

The Second Biggest Infectious Disease Killer in the U.S.: Hepatitis C Virus Infection and Steps Towards its Elimination in Rhode Island and Beyond

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It has been six years since our first hepatitis C virus infection (HCV)-themed edition of the *Rhode Island Medical Journal* (RIMJ) and 31 years since the discovery of this small, single-stranded, enveloped RNA virus.¹ An evolving understanding of this pathogen and the shifting HCV epidemic lead to continual changes in the standard of care. The past months mark the convergence of many steps taken to address the global and national problem of HCV.

In April 2020, the U.S. Centers for Disease Control and Prevention (CDC) released revised HCV testing recommendations, advising universal HCV screening for all adults – not just persons born from 1945 to 1969 and those with risk factors.² The CDC also recommended HCV screening for all women who are pregnant during each pregnancy. CDC continues to instruct that people with risk factors be tested regularly. This followed the March 2020 U.S. Preventive Services Task Force (USPSTF) updated recommendations advising that clinicians screen all adults aged 18 to 79 for HCV at least once, regardless of their risk level for contracting the disease.³ The USPSTF also counseled that those outside this age range at high risk of infection be screened.

These recommendations are consistent with November 2019 modified U.S. society guidelines from the American Association for the Study of Liver Diseases (AASLD) and the Infectious Disease Society of America (IDSA) endorsing one-time, routine, opt-out HCV screening for all individuals 18 years and older.⁴ They also advocate periodic testing for persons with an increased risk of HCV exposure, annual HCV testing for people who inject drugs (PWID) and HIV-infected men who have unprotected sex with men, and one-time testing for all persons younger than 18 years at increased risk of HCV. These updated guidelines stipulate that all patients with chronic HCV be treated, except those with short life expectancies that cannot be remediated, with no restrictive prioritization of HCV medications.

Rapidly advancing therapeutic options and complex treatment algorithms hinder treatment scale-up at the population level; AASLD/IDSA also issued simplified treatment approaches for HCV treatment-naïve patients with and without cirrhosis in November 2019.⁴ Ninety-nine percent of HCV infections are now curable with pan-genotypic direct-acting antiviral (DAA) agents with all-oral medication regimens for 8–12 weeks (longer for advanced liver disease and complex patients). Benefits of cure include

reduced transmission, decreased liver-related morbidity and mortality as well as all-cause mortality, diminished need for liver transplantation and improved quality of life.

Additionally, in April 2020, the CDC reported that U.S. HCV incidence tripled from 2009 to 2018, due to the opioid crisis.⁵ While Baby Boomers remain the highest prevalence population in the U.S., increases in acute HCV infections are attributable to rising rates of injection drug use among younger persons. Compelling evidence demonstrates that DAAs are effective for PWID, and that high levels of HCV treatment and cure for PWID can reduce HCV incidence and prevalence.^{6–11} Consequently, national and international guidelines support prioritization and HCV treatment expansion for this population.^{4,12} In the absence of a vaccine, and no effective pre- or post-exposure prophylaxis, it is DAA treatment, opioid agonist therapy plus high-level needle syringe provision that are the necessary trifecta to facilitate prevention and the path to cure.

The World Health Organization (WHO) Global Health Sector Strategy provides a roadmap to HCV elimination.¹³ In line with WHO goals, there should be a 30% reduction in new infections and a 10% reduction in hepatitis-related deaths by the end of this year. The U.S., along with 80% of high-income countries, is not on track to meet these targets.¹⁴ Of 45 high-income countries, only nine (Australia, France, Iceland, Italy, Japan, South Korea, Spain, Switzerland and the United Kingdom) are on course towards meeting WHO's 2030 targets of 90% reduction in new infections and a 65% reduction in mortality. Thirty nations including the U.S are off-track by at least 20 years, as they are not projected to achieve HCV elimination before 2050. Our national plan, the U.S. National Academies of Sciences, Engineering, and Medicine report, presents strategies and priorities to eliminate HCV as a serious public health threat.¹⁵ Lack of funding impedes full implementation of these plans. For example, for fiscal year 2019, the enacted budget shows that the CDC's Division of Viral Hepatitis received 39 million dollars, representing 0.5% of CDC's total program budget.¹⁶ Viral hepatitis accounts for less than one percent of the National Institutes of Health research budget.¹⁷

Rhode Island data

What is the data from Rhode Island (RI)? Chronic HCV prevalence exceeds national averages.¹⁸ Per a March 2020

modeling study (we lack robust national surveillance data), RI, with a prevalence estimate of 1.78% for men, ties with Arizona for the eighth highest prevalence among men behind the District of Columbia, Louisiana, New Mexico, Oklahoma, Oregon, Tennessee and West Virginia. RI has the ninth highest prevalence estimate among females, behind the District of Columbia, Kentucky, Louisiana, New Mexico, Oklahoma, Oregon, Tennessee and West Virginia with a prevalence estimate of 0.67%. Among the U.S. states and District of Columbia, RI has the 10th highest HCV prevalence estimate among the birth cohort, those born between 1945 and 1969.

Manuscripts from the current edition of the Journal exhibit the wide-ranging expertise needed to make a difference in providing life-saving preventive measures and care. These articles highlight the expertise of a diverse group across RI as they address barriers and facilitators of HCV elimination.

Public health leadership and initiatives provide the foundation for combating RI's HCV epidemic. **MATTHEW MURPHY, MD**, et al describe the Rhode Island Department of Health's HCV elimination efforts.

The advent of DAAs ended the interferon era, and ushered in the use of non-invasive approaches for assessing hepatic fibrosis. **ADIB R. KARAM, MD**, and **MICHAEL D. BELAND, MD**, explain the varied techniques of liver ultrasound elastography, elucidating benefits and limitations.

The HCV cascade to cure has not reached PWID in sufficient numbers. Delivering all elements of care at a single site, and streamlining care to reduce time from infection to cure, may be accomplished with co-location of HCV and addiction care. **SOUMITRI BARUA, MD'21**, along with her co-authors, illuminates these lessons and reminds us of an aggressive HCV-associated malignancy, intra-hepatic cholangiocarcinoma. As HCV is typically asymptomatic, older adults may be unknowingly living with HCV for decades; the largest burden of HCV-related complications falls on those age 60 and older. Highlighting the important role of pharmacists in HCV treatment, **ALYSSA K. GREENWOOD FRANCIS, MPH**, and colleagues evaluate DAA efficacy in older versus younger patients.

The U.S. spends more on healthcare than any other country.¹⁹ Interventions to reduce waste in U.S. healthcare spending include cutting inflation in pricing of medications and easing administrative complexity.¹⁹ **PATRICK DURYEA** et al discuss RI's DAA Prior Authorization process, providing opportunity to consider steps to alleviate administrative burdens and inefficiencies.

Due to the COVID-19 pandemic, RI Defeats Hep C cannot hold C is for Cure Waterfire this summer in honor of July 28's World Hepatitis Day (it would have been our 7th annual event, one of the world's largest HCV festivals). We hope this issue of the Journal keeps HCV on your mind as its contributors address key domains of prevention, stigma, screening and diagnostic testing, evaluation of liver disease,

treatment, medical complications, healthcare disparities and public health policy. Best of health to all and thank you to RI's extraordinary medical community.

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Thank you to the many patients living with and cured of HCV, for your courage and endurance.

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