



## When and in Whom to Initiate HCV Therapy

Successful hepatitis C treatment results in sustained virologic response (SVR), which is tantamount to virologic cure and, as such, is expected to benefit nearly all chronically infected persons. When the US Food and Drug Administration (FDA) approved the first interferon-sparing treatment for HCV infection, many patients who had previously been “warehoused” sought treatment. The infrastructure (ie, experienced practitioners, budgeted healthcare dollars, etc) did not yet exist to treat all patients immediately. Thus, the panel offered guidance for prioritizing treatment first for those with the greatest need.

Since that time, there have been opportunities to treat many of the highest-risk patients and accumulate real-world experience regarding the tolerability and safety of interferon-free HCV regimens. More importantly, from a medical standpoint, data continue to accumulate that demonstrate the many benefits, both intrahepatic and extrahepatic, that accompany HCV eradication. Therefore, the panel continues to recommend treatment for all patients with chronic HCV infection, except those with a short life expectancy that cannot be remediated by HCV treatment, liver transplantation, or another directed therapy. Accordingly, prioritization tables have been removed from this section.

Despite the strong recommendation for treatment of nearly all HCV-infected patients, pretreatment assessment of a patient’s understanding of treatment goals and provision of education about adherence and follow-up are essential. A well-established therapeutic relationship between clinician and patient remains crucial for optimal outcomes with direct-acting antiviral (DAA) therapies. Additionally, in certain settings there remain factors that impact access to medications and the ability to deliver them to patients. In these settings, clinicians may still need to decide which patients should be treated first. The descriptions of unique populations discussed in this section may help physicians make more informed treatment decisions for these groups. For additional information, see unique patient populations: [Patients With HIV/HCV Coinfection](#), [Patients With Decompensated Cirrhosis](#), [Patients Who Develop Recurrent HCV Infection Post Liver Transplantation](#), [Patients With Renal Impairment](#), [HCV in Children](#), and [HCV Post Kidney Transplant](#).

Goal of Treatment	
RECOMMENDED	RATING 
The goal of treatment of HCV-infected persons is to reduce all-cause mortality and liver-related health adverse consequences, including end-stage liver disease and hepatocellular carcinoma, by the achievement of virologic cure as evidenced by a sustained virologic response.	I, A

Recommendation for When and in Whom to Initiate Treatment	
RECOMMENDED	RATING 
Treatment is recommended for all patients with chronic HCV infection, except those with a short life expectancy that cannot be remediated by HCV therapy, liver transplantation, or another directed therapy. Patients with a short life expectancy owing to liver disease should be managed in consultation with an expert.	I, A

## Clinical Benefit of Cure

The proximate goal of HCV therapy is SVR (virologic cure), defined as the continued absence of detectable HCV RNA for at least 12 weeks after completion of therapy. SVR is a marker for cure of HCV infection and has been shown to be durable in large prospective studies in more than 99% of patients followed-up for  $\geq 5$  years ([Swain, 2010](#)); ([Manns, 2013](#)). Patients in whom SVR is achieved have HCV antibodies but no longer have detectable HCV RNA in serum, liver tissue, or mononuclear cells, and achieve substantial improvement in liver histology ([Marcellin, 1997](#)); ([Coppola, 2013](#)); ([Garcia-Bengochea, 1999](#)). Assessment of viral response, including documentation of SVR, requires use of an FDA-approved quantitative or qualitative nucleic acid test (NAT) with a detection level of  $\leq 25$  IU/mL.

Patients who are cured of their HCV infection experience numerous health benefits, including a decrease in liver inflammation as reflected by improved aminotransferase levels (ie, alanine aminotransferase [ALT] and aspartate aminotransferase [AST]), and a reduction in the rate of liver fibrosis progression ([Poynard, 2002b](#)). Among 3,010 treatment-naïve patients from 4 randomized trials who had pretreatment and posttreatment liver biopsies (separated by a mean of 20 months) and were treated with 10 different interferon-based regimens, 39% to 73% of participants who achieved SVR had improvement in liver fibrosis and necrosis ([Poynard, 2002b](#)). Additionally, cirrhosis resolved in 49% of the cases. Portal hypertension, splenomegaly, and other clinical manifestations of advanced liver disease also improved. Among HCV-infected persons, SVR is associated with a  $>70\%$  reduction in the risk of liver cancer (hepatocellular carcinoma [HCC]), and a 90% reduction in the risk of liver-related mortality and liver transplantation ([Morgan, 2013](#)); ([van der Meer, 2012](#)); ([Veldt, 2007](#)).

Cure of HCV infection also reduces symptoms and mortality from severe extrahepatic manifestations, including cryoglobulinemic vasculitis, a condition affecting 10% to 15% of HCV-infected patients ([Fabrizi, 2013](#)); ([Landau, 2010](#)); ([Sise, 2016](#)). HCV-infected persons with non-Hodgkin lymphoma and other lymphoproliferative disorders achieve complete or partial remission in up to 75% of cases following successful therapy for HCV infection ([Gisbert, 2005](#)); ([Takahashi, 2012](#)); ([Svoboda, 2005](#)); ([Mazzaro, 2002](#)); ([Hermine, 2002](#)). These reductions in disease severity contribute to dramatic reductions in all-cause mortality ([van der Meer, 2012](#)); ([Backus, 2011](#)). Furthermore, patients who achieve SVR have a substantially improved quality of life, which spans their physical, emotional, and social health ([Boscarino, 2015](#)); ([Neary, 1999](#)); ([Younossi, 2013](#)); ([Gerber, 2016](#)). Because of the many benefits associated with successful HCV treatment, clinicians should treat HCV-infected patients with antiviral therapy with the goal of achieving SVR, preferably early in the course of chronic HCV infection before the development of severe liver disease and other complications.

## Benefits of Treatment at Early Fibrosis Stages (Metavir Stage Less Than F2)

Initiating therapy in patients with lower-stage fibrosis augments the benefits of SVR. In a long-term follow-up study, 820 patients with biopsy-confirmed Metavir stage F0 or F1 fibrosis were followed for up to 20 years ([Jezequel, 2015](#)). The 15-year survival rate was significantly better for those who experienced SVR than for those whose treatment failed or for those who remained untreated (93%, 82%, and 88%, respectively;  $P = .003$ ). The study results argue for consideration of earlier initiation of treatment. Several modeling studies also suggest a greater mortality benefit if treatment is initiated at fibrosis stages prior to F3 ([Øvrehus, 2015](#)); ([Zahnd, 2015](#)); ([McCombs, 2015](#)).

Treatment delay may decrease the benefit of SVR. In a report from France, 820 patients with biopsy-confirmed Metavir stage F0 or F1 fibrosis were followed for as long as 20 years ([Jezequel, 2015](#)). The authors noted rapid progression of fibrosis in 15% of patients during follow-up, and in patients treated successfully, long-term survival was better. Specifically, at 15 years, survival rate was 92% for those with SVR versus 82% for treatment failures and 88% for those not treated. In a Danish regional registry study, investigators modeled treatment approaches with the aim of evaluating the benefit to the region in terms of reductions in morbidity and mortality and HCV prevalence ([Øvrehus, 2015](#)). Although they note that in their situation of low HCV prevalence (0.4%) with approximately 50% undiagnosed, a policy that restricts treatment to those with Metavir fibrosis stage F3 or higher would decrease mortality from HCC and cirrhosis, the number needed to treat to halve the prevalence of the disease is lower if all eligible patients receive treatment at diagnosis.

A modeling study based on the Swiss HIV cohort study also demonstrated that waiting to treat HCV infection until Metavir fibrosis stages F3 and F4 resulted in 2- and 5-times higher rates of liver-related mortality, respectively, compared with treating at Metavir stage F2 ([Zahnd, 2015](#)). A US Veterans Administration dataset analysis that used very limited end points of virologic response dating from the interferon-treatment era suggested that early initiation of therapy (at a fibrosis-4 [FIB-4] score of <3.25) increased the benefit attained with respect to likelihood of treatment success and mortality reduction, and ultimately decreased the number of patients needed to treat to preserve 1 life by almost 50% ([McCombs, 2015](#)).

## Considerations in Specific Populations

Despite the recommendation for treatment of nearly all patients with HCV infection, it remains important for clinicians to understand patient- and disease-related factors that place individuals at risk for HCV-related complications (liver and extrahepatic) as well as for HCV transmission. Although these groups are no longer singled out for high prioritization for treatment, it is nonetheless important that clinicians recognize the unique dimensions of HCV disease and its natural history in these populations. The discussions offered below may assist clinicians in making compelling cases for insurance coverage of treatment when necessary.

### ***Persons With Advanced Liver Disease***

For persons with advanced liver disease (Metavir stage F3 or F4), the risk of developing complications of liver disease, such as hepatic decompensation (Child-Turcotte-Pugh [CTP] class B or C [[Methods Table 3](#)] <sup>i</sup>) or HCC, is substantial and may occur in a relatively short timeframe. A large prospective study of patients with cirrhosis resulting from HCV infection examined the risk of decompensation—including HCC, ascites, jaundice, bleeding, and encephalopathy—and found that the overall annual incidence rate was 3.9% ([Sangiovanni, 2006](#)). The National Institutes of Health (NIH)-sponsored HALT-C study included a group of 220 patients with cirrhosis resulting from HCV infection who were observed for approximately 8 years. A primary outcome of death, hepatic decompensation, HCC, or an increase in CTP score  $\geq 2$  occurred at a rate of 7.5% per year ([Everson, 2006](#)); ([Di Bisceglie, 2008](#)). Patients with a CTP score of  $\geq 7$  experienced a death rate of 10% per year.

Numerous studies have demonstrated that hepatitis C therapy and the achievement of SVR in this population results in dramatic decreases in hepatic decompensation events, HCC, and liver-related mortality ([Morgan, 2013](#)); ([van der Meer, 2012](#)); ([Backus, 2011](#)); ([Dienstag, 2011](#)); ([Berenguer, 2009](#)); ([Mira, 2013](#)). In the HALT-C study, patients with advanced fibrosis secondary to HCV infection who achieved SVR, compared with patients with similarly advanced liver fibrosis who did not achieve SVR, had a decreased need for liver transplantation (HR, 0.17; 95% CI, 0.06-0.46), decreased development of liver-related morbidity and mortality (HR, 0.15; 95% CI, 0.06-0.38), and decreased HCC (HR, 0.19; 95% CI, 0.04-0.80) ([Dienstag, 2011](#)). Importantly, persons with advanced liver disease also require long-term follow-up and HCC surveillance regardless of treatment outcome (see [Monitoring Patients Who Are Starting Hepatitis C Treatment, Are on Treatment, or Have Completed Therapy](#)).

Given the clinical complexity and need for close monitoring, patients with advanced liver disease that has already decompensated (CTP class B or C [[Methods Table 3](#)] <sup>i</sup>) should be treated by physicians with experience treating HCV in conjunction with a liver transplantation center, if possible (see [Patients with Decompensated Cirrhosis](#)).

### ***Persons Who Have Undergone Liver Transplantation***

In HCV-infected individuals, HCV infection of the liver allograft occurs universally in those with viremia at the time of transplantation. Histologic features of hepatitis develop in about 75% of recipients within the first 6 months following liver transplantation ([Neumann, 2004](#)). By the fifth postoperative year, up to 30% of untreated patients have progressed to cirrhosis ([Neumann, 2004](#)); ([Charlton, 1998](#)). A small proportion of patients (4% to 7%) develop an accelerated course of liver injury (cholestatic hepatitis C, associated with very high levels of viremia) with subsequent rapid allograft failure. Recurrence of HCV infection post transplantation is associated with decreased graft survival for recipients with HCV

infection compared to recipients who undergo liver transplantation for other indications ([Forman, 2002](#)).

Effective HCV therapy prior to transplantation resulting in SVR (virologic cure) prevents HCV recurrence post transplantation ([Everson, 2003](#)). In addition, complete HCV viral suppression prior to transplantation prevents recurrent HCV infection of the graft in the majority of cases ([Forns, 2004](#)); ([Everson, 2005](#)). Preliminary data from a study of patients with complications of cirrhosis secondary to HCV infection who were wait-listed for liver transplantation (included patients with MELD scores up to 14 and CTP scores up to 8) found that treatment with sofosbuvir and weight-based ribavirin for up to 48 weeks was well tolerated and associated with an overall posttransplant SVR rate of 70% ([Curry, 2015](#)). Posttransplant SVR was nearly universal among patients who had undetectable HCV RNA for 28 days or longer prior to transplantation.

Treatment of established HCV infection post transplantation also yields substantial improvements in patient and graft survival ([Berenguer, 2008](#)); ([Picciotto, 2007](#)). The availability of effective, interferon-free antiviral therapy has addressed the major hurdles to treating HCV recurrence post transplantation—poor tolerability and efficacy. A multicenter, open-label study evaluated the efficacy of sofosbuvir plus ribavirin to induce virologic suppression in 40 patients after liver transplantation with compensated recurrence of HCV infection. Daily sofosbuvir plus ribavirin for 24 weeks achieved SVR12 in 70% of these patients ([Charlton, 2015](#)). No deaths, graft losses, or episodes of rejection occurred. Six patients had serious adverse events, all of which were considered unrelated to the study treatment. There were no drug interactions reported between sofosbuvir and any of the concomitant immunosuppressive agents. In contrast, treatment with sofosbuvir plus ribavirin, with or without peginterferon, in 64 patients with severe, decompensated cirrhosis resulting from recurrence of HCV infection following liver transplantation was associated with an overall SVR12 rate of 59% and a mortality rate of 13% ([Forns, 2015](#)). On an intent-to-treat basis, treatment was associated with clinical improvement in 57% and stable disease in 22% of patients. Given the clinical complexity (including drug interactions and the need for close monitoring), patients with liver transplant should be treated by physicians with experience in treating this population (see [Patients Who Develop Recurrent HCV Infection Post-Liver Transplantation](#)).

### ***Persons at Increased Risk for Rapidly Progressive Fibrosis and Cirrhosis***

Fibrosis progression is variable across different patient populations as well as within the same individual over time. Many of the components that determine fibrosis progression and development of cirrhosis in an individual are unknown. However, certain factors, such as coinfection with HIV or the hepatitis B virus (HBV) and prevalent coexistent liver diseases (eg, nonalcoholic steatohepatitis [NASH]), are well-recognized contributors to accelerated fibrosis progression (see [Table](#) below).

#### HIV/HCV Coinfection

HIV coinfection accelerates fibrosis progression among HCV-infected persons ([Benhamou, 1999](#)); ([Macias, 2009](#)); ([Konerman, 2014](#)), although control of HIV replication and restoration of CD4 cell count may mitigate this to some extent ([Benhamou, 2001](#)); ([Bräu, 2006](#)). However, antiretroviral therapy is not a substitute for HCV treatment. In the largest paired-biopsy study, 282 HIV/HCV-coinfecting patients with 435 paired biopsies were prospectively evaluated ([Konerman, 2014](#)). Thirty-four percent of patients showed fibrosis progression of at least 1 Metavir stage at a median of 2.5 years. Importantly, 45% of patients with no fibrosis on initial biopsy had progression. Finally, a more rapid progression to death following decompensation combined with lack of widespread access to liver transplantation and poor outcomes following transplantation highlight the need for HCV treatment in this population regardless of current fibrosis stage (see [Patients with HIV/HCV Coinfection](#)) ([Pineda, 2005](#)); ([Merchante, 2006](#)); ([Terrault, 2012](#)).

#### HBV/HCV Coinfection

The prevalence of HBV/HCV coinfection is estimated at 1.4% in the United States and 5% to 10% globally ([Tyson, 2013](#)); ([Chu, 2008](#)). Persons with HBV/HCV coinfection and detectable viremia of both viruses are at increased risk for disease progression, decompensated liver disease, and the development of HCC. HBV/HCV-coinfecting individuals are susceptible to a process called viral interference wherein one virus may interfere with the replication of the other virus. Thus, when treating one or both viruses with antiviral drugs, periodic retesting of HBV DNA and HCV RNA levels during and after therapy is prudent, particularly if only one of the viruses is being treated at a time. Treatment of HCV infection in

such cases utilizes the same genotype-specific regimens as are recommended for HCV mono-infection (see [Initial Treatment of HCV Infection](#)). HBV infections in such cases should be treated as recommended for HBV mono-infection ([Lok, 2009](#)).

### Other Coexistent Liver Diseases

Persons with other chronic liver diseases who have coincident chronic HCV infection should be considered for HCV therapy given the potential for rapid liver disease progression. An interferon-free regimen is generally preferred for immune-mediated liver diseases, such as autoimmune hepatitis, because of the potential for interferon-related exacerbation.

## ***Persons With Extrahepatic Manifestations of Chronic HCV Infection***

### Cryoglobulinemia

Chronic hepatitis C is associated with a syndrome of cryoglobulinemia, an immune complex and lymphoproliferative disorder that leads to arthralgias, fatigue, palpable purpura, renal disease (eg, membranoproliferative glomerulonephritis), neurologic disease (eg, peripheral neuropathy, central nervous system vasculitis), and reduced complement levels ([Agnello, 1992](#)). Because patients with chronic hepatitis C frequently have laboratory evidence of cryoglobulins (>50% in some series), antiviral treatment is imperative for those with the syndrome of cryoglobulinemia and symptoms or objective evidence of end-organ manifestations. Interferon-based regimens can produce clinical remission; however, the adverse effects of interferon may mimic manifestations of cryoglobulinemia ([Saadoun, 2014](#)).

Glomerular disease results from deposition of HCV-related immune complexes in the glomeruli ([Johnson, 1993](#)). Successful treatment of HCV using interferon-based regimens can reverse proteinuria and nephrotic syndrome but usually does not fully ameliorate azotemia ([Johnson, 1994](#)). There is building new evidence of effective resolution of cryoglobulinemia upon clearance of HCV in most patients, making a strong case for HCV treatment in this clinical setting.

### Diabetes

The relationship between chronic hepatitis C and diabetes (most notably type 2 diabetes and insulin resistance) is complex and incompletely understood. The prevalence and incidence of diabetes is increased in the context of hepatitis C ([White, 2008](#)). In the United States, type 2 diabetes occurs more frequently in HCV-infected patients, with a >3-fold greater risk in persons older than 40 years ([Mehta, 2000](#)). The positive correlation between quantity of plasma HCV RNA and established markers of insulin resistance confirms this relationship ([Yoneda, 2007](#)). Insulin resistance and type 2 diabetes are independent predictors of accelerated liver fibrosis progression ([Petta, 2008](#)). Patients with type 2 diabetes and insulin resistance are also at increased risk for HCC ([Hung, 2010](#)).

Successful antiviral treatment has been associated with improved markers of insulin resistance and a greatly reduced incidence of new-onset type 2 diabetes and insulin resistance in HCV-infected patients ([Arase, 2009](#)). Most recently, antiviral therapy for HCV infection has been shown to improve clinical outcomes related to diabetes. In a large prospective cohort from Taiwan, the incidence rates of end-stage renal disease, ischemic stroke, and acute coronary syndrome were greatly reduced in HCV-infected patients with diabetes who received antiviral therapy compared with untreated, matched controls ([Hsu, 2014](#)). Therefore, antiviral therapy may prevent progression to diabetes in HCV-infected patients with prediabetes, and may reduce renal and cardiovascular complications in HCV-infected patients with established diabetes.

### Fatigue

Fatigue is the most frequently reported symptom in patients with chronic hepatitis C, and has a major effect on quality of life and activity level as evidenced by numerous measures of impaired quality of life ([Foster, 1998](#)). The presence and severity of fatigue appears to correlate poorly with disease activity, although it may be more common and severe in HCV-infected individuals with cirrhosis ([Poynard, 2002a](#)). Despite difficulties in separating fatigue symptoms associated with hepatitis C from those associated with other concurrent conditions (eg, anemia, depression), numerous studies have reported a reduction in fatigue after cure of HCV infection ([Bonkovsky, 2007](#)). In the Virahep-C study, 401 patients with HCV infection were evaluated for fatigue prior to and after treatment, using validated scales to assess the presence and

severity of fatigue ([Sarkar, 2012](#)). At baseline, 52% of patients reported having fatigue, which was more frequent and severe in patients with cirrhosis than in those without cirrhosis. Achieving SVR was associated with a substantial decrease in the frequency and severity of fatigue.

A recent analysis of 413 patients from the NEUTRINO and FUSION trials who were treated with a sofosbuvir-containing regimen and achieved SVR12 demonstrated improvement in patient fatigue (present in 12%) from the pretreatment level ([Younossi, 2014](#)). After achieving SVR12, participants had marked improvements in fatigue over their pretreatment scores, measured by 3 separate validated questionnaires. Additional studies support and extend these findings beyond fatigue, with improvements in overall health-related quality of life and work productivity observed following successful HCV therapy ([Gerber, 2016](#)); ([Younossi, 2015b](#)); ([Younossi, 2015c](#)); ([Younossi, 2015d](#)); ([Younossi, 2015e](#)); ([Younossi, 2016a](#)).

### Dermatologic Manifestations

The reported prevalence of HCV infection in patients with porphyria cutanea tarda approximates 50% and occurs disproportionately in those with cirrhosis ([Gisbert, 2003](#)). The treatment of choice for active porphyria cutanea tarda is iron reduction by phlebotomy and maintenance of a mildly iron-reduced state without anemia. However, although improvement of porphyria cutanea tarda during HCV treatment with interferon has frequently been described ([Takikawa, 1995](#)), there are currently insufficient data to determine whether treating HCV infection with DAAs and achievement of SVR results in porphyria cutanea tarda improvement.

Lichen planus is characterized by pruritic papules involving mucous membranes, hair, and nails. HCV antibodies are present in 10% to 40% of patients with lichen planus but a causal link with chronic HCV infection is not established. Resolution of lichen planus has been reported with interferon-based regimens, but there have also been reports of exacerbation with these treatments. Although it is unknown whether DAAs will have more success against lichen planus, treatment with interferon-free regimens would appear to be a more advisable approach to addressing this disorder ([Gumber, 1995](#)); ([Sayiner, 2017](#)).

## **Benefit of Treatment to Reduce Transmission**

Persons who have successfully achieved SVR (virologic cure) no longer transmit the virus to others. As such, successful treatment of HCV infection benefits public health. Several health models have shown that even modest increases in successful treatment of HCV infection among persons who inject drugs can decrease prevalence and incidence ([Martin, 2013a](#)); ([Durier, 2012](#)); ([Martin, 2013b](#)); ([Hellard, 2012](#)); ([Harris, 2016](#)). Models developed to estimate the impact of HCV testing and treatment on the burden of hepatitis C at a country level reveal that large decreases in HCV prevalence and incidence are possible as more persons are successfully treated ([Wedemeyer, 2014](#)).

There are also benefits to eradicating HCV infection between couples and among families, thus eliminating the perception that an individual might be contagious. In addition, mother-to-child transmission of HCV does not occur if the woman is not viremic, providing an additional benefit of curing a woman before she becomes pregnant ([Thomas, 1998](#)). However, the safety and efficacy of treating women who are already pregnant to prevent transmission to the fetus have not yet been established; thus, treatment is not recommended for pregnant women.

The Society for Healthcare Epidemiology of America (SHEA) advises that healthcare workers who have substantial HCV viral replication ( $\geq 10^4$  genome equivalents/mL) be restricted from performing procedures that are prone to exposure ([Henderson, 2010](#)) and that all healthcare workers with confirmed chronic HCV infection should be treated. For reasons already stated, the achievement of SVR in such individuals will not only eliminate the risk of HCV transmission to patients but also decrease circumstantial loss of experienced clinicians. Given concerns about underreporting of infection and transmission ([Henderson, 2010](#)), the availability of effective, all-oral regimens should lead to greater willingness on the part of exposure-prone clinicians to be tested and treated.

Successful treatment of HCV-infected persons at greatest risk for transmission represents a formidable tool to help stop HCV transmission in those who continue to engage in high-risk behaviors. To guide implementation of hepatitis C treatment as a prevention strategy, studies are needed to define the best candidates for treatment to stop transmission, the additional interventions needed to maximize the benefits of HCV treatment (eg, preventing reinfection), and the cost-

effectiveness of the strategies when used in target populations.

### ***Persons Who Inject Drugs***

Injection drug use (IDU) is the most common risk factor for HCV infection in the United States and Europe, with an HCV seroprevalence rate of 10% to 70% ([Amon, 2008](#)); ([Nelson, 2011](#)). IDU also accounts for the majority of new HCV infections (approximately 70%) and is the key driving force in the perpetuation of the epidemic. Given these facts and the absence of an effective vaccine against HCV, testing and linkage to care combined with treatment of HCV infection with potent interferon-free regimens has the potential to dramatically decrease HCV incidence and prevalence ([Martin, 2013b](#)). However, treatment-based strategies to prevent HCV transmission have yet to be studied, including how to integrate hepatitis C treatment with other risk-reduction strategies (eg, opiate substitution therapy, and needle and syringe exchange programs) ([Martin, 2013a](#)).

In studies of interferon-based treatments in persons who inject drugs, adherence and efficacy rates are comparable to those of patients who do not use injected drugs. A meta-analysis of treatment with peginterferon, with or without ribavirin, in active or recent injection drug users showed SVR rates of 37% and 67% for genotype 1 or 4 and 2 or 3, respectively ([Aspinall, 2013](#)). With the introduction of shorter, better-tolerated, and more efficacious interferon-free therapies, these SVR rates are expected to improve. Importantly, the rate of reinfection in this population is lower (2.4/100 person-years of observation) than that of incident infection in the general population of injection drug users (6.1 to 27.2/100 person-years), although reinfection increases with active or ongoing IDU (6.44/100 person-years) and available data on follow-up duration are limited ([Aspinall, 2013](#)); ([Grady, 2013](#)).

Ideally, treatment of HCV-infected persons who inject drugs should be delivered in a multidisciplinary care setting with services to reduce the risk of reinfection and for management of the common social and psychiatric comorbidities in this population ([Murphy 2015](#)); ([Dore, 2016](#)); ([Mathei 2016](#)); ([Midgard 2016](#)). Regardless of the treatment setting, recent or active IDU should not be seen as an absolute contraindication to HCV therapy. There is strong evidence from various settings in which persons who inject drugs have demonstrated adherence to treatment and low rates of reinfection, countering arguments that have been commonly used to limit treatment access in this patient population ([Aspinall, 2013](#)); ([Hellard, 2014](#)); ([Grebely, 2011](#)). Indeed, combining HCV treatment with needle exchange and opioid agonist therapy programs in this population with a high prevalence of HCV infection has shown great value in decreasing the burden of HCV disease. Elegant modeling studies illustrate high return on the modest investment of addressing this often-ignored segment of the HCV-infected population ([Martin, 2013b](#)). These conclusions were drawn before the introduction of the latest DAA regimens. Conversely, there are no data to support the utility of pretreatment screening for illicit drug or alcohol use in identifying a population more likely to successfully complete HCV therapy. These requirements should be abandoned because they create barriers to treatment, add unnecessary cost and effort, and potentially exclude populations that are likely to obtain substantial benefit from therapy. Scaling up HCV treatment in persons who inject drugs is necessary to positively impact the HCV epidemic in the US and globally.

### ***HIV-Infected Men Who Have Sex With Men***

Since 2000, a dramatic increase in incident HCV infections among HIV-infected men who have sex with men (MSM) who did not report IDU as a risk factor has been demonstrated in several US cities ([van de Laar, 2010](#)); ([Samandari, 2017](#)). Recognition and treatment of HCV infection (including acute infection) in this population may represent an important step in preventing subsequent infections ([Martin, 2016](#)). As with persons who inject drugs, HIV/HCV-coinfected MSM who engage in ongoing high-risk sexual practices should be treated for their HCV infection in conjunction with continued education about risk-reduction strategies. In particular, safer-sex strategies should be emphasized given the high rate of reinfection after SVR, which may approach 30% over 2 years in HIV-infected MSM with acute HCV infection ([Lambers, 2011](#)).

### ***Incarcerated Persons***

Among incarcerated individuals, the rate of HCV seroprevalence ranges from 30% to 60% ([Post, 2013](#)) and the rate of acute infection is approximately 1% ([Larney, 2013](#)). Screening for HCV infection is relatively uncommon in state prison

systems. Treatment uptake has historically been limited, in part because of the toxic effects and long treatment duration of older interferon-based therapies as well as concerns about cost ([Spaulding, 2006](#)). In particular, truncation of HCV treatment owing to release from prison has been cited as a major limitation to widespread, effective HCV treatment in correctional facilities ([Post, 2013](#)); ([Chew, 2009](#)). Shorter HCV treatment duration with DAAs reduces stay-related barriers to HCV treatment in prisons. Likewise, the improved safety of DAA regimens diminishes concerns about toxic effects. Coordinated treatment efforts within prison systems would likely rapidly decrease the prevalence of HCV infection in this at-risk population ([He, 2016](#)), although research is needed in this area.

### Persons on Hemodialysis


The prevalence rate of HCV infection is markedly elevated in persons on hemodialysis, ranging from 2.6% to 22.9% in a large multinational study ([Fissell, 2004](#)). Studies in the US found a similarly elevated prevalence rate of 7.8% to 8.9% ([CDC, 2001](#)); ([Finelli, 2005](#)). Importantly, the seroprevalence of HCV was found to increase with time on dialysis, suggesting that nosocomial transmission, among other risk factors, plays a role in HCV acquisition in these patients ([Fissell, 2004](#)). Improved education and strict adherence to universal precautions can drastically reduce nosocomial HCV transmission risk for persons on hemodialysis ([Jadoul, 1998](#)), but clearance of HCV viremia through treatment-induced SVR eliminates the potential for transmission.

HCV-infected persons on hemodialysis have a decreased quality of life and increased mortality compared with those who are uninfected ([Fabrizi, 2002](#)); ([Fabrizi, 2007](#)); ([Fabrizi, 2009](#)). HCV infection in this population also has a deleterious impact on kidney transplantation outcomes with decreased patient and graft survival ([Fabrizi, 2014](#)). The increased risk for nosocomial transmission and the substantial clinical impact of HCV infection in those on hemodialysis are compelling arguments for HCV therapy as effective antiviral regimens that can be used in persons with advanced renal failure are now available (see [Patients with Renal Impairment](#)).

### Patients Unlikely to Benefit From HCV Treatment

Patients with a limited life expectancy that cannot be remediated by HCV treatment, liver transplantation, or another directed therapy do not require antiviral treatment. Patients with a short life expectancy owing to liver disease should be managed in consultation with an expert. Chronic hepatitis C is associated with a wide range of comorbid conditions ([Butt, 2011](#)); ([Louie, 2012](#)). Little evidence exists to support initiation of HCV treatment in patients with a limited life expectancy (<12 months) owing to nonliver-related comorbid conditions. For these patients, the benefits of HCV treatment are unlikely to be realized and palliative care strategies should take precedence ([Holmes, 2006](#)); ([Maddison, 2011](#)).

### Pretreatment Assessment

Recommendation for Pretreatment Assessment	
RECOMMENDED	RATING 
Evaluation for advanced fibrosis using liver biopsy, imaging, and/or noninvasive markers is recommended for all persons with HCV infection, to facilitate decision making regarding HCV treatment strategy and to determine the need for initiating additional measures for the management of cirrhosis (eg, hepatocellular carcinoma screening) (see <a href="#">HCV Testing and Linkage to Care</a> ).	I, A

An accurate assessment of fibrosis remains vital as the degree of hepatic fibrosis is one of the most robust prognostic factors used to predict HCV disease progression and clinical outcomes ([Everhart, 2010](#)). Individuals with severe fibrosis require surveillance monitoring for liver cancer, esophageal varices, and hepatic function ([Garcia-Tsao, 2007](#)); ([Bruix, 2011](#)). In some instances, the recommended duration of treatment is also longer.




Although liver biopsy is the diagnostic standard, sampling error and observer variability limit test performance, particularly when inadequate sampling occurs. Up to one-third of bilobar biopsies had a difference of at least 1 stage between the lobes ([Bedossa, 2003](#)). In addition, the test is invasive and minor complications are common, limiting patient and practitioner acceptance. Although rare, serious complications such as bleeding are well recognized.

Noninvasive tests to stage the degree of fibrosis in patients with chronic HCV infection include models incorporating indirect serum biomarkers (routine tests), direct serum biomarkers (components of the extracellular matrix produced by activated hepatic stellate cells), and vibration-controlled transient liver elastography. No single method is recognized to have high accuracy alone, and each test must be interpreted carefully. A publication from the Agency for Healthcare Research and Quality found evidence in support of a number of blood tests; however, at best, they are only moderately useful for identifying clinically significant fibrosis or cirrhosis ([Selph, 2014](#)).

Vibration-controlled transient liver elastography is a noninvasive way to measure liver stiffness and correlates well with measurement of substantial fibrosis or cirrhosis in patients with chronic HCV infection. The measurement range, however, overlaps between stages ([Ziol, 2005](#)); ([Afdhal, 2015](#)); ([Castera, 2005](#)).

The most efficient approach to fibrosis assessment is to combine direct biomarkers and vibration-controlled transient liver elastography ([Boursier, 2012](#)); ([European Association for the Study of the Liver and Asociacion Latinoamericana para el Estudio del Hgado, 2015](#)). A biopsy should be considered for any patient who has discordant results between the 2 modalities that would affect clinical decision making (eg, one shows cirrhosis and the other does not). The need for liver biopsy with this approach is markedly reduced.

Alternatively, if direct biomarkers or vibration-controlled transient liver elastography are not available, the AST-to-platelet ratio index (APRI) or fibrosis-4 (FIB-4) index score can prove helpful—although neither is sensitive enough to rule out substantial fibrosis ([Sebastiani, 2009](#)); ([Castera, 2010](#)); ([Chou, 2013](#)). Biopsy should be considered for those in whom more accurate fibrosis staging would impact treatment decisions. Individuals with clinically evident cirrhosis do not require additional staging (biopsy or noninvasive assessment).

Recommendation for Repeat Liver Disease Assessment	
RECOMMENDED	RATING 
Ongoing assessment of liver disease is recommended for persons in whom therapy is deferred.	I, C

Ongoing assessment of liver disease is especially important in patients for whom therapy has been deferred. In line with evidence-driven recommendations for treatment of nearly all HCV-infected patients, several factors must be taken into consideration if treatment deferral is entertained or mandated by lack of medication access. As noted, strong and accumulating evidence argue against deferral because of decreased all-cause morbidity and mortality, prevention of onward transmission, and quality-of-life improvements for patients treated regardless of baseline fibrosis. Additionally, treatment of HCV infection may improve or prevent extrahepatic complications, including diabetes mellitus, cardiovascular disease, renal disease, and B-cell non-Hodgkin lymphoma ([Conjeevaram, 2011](#)); ([Hsu, 2015](#)); ([Torres, 2015](#)), which are not tied to fibrosis stage ([Allison, 2015](#)); ([Petta, 2016](#)). Deferral practices based on fibrosis stage alone are inadequate and shortsighted.

Fibrosis progression varies markedly between individuals based on host, environmental, and viral factors ([Table 1](#)); ([Feld, 2006](#)). Fibrosis may not progress linearly. Some individuals (often those aged >50 years) may progress slowly for many years followed by an acceleration of fibrosis progression. Others may never develop substantial liver fibrosis despite longstanding infection. The presence of existing fibrosis is a strong risk factor for future fibrosis progression. Fibrosis

results from chronic hepatic necroinflammation; thus, a higher activity grade on liver biopsy and higher serum transaminase values are associated with more rapid fibrosis progression ([Ghany, 2003](#)). However, even patients with normal ALT levels may develop substantial liver fibrosis over time ([Pradat, 2002](#)); ([Nutt, 2000](#)). The limitations of transient elastography and liver biopsy in ascertaining the progression of fibrosis must be recognized.

Host factors associated with more rapid fibrosis progression include male sex, longer duration of infection, and older age at the time of infection ([Poynard, 2001](#)). Many patients have concomitant nonalcoholic fatty liver disease. The presence of hepatic steatosis (with or without steatohepatitis) on liver biopsy, elevated body mass index, insulin resistance, and iron overload are associated with fibrosis progression ([Konerman, 2014](#)); ([Everhart, 2009](#)). Chronic alcohol use is an important risk factor because alcohol consumption has been associated with more rapid fibrosis progression ([Feld, 2006](#)). A safe amount of alcohol consumption has not been established. Cigarette smoking may also lead to more rapid fibrosis progression. For more counseling recommendations, see [Testing and Linkage to Care](#).

Immunosuppression leads to more rapid fibrosis progression, particularly in the settings of HIV/HCV coinfection and solid organ transplantation ([Macias, 2009](#)); ([Konerman, 2014](#)); ([Berenguer, 2013](#)). Therefore, immunocompromised patients should be treated even if they have mild liver fibrosis at presentation.

Level of HCV RNA does not correlate with stage of disease (degree of inflammation or fibrosis). Available data suggest that fibrosis progression occurs most rapidly in patients with genotype 3 infection ([Kanwal, 2014](#)); ([Bochud, 2009](#)). Aside from coinfection with HBV or HIV, no other viral factors are consistently associated with disease progression.

Although an ideal interval for assessment has not been established, annual evaluation is appropriate to discuss modifiable risk factors and update testing for hepatic function and markers for disease progression. For all individuals with advanced fibrosis, liver cancer screening dictates a minimum of evaluation every 6 months.

**Table. Factors Associated With Accelerated Fibrosis Progression**

Host	Viral
<p><b>Nonmodifiable</b></p> <ul style="list-style-type: none"> <li>• Fibrosis stage</li> <li>• Inflammation grade</li> <li>• Older age at time of infection</li> <li>• Male sex</li> <li>• Organ transplant</li> </ul> <p><b>Modifiable</b></p> <ul style="list-style-type: none"> <li>• Alcohol consumption</li> <li>• Nonalcoholic fatty liver disease</li> <li>• Obesity</li> <li>• Insulin resistance</li> </ul>	<ul style="list-style-type: none"> <li>• Genotype 3 infection</li> <li>• Coinfection with hepatitis B virus or HIV</li> </ul>

**Last update:** September 21, 2017

## Related References

- Afdhal NH, Bacon BR, Patel K, Lawitz EJ, Gordon SC, Nelson DR, et al. [Accuracy of fibroscan, compared with histology, in analysis of liver fibrosis in patients with hepatitis B or C: a United States multicenter study](#). Clin. Gastroenterol. Hepatol. 2015;13(4):772-779.
- Agnello V, Chung RT, Kaplan LM. [A role for hepatitis C virus infection in type II cryoglobulinemia](#). N Engl J Med. 1992;327(21):1490-1495.
- Allison RD, Tong X, Moorman AC, Ly KN, Rupp L, Xu F, et al. [Increased incidence of cancer and cancer-related mortality among persons with chronic hepatitis C infection, 2006-2010](#). J Hepatol. 2015;63(4):822-828.
- Amon JJ, Garfein RS, Ahdieh-Grant L, Armstrong GL, Ouellet LJ, Latka MH, et al. [Prevalence of hepatitis C virus infection among injection drug users in the United States, 1994-2004](#). Clin Infect Dis. 2008;46(12):1852-1858.
- Arase Y, Suzuki F, Suzuki Y, Akuta N, Kobayashi M, Kawamura Y, et al. [Sustained virological response reduces incidence of onset of type 2 diabetes in chronic hepatitis C](#). Hepatology. 2009;49(3):739-744.
- Aspinall EJ, Corson S, Doyle JS, Grebely J, Hutchinson SJ, Dore GJ, et al. [Treatment of hepatitis C virus infection among people who are actively injecting drugs: a systematic review and meta-analysis](#). Clin Infect Dis. 2013;57(Suppl 2):S80-S89.
- Backus LI, Boothroyd DB, Phillips BR, Belperio P, Halloran J, Mole LA. [A sustained virologic response reduces risk of all-cause mortality in patients with hepatitis C](#). Clin Gastroenterol Hepatol. 2011;9(6):509-516.
- Bedossa P, Dargère D, Paradis V. [Sampling variability of liver fibrosis in chronic hepatitis C](#). Hepatology. 2003;38(6):1449-1457.
- Benhamou Y, Bochet M, Di Martino V, Charlotte F, Azria F, Coutellier A, et al. [Liver fibrosis progression in human immunodeficiency virus and hepatitis C virus coinfecting patients. The Multivirc Group](#). Hepatology. 1999;30(4):1054-1058.
- Benhamou Y, Di Martino V, Bochet M, Colombet G, Thibault V, Liou A, et al. [Factors affecting liver fibrosis in human immunodeficiency virus- and hepatitis C virus-coinfecting patients: impact of protease inhibitor therapy](#). Hepatology. 2001;34(2):283-287.
- Berenguer M, Palau A, Aguilera V, Rayon JM, Juan FS, Prieto M. [Clinical benefits of antiviral therapy in patients with recurrent hepatitis C following liver transplantation](#). Am J Transplant. 2008;8(3):679-687.
- Berenguer J, Álvarez-Pellicer J, Martín PM, López-Aldeguer J, Von-Wichmann MA, Quereda C, et al. [Sustained virological response to interferon plus ribavirin reduces liver-related complications and mortality in patients coinfecting with human immunodeficiency virus and hepatitis C virus](#). Hepatology. 2009;50(2):407-413.
- Berenguer M, Schuppan D. [Progression of liver fibrosis in post-transplant hepatitis C: mechanisms, assessment and treatment](#). J Hepatol. 2013;58(5):1028-1041.
- Bochud PY, Cai T, Overbeck K, Bochud M, Dufour JF, Mullhaupt B, et al. [Genotype 3 is associated with accelerated fibrosis progression in chronic hepatitis C](#). J Hepatol. 2009;51(4):655-666.
- Bonkovsky HL, Snow KK, Malet PF, Back-Madruga C, Fontana RJ, Sterling RK, et al. [Health-related quality of life in patients with chronic hepatitis C and advanced fibrosis](#). J Hepatol. 2007;46(3):420-431.
- Boscarino JA, Lu M, Moorman AC, Gordon SC, Rupp LB, Spradling PR, et al. [Predictors of poor mental and physical health status among patients with chronic hepatitis C infection: the Chronic Hepatitis Cohort Study \(CHeCS\)](#). Hepatology

(Baltimore, Md.). 2015;61(3):802 - 811.

Boursier J, de Ledinghen V, Zarski JP, Fouchard-Hubert I, Gallois Y, Oberti F, et al. [Comparison of eight diagnostic algorithms for liver fibrosis in hepatitis C: new algorithms are more precise and entirely noninvasive](#). Hepatology. 2012;55(1):58-67.

Brau N, Salvatore M, Ríos-Bedoya CF, Fernandez-Carbia A, Paronetto F, Rodriguez-Orengo JF, et al.. [Slower fibrosis progression in HIV/HCV-coinfected patients with successful HIV suppression using antiretroviral therapy](#). J Hepatol. 2006;44:47-55.

Bruix J, Sherman M. [Management of hepatocellular carcinoma: an update](#). Hepatology. 2011;53(3):1020-1022.

Butt AA, McGinnis K, Skanderson M, Justice AC. [A comparison of treatment eligibility for hepatitis C virus in HCV-monoinfected versus HCV/HIV-coinfected persons in electronically retrieved cohort of HCV-infected veterans](#). AIDS Res Hum Retroviruses. 2011;27(9):973-979.

Castera L, Vergniol J, Foucher J, Le BB, Chanteloup E, Haaser M, et al. [Prospective comparison of transient elastography, Fibrotest, APRI, and liver biopsy for the assessment of fibrosis in chronic hepatitis C](#). Gastroenterology. 2005;128(2):343-350.

Castera L, Sebastiani G, Le BB, de Ledinghen V, Couzigou P, Alberti A. [Prospective comparison of two algorithms combining non-invasive methods for staging liver fibrosis in chronic hepatitis C](#). J Hepatol. 2010;52(2):191-198.

[CDC: Recommendations for preventing transmission of infections among chronic hemodialysis patients](#). MMWR Recomm Rep. 2001;50(RR-5):1-43.

Charlton MR, Seaberg E, Wiesner R, Everhart J, Zetterman R, Lake J, et al. [Predictors of patient and graft survival following liver transplantation for hepatitis C](#). Hepatology. 1998;28(3):823-830.

Charlton MR, Gane EJ, Manns MP, Brown, Jr. RS, Curry MP, Kwo PY, et al. [Sofosbuvir and ribavirin for treatment of compensated recurrent hepatitis C virus infection after liver transplantation](#). Gastroenterology. 2015;148(1):108-117.

Chew KW, Allen SA, Taylor LE, Rich JD, Feller E. [Treatment outcomes with pegylated interferon and ribavirin for male prisoners with chronic hepatitis C](#). J Clin Gastroenterol. 2009;43(7):686-691.

Chou R, Wasson N. [Blood tests to diagnose fibrosis or cirrhosis in patients with chronic hepatitis C virus infection: a systematic review](#). Ann Intern Med. 2013;158(11):807-820.

Chu CJ, Lee SD. [Hepatitis B virus/hepatitis C virus coinfection: epidemiology, clinical features, viral interactions and treatment](#). J Gastroenterol Hepatol. 2008;23(4):512-520.

Conjeevaram HS, Wahed AS, Afdhal NH, Howell CD, Everhart JE, Hoofnagle JH. [Changes in insulin sensitivity and body weight during and after peginterferon and ribavirin therapy for hepatitis C](#). Gastroenterology. 2011;140(2):469-477.

Coppola N, De PS, Pisaturo M, Paradiso L, Macera M, Capoluongo N, et al. [Sustained virological response to antiviral treatment in chronic hepatitis C patients may be predictable by HCV-RNA clearance in peripheral blood mononuclear cells](#). J Clin Virol. 2013;58(4):748-750.

Curry MP, Fornis X, Chung RT, Terrault NA, Brown, Jr. RS, Fenkel JM, et al. [Sofosbuvir and ribavirin prevent recurrence of HCV infection after liver transplantation: an open-label study](#). Gastroenterology. 2015;148(1):100-107.

Di Bisceglie AM, Shiffman ML, Everson GT, Lindsay KL, Everhart JE, Wright EC, et al. [Prolonged therapy of advanced chronic hepatitis C with low-dose peginterferon](#). N Engl J Med. 2008;359(23):2429-2441.

Dienstag JL, Ghany MG, Morgan TR, Di Bisceglie AM, Bonkovsky HL, Kim HY, et al. [A prospective study of the rate of](#)

[progression in compensated, histologically advanced chronic hepatitis C](#). Hepatology. 2011;54(2):396-405.

Dore GJ, Altice F, Litwin AH, Dalgard O, Gane EJ, Shibolet O, et al. [Elbasvir-Grazoprevir to Treat Hepatitis C Virus Infection in Persons Receiving Opioid Agonist Therapy: A Randomized Trial](#). Annals of Internal Medicine. 2016;165(9):625 - 634.

Durier N, Nguyen C, White LJ. [Treatment of hepatitis C as prevention: a modeling case study in Vietnam](#). PLoS One. 2012;7(4):e34548.

[EASL-ALEH Clinical Practice Guidelines: Non-invasive tests for evaluation of liver disease severity and prognosis](#). J Hepatol. 2015;63(1):237-264.

Everhart JE, Lok AS, Kim HY, Morgan TR, Lindsay KL, Chung RT, et al. [Weight-related effects on disease progression in the hepatitis C antiviral long-term treatment against cirrhosis trial](#). Gastroenterology. 2009;137(2):549-557.

Everhart JE, Wright EC, Goodman ZD, Dienstag JL, Hoefs JC, Kleiner DE, et al. [Prognostic value of Ishak fibrosis stage: findings from the hepatitis C antiviral long-term treatment against cirrhosis trial](#). Hepatology. 2010;51(2):585-594.

Everson GT. [Treatment of patients with hepatitis C virus on the waiting list](#). Liver Transpl. 2003;9(11):S90-S94.

Everson GT, Trotter J, Forman L, Kugelmas M, Halprin A, Fey B, et al. [Treatment of advanced hepatitis C with a low accelerating dosage regimen of antiviral therapy](#). Hepatology. 2005;42(2):255-262.

Everson GT, Hoefs JC, Seeff LB, Bonkovsky HL, Naishadham D, Shiffman ML, et al. [Impact of disease severity on outcome of antiviral therapy for chronic hepatitis C: Lessons from the HALT-C trial](#). Hepatology. 2006;44(6):1675-1684.

Fabrizi F, Poordad F, Martin P. [Hepatitis C infection and the patient with end-stage renal disease](#). Hepatology. 2002;36(1):3-10.

Fabrizi F, Takkouche B, Lunghi G, Dixit V, Messa P, Martin P. [The impact of hepatitis C virus infection on survival in dialysis patients: meta-analysis of observational studies](#). J Viral Hepat. 2007;14(10):697-703.

Fabrizi F, Messa P, Martin P. [Health-related quality of life in dialysis patients with HCV infection](#). Int J Artif Organs. 2009;32(8):473-481.

Fabrizi F, Dixit V, Messa P. [Antiviral therapy of symptomatic HCV-associated mixed cryoglobulinemia: meta-analysis of clinical studies](#). J Med Virol. 2013;85(6):1019-1027.

Fabrizi F, Martin P, Dixit V, Messa P. [Meta-analysis of observational studies: hepatitis C and survival after renal transplant](#). J Viral Hepat. 2014;21(5):314-324.

Feld JJ, Liang TJ. [Hepatitis C -- identifying patients with progressive liver injury](#). Hepatology. 2006;43(2 Suppl 1):S194-S206.

Finelli L, Miller JT, Tokars JI, Alter MJ, Arduino MJ. [National surveillance of dialysis-associated diseases in the United States, 2002](#). Semin Dial. 2005;18(1):52-61.

Fissell RB, Bragg-Gresham JL, Woods JD, Jadoul M, Gillespie B, Hedderwick SA, et al. [Patterns of hepatitis C prevalence and seroconversion in hemodialysis units from three continents: the DOPPS](#). Kidney Int. 2004;65(6):2335-2342.

Forman LM, Lewis JD, Berlin JA, Feldman HI, Lucey MR. [The association between hepatitis C infection and survival after orthotopic liver transplantation](#). Gastroenterology. 2002;122:889-896.

Forns X, Navasa M, Rodes J. [Treatment of HCV infection in patients with advanced cirrhosis](#). Hepatology.

2004;40(2):498.

Forns X, Charlton MR, Denning J, McHutchison JG, Symonds WT, Brainard D, et al. [Sofosbuvir compassionate use program for patients with severe recurrent hepatitis C after liver transplantation](#). Hepatology. 2015;61(5):1485-1494.

Foster GR, Goldin RD, Thomas HC. [Chronic hepatitis C virus infection causes a significant reduction in quality of life in the absence of cirrhosis](#). Hepatology. 1998;27(1):209-212.

Garcia-Bengoechea M, Basaras M, Barrio J, Arrese E, Montalvo II, Arenas JI, et al. [Late disappearance of hepatitis C virus RNA from peripheral blood mononuclear cells in patients with chronic hepatitis C in sustained response after alpha-interferon therapy](#). Am J Gastroenterol. 1999;94(7):1902-1905.

Garcia-Tsao G, Sanyal AJ, Grace ND, Carey W. [Prevention and management of gastroesophageal varices and variceal hemorrhage in cirrhosis](#). Hepatology. 2007;46(3):922-938.

Gerber L, Estep M, Stepanova M, Escheik C, Weinstein A, Younossi ZM. [Effects of Viral Eradication With Ledipasvir and Sofosbuvir, With or Without Ribavirin, on Measures of Fatigue in Patients With Chronic Hepatitis C Virus Infection](#). Clinical Gastroenterology and Hepatology: The Official Clinical Practice Journal of the American Gastroenterological Association. 2016;14(1):156 - 164.e3.

Ghany MG, Kleiner DE, Alter H, Doo E, Khokar F, Promrat K, et al. [Progression of fibrosis in chronic hepatitis C](#). Gastroenterology. 2003;124(1):97-104.

Gisbert JP, Garcia-Buey L, Pajares JM, Moreno-Otero R. [Prevalence of hepatitis C virus infection in porphyria cutanea tarda: systematic review and meta-analysis](#). J Hepatol. 2003;39(4):620-627.

Gisbert JP, Garcia-Buey L, Pajares JM, Moreno-Otero R. [Systematic review: regression of lymphoproliferative disorders after treatment for hepatitis C infection](#). Aliment Pharmacol Ther. 2005;21(6):653-662.

Grady BP, Schinkel J, Thomas XV, Dalgard O. [Hepatitis C virus reinfection following treatment among people who use drugs](#). Clin Infect Dis. 2013;57(Suppl 2):S105-S110.

Grebely J, Matthews GV, Hellard M, Shaw D, Shaw D, Petoumenos K, Yeung B, et al. [Adherence to treatment for recently acquired hepatitis C virus \(HCV\) infection among injecting drug users](#). J Hepatol. 2011;55(1):76-85.

Gumber SC, Chopra S. [Hepatitis C: a multifaceted disease. Review of extrahepatic manifestations](#). Ann Intern Med. 1995;123(8):615-620.

He T, Li K, Roberts MS, Spaulding AC, Ayer T, Grefenstette JJ, et al. [Prevention of Hepatitis C by Screening and Treatment in U.S. Prisons](#). Ann Intern Med. 2016;164(2):84-92.

Hellard ME, Jenkinson R, Higgs P, Stooze MA, Sacks-Davis R, Gold J, et al. [Modelling antiviral treatment to prevent hepatitis C infection among people who inject drugs in Victoria, Australia](#). Med J Aust. 2012;196(10):638-641.

Hellard M, Doyle JS, Sacks-Davis R, Thompson AJ, McBryde E. [Eradication of hepatitis C infection: the importance of targeting people who inject drugs](#). Hepatology. 2014;59(2):366-369.

Henderson DK, Dembry L, Fishman NO, Grady C, Lundstrom T, Palmore TN, et al. [SHEA guideline for management of healthcare workers who are infected with hepatitis B virus, hepatitis C virus, and/or human immunodeficiency virus](#). Infect Control Hosp Epidemiol. 2010;31(3):203-232.

Hermine O, Lefrere F, Bronowicki JP, Mariette X, Jondeau K, Eclache-Saudreau V, et al. [Regression of splenic lymphoma with villous lymphocytes after treatment of hepatitis C virus infection](#). N Engl J Med. 2002;347(2):89-94.

Holmes HM, Hayley DC, Alexander GC, Sachs GA. [Reconsidering medication appropriateness for patients late in life](#).

Arch Intern Med. 2006;166(6):605-609.

Hsu YC, Lin JT, Ho HJ, Kao YH, Huang YT, Hsiao NW, et al. [Antiviral treatment for hepatitis C virus infection is associated with improved renal and cardiovascular outcomes in diabetic patients](#). Hepatology. 2014;59(4):1293-1302.

Hsu YC, Ho HJ, Huang YT, Wang HH, Wu MS, Lin JT, et al. [Association between antiviral treatment and extrahepatic outcomes in patients with hepatitis C virus infection](#). Gut. 2015;64(3):495-503.

Hung CH, Wang JH, Hu TH, Chen CH, Chang KC, Yen YH, et al. [Insulin resistance is associated with hepatocellular carcinoma in chronic hepatitis C infection](#). World J Gastroenterol. 2010;16(18):2265-2271.

Jadoul M, Cornu C, van Ypersele de Strihou C. [Universal precautions prevent hepatitis C virus transmission: a 54 month follow-up of the Belgian Multicenter Study. The Universitaires Cliniques St-Luc \(UCL\) Collaborative Group](#). Kidney Int. 1998;53(4):1022-1025.

Jezequel C, Bardou-Jacquet E, Desille Y, Renard I, Laine F, Lelan C, et al. [Survival of patients infected by chronic hepatitis C and F0F1 fibrosis at baseline after a 15 year follow-up](#). 50th Annual Meeting of the European Association for the Study of the Liver (EASL). 2015;:S589.

Johnson RJ, Gretch DR, Yamabe H, Hart J, Bacchi CE, Hartwell P, et al. [Membranoproliferative glomerulonephritis associated with hepatitis C virus infection](#). N Engl J Med. 1993;328(7):465-470.

Johnson RJ, Gretch DR, Couser WG, Alpers CE, Wilson J, Chung M, et al. [Hepatitis C virus-associated glomerulonephritis. Effect of alpha-interferon therapy](#). Kidney Int. 1994;46(6):1700-1704.

Kanwal F, Kramer JR, Ilyas J, Duan Z, El-Serag HB. [HCV genotype 3 is associated with an increased risk of cirrhosis and hepatocellular cancer in a national sample of U.S. Veterans with HCV](#). Hepatology. 2014;60(1):98-105.

Konerman MA, Mehta SH, Sutcliffe CG, Vu T, Higgins Y, Torbenson MS, et al. [Fibrosis progression in human immunodeficiency virus/hepatitis C virus coinfecting adults: prospective analysis of 435 liver biopsy pairs](#). Hepatology. 2014;59(3):767-775.

Lambers FA, Prins M, Thomas X, Molenkamp R, Kwa D, Brinkman K, et al. [Alarming incidence of hepatitis C virus re-infection after treatment of sexually acquired acute hepatitis C virus infection in HIV-infected MSM](#). AIDS. 2011;25(17):F21-F27.

Landau DA, Scerra S, Sene D, Resche-Rigon M, Saadoun D, Cacoub P. [Causes and predictive factors of mortality in a cohort of patients with hepatitis C virus-related cryoglobulinemic vasculitis treated with antiviral therapy](#). J Rheumatol. 2010;37(3):615-621.

Larney S, Kopinski H, Beckwith CG, Zaller ND, Jarlais DD, Hagan H, et al. [Incidence and prevalence of hepatitis C in prisons and other closed settings: Results of a systematic review and meta-analysis](#). Hepatology. 2013;58(4):1215-1224.

Lok AS, McMahon BJ. [Chronic hepatitis B: update 2009. AASLD practice guideline update](#). Hepatology. 2009;50(3):661-662.

Louie KS, St Laurent S, Forssen UM, Mundy LM, Pimenta JM. [The high comorbidity burden of the hepatitis C virus infected population in the United States](#). BMC Infect Dis. 2012;12:86.

Macias J, Berenguer J, Japon MA, Giron JA, Rivero A, Lopez-Cortes LF, et al. [Fast fibrosis progression between repeated liver biopsies in patients coinfecting with human immunodeficiency virus/hepatitis C virus](#). Hepatology. 2009;50(4):1056-1063.

Maddison AR, Fisher J, Johnston G. [Preventive medication use among persons with limited life expectancy](#). Prog Palliat Care. 2011;19(1):15-21.

- Manns MP, Pockros PJ, Norkrans G, Smith CI, Morgan TR, Haussinger D, et al. [Long-term clearance of hepatitis C virus following interferon alpha-2b or peginterferon alpha-2b, alone or in combination with ribavirin](#). J Viral Hepat. 2013;20(8):524-529.
- Marcellin P, Boyer N, Gervais A, Martinot M, Pouteau M, Castelnau C, et al. [Long-term histologic improvement and loss of detectable intrahepatic HCV RNA in patients with chronic hepatitis C and sustained response to interferon-alpha therapy](#). Ann Intern Med. 1997;127(10):875-881.
- Martin NK, Hickman M, Hutchinson SJ, Goldberg DJ, Vickerman P. [Combination interventions to prevent HCV transmission among people who inject drugs: modeling the impact of antiviral treatment, needle and syringe programs, and opiate substitution therapy](#). Clin Infect Dis. 2013;57(Suppl 2):S39-S45.
- Martin NK, Vickerman P, Grebely J, Hellard M, Hutchinson SJ, Lima VD, et al. [Hepatitis C virus treatment for prevention among people who inject drugs: Modeling treatment scale-up in the age of direct-acting antivirals](#). Hepatology. 2013;58(5):1598-1609.
- Martin NK, Thornton A, Hickman M, Sabin C, Nelson M, Cooke GS, et al. [Can Hepatitis C Virus \(HCV\) Direct-Acting Antiviral Treatment as Prevention Reverse the HCV Epidemic Among Men Who Have Sex With Men in the United Kingdom? Epidemiological and Modeling Insights](#). Clin Infect Dis. 2016 Feb 16.th ed. 2016;62(9):1072-80.
- Matheï C, Bourgeois S, Blach S, Brixko C, Mulkay JP, Razavi H, et al.. [Mitigating the burden of hepatitis C virus among people who inject drugs in Belgium](#). Acta Gastro-Enterologica Belgica. 2016;79(2):227 - 232.
- Mazzaro C, Little D, Pozzato G. [Regression of splenic lymphoma after treatment of hepatitis C virus infection](#). N Engl J Med. 2002;347(26):2168-2170.
- McCombs JS, Tonnu-MiHara I, Matsuda T, McGinnis J, Fox S. [Can hepatitis C treatment be safely delayed? Evidence from the Veterans Administration Healthcare System](#). 50th Annual Meeting of the European Association for the Study of the Liver (EASL). 2015;:S191.
- Mehta SH, Brancati FL, Sulkowski MS, Strathdee SA, Szklo M, Thomas DL. [Prevalence of type 2 diabetes mellitus among persons with hepatitis C virus infection in the United States](#). Ann Intern Med. 2000;133(8):592-599.
- Merchante N, Giron-Gonzalez JA, Gonzalez-Serrano M, Torre-Cisneros J, Garcia-Garcia JA, Arizcorreta A, et al. [Survival and prognostic factors of HIV-infected patients with HCV-related end-stage liver disease](#). AIDS. 2006;20(1):49-57.
- Midgard H, Bramness JG, Skurtveit S, Haukeland JW, Dalgard O. [Hepatitis C Treatment Uptake among Patients Who Have Received Opioid Substitution Treatment: A Population-Based Study](#). PloS One. 2016;11(11):e0166451.
- Mira JA, Rivero-Juárez A, Lopez-Cortes LF, Giron-Gonzalez JA, Tellez F, Santos-Gil ID, et al.. [Benefits from sustained virologic response to pegylated interferon plus ribavirin in HIV/hepatitis C virus-coinfected patients with compensated cirrhosis](#). Clin Infect Dis. 2013;56(11):1646-1653.
- Morgan RL, Baack B, Smith BD, Yartel A, Pitasi M, Falck-Ytter Y. [Eradication of hepatitis C virus infection and the development of hepatocellular carcinoma: a meta-analysis of observational studies](#). Ann Intern Med. 2013;158(5 Pt 1):329-337.
- Murphy SM, Dweik D, McPherson S, Roll JM. [Association between hepatitis C virus and opioid use while in buprenorphine treatment: preliminary findings](#). The American Journal of Drug and Alcohol Abuse. 2015;41(1):88 - 92.
- Neary MP, Cort S, Bayliss MS, Ware, Jr. JE. [Sustained virologic response is associated with improved health-related quality of life in relapsed chronic hepatitis C patients](#). Semin Liver Dis. 1999;19(Suppl 1):77-85.
- Nelson PK, Mathers BM, Cowie B, Hagan H, Des Jarlais D, Horyniak D, et al. [Global epidemiology of hepatitis B and](#)



- [hepatitis C in people who inject drugs: results of systematic reviews](#). Lancet. 2011;378(9791):571-583.
- Neumann UP, Berg T, Bahra M, Seehofer D, Langrehr JM, Neuhaus R, et al. [Fibrosis progression after liver transplantation in patients with recurrent hepatitis C](#). J Hepatol. 2004;41(5):830-836.
- Nutt AK, Hassan HA, Lindsey J, Lamps LW, Raufman JP. [Liver biopsy in the evaluation of patients with chronic hepatitis C who have repeatedly normal or near-normal serum alanine aminotransferase levels](#). Am J Med. 2000;109(1):62-64.
- Petta S, Camma C, di Marco V, Alessi N, Cabibi D, Caldarella R, et al. [Insulin resistance and diabetes increase fibrosis in the liver of patients with genotype 1 HCV infection](#). Am J Gastroenterol. 2008;103(5):1136-1144.
- Petta S, Maida M, Macaluso FS, Barbara M, Licata A, Craxi A, et al. [Hepatitis C Virus Infection Is Associated With Increased Cardiovascular Mortality: A Meta-Analysis of Observational Studies](#). Gastroenterology. 2015 Sep 18th ed. 2016;150(1):145-155.e4.
- Picciotto FP, Tritto G, Lanza AG, Addario L, De LM, Di Costanzo GG, et al. [Sustained virological response to antiviral therapy reduces mortality in HCV reinfection after liver transplantation](#). J Hepatol. 2007;46(3):459-465.
- Pineda JA, Romero-Gomez M, Díaz-García F, Giron-Gonzalez JA, Montero JL, Torre-Cisneros J, et al. [HIV coinfection shortens the survival of patients with hepatitis C virus-related decompensated cirrhosis](#). Hepatology. 2005;41:779-789.
- Post JJ, Arain A, Lloyd AR. [Enhancing assessment and treatment of hepatitis C in the custodial setting](#). Clin Infect Dis. 2013;57(Suppl 2):S70-S74.
- Poynard T, Ratziu V, Charlotte F, Goodman Z, McHutchison JG, Albrecht J. [Rates and risk factors of liver fibrosis progression in patients with chronic hepatitis c](#). J Hepatol. 2001;34(5):730-739.
- Poynard T, Cacoub P, Ratziu V, Myers RP, Dezailles MH, Mercadier A, et al. [Fatigue in patients with chronic hepatitis C](#). J Viral Hepat. 2002;9(4):295-303.
- Poynard T, McHutchison JG, Manns M, Trepo C, Lindsay K, Goodman Z, et al. [Impact of pegylated interferon alfa-2b and ribavirin on liver fibrosis in patients with chronic hepatitis C](#). Gastroenterology. 2002;122(5):1303-1313.
- Pradat P, Alberti A, Poynard T, Esteban JI, Weiland O, Marcellin P, et al. [Predictive value of ALT levels for histologic findings in chronic hepatitis C: a European collaborative study](#). Hepatology. 2002;36(4 Pt 1):973-977.
- Saadoun D, Resche RM, Thibault V, Longuet M, Pol S, Blanc F, et al. [Peg-IFN \$\alpha\$ /ribavirin/protease inhibitor combination in hepatitis C virus associated mixed cryoglobulinemia vasculitis: results at week 24](#). Ann Rheum Dis. 2014;73(5):831-837.
- Samandari T, Tedaldi E, Armon C, Hart R, Chmiel JS, Brooks JT, et al. [Incidence of Hepatitis C Virus Infection in the Human Immunodeficiency Virus Outpatient Study Cohort, 2000-2013](#). Open Forum Infectious Diseases. 2017;4(2):ofx076.
- Sangiovanni A, Prati GM, Fasani P, Ronchi G, Romeo R, Manini M, et al. [The natural history of compensated cirrhosis due to hepatitis C virus: a 17-year cohort study of 214 patients](#). Hepatology. 2006;43(6):1303-1310.
- Sarkar S, Jiang Z, Evon DM, Wahed AS, Hoofnagle JH. [Fatigue before, during and after antiviral therapy of chronic hepatitis C: results from the Virahep-C study](#). J Hepatol. 2012;57(5):946-952.
- Sayiner M, Golabi P, Farhat F, Younossi ZM. [Dermatologic Manifestations of Chronic Hepatitis C Infection](#). Clinics in Liver Disease. 2017;21(3):555 - 564.
- Sebastiani G, Halfon P, Castera L, Pol S, Thomas DL, Mangia A, et al. [SAFE biopsy: a validated method for large-scale staging of liver fibrosis in chronic hepatitis C](#). Hepatology. 2009;49(6):1821-1827.

- Selph S, Chou R. [Impact of contacting study authors on systematic review conclusions: diagnostic tests for hepatic fibrosis](#). 2014.
- Sise ME, Bloom AK, Wisocky J, Lin MV, Gustafson JL, Lundquist AL, et al. [Treatment of hepatitis C virus-associated mixed cryoglobulinemia with direct-acting antiviral agents](#). Hepatology (Baltimore, Md.). 2016;63(2):408 - 417.
- Spaulding AC, Weinbaum CM, Lau DT, Sterling RK, Seeff LB, Margolis HS, et al. [A framework for management of hepatitis C in prisons](#). Ann Intern Med. 2006;144(10):762-769.
- Svoboda J, Andreadis C, Downs LH, Miller WT, Tsai DE, Schuster SJ. [Regression of advanced non-splenic marginal zone lymphoma after treatment of hepatitis C virus infection](#). Leuk Lymphoma. 2005;46(9):1365-1368.
- Swain MG, Lai MY, Shiffman ML, Cooksley WG, Zeuzem S, Dieterich D, et al. [A sustained virologic response is durable in patients with chronic hepatitis C treated with peginterferon alfa-2a and ribavirin](#). Gastroenterology. 2010;139(5):1593-1601.
- Takahashi K, Nishida N, Kawabata H, Haga H, Chiba T. [Regression of Hodgkin lymphoma in response to antiviral therapy for hepatitis C virus infection](#). Intern Med. 2012;51(19):2745-2747.
- Takikawa H, Yamazaki R, Shoji S, Miyake K, Yamanaka M. [Normalization of urinary porphyrin level and disappearance of skin lesions after successful interferon therapy in a case of chronic hepatitis C complicated with porphyria cutanea tarda](#). J Hepatol. 1995;22(2):249-250.
- Terrault NA, Roland ME, Schiano T, Dove L, Wong MT, Poordad F, et al. [Outcomes of liver transplant recipients with hepatitis C and human immunodeficiency virus coinfection](#). Liver Transpl. 2012;18(6):716-726.
- Thomas DL, Villano SA, Riester KA, Hershow R, Mofenson LM, Landesman SH, et al. [Perinatal transmission of hepatitis C virus from human immunodeficiency virus type 1-infected mothers. Women and Infants Transmission Study](#). J Infect Dis. 1998;177(6):1480-1488.
- Torres HA, Mahale P. [Most patients with HCV-associated lymphoma present with mild liver disease: a call to revise antiviral treatment prioritization](#). Liver Int. 2015;35(6):1661-1664.
- Tyson GL, Kramer JR, Duan Z, Davila JA, Richardson PA, El-Serag HB. [Prevalence and predictors of hepatitis B virus coinfection in a United States cohort of hepatitis C virus-infected patients](#). Hepatology. 2013;58(2):538-545.
- van de Laar TJ, Matthews GV, Prins M, Danta M. [Acute hepatitis C in HIV-infected men who have sex with men: an emerging sexually transmitted infection](#). AIDS. 2010;24(12):1799-1812.
- van der Meer AJ, Veldt BJ, Feld JJ, Wedemeyer H, Dufour JF, Lammert F, et al. [Association between sustained virological response and all-cause mortality among patients with chronic hepatitis C and advanced hepatic fibrosis](#). JAMA. 2012;308(24):2584-2593.
- Veldt BJ, Heathcote EJ, Wedemeyer H, Reichen J, Hofmann WP, Zeuzem S, et al. [Sustained virologic response and clinical outcomes in patients with chronic hepatitis C and advanced fibrosis](#). Ann Intern Med. 2007;147(10):677-684.
- Wedemeyer H, Duberg AS, Buti M, Rosenberg WM, Frankova S, Esmat GE, et al. [Strategies to manage hepatitis C virus \(HCV\) disease burden](#). J Viral Hepat. 2014;21(Suppl 1):60-89.
- White DL, Ratziu V, El-Serag HB. [Hepatitis C infection and risk of diabetes: a systematic review and meta-analysis](#). J Hepatol. 2008;49(5):831-844.
- Yoneda M, Saito S, Ikeda T, Fujita K, Mawatari H, Kirikoshi H, et al. [Hepatitis C virus directly associates with insulin resistance independent of the visceral fat area in nonobese and nondiabetic patients](#). J Viral Hepat. 2007;14(9):600-607.

- Younossi ZM, Stepanova M, Henry L, Gane EJ, Jacobson IM, Lawitz EJ, et al. [Effects of sofosbuvir-based treatment, with and without interferon, on outcome and productivity of patients with chronic hepatitis C](#). Clin Gastroenterol Hepatol. 2013;[Epub ahead of print].
- Younossi ZM, Stepanova M, Nader F, Jacobson IM, Gane EJ, Nelson DR, et al. [Patient-reported outcomes in chronic hepatitis C patients with cirrhosis treated with sofosbuvir-containing regimens](#). Hepatology. 2014;59(6):2161-2169.
- Younossi ZM, Jiang Y, Smith NJ, Stepanova M, Beckerman R. [Ledipasvir/sofosbuvir regimens for chronic hepatitis C infection: Insights from a work productivity economic model from the United States](#). Hepatology. 2015;61(5):1471-1478.
- Younossi ZM, Stepanova M, Afdhal NH, Kowdley KV, Zeuzem S, Henry L, et al. [Improvement of health-related quality of life and work productivity in chronic hepatitis C patients with early and advanced fibrosis treated with ledipasvir and sofosbuvir](#). J Hepatol. 2015;63(2):337-345.
- Younossi ZM, Stepanova M, Sulkowski MS, Naggie S, Puoti M, Orkin C, et al. [Sofosbuvir and ribavirin for treatment of chronic hepatitis C in patients coinfecting with hepatitis C virus and HIV: the impact on patient-reported outcomes](#). J Infect Dis. 2015;212(3):367-377.
- Younossi ZM, Stepanova M, Feld J, Zeuzem S, Jacobson I, Agarwal K, et al. [Sofosbuvir/velpatasvir improves patient-reported outcomes in HCV patients: Results from ASTRAL-1 placebo-controlled trial](#). Journal of Hepatology. 2016;65(1):33 - 39.
- Younossi ZM, Stepanova M, Henry L, Nader F, Hunt S. [An In-Depth Analysis of Patient-Reported Outcomes in Patients With Chronic Hepatitis C Treated With Different Anti-Viral Regimens](#). The American Journal of Gastroenterology. 2016;111(6):808 - 816.
- Zahnd C, Salazar-Vizcaya LP, Dufour JF, Mullhaupt B, Wandeler G, Kouyos R, et al. [Impact of deferring HCV treatment on liver-related events in HIV+ patients](#). In Conference on Retroviruses and Opportunistic Infections (CROI) February 23-26. Seattle, WA; 2015.
- Ziol M, Handra-Luca A, Kettaneh A, Christidis C, Mal F, Kazemi F, et al. [Noninvasive assessment of liver fibrosis by measurement of stiffness in patients with chronic hepatitis C](#). Hepatology. 2005;41(1):48-54.
- Øvrehus ALH, Blach S, Christensen PB, Gerstoft J, Weis N, Krarup H, et al. [Impact of prioritizing treatment in a high resource setting - minimizing the burden of HCV related disease in 15 years](#). 50th Annual Meeting of the European Association for the Study of the Liver (EASL). 2015;;S591.