

ADVANCES IN HEPATOLOGY

Current Developments in the Treatment of Hepatitis and Hepatobiliary Disease

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Identification of People Infected With Hepatitis C Virus Who Have Never Been Diagnosed



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G&H What is the current prevalence of hepatitis C virus infection in the United States?

KK A recent population-based survey of the United States found that the national prevalence of hepatitis C virus (HCV) infection between 2013 and 2016 was 0.93%, varying from 0.45% to 2.34%. This means that there are approximately 2.4 million persons infected with HCV in the United States.

G&H What are the most recent estimates on how many people are infected with HCV but have never been diagnosed?

KK According to a 2016 study, approximately 1 out of 2 people infected with HCV are unaware of their diagnosis, but the rates of undiagnosed HCV infection range from 45% to 85%. With increased screening of Baby Boomers (individuals born between 1945 and 1965, who have an increased risk of HCV infection), it has been possible to identify a large proportion of these individuals with chronic HCV infection. However, I suspect that the undiagnosed population is even higher among certain groups, such as people who inject drugs (PWID), incarcerated people, people in rural areas, and people who do not have routine access to preventive health care. Globally, the World Health Organization estimates that only 1 in 5 individuals with HCV infection is aware of their diagnosis.

G&H What are the potential consequences of undiagnosed HCV infection?

KK In the majority of individuals, HCV infection does not spontaneously resolve, which means that the infection is chronic. A significant proportion of individuals with chronic HCV infection will go on to develop end-stage liver disease and other complications of cirrhosis, such as hepatocellular carcinoma. There is now also a growing body of evidence that HCV infection is a chronic inflammatory state similar to diabetes. Thus, patients infected with HCV appear to have an increased likelihood of cardiovascular disease and diabetes.

G&H What have been the most significant challenges to identifying people who are infected with HCV?

KK Historically, the challenges were related to a lack of recognition of HCV infection as a chronic disease. There was also stigmatization and fear of discrimination that caused some people who may have been exposed to the virus, or may have had risk factors for it, to be unwilling to present themselves for testing. The lack of highly effective and inexpensive therapies may have been another factor that diminished enthusiasm for large-scale testing of the population. HCV infection was historically treated with interferon injections, which were costly, painful, associated with many side effects, and required frequent clinical and laboratory monitoring of patients. The treatment duration was frequently 48 weeks or longer, and only a small proportion of patients (10%-30%) achieved a cure (also called sustained virologic response).

Much has changed over the past several years; as of 2014, we have highly safe and effective all-oral therapies

with direct-acting antiviral agents. Cure is now possible in over 95% of most patient populations with as little as 8 weeks of all-oral treatment regimens that have minimal to no side effects. As a result, the US Preventive Services Task Force (USPSTF), the Centers for Disease Control and Prevention (CDC), other public health organizations, and medical societies now support universal testing for Baby Boomers, who have historically comprised the majority of the HCV-infected population. Furthermore, there is now a growing consensus that all adults should be tested for HCV infection at least once.

However, despite these advances in diagnosis and treatment, several challenges in achieving the goal of elimination of HCV infection remain. The cost of treatment has declined significantly but remains expensive. The demographics of the HCV population have changed over the past several years. The opioid epidemic has resulted in a high incidence and prevalence of HCV infection among PWID. The PWID population is younger than the Baby Boomer population and more likely to have other comorbid social, financial, and health challenges, such as poverty, food insecurity, increased rates of mental illness, and lack of access to health care and other social services. Thus, this population requires a comprehensive approach to diagnosis and treatment. There is a growing recognition and resolve on the part of stakeholders committed to elimination of HCV infection to treating this at-risk population, but access to skilled providers and ongoing health care in a comprehensive manner remains a concern.

G&H Do you support universal HCV screening?

KK In my opinion, one-time HCV screening should be offered to all adults. This would increase the rate of diagnosis in the growing population of younger HCV-infected patients. The implementation of Baby Boomer screening has definitely played an important role in identifying patients with HCV infection and, in my opinion, contributed to reduced fear of stigmatization associated with testing. Universal screening and linkage to care would further increase case detection and advance the goal of elimination of HCV infection.

G&H Are there any concerns about whether universal screening would be feasible or cost-effective?

KK A change from risk-based screening to universal screening would result in the test being conducted in a population with a lower prevalence of the disease, which would yield a higher rate of false-positive results. Therefore, universal screening requires a sensitive screening test (such as an enzyme-linked immunosorbent assay-based

screening antibody test) and a confirmatory test with high specificity. Inexpensive HCV antibody tests are available, but the confirmatory test requires measurement of HCV RNA in the serum and is more expensive. Additionally, the patient will need to return for the confirmatory test. The time, effort, and cost involved in this process could temper the enthusiasm for universal screening.

It is possible for reflex confirmatory testing to be performed from the same sample collected for the screening antibody test, but such a system is not widely available at this time to my knowledge.

G&H How can the identification of people infected with HCV who are unaware of their status be improved?

KK The CDC and USPSTF recommendations regarding Baby Boomer screening have been successful in increasing awareness among patients and health care providers. However, a significant proportion of the population has yet to be screened, and we should continue to highlight the ease and efficacy of therapies in achieving a cure for the vast majority of patients. Given the simplicity and safety of current HCV treatment regimens, more primary care providers should be trained to identify HCV infection, accurately stage liver disease, evaluate liver function, and treat HCV infection. The cost of treatment has been reduced and is likely to decrease further, which should allow more people to be treated. In the United States, our efforts should be focused where the incidence and prevalence of the disease is highest at the current time, namely the PWID population. I think that partnering with public health organizations, federally qualified health centers, methadone or opiate agonist programs, and addiction medicine specialists will be very important. Increased awareness and education among providers who treat these patients is important via educational outreach programs, telementoring, and other means of training.

G&H Has the use of electronic medical record prompts or reminders been shown to help increase the identification of people infected with HCV?

KK Automated prompts via electronic health records can be very helpful in increasing case detection. A prompt to patients and providers via electronic health records significantly increased the proportion of Baby Boomers screened by primary care providers. However, it is critical that such automated screening programs be coupled with education of primary care providers to empower them to interpret the tests correctly and link patients to appropriate tests for staging of liver disease and a pharmacy program able

to help navigate them through the process of obtaining treatment. Otherwise, adding yet another task to the already overburdened primary care provider's workload may prove challenging and unpopular.

G&H Have there been any attempts to target particular at-risk populations, such as individuals in the correctional system?

KK There has been increasing interest in identifying and treating patients in the correctional system. Because of the short duration of HCV therapy, we now have the ability to treat patients while they are incarcerated. The challenge has been the cost of treatment and the limited resources available to the providers taking care of patients in a correctional environment. However, this is clearly one of the areas that should be focused on because it has been shown that the prevalence of HCV infection is much higher among individuals in the correctional system. Especially for patients with insecure housing after release from incarceration, the opportunity to treat them while they are in prison is an opportunity that should not be missed.

G&H What are the most important next steps that should be taken?

KK There has to be a coordinated effort to make treatment accessible without restrictions to both privately and publicly insured individuals and those who are uninsured. There needs to be greater outreach, awareness, and education so that people at increased risk of HCV infection engage with health care and receive care. An important first step is to implement cost-effective and seamless

point-of-care testing with reflex confirmatory testing available simultaneously and to link patients found to be HCV-positive to care.

Dr Kowdley serves as a consultant and speaker for AbbVie and Gilead Sciences, and receives research support from Gilead Sciences.

Suggested Reading

AASLD-IDSA. Recommendations for testing, managing, and treating hepatitis C. <http://www.hcvguidelines.org>. Accessed November 13, 2019.

Centers for Disease Control and Prevention. Testing recommendations for hepatitis C virus infection. <https://www.cdc.gov/hepatitis/hcv/guidelinesc.htm>. Accessed November 13, 2019.

Eckman MH, Ward JW, Sherman KE. Cost effectiveness of universal screening for hepatitis C virus infection in the era of direct-acting, pangenotypic treatment regimens. *Clin Gastroenterol Hepatol*. 2019;17(5):930-939.e9.

Lyons MS, Kunnathur VA, Rouster SD, et al. Prevalence of diagnosed and undiagnosed hepatitis C in a Midwestern urban emergency department. *Clin Infect Dis*. 2016;62(9):1066-1071.

Rosenberg ES, Rosenthal EM, Hall EW, et al. Prevalence of hepatitis C virus infection in US states and the District of Columbia, 2013 to 2016. *JAMA New Open*. 2018;1(8):e186371.

Suryaprasad AG, White JZ, Xu F, et al. Emerging epidemic of hepatitis C virus infections among young nonurban persons who inject drugs in the United States, 2006-2012. *Clin Infect Dis*. 2014;59(10):1411-1419.

World Health Organization. Combating hepatitis B and C to reach elimination by 2030. <https://www.who.int/hepatitis/publications/hep-elimination-by-2030-brief/en/>. Published May 2016. Accessed November 21, 2019.

World Health Organization. Hepatitis C key facts. <https://www.who.int/news-room/fact-sheets/detail/hepatitis-c>. Published July 9, 2019. Accessed November 21, 2019.

Zibbell JE, Iqbal K, Patel RC, et al; Centers for Disease Control and Prevention (CDC). Increases in hepatitis C virus infection related to injection drug use among persons aged ≤30 years—Kentucky, Tennessee, Virginia, and West Virginia, 2006-2012. *MMWR Morb Mortal Wkly Rep*. 2015;64(17):453-458.