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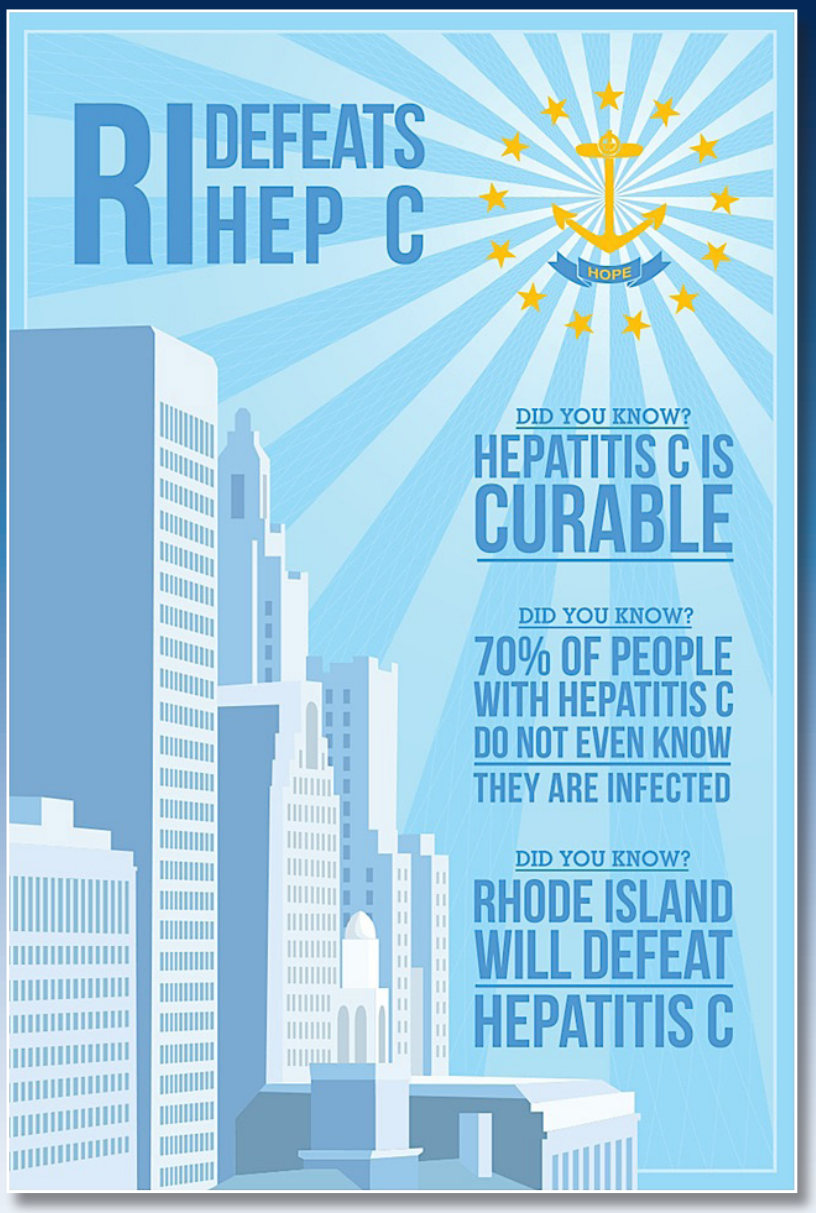

SPECIAL SECTION

HEPATITIS C

LYNN E. TAYLOR, MD; GUEST EDITOR

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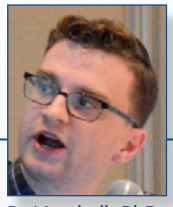

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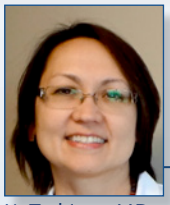

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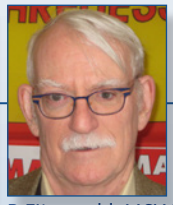

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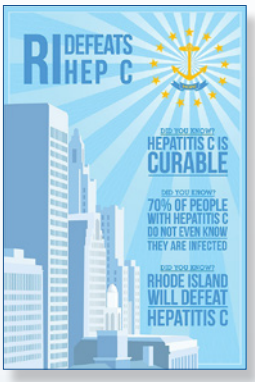


Cover image – Earlier this year, RI Defeats Hep C and renowned graphic artist and RISD grad Shepard Fairey named two winners of its poster design competition: Hayward H. Gatch, IV, whose image is on this month's cover of RIMJ, and Brandon Bruzzi.

Hepatitis C Virus Infection: From Margin to Center in Rhode Island and Beyond

Physicians, Research Scientists and Public Health Experts Collaborate to Combat Rhode Island's Hepatitis C Epidemic

LYNN E. TAYLOR, MD, FACP
GUEST EDITOR

KEYWORDS: Hepatitis C, Rhode Island

BACKGROUND

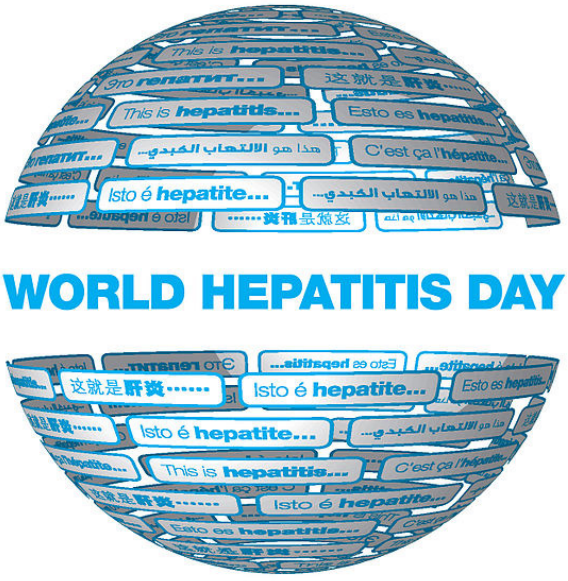
July 28 is World Hepatitis Day – in honor of Nobel Laureate Baruch Samuel Blumberg, MD, who discovered the hepatitis B virus (HBV), demonstrated it could cause liver cancer, developed the HBV vaccine, and implemented HBV vaccination worldwide. Each year on Dr. Blumberg's birthday, the World Health Organization (WHO) and partners acknowledge World Hepatitis Day to increase awareness of all types of viral hepatitis; strengthen prevention, detection and treatment; and promote action to improving access to care and control of these epidemics.

This year marks the convergence of many steps taken to address the global and national problem of hepatitis C virus infection (HCV). The WHO unveiled its first-ever HCV treatment guidelines.[1] The American Association for the Study of Liver Diseases/Infectious Diseases Society of America in partnership with the U.S. Centers for Disease Control and Prevention (CDC), developed HCV care recommendations.[2] The U.S. Department of Health and Human Services updated its Viral Hepatitis Action Plan.[3] Thus coinciding with World Hepatitis Day, this issue of the *Rhode Island Medical Journal* focuses on HCV, the biggest killer of Americans among the viral hepatidities.

More than 185 million people worldwide, 3% of the world's population, are living with HCV, of whom 350,000 die each year.[1] Three to 4 million people are newly infected annually. HCV is the most common chronic blood-borne infection in the U.S. Yet most people with HCV are unaware of their infection. Most individuals are asymptomatic when they become infected. They remain symptom-free for decades, during which time diagnosis will not occur without screening and the virus may be unknowingly be transmitted to others – until they develop severe liver disease including cirrhosis and liver cancer, and develop symptoms. This causes the "silent epidemic" we face today. HCV burdens healthcare systems due to high costs of treatment of end-stage liver disease and liver cancer. In the U.S., HCV is the leading reason for liver transplantation. Nevertheless, this epidemic has not been addressed in a comprehensive way in most locales.

HCV HISTORY

We have come a long way since 1957 when Alick Isaacs, a Scottish virologist, and his Swiss colleague Jean Lindenmann discovered interferon, a natural antiviral agent. This protein "interfered" with infections and cancers – thus their name, "interfer-on." Cynics dubbed their cytokine, "misinterpreton." Eventually interferon became the mainstay of HCV therapy. More than 50 years later we still use interferon alfa against HCV, HBV and melanoma.



In the 1970s, Harvey Alter, MD, at the National Institutes of Health (NIH), demonstrated that hepatitis acquired via transfusion was not due to hepatitis A or B. In 1987, Daniel Bradley, PhD, at the CDC, in collaboration with Chiron Corporation scientists, identified the virus. In 1988, Alter confirmed its presence in non-A, non-B hepatitis specimens. In 1989, the discovery of HCV was published in journal *Science*.[5,6] By 1992 the blood test was perfected that essentially eliminated HCV from the blood supply.

The first patients treated with interferon were cured in 1984 and 1985 before it was known that HCV caused their disease. Jay Hoofnagle and his NIH colleagues used interferon to treat patients with non-A, non-B hepatitis and observed normalization of hepatic enzymes.[7] It was not until 1991 that the U.S. Food and Drug Administration (FDA) approved the first alpha interferon, administered by subcutaneous injection three times weekly, to treat HCV.

Cure rates were abysmal – less

than 10% for genotype 1, which accounts for 75% of U.S. infections. By 1998, ribavirin, a nucleoside analogue active against some RNA and DNA viruses, with unclear mechanism of action, was approved for use with interferon, to be taken twice daily in pill form. Pegylation, the attachment of large polyethylene glycol (PEG) molecule to interferon, prolonged the half-life, reduced clearance and extended therapeutic action. The FDA approved the first once-weekly pegylated interferon in 2001. At this time, one was still considered a charlatan if you stated that HCV was curable.

Although cure rates remained low with PEG-interferon plus ribavirin, cure was established to be beneficial. HCV viral eradication decreases liver-related morbidity and mortality, as well as overall mortality. While there were many systems-, provider-, and patient-level barriers to treatment, interferon itself was central. Interferon is a "hard sell." Physicians must ask patients who feel well to take injections for up to a year. These may cause depression, suicidality, cytopenias, fatigue, flu-like symptoms, bacterial infection and permanent thyroid dysfunction and vision loss, to name a subset of potential adverse effects. Ribavirin causes a dose-dependent, reversible hemolytic anemia that has precipitated myocardial infarction, respiratory distress and death. Ribavirin is teratogenic for both women and men. Taking the time to evaluate and treat comorbidities to permit this therapy, manage co-existing disorders, shepherd patients safely through, manage side effects by titrating interferon and ribavirin doses and adding adjunct medications, is poorly reimbursed in our current medical system. Given the low efficacy, toxicity, poor tolerability, contraindications, dangers, extended duration of therapy and low reimbursement for providers, it is no wonder that a minority of patients have been treated and cured. Consequently, mortality from HCV in the U.S. has continued to increase and now exceeds that from HIV infection.[8]

DIRECT-ACTING ANTIVIRAL AGENTS (DAAs)

Cure rates with immune-modulating therapy remained stagnant until the advent of direct-acting antiviral agents (DAAs) in 2011. A better understanding of HCV's life cycle resulted in development of DAA pills that stop the virus' ability to copy itself. DAAs directly interfere with HCV replication by targeting viral proteins that inhibit enzymes and steps in viral replication. Combining DAAs from various classes yields consistent, astonishingly high cure rates (100% in some studies), brief treatment durations (perhaps 4 weeks within a few years), and vastly improved tolerability and safety. This transformative breakthrough in antiviral therapeutics is unprecedented; it is as if we are experiencing three decades of gradual improvements in antiretroviral therapies for HIV condensed into a few years. Four DAAs are now available; already the first two are obsolete in the U.S., supplanted by safer, more effective DAAs with simpler dosing schedules.

As of December 2013, we entered the era of interferon-free and ribavirin-free therapies. We now have a simple genotype 1 option of 2 pills, once daily, for 12 weeks, leading to cure in over 90% of patients. By the end of 2014, the FDA is expected to approve the first combination pill – one pill integrating 2 DAAs, once daily – to cure HCV. We are approaching ideal regimens with high-cure rates in all genotypes and subpopulations (interferon treatment-experienced, patients with cirrhosis), with minimal to no side effects. Physicians and patients alike must stay on top of the rapidly changing standard of care.[2] Treatment paradigms will continue to shift as new agents become available.

THE PROBLEM OF THE BABY BOOMERS

Screening with a blood test identifies people so they may be engaged in care and treatment, and evaluated for cirrhosis (Determining if a person has cirrhosis is always the first step in HCV

COMMENTARY

What price for a cure?

LYNN E. TAYLOR, MD

DAAs are not expensive drugs to manufacture. The high pricing of the new pills will limit their impact. Already payers are devising schemes to ration these potentially life-saving medications. Some algorithms are aligned with principles of distributive justice,[11] such as prioritizing patients with advanced liver scarring. Other rules support long-held prejudices and misperceptions rather than evidence-based science, about certain people with HCV being more deserving than others, about some subpopulations being more able to adhere to DAAs than others. Removing interferon from the treatment armamentarium will not eradicate barriers for people who use drugs and alcohol, for people who are poor and underinsured. We need advocacy from diverse stakeholders and political action to dismantle the hurdles that have been built over decades. We need experts to step up and participate. Otherwise, non-specialists in payer organizations and business people in medical organizations who prioritize lucrative types of medical practice, will make decisions about which patients we can treat.

DAA price reform will require social and political action. Some are already able to negotiate much lower DAA prices – countries with universal healthcare systems, countries with high disease prevalence. Egypt negotiated a deal whereby sofosbuvir, a pan-genotypic (effective against genotypes 1-6) DAA that may be used without interferon, costs 1% of the U.S. price. These issues go way beyond those of HCV. The U.S. bears research and development costs and pharmaceutical company profits for drugs for many diseases, while middle- and lower-resourced countries and nations with universal health care pay less. The pressure for lower drug prices must remain in the context of our promise to treat more patients. By lowering DAA prices to facilitate treatment for everyone in need, drug manufacturers

care). Baby Boomers who never suspected they were infected are now discovering their liver disease in advanced form. One in 30 U.S. Baby Boomers, those born from 1945-1965, has HCV, comprising 75% of the U.S. epidemic. In 2013, the CDC revised its guidelines to recommend 1-time screening for everyone born from 1945 to 1965, in addition to risk-based screening. The U.S. Preventive Services Task Force supports this recommendation.

CHALLENGES AHEAD

Excitement over the striking advances in therapeutics is tempered by concerns about challenges ahead. Without a parallel revolution in treatment delivery, HCV-related morbidity and mortality in the U.S will continue to rise.[9] Will we be able to treat enough patients in time to avert the looming disaster of early illness, suffering and death, as Baby Boomers infected in the 1960s–1990s progress to cirrhosis? Will we be able to treat enough patients in time to avoid the enormous costs of the complications of cirrhosis? "…treatment of half or all of HCV persons with these new agents would reduce cirrhosis by 15.2% and 30.4%, respectively, after just 10 years."[10] (*See Commentary: What Price for a Cure*?)

CONTRIBUTORS

This issue of the Journal features articles on various aspects of the RI HCV epidemic. We address key domains including epidemiology, prevention, screening, treatment, public health policy and advocacy.

Tackling HCV begins with understanding the scope of the problem. In, "Estimating the True Prevalence of Hepatitis C in Rhode Island," authors **ELIZABETH KINNARD, BA**; **OMAR GALÁRRAGA, PhD**; **BRANDON MARSHALL, PhD**, and I model the first estimates of the disease burden in our state.

Public health leadership and initiatives provide foundation for combating RI's HCV epidemic. "Prevention and Control of Hepatitis C in Rhode Island," by **NICOLE ALEXANDER-SCOTT, MD**; **ANGELA LEMIRE**, **H. ELSA LARSON, MA, MS**; and **UTPALA BANDY, MD, MPH**, delineates the RI Department of Health's commitment to addressing HCV.

The DAA drug pipeline is robust, with many DAAs under investigation. The rapid development of multiple classes of DAAs demonstrates that HCV research field has benefited from the arduous path of HIV therapeutics.[17] Who better to discuss, "Therapeutic Revolution in Antiviral Medications for Hepatitis C Virus Infection," than **KAREN TASHIMA, MD**, RI's leader in studies of antiretroviral agents for HIV.

An anti-HCV vaccine remains elusive. Incident HCV occurs due to nosocomial transmission. HCV outbreaks have occurred due to lack of infection control in U.S. healthcare facilities, primarily at ambulatory surgery centers.[18,19] HCV maintains infectivity for weeks after drying on inanimate surfaces at room temperature.[20] Most incident HCV in the U.S. is due to use of injection equipment contaminated with HCV. Evidence-based preventive interventions exist via needle exchange programs (NEPs). The Congressional ban on federal funding for NEPs has thwarted expanded preventive efforts. Providence is one of only 166 U.S. cities with a NEP. In, "ENCORE: Rhode Island's Needle Exchange Program," **RAYNALD JOSEPH, AARON KOFMAN, MD**; **SARAH LARNEY, PhD**; and **PAUL FITZGERALD, MSW**, focus on the history and current status of this critical prevention program.

In accordance with CDC recommendations, RI could and should become the first state to implement statewide HCV screening of Baby Boomers among primary care physicians using electronic medical records (EMRs). **ROLAND MERCHANT, MD, MPH, ScD**; **JANETTE BAIRD, PhD**; **TAO LIU, PhD**, and I, in, "Hepatitis C Seroprevalence among The Miriam Hospital and Rhode Island Hospital Adult Emergency Department Patients," consider one approach to RI HCV screening to date.

COMMENTARY continued

will receive less money per pill but will garner greater societal commitment to treat more individuals. When considering costs, we must consider the costs of not treating, costs of advanced liver disease, and costs of removing people at the prime of their lives from the workforce. As Harvard's Camilla Graham, MD, teaches us, we must use the metric of cost per cure when comparing DAA regimens.[12]

Eliminating HCV is technically feasible. Eliminating HCV can provide economic benefits, enhance capacity to address other health challenges, and ameliorate healthcare disparities.[13,14] Eliminating HCV is likely going to be cost-effective, but up-front resources will be needed.[15,16] Barriers to eliminating HCV in the U.S. include lack of NIH funding earmarked for HCV research, sparse federal funding for HCV prevention and care, underinsured and disenfranchised populations disproportionately affected by HCV, and low reimbursement for HCV care. How will we build the infrastructure to get the new drugs to the people who need them? How will we utilize scientific breakthroughs to benefit those in need? Rational decision-making requires change at the governmental, health systems, pharmaceutical industry and payer levels. For example, the ban on Medicare negotiating drug prices means that Baby Boomers will overpay. The crisis over DAA costs should prompt deliberate, thoughtful discourse and plans about what to do about HCV in RI, and stimulate development of a business case for a cost-saving HCV model. ❖

Acknowledgments

I appreciate the opportunity to edit this Special Edition of the *Rhode Island Medical Journal*. Many thanks to Edward R. Feller, MD; Journal editors, and my many HCV patients over the years. I admire your perseverance. I am sorry and sad for those who died prematurely of preventable liver disease. As Stephen Shwartz wrote in the song, *For Good*, "But because I knew you, I have been changed for good."

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Disclosures

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'C' is for Cure: A WaterFire Lighting for RI Defeats Hep C

Saturday, July 26
Full Lighting – Sunset 8:11 pm

Please join us for this special WaterFire on Saturday, July 26. We will raise awareness; build Community, Connection, Cooperation and Camaraderie around HCV; help diminish stigma; inspire those living with HCV to seek cure; and have a family-oriented, artistic, musical, creative, enchanting, free summer night out on the town. This Waterfire will include entertainers, food, music and HCV testing. WaterFire Providence is an independent, non-profit arts organization whose mission is to inspire its visitors by revitalizing the urban experience, fostering community engagement and creatively transforming the city. WaterFire centers around the installation of 80 bonfires floating on Providence's rivers, with 65,000 people attending each WaterFire event.

Estimating the True Prevalence of Hepatitis C in Rhode Island

ELIZABETH N. KINNARD, BA; LYNN E. TAYLOR, MD; OMAR GALÁRRAGA, PhD; BRANDON DL MARSHALL, PhD

ABSTRACT

Although there is a large health, social, and economic burden of hepatitis C virus (HCV) infection in the United States, the number of persons infected with HCV in Rhode Island (RI) is unknown. To inform the expansion of HCV-related public health efforts in RI, and because surveillance data are lacking and national surveys, including the National Health and Nutrition Examination Survey (NHANES), likely underestimate true HCV prevalence, we reviewed published peer-reviewed and grey literature to more accurately estimate the prevalence of HCV in RI. The results of our review suggest that between 16,603 and 22,660 (1.7%–2.3%) persons in RI have ever been infected with HCV. Assuming a spontaneous clearance rate of 26%, we estimate that between 12,286 and 16,768 (1.2%–1.7%) have ever been or are currently chronically infected with HCV. Findings suggest the urgent need for improved HCV screening in RI, and that reducing morbidity and mortality from HCV will require a dramatic scale-up of testing, linkage to care, treatment and cure.

KEYWORDS: Hepatitis C, HCV, epidemiology, prevalence, Rhode Island

INTRODUCTION

Hepatitis C virus (HCV) infection is the most common chronic blood-borne infection in the United States.[1–5] If left untreated, chronic HCV infection can lead to cirrhosis, hepatocellular carcinoma, liver failure, and death.[1,2,6,7] Because new HCV infections are typically asymptomatic, most go undiagnosed until chronic HCV causes morbidity such as liver-related complications.[6] These advanced stages of disease are when screening for chronic HCV typically occurs, and when the majority of cases are first made known to the healthcare system.[3] Most Americans remain unaware of their infection status and are not receiving appropriate care and treatment.[8]

Currently, deaths due to HCV in the U.S. are higher than those due to HIV.[9] Cirrhosis resulting from chronic HCV is the leading cause for liver transplant,[10] and the subsequent effect on healthcare utilization is high.[3,11] A significant number of HCV-infected persons are now reaching an age when liver complications may start to develop, and multiple studies have predicted a rise in future HCV-related morbidity and mortality rates.[2,12–15] HCV infection is disproportionally represented among marginalized populations, particularly those under-represented in health surveillance programs and underserved by the healthcare system.[5] Specifically, chronic HCV signifies a public-health challenge due to its higher prevalence among groups such as middle-aged African-American men, hospitalized patients, individuals with serious mental illness, prisoners, people who are homeless, people living with HIV, and people who inject drugs (PWID).[5,7]

In RI, the true number of prevalent chronic HCV cases is unknown. Preventing new cases of HCV, improving access to HCV testing, screening, and diagnosis, as well as identifying those chronically infected and linking them to curative treatment, are urgent matters of public health. HCV treatment leading to viral eradication – termed sustained virologic response (SVR), defined as undetectable HCV RNA 12 weeks post-treatment – reduces liver-related morbidity and mortality, as well as all-cause mortality.[16,17] By estimating the true prevalence of chronic HCV in RI, specifically focusing on groups under-represented by or excluded from nationally representative surveys including the National Health and Nutrition Examination Survey (NHANES), the objective of this paper is to inform intervention efforts to better manage and improve assessment and treatment for HCV in the state.

METHODS

We adapted a method used in previous epidemiological studies to identify groups under-represented by or excluded from the NHANES (survey years 2007–2008).[18,19] The method focused on determining HCV infection prevalence in high-risk groups not captured by the NHANES. Specifically, these groups include persons who are: homeless, incarcerated, residing in nursing homes, on active military duty, on long-term hemodialysis, recipients of chronic blood transfusions before 1992 (i.e., hemophiliacs), veterans, healthcare workers, and persons who inject drugs. Of these groups, only PWID were found to be accurately represented in the NHANES, as the estimated prevalence of 57.5% appeared to be a reasonable estimation of the true HCV prevalence among PWID, falling within the range of the studies available in the literature, from 27% to 93%.[18]

We reviewed published, peer-reviewed studies as well as grey literature to estimate the HCV prevalence among these subpopulations in RI, as well as how many people are estimated to belong to each group in the state. Whenever possible, we used RI-specific point-estimates for the total numbers of individuals in each subpopulation to estimate how many people are currently HCV antibody-positive. Using a point-prevalence methodology, rather than period-prevalence, aided in avoiding double counting across groups. For example, someone who was counted as incarcerated in RI at a specific point in time would not also be counted as homeless; this prevents double counting across the two groups.

As a first step, we estimated the RI-specific population size for each group under-represented by or excluded from the NHANES.[18,19] When searching grey literature to determine the population sizes in RI, if only one source was available, we used that one estimate for all subsequent calculations. If more than one estimate was available, we computed an average to more accurately capture the number of individuals in that group. Specifically, the population size of homeless persons was estimated from reports published by Opening Doors RI and RI Coalition for the Homeless;[20,21] the incarcerated persons estimate was obtained from the RI Department of Corrections;[22] the veterans estimate was obtained from the United States Department of Veterans Affairs and the RI Department of Human Services (Division of Veterans Affairs);[23,24] the active military duty count was taken from the U.S. Census Bureau (National Security and Veterans Affairs);[25] the healthcare workers estimate was taken from the Kaiser Family Foundation and RI Department of Labor and Training;[26,27] the nursing home residents estimate was taken from the Kaiser Family Foundation and SkilledNursingFacilities.org;[28,29] the number on chronic hemodialysis was estimated from personal correspondence with Douglas Shemin, MD, (medical director of two dialysis clinics in RI);[30] and the number of hemophiliacs with transfusions before 1992 was calculated by taking RI's percentage of the total U.S. population (0.335%) and multiplying it by the estimated range of HCV cases for this group in the U.S. population.[18]

Second, after the population size for each group was estimated, we searched peer-reviewed and grey literature to obtain group-specific estimates for HCV prevalence. RI-specific HCV prevalence estimates were available for the following subpopulations: incarcerated persons, veterans, and individuals on chronic hemodialysis (see references in **Table 1**). For the remaining subpopulations, we used ranges provided in a recently published national review of HCV prevalence in these groups.[18,19]

Third, to calculate the number of HCV cases in each subpopulation of interest, we multiplied each population size by the range of group-specific HCV prevalence estimates (see **Table 1**). Once the range of HCV cases in RI was calculated, we added these totals to the NHANES estimate for RI (i.e., 1.3% HCV prevalence among individuals above age 5). With regards to veterans, the NHANES study appears to have underestimated the prevalence of HCV in this population.[2,18] To correct this, Chak et al. calculated a revised estimate of HCV prevalence in veterans based on previously published epidemiological studies, and subtracted the number of HCV cases attributed to veterans reported by the NHANES before adding the revised estimate to prevent double counting.[18] We adopted this approach, subtracting 1,835 veterans from the NHANES total estimate of 12,944 HCV cases in RI before adding in our own calculation for veterans.

Fourth, given the observed racial disparities in HCV prevalence in the United States,[31] we conducted indirect standardization by race to adjust the RI-specific NHANES estimate, as RI differs notably from the national population in terms of race and ethnicity.[32] As RI does not differ greatly from the national estimates in terms of age structure, we did not conduct age-standardization calculations.

Finally, to determine the number of people who have ever been or are currently chronically infected with HCV in the state, we assumed, consistent with basic HCV biology, that approximately 26% of persons ever exposed to HCV would spontaneously clear the virus within the first six months of infection.[33] To improve the precision of the estimated rate of spontaneous viral clearance, a systematic review was conducted of longitudinal studies. Factors associated with viral clearance were also examined. Inclusion criteria for studies were: longitudinal assessment from time of acute HCV; HCV RNA analysis as determinant of viral clearance; untreated for acute HCV. Information on study population, and factors that may influence viral clearance were extracted from each study. Viral clearance was defined among individuals with at least 6 months follow-up following acute HCV. The number of subjects with viral clearance was expressed as a proportion for each study and a weighted mean for proportion was calculated. A total of 31 studies were examined. Study populations included nine studies of post-transfusion hepatitis, 19 of acute clinical hepatitis, and three of seroincident cases. In total, data was available for 675 subjects and the mean study population was 22 (range 4-67). This means that these individuals remain HCV Ab-positive by blood tests, but no longer have chronic HCV infection, do not have HCV RNA in the blood, are not infectious to others, but can be re-infected. We applied this proportion to the total number of HCV-infected persons in RI (both before and after race standardization).

RESULTS

Prevalence Estimates in Rhode Island

The estimated range of HCV prevalence and population size for each group under-represented by or excluded from the NHANES is shown in **Table 1**. As shown in the table, we estimate that between 5,811 and 11,868 HCV cases in RI would be unaccounted for by the NHANES.

The total number of HCV cases in RI (estimated by the NHANES and from our review) is shown in **Table 2**. As shown

in the table, approximately 16,603 to 22,660 individuals are estimated to be HCV antibody-positive in RI, corresponding to an overall prevalence of 2.0% (range = 1.7% to 2.3%) in the state. Assuming a 26% spontaneous clearance rate, there are approximately 12,286 to 16,768 individuals who have ever been or are currently chronically infected in RI, corresponding to an overall prevalence of approximately 1.5% (range = 1.2% to 1.7%). Using the race-adjusted estimates for HCV cases (HCV antibody-positive), our calculations indicate that the NHANES estimate of 1.3% in the state likely underestimates the true population of HCV-infected persons by about 6,000 to 12,000 cases.

Table 1. Estimated total prevalence of hepatitis C in RI for populations under-represented by or excluded from the NHANES (RI population in 2012 above age 5 = 995,677)

Population	HCV Prevalence	Point-estimate of Population Size in RI	Estimated Range of HCV Cases in RI
Homeless	22.2%–52.5%[35–40]e	1048[20,21]	233–550
Incarcerated	20.0%–25.0%[41,42]	3191[22]	638–798
Veterans	5.40%–10.7%[43–49]	73420[23,24]	3965–7856
Active Military Duty	0.48%[50]V	1490[25]	7**
Healthcare Workers	0.90%–3.60%[51–61]	59894[26,27]	539–2156
Nursing Home Residents	4.50%[62]	8040[28,29]	362**
Chronic Hemodialysis	2.30%–7.90%[30]	1041[30]	24–82
Hemophiliacs with Transfusions Before 1992	76.3%–100%[63–6]	*	43–57
		Total	**5811–11868**

*We estimated the R.I. range of HCV cases for "hemophiliacs with transfusions before 1992" by taking R.I.'s percentage of the total U.S. population (.335%) and multiplying it by Chak's estimated range of HCV cases for this group in the U.S. population.

**We did not report ranges of HCV cases in instances where only one reference was available for the HCV prevalence of the subpopulation.

Table 2. Estimated total number of hepatitis C cases in Rhode Island

Unaccounted # of HCV Antibody Positive in RI from Table 1	5811–11868		
***Total # of HCV Positive in RI Estimated by NHANES**	11109*		
Total # of HCV Positive in RI Estimated by NHANES, Race Adjusted	10792		
Total RI HCV Cases (HCV Antibody +)	16920–22977	**Chronically Infected in RI**	12521–17003
Total RI HCV Cases, Race Adjusted (HCV Antibody +)	16603–22660 (1.7%–2.3%)	**Chronically Infected in RI, Race Adjusted**	12286–16768 (1.2%–1.7%)

*Original NHANES estimate minus HCV cases attributed to veterans (12944 total – 1835 veterans)

DISCUSSION

Our prevalence estimate of approximately 2.0% of the RI population ever infected with HCV (HCV antibody-positive) highlights the underestimation of national surveys, including the NHANES, but is consistent with recently published national estimates that seek to account for under-represented populations.[18,19] In the state, surveillance systems also fail to capture many acute and chronic HCV cases. Missed diagnoses are extremely common; acute HCV is a silent infection due to the fact that most individuals are asymptomatic, or have symptoms that are mild and non-specific. Similarly, chronic HCV is clinically silent in most infected individuals until late stages.[6] When assuming a spontaneous 26% clearance rate,[33] we determined that approximately 1.5% of RIers above 5 years old have ever been or are currently chronically infected with HCV. If left untreated, many of these individuals could experience health problems including but not limited to cirrhosis, hepatocellular carcinoma, liver failure, and death.[1,2,6,7] At the same time, these individuals could infect others, perpetuating the HCV epidemic in the state.

This study is subject to a number of limitations. First, wherever possible, we used RI-specific subpopulation and HCV prevalence estimates to conduct the most accurate calculation of total persons infected in the state. However, we were unable to capture RI-specific estimates for the HCV prevalence for every subpopulation of interest, as well as point estimates for the total number of state residents belonging to each population. Therefore, calculations may be inaccurate when using national estimates and applying them to the RI population, as the inhabitants of the state may have different characteristics than the national average. Second, it is possible that we "double counted" individuals who may belong to more than one subpopulation excluded or under-represented by the NHANES. However, we made our best attempt at preventing double counting by using point-estimates for population sizes wherever possible. Third, we used the HCV prevalence estimate from the NHANES 2007-2008 dataset rather than the NHANES 2011-2012, which only very recently became available. However, the overall HCV prevalence reported in both surveys is very similar (i.e., 1.3%); thus, we expect the older NHANES data to provide a reasonably accurate estimate of current prevalence. We likely underestimated the number chronically infected by using a conservative estimate of 26% spontaneously resolving infection. For example, at

RI's needle exchange program and amongst HIV-infected persons, spontaneous clearance rates are considerably lower at 16%. Finally, although HCV prevalence is elevated among some immigrant groups, neither the NHANES nor we were able to consider country of origin in our estimates. Thus, we may have underestimated prevalence among a number of immigrant groups residing in RI who may be disproportionately represented (e.g., Egyptians, Pakistanis, Taiwanese).[34]

In order to "test and treat this silent killer,"[5] the results of this work demonstrate that RI public health professionals and the medical community must scale up screening and respond to the medical needs of those who are infected with testing, counseling and curative treatment to avert preventable morbidity and mortality. Coordinated approaches to prevention and treatment of HCV in RI are imperative. HCV screening should be accompanied by education about prevention, transmission, natural history, and evolving therapies. The availability of new oral therapies for chronic HCV, with improved tolerability and efficacy, and the movement away from interferon-based regimens, are very promising. Given the high upfront investment costs of these therapies at the individual and population levels, research studies on the economic efficiency and potential cost savings in the long term are urgently needed.

In summary, our findings support the need for greatly expanded public health efforts for prevention, screening and diagnostic testing, liver wellness counseling, and treatment of HCV-infected individuals, as recommended by the CDC.[8] Further research is being conducted to determine the cost-effectiveness of new direct-acting antiviral therapies, as well as implementing and evaluating cost-efficient models of linking individuals infected with HCV in RI to care.

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Prevention and Control of Hepatitis C in Rhode Island

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ABSTRACT

Concern about the morbidity and mortality of hepatitis C infection is increasing. Persons born from 1945 to 1965 are most significantly affected, with the majority unaware of their infection, and will otherwise go untreated. Up to three-fourths of hepatitis C-related deaths occur in this population of "baby boomers." Since 2007, mortality from hepatitis C has exceeded that from HIV, nationally and in Rhode Island. New treatment options for hepatitis C emphasize the potential for cure of hepatitis C that is distinct from HIV. Financial resources and integration of hepatitis C partners and services in Rhode Island will be instrumental in reducing hepatitis C infections and increasing the number of cases cured. We describe public health investments in the past, present, and future to implement strategies for effectively addressing hepatitis C in the state.

KEYWORDS: Hepatitis C, Curative therapy, Rhode Island, Social marketing campaign

INTRODUCTION

Hepatitis C virus is a chronic blood-borne pathogen with a slow progression of illness that is often unrecognized until liver damage is severe. In the United States (US), approximately, 3.2 million people (~1% of the population) are chronically infected with hepatitis C and most (up to 75%) are unaware of their infection.[1-3] The burden of hepatitis C in the US exceeds the burden of HIV, currently estimated to be 1.1 million people, with only 16% of those with HIV unaware.[4-6] Among all the people living with hepatitis C in the US, 75% are "baby boomers" or people born between 1945 and 1965, who make up only 27% of the population.[7,8] About 15,000 people die each year from hepatitis C, and "baby boomers" represent more than 70% of hepatitis C-related mortality.[8,9] Research indicates that hepatitis C mortality estimates are expected to triple over the next eight years.[10-12] Similarly, without increased detection and improved access to treatment for hepatitis C, costs associated with hepatitis C care may increase over the next 20 years from $30 billion to $85 billion per year.[13] The impending tsunami of hepatitis C cases and costs requires increased recognition, funding, and public health intervention at the national and local level.

A helpful model for addressing hepatitis C from a public health perspective is to replicate the stages of the HIV care continuum first described by Gardner et al[14] to quantify key components of hepatitis C care engagement and target resources accordingly.[15,16] Using data from two large national surveys, researchers estimated the following: 1) the number of people infected with hepatitis C in the United States (3.2 million), 2) the proportion of infected individuals that are diagnosed and aware of their hepatitis C infection (50%), 3) the proportion of persons infected with hepatitis C who were referred to care (32–38%), and d) the proportion of persons infected with hepatitis C who were successfully treated (5–6%).[17] New FDA-approved hepatitis C therapies (Direct-Acting Antiviral Agents [DAAs]) are now available that can cure hepatitis C in over 70–80% of persons infected, with imminent cure rates of 90–100% with soon-to-be-approved DAAs.[10,18] These new regimens have the potential to significantly reduce morbidity and mortality, and prevent further transmission, but only if hepatitis C provider capacity is in place with integrated services to support case management and retention in care that will lead to cure. Findings from the hepatitis C continuum underscore the public health need for persons with hepatitis C to gain access to effective care, and to successfully treat and cure each person.

In Rhode Island (RI), the number of hepatitis C infections reported by the Rhode Island Department of Health (HEALTH) for 2007–2008 exceeded HIV cases by more than 7-to-1 (compared to an estimated national ratio of 5-to-1), indicating a higher rate of hepatitis C infection in RI than in the rest of the country. HEALTH estimates for the burden of hepatitis C disease in RI cite prevalence to be approximately 11,000 cases, with modeling studies estimated to be between 12,286 and 16,768 cases.[19]

PUBLIC HEALTH INVESTMENTS ON THE PREVENTION AND CONTROL OF HEPATITIS C IN THE RECENT PAST

Before 2013, there was little federal or state funding specific to hepatitis C prevention and control efforts, which restricted statewide capacity to advance comprehensive surveillance and case management. Hepatitis prevention activities were successfully integrated with HIV-prevention activities, and have focused on the steady expansion of bundled hepatitis C and HIV testing throughout RI. Since 2001, HEALTH has supported funding for community-based integrated

prevention services that have included education and counseling (integrated with HIV counseling, testing, and referral), community-based syringe exchange programs, and hepatitis A and B vaccination for persons who inject drugs and for men who have sex with men. By 2002, hepatitis A and B vaccination programs were expanded throughout the state, and new sites included a gay bath house, sexually transmitted disease clinic, a homeless shelter, and a substance abuse treatment facility. A subsequent increase in vaccination rates was noted by 2005; however, no similar targeted intervention (vaccine) currently exists for hepatitis C.

A Viral Hepatitis Advisory Group of over 60 community members was convened in 2008, with the objective of establishing a statewide coalition of partners to develop and implement a strategic plan. The Group published a, "*Comprehensive Strategic Plan for the Prevention and Control of Viral Hepatitis in Rhode Island*."[20] An overall goal from this initiative was to "gain a better understanding of viral hepatitis prevention, control, and medical care resource needs for people living with the disease and the providers who serve them."

A subcommittee of this Advisory Group successfully developed and implemented a perinatal hepatitis prevention plan. Perinatal medical providers collaborated with the RI Immunization Program to identify women infected with hepatitis B or C early in their pregnancy in order to assure referral to care, appropriate management during pregnancy, and postpartum care for their newborns.

Another subcommittee worked on and published a, " RI Viral Hepatitis Resource and Services Directory" intended for use by a wide range of care providers in the community such as RI clinical providers, substance abuse counselors, and school nurse teachers. The Directory included contact information for hepatitis C resources such as treatment providers, support groups, syringe exchange programs, substance use treatment facilities, and included factsheets about viral hepatitis and HIV/hepatitis C co-infection.

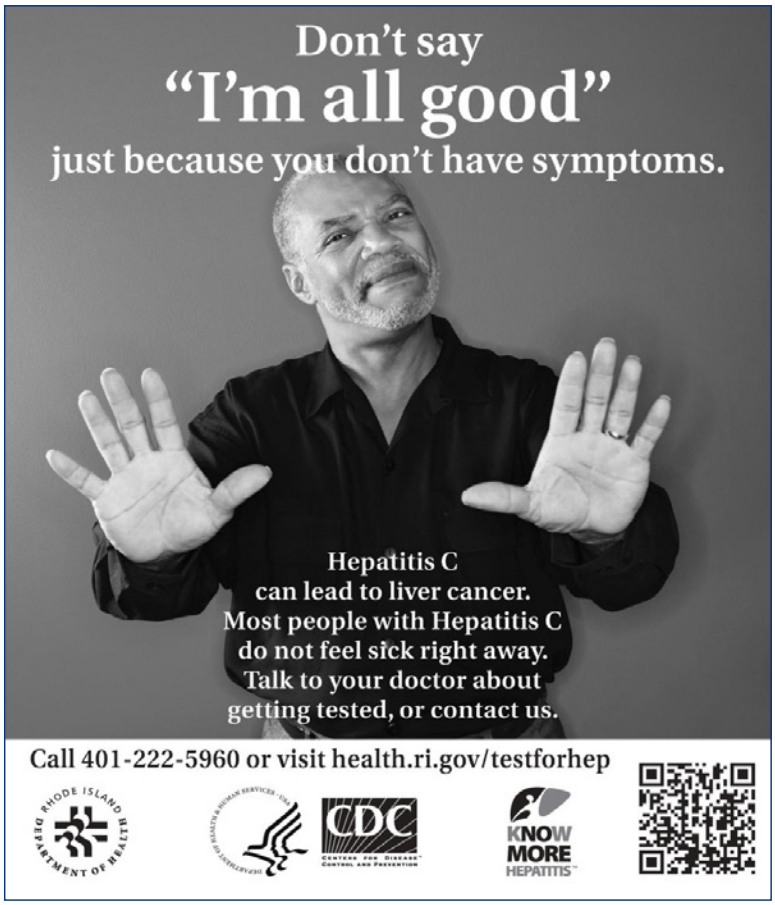
Provider and public education are a cornerstone of prevention. Since 2001, over 83 presentations have been provided throughout RI to engage and educate over 3,000 stakeholders in hepatitis C prevention and care including physicians, nurses, substance abuse treatment counselors, community outreach workers, and hepatitis C consumers.

CURRENT PUBLIC HEALTH ACTIVITIES FOR HEPATITIS C IN RI

The Centers for Disease Control and Prevention (CDC) provided HEALTH with funding in 2013 to conduct a social marketing campaign to increase public awareness and promote hepatitis C testing for all "baby boomers," in keeping with the latest screening guidelines.[8] The multimedia campaign launch coincided with National Hepatitis C Testing Day on May 19, 2013 and ran through October 2013. Messaging emphasized that an estimated 11,000 Rhode Islanders of all ages are infected with the hepatitis C, with many people unaware of their status. Campaign ads stated that "all Rhode Islanders born between 1945 and 1965 should be tested for hepatitis C at least once or more often if they have known risk factors. Also, "baby boomers" are five times more likely than others to be infected with hepatitis C, and often have no symptoms."

The social marketing campaign utilized iconic imagery with broad, universal appeal specific to the "baby-boomer" generation (e.g., man on the moon, cassette tape, disco ball). The "Born 1945-1965?" ad prompted self-identification for hepatitis C risk while others stated that " 'baby boomers' are 5 times more likely to be infected with hepatitis C." (**Figure 1**)

Figure 1. Examples of bus shelter ads targeting populations at risk for undiagnosed hepatitis C infection (1a) and newspaper print ads for Rhode Island-specific audiences (1b).



The campaign adopted existing CDC messaging for the targeted RI audiences, utilizing radio, print, and online ads, as well as exterior bus ads, bus shelters, and billboards. Billboard and bus shelter ads were placed near methadone clinics and drug treatment centers to geo-target high-risk populations who inject drugs. Spanish-language ads and culturally appropriate ads were also utilized. Online ads were placed on the AARP website, Google news, and topical websites. All ads drove audiences to the HEALTH webpage that lists free and low-cost hepatitis C testing sites, and provides more resources, including a CDC hepatitis risk-assessment questionnaire.

Web-based tools and other related guidance were shared with RI's physician community via the HEALTH website and in HEALTH Connections, the agency's monthly e-newsletter. Updated information, such as the list of insurers in RI that cover hepatitis C antibody testing, in order to most effectively test all patients born between 1945 and 1965 continues to be shared with providers as they become available.

In RI, four counseling, testing, and referral sites report hepatitis C testing statistics to HEALTH. Data from 2013 show that prior to the campaign launch (i.e., January–April), a total of 466 hepatitis C rapid tests were conducted, with 10 new cases of hepatitis C identified. By comparison, after the campaign launch (i.e., May–August), hepatitis C testing nearly doubled to 841 tests conducted, with 33 new cases of hepatitis C identified. As the campaign was expanded to Google ads targeting more "baby boomers," the apparent upswing of hepatitis C testing continued, with another 771 tests conducted and 41 additional new cases of hepatitis C identified between September and December of 2013.

When compared to web traffic during the previous year with no active campaign, Google analytics showed that traffic to the same hepatitis C webpage increased by 1,159% from May through August, with 856 unique visitors (UVs) in 2013 compared to 68 UVs in 2012. Similarly, from September to December of 2013, the webpage saw a 1,648% increase in UV traffic, with 909 UVs in 2013 compared to 52 in 2012 during the same four-month reporting period. Evidence for the effectiveness of the social marketing campaign was also supported by a decrease in webpage hits from more than 100 daily visits to nearly zero as soon as the hepatitis C radio ads ceased.

Additionally, HEALTH has fostered collaboration with hepatitis C partners to help promote similar prevention, treatment, and awareness campaigns. HEALTH has expressed support for the Rhode Island Innovation Fellowship initiative, RI Defeats Hep C (http://ridefeatshepc.com) which provides extensive resources to improve hepatitis C testing and treatment services, direct stakeholders to important links, and raise awareness for targeted communities. HEALTH also helped to promote the May 2014 RI Defeats Hep C conference to statewide providers, and participated in the conference as a co-facilitator and panelist for in-depth discussions on the diagnosis and management of patients with hepatitis C infection.

FUTURE DIRECTIONS TO REDUCE HEPATITIS C IN RI

The advent of DAAs recently approved by the FDA is a game changer for strategic approaches to hepatitis C control through treatment to cure. While providers, patients, and HEALTH have recognized the significance of hepatitis C disease, the timing to increase engagement with insurers cannot be any more crucial than right now because of the cost burden of hepatitis C prevention and care.

The continuum of care analogy for hepatitis C is a helpful frame of reference because it highlights how critical it is for organizations, agencies, and advocates to jointly contribute to the public health efforts that range from education about hepatitis C care for providers, to maintaining adequate hepatitis C provider capacity, and access to curative hepatitis C therapy with integrated services for care. HEALTH must partner with stakeholders who are committed to addressing aspects of the hepatitis C continuum that will most effectively result in curing as many cases of hepatitis C as possible.

Goals for RI to tackle hepatitis C at the public health level can be taken not only from the foundation laid in the Comprehensive Strategic Plan for the Prevention and Control of Viral Hepatitis in Rhode Island[20] and from the recently published National Action Plan for the Prevention, Care, and Treatment of Viral Hepatitis – Updated 2014-2016,[18] but also from such literature as Mehta et al[21] who emphasizes strategies that address barriers along the continuum at the patient, provider, and structural levels – in order to effectively achieve the goal of hepatitis C viral clearance. A few of the key target objectives to highlight for RI to reduce hepatitis C infections include, but are not limited to:

1. Increasing education, counseling, and harm reduction activities that target individuals at risk for infection with hepatitis C
2. Expanding hepatitis C provider capacity and integrated services that increase potential to cure
3. Improving access to care and improving quality of care and treatment for persons infected with hepatitis C
4. Conducting surveillance to monitor all stages of the continuum of care and to provide meaningful population-based metrics to guide policy

HEALTH looks forward to working together with hepatitis C partners throughout the state to coordinate public health efforts and reach the goals that will reduce hepatitis C infections in RI.

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Q & A with Karen Tashima, MD

New Direct-Acting Antiviral Agents Offer Therapeutic Revolution for Hepatitis C Virus Infection

MARY KORR
RIMJ MANAGING EDITOR

MARY KORR

Dr. Karen Tashima, Professor of Medicine in the Division of Infectious Diseases at Brown, stands by a painting in her office, a memento of her years as ID Fellowship Director, 2005-2012, presented to her by the Infectious Disease Fellows last year.

PROVIDENCE – Hope is here for the estimated 5.2 million persons[1] in the United States with chronic hepatitis C virus (HCV) infections. Twenty-five years after the identification of the virus through cloning techniques, revolutionary direct-acting antiviral agents (DAAs) offer the promise of a cure for a significant number of those affected.

Dr. Karen Tashima, Site Director of HIV Clinical Studies and Clinical Research Site Leader of the AIDS Clinical Trials Unit at The Miriam Hospital, is also a principal investigator in studies of these new DAA medications. In addition, she is engaged in follow-up studies with those patients whose virus been eradicated to make sure it is cured for the long-term; there are also two trials underway at Miriam for HIV-HCV co-infected patients.

Recently Dr. Tashima discussed these revolutionary therapeutic agents and the economic challenges they present.

Q. The mainstay of care to treat HCV infection has been interferon and ribavirin. Do the new direct-acting antivirals (DAAs) replace that?

A. There had been incremental advances in the treatment of HCV with interferon, such as giving injections in the pegylated form once a week, rather than injections three times a week. Then ribavirin came along and increased a patient's chance of cure. Cure rates were still pretty low, around 50 percent. But only 10-20 percent of patients with HCV infection could be cured if they also had HIV infection.

We've been waiting a long time for direct-acting agents. Interferon is poorly tolerated in many people, with side effects such as flu-like symptoms, often resulting in time loss from work. There are also contraindications in the use of interferon in patients with significant cardiac, pulmonary, and psychiatric diseases such as uncontrolled depression, or in poorly controlled diabetes.

Understanding how well these DAAs work, and if we still need to use pegylated interferon and ribavirin, is what we are investigating. Studies are underway testing different genotypes and different combinations of drugs. So, for example, in patients with genotypes 1-4, the FDA has approved the DAA Sovaldi (sofosbuvir) to be given with pegylated interferon and ribavirin for 12 weeks. For a sub-group of patients, the FDA approved sofosbuvir for genotype 1 and 4 patients even without interferon. For patients with genotypes (2 and 3), Sovaldi can be given with ribavirin alone for a high rate of cure.

Q. Are different DAAs combined in treatment protocols?

A. These are really targeted designer medications. The first one to be FDA-approved was Sovaldi (sofosbuvir) made by Gilead Sciences. We have a study going on now with Gilead combining different oral agents. We are also working with Bristol-Myers Squibb (BMS) on a drug called daclatasvir and combining that with other drugs. And Abbott has a three-drug regimen that we think will be approved by the FDA within this year.

Q. Can DAAs be used in people with hepatitis C-related liver cancer, advanced liver disease, or after liver transplant?

A. We're prioritizing the patients who have advanced liver disease, such as stage 3 or 4 fibrosis, and those who are most at risk for liver failure. Some of the DAAs, such as sofosbuvir, are safe in people with advanced liver disease, including decompensated cirrhosis, while awaiting liver transplant. If we cure the hepatitis C we might prevent liver cancer. The FDA approved sofosbuvir for use in patients with hepatitis C-induced liver cancer. If a patient needs a liver transplant, the DAAs are used to prevent hepatitis C from coming back in the newly transplanted liver.

Q. What are the prospects for the development of an HCV vaccine?

A. Currently there is no effective vaccine but researchers are investigating possible approaches.

Q. According to the Centers for Disease Control (CDC), more than 75% of adults infected with HCV are Baby Boomers, people born from 1945 through 1965. Why is the highest prevalence in this cohort?

A. Before hepatitis C was identified, the disease was called non-A, non-B hepatitis.

Non-A, non-B was transmitted through unsafe blood transfusions before widespread screening of the blood supply, through high-risk behaviors such as injection drug use; and there were transmissions in the healthcare settings back then, before widespread institution of universal precautions. With screening of the blood supply and safe infection control practices, we avoid HCV transmission in the healthcare setting.

Q. What should practicing physicians know about HCV?

A. It's a reflex for doctors to check for hepatitis A, B, C when they see elevated liver enzyme levels. But people can be fully asymptomatic for 20-40 years, and may even have normal liver-related blood tests. The only hint might be the appearance of cirrhosis. Knowing which patients should be tested is important. (*See sidebar.*) The hepatitis C antibody test is

the first you should do. If it comes back positive there is a specific RNA test for the virus to identify patients with chronic hepatitis C infection (as opposed to prior infection and clearance of the virus spontaneously or due to prior effective therapy).

Q. There has been controversy about the cost of these DAAs – as much as $1,000 a pill. A combination of these agents could double or triple the price. What are your thoughts on this?

A. There are a lot of companies working on hepatitis C treatment, and with more competition hopefully the prices will come down. It's very early on with the hepatitis C drugs and I think insurance companies will help pay for the cost. We are talking about three months of treatment and that's it. The downside of not treating HCV is expensive care for complications of liver failure, need for liver transplantation, or death.

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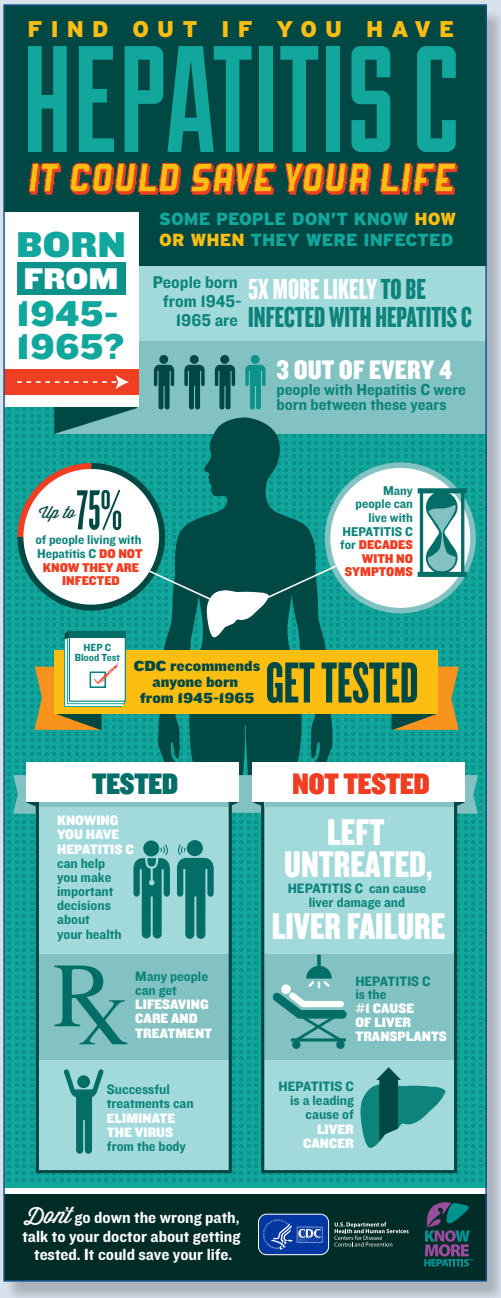

WHO SHOULD BE TESTED?

Routine testing of asymptomatic persons:

Persons who should be tested once for hepatitis C virus (HCV) infection without prior ascertainment of HCV risk factors include:

- People born during 1945 through 1965

Persons who should be tested routinely for hepatitis C virus (HCV) infection based on their risk for infection include those who:

Currently inject drugs

Ever injected drugs, including those who injected once many years ago

Have certain medical conditions, including persons:

- who received clotting factor concentrates produced before 1987
- who were ever on long-term hemodialysis
- with persistently elevated alanine aminotransferase levels (ALT)
- infected with HIV

Were prior recipients of transfusions or organ transplants, including persons who:

- were notified that they received blood from a donor who later tested positive for HCV infection
- received a transfusion of blood, blood components or an organ transplant before July 1992

Persons who should be tested routinely for HCV-infection based on a recognized exposure:

- Healthcare, emergency medical, and public safety workers after needle sticks, sharps, or mucosal exposures to HCV-infected blood
- Persons who have received medical or dental interventions in health care settings where infection control practices are substandard
- Persons who have received blood in countries where serological testing of blood donations for HCV is not routinely performed
- Persons who have had tattoos, body piercing or scarification procedures done where infection control practices are substandard
- Children born to mothers infected with HCV
- Persons who have used intranasal drugs
- Prisoners and previously incarcerated persons

(Source: CDC) http://www.cdc.gov/hepatitis/HCV/GuidelinesC.htm

Hepatitis C Prevention and Needle Exchange Programs in Rhode Island: ENCORE

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ABSTRACT

As Rhode Island's only needle exchange program, ENCORE (**E**ducation, **N**eedle Exchange, **C**ounseling, **O**utreach, and **RE**ferrals) serves a wide range of clients infected or at risk for infection with hepatitis C virus (HCV). Through its on-site and outreach platforms across Rhode Island, ENCORE is in a unique position to serve at-risk individuals who may not otherwise present for prevention, testing and care for HCV, as well as human immunodeficiency virus (HIV). In this article, we discuss the role of needle exchange programs in preventing HCV transmission, and provide an overview of the history and current operations of ENCORE.

KEYWORDS: Hepatitis C, needle exchange program, Rhode Island, drug injection

INTRODUCTION

Needle exchange programs are a core component of harm reduction programs for people who inject drugs (PWID).[1] At a minimum, needle exchange programs (also known as needle and syringe programs) provide sterile needles and syringes to PWID; most also provide other injecting paraphernalia (e.g., alcohol swabs, sterile water and tourniquets) as well as health information and referrals. In this article, we describe the role of needle exchange programs in preventing hepatitis C virus (HCV) transmission, and provide an overview of the history and current operations of Rhode Island's only needle exchange program, ENCORE.

NEEDLE EXCHANGE PROGRAMS AND HEPATITIS C PREVENTION

In middle- and high-income countries, injecting drug use is the primary route of HCV transmission.[2] HCV is easily transmitted through shared use of needles and other drug injecting equipment, with transmission requiring the transfer of only microscopic amounts of blood from an infected person to an uninfected person, and the virus maintaining infectivity in dried blood for as long as 6 weeks.[3] Globally, it is estimated that 10 million PWID, or 67% of the PWID population, are infected with HCV.[4] By way of contrast, an estimated 3 million PWID are infected with human immunodeficiency virus (HIV).[5]

There is very strong evidence that needle exchange programs reduce HIV transmission among PWID.[6,7] Although the evidence for needle exchange programs is less conclusive in relation to HCV prevention,[7,8] needle exchange programs are an essential part of any comprehensive intervention strategy to prevent HCV transmission.[1,2] Other components of health care for PWID, recommended by the World Health Organization (WHO), include opioid substitution therapy (also known as methadone maintenance treatment; the medical prescription of opioids such as methadone and buprenorphine to people with opioid dependence, in order to reduce illicit opioid use and injection) and other drug treatment; hepatitis B vaccination, with incentives to initiate and complete the vaccination schedule; integration of medical services for hepatitis with treatment of opioid dependence; and peer-led interventions.[2] These are in addition to the WHO-recommended comprehensive package of intervention for HIV prevention, treatment and care in PWID, including blood-borne virus testing and counseling; antiviral therapy, prevention and treatment of sexually transmitted infections, condom distribution to PWID and their sexual partners, targeted information and education, and prevention, diagnosis and treatment of tuberculosis.[2]

THE ENCORE PROGRAM

ENCORE (**E**ducation, **N**eedle Exchange, **C**ounseling, **O**utreach, and **RE**ferrals) is Rhode Island's only needle exchange program. It aims to reduce risk and transmission of HCV, HIV and other drug-related harms among PWID through a range of harm reduction services (**Box 1**). Harm reduction

Box 1. Harm reduction services provided by ENCORE

- **E**ducation – on HIV, viral hepatitis and other blood-borne pathogens prevention
- **N**eedle Exchange – to reduce the risk of transmitting HIV, viral hepatitis and other blood-borne pathogens prevention
- **C**ounseling – on reducing risks, HIV and viral hepatitis testing, following through on medical care and substance abuse treatment options
- **O**utreach – into the community to help identify clients for the ENCORE program
- **RE**ferrals – to health care and social service agencies and drug treatment

services focus on preventing harms associated with drug use, rather than preventing drug use *per se*, in acknowledgement that there are people who are unwilling or unable to stop using drugs.[9]

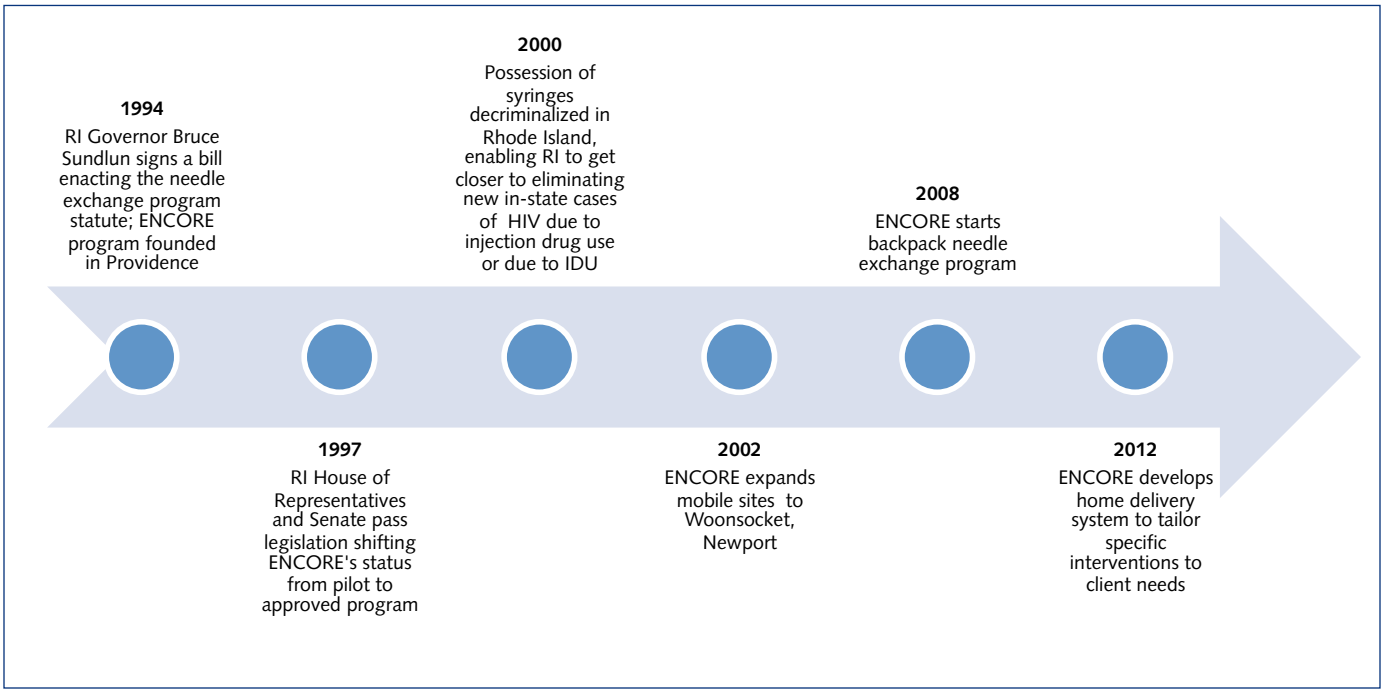
ENCORE has been coordinated by AIDS Care Ocean State (ACOS) since 1998. ACOS is a 501(c)(3) nonprofit AIDS Service Organization and the largest provider of HIV support services in Rhode Island. ACOS has an extensive infrastructure to support HIV prevention and harm reduction services, and has an established reputation in the community of being able to service hard-to-reach, high-risk individuals.

Local development of a needle exchange program in Rhode Island has its roots in the epidemic of HIV transmission through PWID. As early as 1988 in New York City, community advocates such as Edith Springer pioneered harm reduction techniques and needle exchanges to prevent HIV and HCV transmission. In Rhode Island, methadone maintenance treatment programs were expanded into pilot needle exchange programs as acceptable interventions for PWID. Local political opposition to pilot needle exchange shifted when the Rhode Island Department of Health partnered with a community-based AIDS service organization, ACOS, with roots in the urban neighborhoods of Providence.

The ENCORE program has existed in Rhode Island since 1994 (**Figure 1**), and currently operates three fixed sites and mobile/street-based exchange units, where a van and a team of outreach workers go out into the community to actively seek out PWID in five cities: Providence, Woonsocket, Newport, Pawtucket and Central Falls. The main hub for ENCORE is located at 557 Broad Street, Providence. ENCORE also has a home delivery system where clients can call in an order and have their supplies delivered directly to them. Services are provided anonymously and are open to anyone over the age of 18. Clients are recruited through referrals from substance treatment facilities, the street outreach component of the program, or through word of mouth. Harm reduction tools provided to clients include: new syringes, alcohol swabs, antibiotic ointment, ascorbic acid, band-aids, bio-hazard sharps containers, cookers, cotton, rubber tip covers, sterile water, and tourniquets. These items are given to clients to help reduce the spread of HIV and HCV. All staff undergo training sessions on agency policy, Harm Reduction 101, safety guidelines of collection and disposal or syringe, HIV and viral hepatitis basics and prevention, safer injection and overdose prevention, referral networks and cultural competency.

As of 2005, ENCORE became Rhode Island's first free testing site for anti-HCV antibodies, markers of exposure to HCV in the blood, in collaboration with Dr. Lynn E. Taylor of Miriam Hospital and Brown University. Used as an initial screening test to identify patients who have been exposed to HCV, the HCV antibody test requires a confirmatory test, if it is reactive/positive, for the HCV virus itself, HCV RNA. Some 15-25% of patients who are exposed to HCV develop the antibody but clear the virus spontaneously in the first six months of infection, and thus have a negative HCV RNA test. From August 2012 – January 2013, HCV antibody screenings at ACOS have a 13% positivity rate, 10 times higher than the 1.3% for the U.S. population overall. In 2013, Dr. Taylor's program Rhode Island Defeats Hep C began offering free confirmatory HCV RNA testing through ACOS, and referred those individuals with detectable HCV

Figure 1. History of needle exchange in Rhode Island



RNA to HCV care in Rhode Island. Of the 13% of individuals with positive HCV antibody screens who underwent confirmatory RNA testing, 84% had detectable HCV RNA.

In addition to HCV testing, ENCORE also offers free, anonymous and confidential HIV and hepatitis B virus testing; distributes a variety of both male and female condoms as well as lubrication and hygiene packs (combs, deodorant, razors, shaving cream, soap, toothbrushes and toothpaste); and provides referrals to an array of social services. Since ENCORE's inception, the Rhode Island Department of Health has supported the program with State resources for the purchase of supplies and volunteer training.

CLIENT CHARACTERISTICS

The ENCORE Program collects data on its clients through a pre-enrollment interview completed on first presentation to an ENCORE service. The interview also introduces the client to all of the services ENCORE offers. The interviews contain questions pertaining to client demographics, drug use, sharing of injection supplies, and HIV and HCV testing. ENCORE completes follow-up interviews with clients every three months.

Each client is assigned a unique identifier (their ENCORE Code) at the pre-enrollment interview for the purposes of tracking client activity. In 2012, a new coding system was introduced to match the Rhode Island Department of Health's Counseling Testing and Referral (CTR) codes. **Table 1** presents data from pre-enrollment interviews with ENCORE clients between 1994 and 2011, and 2012–2013. The majority of clients were male and Caucasian, with a substantial minority identifying as Hispanic. The majority of clients first injected drugs prior to 30 years of age, and heroin was the most common primary drug. One in five clients reported sharing needles to inject drugs.

On the basis of client self-reports, 44% of ENCORE clients in 2012-2013 were HCV-infected (**Table 1**). It is unclear if clients reporting HCV infection were reporting positive antibody test results, signifying exposure, or confirmed infection. By way of comparison, 10% of clients over the same time period reported that they were HIV-positive (which unlike HCV positive testing, always indicates active infection). Additionally, 7% of clients in 2012-2013 were unaware of their HCV status, and 6% of clients were unaware of their HIV status. Among clients between 1994 and 2011, low levels of blood borne virus testing were reported, with only 26% having received an HCV test in the past year, and 30% having received an HIV test in the past year.

IMPLICATIONS FOR PUBLIC HEALTH IN RHODE ISLAND

There is potential for HCV transmission among PWID in Rhode Island, with nearly half of ENCORE clients reporting prior HCV exposure or infection, and a substantial minority

Table 1. Characteristics of ENCORE clients, 1994-2011 (n=2,525) and 2012–2013 (n=596)

	%	
CHARACTERISTIC	**1994-2011**	**2012-2013**
Sex		
Male	70	77
Female	29	22
Transgender	<1	1
Unknown	2	0
Race		
Caucasian	69	65
African-American	4	6
Native American	2	3
Asian	<1	1
Other	2	<1
More than 1 Race	<1	0
Unknown/blank	21	0
Hispanic ethnicity	15	25
Homeless	22	40
Drug of choice		
Heroin	72	81
Crack/cocaine	15	9
Speedball[1]	4	5
Other/unknown[2]	9	5
First injected drugs aged <30 years	81	81
Report needle sharing	22	20
Of sharers, sharing with friends	34	55
Of sharers, sharing with sexual partners	38	37
Ever enrolled in drug treatment	50	75
HCV test in the past year		
Yes	26	—
No	10	—
Unknown	63	—
HCV status		
Self-reported HCV positive[3]	—	44
Unaware of HCV status	—	7
HIV test in the past year		
Yes	30	—
No	7	—
Unknown	63	—
HIV status		
Self-reported HIV positive	—	10
Unaware of HIV status	—	7

HCV: hepatitis C virus.
[1] Speedball refers to injection of cocaine and heroin or morphine in the same mixture.
[2] Includes amphetamine and steroids.
[3] May refer to either HCV antibody positive, or confirmed HCV infection.

of clients sharing needles. Furthermore, a small proportion of clients are unaware of their infection status, suggesting that they have not been tested for HCV, or at the least have not been tested recently. Between 1994 and 2011, only one-quarter of clients reported HCV testing in the past year. There are considerable opportunities to increase HCV testing among this group, including through ENCORE. These include better follow-up of clients through ENCORE's home delivery system, and increasing awareness among PWID of the benefits of testing and the availability of highly effective treatments with fewer side effects than in the past. These actions will complement broader ACOS and Rhode Island Defeats Hepatitis C efforts.

Studies of needle exchange programs and HCV have demonstrated that a high level of coverage (i.e., contact with a high proportion of local PWID) is necessary to have an impact on HCV incidence and prevalence.[7] Coverage of needle exchange programs in the United States is among the lowest in the world,[10] in part due to a ban on federal funding for such services. The extent to which ENCORE reaches the population of PWID in Rhode Island has not been formally estimated, but in 2008–2009, only 28% of a small sample of PWID seeking detoxification services in Rhode Island reported having accessed a needle exchange program in the last six months.[11] ENCORE outreach and home delivery services have expanded since 2008, so it is possible that coverage has increased in recent years. There is a need for data estimating ENCORE's coverage of PWID in Rhode Island, as well as the potential impacts of increased needle exchange coverage on HCV incidence and prevalence in the state.

CONCLUSION

ENCORE is a long-standing program providing harm reduction services, including needle exchange, to PWID in Rhode Island. As the only needle exchange program in the state, it serves as a vital resource for a highly vulnerable population that is at risk of HCV infection. Continued scale-up of ENCORE's reach and services will have a positive impact on the HCV epidemic in Rhode Island.

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HCV among The Miriam Hospital and Rhode Island Hospital Adult ED Patients

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ABSTRACT

The Emergency Department (ED) appears to be an ideal place to conduct hepatitis C virus (HCV) screening. We aimed to estimate the prevalence of prior HCV test positivity among adult (18–64 year-old) patients at The Miriam Hospital and Rhode Island Hospital EDs, as well as the undiagnosed HCV antibody seroprevalence among patients with any self-reported injection or non-injection drug use who agreed to undergo rapid HCV antibody testing. The prevalence of prior HCV test positivity among 8,500 adult ED patients was approximately 4.6%, and the previously undiagnosed HCV antibody seroprevalence among 621 drug-using adult ED patients was 1.6%. Among the ten ED patients with a positive rapid HCV antibody test not previously diagnosed, eight were born after 1965 and six never had injected drugs. If current HCV screening recommendations were followed exclusively in this setting, this practice would have missed half of those with a positive rapid HCV antibody test.

KEYWORDS: hepatitis C, mass screening, substance abuse, emergency medicine, seroepidemiologic studies

INTRODUCTION

The United States (US) Centers for Disease Control and Prevention (CDC) and US Public Health Service Task Force (USPHSTF) currently recommend a one-time screening test for the hepatitis C virus (HCV) for those born between 1945 and 1965 ("baby boomers") and continuous risk-based screening for those at higher risk for infection, such as people who inject drugs.[1-3] However, HCV screening for other populations, particularly for those who use non-injection drugs, has been encouraged by others,[4,5] especially since most people who use drugs do not inject them. The need to understand the value of HCV antibody screening among those who use any type of drug is particularly relevant to Rhode Island. Our state has one of the highest reported prevalences of drug dependency (9-13%) and has one of the highest percentages of its citizens reporting illicit drug use.[6]

Because of the success of HIV-screening efforts in emergency departments (EDs),[7-13] the overlapping risk for HIV and HCV, high prevalence of drug use,[14] and access-to-care challenges faced by many ED patients,[15] the ED would appear to be an ideal location to conduct HCV screening and link patients to care. Further, if the prevalence of prior HCV test positivity is high among ED patients, interventions to increase linkage to care also could be a viable means to expand our capacity to cure and reduce the downstream damage of HCV, including end-stage liver disease and liver cancer. We aimed to estimate the prevalence of patient-reported prior HCV test positivity among a random sample of adult (18-64 years-old) patients at The Miriam Hospital and Rhode Island Hospital EDs, as well as the HCV antibody seroprevalence among patients with any self-reported drug use who agreed to undergo rapid HCV antibody testing.

METHODS

Study Design and Setting

This investigation involved a secondary analysis from two studies: Increasing Viral Testing in the ED (InVITED) and Brief Intervention for Drug Misuse in the ED (BIDMED). These two studies were conducted concurrently at The Miriam Hospital and Rhode Island Hospital EDs from July 2010-December 2012. The Lifespan Institutional Review Board approved the two studies.

Data Collection

The InVITED and BIDMED studies included two components: (1) an assessment of the prevalence of patient-reported prior HCV test positivity (i.e., a positive HCV test of any kind – an HCV antibody test, which is a screening test that identifies prior exposure to HCV; or an HCV ribonucleic acid (RNA) polymerase chain reaction (PCR) test, which is a confirmatory test that identifies a current HCV infection and ongoing viral replication) among a random sample of adult ED patients, and (2) rapid HCV antibody screening among drug-using study participants who self-reported that they never had a positive HCV test.

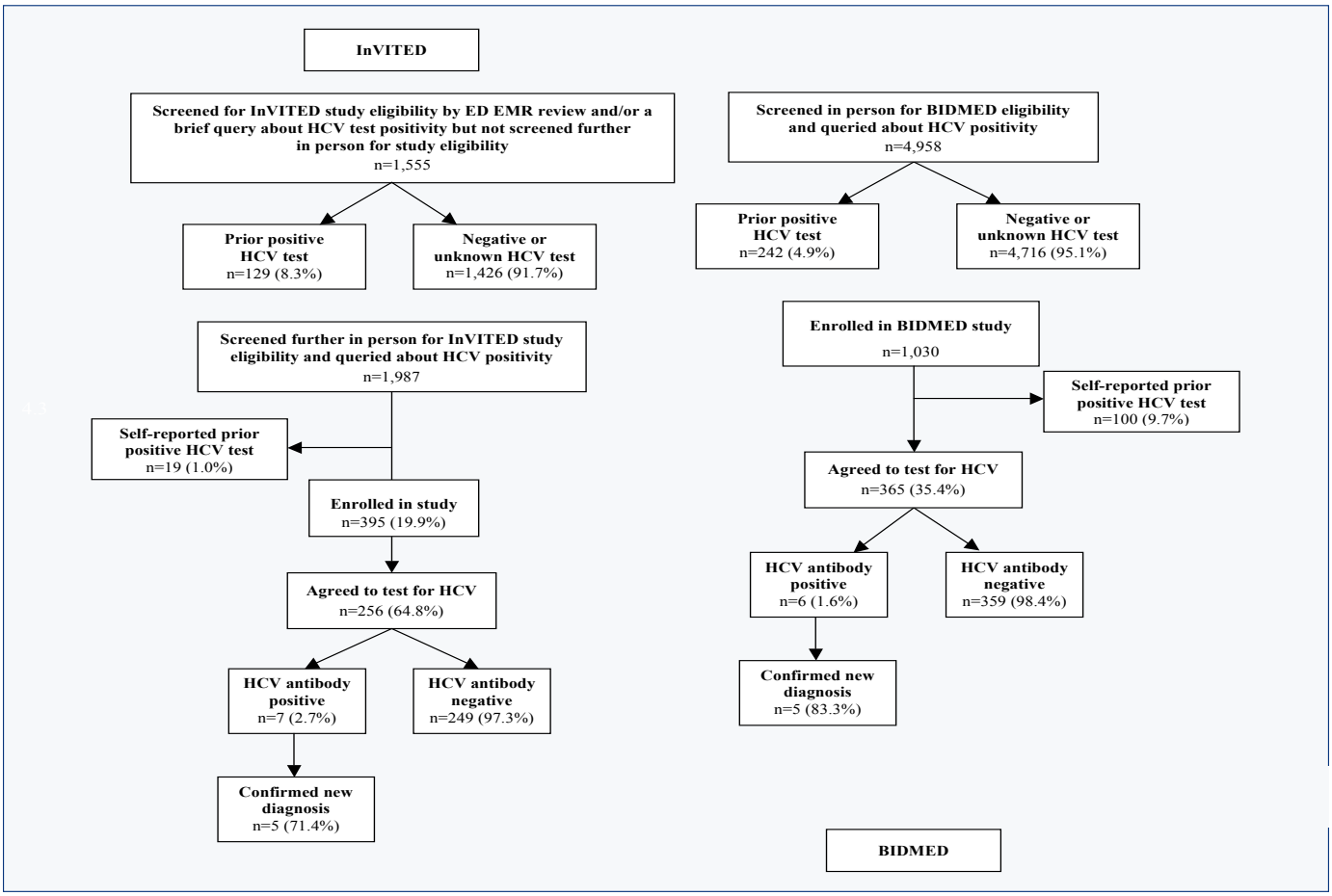
Efforts to estimate the prevalence of patient-reported prior HCV test positivity differed slightly between the two studies. For the InVITED study, trained research assistants (RAs) first reviewed the ED electronic medical records (EMRs) of a random sample of ED patients awaiting medical care and noted if the nursing or medical staff had recorded that the patient previously had been diagnosed with HCV (regardless of status of the infection – chronic, cured with medications, or spontaneously resolved). For patients who had

no other apparent exclusion criteria for InVITED by the ED EMR review, the RAs would approach those who otherwise appeared to be study eligible and briefly ask them if they ever had a positive HCV test (of any kind). If they answered affirmatively or met any other study exclusion criteria, they were not evaluated further. Those who were potentially study eligible, whose EMR ED did not indicate a history of any positive HCV test, and who denied on initial query that they ever had a positive HCV test were asked a series of follow-up questions to determine study eligibility, including a more extensive assessment of their HCV testing history. For BIDMED, a random sample of patients underwent a similar EMR review, and those whose review indicated that they might be study eligible were interviewed in person. This group had the same extensive assessment of their HCV testing history as those for the InVITED study. However, HCV was not an exclusion criterion for BIDMED. If patients in either study informed the RAs during this extensive assessment that they had previously tested positive for HCV, these data were recorded.

As part of the eligibility assessments for both studies, patients self-administered the *Alcohol, Smoking and Substance Involvement Screening Test, Version 3* (ASSIST V.3.) using an audio computer-assisted self-interviewer (ACASI).[16] The ASSIST queried them about their lifetime and past three-month drug use or misuse. Using the ACASI system, patients also completed questionnaires about the specific drugs that they had used and their sexual and drug use/misuse risk-taking behaviors within the past three months. For the InVITED study, patients were study eligible if they reported any drug use within the previous three months, were not known to be HIV-infected, or never had a positive HCV test. For BIDMED, patients were study eligible if their responses to the ASSIST indicated that they would qualify for a brief or more intensive intervention for their drug misuse. Patients were otherwise eligible for both studies if they were 18-64 years-old; English- or Spanish-speaking; not critically ill or injured; not prison inmates, under arrest, nor undergoing home confinement; not presenting for an acute psychiatric illness or an evaluation for substance misuse; not intoxicated; and did not have a physical disability or mental impairment that prevented them from providing consent for participating in the study.

All participants in the InVITED study were offered rapid HCV antibody screening. Participants who self-reported in the BIDMED study that they never had a positive HCV

Figure 1. InVITED and BIDMED studies HCV positive test history and HCV antibody test prevalence



Key: ED = Emergency Department; EMR = Electronic Medical Record; HCV = Hepatitis C Virus

test also were offered rapid HCV antibody testing. The RAs performed the rapid HCV antibody test using a fingerstick for blood (OraQuick® HCV rapid antibody test, OraSure Technologies, Inc., Bethlehem, PA). Test results were available within 20 minutes.

Data Analysis

To estimate patient-reported prior HCV test positivity among adult ED patients, for the InVITED study we tabulated the number of patients whose ED EMR indicated or who informed the RAs during the initial study-eligibility assessment that they previously had been informed that they had a positive HCV test. For the InVITED and the BIDMED studies, we also tabulated the number of patients who informed the RAs during the HCV testing history assessment that they ever had a positive HCV test. We compared patients who reported a positive HCV test to those who denied ever having a positive HCV test (i.e., prior negative test, never tested, or did not know if they had been tested) by their demographic characteristics using Wilcoxon rank-sum or Pearson's X^2 testing, as appropriate. An α=0.05 level of significance was used for these comparisons. We also calculated HCV antibody-testing uptake among study participants and the HCV antibody seroprevalence among those tested. We recorded the demographic characteristics, self-reported potential HCV risk factors, and self-reported drugs used of those with a positive test.

RESULTS

Figure 1 depicts the patient-reported prior HCV test positivity, HCV antibody-screening uptake, and HCV antibody-screening results for the two studies. Of the 3,542 ED 18–64 year-old patients assessed for InVITED study eligibility (EMR review, brief query and/or in-person study-eligibility assessment), the prevalence of a self-reported history of any positive HCV test was 3.9%. Of the 4,958 assessed in-person for BIDMED study eligibility, this prevalence was 4.9%. When data from both studies was combined, the self-reported prevalence was approximately 4.6%. Of those who completed the ASSIST in both studies, 49.5% reported any drug use within the past three months. Among the 390 patients across both studies who reported ever having a positive HCV test, 50.3% were under 50-years-old (i.e., were not "baby boomers" – not born between 1945 and 1965). In comparing the demographic characteristics of the 390 patients across both studies who reported ever having a positive HCV test vs. the 8,110 who denied ever having a positive HCV test (**Table 1**), more of those with a history of a positive HCV test were male and white or white/non-Hispanic.

Among the 621 patients in both studies who agreed to be tested for HCV, 1.6% had a previously undiagnosed positive HCV antibody test. As shown in **Table 2**, among the ten participants from both studies with a previously undiagnosed positive HCV antibody test, only one was female, none were HIV-infected, eight were born after 1965, most identified the

Table 1. Comparison of demographic characteristics by history of any positive HCV test

	InVITED EMR & brief query screen			InVITED in-person screen			BIDMED in-person screen		
	HCV (+)	HCV (–) or unknown status		HCV (+)	HCV (–) or unknown status		HCV (+)	HCV (–) or unknown status	
Demographic Characteristics	**n=129**	**n=1426**	**p-value**	**n=19**	**n=1968**	**p-value**	**n=242**	**n=4716**	**p-value**
	%	%	p <	%	%	p <	%	%	p <
Age (years)									
18-24	2.3	12.8	0.0	0.0	21.8	0.1	2.5	20.9	0.0
25-34	8.5	17.7		26.3	24.8		13.2	24.6	
35-49	34.9	33.0		36.8	30.0		36.0	31.7	
50-64	54.3	36.4		36.8	23.5		48.4	22.7	
Gender									
Male	66.7	54.5	0.0	68.4	42.7	0.0	57.4	43.4	0.0
Female	33.3	45.4		31.6	57.3		42.6	56.6	
Ethnicity/Race									
White	69.0	60.8	0.4			0.8			0.0
Black	17.8	16.4							
White, non-Hispanic				73.7	64.0		69.0	59.8	
White, Hispanic				5.3	10.4		6.6	11.6	
Black/African-American, non-Hispanic				15.8	16.2		16.5	16.2	
Black/African-American, Hispanic				0.0	5.1		5.0	6.8	
Other	12.4	20.2		5.3	4.3		2.9	5.6	
Health insurance status									
Private	13.2	20.9	0.0	10.5	44.1	0.1	10.3	40.6	0.0
Governmental	55.8	31.1		52.6	32.2		57.4	34.3	
None	11.6	22.0		36.8	23.5		32.2	24.9	
Don't know/Refuse to answer	19.4	26.0		0.0	0.2		0.0	0.2	

EMR=Electronic Medical Record; HCV=Hepatitis C Virus; HCV (+)=history of any positive HCV test; HCV (-)=no history of any positive HCV test

Table 2. Confirmed new HCV antibody positive study participants

		Usual source of medical care	Prior HCV testing	Time elapsed since last HCV test	Injection drug use	Lifetime drug use	Past 3 months drug use
Male							
Subject	**Age**						
A	25	ED	Don't know	N/A	Never	Marijuana, cocaine or crack, methamphetamines, inhalants, illicit opioid, amphetamines	Marijuana, cocaine or crack, methamphetamines, inhalants
B*	25	ED	No	N/A	P3M	Marijuana, cocaine or crack, methamphetamines, hallucinogens, illicit opioid, benzodiazepines, methadone or buprenorphine, prescription opioid analgesics	Marijuana, cocaine or crack, Methamphetamines, hallucinogens, illicit opioids, benzodiazepines, methadone or buprenorphine, prescription opioid analgesics
C	29	PC	Yes	Don't know	Never	Marijuana, cocaine or crack, hallucinogens, illicit opioids, amphetamines, benzodiazepines, prescription opioid analgesics	Illicit opioids, benzodiazepines
D	32	CHC	Yes	< 2 years but > 1 year	Never	Marijuana, illicit opioids, benzodiazepines, methadone or buprenorphine	Marijuana
E*	32	ED	Yes	≤ 5 years but > 2 years	P3M	Marijuana, cocaine or crack, hallucinogens, illicit opioids, benzodiazepines, methadone or buprenorphine, prescription opioid analgesics	Cocaine or crack, illicit opioids, prescription opioid analgesics
F	34	ED	Yes	< 5 years but > 2 year	Never	Marijuana	Marijuana
G	35	ED	No	N/A	Never	Marijuana, cocaine or crack, hallucinogens	Marijuana, cocaine or crack
H*	41	ED	Yes	< 6 months	Ever	Marijuana, cocaine or crack, illicit opioids	Marijuana
I*	49	PC	Yes	< 6 months	Ever	Marijuana, cocaine or crack, illicit opioids, benzodiazepines	Marijuana
Female							
Subject	**Age**						
J*	52	PC	No	N/A	Never	Marijuana, cocaine or crack, illicit opioids, methadone	Marijuana

*Met Centers for Disease Control & Prevention recommendations for HCV screening by age cohort (born 1945-1965) or IDU

CHC=Community Health Clinic; ED=Emergency Department; HCV=Hepatitis C Virus; IDU=Injection Drug Use; P3M=Past 3 Months; N/A =Not Applicable; PC=Primary Care; IDU=Injection Drug Use

ED as their usual source of medical care, most had previously been tested for HCV, six had never injected drugs, and marijuana was the drug most often reported used within the past three months. Of these ten participants, five did not meet current CDC HCV screening criteria: were not born between 1945 and 1965 (not "baby boomers") and never injected drugs.

DISCUSSION

Extrapolating from the data from this study and the annual patient volumes among 18–64 year-olds at The Miriam Hospital and Rhode Island Hospital EDs, approximately 5,346 non-critically ill or injured, non-acutely psychiatrically ill 18–64 year-olds per year could be estimated ever to have had a positive HCV test (116,225 patients/year x 4.6% prevalence). Although not directly comparable, this prevalence is much greater than the 1.3% estimated prevalence of HCV antibody positivity reported for the US general population (all ages) using data from the 2001–2010 National Health and Nutrition Examination survey (NHANES).[17] Further, if HCV antibody screening were instituted among a similar group of 18–64 year-olds at these EDs who might report any type of drug use within the prior three months (49.5%), we can anticipate that 920 people (116,225 patients/year x 49.5% drug use prevalence x 1.6% HCV seropositivity) over a one-year period would have a positive HCV antibody test. These results indicate that a substantial number of patients are known to have been or could have a positive HCV test at these EDs. This finding suggests the need to consider screening and assure linkage to care for those with HCV from the ED who are not already in care. Many of these patients do not have regular sources of medical care, which leaves the ED as the place where they would be tested for HCV. The study results also indicate that despite the current focus on "baby boomers" and people who inject drugs, half of those newly diagnosed with HCV had never injected drugs and were not "baby boomers."

This investigation had a number of limitations. The study cannot estimate the HCV antibody seroprevalence among patients not evaluated for study eligibility (e.g., critically ill or injured patients, intoxicated patients, patients with an acute psychiatric problem) and cannot assess the extent of HCV positivity among those patients evaluated at other EDs in Rhode Island. It also is likely that the patient-reported history of prior HCV test positivity among ED patients was underestimated, since patients whose ED EMR indicated that they were otherwise not study eligible were not interviewed. The study also could not determine the status of these patients' current HCV care, which would impact estimates on need for linkage to care. Nevertheless, the results provide a minimum estimate of the extent of prior HCV

test positivity and HCV antibody test seroprevalence among these patients. Also, we do not know the risk-taking behaviors (e.g., injection-drug use) among those who were not interviewed. In addition, if our study exclusively had focused instead on all "baby boomers," the estimates of undiagnosed HCV antibody seroprevalence might have been different.

In conclusion, a substantial number of The Miriam Hospital and Rhode Island Hospital adult ED patients are impacted by HCV. Approximately 1.6% of drug-using patients have HCV and are unaware of their status. Further, it appears that if current HCV screening recommendations were followed exclusively, this practice might miss a substantial number of those impacted by HCV. We are hopeful that these findings might lead to an expansion of HCV screening in Rhode Island EDs and linkage to care efforts and perhaps revision of current HCV screening recommendations.

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