Review Article
Hepatitis C screening in the United States: current models and challenges

Mel A Ona1, Haris Papafragkakis1, Calvin Q Pan2

1Division of Gastroenterology, The Brooklyn Hospital Center, The Icahn School of Medicine at Mount Sinai, Brooklyn, NY, U.S.A; 2Division of Gastroenterology, Department of Medicine, NYU Langone Medical Center, NYU School of Medicine, New York, NY, U.S.A

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Abstract: Background: The prevalence of hepatitis C in the United States is estimated to be 1-1.5% (2.7 to 3.9 million persons). Birth-cohort screening with linkage to care is recommended to augment risk-based screening programs in reducing hepatitis C-associated morbidity and mortality. However, only a small percentage of hepatitis C patients are identified and have received treatment. Aims: To better understand the challenge of screening and linkage to care, we review the reported prevalence of hepatitis C infection among different risk groups in the United States, examine current hepatitis C screening models, identify barriers for hepatitis C screening, and discuss approaches for improving screening. Methods: We searched electronic databases (PubMed and Cochrane Library) to identify articles published from 2008 to 2014 on risk-based and birth-cohort hepatitis C screening programs. Results: Studies have revealed that risk-based and birth-cohort screening programs alone are insufficient to reduce hepatitis C-related morbidity and mortality. Hepatitis C infection is more prevalent in high-risk groups such as persons who inject drugs, incarcerated inmates, persons living with HIV, and persons born between 1945 and 1965. Barriers to hepatitis C screening are observed in patients, providers, and structural insufficiency in the health care system. Gaps exist in the linkage to care after hepatitis C diagnosis, which include bridging patients to subspecialty care providers, medication access with resources for on-treatment monitoring, and patient motivation to receive treatment. Conclusions: Risk-based screening approaches should be expanded to birth-cohort screening to improve the capture rate of patients infected with hepatitis C. Hepatitis C remains an underdiagnosed and undertreated disease in the United States. Thus, patient and physician education with structured programs are needed to address the issues of implementing risk-based and birth-cohort screening. Further studies are needed to determine the appropriate model of linkage to care after identifying those patients from screening as current therapies are highly effective and treatment can reduce disease progression with the possibility of global eradication of hepatitis C infection.

Keywords: Hepatitis C virus (HCV), HCV infection, birth-cohort, screening

Introduction

Hepatitis C virus (HCV) infection is a global problem with an estimated 150 million (range of 130-170 million) persons having chronic HCV infection [1, 2]. In the United States (U.S.), approximately 4.1 million persons are HCV-antibody positive. Of these, an estimated 75% or approximately 2.7 to 3.9 million persons (1-1.5%) are chronically infected with HCV [3]. A recently published study of 30,074 participants in the National Health and Nutrition Examination Survey between 2003 and 2010 estimated the prevalence of HCV infection to be 1% of the U.S. population (approximately 2.7 million persons) [4]. This estimate did not include institutionalized and homeless individuals, so the actual number of infected persons is probably higher. Chronically infected persons with hepatitis C is more prevalent in non-Hispanic black men between 40 to 59 years, with low education and income. History of drug use and blood transfusions before 1992 are significant risk factors for disease acquisition, however, almost half of the surveyed population did not demonstrate these risk factors. Acute HCV infection may present as mild to severe illness, however, up to 70% of HCV-infected persons are asympt-
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HCV infection is often clinically silent with most patients unaware of their infection status. Chronic hepatitis C infection is the most common cause of death from liver disease and is the leading indication for liver transplantation in the U.S. In fact, HCV-related deaths now outnumber deaths due to HIV/AIDS in developed countries [5].

Many HCV screening programs in the U.S. have focused on high-risk populations. Recently, the United States Preventive Services Task Force (USPSTF) updated its 2004 hepatitis C guideline and now recommends screening asymptomatic adults who are born between 1945 and 1965 (the “baby boomer” cohort) as these persons have an estimated prevalence of anti-HCV positivity of 3.25%, which accounts for nearly three quarters of all chronic HCV infections in the U.S. [6]. As a high prevalence disease with significant mortality if untreated, HCV infection should be diagnosed early. Screening and linkage to care are the fundamental steps to reduce morbidity and mortality in the infected population. In this brief review, we describe current models for HCV screening in the U.S., examine challenges, and discuss approaches for improving HCV screening.

Natural history of HCV infection

HCV is the most common blood-borne infection in the U.S. that is most efficiently transmitted through parenteral exposure. The highest prevalence of HCV infection occurs among those with significant and repeated percutaneous exposures, such as persons who inject drugs (PWID), hemodialysis patients, recipients of infected donor blood transfusions and hemophiliacs who received blood prior to July 1992 [6]. Traditionally, patients with the above risk factors are considered the key affected population (KAP) and received routine screening for HCV infection as the standard of care. In the past, community screening activities were also focused on the KAP but the majority of funding resources were from non-profit organizations. With no public funding (government-sponsored structural programs) in the U.S., many individuals who are infected with HCV have not been identified. In addition, HCV infection is a silent killer with a protracted and indolent course and asymptomatic individuals often fail to come forward for screening and medical intervention before serious disease complications occur such as decompensated cirrhosis and hepatocellular carcinoma (HCC).

HCV, a flavivirus cloned in 1989, has genetic variability allowing it to evade the immune response, which is predominantly mediated by type 1 helper T-cells [7, 8]. Cirrhosis occurs in 15% to 30% of patients after 30 years of chronic HCV infection and progresses at a variable rate that is influenced by alcohol consumption, older age, co-infection with hepatitis B virus or HIV, degree of inflammation and fibrosis on liver biopsy, comorbid conditions (e.g. immunosuppression and insulin resistance), with consequent increased risk for developing HCC [9].

Current HCV screening recommendations

In 1998, the Centers for Disease Control and Prevention (CDC) recommended risk-based HCV testing for persons likely to be infected. This KAP focused approach called for HCV screening for the following individuals: 1) ever injected illegal drugs, 2) received clotting factor concentrates produced prior to 1987, 3) ever were on long-term hemodialysis, 4) had persistently abnormal alanine aminotransferase (ALT) levels, 5) received blood or a blood component transfusion or 6) received an organ transplant before July 1992. Screening was also recommended for persons with recognized exposures to HCV such as healthcare providers, emergency medical personnel, and public safety workers exposed to needle sticks, sharps, or mucosal exposures to HCV-positive blood, and children born to mothers with HCV infection. In 1999, persons with HIV infection were also recommended to undergo HCV testing [6]. In 2002, the National Institutes of Health (NIH) also recommended HCV testing for persons at high risk [10]. In 2004, the USPSTF had recommended against HCV screening for asymptomatic adults who were not at increased risk for HCV infection. However, after the CDC updated its guideline in 2012 and expanded the KAP to a much larger scale with the recommendation of one-time screening for HCV infection in persons born between 1945 and 1965, the USPSTF endorsed this new screening approach in June 2013 and recommended the screening expense be covered by insurance [11].

The rationale for augmenting previous recommendations is based on the limitations of risk-based HCV testing. Many of the estimated 2.7
Table 1. HCV Screening Programs

<table>
<thead>
<tr>
<th>Author (Year) [Ref.]</th>
<th>Years of Data Collection</th>
<th>Study Design</th>
<th>Population</th>
<th>Screening Program Setting</th>
<th>Screening Program Duration</th>
<th>Screening Uptake and anti-HCV Prevalence (95% CI)</th>
<th>Limitations</th>
<th>Strengths</th>
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<tbody>
<tr>
<td>Cartwright, et al. [31]</td>
<td>2011</td>
<td>Retrospective</td>
<td>VA patients</td>
<td>VA Medical Center (inpatient) or VA clinic (outpatient)</td>
<td>12 months</td>
<td>Screening uptake: 48% (41556/87144); Prevalence: 10% (4107/41556); Prevalence among those born from 1945 to 1965: 15% (95% CI: 5.32-6.78)</td>
<td>Analysis used administrative databases (lack information regarding behavioral risk factors, medical comorbidities, provider rationale for HCV testing), predominantly male population</td>
<td>Confirm higher HCV prevalence in persons born between 1945 and 1965, high confirmatory HCV RNA testing rate</td>
</tr>
<tr>
<td>Corcoros, et al. [14]</td>
<td>2009 to 2012</td>
<td>Prospective</td>
<td>Correctional facility inmates</td>
<td>Correctional facility</td>
<td>July 2009 through April 2012</td>
<td>Screening uptake: 22% (596/2716); Prevalence: 20.5% (122/596)</td>
<td>Delayed follow-up after release; HCV care/treatment costs; short-term detention may impede initial evaluation and continuity of care</td>
<td>HCV education and screening is feasible and well accepted by inmates/detainees; high yield risk-based screening</td>
</tr>
<tr>
<td>Sears, et al. [32]</td>
<td>2010 to 2011</td>
<td>Prospective</td>
<td>Outpatients for colonoscopy</td>
<td>Endoscopy/GI department</td>
<td>3 months</td>
<td>Screening uptake: 75% (376/500); Prevalence: 1.2% (4/346; 95% CI 0.3-3)</td>
<td>Exclusion of uninsured; lack data regarding decliners for HCV screening; non-urban setting with low-risk factor prevalence</td>
<td>High acceptability for HCV screening during colonoscopy, no additional needle sticks (IV site for blood collection)</td>
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<tr>
<td>Kim, et al. [15]</td>
<td>2006 to 2008</td>
<td>Cross-sectional</td>
<td>Incarcerated inmates</td>
<td>Two correctional facilities</td>
<td>18 months</td>
<td>Screening uptake: 55% (3470/6342); Prevalence: 1% (95% CI: 0.7-1.4)</td>
<td>Initial screening not done by trained research staff, only 28% of newly incarcerated inmates screened</td>
<td>Streamlined (6 question) questionnaire enhanced case-finding rate</td>
</tr>
<tr>
<td>Woo, et al. [22]</td>
<td>Annual</td>
<td>Single-center experience</td>
<td>General population</td>
<td>Community festival</td>
<td>2-days</td>
<td>Screening uptake: 2.6% (231/9000); Prevalence: &lt;1% (1/231)</td>
<td>Screening setting at festival (focus not on healthcare); language barriers; goal to increase awareness and screen persons at high-risk (study did not assess barriers to screening)</td>
<td>NR</td>
</tr>
<tr>
<td>Litwin, et al. [19]</td>
<td>2008; 2009</td>
<td>Cross-sectional</td>
<td>GP patients</td>
<td>GP clinics</td>
<td>Baseline period (2 months); Risk-based (15 weeks); Birth-cohort (16 weeks)</td>
<td>Screening uptake: NR; Prevalence (risk-based): 5.3%; Prevalence (birth-cohort): 5.8%</td>
<td>Intervention duration only 31 weeks (unclear sustainability); contemporaneous comparison group not used; study evaluated change in HCV testing, not HCV testing yield</td>
<td>Electronic medical record clinical reminders associated with significantly increased HCV testing rates</td>
</tr>
<tr>
<td>Southern, et al. [18]</td>
<td>2008</td>
<td>Cross-sectional</td>
<td>GP patients</td>
<td>GP clinics</td>
<td>Baseline period (2 months)</td>
<td>Screening uptake: 39.7% (3803/9579); Prevalence: 11.5%; Estimated floor prevalence (assuming all untested subjects are negative): 4.6%; Estimated ceiling prevalence (assuming untested subjects would test positive at the same rate as those tested, based on risk profile): 7.7%</td>
<td>Not all patients tested for anti-HCV (reported prevalence estimate based on risk profile); patient data from electronic medical record unable to determine all risks for HCV infection; unclear temporal relationship between risk factors and HCV testing</td>
<td>Strong relationship between high-risk comorbidities and physical testing behavior</td>
</tr>
<tr>
<td>Taylor, et al. [17]</td>
<td>2007</td>
<td>Prospective, feasibility study</td>
<td>HIV-infected patients</td>
<td>HIV clinic</td>
<td>9 months</td>
<td>Screening uptake: NR; Prevalence: NR; Incidence: 2% (1/58 in 50 person-years of observation) per year (95% CI: 0.05-11.1)</td>
<td>Short screening duration; small number of participants; cost analysis not performed</td>
<td>Screening algorithm identified at-risk patients; integrated HCV screening in established HIV care setting; ALT quarterly tracking prompted HCV RNA testing</td>
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</table>
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<table>
<thead>
<tr>
<th>Study Abbreviation</th>
<th>Year Range</th>
<th>Study Design</th>
<th>Setting</th>
<th>Screening Uptake</th>
<th>Prevalence</th>
<th>Time Constraints</th>
<th>Referrals Provided</th>
<th>Challenges and Considerations</th>
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<tbody>
<tr>
<td>Kallman et al. [30]</td>
<td>NR</td>
<td>Single-center experience and health fair</td>
<td>GP patients</td>
<td>NR</td>
<td>Screening uptake: NR; Prevalence: 2.2% (7/322), 1.2% (3/245 tested in clinic), 5.2% (4/77 screened at community health fair)</td>
<td>Time constraints to obtain complete clinical history (health fair), selection bias (health fair), recall bias (health fair)</td>
<td>Referrals provided for follow-up and treatment</td>
<td></td>
</tr>
<tr>
<td>Hwang, et al. [21]</td>
<td>2006</td>
<td>Cross-sectional</td>
<td>Asian Americans</td>
<td>Community health fair</td>
<td>Screening uptake: 58.4% (118/202); Prevalence: 6% (7/118; 95% CI: 2.9-11.7), 15.4% (6/39; among Vietnamese)</td>
<td>Screening fair participants may have increased awareness/knowledge leading to elevated prevalence estimate; unknown follow-up outcomes; unknown specific Asian ethnicities</td>
<td>Referrals provided for further care</td>
<td></td>
</tr>
<tr>
<td>Valway, et al. [20]</td>
<td>2004 to 2006</td>
<td>Prospective, risk assessment</td>
<td>Truck drivers</td>
<td>Mobile clinic</td>
<td>Screening uptake: 97.5% (636/652); Prevalence: 8.5% (54/636)</td>
<td>Convenience sample (volunteer participants' behaviors may differ from non-participants); self-reported data during interview</td>
<td>Identification of at-risk population</td>
<td></td>
</tr>
<tr>
<td>Groom, et al. [28]</td>
<td>2000 to 2001</td>
<td>Retrospective</td>
<td>VA patients</td>
<td>VA clinic</td>
<td>Screening uptake: NR; Prevalence: 5.4% (681/12485; 95% CI: 5.1-5.9)</td>
<td>Data for study population had high proportion of unknown characteristics</td>
<td>Relatively high referral and follow-up, treatment, treatment success rates</td>
<td></td>
</tr>
<tr>
<td>Mallette, et al. [29]</td>
<td>1998 to 2004</td>
<td>Prospective, risk-based screening</td>
<td>VA patients</td>
<td>VA clinic</td>
<td>Screening uptake: 66.7% (5646/8471); Prevalence: 7.3% (412/5646; 95% CI: 6.6-8); Prevalence without already known HCV+: 4.6% (260/5646; 95% CI: 4.1-5.2)</td>
<td>Non-standardized recall protocol for abnormal results: 19% of patients did not have confirmatory testing (loss to follow-up outside VA system); lack of convenient and effective antiviral therapy</td>
<td>Risk stratification integration into screening improves HCV detection rate; referral for subspecialty care and treatment provided</td>
<td></td>
</tr>
</tbody>
</table>

NR = Not reported, PCP = Primary care providers, GP = General practitioners, VA = Veterans Affairs. *34.3% tested (12485 of 36422).
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millon persons with HCV are unaware of their infection. Risk-based screening strategies alone failed to identify more than 50% of HCV infections, and persons born between 1945 and 1965 comprise nearly three-quarters of all HCV infections [12]. Moreover, 73.4% of the 15,000 HCV-related deaths in 2007 were persons aged 45 to 64 years [6] with more than 18,000 deaths per year from HCV projected by year 2020 and more than 35,000 per year by 2030 [13].

Risk-based models for hepatitis C screening

The majority of recently published studies of HCV screening comprise risk-based screening methodology (Table 1). HCV screening programs targeted at high-risk groups such as incarcerated inmates in correctional facilities and jails [14-16], HIV-infected individuals [17], urban community general practitioner clinic patients [18, 19], and long-distance truck drivers [20] have revealed HCV prevalence rates much higher than the reported U.S. prevalence. Community-based HCV screening programs have yielded mixed results with one study by Hwang and colleagues having reported an HCV prevalence of 6%, while Woo and colleagues reported only one person (of 231 total people screened) with anti-HCV positivity and undetectable HCV RNA levels [21, 22]. Another community-based screening program by Pan et al. indicated 1.5% HCV infection rate in an Asian community but the risk factors were mainly from blood transfusion prior to 1992 [23].

Acute HCV prevalence was 20.5% (35/171) among incarcerated persons classified as high-risk in a cross-sectional study evaluating whether risk-based screening of newly incarcerated inmates would identify more HCV infections [15]. HCV prevalence among total incarcerated inmates who were screened was 1% (35/3470). Similarly, a pilot HCV screening program linked to an established HIV screening program at a Massachusetts correctional facility, screened 596 of 2716 inmates, with a reported HCV prevalence of 20.5% (122/596). However, only 37.8% received follow-up medical care after release [14]. Because incarcerated inmates have high prevalence of HCV infection and more than 7 million are estimated to have been jailed and/or imprisoned annually in the late 1990s, a large proportion of those inmates released since then may represent a large proportion of the estimated 2.7 million persons infected with HCV. According to the 2014 U.S. Department of Justice Bulletin, an estimated 1.57 million prisoners were in state and federal prisons by the end of 2013. Male prisoners comprised the majority (1.46 million), 37% of whom were non-Hispanic black men, who have been shown to encompass the highest prevalence of HCV infection in the non-incarcerated population [24]. Screening for HCV infection among incarcerated persons, especially among those in short-term correctional facilities or jail detainees, presents a significant opportunity for identifying new cases of HCV [16].

Another challenge regarding HCV screening involves homeless persons. People who are homeless are usually excluded from regular household surveys of HCV infection prevalence, and surely encompass an underrepresented but important cohort. The 2013 annual homeless assessment report to Congress calculated the number of homeless persons to be approximately 600,000. A survey that intended to screen homeless persons in downtown Los Angeles demonstrated a 26.7% prevalence of HCV infection, about half of whom did not know that they were infected [25]. In contrast, a screening study conducted at a single homeless shelter in Hawaii found 7% with positive HCV (3/40 participants tested) [26]. The presumed high prevalence of HCV infection in the homeless and the unawareness of their disease, pose significant health risks to themselves and others through high-risk behaviors.

The Veteran Affairs (VA) health care system developed a national mandate for routine HCV screening for all VA patients [27] due to increased HCV diagnoses among veterans. Groom and colleagues conducted a two-year, three-stage, retrospective review of risk-based HCV screening and referral (stage one), evaluation of patients in the chronic hepatitis clinic (stage two), and determination of treatment (stage 3) of all patients tested for HCV antibody (Ab) at a VA Medical Center. Of 12,485 HCV Ab tests, 4.16% (520/12,485) were HCV RNA positive. 83% (430/520) of patients were referred to a specialty clinic, of which 73% (382/430) attended their scheduled appointment. 32% (124/382) received antiviral treatment with resultant sustained virologic response (SVR) achieved in 37% (46/124) of patients (9% of
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An earlier study conducted at a VA hospital by Mallette and colleagues [29], reported an anti-HCV prevalence of 4.6% (260/5646). Of those newly diagnosed, 81.1% (211/260) received confirmatory HCV RNA testing, of which 57.8% (122/211) were confirmed to have chronic HCV infection with 46.7% (57/122) deemed eligible for treatment, with 32% (18/57) treated. 33% (6/18) achieved SVR.

High HCV Ab prevalence (8.5%) was reported among long-distance truck drivers in New Mexico in a risk-assessment and screening program that enrolled 652 drivers at a trucking terminal and ten other truck stops throughout the state. 97.5% (636/652) of drivers had blood collected for sexually transmitted infection (STI) and hepatitis screening, of which 8.5% (54/636) tested positive for HCV Ab. The majority of HCV Ab positive drivers reported engaging in high-risk behaviors such as prior or current injection drug use (66.7%, 36/54 drivers) [20].

A prospective, longitudinal, nine-month pilot project to screen HIV-infected persons for acute HCV, was conducted by Taylor and colleagues in a Rhode Island HIV care center. Investigators used routine HIV clinical care schedules and quarterly tracking of ALT levels, which would prompt HCV RNA testing if the ALT level was elevated. HCV RNA testing was pooled for underinsured participants and plasma screened in batches. They reported a 2% (one newly diagnosed case of acute HCV out of 58 enrolled participants) annual incidence of HCV infection [17].

Community-based HCV screening programs among different racial/ethnic populations have yielded a broad range of reported anti-HCV prevalence [21, 22, 30]. Hwang and colleagues provided HBV and HCV screening at a one-day community health fair in Houston, Texas. Fifty eight percent (118/202) of consenting participants were Asian Americans (33%, or 39/118 were Vietnamese American). Overall, 6% (7/118) tested positive for HCV Ab. Among the Vietnamese Americans, HCV prevalence was 15.4% (6/39). Kallman et al. screened 322 subjects for HBV and HCV in Northern Virginia, a region known to have immigrant populations from areas highly endemic for viral hepatitis. 77 of the 322 subjects were screened at community health fairs and 245 were screened at a local private practice clinic. HCV prevalence was 2.2% (7/322) with 5.2% (4/77) screened at the community health fairs and 1.2% (3/245) screened in the clinic [30]. Woo and colleagues conducted HBV and HCV screening for 231 of 9000 attendees at a community festival in Miami-Dade County. Only one participant tested positive for anti-HCV (subsequent HCV RNA testing was not detected) [22].

HCV screening of high-risk populations served by urban ambulatory clinics have demonstrated high prevalence of HCV compared to the estimated U.S. prevalence. Southern et al. retrospectively examined data from 9579 patients at three primary care clinics. Of the 39.7% (3803/9579) tested, 11.5% (438/3803) tested positive for HCV. Of the 438 HCV Ab positive patients, 73.3% (321/438) were born between 1945 and 1965 [18]. Overall, the estimated HCV prevalence was 4.6% assuming all untested subjects were negative (floor estimate), whereas the estimated HCV prevalence was 7.7% assuming untested subjects would test positive equally as those tested based on risk factors (ceiling estimate). Litwin and colleagues conducted two serial interventions, a 15-week risk-based screener and 16-week birth-cohort intervention respectively, at three urban primary care clinics [19]. Both interventions involved clinical reminder stickers that prompted physicians to order HCV tests based on nine HCV risk-factor related questions (risk-based screener) or for patients born between 1946 to 1965 (high prevalence birth-cohort) and resulted in statistically significant increases in HCV testing-13.1% (risk-screener) and 9.9% (birth-cohort)-compared to 6% screened at baseline. Prevalence of HCV Ab positivity was 5.3% (risk-based screener) and 5.8% (birth-cohort).

Birth-cohort screening for hepatitis C infection

Currently, very few data exist for birth-cohort based screening. Southern and colleagues conducted The Hepatitis C Assessment and Testing Project (HepCAT), a serial cross-sectional study at three large, urban clinics in the Bronx, NY, that aimed to increase rates of HCV testing after two serial community-based interventions (risk-based screener intervention and a birth-cohort intervention). The estimated overall prevalence of HCV infection was 7.7% among patients with known risk factors (i.e.
Figure 1. Barriers to Hepatitis C Screening and Treatment.
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Substance abuse, alcohol abuse, HIV, cirrhosis, end-stage renal disease, ALT elevation, STIs, or psychiatric diagnosis) associated with anti-HCV positivity. While 73.3% of the anti-HCV positive patients were born between 1945 and 1964, the data suggest that 26.7% of those infected with HCV would not be identified by birth-cohort screening alone. Furthermore, high rates of HCV infection were found in high-risk patients who were born outside the birth-cohort, which underscores the importance to continue risk-based screening methods. The HepCAT study investigators noted that the anti-HCV-positivity rates for the risk-based screener intervention and birth-cohort screening were 5.3% and 5.8% respectively [18, 19].

Cartwright and colleagues analyzed data of 87,144 veterans seen at Atlanta VA Medical Center of which 48% (41,556) had HCV Ab testing. 10% (4,107/41,556) tested positive for HCV Ab of which 73% (3,004/4,107) were identified as having chronic hepatitis C (positive HCV Ab and detectable HCV RNA viral load). When the veterans were age-stratified (i.e. those born between 1945 and 1965), 54% (25,097/41,556) were tested for HCV, of which 14.5% (3,644/25,097) were HCV Ab positive with 76% (2,775/3,644) confirmed with chronic infection [31]. A unique setting for birth-cohort HCV screening was explored by Sears and colleagues, by implementing a viral hepatitis screening program in an endoscopy suite. Five hundred people who underwent screening colonoscopy were invited to participate in the study, 483 of whom were deemed eligible (17 patients already had known chronic hepatitis C). 78% (376/483) agreed to participate, of which 92% (346/376) had sufficient blood draws for analysis. HCV prevalence was 1.2% (4/346) with only one patient found to have detectable HCV RNA [32].

Barriers to HCV screening

HCV treatment uptake has been historically and unacceptably low. Gaps in linkage to care have been attributed to multiple barriers at the patient, provider, healthcare organizations, hospital and institutions, and payer level, which impede delivery of care along the HCV infection-to-diagnosis-to-treatment continuum (Figure 1) [33].

Patient-related barriers

In a recent survey conducted by Barocas and colleagues of 553 individuals, a subset of 362 respondents reported that fear represented a barrier to HCV testing. Responses such as being “not ready” or “scared of the result” or “I don’t want to hear that I have it” further characterized this psychological barrier. Other respondents had a low perceived risk for HCV infection [34]. Lack of rapport with a healthcare provider and perceptions of feeling judged and stigmatized were other patient-related barriers to HCV screening.

Other patient-related barriers such as poor knowledge related to HCV infection and treatment, non-adherence to specialist follow-up upon referral, lack of insurance, socio-economic constraints, lower education level, psychiatric disease, injection drug use, and inadequate healthcare access have been elucidated [35, 36].

In a recent global survey of 697 HCV treatment providers from 29 countries, McGowan and colleagues reported that patient-level barriers; particularly, fear of side effects and concerns regarding treatment cost/duration, were the most significant obstacles to treatment, which mirrored prior surveys [37].

Healthcare provider-related barriers

A survey of 214 physicians showed that a large percentage of primary care physicians lacked knowledge regarding HCV screening guidelines, which was associated with less HCV screening compared to hepatologists. Knowledge deficits in primary care providers may be attributed to limited training, lower caseloads, and consequent lack of confidence to start HCV treatment [35]. Limited availability of specialists has also contributed to infrequent referrals by primary care providers. Ongoing substance abuse by patients co-infected with HIV and HCV and the perceived priority of clinicians to treat HIV infection in these patients were also suggested provider-related barriers to HCV screening [38]. Providers often perceive patients with psychiatric conditions or substance abuse problems as poor treatment candidates with resultant lack of subspecialist referral and/or treatment initiation [35].
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Healthcare system-related barriers

Gaps in follow-up care for patients diagnosed with HCV infection may be attributed to healthcare system-related barriers such as lack of specialist availability, lack of healthcare access, under-insurance or lack of insurance, and failure of healthcare providers to provide referrals [6, 35]. Thus far, there is no published data evaluating the impact of the Affordable Care Act on HCV screening.

Medication access and payer barriers

Current treatment for HCV with direct-acting antiviral agents (DAA) pose significant challenges to the payer as most of the regimens cost at least $80,000 USD to complete a 12-week treatment course. Most insurance companies in the U.S. restrict DAA treatment to patients who meet the criteria set by the American Association for the Study of Liver Diseases (AASLD) for priority candidates of HCV treatment, which consequently results in no coverage for the majority of patients with histologically mild disease [39]. However, many of these non-covered patients indeed have significant HCV RNA levels and elevated liver enzymes, which is often indicative of continued liver necro-inflammation.

For many years, HIV patients in the U.S. have gained free access to public funding for treatment. In contrast, despite the fact that HCV causes more mortality and higher societal financial burden than HIV infection, there is no funding mechanism that exists for using public resources to cover treatment for all HCV infected individuals. It is critical for healthcare policy makers in the U.S. to respond to this urgent need to reduce harm for the KAP infected with HCV. Insurance plans requiring high deductibles limit access to medications and without universal access supported by public funding to treat those with HCV, patients with mild or even significant liver damage cannot afford treatment. Consequently, HCV screening may unfortunately become irrelevant because the majority of patients will have no access to treatment and healthcare providers will lack motivation to prescribe it.

Conclusion and future directions to improve HCV screening

Although the approach of using birth-cohort and risk-factor based screening for HCV infection has been endorsed by both the CDC and the USPSTF, challenges remain regarding its application in the target population. Systematic targeted assessment of screening strategies is needed (e.g. screening incarcerated persons on admission in the correctional system). Quality improvement initiatives such as computerized reminders that prompt healthcare clinicians to screen and test patients for HCV may be effective in increasing screening [40]. Further improvement on screening technique may enhance the ability to capture those patients at risk. For example, the rapid antibody test (oral swab) for HCV may enhance urban outreach testing programs and target high-risk groups who are likely unaware of their HCV status [41]. The U.S. Food and Drug Administration has approved a home-based qualitative HCV screening test, which may be done in the privacy of a person’s home. This test is highly accurate and provides toll-free telephone counseling from medical professionals. This testing option may reduce patient fears of being stigmatized and labeled, increase HCV screening, and enhance linkage to care [42].

Strategies to expand primary care capacity and improve linkage to care and treatment include innovative programs such as Project ECHO. This telehealth technology model involves didactic teleconferencing by multidisciplinary specialists for PCPs and case-based shared learning between PCPs and specialists to create guided comprehensive treatment plans for underserved patients [43]. Mitruka and colleagues implemented this model in Utah and Arizona to start treatment in 129 of 280 patients (46.1%) with HCV infection over a 17-month period [44].

Opportunities to enhance HCV screening and adherence to treatment using proven models such as substance use detoxification clinics, directly observed therapy programs, HIV clinics, and peer-support groups, will continue to develop and evolve [35] along with novel settings such as the emergency department [45] and outpatient screening settings such as colonoscopy [32]. Broadening the base of HCV screening seeks to identify more patients with HCV infection and potentially link them to care to achieve cure. However, potential harms may exist. New DAAs are very expensive and insurance companies may not approve these medications for patients unless there is evidence of
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advanced liver disease. Thus, these HCV-infected patients are left untreated and may suffer social stigmatization and isolation. Further studies are needed to clarify the cost-effectiveness of birth-cohort screening among sub-groups that may be at low-risk for HCV infection. For example, immigrants from historically low endemic areas for HCV infection may represent a low-risk population that may not benefit from birth-cohort screening. However, there are 40 million foreign-born persons who reside in the U.S. and over one million new immigrants entering the U.S. every year, many of whom may have come from highly endemic areas such as Egypt (10% HCV prevalence), Africa (2% to >3%), Eastern Europe (2% to 3%), and Latin America (3%) [46, 47]. Therefore, these persons should be screened for HCV infection. One area of research may study whether HCV infection rates of immigrants residing in the U.S. mirror the HCV prevalence rates in their country of origin. Moreover, healthcare providers must inform and counsel their patients of potential exposure risks (e.g. acupuncture, blood transfusions, routine medical injections) when traveling in these endemic areas [2].

The advent of new DAAs to treat HCV infection with one-pill, once-daily dosing, minimal side effects, and high SVR rates, are expected to eliminate the gap between HCV diagnosis and cure. Indeed, there is great urgency for U.S. healthcare policy to respond to the needs of reducing harm in KAP with HCV infection before the devastating complications of end stage liver disease are manifest. Although current DAA treatment is highly effective and cost-saving in the long term with the possibility of global HCV eradication, screening and treatment uptakes remain inadequate and have resulted in an unacceptably large number of patients unable to receive treatment and achieve cure. Access to HCV treatment may be secured with a shift in coverage from the private sector to publicly-funded programs. Such policy change is paramount for enhancing screening and linkage to care. Patient advocacy groups and healthcare provider organizations must work together and promote awareness and facilitate universal coverage for HCV treatment.

Disclosure of conflict of interest

The authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest or non-financial interest in the subject matter discussed in this manuscript.

Address correspondence to: Calvin Q Pan, Division of Gastroenterology, Department of Medicine, NYU Langone Medical Center, NYU School of Medicine, 132-21 Forty First Ave, Flushing, New York, 11355 U.S.A. Tel: 1-718-888-7728; Fax: 1-718-353-6901; E-mail: cpan11355@yahoo.com

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