

Nearly a Decade of Treatment Advances Bring Cures to the Vast Majority of Hepatitis C Patients

JUST THE FACTS



2.4 MILLION

Americans live with Hepatitis C (HCV)¹



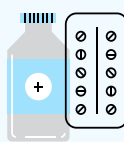
**IT IS ESTIMATED
23,000 TO 46,000**

children in the U.S. have an HCV infection



21%

of people with HIV are also coinfecting with HCV



MORE THAN 95%

of HCV infected persons can be cured of HCV infection with 8-12 weeks of treatment²

The Hepatitis C virus, or HCV, is a devastating viral disease that progresses slowly over time and can cause severe damage to the liver. Historically, HCV was the leading cause of liver cancer and the most common reason for a liver transplant. However, recent scientific advancements have led to a new era of treatments, with cure rates approaching nearly 100%.

SCIENTIFIC INNOVATION FUELS SEA CHANGE IN TREATMENT

2013 marked a paradigm shift in the treatment of HCV, ushering in a new era of highly effective treatment with Direct-Acting Antivirals (DAAs). DAAs treat patients with HCV by interfering with the ability of the virus to replicate and are more effective and better tolerated than the prior standard of care: interferon-based therapy. Unfortunately, interferon can be associated with severe flu-like side effects and even among those who could tolerate six months to a year of treatment, only about half could hope to be cured. 2013 was regarded as a pivotal moment, as it marked the availability of the first “interferon-free” treatment regimen for many patients, offering cure rates over 90% in just 12 weeks.³

Over the past decade, subsequent DAA regimens have offered continued improvements in cure rates, dramatically simplified treatment regimens and provided curative treatment options for the vast majority of patients with HCV.

WHAT IS HEPATITIS C?

HCV was only discovered in 1989. Since then, much has been learned about the virus, its various genotypes and the best approaches to treatment. In the United States, there are at least six distinct HCV genotypes, or strains. Each represents genetically distinct forms of the virus. Genotype 1 is the most common, affecting 75% of Americans with HCV. Another 20-25% have genotypes 2 or 3; and a relatively smaller proportion have genotypes 4, 5 or 6. Some have been historically more difficult to treat—including genotype 3, which is also associated with faster disease progression.⁴

Chronic HCV progresses slowly over time, causing damage to the liver, often progressing from inflammation to scarring (fibrosis) to permanent, irreversible scarring (cirrhosis), leading to liver failure, liver cancer and premature mortality.⁵

THE INTRODUCTION OF FIXED-DOSE COMBINATION REGIMENS

Following 2013, an improved approach to increasing cure rates for HCV emerged. Fixed-dose combination regimens combine two to three classes of antivirals with different mechanisms of action into a single tablet, each capable of interfering with various processes involved in viral replication. The first fixed-dose combination therapies introduced after 2014 greatly improved the efficacy of treatment and adherence for patients with genotypes 1 through 4, with cure rates ranging from 84% to 97%.⁶

Importantly, effective fixed-dose combination regimens also provided critical options for patients with certain genotypes previously associated with treatment resistance. These treatments also demonstrated high cure rates for patients who had already progressed to cirrhosis and for patients with human immunodeficiency virus (HIV) coinfection.

Approximately 21% of people with HIV are also coinfecting with HCV.⁷ HCV-HIV coinfection significantly increases the risk of more severe forms of the disease, favoring the development of cirrhosis, liver cancer and liver failure. Prior to DAAs, interferon-based treatment had been used infrequently in this population due to its limited efficacy, high prevalence of comorbidities and increased risk of severe adverse reactions. Therefore, the advent of fixed-dose combination DAA therapy—which not only offered high cure rates but a reduced pill burden for a population already chronically managed on HIV medication—represented a critical advance for a significant proportion of the HCV population in the United States.⁸

PAN-GENOTYPIC REGIMENS

While fixed-dose combinations provided critical treatments for patients with genotypes 1 through 4, cure rates were still variable across genotypes, and genotypes 5 and 6 continued to lack DAA treatment options. The introduction of pan-genotypic treatment regimens after 2016 enabled treatment across all six genotypes, offering cure rates ranging from 97% to 100%. Importantly, they could also be used in patients with or without cirrhosis, including severe forms of cirrhosis.⁹ For these reasons, these “one-pill-fits-all” regimens dramatically simplified treatment by reducing the need to determine a patient’s genotype, the presence of resistant forms of the virus, or the extent of liver damage in advance of treatment initiation.¹⁰ Likewise, pan-genotypic regimens have paved the way for a more effective global strategy to eliminate HCV.

More recently, pan-genotypic regimens have also been approved and recommended for use in children as young as three years of age.¹¹ Children born to HCV-positive mothers are at risk for HCV infection. It is estimated 23,000 to 46,000 children in the U.S. have an HCV infection. Effective treatment options for this treatment population, before the virus can cause progressive damage to the liver, thus represented a critically important treatment advance.¹² For children with HCV who are unable to swallow pills, formulations such as pellets have also been approved to help facilitate administration to younger children.¹³

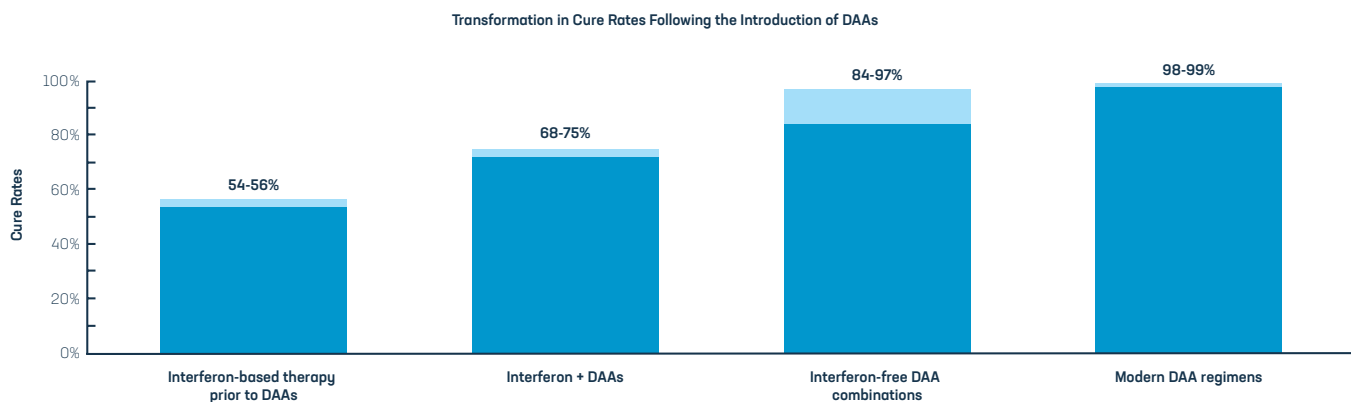
SPILLOVER EFFECTS OF CURING A DEVASTATING VIRAL ILLNESS

The introduction of highly effective treatments for a broader range of HCV patients at various stages of disease progression has enabled the treatment of HCV even after a patient has progressed to requiring liver transplantation. Not only do modern DAAs offer cure rates exceeding 95% in post-transplant patients, but the ability to cure these patients post-transplant has markedly increased survival since 2015. Perhaps more incredibly, the ability to cure Hepatitis C post-liver transplant was not limited to patients previously infected with the

virus. In transplant recipients who receive an organ from a donor infected with HCV, safe and highly effective antiviral treatment after liver, kidney, lung and heart transplantation is now also an option. In other words, modern DAAs have not only saved the lives of countless HCV patients, but by increasing the supply of donor organs that previously had not been considered viable for transplant, they have also potentially saved the lives of many more patients with a wide range of conditions.¹⁴

TREATMENT RESISTANT FORMS OF HCV

Despite significant improvements in cure rates since the introduction of interferon-free DAAs in 2014, a small proportion of patients remained without a treatment option who had failed treatment on previous DAA treatment regimens. The approval of a pan-genotypic regimen in 2016 provided the first FDA-approved treatment regimen for patients who had failed on previous DAA therapy. This fixed-dose combination offered cure rates ranging from 96% to 98% in 12 weeks in patients with a previous DAA treatment failure.^{15 16}



*Manns MP, Maasoumy B. Breakthroughs in hepatitis C research: from discovery to cure. *Nat Rev Gastroenterol Hepatol.* 2022 May 20:1-18. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9122245/>

In the span of just nearly 10 years, DAA regimens have been developed to offer cure rates closely approaching 100%, including for patients with various comorbid conditions.¹⁷ Today, greater than 95% of HCV infected persons can be cured of HCV infection with 8-12 weeks of DAA therapy regardless of genotype, prior treatment experience or failure, stage of liver damage or presence of cirrhosis.¹⁸ **Considering the countless number of lives this transformation has saved, and the cases of liver failure, liver cancer and organ transplants that have been avoided, the remarkable impact of these treatment advances cannot be overstated.**

SOURCES

- 1 HHS, Viral Hepatitis in the United States: Data and Trends, <https://www.hhs.gov/hepatitis/learn-about-viral-hepatitis/data-and-trends/index.html>
- 2 Kish T, Aziz A, Sorio M. Hepatitis C in a New Era: A Review of Current Therapies. P T. 2017 May;42(5):316-329. PMID: 28479841
- 3 Manns MP, Maasoumy B. Breakthroughs in hepatitis C research: from discovery to cure. Nat Rev Gastroenterol Hepatol. 2022 May 20:1-18. doi: 10.1038/s41575-022-00608-8.
- 4 HCV Epidemiology in the United States, <https://www.hepatitis.cu.edu/pdf/screening-diagnosis/epidemiology-us/core-concept/all>
- 5 NIH, National Institute of Diabetes and Digestive and Kidney Diseases, Hepatitis C, <https://www.niddk.nih.gov/health-information/liver-disease/viral-hepatitis/hepatitis-c#:~:text=for%20hepatitis%20C-. ,What%20are%20the%20complications%20of%20hepatitis%20%20C%3F,C%20can%20prevent%20these%20complications>
- 6 Manns MP, Maasoumy B. Breakthroughs in hepatitis C research: from discovery to cure. Nat Rev Gastroenterol Hepatol. 2022 May 20:1-18. doi: 10.1038/s41575-022-00608-8.
- 7 HIV and Opportunistic Infections, Coinfections, and Conditions, <https://hivinfo.nih.gov/understanding-hiv/fact-sheets/hiv-and-hepatitis-c>
- 8 Coppola N, Martini S, Pisaturo M, Sagnelli C, Filippini P, Sagnelli E. Treatment of chronic hepatitis C in patients with HIV/HCV coinfection. World J Virol. 2015 Feb 12;4(1):1-12. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4308522/>
- 9 Manns MP, Maasoumy B. Breakthroughs in hepatitis C research: from discovery to cure. Nat Rev Gastroenterol Hepatol. 2022 May 20:1-18. doi: 10.1038/s41575-022-00608-8.
- 10 V. Soriano et al, Treatment of hepatitis C with new fixed dose combinations, Expert Opinion on Pharmacotherapy. 2017. <https://www.tandfonline.com/doi/abs/10.1080/14656566.2017.1346609?journalCode=ieop20>
- 11 HCV Guidance: Recommendations for Testing, Managing, and Treating Hepatitis C, HCV in Children. <https://www.hcvguidelines.org/unique-populations/children#:~:text=Sofosbuvir%2Fvelpatasvir%20was%20approved%20by,least%206%20years%20of%20age.>
- 12 American Academy of Pediatrics, Hepatitis C: What Parents Need to Know, <https://www.healthychildren.org/English/health-issues/conditions/abdominal/Pages/Hepatitis-C.aspx>
- 13 FDA, First oral pan-genotypic HCV drugs approved for children as young as 3 years, Nov. 2021. <https://www.fda.gov/media/154745/download>
- 14 Manns MP, Maasoumy B. Breakthroughs in hepatitis C research: from discovery to cure. Nat Rev Gastroenterol Hepatol. 2022 May 20:1-18. doi: 10.1038/s41575-022-00608-8.
- 15 Manns MP, Maasoumy B. Breakthroughs in hepatitis C research: from discovery to cure. Nat Rev Gastroenterol Hepatol. 2022 May 20:1-18. doi: 10.1038/s41575-022-00608-8.
- 16 <https://www.vosevi.com/about-vosevi>
- 17 Manns MP, Maasoumy B. Breakthroughs in hepatitis C research: from discovery to cure. Nat Rev Gastroenterol Hepatol. 2022 May 20:1-18. doi: 10.1038/s41575-022-00608-8.
- 18 Kish T, Aziz A, Sorio M. Hepatitis C in a New Era: A Review of Current Therapies. P T. 2017 May;42(5):316-329. PMID: 28479841. Manns MP, Maasoumy B. Breakthroughs in hepatitis C research: from discovery to cure. Nat Rev Gastroenterol Hepatol. 2022 May 20:1-18. doi: 10.1038/s41575-022-00608-8.