

EDITORIAL

Updated Hepatitis C Virus Screening Recommendation—A Step Forward

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Hepatitis C virus (HCV) is the most common blood-borne pathogen in the United States, with an estimated 2.4 million people in the US living with HCV, and leads to substantial morbidity and mortality.¹ Between 2003 and 2013, the number of



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HCV-associated deaths in the US exceeded that of the top 60 other notifiable infectious conditions combined.² Moreover, prior to 2014, only half of people living with HCV were aware that they were infected, and just 9% had been treated and cured.³ In 2013, the US Preventive Services Task Force (USPSTF) recommended screening for HCV infection in persons at high risk for infection and one-time screening in adults born between 1945 and 1965.⁴ In 2020, the USPSTF has updated its recommendation,⁵ as well as the evidence report and systematic review,⁶ to expand the ages for screening to all adults aged 18 to 79 years (B recommendation) and concluded with moderate certainty that implementing such screening will have substantial net benefit. The updated recommendation aligns with joint American Association for the Study of Liver Diseases-Infectious Diseases Society of America recommendations for one-time HCV testing in all adults 18 years or older.⁷ Recent developments inform the updated USPSTF HCV screening recommendation.

Effectiveness of Direct Acting Antivirals and the Influence of Cure

In 2014, highly effective all-oral direct acting antivirals (DAAs) became available. With pan-genotypic regimens and sustained virologic response (SVR) rates 95% and higher, HCV is now curable in most patients who complete treatment, including people living with HIV, patients with end-stage renal disease, and patients with cirrhosis.⁷ Furthermore, in contrast with older HCV regimens containing peginterferon, the all-oral regimens are better tolerated. When DAAs were introduced, patients with advanced fibrosis or cirrhosis and others at highest risk of HCV-related adverse events were prioritized for treatment. This population stood to derive the most benefit from treatment. Additionally, wholesale acquisition costs of DAAs were very high, ranging from \$83 000 to \$189 000 depending on the regimen and duration. Treatment costs have since decreased, but the specific amounts paid per regimen are not known because payer-pharmaceutical company negotiations are not publicly available.

The systematic review⁶ that informs the updated USPSTF HCV screening recommendation demonstrates that direct evidence on the effects of current DAA regimens on health

outcomes is limited because nearly all DAA trials relied on SVR as the primary efficacy outcome. However, SVR was associated with a decreased risk of all-cause mortality (pooled hazard ratio [HR], 0.40; 95% CI, 0.28-0.56), liver-related mortality (pooled HR, 0.11; 95% CI, 0.04-0.27), cirrhosis (pooled HR, 0.36; 95% CI, 0.33-0.40), and hepatocellular carcinoma (pooled HR, 0.29; 95% CI, 0.23-0.38).⁸ Based on this observational data, HCV treatment is recommended in all patients living with HCV, regardless of disease stage, except those with shortened life expectancies that would not be affected by treatment.^{7,9} Importantly, ongoing substance use is not a contraindication to HCV treatment. The 12-week SVR rates are more than 90% among people with recent and ongoing injection drug use,^{10,11} and evidence supports scaling up HCV treatment among people who inject drugs as a strategy to prevent transmission.¹²

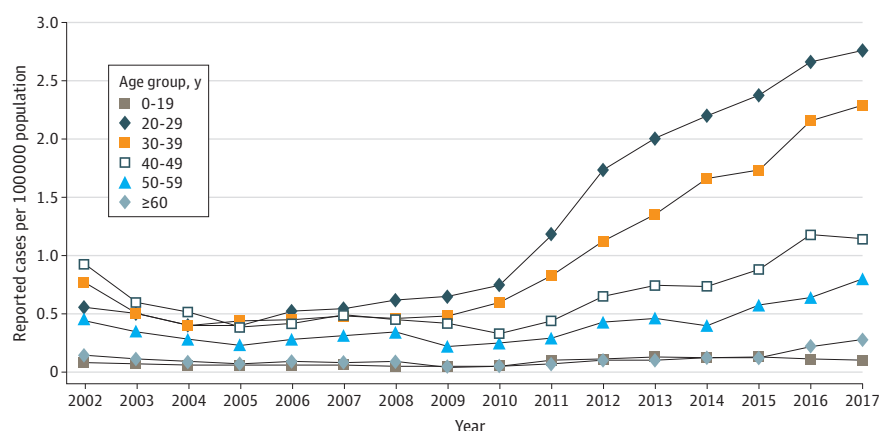
Changing Epidemiology of HCV Infection

Despite the advances in therapeutics, HCV incidence is increasing in the US (**Figure**) in parallel with the increase in injection opioid use. In 2017, there were an estimated 44 700 new HCV infections in the US, representing a 3.8-fold increase since 2010; most cases were attributable to drug use.¹³ Although HCV incidence has increased across all age groups, the increase has been most rapid among adults younger than 40 years and in nonurban settings.^{13,14} In 2007 through 2008, the majority of newly reported cases of HCV were in people in the 1945-1965 birth cohort—the population targeted in the 2013 USPSTF HCV screening recommendation.⁴ Importantly, the percentage of people in the birth cohort whose HCV was identified and cured increased from 17% in 2011 to 40% in 2018, and 67% are expected to be cured by 2030.¹⁵ However, the proportion cured is much lower (4%) in the largest population of HCV-infected persons, incarcerated persons, so efforts for treatment must include this group. In recent years, infections show a bimodal distribution, with a second wave of newly reported HCV cases among younger adults. The expansion of HCV screening in the updated USPSTF recommendation⁵ to adults aged 18 to 79 years is a response to the changing demographics of HCV infection.

HCV Screening and the Path to HCV Elimination

In 2016, the World Health Organization set the goal of eliminating viral hepatitis as a major public health threat by 2030, defined as a 90% reduction in incident infections and 65% reduction in mortality compared with a 2015 baseline.¹⁶ At present, the US is not on track to achieve these goals. One estimate is that at present rates of HCV screening, treatment, and new infections, 62% of people with HCV in the US will be aware of their infection by 2030 and 49% will have been cured.¹⁵ Clearly, reducing incident infections will require programs to

Figure. Rates of Reported Acute Hepatitis C by Age Group in the United States, 2002-2017



Source: Centers for Disease Control and Prevention, National Notifiable Diseases Surveillance System.

reduce transmission during intravenous drug use, such as needle-exchange or other programs. A simulation study projected that HCV screening in all adults 18 years and older would result in increased rates of HCV detection (from 74% to 85%) and cure (from 49% to 61%), and ultimately reduce the incidence of liver-related death by 21%.¹⁷ While projected cost of testing increased using this approach, it ultimately was more cost-effective than the birth cohort approach.

Over the past decade, the advancements in HCV diagnosis and treatment have been extraordinary. The updated USPSTF screening recommendation⁵ are necessary but not sufficient for further progress. Implementation of HCV screening and linkage to treatment requires large-scale coordinated efforts, innovation, and resources. For example, point-of-care HCV RNA testing would enable scale-up of HCV screening and confirmatory testing among individuals at greatest risk of HCV infection. Additionally, barriers remain between diagnosis and treatment, such as access to a health care provider who can treat HCV and authorization to receive affordable DAAs. This can be accomplished by simplifying treatment regimens and colocalizing treatment in settings more easily accessible to marginalized populations, such as syringe service programs and opioid sub-

stitution programs, and increasing treatment capacity. There should be expanded access to clinicians, including primary care physicians, who can treat patients with HCV, as well as continued attention to preventing transmission through programs that offer patient education and harm reduction.

The cost of HCV treatment remains very high and drives the present payer restrictions. Innovative payment strategies such as the Netflix model adopted by Louisiana could increase treatment access without completely consuming state Medicaid budgets.¹⁸ Similar to Netflix, in which customers pay a monthly fee for unlimited video-streaming services, this model allows the state to negotiate a fixed annual fee with pharmaceutical companies in exchange for unlimited access to DAAs to treat all infected state residents. People living with HCV should be treated regardless of disease stage or ongoing substance use. Remaining questions include the frequency of screening for people with ongoing risk factors for HCV infections and preventing transmission from mother to child. Although the USPSTF HCV screening recommendation is a step forward for controlling HCV infection in the US, it will take a coordinated and funded effort to ensure that the anticipated benefits are realized.

ARTICLE INFORMATION

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