HIV community. Particular emphasis has been on addressing the needs of vulnerable populations who bear a disproportionate burden of HIV. In order to address HIV and associated health disparities, scalable, cost-effective, and targeted initiatives, such as the Hepatitis C Initiative, are vital.

Unlike HIV, HCV can be cured. Being cured of HCV—even in people who have cirrhosis—reduces the risk of liver-related, AIDS-related, and all-cause mortality for coinfecting people.^{179–181} There are other

HEPATITIS C INITIATIVE AT A GLANCE

The Initiative

- 29 grantees funded from across the country
- Each grantee received \$80,000 in annual funding
- Grantees split into two cohorts (over four years) due to the significant interest in HCV treatment implementation
 - Cohort 1: first two years
 - Cohort 2: second two years
- The University of South Florida in Tampa, FL was the evaluation and technical assistance center for the Initiative
 - Provided technical assistance to grantees in the form of clinical assistance and evaluation

benefits to being cured, regardless of HIV status: SVR improves fatigue and physical health, can halt HCV progression, and sometimes even reverse liver disease progression (thereby reducing the risk for liver cancer and transplantation).^{182–188}

Initiative grantees and patients were motivated by the possibility of curing HCV, despite the range of potential side effects and complexity of HCV treatment. Given the growing prevalence of HCV coinfection among PLWH and its severity, coupled with the benefits of SVR, significant interest was expressed by grantees for participation in the Hepatitis C Initiative to facilitate implementation or expansion of HCV treatment within their care clinics.

The Initiative was thus rolled out in two separate cohorts. Both cohorts, however, were supported and evaluated by the same ETAC. Grantees implemented 1 of 4 possible HCV models of care. (See “Hepatitis C Initiative at A Glance” and “Organizational Models Studied.”)

RESULTS FROM THE SPNS HEPATITIS C TREATMENT EXPANSION INITIATIVE

When the SPNS Hepatitis C Initiative started, the standard of care for HCV was PEG-IFN. In 2011, the HCV protease inhibitors Incivek and Victrelis were approved; grantees began treating coinfecting genotype 1 patients with triple combination therapy, while continuing to use PEG-IFN in the 48 patients with non-1 genotypes (16 of them discontinued treatment).¹⁸⁹

Of the 191 genotype 1 patients treated during the Initiative, 41% were cured. Additional information on the type and outcome of treatment in patients coinfecting with HCV genotype 1 is listed in Table 1. Overall,

40% (94 of 239) patients discontinued treatment, more than half during the first 12 weeks of treatment. The reasons for discontinuation were: physical side effects (N = 36); nonresponse (N = 33); psychiatric side effects (N = 7); patient request (N = 4); loss to follow-up (N = 3); alcohol use (N = 2); and other (N = 9).¹⁹⁰ Discontinuation rates were lowest in Model 3 (30%) and similar for models 1, 2, and 4 (~40%).¹⁹¹

ORGANIZATIONAL MODELS STUDIED

The Hepatitis C Initiative included four models of care. These were:

1. Integrated HCV treatment without a designated HCV clinic
2. Integrated HCV treatment with a designated clinic day
3. Primary care with expert backup
4. Co-located care with a specialist.

The models themselves have all been successful within respective grantee sites and there is no “right” way or model to use. Primarily, model selection was determined not by preferences but by what resources and personnel clinics had at their disposal. A few grantee sites changed models when their circumstances changed (e.g., a specialist didn’t relate well to their patients; staff was spread thin and weren’t always available, so they shifted to a designated clinic day model).

TABLE 1
HCV Treatment Outcomes in HIV/HCV Genotype 1 from the SPNS Initiative

Treatment Type and Number of Patients	Achieved SVR	Discontinued	Relapse	Unknown
PEG-IFN and RBV N = 74	46% (35/74)	45% (34/74)	~2% (2/74)	~3% (3/74)
Incivek, PEG-IFN and RBV N = 84	35% (29/84)	35% (29/84)	~1% (1/84)	29% (25/84)
Victrelis, PEG-IFN and RBV N = 22	27% (6/22)	60% (13/22)	0	10% (3/22)
Experimental N = 9	70% (6/9)	~10% (1/9)	0	~20% (2/9)
Unknown N = 2	50% (1/2)	50% (1/2)	50% (1/2)	0

Source: HRSA. ETAC Project Summary Webinar, May 2014. [unpublished.]

MODEL 1: INTEGRATED HCV TREATMENT WITHOUT DESIGNATED HCV CLINIC

To summarize, this model:

- Is one in which the clinic has a designated HCV program, but does not have a designated time slot for HCV;
- The medical provider and team at the HIV clinic are responsible for the initial evaluation, initiation of treatment (if indicated), evaluation of patient response to medication, and the monitoring for adverse reactions;
- Typically involves a formal HCV coinfection treatment program;
- Typically involves a multidisciplinary team approach; and
- Expert consultation occurs only when patient has a major complication related to liver disease.

This was the most commonly seen model within the Hepatitis C Initiative and clinics employing this model appeared to treat slightly more HIV-infected patients than clinics employing other models. However, overall differences in mean number of HIV-infected patients treated were not statistically significant across models.

In this model, the patient receives HCV clinical care in the setting of their primary HIV care clinic by their primary care provider. Liver biopsies are usually obtained through interventional radiology.¹⁹²

An advantage of this model is that it makes use of existing patient-provider relationships and is often seen as ideal from the patient perspective. This clinic model typically involves a formal HCV coinfection treatment program and team-based approach. Expert consultation is used only in a situation where a patient has major complications related to their underlying liver disease, otherwise the primary care provider continues to be the main point of contact for the patient.

Possible challenges to this model, however, do exist. Particularly if patients disagree on the importance of treatment or perform poorly on HCV treatment, then it may put strain on the existing patient-provider relationship. Patients may also feel fearful of failure both in terms of HCV treatment and in letting their provider down. Additionally, this model places the greatest demands on the existing clinic staff who may require HCV training and ongoing support to treat HCV alongside HIV.

While many grantees readily implemented this model, they still had access to ETAC clinicians and ETAC conference calls for any expert backup as needs arose. As such, new clinics considering this model may wish to identify a local AIDS Education and Training Center (AETC) or other resources to have accessible should challenging patient cases arise.

MODEL 2: INTEGRATED HCV TREATMENT WITH DESIGNATED HCV CLINIC

To summarize, this model:

- Is for clinics with high volume of co-infection;
- Includes a HCV Co-infection Clinic at a designated time, with team of providers who have experience, interest, and training in the management of HCV coinfections; and
- Involves patient monitoring, typically by a team member such as a nurse, nurse practitioner, or pharmacist who has frequent interactions with a physician provider.

In this model, the coinfection clinic is typically held at a designated time, with a team of providers who have experience, interest, and training in managing HCV in coinfecting persons. In most cases, PLWH treated at the HCV clinic are also receiving their HIV care at the same facility.¹⁹³

A nurse, nurse practitioner, or even pharmacist is most often the team member in charge of monitoring patient treatment. The person designated for this responsibility must have frequent interaction with the physician provider and be readily entrenched within the clinic site.¹⁹⁴

This model of care allows the clinic to provide HCV treatment without requiring the entire staff to develop HCV expertise. It also facilitates the scheduling of support groups, as HCV-infected patients are having appointments on the same clinic days. Support groups, particularly for treatment as intense as that of HCV treatment, can play a critical part in encouraging patients during their treatment course, validating their concerns, and hearing from others who have either gone through treatment before them or are currently undergoing treatment. This model type had the most success sustaining support groups.

Having relevant staff members such as physicians, nurses, psychiatrists, nutritionists, and pharmacists all

available on the same clinic day can facilitate collaboration and patient engagement. Challenges, however, do exist within this model, primarily if patient schedules cannot accommodate the clinic HCV schedule day. As such, some grantee sites found themselves having to treat HCV patients on nonclinic days anyway.¹⁹⁵

MODEL 3: PRIMARY CARE WITH EXPERT BACKUP

To summarize, this model:

- Is generally employed by clinics with lower HCV volume or that lack a formal HCV treatment program;
- Generally utilizes an expert who is either an hepatologist (possibly a gastrointestinal (GI) specialist with HCV experience), or an infectious disease specialist, who is able to serve as an expert in HCV management; and
- Has the provider make an initial patient evaluation and treatment recommendations while the primary care team follows up with the patient for response and adverse reactions.

This model allows a clinic to provide HCV treatment along with HIV treatment within a primary care setting. A collaborative management arrangement is made involving a primary care HIV provider who is not considered an expert in HCV management and a specialist who is expert in HCV management. Clients receive HCV therapy in the setting of their primary HIV care clinic, and liver biopsies are typically obtained through interventional radiology.

The expert is typically a hepatologist, infectious disease specialist, or gastroenterologist. This arrangement may include an initial patient evaluation, approval for treatment initiation, and specific regimen recommendation all done by the specialist. If the patient undergoes HCV therapy, the primary care provider monitors the patient for response and adverse effects, utilizing the specialist as a backup for information during the treatment course.¹⁹⁶

It has the advantages of a “one-stop shop” in that patient is centrally located and they can receive both HIV and HCV treatment within the same clinic. The consistency of the patient’s clinic environment can help

patients feel comfortable as they consider starting HCV treatment as well as stay motivated and engaged as they receive continued support from the primary care staff that they know.¹⁹⁷

Additionally, this model reduces stress on HIV primary care providers from being fully accountable while still connecting patients with an HCV specialist. Like other patient-centered medical home models, there are cost savings with accessing HIV and HCV treatment within a single visit.¹⁹⁸

As the ETAC summarized:¹⁹⁹

The ability of the experts to impact quality of care in more patients than they could by providing direct care is a great systemic advantage. Using telehealth technology like the Project ECHO model further extends the reach of experts and improves access to care that would be otherwise unavailable.

One grantee added, “The force multiplier effect applies [to] us being able to increase our capacity and knowledge, [and] we’ve been able to pay it forward by doing education for our nurses, and other providers and make everything more routine.”²⁰⁰

PROJECT ECHO: HOW DOES IT CONNECT PRIMARY CARE PROVIDERS TO CLINICAL SPECIALISTS?

Project ECHO is an innovative clinical consultation model first created and pioneered in New Mexico. It has since been implemented within several HAB AIDS Education and Training Centers (AETCs). All a provider needs is a computer, an Internet connection, webcam, and a willingness to learn. An online conference call includes a video chat component where a provider presents a patient case to participating experts. In particular, Project ECHO has been used to help connect specialists to primary care providers who, because of geography, low prevalence, or other challenges, are unable to refer patients out for specialty care. (See Chapter 6 resources for links to Project ECHO sites.)

MODEL 4: CO-LOCATED CARE WITH SPECIALIST

To summarize, this model:

- Usually involves either clinics with a relatively low volume of HIV patients or a larger academic center with a strong relationship between the HIV and hepatology clinic/provider(s);
- Provides expert HCV therapy through integrating this care into the patient's primary care setting; and
- Generally requires a hepatologist who has significant interest in managing HCV in patients coinfecting with HIV (or nurse practitioner specialized in gastrointestinal/hepatology or a physician hepatologist).

In settings where this expertise is available, it is seen as one of the simplest ways to bring HCV care into an HIV primary care clinic. The goal of this model is to provide expert HCV therapy by integrating this care into the patient's primary care setting.

In this way, it offers the “one-stop shop” medical home model without primary care clinicians having

to learn how to treat or be fully responsible for HCV treatment.²⁰¹

For this model to be successful, however, the HIV primary care clinic and HCV primary care clinic must be willing to collaborate with one another and the hepatologist (or liver specialist) must have a genuine interest in managing HCV in coinfecting patients. The model generally consists of the hepatologist providing initial evaluation and treatment decisions. Ongoing treatment monitoring is variable, however, and may be performed by the hepatologist, the primary care provider, or a combination of both.²⁰²

Similar to Model 3 (primary care with expert backup), this model requires a patient to get to know a new provider and often to discuss personal issues with someone they see as a stranger.²⁰³ Similarly, the patient is undergoing very difficult treatment while needing to lean on the specialist provider for support. As such, the specialist being personable and having a sincere interest in working with coinfecting patients is critical.

This model may make the most sense for clinics with relatively low volume of HIV patients or within larger academic centers with strong relationships between HIV and hepatology clinics.²⁰⁴ Changes in the specialist's availability as well as peer oversight were cited as challenges.²⁰⁵

TABLE 2
Overview of the SPNS Grantees and Organizational Models Studied

	Integrated Care	Integrated Care with HCV Clinic	Primary Care Expert Backup	Co-located Care with Specialist
Cohort 1				
AIDS Resource Center of Wisconsin				X
Bronx-Lebanon Hospital Center		X		
Cambridge Health Alliance			X	
Carillion Medical Center	X			
Clarion University of Pennsylvania	X			
East Bay AIDS Center (EBAC)			X	
Harlem United Community AIDS Center	X			
Inova Health Care Services	X			
Kansas City Free Health Clinic			X	
St. Mary Medical Center Foundation		X		
SUNY Downstate Medical Center	X			
University of California, San Francisco		X		
Washington University				X
William F. Ryan Community Health Center			X	
Cohort 2				
AIDS Care Group				X
Alta Med Health Services Corporation				X
Boston Health Care for the Homeless			X	
Chase Brexton Health Services	X			
City of Portland Maine	X			
Cooper Health System		X		
Harlem Hospital Center		X		
Health Delivery, Inc.				X
Health Services Center	X			
Housing Works			X	
Howard Brown Health Center		X		
Idaho State University			X	
Siouxland Community Health Center	X			
St. Hope Foundation		X		
St. Luke's Roosevelt Institute for Health Sciences	X			

ETAC: University of South Florida; for Cohorts 1 and 2.



SPNS BEST PRACTICES FOR BUILDING AN HCV TREATMENT PROGRAM

Building or expanding a coinfection program requires buy-in from leadership, clinic directors, administrators, and staff. Underscoring the need for and benefits of this work, having a champion to bring it to the forefront of discussions, and highlighting the success of other similar programs are all useful approaches. Doing a thorough evaluation of your agency's strengths, and as well as available resources to be able to take on this work, will also help drive the direction, model, and partnerships your organization chooses to pursue.

ESTABLISHING A STRONG FOUNDATION FOR A SUCCESSFUL PROGRAM

Selecting a Model to Treat HIV-HCV Coinfection

The Hepatitis C Initiative grantees selected their models based on clinic resources and personnel capacity. The ETAC explained that for grantees it was very clear which model would be the right fit for organizations based on resources they had access to internally and within their larger institutions and communities.

It is, therefore, important for health care providers considering similar work to do a thorough assessment of

both their organization's capacity as well as that of local partnering agencies, and to assess what resources they may have access to within the broader community.

Consider the following questions to assess your organization's capacity:

- How many patients have been screened for HCV?
- How many of your current patients are coinfecting and eligible for HCV treatment?
- What is currently in place?
 - How many patients do you have the capacity to treat for HCV at one time?
 - Do you have HCV expertise in-house?
 - What would need to be modified or created?
 - What additional resources are needed to expand treatment?
- What HCV treatment is currently offered by your clinic or in your community?
- Where are there gaps? Will direct-acting antivirals (DAAs) change this?
- If your clinic is unable to fill a certain gap in treatment, are there other organizations in your community that could? Are there existing partnerships with these organizations or would new partnerships need to be established?

RECOMMENDED COMPONENTS OF AN HCV COINFECTION TREATMENT PROGRAM IN A HIV PRIMARY CARE SETTING

When initiating an HCV coinfection treatment program, clinics may want to consider the following components as ways to build capacity and enhance infrastructure.

- 1. Identify and designate a physician to serve as lead medical provider for the program.** Establishing and maintaining an HCV coinfection treatment program requires a critical commitment from a physician who is interested and dedicated to the success of the coinfection treatment program. Identifying a lead “champion” medical director is critical regardless of the proposed capacity of the coinfection program.
- 2. Describe the basic clinic model for providing treatment of hepatitis C in the Ryan White HIV/AIDS Program clinic setting.** Multiple options exist for establishing a treatment model for the clinical care of HCV in people coinfecting with HIV. Thus, it is very important to clearly define the proposed basic treatment model to staff and any outside partners or experts who will be participating, and to assure that the model is consistent with the clinic’s capacity and available resources before moving forward.
- 3. Summarize the structure of the clinical care delivery model.** A successful coinfection program will likely require a coordinated effort of the multiple medical providers involved. The HCV program proposal should include a clear description of the roles of each provider directly involved in the HCV program. Most but not all programs have used a core provider at the level of advanced registered nurse practitioner (ARNP), physician assistant (PA), or pharmacist who serves a critical role in patient education, treatment monitoring, and patient correspondence. If a designated core provider is not used, then the mechanism for patient treatment monitoring should be in place. Designated funding for other personnel, such as hepatologists, educators, addiction specialists, and psychiatrist should also be considered.
- 4. Develop a clinic system that identifies all people coinfecting with HCV.** The clinic should establish a system for screening all HIV-infected clients for possible HCV coinfection. Most clients already have a system in place for HCV screening. The screening process should include a protocol that determines whether HCV-antibody positive patients have chronic HCV infection (HCV viremia) and indications for qualitative HCV RNA testing in individuals with a negative HCV antibody test.
- 5. Understand how HCV-infected clients will be evaluated and prepared for potential treatment with peginterferon and ribavirin.** A critical element of a successful HCV coinfection treatment program includes systematic evaluation of all HCV-infected individuals for potential HCV treatment. All people identified as having chronic HCV infection (HCV documented viremia) should have regular evaluations of their treatment eligibility. Many factors can change over time and patients previously considered ineligible may transition to an eligible status. Accordingly, regular evaluation of patients for possible HCV therapy should be performed, even for those who do not appear interested in receiving therapy. Overall, this system should provide a mechanism to move clients in the direction of readiness for HCV treatment, if indicated. For example, patients should receive counseling and education regarding treatment of HCV, and efforts should be made to address existing barriers to treatment, such as ongoing substance abuse, active psychiatric issues, or living situations not conducive to HCV treatment.
- 6. Identify a process for providing patient education related to HCV therapy.** Patient education plays a critical role in multiple aspects of patients’ HCV therapy, and should include understanding their need for treatment, the importance of high level of adherence, and self-monitoring for adverse effects. Accordingly, all clinics should have a system for providing patient education related to the treatment of HCV. Treatment education should be available prior to starting therapy as well as during therapy.

RECOMMENDED COMPONENTS OF AN HCV COINFECTION TREATMENT PROGRAM IN A HIV PRIMARY CARE SETTING (*continued*)

7. Establish a system for evaluating and managing patient alcohol use, drug treatment, and psychiatric disorders. All clinics should have a system in place for management (or referral to services) for substance abuse and psychiatric disorders. These services should be in place for clients prior to, at the time of, and after starting therapy. Ongoing psychiatric and/or mental health disorders often serve as a barrier that prevents a client from initiating HCV. (It should be noted that treatment with peginterferon can cause or exacerbate psychiatric disorders and thus access to psychiatric services is essential during therapy. Optimal treatment with peginterferon and ribavirin requires excellent adherence and relapses in alcohol or drug use can impair a client's ability to remain adherent with therapy.

8. Establish a mechanism for evaluating liver fibrosis (when indicated). Evaluation of the patient's degree of fibrosis and progression of liver disease can play a critical role in treatment indications, particularly for patients with HCV genotypes 1 and 4. Clinics will need access to liver biopsy to evaluate the extent of liver fibrosis if indicated unless they have access to noninvasive methods for evaluating liver fibrosis (in lieu of liver biopsy) that would be applicable (e.g. Fibroscan for minimal fibrosis; see page 24 for more information).

9. Establish or identify existing treatment protocols that address laboratory monitoring, frequency of clinic visits, indications, and dosing of factors to support neutropenia or anemia. Treatment of HCV can result in numerous adverse clinical side effects and laboratory abnormalities. Accordingly, all programs should have a formal protocol in place for regularly evaluating patients on HCV therapy for clinical adverse effects as well as monitoring specific laboratory parameters. Maintaining an optimal ribavirin dose may play an important role in treatment success, and thus, a system should be in place for support of anemia and neutropenia, including indications for the appropriate factors, such as erythropoietin and granulocyte macrophage colony-stimulating factor.

Source: Adapted from U.S. Department of Health and Human Services, Health Resources and Services Administration, HIV/AIDS Bureau, Special Projects of National Significance. Hepatitis C Treatment Expansion Initiative – Evaluation and Technical Assistance Center. Funding Opportunity Announcement. HRSA-10-216.

In addition, determine the level of staff participation you can expect if you build or expand HCV activities. For example, who would be your HCV champion? The Hepatitis C ETAC and Initiative grantees underscored the importance of having someone within the clinic who is going to be the driving force in securing buy-in and paving the way for treatment. This does not necessarily have to be a physician; it simply could be a staff member committed to making HCV treatment happen.

Memorandums of understanding (MOUs), particularly if partnering with an outside expert or agency, can be advantageous but remember that MOUs and contracts are pieces of paper. Clear communication and transparency will be key in building out HCV activities. As underscored in Chapter 3, staff (including any specialists brought on specifically for this work) will

need to be individuals who want to work with coinfecting patients.

DEVELOP STAFF

It is important that all staff involved in the project have a vested interest in participating in HCV treatment. Talking with staff and hiring/assigning staff who really want to be doing this work will go far in setting your organization up for success.

Recognize ahead of time, however, that staff turnover can happen and that this will be more impactful on models relying on a single person, particularly if the turnover involves that critical individual. During the Hepatitis C Initiative, when this did occur, case duties were shifted to another discipline/individual. As part of

a programmatic plan, it may thus be important to have a backup plan/person in place to ensure as much continuity for clients as possible.

Clinical staff should also know how to monitor for drug-drug interactions and complications. Staff should also be skilled in HCV screening and diagnosis, as well as assessing liver damage and monitoring for comorbidities such as mental health issues and substance use; if this expertise is not available, models that include linkage with specialists will be important.

Grantees also found it useful to tap into specialists and learn from other successful programs. These individuals can conduct a training or serve in a broader mentorship role for your organization, particularly as training needs evolve.

Other key staffing tips to remember are that coinfected patients will have myriad needs to address. As such, having an interdisciplinary team will be important. This includes not only physicians and nurses but also case managers, patient navigators, pharmacists, psychiatrists or psychologists, and other specialists either in-house, locally, or accessible via telemedicine. (See the *HRSA CAREAction* newsletter “Interdisciplinary Care Teams: A Lifeline for People with HIV/AIDS” to learn more about building an interdisciplinary team: www.hrsa.gov/deliverhivaidscares/interdisciplinarycare-teamsnewsletter.pdf.)

IDEAS FOR EDUCATING STAFF

- Establish linkages with other staff who have experience in treating HIV/HCV.
- Hold joint conferences or journal clubs with HIV providers and liver specialists.
- Stay connected with other treatment providers to talk about experiences.
- Connect to AIDS Education and Training Center (AETC) preceptorships to work alongside other clinicians to gain more knowledge about HCV care and treatment (e.g., www.fxbcenter.org/preceptorships.html).
- Stay informed about HCV treatment from conferences, and Internet and telemedicine resources, such as the University of Washington’s Project ECHO, and the AETC network.

Even those individuals not intricately involved in the oversight of HCV treatment and patient management should be aware of the clinic’s involvement in this work and understand its importance. Initiative grantees recommended holding organization-wide education sessions, so that everyone from physicians to front desk staff know about the clinic’s involvement in HCV treatment. Doing so may also help with broader organizational buy-in. Providing ongoing and extensive training to the whole staff will continue to be important as staff turnover occurs and/or as HCV treatment and guidelines change.

Initiative grantees benefited from the didactic ETAC presentations, particularly case examples and Q&A. Moving forward, many grantees planned to tap their local AETCs to assist in meeting continuing education needs. In a few instances, grantee sites had enough expertise in-house that they could keep up with the evolving clinical standards of HCV.²⁰⁶

PROGRAMMATIC BARRIERS

Initiative grantee barriers varied based on organizational size and geographic locations. In some instances, lack of local resources such as lack of hepatologists, psychiatrists, and other specialists were cited. Mental health and substance abuse treatment were available onsite at some grantee locations, but were simply unavailable within other communities at large.

Financial issues such as reimbursement also varied by state. For example, insurance prior authorization procedures could be troublesome; HCV medications may be covered but not HCV labs or other diagnostic procedures. Pharmaceutical patient assistance programs were cited as generally being helpful and providers were optimistic about the impact of the Affordable Care Act (ACA). According to the ETAC focus group summary, “It is encouraging to note that the two sites in Massachusetts (which has had its own version of the ACA) reported no financial barriers.”²⁰⁷

Administrative burdens also involved handling prior authorizations to obtain necessary medications or to respond to treatment needs. Overall, HCV treatment added to total paperwork and scheduling burden.

Providers faced challenges, due to lack of time and support from other staff, inexperience, and complexity of HCV treatment, especially with new drugs. Typically, protease-inhibitor-based triple therapy for HCV

“Overall, the lack of treatment options without interferon was reported to be the greatest obstacle to treating HCV in the coinfecting population, whether clinics described this as clinicians’ resistance [or] patient resistance.”

Source: ETAC. Report. 2014. n.d. [unpublished.]

involves up to eight clinic visits and as many as 66 laboratory tests.²⁰⁸

Simpler, shorter, safer and more effective HCV treatment is on the way, which will remove some of the barriers noted by grantees and reduce burdens on patients and providers alike. PEG-IFN is being replaced by oral DAAs. These drugs have dramatically simplified, shortened, and improved HCV treatment; cure rates topping 85% have been reported from HCV clinical trials in people with HIV/HCV.^{209–211}

Given newer interferon-free HCV treatment regimens, a clinic barrier was sometimes simply provider

buy-in to move forward with this work knowing that the treatment landscape is rapidly changing. However, questions of coverage and exclusion criteria persist, particularly as interferon-free treatment remains incredibly expensive. For example, it is estimated that if all Americans estimated to be infected with HCV were treated with newer, interferon-free medication, the amount the U.S. spends on prescription drugs would double.²¹²

Although the landscape of HCV treatment is shifting dramatically, affordability and reimbursement for newer treatments may not always be feasible for all patients. As such, PEG-IFN and RBV, like those used during the Hepatitis C Initiative, may still be necessary for some patients.²¹³

If patients are able to access interferon-free treatment, the regimen will be simpler but still require an expert, particularly for people with advanced liver disease. Drug-drug interactions remain a major concern and there will still be side effects from HCV drugs, although these will likely be much milder.

Lessons learned and types of care models available—and tested in the SPNS Hepatitis C Initiative—will still remain relevant as clinics move into the next phase of HCV treatment and care.

LESSONS LEARNED

No matter what organizational model a provider selects to implement, there are several best practices for establishing a successful treatment program that apply across models. The following elements were cited by SPNS Hepatitis C Initiative grantees as crucial ingredients for the success of their programs.

- Identify a HCV champion at your organization (e.g., medical director or physician) dedicated to the treatment of HCV and enlist them to help put together a HCV treatment program.
- Ensure that you are meeting an unmet patient need within your community.
- Pull together an interdisciplinary care team to work with coinfecting patients.
- Understand and really want to treat the HIV-HCV coinfecting population.
- Have another key medical provider available for monitoring of patients on treatment (such as a physician assistant or even a pharmacy technician to monitor for drug–drug interactions and other drug events).
- Establish a system to track lab results and identify coinfecting patients.
 - Continue to track (either through electronic medical records or a designated individual) coinfecting patients.
 - Actively track referrals.
- Start slowly and with the easiest patients and build out your program from there.
- Use treatment protocols that are clear and up-to-date with the latest recommendations.
- Educate staff and establish calls (e.g., monthly) for counselors and case managers.
- Improve patient readiness through targeted and (ideally) coordinated substance abuse and other pretreatment options to improve patient readiness.
- If you have the resources, consider:
 - Establishing patient support groups
 - Providing patient education (this can be linked with a patient support group, or be offered separately)
 - Ensuring patients have access to mental health and psychiatric care as well as substance use treatment programs (either onsite or through linking with another provider)
 - If you do not have the resources, develop a good relationship with a psychiatrist who can be available for immediate appointments.
 - Enhancing medication access for patients: developing linkage to pharmacy services, applying for ADAP and pharmaceutical companies' drug assistance programs; providing weekly pill supplies for patients and providing guidance regarding monitoring side effects
 - Arranging for access to liver biopsy or less invasive services such as the U.S. Food and Drug Administration (FDA)-approved Fibroscan (now portable models) and blood tests
 - Conduct outreach/follow-up with patients as necessary to keep them engaged.

Sources: SPNS Hepatitis C Initiative grantees. ETAC. Report. 2014. n.d. [unpublished.]



CLINICAL GUIDE TO HCV TREATMENT IN THE HIV PRIMARY CARE SETTING

Good practices for HCV diagnosis, care, and treatment include patient support and education, referral to syringe exchange programs to reduce risk of HCV reinfection for people who inject drugs, counseling to reduce alcohol intake, and screening all PLWH for anti-HCV; people with positive antibody test results should be tested for HCV RNA to confirm or rule out chronic HCV infection (unlike HIV, presence of antibodies to HCV does not indicate current, chronic infection). Chronically infected patients should have HCV genotyping and fibrosis assessment.^{214–216}

The standard of care for HCV has changed dramatically; drugs used to treat HCV during the SPNS Hepatitis C Treatment Expansion Initiative are complex due to their side effects, drug-drug interactions, and contraindications. By 2015, interferon-free, DAA treatment that can cure over 85% of people in 12 weeks—regardless of HIV status—will be available.^{217–219} Although HCV treatment has gotten easier and will continue to do so, patients still have complex lives; the lessons learned, processes, and experience from the *SPNS Hepatitis C Treatment Expansion Initiative* remain relevant.

BEST PRACTICES FOR HCV CLINICAL MANAGEMENT

HIV Antiretroviral Therapy for Coinfected People

Inflammation from HIV infection contributes to liver damage, even in people who are not coinfecting with viral hepatitis or heavy drinkers.²²⁰

The benefits of ART outweigh the risks for people with HIV/HCV—and may actually delay HCV progression by maintaining the immune system.²²¹ But many of these drugs are metabolized through the liver. Some are more “liver friendly” than others, especially for coinfecting people, who are at increased risk for liver toxicity (called *hepatotoxicity*) from HIV treatment.²²² In addition to direct hepatotoxicity, some antiretrovirals cause metabolic changes (such as insulin resistance and type 2 diabetes) that increase the risk for liver disease and cirrhosis, even in people who do not have viral hepatitis.²²³

Although HCV treatment is becoming simpler, shorter, more effective and easier to tolerate, interferon-free regimens still increase pill burden for coinfecting

people, and add side effects. In addition, clinicians must be vigilant about avoiding drug-drug interactions between HIV and HCV treatment and should keep this in mind when evaluating ART regimens.

HCV: EDUCATION, SCREENING AND DIAGNOSIS

Fully informing patients about HCV transmission is essential. In particular, patients need information about risk for, and prevention of HCV reinfection (sometimes with a different, harder-to-cure genotype), and referrals and resources that help them prevent reinfection before, during, and after HCV treatment.

Maintaining a high CD4 cell count and limiting alcohol intake can delay liver disease progression.²²⁴ Alcohol is known to worsen liver damage from HCV (whether it is beer, wine, or hard liquor). Patients should receive information about alcohol and the liver, and be offered counseling if indicated.

Before treatment in the SPNS Hepatitis C Initiative, patients were provided with comprehensive information about HCV and services, including:

- Basic hepatitis information
- Liver health
 - Education about alcohol use since it is known to cause and accelerate liver damage
 - If indicated, offer counseling on alcohol use.
 - Vaccination against hepatitis A and hepatitis B, if susceptible
- Transmission and prevention
 - Lack of vaccine
 - Risk of reinfection (sometimes with a different genotype that complicates treatment) before, during, and after HCV treatment
 - Referral to syringe exchange as indicated
 - When relevant, patients should be offered information about safer injection and referral to syringe exchange programs.

SCREENINGS

It is important for clinics to establish an HCV screening system for all HIV patients (if one is not currently in place), especially high-risk groups such as injection drug users (IDUs) and men who have sex with men (MSM). High-risk individuals should be rescreened annually. HCV antibody positive patients should be confirmed with an HCV RNA, as a proportion of infected patients will clear their infection without treatment.

Other screenings should be considered as well, such as:

- assessment of acute HCV infection
- estimated duration of HCV infection (e.g., history and signs of hepatic decompensation and prior HCV treatment history)
- evaluation of comorbidities
- if HIV-positive, assess CD4 count and current antiretroviral (ART) medications, as drug-drug interactions may exist with HCV medications
- screen for mental health prior to HCV treatment initiation (note, depression is a possible side effect of interferon and all patients should be screened at baseline and during regular intervals during therapy)
- substance use screening
- liver disease
- hepatocellular carcinoma (HCC) screening as HCC screening is only indicated in HCV infected patients with cirrhosis
- social history (e.g., stability of living situation, social support)
- any other contraindications to PEG/RBV-containing HCV treatment (e.g., pregnancy, allergy to HCV treatment, severe concurrent medical disease that is poorly controlled, and others).

Source: University of California, San Francisco (UCSF). *San Francisco hepatitis C: primary care initiative, hepatitis C treatment and management*. [SPNS grantee report.] May 8, 2012.

- Referral to medication-assisted treatment, upon request
- Referral to drug treatment, upon request (Offer, but do not require any of these as a prerequisite for treatment.)
- Screening, diagnostic and staging tests, and what their results mean
 - Antibody testing
 - Confirmatory testing with HCV RNA for people who are anti-HCV positive or immunocompromised; have a recent risk, or signs and symptoms of liver disease
 - Genotyping
 - Stage liver disease
 - Biopsy versus noninvasive testing
- Treatment options
 - Side effects and strategies to manage them
 - Adherence support
 - Potential drug-drug interactions with antiretroviral agents, and alternatives or plan/options for switching
 - Potential drug-drug interactions with other medications, and alternatives
 - Need for contraception.

Grantees developed the *HCV Treatment Referral Protocol*, a Referral Checklist and the *Doctor Reminder Sheet* to track whether patients had been educated, vaccinated, had HCV RNA testing, genotyping and liver disease staging, and assessment by mental health and other medical providers. They created additional resources and checklists to prepare patients for treatment and monitor them during treatment: *Is Your Patient Ready for HCV Treatment*, *Hepatitis C Treatment Agreement*, *Lab Monitoring*, *Side Effect Monitoring*, and the *Hep C Treatment Reminder Sheet for Charts*.

Diagnosing HCV is a two-step process. Screening for anti-HCV is recommended for *all* PLWH in the *HAB Guide for HIV/AIDS Clinical Care* and *HHS Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents*, and by the American Association for the Study of Liver Diseases (AASLD) and the Infectious Diseases Society of America (IDSA/IAS-USA). *HAB's Guide for HIV/AIDS Clinical Care* also recommends that all patients with anti-HCV positive test results be tested for HCV RNA (as well as patients who are anti-HCV negative but who have recent exposure to HCV, or patients with persistently elevated liver enzymes and past risk for HCV infection).

HCV screening is a HAB clinical HIV Performance measure also for adults and adolescents; it is considered a critical part of care and treatment for PLWH.²²⁵ Guidelines from HAB and AASLD/IDSA/ IAS-USA also recommend annual HCV screening for people at ongoing risk (e.g., MSM who engage in condomless sex and individuals who inject drugs).

The Hepatitis C Initiative grantees recognized the limitations of antibody testing, since it does not identify patients with chronic HCV in the absence of confirmatory testing for HCV viral load (HCV RNA). Unlike HIV, a positive HCV antibody test result identifies people who have been infected with HCV at some point, but it cannot distinguish between a past infection that has been spontaneously cleared or cured from a current infection.

- Most people develop anti-HCV within three months of infection. Recently infected patients may be in the “window period.” Patients with a low CD4 cell count (<200 cells/mL) may not develop anti-HCV, although they are HCV-infected.²²⁶ This means that patients with chronic HCV may test negative for anti-HCV, because they have not finished making antibodies or are immunocompromised.
- In contrast, spontaneous viral clearance of HCV occurs in 15% to 33% of PLWH, although they retain HCV antibodies, they are not infected with HCV virus.^{227,228}

Thus, HCV RNA testing should be performed in people who test anti-HCV positive, and in anti-HCV negative people who were recently exposed, or people with low CD4 cells who have signs and symptoms of viral hepatitis and/or a risk history.

Preparing for Treatment: HCV Genotyping and Liver Disease Staging

After HCV has been diagnosed, patients and clinicians need more information before they make an HCV treatment decision. The type and length of HCV treatment differs by HCV genotype. HCV can be genotyped with a blood test.

Staging liver disease is an important part of HCV care. Starting HCV treatment is more urgent for people who have already developed serious liver scarring (*bridging*

fibrosis or *cirrhosis*) than it is for people with very mild liver scarring (who should be monitored).

Although liver biopsy is considered a gold standard for assessing liver disease, it creates additional barriers to HCV treatment. The procedure can be painful, there is a small risk of complications, it is expensive, and it must be performed by a specialist. Fortunately, there are alternatives to biopsy: noninvasive methods that can distinguish between mild and advanced liver damage.

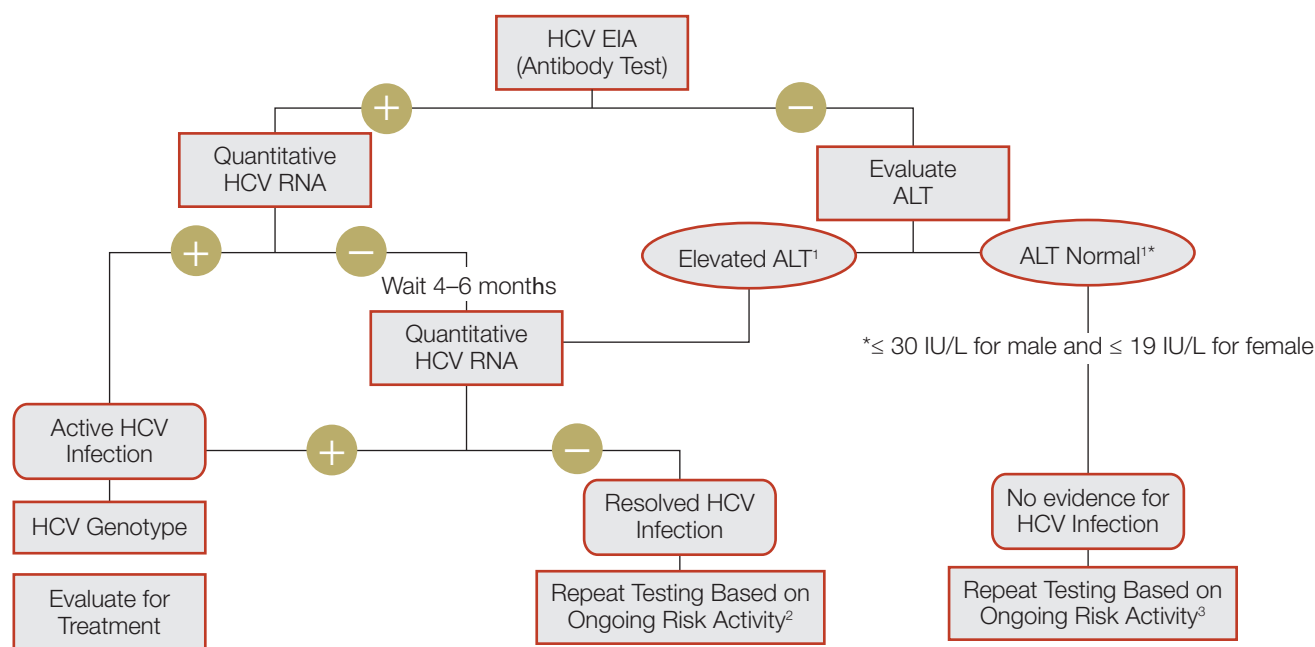
In 2013, the U.S. Food and Drug Administration (FDA) approved Fibroscan, a noninvasive device that uses sound waves to measure liver stiffness. Fibroscan can detect minimal versus severe fibrosis, but is less accurate for midstage liver damage. Researchers have reported

that Fibroscan is as reliable as biopsy for predicting liver disease progression in HIV/HCV coinfection.^{229,230}

Fibroscan is not available everywhere, but clinicians can use other noninvasive means to assess liver disease, such as ultrasound and combinations of blood tests (called *serum panels*).

The benefits of treating people with HIV/HCV at any stage of liver disease—since they may experience rapid HCV disease progression—have increased. However, people with advanced liver disease are one of the groups that is prioritized for treatment, due to limited workforce and resources, so staging—but not necessarily biopsy—remains an important part of the pretreatment assessment.²³¹

FIGURE 1
HCV Testing Algorithm



1. Definitions of “normal and elevated” ALT (alanine aminotransferase level) vary. Most clinical laboratories and studies for persons coinfectd with HIV and HCV use ALT > 40 IU/L as the cut-off for elevated ALT. Prior studies in monoinfected pts have defined elevated ALT as > 30 IU/L (for men) and > 19 IU/L (for women).

2. Positive HCV EIA, but confirmed negative RNA, indicates resolved HCV infection. Patients may become reinfected; repeat HCV RNA annually if patient has ongoing risk (e.g., unprotected sex, exposure to blood or instruments that could be contaminated with blood, risky behavior).

3. For patients without HCV infection, repeat HCV EIA should be done annually only in those individuals with ongoing risk for acquiring HCV.

Source: Beal J, Fernandes F, Orrick JJ, et al. Florida/Caribbean AIDS Education and Training Center (AETC). *Hepatitis C in HIV/AIDS*. September 2013. Available at: http://fcaetc.org/files/HepC_Final%20Web%20Version%20with%20highlights.pdf. Adapted from Sulkowski MS, Cheever LW, Spach DH. *A Guide for Evaluation and Treatment of Hepatitis C in Adults Coinfected with HIV*. 2011. Available at: <http://hab.hrsa.gov/deliverhivaidscafe/files/hepccoinfectguide2011.pdf>.

Current HCV Treatment Options

When the Hepatitis C Initiative began, the standard of care for HCV was 48 weeks of PEG-IFN and RBV. (See Chapter 2, section “HCV Treatment” to learn more.) Pegylated interferon was the backbone of hepatitis C treatment, as well as a major barrier to treatment access, uptake, and completion due to debilitating side effects and low cure rates, especially in people coinfecting with HCV genotype 1 and HIV.^{232–234}

In 2011, the hepatitis C treatment revolution began with approval of the first oral DAAs: Incivek and Victrelis. Adding one of these drugs to PEG-IFN and RBV increased SVR in people with HCV genotype 1—from 43% to almost 70%.^{235,236}

When Incivek and Victrelis were approved, information for PLWH was limited, but experts issued provisional guidelines for their use in HIV/HCV coinfection in recognition that their benefits could outweigh the risks in certain patients.²³⁷ But actual eligibility for

Incivek- or Victrelis-based treatment in HIV/HCV coinfecting patients is limited (<40%) by contraindications, and complicated by drug-drug interactions with antiretroviral agents.²³⁸ In fact, one study reported that ART would have to be changed in 61% of patients with Incivek, and 84% of patients with Victrelis to avoid drug-drug interactions between these drugs and their antiretroviral regimens.²³⁹

By the end of 2013, when the *SPNS Hepatitis C Treatment Expansion Initiative* demonstration sites ended, the standard of care for HCV was transformed by approval of two game-changing HCV DAAs: sofosbuvir (Sovaldi), a nucleotide HCV polymerase inhibitor, and simeprevir (Olysio), an HCV protease inhibitor. These two DAAs made it possible to treat some patients without interferon. (See Table 3, Hepatitis C Treatment Recommendations). As a result of these therapeutic advances, boceprevir or telaprevir-based regimens are no longer recommended.²⁴²

The second milestone in the HCV treatment revolution was establishment of proof-of-concept for a cure without interferon. Researchers demonstrated that two DAAs could be combined to cure people after 24 weeks of treatment.²⁴³ Since then, interferon-free regimens have cured over 85% of HIV/HCV coinfecting people in clinical trials.^{244–246} By 2015, interferon-free HCV treatment options are expected to increase, with approval of additional DAA regimens; many are also being studied in HIV/HCV.

HCV MEDICATIONS AVAILABLE DURING THE SPNS HEPATITIS C INITIATIVE

- Incivek (telaprevir; an HCV protease inhibitor taken every eight hours with a high-fat meal or snack): used with peginterferon and ribavirin. After 12 weeks of treatment with all three drugs, Incivek is discontinued, and treatment with PEG-IFN and RBV continues for an additional 36 weeks.²⁴⁰
- Peginterferon alfa-2a (Pegasys; injected once weekly): used with ribavirin, with or without an HCV protease inhibitor, for 48 weeks.
- Peginterferon alfa-2b (PEG-Intron; injected once weekly): used with ribavirin, with or without an HCV protease inhibitor, for 48 weeks.
- Ribavirin (Copegus, Rebetol; also available as a generic, dosed according to weight, taken twice daily): used with pegylated interferon, with or without an HCV protease inhibitor.
- Victrelis (boceprevir; an HCV protease inhibitor, taken every eight hours): used with peginterferon and ribavirin. After a four-week “lead in” with peginterferon and ribavirin, treatment with all three drugs continues for 44 weeks.²⁴¹

CURRENTLY AVAILABLE TREATMENT OPTIONS

Many DAAs were developed to work against HCV genotype 1, which is the most common genotype in the United States—and the least likely to be cured by PEG-IFN and RBV.^{247–249} Some DAAs are also active against other genotypes. As of August 2014, the following medications have been approved to treat HCV:

- Incivek (telaprevir): genotype 1
- Olysio (simeprevir) : genotypes 1 and 4
- PEG-IFN (alfa-2a [Pegasys] or alfa-2b [PEG-Intron]): all genotypes
- Ribavirin (Copegus; Rebetol; generics): all genotypes
- Sovaldi (sofosbuvir): genotypes 1,2,3 and 4
- Victrelis (boceprevir): genotype 1

TABLE 3
Current HCV Treatment Recommendations in HIV/HCV Coinfection*
(Updated August 2014)

Population	Regimen(s)	SVR in HIV/HCV	ARVs	Comments
Genotype 1; treatment-naïve and relapsers	Sofosbuvir + PEG-IFN and weight-based RBV 12 weeks	89%	CONTRAINDICATED: didanosine, zidovudine, tipranavir	Interferon may limit uptake of this regimen, since all-oral regimens will be available soon
	ALTERNATIVE REGIMEN			
	Simeprevir + PEG-IFN and weight-based RBV for 12 weeks, followed by 12 additional weeks of PEG-IFN and weight-based RBV 24 weeks	79%	CONTRAINDICATED: protease inhibitors, efavirenz and etravirine ALLOWED: enfuvirtide, maraviroc, raltegravir, ripivirine, abacavir, emtricitabine, lamivudine and tenofovir	Not recommended for use in people with HCV genotype 1a and the Q80K mutation (subtyping and resistance testing may be required before use of this regimen) Simeprevir is not recommended for use in advanced cirrhosis (Child-Pugh Class B or C)
	IFN-INELIGIBLE* PATIENTS			
	Sofosbuvir + weight-based RBV 24 weeks	76% to 85%	CONTRAINDICATED: didanosine, zidovudine, tipranavir	
Genotype 1, treatment-experienced (PEG-IFN and RBV)	Sofosbuvir + simeprevir, with or without weight-based RBV for 12 weeks**	N/A; Trial in HIV/HCV underway	CONTRAINDICATED: protease inhibitors, efavirenz and etravirine, didanosine, zidovudine, tipranavir ALLOWED: enfuvirtide, maraviroc, raltegravir, ripivirine, abacavir, emtricitabine, lamivudine and tenofovir	Simeprevir is not recommended for use in advanced cirrhosis (Child-Pugh Class B or C)
	ALL PATIENTS			
	Sofosbuvir + simeprevir, with or without weight-based RBV for 12 weeks**	Trial in HIV/HCV expected to launch in 2014	CONTRAINDICATED: protease inhibitors, efavirenz and etravirine, didanosine, zidovudine, tipranavir ALLOWED: enfuvirtide, maraviroc, raltegravir, ripivirine, abacavir, emtricitabine, lamivudine and tenofovir	Simeprevir is not recommended for use in advanced cirrhosis (Child-Pugh Class B or C)
	IFN-ELIGIBLE PATIENTS			
	Sofosbuvir + PEG-IFN and weight-based RBV for 12 weeks	No data	CONTRAINDICATED: didanosine, zidovudine, tipranavir	No data in treatment-experienced, coinfecting genotype 1 patients; In HCV-monoinfected, treatment-experienced genotype 1 patients, SVR was 74%

TABLE 3
Current HCV Treatment Recommendations in HIV/HCV Coinfection (*continued*)

Population	Regimen(s)	SVR in HIV/HCV	ARVs	Comments
Genotype 1, treatment-experienced (PEG-IFN and RBV) (<i>continued</i>)	IFN-INELIGIBLE* PATIENTS			
	Sofosbuvir + RBV 24 weeks	No data	CONTRAINDICATED: didanosine, zidovudine, tipranavir	No data in treatment-experienced, coinfecting genotype 1 patients (SVR: 75% to 86% in coinfecting, treatment-naïve patients) In HCV monoinfection, SVR was 68% in treatment-naïve genotype 1 patients considered “hard to treat” (many were African-American, had IL-28B non-CC genotypes, HCV genotype 1a and high baseline HCV RNA)
Genotype 2, treatment-naïve and relapsers	Sofosbuvir + RBV 12 weeks	88% to 90% in treatment-naïve coinfecting genotype 2 patients treated for 12 weeks	CONTRAINDICATED: didanosine, zidovudine, tipranavir	Although data are available in treatment-experienced, coinfecting genotype 2 patients, they were treated for 24 weeks
Genotype 2, treatment-experienced (PEG-IFN and RBV)	Sofosbuvir + PEG-IFN and RBV 12 weeks	No data	CONTRAINDICATED: didanosine, zidovudine, tipranavir	No data on this regimen in treatment-experienced, coinfecting genotype 2 patients In HCV monoinfection treatment-experienced genotype 2 patients, SVR was 96% to 100% in two (small) trials of sofosbuvir + PEG-IFN and RBV for 12 weeks In coinfecting, treatment-experienced, genotype 2 patients, SVR was 85% to 92% in two (small) trials of sofosbuvir + RBV for 24 weeks
Genotype 3, treatment-naïve and treatment-experienced	ALL PATIENTS			
	Sofosbuvir + RBV 24 weeks	67% in coinfecting, treatment-naïve genotype 3 patients after 12 weeks of treatment 91% in coinfecting, treatment-naïve genotype 3 patients after 24 weeks of treatment 85% to 94% in coinfecting, treatment-experienced genotype 3 patients after 24 weeks of treatment	CONTRAINDICATED: didanosine, zidovudine, tipranavir	SVR rates generally lower in cirrhotic patients treated with sofosbuvir + RBV
	IFN-ELIGIBLE, TREATMENT-EXPERIENCED PATIENTS (PEG-IFN and RBV)			
	Sofosbuvir + PEG-IFN and RBV 12 weeks	No data	CONTRAINDICATED: didanosine, zidovudine, tipranavir	No data in treatment-experienced coinfecting genotype 3 patients In HCV monoinfection, SVR in (sofosbuvir) treatment-experienced genotype 3 patients was 91%

TABLE 3
Current HCV Treatment Recommendations in HIV/HCV Coinfection (*continued*)

Population	Regimen(s)	SVR in HIV/HCV	ARVs	Comments
Genotype 4, Treatment-naïve and treatment experienced	Sofosbuvir + PEG-IFN and RBV 12 weeks	No data	CONTRAINDICATED: didanosine, zidovudine, tipranavir	In HCV mono-infection, SVR in treatment-naïve patients was 96%
	INTERFERON-INELIGIBLE PATIENTS, TREATMENT- NAIVE or TREATMENT-EXPERIENCED			
	Sofosbuvir + RBV, 24 weeks	83%	CONTRAINDICATED: didanosine, zidovudine, tipranavir	In HCV mono-infected, treatment-experienced genotype 4 patients, SVR-4 was 93%
	ALTERNATIVE REGIMEN, INTERFERON-ELIGIBLE, TREATMENT NAIVE			
	Simeprevir + PEG-IFN and weight-based RBV for 12 weeks, followed by 12 or 36 weeks of PEG-IFN and RBV	No data	CONTRAINDICATED: protease inhibitors, efavirenz and etravirine, didanosine, zidovudine, tipranavir ALLOWED: enfuvirtide, maraviroc, raltegravir, ripivirine, abacavir, emtricitabine, lamivudine and tenofovir	In HCV mono-infected genotype 4 patients , overall SVR was 65%; in treatment-naïve patients and relapsers (most treated for 25 weeks)
Genotypes 5 and 6, all patients	Sofosbuvir + PEG-IFN and RBV	No data	CONTRAINDICATED: didanosine, zidovudine, tipranavir	In HCV mono-infection, only small numbers of treatment-naïve genotype 5 (N = 1) and genotype 6 (N = 6) patients; all achieved SVR Simeprevir is not recommended for use in advanced cirrhosis (Child-Pugh Class B or C)

Adapted from AASLD/IDSA/IAS–USA. Recommendations for testing, managing, and treating hepatitis C. Unique Patient Populations: HIV/HCV Coinfection Box. Recommendations for HIV/HCV Coinfected Patients Who are Being Treated for HCV, by Genotype. Accessed August 1, 2014. Available at: <http://www.hcvguidelines.org>.

*IFN ineligible is defined as one or more: intolerance to IFN; autoimmune hepatitis; and other autoimmune disorders; hypersensitivity to PEG or any of its components; decompensated hepatic disease; major uncontrolled depressive illness; a baseline neutrophil count below 1500/μL, a baseline platelet count below 90,000/μL or baseline hemoglobin below 10 g/dL; a history of pre-existing cardiac disease.

**This regimen should be considered only in those patients who require immediate treatment, because it is anticipated that safer and more effective IFN-free regimens will be available by 2015.

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**RECOMMENDATIONS FOR
HCV TREATMENT IN HIV/HCV**

As of August 2014, guidelines from the AASLD, IDSA and IAS-USA consider HCV treatment a high priority in people who are HIV/HCV coinfecting, and recommend HCV treatment for HIV/HCV coinfecting persons at any fibrosis stage, due to rapid disease progression, shorter survival after hepatic decompensation, and lack of access to and poor outcomes after liver transplantation.²⁵⁰

**LATEST TREATMENT ADVANCES:
A BRIGHT FUTURE AHEAD**

The great progress against HCV virus began when researchers developed cell culture systems; these allowed them to test antiviral drugs. Since then, four classes of HCV DAAs have been developed: protease inhibitors, non-nucleoside or nucleoside/tide polymerase inhibitors, and NS5A inhibitors. HCV DAAs are not active against HIV—although the viruses have some of the same enzyme, they are very different from one another.

Eligibility for, and delivery and uptake of, HCV treatment among both HCV monoinfected and HIV/HCV coinfecting people are likely to increase dramatically with the advent of all-oral, interferon-free

treatment with HCV DAAs. Several DAA combinations are in clinical trials.

The new oral DAA regimens will require less monitoring during treatment for both safety and efficacy, and cure rates from clinical trials have topped 90%. But clinicians will still need to select DAA regimens carefully to avoid drug-drug interactions with these and HIV.

WHAT'S NEXT?

All-oral HCV treatment is on the way for people with HCV genotype 1. By 2015, approval of a one pill, once-a-day regimen, or a twice-daily combination—both with cure rates over 85% in clinical trials—is anticipated.^{251–253} (See Table 4 Interferon-Free Regimens: Phase 3 Results in HCV Genotype 1).

Phase 3 trials are exploring the combination of sofosbuvir and daclatasvir (an NS5A inhibitor that awaits FDA approval) in all HCV genotypes, in people with HIV/HCV, in people with cirrhosis, and after liver transplantation.

With better HCV treatment on the way, grantees will not only be able to reap the benefits from these medications, they will also be able to apply the lessons learned from the *SPNS Hepatitis C Treatment Expansion Initiative* and grantees' years of experience caring for marginalized, underserved populations.

TABLE 4
Interferon-Free Regimens in HCV Genotype 1 (all phase 3, unless indicated)

Sponsor and regimen	Population	SVR	Common Adverse Events (mild to moderate)	Comments
ABT-450/r/ ombitasvir and dasabuvir + or – RBV 12 weeks AbbVie	HCV monoinfection treatment naive, no cirrhosis	Genotype 1b: 99% (no RBV) 99.5% (+ RBV) Genotype 1a: 90% (no RBV) 97% (+ RBV) Genotypes 1a and 1b 96% (+ RBV)	headache, fatigue, pruritus, rash, nausea, insomnia, diarrhea, asthenia	Genotype 1b can be treated without ribavirin
ABT-450/r/ ombitasvir and dasabuvir + or – RBV 12 or 24 weeks AbbVie	HCV monoinfection treatment-naive, cirrhosis	94% (12 weeks) 95% (24 weeks)	fatigue, headache, nausea, pruritus, insomnia, diarrhea, asthenia, rash, irritability, anemia, dyspnea	
ABT-450/r/ ombitasvir and dasabuvir + or – RBV 12 weeks AbbVie	HCV monoinfection treatment-experienced, no cirrhosis	Genotype 1b 100% (no RBV) 97% (+ RBV) Genotypes 1a and 1b 96%(+ RBV)		
ABT-450/r/ ombitasvir and dasabuvir + or – RBV 12 or 24 weeks AbbVie	HCV monoinfection treatment-experienced, compensated cirrhosis	90% (12 weeks) 97% (24 weeks)	fatigue, headache, nausea, pruritus, insomnia, diarrhea, asthenia, rash, irritability, anemia, dyspnea	24 weeks of treatment more effective for null responders with genotype 1a and cirrhosis
ABT-450/r/ ombitasvir and dasabuvir + RBV 12 or 24 weeks AbbVie	HIV/HCV treatment-naive or-experienced compensated cirrhosis (19%)	93% (12 week treatment group only) Interim results: (SVR-4) 96% (24-week treatment group)	fatigue, headache, nausea, insomnia, upper respiratory tract infection, pruritus anemia, cough, ocular icterus	ARVs: raltegravir, unboosted atazanavir, tenofovir and emtricitabine Regimen less effective for null responders with genotype 1a and cirrhosis
Sofosbuvir + ledipasvir (fixed-dose combination) + or – RBV 8 or 12 weeks Gilead Sciences	HCV monoinfected, treatment-naive no cirrhosis	93% to 94% (8-week treatment groups) 95% (no RBV; 12-week treatment group)	fatigue, headache, nausea, insomnia, irritability, diarrhea, arthralgia, constipation, dizziness, rash, pruritus,, cough, anemia, muscle spasms, dyspnea	Ribavirin is not needed

TABLE 4
Interferon-Free Regimens in HCV Genotype 1 (all phase 3, unless indicated) (*continued*)

Sponsor and regimen	Population	SVR	Common Adverse Events (mild to moderate)	Comments
Sofosbuvir + ledipasvir (fixed-dose combination) + or – RBV 12 or 24 weeks Gilead Sciences	HCV monoinfected, treatment-naïve 16% cirrhosis	97% to 99% (12-week treatment groups) 99% (24-week treatment group)	fatigue, headache, insomnia, nausea, asthenia, diarrhea, rash, irritability, cough, pruritus, arthralgia, anemia	SVR did not differ in cirrhosis
Sofosbuvir + ledipasvir (fixed-dose combination) + or – RBV 12 or 24 weeks Gilead Sciences	HCV monoinfected, treatment-experienced (50% with an HCV protease inhibitor); 20% cirrhosis	94% to 96% (12 week treatment groups (no RBV and + RBV) 99% (24 weeks, with and without RBV)	nausea, insomnia, arthralgia, cough, diarrhea rash, irritability, dizziness, dyspnea, upper respiratory tract infection, muscle spasms, anemia, dry skin	
Sofosbuvir + ledipasvir 12 weeks Phase 2 Gilead Sciences	HIV/HCV coinfectd (12 no ARV; 37 taking ARV) treatment-naïve, no cirrhosis	Interim results (SVR-4) 100% (ARV group) 100% (no ARV group)		ARVs: efavirenz, raltegravir, rilpivirine, tenofovir, emtricitabine

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PROGRAM SUSTAINABILITY

Clinics not treating HCV *prior* to the Hepatitis C Initiative SPNS grant found it difficult to either 1) find specialists within their communities to refer patients to due to a general shortage of specialists or 2) identify specialists willing to treat their patients. Other clinic sites were treating HCV but in smaller numbers. In both cases, grantees were seeing unmet need which the SPNS grant helped fill. Today, virtually all grantees are working to sustain their HCV treatment efforts.

Sustainable programs typically feature at least one of the following: securing new funding stream(s), optimizing existing resources, or leveraging the Ryan White HIV/AIDS Program network.

SECURING FUNDING

By demonstrating the effectiveness of programs and infrastructures established during the SPNS project, grantees are well positioned to seek out new grants and other funding streams (e.g., from state or local health departments, foundations/nongovernment organizations).

In addition, the ACA has facilitated Medicaid expansion in many states and expanded mental health and substance use screenings and treatment. ACA also has

ended discrimination against individuals with pre-existing conditions (such as HIV and HCV), and eliminated co-pays for particular screenings and vaccinations.

Some Hepatitis C Initiative grantees have been successful in securing support under other Ryan White HIV/AIDS Program Parts while others have sustained HCV work with current funding but at a smaller capacity than during SPNS grant years. Use of Ryan White HIV/AIDS Program (ADAP) funds and application to pharmaceutical drug assistance programs have also assisted in covering medication costs. In addition, Initiative grantees have cited the importance of the 340B Drug Pricing Program in assisting with the cost of medications (through 340B discounts) and, for those with 340B pharmacies, generating revenue.

In the case of Idaho State University, the grantee has not only enabled its HCV program to be self-sustaining, but the capacity built over the tenure of the SPNS Initiative has positioned the program to become a regional treatment center. As the Idaho State grantee summarized:

We have seamlessly integrated coinfecting patients into routine care, and with established protocols, we are able [to] work patients up for hepatitis C

*treatment readiness, provide education, and generate revenue from office visits. More importantly, we plan to maximize profits from the 340B program in the near future. At nearly \$60,000 for a treatment course for available medications (and projected at least that with new medications), there is a strong likelihood for significant revenue to return to our program, and which would support provider time and other needs. [In addition, on the topic of hepatitis C mono-infection] . . . our community health center has now become a community resource for patients infected with hepatitis C. In conjunction with new CDC screening guidelines for baby boomers, we are poised to be a major regional treatment center for hepatitis C.*²⁵⁴

OPTIMIZING EXISTING RESOURCES AND LEVERAGING THE RYAN WHITE HIV/AIDS PROGRAM NETWORK

Grantees readily took advantage of HCV technical assistance and education resources during the grant's tenure and nearly all stated that they planned to continue to do so. (A list of useful online resources can be found on the following page.) Grantees optimized what resources they

had accessible. For example, group visits to specialty trainings can maximize the number of staff up-to-date on HCV and foster collaboration.

Meanwhile, clinics similar to Idaho State University can also choose to expand treatment beyond HIV/HCV coinfecting patients to be inclusive of HCV monoinfecting patients as a way to recruit more individuals into their programs.

CONCLUSION

Grantees found a singular model that clearly fit their organizational needs. They sought—and continue to seek—guidance on evolving HCV practices and tapping into specialty care. Through new funding streams, modifications of current funding streams, smaller project scope, 340B-related revenue, or broadening their HCV patient base, SPNS grantees are actively seeking ways to sustain this work. HCV is a serious and complicated coinfection. Ryan White HIV/AIDS Program grantees are well-positioned to meet the challenges that HCV-infected PLWH face, offer culturally competent care, encourage these patients throughout the course of their HCV treatment, however, and help them advance along the broader HIV Care Continuum.



HELPFUL WEB-BASED HCV RESOURCES

Action Plan for the Prevention, Care and Treatment of Viral Hepatitis: <http://www.hhs.gov/ash/initiatives/hepatitis/>

A Guide for Evaluation and Treatment of Hepatitis C in Adults Coinfected with HIV: <http://hab.hrsa.gov/deliverhivaidsare/files/hepccoinfectguide2011.pdf>

AIDS Education and Training Centers: www.aidseduc.org

- Hepatitis in 2014 Webinar Series, New York/New Jersey AIDS Education and Treatment Center: www.nynjaetcc.org/on-demand/index.html#HCV

A Toolkit for Screening, Counseling and Patient Education: Hepatitis C Infection and People Living with HIV: www.projectinform.org/hcvtoolkit/

American Association for the Study of Liver Diseases (AASLD) and the Infectious Diseases Society of America (IDSA). Recommendations for Testing, Managing, and Treating of Hepatitis C: www.hcvguidelines.org/

CME Education on Coinfection: <http://clinicaloptions.com/Hepatitis.aspx> and <http://clinicaloptions.com/HIV.aspx>

European Association for the Study of the Liver (EASL). EASL Recommendations on the Treatment of Hepatitis C 2014. Available at: <http://files.easl.eu/easl-recommendations-on-treatment-of-hepatitis-c-summary/index.html>. April 2014.

Guide for HIV/AIDS Clinical Care (see Chapter 6 “Comorbidities, Coinfections, and Complications”): www.hab.hrsa.gov/deliverhivaidsare/2014guide.pdf

HCV Guidance, Management, and Treatment: <http://aasld.org/practiceguidelines/pages/guidelinelisting.aspx>

Hepatitis C in HIV/AIDS Pocket Guide: http://fcaetc.org/files/HepC_Final%20Web%20Version%20with%20highlights.pdf

HIV/HCV (requires registration; search “HIV/HCV”): www.medscape.com/hiv

Modular Training with Free CME for Hepatitis B and C: <http://aasld.org/liverlearning%C2%AE/Pages/LiverProgramforPrimaryCareProviders.aspx>

SAMHSA-HRSA Center for Integrated Health Solutions: <http://www.integration.samhsa.gov/>

Screening for Viral Hepatitis within Behavioral Health Organizations: <http://www.integration.samhsa.gov/about-us/webinars>

Self-study online course for medical providers (includes modules, lectures, core concepts, and bibliography): <https://careacttarget.org/library/hepatitis-c-online-course>

Take Action Against Hepatitis C: For People in Recovery From Mental Illness or Addiction: <http://store.samhsa.gov/product/Take-Action-Against-Hepatitis-C/SMA14-4853>

TARGET Center Website: <https://careacttarget.org>

Telehealth/Project ECHO:

- <http://echo.unm.edu>
- <http://fcaetc.org/echo>
- <http://depts.washington.edu/nwaetc/echo/index.html>

The University of Liverpool and eMedFusion. Drug Interaction Charts. Last revised March 27, 2014: www.hep-druginteractions.org/.

University of Washington, Hepatitis C Training Modules: <http://hepatitisc.uw.edu/>

Veteran Affairs (VA) National Hepatitis C Program and Hepatitis C Resource Centers (HCRCs):

- The VA is the top provider of medical care for people living with HCV in the United States
- HCRCs develop HCV best practices for use in the VA and around the country
- Four centers are located in Minneapolis, San Francisco, Connecticut, and the Northwest: www.hepatitis.va.gov/hcrc-index.asp

2014 – Optimal Management of HIV and Hepatitis: Clinical Conference XXII: www.practicepointhepatitis.com



APPENDIX

The appendix includes a compilation of useful grantee tools that may be used as templates for organizations looking to expand or develop HCV treatment within their clinics. Providers should be cognizant to tailor these forms to their particular needs.

- HCV Treatment Referral Protocol
- HCV Treatment Referral Protocol Checklist
- HCV Doctor Reminder Sheet
- Is Your Patient Ready to Start HCV Treatment?
- Hepatitis C Treatment Agreement
- HCV Side Effects Monitoring
- HCV Lab Monitoring
- Hepatitis C Treatment Reminder for Charts

HEPATITIS C TREATMENT REFERRAL PROTOCOL

Effective Date: _____

PROTOCOL: HEPATITIS C PATIENT REFERRALS

DESCRIPTION:

1. The provider will identify patients that would benefit from Hepatitis treatment by reviewing necessary labs such as: results of liver biopsy/sonogram, Hepatitis C genotype, Hepatitis C viral load etc. (refer to Hepatitis C treatment protocols).
2. The Provider will make an appointment with the patient to discuss treatment. During this visit the Provider will assess whether the patient is a good candidate for treatment by determining if the patient is ready physically and mentally for treatment. Once the provider has determined that the patient may be a candidate for treatment an initial referral will be made for Hepatitis C education. Family and support persons are encouraged to attend the Hepatitis C education session with the patient. **The patient must attend an education session before the referral process can proceed.**
3. Once the Hepatitis C education session is completed the patients will need time to decide if they wish to participate in treatment. They may need to discuss this with their family/support team or other significant persons. If the patient decides they wish to continue with the Hepatitis C treatment process they will need to meet again with their medical provider.
4. If the above patient does not wish to participate in Hepatitis C treatment, this information will be relayed to the medical provider. If and when the patient decides that they want to participate in treatment the educator will be notified either by the medical provider or patient. The educator will then discuss the patient with their medical provider to see if additional education will be needed. The protocol will then be followed beginning with #5.
5. The provider will make an initial referral to social services for a mental health assessment by a Behavioral Health Counselor. The results of this mental health assessment will be used to make a final determination of the patient's appropriateness for Hepatitis C treatment by using the Criteria for Hepatitis C Therapy Scoring system. Once the patient starts treatment the Behavioral Health Counselor will conduct a 60-minute session to assess the patient's mental health status every month throughout therapy.
6. If the patient is currently under the care of a psychiatrist or other mental health provider this provider must sign off on the patients' appropriateness for treatment before treatment can be considered. If the psychiatrist or other mental health provider approves their patient for treatment the social service Behavioral Health Counselor will follow the patient monthly during their Hepatitis C treatment. The patient will keep appointments with their psychiatric/mental health provider as appropriate/necessary.
7. If the patient is found to be appropriate for treatment after their mental health assessment and the patient wishes to initiate treatment for Hepatitis C treatment social services will notify the patient's provider and Team 8.
8. If the patient has completed the mental health exam and is found to be appropriate for treatment then the patients will need to complete a baseline ophthalmoscopic examination. A referral will be made to [physician name] if the patient has no insurance or to their choice of provider if they have insurance.

HEPATITIS C TREATMENT REFERRAL PROTOCOL (*continued*)

9. Once the baseline ophthalmoscopic examination has been successfully completed the process for ordering medications will be initiated. Medications will be ordered either by their pharmacy if they have insurance or through pharmaceutical programs if they do not have insurance coverage. The pharmaceutical programs will be accessed through the pharmacy. Medication initiation and monitoring will be done according to Hepatitis C Treatment protocols. It is preferred that medications be sent to [facility name] for better monitoring. Once the medication arrives the patients will need an appointment with their provider before therapy initiation. The patient will need monthly medical follow up appointments scheduled with their provider.
10. Team 8 will then be informed of the initiation date of the patient's treatment and will make referrals to social services for monthly follow up appointments for the duration of their treatment. A brief refresher on medication administration may need to be completed with the patient before medication initiation and possible side effects readdressed.
11. If a patient experiences medication side effects or other problems during their treatment course the patient will call their medical provider for further evaluation and an appointment if necessary.
12. Team 8 will monitor patients during the course of their treatment to be sure that they are followed appropriately by social services, keep all their provider appointments, and for support and additional education if needed.

Medical Director Signature: _____

CEO Signature: _____

HCV TREATMENT REFERRAL PROTOCOL CHECKLIST

Patient identified by their medical provider as appropriate for, interested in, and would benefit from HCV treatment

- ☐ Referral made for HCV treatment per protocol:
 - ☐ HCV Viral load
 - ☐ HCV Genotype
 - ☐ Hepatitis immunizations completed:
 - ☐ Twinrix #1, ☐ Twinrix #2, ☐ Twinrix #3
 - OR
 - ☐ Hepatitis A #1, ☐ Hepatitis A #2
 - ☐ Hepatitis B #1, ☐ Hepatitis B #2, ☐ Hepatitis B #3
 - ☐ Attended HCV treatment group education: Date _____
 - ☐ *Two methods of birth control discussion (note in dictation)
 - ☐ *Two barrier methods of birth control discussion if on protease inhibitors
 - ☐ If still interested in treatment patient needs appt with provider and may continue on with the rest of the referral protocol.
 - ☐ Baseline mental health assessment completed by social services:
 - ☐ IF NOT APPROPRIATE NOTE REASON AND PLAN: _____
 - ☐ If appropriate for treatment continue with protocol (BELOW)
 - ☐ Baseline Ophthalmoscopic examination completed:
 - ☐ Date: _____
 - ☐ Doctor: _____
 - ☐ Copy of results on file
 - ☐ *Provider orders HCV treatment medications:
 - ☐ Insurance
 - ☐ Patient Assistance with pharmacist
 - ☐ Date application completed _____
 - ☐ expected arrival date of medications to Pharmacy: _____
- * After HCV treatment medications arrive patient must:
- ☐ Meet with medical provider to have baseline labs completed (if not done)
 - ☐ Provider to reinforce the need for 2 methods of birth control use while on HCV treatment and for 6 months after treatment is completed if on standard interferon/ribavirin regimen, 2 BARRIER methods discussed if patient is on standard HCV treatment with a protease inhibitor-note in dictation
 - ☐ Meet with HCV case manager for a review of expected side effects and injection techniques
 - ☐ HCV Treatment agreement signed

HCV Treatment start date: _____

If COINFECTED:

- ☐ HIV stable
- ☐ HAART regimen: _____

HCV DOCTOR REMINDER SHEET

Name _____ Date _____

After reviewing this patient's chart it appears that the patient may need some items completed. Any highlighted items may need to be completed during today's visit.

Please check the box of each item completed today and place in yellow Hep C folder.

If a highlighted item does not need completed today please explain.

- ☐ HCV Viral load
- ☐ HCV Genotype
- ☐ Baseline Ophthalmoscopic examination
- ☐ *Two methods of birth control discussion (note in dictation)
- ☐ HCV Group education
- ☐ Baseline mental health assessment
- ☐ Hepatitis C Treatment agreement signed
- ☐ Twinrix #1, ☐ Twinrix #2, ☐ Twinrix #3
- OR
- ☐ Hepatitis A #1 Vax ☐ Hepatitis A #2 Vax
- ☐ Hepatitis B #1 Vax ☐ Hepatitis B #2 Vax
- ☐ Hepatitis B #3 Vaccination
- ☐ Monthly mental health assessment
- ☐ CBC to be completed immediately prior to treatment as a baseline and throughout treatment-see lab draw schedule on your Hepatitis C Treatment Flow Sheet
- ☐ LFT to be completed immediately prior to treatment as a baseline and throughout treatment-see lab draw schedule on your Hepatitis C Treatment Flow Sheet
- ☐ TSH to be completed immediately prior to treatment as a baseline and throughout treatment-see lab draw schedule on your Hepatitis C Treatment Flow Sheet
- ☐ AFP to be completed immediately prior to treatment as a baseline and throughout treatment-see lab draw schedule on your Hepatitis C Treatment Flow Sheet
- ☐ *Beta HCG to be completed immediately prior to treatment as a baseline and throughout treatment-see lab draw schedule on your Hepatitis C Treatment Flow Sheet

***The medical provider may decide that this item is unnecessary due to age, menopause, hysterectomy, or other reason but this must be noted in the provider's dictation.**

PLEASE DISCUSS: _____

IS YOUR PATIENT READY TO START HCV TREATMENT?

Has this patient completed the HCV referral process-check below:

- ☐ HCV Viral load
- ☐ HCV Genotype
- ☐ Baseline Ophthalmoscopic examination
- ☐ *Two methods of birth control discussion,
 - ☐ Standard treatment with just ribavirin and interferon: one method must be barrier method like condoms (note in dictation)
 - ☐ Standard treatment plus protease inhibitors Incivik or Victrelis: the 2 methods of birth control MUST both be BARRIER methods like condoms and a diaphragm or cervical cap
- ☐ HCV Group education
- ☐ Baseline mental health assessment
- ☐ Hepatitis C Treatment agreement signed
- ☐ Twinrix #1, ☐ Twinrix #2, ☐ Twinrix #3
- OR
- ☐ Hepatitis A #1 Vax ☐ Hepatitis A #2 Vax
- ☐ Hepatitis B #1 Vax ☐ Hepatitis B #2 Vax
- ☐ Hepatitis B #3 Vaccination

If all the above have been completed satisfactorily then:

- ☐ notify the HCV case Manager
- ☐ Scripts need to be written for medications: Pegasys (pegylated interferon) and Ribavirin (Copegus if the patient has no insurance and needs the patient assistance program) See dosing recommendations below:

Genotype	Peginterferon alfa-2a dose (weekly)	Ribavirin Tablets Dose (Daily)	Duration
Genotype 1, 4	180 mcg	<75 kg (165 #) = 1000 mg, (women 2, 200 mg tablets in the morning and 3, 200 mg tablets with the evening meal at least 3-4 hours before bedtime)	48 weeks
		Men; 3, 200 mg tablets by mouth twice daily with food- the last daily dose needs to be at least 3-4 hours before bedtime)	48 weeks
		>75 kg (165 #) = 1200 mg	
Genotype 2, 3	180 mcg	800 mg	24 weeks

IS YOUR PATIENT READY TO START HCV TREATMENT? *(continued)*

Incivik (Telaprevir) & Victrelis (Boceprevir) Dosing:

Medication	Dosing	Route	Schedule	Storage	Length	Evaluate
Incivik (Telaprevir)	2, 375 mg tablets	By mouth with food containing at least 20 grams of fat per dose	Every 7-9 hours	Store at room temperature	12 weeks	Need RVR at 4 weeks with HCV viral load
Victrelis (Boceprevir)	4, 200 mg tablets with food, Lead in dosing of 4 weeks with ribavirin and interferon-start Victrelis at week 5	By mouth with food	Every	Refrigerate	28 weeks,	Need HCV viral load at 8 weeks

Scripts for patients needing patient assistance need to be sent to the pharmacist so she can begin the process to apply for the pharmaceutical assistance programs for those medications. She cannot begin this process without the scripts.

*all patients on patient assistance programs will also complete paper work for the Neupogen replacement program.

For patient assistance patients the program only offers the ribavirin in the 200 mg tablet formulation. Genotype 1 patients under 75 kg (165 #) will need to take 2 tablets in the morning and 3 tablets in the evening . . . (take the 3 tabs with the largest meal). The pharmaceutical program will also only give a month worth of medication at a time as well. A month of Ribavirin for genotype 1 > 75 kg (165 #) order 3, 200 mg tablets twice daily with meals, dispense #180 and for genotype 1's < 165 # order as described above, dispense 150 tablets for a month's worth.

Please note that ribavirin tablets are available in the following strengths for patients not on pharmaceutical assistance programs: 200mg, 400 mg, 500 mg, & 600 mg.

IS YOUR PATIENT READY TO START HCV TREATMENT? *(continued)*

Patients are not to begin the medications until they have:

- ☐ Met with their provider one more time to review blood work (see below) and answer any lingering questions. The patient needs to sign the Hepatitis C treatment agreement with their medical provider.
- ☐ Met with the HCV case manager to review side effects, develop medication time schedule, and review injection techniques (this appointment should coincide with the last meeting with the provider before treatment initiation above)
- ☐ Had the following blood work completed and reviewed by the provider (this needs to be completed on all HCV Treatment patients just prior to treatment initiation):
 - ☐ HCV Viral load to be completed immediately prior to treatment as a baseline and throughout treatment
 - ☐ CBC to be completed immediately prior to treatment as a baseline and throughout treatment-see lab draw schedule on your Hepatitis C Treatment Flow Sheet
 - ☐ LFT to be completed immediately prior to treatment as a baseline and throughout treatment-see lab draw schedule on your Hepatitis C Treatment Flow Sheet
 - ☐ TSH to be completed immediately prior to treatment as a baseline and throughout treatment-see lab draw schedule on your Hepatitis C Treatment Flow Sheet
 - ☐ AFP to be completed immediately prior to treatment as a baseline and throughout treatment-see lab draw schedule on your Hepatitis C Treatment Flow Sheet
 - ☐ *Beta HCG to be completed immediately prior to treatment as a baseline and throughout treatment-see lab draw schedule on your Hepatitis C Treatment Flow Sheet

After all the above is completed the patient can begin treatment! See below for the routine blood draw schedule. Patients will also need to meet with Social services monthly throughout their treatment course-please make sure these are scheduled preferably to coincide with the patient's other monthly appointments.

Test	Treatment weeks															Post Treatment Follow up		
	0	1	2	4	8	12	16	20	24	28	32	36	40	44	48	4	12	24
CBC																		
LFT																		
HCV Viral load				Incivek	Victrelis													
TSH																		
INR																		
AFP																		
Serum Beta HCG ♀																		

HEPATITIS C TREATMENT AGREEMENT

I am requesting treatment of my Hepatitis C. Treatment most often used is a combination of Pegylated Interferon and Ribavirin. This treatment may also include additional protease inhibitor medications.

Nearly all patients experience one or more side effects. Some common side effects may include:

- Mood changes such as depression, irritability, and anxiety
- Flu-like symptoms such as fatigue, fever, body aches, headache, and chills
- Rash or skin reaction including dry skin or hair loss/thinning. **Report any rash to your medical provider**
- Decrease in red blood cells (anemia), white blood cells, or platelets
- Diarrhea
- Nausea and vomiting
- Thyroid abnormalities
- Decreased appetite

Good communication with my medical provider and nurses will help to manage the side effects that you may experience during your treatment. It is also important to incorporate other support systems such as family and close friends.

Severe side effects can occur, although they are relatively uncommon. These include hearing loss or ringing in the ears, seizures, diabetes, heart problems, stroke, eye problems, kidney failure, and worsening of liver disease. If you experience any of the conditions below, contact your medical provider (or seek urgent medical attention):

- You become very depressed or think about suicide
- You have trouble breathing
- You notice unusual bruising or bleeding
- You have psoriasis (a skin disease) that gets worse during treatment
- You have severe stomach pain or lower back pain
- You have severe chest pain
- You have a change in vision
- You become pregnant
- High fever or a fever that does not go away
- Bloody diarrhea

Information about Ribavirin:

The side effects of ribavirin include hemolytic anemia, difficulty sleeping, poor appetite, rash/itching, cough/shortness of breath. In addition **Ribavirin may cause birth defects and/or death of your unborn child. Extreme care must be taken to avoid pregnancy in female patients and in female partners of male patients, use two forms of birth control during treatment and for the 6 months after treatment is completed. One method must be a barrier such as condoms.** ____ initial here indicating understanding

If you are prescribed either Incivek (Telaprevir) or Victrelis (boceprvir) along with the standard HCV treatment of Pegylated interferon and Ribavirin it is imperative that you use 2 BARRIER METHODS of birth control (example: condoms and a cervical cap or diaphragm) while on these medications. Both of these medications make estrogen based birth control pills ineffective. ____ initial here indicating understanding

HEPATITIS C TREATMENT AGREEMENT (*continued*)

Patient Statement:

Medication guides or Product information all my treatment medications are provided to me with my prescriptions. I understand that good communication with my medical provider's office will help me in the management of side effects that I may experience. I also understand that it is uncommon, but should I experience any serious side effects, I will seek urgent medical care and will contact my medical provider's office.

I understand that my HCV treatment requires close supervision. I agree to monthly follow up appointments with my medical provider and mental health worker. I agree to answer phone calls and letters promptly. I understand the importance of taking all my medications exactly as ordered. I agree that I will not skip medication doses or stop any of my medications without consulting with my medical provider first. I understand that I need to report any medications that I use whether over the counter, prescribed, or recreational to my medical provider. I understand that if I do not follow through with keeping my appointments or taking my medications that I may not be able to continue my HCV treatment. My treatment may also be discontinued if I use any substances including alcohol that are not prescribed by or approved by my medical provider. I will agree to a drug screen should my medical provider request one.

_____ initial here indicating understanding

All of my questions have been answered about interferon, ribavirin, Incivik, and Victrelis and I understand the seriousness of pregnancy during treatment and 6 months following the end of treatment. I agree to take responsibility for contraception.

Patient name printed _____

Patient Signature _____ Date _____

Staff Witness: _____

Print Name & Title _____

Staff Signature _____ Date _____

HCV SIDE EFFECTS MONITORING

Side effect Monitoring	Treatment weeks														Post treatment Follow up		
	1	2	4	8	12	16	20	24	28	32	36	40	44	48	4	12	24
Fatigue																	
Insomnia																	
Irritability																	
Lack of concentration																	
Depression																	
Nausea																	
Loss of appetite																	
Headaches																	
Muscle Aches																	
Chills																	
Fever																	
Cough																	
Itchy Skin																	
Injection site reaction																	
Hair loss																	
Rash grade 1																	
Rash grade 2																	
Rash grade 3																	
Anemia																	

NOTES: _____

Treatment initiation Date: _____ Treatment completion Date: _____

Was treatment stopped prematurely? : ☐ yes ☐ no

If "yes" why: _____

HCV LAB MONITORING

Test	Treatment weeks															Post Treatment Follow up		
	0	1	2	4	8	12	16	20	24	28	32	36	40	44	48	4	12	24
CBC																		
LFT																		
HCV Viral load				Incivek & SPNS	Victrelis													
TSH																		
INR																		
AFP																		
Beta HCG ♀																		

Viral Load draws	Treatment weeks							
	0	4 weeks	8 weeks	12 weeks	24 weeks Genotypes 2 & 3	28 weeks	48 weeks genotypes 1 & 4	72 weeks
Starting Viral load								
RVR (rapid viral response)		INCIVIK	VICTRELIS					
EVR (Early viral response)								
EOT (end of treatment)				INCIVIK		VICTRELIS		
SVR (sustained viral response)								
Ending viral load								

HEPATITIS C TREATMENT REMINDER FOR CHARTS

NAME _____ DATE _____

Hepatitis C treatment initiation date: _____

- ☐ Hepatitis C Genotype _____
- ☐ Hepatitis C group education
- ☐ Baseline mental health assessment completed prior to treatment initiation
- ☐ Baseline ophthalmoscopic examination completed
- ☐ Beta HCG on women prior to treatment
- ☐ Discussed necessity of 2 methods of birth control during treatment
Date _____ Methods: #1 _____ #2 _____

☐ Beta HCG on women **monthly** during treatment & Post treatment follow up weeks 4, 12, & 24

☐ Monthly Mental health assessment during treatment:

☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10 ☐ 11 ☐ 12

☐ Hepatitis C Viral load prior to treatment

☐ Hepatitis C Viral load during treatment at:

☐ 4 weeks ☐ 16 weeks ☐ 48 weeks

☐ CBC prior to treatment and during treatment weeks: 1,2,3,4,8,12,16,20,24,28,32,36,40,44,48 & Post treatment follow up weeks 4 & 24

☐ LFT prior to treatment and during treatment weeks: 4,8,12,16,20,24,28,32,36,40,44,48 & Post treatment follow up weeks 4, 12, 24

☐ HCV viral load prior to treatment and during treatment weeks: 12, 24,48 & Post treatment follow up week 24

☐ TSH prior to treatment and during treatment weeks: 12,24,36,48

☐ AFP prior to treatment and during treatment weeks: 48 & Post treatment follow up week 24

☐ Hepatitis A Vaccination should be completed on all Hepatitis C patients

☐ initial ☐ 6 months

☐ Hepatitis B Vaccination should be completed on all hepatitis C patients

☐ initial ☐ 1 month ☐ 6 months

OR

☐ Twinrix Vaccination completed

☐ initial ☐ 1 month ☐ 6 months

HEPATITIS C TREATMENT REMINDER FOR CHARTS *(continued)*

Side effect Monitoring	Treatment weeks														Post treatment Follow up		
	1	2	4	8	12	16	20	24	28	32	36	40	44	48	4	12	24
Fatigue																	
Insomnia																	
Irritability																	
Lack of concentration																	
Depression																	
Nausea																	
Loss of appetite																	
Headaches																	
Muscle Aches																	
Chills																	
Fever																	
Cough																	
Itchy Skin																	
Injection site reaction																	
Hair loss																	

Other: _____

*any circled items may need to be completed during today's visit. Please check the box of each item completed today and place in yellow Hep C folder.



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