

# Universal Screening for Hepatitis C Virus Infection A Step Toward Elimination

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**In this issue of JAMA**, the US Preventive Services Task Force (USPSTF) has issued new recommendations for hepatitis C virus (HCV) infection screening in the asymptomatic US population.<sup>1</sup> Based on an updated review of the evidence,<sup>2</sup> the



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task force now “recommends screening for HCV infection in adults aged 18 to 79 years (B recommendation),”<sup>1</sup> regardless of known risk factors. Adolescents who engage in injection drug use or other behaviors associated with acquisition of HCV should also be screened. Screening all adults

has been shown to be cost-effective, and a B recommendation means that insurance companies will provide reimbursement for hepatitis C testing without cost-sharing by patients. To understand the significance of this new recommendation, the evolution in HCV management over the last decade provides context. In 2010 in the US, the need for HCV screening was based on assessing a series of potential exposures, many of which were stigmatizing, such as having engaged in injection drug use years earlier.<sup>3</sup> The only available antiviral treatment for HCV was injectable pegylated interferon alfa combined with oral ribavirin, and this combination was associated with cure rates less than 50% for the most common genotype-1 HCV infections.<sup>4</sup> Screening rates for HCV infection were low (only 12% of baby boomers, ie, individuals born from 1945 through 1965, reported being tested for HCV in a 2013 national patient survey), and patients were reluctant to embark on treatment that was similar to experiencing a flu-like illness for 48 weeks with a less than 50% chance of cure.<sup>5</sup>

In 2012, the Centers for Disease Control and Prevention noted that 75% of persons living with HCV infection were born from 1945 through 1965 and recommended 1-time “baby boomer” HCV screening along with continued risk-based screening.<sup>6</sup> In 2013, the USPSTF issued a B recommendation for HCV screening for the 1945-1965 birth cohort, along with risk-based screening.<sup>7</sup> The timing of that recommendation coincided with an important advance in medicine. With the approvals of sofosbuvir and simeprevir in 2013, patients with hepatitis C, a chronic viral illness associated with the deaths of more US patients than the next 60 reportable infectious diseases combined, including HIV and tuberculosis, could expect a greater than 90% rate of achieving sustained virologic response (SVR, defined as undetectable HCV levels 12 weeks or longer after treatment completion, which is consistent with virologic cure of HCV infection) following 12 weeks of treatment.<sup>8</sup>

As reviewed by the USPSTF,<sup>2</sup> data from additional randomized clinical trials demonstrated that newer all-oral regimens were associated with up to 99% SVR rates after 8 to 12 weeks of treatment, and observational studies showed that a wide variety of patient populations, including people who used drugs, had similarly high SVR rates. It also became clear that treatment of HCV infection changed the natural history of this disease. According to the USPSTF Evidence Review,<sup>2</sup> SVR was associated with decreased risk of liver-related mortality (4 studies, n = 5953; pooled hazard ratio [HR], 0.11 [95% CI, 0.04-0.27]), risk of hepatocellular carcinoma (20 studies, n = 84 491; pooled HR, 0.29 [95% CI, 0.23-0.38]), and all-cause mortality (13 studies, n = 36 986; pooled HR, 0.40 [95% CI, 0.28-0.56]).

These advances should have led to implementation of widespread HCV screening programs in all clinics and hospitals. However, one of the new medications was priced at \$1000 per pill, and this high price led to rationing of HCV antiviral treatment by public and private insurance companies on a scale rarely seen before in the US.<sup>9</sup> For many plans, only the patients with the most severe liver scarring who had months of sobriety and access to HCV specialists were able to receive reimbursed treatment. Health centers were reluctant to identify new patients with HCV infection, only to have to inform them that they could not be treated.

From 2014 until now, 2 critical changes happened. First, free-market competition between drug regimens to treat HCV infection has lowered the price of antiviral treatment by at least 70%, with an estimated price of \$26 400 for a typical 8-week regimen in 2020.<sup>10</sup> This is one of only a few recent examples of competition significantly lowering the price of branded drugs. A generic regimen became available to treat all types of HCV viruses in 12 weeks.<sup>11</sup> States such as Louisiana and Washington are testing flat-rate, “all-you-can-treat” drug purchasing plans that reduce the per-patient cost even further.<sup>12</sup> The cost of curing HCV is now less than the cost of a year’s supply of antiretroviral medications for HIV.

Second, the opioid epidemic, which had been building since the late 2000s, is now contributing to thousands of new cases of HCV through injection drug use in persons younger than the 1945-1965 birth cohort. The most rapid increase in acute HCV incidence over the last decade has been in young adults aged 20 to 39 years who have injected drugs.<sup>1</sup> Both the reduced price of hepatitis C regimens, which should make broader access to treatment more feasible, and the increase in HCV infections in younger people are compelling reasons for expanding HCV screening at this time.

The USPSTF also states that clinicians might consider testing adolescents with past or current injection drug use.<sup>1</sup> In the last 3 years, the HCV regimens commonly used in adults were also approved for use in adolescents 12 years and older, so adolescents

now have access to these potent, easier-to-tolerate regimens as well. Appropriate screening of the adolescent population will require diligent assessment of risk factors; clinicians will need to demonstrate great sensitivity while minimizing any stigma and judgment that adolescents may feel related to drug use. This will be critical to facilitating truthful disclosure of risks by adolescents and will be important to help engage and keep them in care.

During 2011-2014, commercial laboratory data indicated that the national rate of HCV detection among women aged 15 to 44 years increased 22%, from 139 to 169 per 100 000, and because many of these women are of reproductive age, cases of perinatal transmission of HCV have also increased.<sup>13</sup> The USPSTF recommends testing all pregnant adults and states that clinicians might consider testing all pregnant adolescents, without regard for known risk factors. There are no approved antiviral regimens to treat HCV during pregnancy, but knowing a pregnant person's HCV status will allow infants to be monitored for perinatal transmission of HCV (which can be treated before serious liver damage occurs in these children) and postpartum HCV treatment to be prioritized.<sup>14</sup>

It is unclear whether the lack of testing and treatment for HCV in younger patients has contributed to ongoing HCV transmission. However, the high rates of new infections and the lack of adequate harm reduction services such as syringe service programs and medication-assisted treatment have decreased the

likelihood that the US will meet World Health Organization (WHO) 2030 targets for HCV elimination.<sup>15</sup> According to 1 estimate, the US will not eliminate HCV until after 2050 unless harm reduction services, HCV screening, and treatment rates change.<sup>16</sup>

The HCV screening recommendation for the baby boomer (1945-1965) birth cohort was an initial step forward in destigmatizing HCV testing by removing behavioral risk factor assessment from the conversation with patients. It is time to revisit the effective but now outdated baby boomer screening recommendations, and the updated recommendations from the USPSTF are welcome. If (1) every hospital, clinic, and emergency department offers HCV screening to all adults aged 18 to 79 years and adolescents with risk factors and ensures that patients are linked to care; (2) substance use disorder treatment programs such as syringe service programs have sustainable resources to perform HCV testing; and (3) all persons who have active HCV infection are offered antiviral treatment regardless of the severity of liver damage, substance use status, or any other factors not detailed in treatment guidelines, there is an opportunity to reduce HCV-related morbidity and mortality and to demonstrate that all people deserve care. Meeting the WHO 2030 targets for reducing new HCV infections and increasing treatment will be more likely to succeed if more primary care clinicians and addiction specialists join in the important efforts to screen, treat, and achieve virologic cure for people living with HCV infection.

#### ARTICLE INFORMATION

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