Estimating the True Prevalence of Hepatitis C in Rhode Island

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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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