CDC Recommendations for Hepatitis C Screening among Adults

Recommendations and Reports

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Summary

Hepatitis C virus (HCV) infection is a major source of morbidity and mortality in the United States, resulting in tens of thousands of deaths each year(1, 2). HCV is transmitted primarily through parenteral exposures to infectious blood or body fluids that contain blood, most commonly through injection drug use(3). Approximately 75%-85% of persons who become infected with HCV will develop chronic infection(4, 5), and 10%-15% will develop progressive liver fibrosis and cirrhosis(4-6). Well-tolerated, all oral medication regimens can cease disease progression and result in a virologic cure in most persons with 8-12 weeks of treatment, although these medications are not currently available for pregnant women or children under 12 years of age. This report updates and summarizes previously published recommendations from the CDC regarding screening for HCV infection in the United

States(7). CDC is augmenting previous guidance to recommend: 1) hepatitis C screening at least once in a lifetime for all adults aged 18 years and older, except in settings where the prevalence of HCV infection is less than 0.1%, and 2) hepatitis C screening for all pregnant women during each pregnancy, except in settings where the prevalence of HCV infection is less than 0.1%. Regardless of age or setting prevalence, all persons with risk factors should be tested for hepatitis C, with periodic testing while risk factors persist. This report is intended to serve as a resource for healthcare professionals, public health officials, and organizations involved in the development, implementation, delivery, and evaluation of clinical and preventive services.

Introduction

Hepatitis C is the most commonly reported blood-borne infection in the United States(3, 8), and during 2013-2016 there were an estimated 2.4 million people (1.0%) in the nation living with hepatitis C(9). Percutaneous exposure is the most efficient mode of hepatitis C virus (HCV) transmission, and injection drug use is the primary risk factor for infection(3). National surveillance data reveal an increase in reported cases of acute HCV infection every year from 2009 through 2017. The highest rates of acute cases are among persons aged 20-39 years. As new HCV infections have risen among reproductive aged adults, rates of HCV infection nearly doubled from 2009-2014 among women with live births(10). In 2015, 0.38% of live births were delivered by mothers with hepatitis C(11).

This report augments previously published CDC recommendations (7, 12) for the identification of hepatitis C in the United States. A list of all abbreviations used is provided (Box 1).

New Recommendations

The following recommendations are new:

- hepatitis C screening at least once in a lifetime for all adults aged 18 years and older, except in settings where the prevalence of HCV infection is less than 0.1%, and
- hepatitis C screening for all pregnant women during each pregnancy, except in settings where the prevalence of HCV infection is less than 0.1%.

This report augments CDC recommendations for hepatitis C testing published in 1998 and 2012. The recommendations in this report do not replace previous recommendations for HCV testing that are based on known risk factors or clinical indications. Previously published recommendations for hepatitis C testing of persons with risk factors, and alcohol use screening and intervention for persons identified as infected with HCV, remain in effect(7, 12).

Epidemiology

In 2017, a total of 3,186 cases (1.0 per 100,000) of acute HCV infection were reported to CDC (Figure 1). The reported number of cases in any given year is believed to represent less than 10% of the actual number of cases, due to under-ascertainment and under-reporting.(13) It is estimated that 44,300 new cases of HCV infection occurred in 2017. The rate of reported acute HCV infections increased from 0.6 cases per 100,000 population in 2012 to 1.0 cases per 100,000 population in 2017. The 2017 acute HCV

incidence was greatest for persons aged 20-29 years (2.8 cases per 100,000 population) and 30-39 years (2.3 cases per 100,000 population). Persons aged 19 years or younger had the lowest incidence (0.1 cases per 100,000 population). Incidence was slightly greater for males than females (1.1 cases and 0.9 cases per 100,000 population, respectively)(3). During 2006-2012, the combined incidence of acute HCV infection in four states (Kentucky, Tennessee, Virginia, and West Virginia) increased 364% among persons aged 30 years or younger. Among cases in these states with identified risk information, injection drug use was most commonly reported (73%). Those infected were primarily non-Hispanic white persons from nonurban areas(14).

Based on National Health and Nutrition Examination Survey (NHANES) data, it is estimated that in 2013-2016 approximately 0.9 % of the noninstitutionalized U.S. population, or 2,139,000 persons, were living with HCV infection (HCV RNA positive). Considering populations not included in NHANES, an additional 247,100 persons were living with HCV infection, adjusting the prevalence to 1.0%(9). Nine states comprise 51.9% of all persons living with HCV infection: California, Texas, Florida, New York, Pennsylvania, Ohio, Michigan, Tennessee, and North Carolina(8).

Strategy to End the Hepatitis C Epidemic

In 1990, serologic tests to detect immunoglobulin G antibody to HCV (anti-HCV) by enzyme immunoassay were licensed and became commercially available in the United States, and U.S. blood banks voluntarily began testing donations for anti-HCV. In 1991, U.S. Public Health Service inter-agency guidelines addressing hepatitis C screening of blood, organs, and tissues were issued. These guidelines recommended hepatitis C testing for all donations of whole blood and components for transfusion, as well as testing serum/plasma from donors of organs, tissues, or semen intended for human use(15).

In 1998, CDC expanded the inter-agency guidelines to provide recommendations for preventing transmission of HCV; identifying, counseling, and testing persons at risk for hepatitis C; and providing appropriate medical evaluation and management of persons with hepatitis C. That guidance recommended testing based on risk factors for HCV infection, for persons: who ever injected drugs and shared needles, syringes, or other drug preparation equipment, including those who injected once or a few times many years ago and do not consider themselves as drug users; with selected medical conditions, including those who received clotting factor concentrates produced before 1987, those who were ever on chronic hemodialysis (maintenance hemodialysis), and those with persistently abnormal alanine aminotransferase (ALT) levels; who were prior recipients of transfusions or organ transplants, including those who were notified that they received blood from a donor who later tested positive for HCV infection, those who received a transfusion of blood or blood components before July 1992, and those who received an organ transplant before July 1992; and with a recognized exposure, including healthcare, emergency medical, and public safety workers after a needlestick injury, sharps injury, or mucosal exposure to blood infected with hepatitis C or children born to mothers infected with hepatitis C(12). In 1999, the U.S. Public Health Service and Infectious Disease Society of America (IDSA) guidelines recommended hepatitis C testing for persons with HIV(16).

Because of the limited effectiveness of risk-based hepatitis C testing, CDC considered strategies to increase the proportion of infected persons who are aware of their status and are linked to care. In 2012, CDC augmented its guidance to recommend one-time hepatitis C screening for persons born during 1945-1965, without prior ascertainment of risk. With an anti-HCV prevalence of 3.25%, persons born in the 1945-1965 birth year cohort accounted for approximately three-fourths of chronic HCV infections among U.S. adults in 1999-2008(17). Many persons (~45%) infected with HCV do not recall or report having specific risk factors. Included in the 2012 guidance were recommendations for alcohol use screening and intervention for those persons identified with HCV infection(7).

Existing CDC guidelines recommend that pregnant women be tested for hepatitis C only if they have known risk factors. However, universal hepatitis C screening during pregnancy was recommended by the American Association for the Study of Liver Diseases and IDSA in 2018(18).

Existing strategies for hepatitis C testing have had limited success, as only about 56% of people with HCV infection reported having ever been told they had hepatitis C in 2013-2016(19); thus, strengthened guidance for universal hepatitis C testing is warranted.

Virus Description, Transmission, Clinical Features, and Natural History

HCV is a small, single-stranded, enveloped RNA virus in the flavivirus family with a high degree of genetic heterogeneity. Seven distinct HCV genotypes and more than 67 subtypes have been identified. Genotype 1 is the most prevalent genotype in the United States and worldwide, accounting for more than 75% and 46% of cases, respectively(20, 21). Geographic differences in global genotype distribution are important as some treatment options are genotype specific(21, 22). High rates of mutation in the HCV RNA genome are believed to play a role in the pathogen's ability to evade the immune system(21). Prior infection with HCV does not protect against subsequent infection with the same or different genotypes.

HCV is primarily transmitted through direct percutaneous exposure to blood. Mucous membrane exposures to blood can also result in transmission, although this route is less efficient. HCV can be detected in saliva, semen, breast milk, and other body fluids, although these body fluids are not believed to be efficient vehicles of transmission(21, 23).

Persons with acute HCV infection are typically either asymptomatic or have a mild clinical illness like that of other types of viral hepatitis. Approximately 70% to 80% of persons have no apparent symptoms(24). Jaundice may occur in 20%-30%, while nonspecific symptoms (e.g., anorexia, malaise, or abdominal pain) may be present in 10%-20% of persons. Fulminant hepatic failure following acute hepatitis C is rare. The average time from exposure to symptom onset is 2-12 weeks (range: 2-26 weeks)(25, 26). Anti-HCV antibodies can be detected 4-10 weeks after infection and are present in more than 97% of persons by 6 months after exposure. HCV RNA can be detected as early as 1-2 weeks after exposure. The presence of HCV RNA indicates current infection(27-29).

Approximately 15%-25% of persons resolve their acute infection without sequelae. Predictors of spontaneous clearance include jaundice; elevated ALT level; hepatitis B virus surface antigen (HBsAg) positivity; female sex; younger age; HCV genotype 1; and host genetic polymorphisms, most notably

those near the IL28B gene(27-29). Chronic HCV infection develops in 75%-85% of persons as viral replication evades the host immune response. The course of chronic liver disease is usually insidious, progressing slowly, without symptoms or physical signs, in most persons during the first 20 years or more following infection. Approximately 10%-15% of persons with hepatitis C will develop cirrhosis over 20-30 years. Those with cirrhosis experience a 1%-5% annual risk for hepatocellular carcinoma and a 3%-6% annual risk of hepatic decompensation, for which the risk of death in the following year is 15%-20%. Persons who are male, older than 50 years, use alcohol, have nonalcoholic fatty liver disease, have hepatitis B virus (HBV) or HIV coinfection, and who are undergoing immunosuppressive therapy have increased rates of progression to cirrhosis. Extrahepatic manifestations of chronic HCV infection may occur and include membranoproliferative glomerulonephritis, essential mixed cryoglobulinemia, and porphyria cutanea tarda(27-29).

Persons at Risk for HCV Infection

HCV is transmitted primarily through parenteral exposures to infectious blood or body fluids that contain blood. Injection drug use is the most common means of HCV transmission in the United States. Invasive medical procedures (e.g., injections, hemodialysis) pose risks for HCV infection when standard infection control practices are not followed(30, 31). Healthcare-related hepatitis C outbreaks also stem from drug diversion (i.e., tampering with fentanyl syringes)(32, 33). Although sexual contact is not an efficient mode of HCV transmission, the risk for HCV infection through sexual contact increases for men and women with HIV, especially MSM(34). Other possible exposures include sharing personal items contaminated with blood (e.g., razors or toothbrushes), unregulated tattooing, needlestick injuries among healthcare personnel, and birth to a mother with hepatitis C. Receipt of donated blood, blood products, and organs was once a common means of transmission but is now rare in the United States(6, 18, 35).

Prior to implementing universal blood product testing in 1992, children acquired hepatitis C predominantly through blood transfusion. Given the increasing incidence of HCV infection among women of childbearing age, perinatal transmission (intrauterine or intrapartum) has become an increasingly important mode of HCV transmission(36, 37). The risk for perinatal transmission is 5.8% for infants born to mothers infected with hepatitis C but not with HIV and doubles for infants born to mothers co-infected with HCV and HIV(38). Nearly 20% of infants with perinatally acquired hepatitis C clear the infection, 50% have chronic asymptomatic infection, and 30% have chronic active infection(39). HCV-related liver disease rarely causes complications during childhood. Because fibrosis increases with disease duration, perinatally infected individuals may develop severe disease as young adults(36, 37).

Clinical Management and Treatment

The treatment for HCV infection has evolved substantially since the introduction of direct-acting antiviral (DAA) agents in 2011. DAA therapy is generally better tolerated, of shorter duration, and more effective than interferon-based regimens used in the past(40, 41). New drugs with different mechanisms of action and fewer negative side effects continue to become available. The latest classes of antivirals for hepatitis C treatment include second- and third-generation DAAs, categorized as either

protease inhibitors, nucleotide analog polymerase inhibitors, non-nucleotide analogs, or nonstructural (NS5A) protein inhibitors. Some agents are pangenotypic, meaning they have antiviral activity against all genotypes(36, 37, 41). A sustained virologic response (SVR) is indicative of cure and is defined as the absence of detectable HCV RNA 12 weeks after completion of treatment. Over 90% of HCV-infected persons can be cured of HCV infection with 8-12 weeks of therapy, regardless of HCV genotype(40, 41).

Despite their favorable safety profile, DAAs are not approved for use in pregnancy, as safety data during pregnancy are lacking. However, testing women during pregnancy for HCV infection allows identification of infants who should receive testing. In 2017, ledipasvir/sofosbuvir became the first DAA approved for use in children aged 12-17 years(36, 37). Although treatment is not approved for children younger than 12 years of age, infected children can be monitored. Furthermore, identification of HCV infection in a pregnant woman may be a marker for other conditions that are associated with a high-risk or substance-exposed pregnancy and may warrant additional monitoring and screening during the pregnancy as well as monitoring for infants as applicable (e.g., for neonatal abstinence syndrome during the post-partum period for opioid-exposed infants).

No vaccine against hepatitis C exists and no effective pre- or post-exposure prophylaxis (e.g., immune globulin) is available currently. HCV infection is not an indication for Cesarean delivery, and is not a contraindication to breastfeeding provided nipples are not bleeding or cracked(42).

Methods

To inform these recommendations, comprehensive systematic reviews of the literature, described in more detail below, were conducted, analyzed, and assessed in two stages. These reviews examined the availability of evidence regarding HCV infection prevalence and the health benefits and harms associated with one-time hepatitis C screening for persons unaware of their status.

CDC determined that the new recommendations constituted scientific information that will have a clear and substantial impact on important public policies and private sector decisions. The Information Quality Act, therefore, required peer review by specialists in the field who were not involved in the development of these recommendations. Additionally, feedback from the public was solicited through a Federal Register notice released on Month XX, 2019, announcing the availability of the draft recommendations for public comment through Month XX, 2019. Feedback attained during both the peer review process and the public comment period was reviewed by CDC, and the draft recommendation statement was modified accordingly.

To facilitate the systematic review of the evidence, two research questions were formulated to guide the development of the recommendations:

- Does universal screening for HCV infection among adults aged 18 years and older, compared to risk-based screening, reduce morbidity and mortality?
- Does universal screening for HCV infection among pregnant women, compared to risk-based screening, reduce morbidity and mortality among mothers and their children?

An analytic framework describing the chain of indirect evidence was developed:

- How would universal screening for hepatitis C affect the number (and composition) of people who screen positive for HCV infection?
- How many additional persons would be linked to care?
- Do desirable treatment effects outweigh undesirable effects?

Key questions (KQ) were formulated for each link of the chain (Figure 2):

- K.Q.1.a. What is the prevalence of HCV infection in the United States by general population and risk groups?
- K.Q.2.a. What is the diagnostic accuracy of HCV antibody testing?
- K.Q.2.b. What are the harms of hepatitis C screening?
- K.Q.2.c. What proportion of people who screen positive for HCV infection are linked to care?
- K.Q.3.a. What is the effect of DAA treatment on HCV viral load?
- K.Q.3.b. What is the effect of DAA treatment on morbidity (including cirrhosis, hepatocellular carcinoma)?
- K.Q.3.c. What is the effect of DAA treatment on mortality (HCV-specific and all-cause)?
- K.Q.3.d. What are the adverse effects of DAA treatment?

Because the diagnostic accuracy of anti-HCV testing and treatment effects have been well described previously, K.Q.2.a. and K.Q.3.a.-d. were not included in this review.

Literature Review

Systematic reviews were conducted to examine benefits and harms of hepatitis C screening. The systematic review process for these recommendations was separated into two stages: 1) a review of evidence to inform the hepatitis C screening strategy among all adults, and 2) a review of the evidence to inform the hepatitis C screening strategy among pregnant women.

Systematic reviews were conducted for literature published worldwide in Medline (OVID), Embase (OVID), CINAHL (Ebsco), Scopus, and Cochrane Library. All age groups were included in the literature search. For the all adult review, the beginning search date was 2010 to capture studies reflecting the changing epidemiology of HCV infection and the availability of DAAs, and the end date was the run date of August 6, 2018 (Figure 3). For the pregnancy review, the beginning search date was 1998 to capture studies published since past recommendations were issued in 1998, and the end date was the run date of July 2, 2018 (Figure 4). Duplicates were identified using the Endnote (Clarivate Analytics, Philadelphia, Pennsylvania, United States) automated "find duplicates" function with preference set to match on title, author and year. Duplicates were removed from the Endnote library.

Following the initial collection of results from the search, titles/abstracts were independently reviewed by two persons. For papers in which the title indicated the study was irrelevant to the research question, abstracts were not reviewed.

Titles/abstracts for the all-adult review were independently reviewed by either LW, SS, AT, SC, NW, or MO; all titles/abstracts had to be screened by either senior abstractor (LW or SS). Conflicts were resolved by SS. If a conflict arose from a study whose title/abstract was reviewed only by both LW and SS, that study was kept for the full text review. All full texts were screened by both MO and LW. SS made the final decision regarding conflicts. Information from the full texts was extracted for the evidence review. A systematic review software program, Covidence (Melbourne, Victoria, Australia) was used to facilitate the all-adult review process.

Titles/abstracts for the pregnancy review were independently reviewed by two senior abstractors (LW or SS). Studies that either abstractor deemed as potentially relevant were retrieved for full text review. All full texts were screened by both senior abstractors. Information from the full texts was extracted for the evidence review.

Studies were excluded if they were conducted in a correctional facility (as separate CDC guidance for screening specifically in correctional facilities is under development), if prevalence data from 2010 forward could not be abstracted (all-adult review only), or if the study reported estimated or projected data. Studies were also excluded if the study population was non-U.S. based, unless the study examined outcomes related to harms of screening. Studies related to harms of screening were included broadly to help ensure all potential harms were captured in the review. Linkage-to-care data were abstracted from 2010 forward, and HCV RNA testing alone was not deemed linkage-to-care for purposes of this review. Study design and setting were abstracted for all applicable studies. After the formal literature review was conducted, relevant studies identified through reference lists and those that were newly published were added for review. Studies that were reported as feasibility or pilot studies, even if they used a prospective design, were deemed pilot studies (and not prospective studies).

To capture recently published studies, a supplementary literature search was conducted on Month XX, 2019, for both all adults and pregnant women. The search strategy was the same as for the original searches, except the end date was extended to Month XX, 2019. Titles/abstracts were independently reviewed by XX and XX. Full texts were screened by XX. Information from the full texts was abstracted and added to the original review.

Results

For the all-adult review, the formal literature search yielded 4,867 studies. Twenty-nine duplicates were identified. Of 4,838 unique studies, 4,170 (86.2%) were deemed irrelevant by title/abstract screening, leaving 668 (13.8%) full texts for review. Among these, 368 studies had data available to extract. Three additional studies (8, 9, 43) were added to the review outside of the formal literature search (e.g., identified from reference lists or newly published) yielding a total 371 studies included.

For the pregnancy review, the formal literature search yielded 1,500 studies. Two duplicates were identified. Of 1,498 unique studies, 1,412 (94.3%) were deemed irrelevant by title/abstract screening, leaving 86 (5.7%) full texts for review. One additional study was added to the review outside of the formal literature search.

The supplementary review yielded an additional XXX and XXX studies among all adults and pregnant women, respectively. Of these, XX (XX.X%) and XX (XX.X%), respectively, were deemed irrelevant by title/abstract screening, leaving XX (X.X%) and XX (X.X%), respectively, full texts for review.

One prospective observational study(44) utilized a screening questionnaire and compared universal versus risk-based screening among pregnant women. Among 419 women at a single clinic, 37 (8.8%) were deemed at high risk for hepatitis C. The prevalence of HCV infection during pregnancy was 10.8% among high-risk women and 1.6% among low-risk women. The sensitivity and specificity of the screening questionnaire was 0.85 and 0.52, respectively. The authors concluded that the use of a screening questionnaire underestimated the number of pregnant women at high risk for hepatitis C, and that a universal screening strategy should be considered. The study was limited by loss to follow-up, as 41.2% of subjects were unavailable to consent or declined participation.

Considering all 86 applicable studies, the median anti-HCV positivity prevalence (indicative of past or current infection) among all adults was 7.5% (range, 0.0%-100.0%). Median anti-HCV positivity prevalence was 3.3% (range, 0%-19.8%) for birth cohort members (34 studies), 7.5% (range, 1.6%-25.8%) for patients seen in the emergency department (ED) (3 studies), 4.7% (range, 3.4%-7.5%) for immigrant populations (3 studies), 9.4% (range: 1.2%-27.4%) for others potentially at-risk for HCV infection (e.g., people experiencing homelessness or who live in communities with high rates of hepatitis C) (24 studies), 15.7% (range, 8.0%-19.3%) for persons with HIV (PWH) (5 studies), 43.6% (range, 1.6%-100%) for persons who use drugs (26 studies), and 1.2% (range, 0.1%-67.0%) for pregnant women (26 studies) (Table 1,2).

Considering all 32 applicable studies, the median rate of HCV RNA positivity (indicative of viremia) among those who were anti-HCV positive was 64.6% (range, 20.0%-97.6%). Median HCV RNA positivity was 55.3% (range, 20.0%-97.6%) for birth cohort members (14 studies), 57.9% for patients seen in the ED (1 study), 81.8% for Egyptian immigrants (1 study), 72.4% (range: 45.5%-82.6%) for others potentially at risk for HCV infection (9 studies), and 73.4% (range, 35.6%-82.6%) for persons who use drugs (2 studies). HCV RNA positivity was not reported for studies among PWH or pregnant women (Table 1,2).

One primary study by Hofmeister, et al.(9) and one follow-up modeling study(8) based entirely on Hofmeister's analysis examined nationally representative anti-HCV and HCV RNA data for adults from the 2013-2016 National Health and Nutrition Examination Survey (NHANES), as well as data from the literature to estimate prevalence among populations not sampled by NHANES. The national estimate for anti-HCV positivity among adults was 1.7% (95% CI: 1.4, 2.0).(9) The HCV RNA prevalence estimate among adults was 1.0% (95% CI, 0.8%-1.1%)(9).

Forty-one studies (14 retrospective cohort, 10 prospective cohort, and 17 others [including pilot studies, cross-sectional, qualitative, mixed methods, interrupted time series, and claims analysis]) informed linkage-to-care among adults (Table 3). Sixteen studies (39.0%) included only or predominantly persons born during 1945-1965; the remainder of studies comprised adults without restriction by age, particularly adults with risk factors for hepatitis C or those living in communities with a high prevalence of hepatitis C or risk factors for HCV infection (e.g., injection drug use). Specific interventions to

facilitate linkage-to-care and treatment of persons with hepatitis C (e.g., CDC's Hepatitis Testing and Linkage to Care initiative studies, medical record prompts) were employed in 16 (39.0%) studies. Follow-up appointments or referrals were made for a median of 80.2% of HCV RNA positive patients (range, 0.0%-100.0%) (9 studies). A median of 49.6% of HCV RNA positive patients attended their first follow-up appointment (range, 0.0%-100.0%) (25 studies). This excludes self-reported data and studies that reported patients who were "linked to care" without explicitly stating the patient attended an appointment. A median of 24.7% of those attending a follow-up appointment received treatment (range, 0.0%-100.0%) (15 studies). Among those who received treatment, a median of 100.0% of patients achieved SVR (range, 79.2%-100.0%) (5 studies). Extrapolating these data reveals that for every 100 persons with hepatitis C, 9.8 received treatment and achieved SVR. Because DAAs are not approved for use during pregnancy, linkage-to-care was not assessed for pregnant women.

Harms associated with hepatitis C screening were informed by 21 and 12 studies from the all adult and pregnancy review, respectively, including U.S.-based and non-U.S.-based studies. No study compared harms systematically using comparison groups associated with different screening approaches. Harms informed by the all adult review included physical harms of screening (1 study)(45), anxiety/stress related to testing or waiting for results (4 studies)(46-49), anxiety related to receiving positive results (1 study)(50), interpersonal outcomes (e.g., problems related to family, friends from learning HCV status) (5 studies)(47, 50-53), attitudes toward people with hepatitis C, including stigma (8 studies)(50, 52-58), and false positive results, including among left ventricular assist device patients, possibly precluding heart transplantation (6 studies)(59-64). Harms informed by the pregnancy review included physical harms of screening (1 study)(65) anxiety (5 studies)(66-70), stigma (1 study) (69), psychological issues (2 studies)(65, 71), fears related to sexual relationships (1 study)(72), legal ramifications and potential loss of infant custody (1 study)(73), decreased quality of life (1 study)(74), social repercussions (1 study)(44), expense (2 studies)(70, 75), and false positive results (1 study)(65). Other plausible harms associated with hepatitis C screening identified outside of these studies include harms associated with undergoing a liver biopsy (e.g., pain, bleeding, intestinal perforation, and death), insurability and employability issues, treatment adverse effects, the need to wait or return for test results, and difficulty accessing treatment. The authors concluded that identified or potential harms did not outweigh the benefits of screening.

These literature reviews are subject to the limitations of the included studies. Publication bias may favor publications of studies reporting high disease prevalence. Other biases, including recall bias and low response rates, may occur. Furthermore, studies performed in high-burden areas may not be representative of the general population.

Cost-effectiveness Considerations

Several recent economic analyses provide information on the cost-effectiveness of hepatitis C screening. Eckman(76) determined universal screening for persons aged 18 years and older, using a healthcare perspective, yielded an incremental cost-effectiveness ratio [ICER] of $11,378 per quality-adjusted life year [QALY] gained when compared to 1945-1965 birth cohort screening, using a base case hepatitis C prevalence of 2.6% and 0.29% for birth cohort members and non-birth cohort members, respectively.

The ICER remained below $50,000 per QALY gained; a threshold sometimes considered as a cut-off for determining cost-effectiveness, until the anti-HCV positivity prevalence dropped below 0.07% among non-birth cohort members. Barocas(77) calculated an ICER of $28,000/QALY gained under a healthcare perspective for a strategy of screening all persons aged 18 years and older compared to birth cohort screening, with an additional 280,000 cures, and 4,400 fewer cases of hepatocellular carcinoma. When the national hepatitis C prevalence was halved from the base case of 0.84%, the ICER increased to $39,400. The ICER remained below $100,000 per QALY gained when varying key parameters across broad ranges (e.g., when there was no improvement in quality of life and costs decreased following early-stage cure, when cost of early-stage disease was $0, when treatment costs varied, and when there was no mortality benefit from SVR). Several other studies provide similar cost-effectiveness estimates of a universal screening strategy for adults, with ICERs ranging from cost-saving to $71,000/QALY gained(78-80).

Analyses focusing on pregnant women have yielded similar results. Using a hepatitis C prevalence of 0.38% among pregnant women, as determined from national birth certificate data, Tasillo (81) reported universal hepatitis C screening during each pregnancy under a healthcare perspective compared to current practice of risk-based screening had an ICER of $41,000/QALY gained. Universal screening reduced HCV-attributable mortality by 16% and more than doubled the proportion of infants born to mothers with hepatitis C who were identified as HCV-exposed, from 44% to 92%. The ICER remained at or below $100,000 per QALY gained if hepatitis C prevalence was higher than 0.16%. Chaillon(82) calculated an ICER of $2,826 for universal screening of pregnant women under the healthcare perspective, compared to risk-based screening at an HCV RNA positivity prevalence of 0.73%; sensitivity analyses generated an ICER of $50,000 per QALY gained or less until the prevalence of chronic hepatitis C infection dropped to 0.03-0.04%. Studies did not account for any cost savings associated with prevention of risks to subsequent pregnancies or the potential benefits to early detection and management of infected infants.

Hepatitis C Testing Strategy

The goal of hepatitis C screening is to identify persons who are currently infected with HCV. Hepatitis C testing should be initiated with a Food and Drug Administration (FDA)-approved anti-HCV test. Persons who test anti-HCV positive are either currently infected or had past infection that has resolved naturally or with treatment. Immunocompetent persons without hepatitis C risks who test anti-HCV negative are not infected and require no further testing. Persons testing anti-HCV positive should have follow-up testing with an FDA-approved nucleic acid test (NAT) for detection of HCV RNA. NAT for HCV RNA detection determines viremia and determines current HCV infection. Persons who test anti-HCV positive, but HCV RNA negative do not have current HCV infection. CDC encourages use of reflex HCV RNA testing, in which specimens testing anti-HCV positive undergo HCV RNA testing immediately and automatically in the laboratory, using the same sample from which the anti-HCV test was conducted. Hepatitis C testing should be provided on-site when feasible.

Determining the Prevalence Threshold for the Recommendation

The recommended HCV RNA prevalence threshold of 0.1% was determined based, in part, on review of published ICERs, as a function of hepatitis C prevalence, and the most up-to-date estimated prevalence of hepatitis C within states. In general, cost analyses determined that for all adults, the ICER would be approximately $50,000 per QALY gained or less at current treatment costs (approximately $25,000 per course of treatment) and an anti-HCV positivity prevalence of 0.07% in the non-birth cohort, which is similar to the HCV RNA prevalence in all adults; at a hepatitis C prevalence of 0.1%, the ICER would be about $36,000 per QALY gained(83). Some economists use $50,000 as a conservative threshold to determine cost-effectiveness. As treatment costs decrease, ICERs will also decrease, assuming other parameters remain stable. According to modeling results using NHANES data, no state currently has a hepatitis C prevalence in adults that is below 0.1%(8). Similarly, for universal testing in pregnant women the ICER would be approximately $50,000 per QALY gained or less at an HCV RNA positivity prevalence of 0.05%; at a prevalence of 0.1%, the ICER would be about $15,000 per QALY gained(82). The ICERs may be higher for testing in subsequent pregnancies when testing during the index pregnancy identifies women with hepatitis C who receive treatment following pregnancy, resulting in a decrease in hepatitis C prevalence among women with more than one pregnancy. According to birth certificate data (likely an underestimate of current maternal HCV infections), only 3 states were below the 0.1% prevalence among pregnant women(11).

While the intent of public health screening is usually to identify undiagnosed disease, many persons previously diagnosed with hepatitis C are not appropriately linked to care and are not cured of their HCV infection, thereby representing an ongoing source of transmission. Therefore, the prevalence threshold of 0.1% should be determined based on seroprevalence estimates of hepatitis C, regardless of diagnostic status.

Recommendations

The following recommendations for hepatitis C screening augment the *Recommendations for the Identification of Chronic Hepatitis C Virus Infection Among Persons Born During 1945-1965* issued by CDC in 2012. The *Recommendations for Prevention and Control of Hepatitis C Virus (HCV) Infection and HCV-Related Chronic Disease* issued by CDC in 1998 remain in effect. CDC recommends (Box 2):

- Universal hepatitis C screening:
  - Hepatitis C screening at least once in a lifetime for all adults aged 18 years and older, except in settings where the prevalence of HCV infection (HCV RNA-positivity) is less than 0.1%
  - Hepatitis C screening for all pregnant women during each pregnancy, except in settings where the prevalence of HCV infection (HCV RNA-positivity) is less than 0.1%

- One-time hepatitis C testing regardless of age or setting prevalence, including among persons with recognized conditions or exposures:
  - Persons with HIV
  - Persons who ever injected drugs and shared needles, syringes, or other drug preparation equipment, including those who injected once or a few times many years ago
  - Persons with selected medical conditions, including:
    - persons who ever received maintenance hemodialysis
    - persons with persistently abnormal ALT levels
  - Prior recipients of transfusions or organ transplants, including;
    - persons who received clotting factor concentrates produced before 1987
    - persons who received a transfusion of blood or blood components before July 1992
    - persons who received an organ transplant before July 1992
    - persons who were notified that they received blood from a donor who later tested positive for HCV infection
  - Healthcare, emergency medical, and public safety personnel after needle sticks, sharps, or mucosal exposures to HCV-positive blood
  - Children born to mothers with HCV infection
- Routine periodic testing for persons with ongoing risk factors, while risk factors persist:
  - Persons who currently inject drugs and share needles, syringes, or other drug preparation equipment
  - Persons with selected medical conditions, including:
    - persons who ever received maintenance hemodialysis
- Any person who requests hepatitis C testing should receive it, regardless of disclosure of risk, because many persons may be reluctant to disclose stigmatizing risks

Hepatitis C screening can be conducted in a variety of settings or programs that serve populations at different risk and with varying hepatitis C prevalence. Regardless of the provider, organization, or program providing testing, healthcare providers should initiate universal screening for adults and pregnant women unless the prevalence of HCV infection (HCV RNA positivity prevalence) in their patients has been documented to be <0.1%. In the absence of existing data for hepatitis C prevalence, healthcare providers should initiate universal hepatitis C screening until they establish that the prevalence of HCV RNA positivity in their population is less than 0.1%, at which point universal screening is no longer explicitly recommended but may occur at the provider's discretion. There are statistical challenges with determining a "number needed to screen" to detect a relatively rare disease in

lower-risk settings; thus providers and program directors are encouraged to consult their state or local health departments or CDC to determine a reasonable estimate of baseline prevalence in their setting or a methodology for determining how many people they need to screen before confidently being able to establish that the prevalence is below 0.1%. As a general guide: as HCV RNA prevalence is predicated on first testing for anti-HCV, and according to the most current serologic data in the United States, approximately 59% of anti-HCV positive people are currently HCV RNA positive(9), it is estimated that 507 randomly selected patients in a setting of any size would need to be tested using any of the currently available anti-HCV tests(84) to detect an anti-HCV prevalence positivity of 0.17% or below, corresponding to an expected HCV RNA positivity prevalence of 0.1% with 95% confidence and 5% tolerance.(85) (http://epitools.ausvet.com.au/content.php?page=PrevalenceSS_1&HTP=0.0017&HSENS=1.00&HSPEC=0.9984&Popsize=&Conf=0.95&Precision=0.025)

Providers and patients can discuss hepatitis C screening as part of an individual's preventive health care. For persons identified with current HCV infection, CDC recommends that they receive appropriate care, including hepatitis C-directed clinical preventive services (e.g., screening and intervention for alcohol or drug use, hepatitis A and hepatitis B vaccination, and medical monitoring of disease).

Recommendations are available to guide treatment decisions. Persons infected with HCV can benefit from counseling messages (Box 3).

- Persons with *negative anti-HCV test results* should be informed of their test results and reassured that they are not infected, unless they were recently exposed to infection (e.g., recent injection-drug use). Repeat testing should occur for persons with ongoing risk behaviors.
  - Persons with *negative anti-HCV* and *positive HCV RNA* test results have recent HCV infection.
- Persons with *positive anti-HCV* and *negative HCV RNA* test results should be informed that they had HCV infection in the past, but do not have current HCV infection, and that they could be re-infected and should have HCV RNA testing, if risk factors persist. Alternatively, this may represent a false-positive anti-HCV test result.
- Persons with *positive anti-HCV* and *positive HCV RNA* test results should be informed that they have active HCV infection and need further evaluation for treatment, medical care for liver disease, and ongoing medical monitoring. Persons with HCV infection should be provided information about HCV infection, risk factors for disease progression, preventive self-care and treatment options, how to prevent transmission of HCV to others, and drug treatment, as appropriate. Persons with hepatitis C also should be informed about the resources available to them within their communities, including providers of medical evaluation and social support.

- At the time positive test results are communicated to patients, healthcare providers should evaluate the patient's level of alcohol and drug use and provide a brief alcohol or drug use intervention, if clinically indicated(86).

Testing Considerations

Universal hepatitis C screening was compared to risk-based screening for adults and pregnant women. As such, the marginal benefits and harms of universal screening compared to birth cohort screening was not directly assessed. For the purposes of this literature review, the birth cohort was deemed a risk group, and studies comparing birth cohort with universal screening strategies were eligible for inclusion. Indeed, the incidence of acute hepatitis C is greatest among persons younger than birth cohort members(2). Because most pregnant women are younger than persons born during the 1945-1965 birth cohort, hepatitis C testing among pregnant women has previously been based upon the presence of risk factors.

Data informing the optimal time during pregnancy for which hepatitis C testing should occur are lacking. Testing at an early prenatal visit harmonizes testing for hepatitis C with testing for other infectious diseases during pregnancy; although this strategy may miss women who acquire HCV infection later during pregnancy. Pregnant women with ongoing risk factors tested early in pregnancy could undergo repeat testing later in pregnancy to identify those who acquired HCV infection later in pregnancy(87).

Cases of hepatitis C should be reported to the appropriate state or local health jurisdiction, in accordance with requirements for reporting acute, perinatal, and chronic HCV infection. Case definitions for the classification of reportable cases of HCV infection have been published previously by the Council of State and Territorial Epidemiologists(88).

Recommendations of Other Organizations

Recommendations in this report for groups of persons for whom hepatitis C screening is recommended differ somewhat from the recommendations of other organizations. The U.S. Preventive Services Task Force(89) as well as AASLD and IDSA(40) also make recommendations for hepatitis C testing.

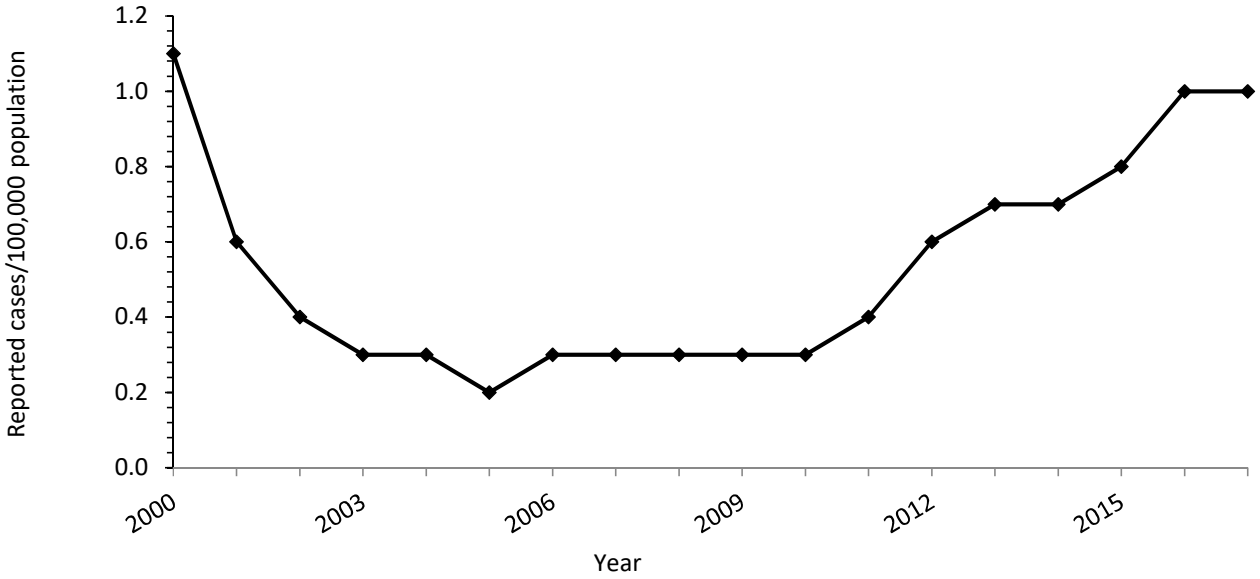
Future Directions

CDC will review these recommendations as new epidemiology or other information-- related to hepatitis C, including potential availability of DAA treatments for pregnant women, infants, and younger children, and the experience gained from the implementation of these recommendations-- becomes available. As additional evidence becomes available, these recommendations may be revised.

Box 1. Abbreviations used in this report

ALT	alanine aminotransferase
anti-HCV	antibody to HCV
DAA	direct acting antiviral
FDA	Food and Drug Administration
HBsAg	Hepatitis B surface antigen
HBV	hepatitis B virus
HCV	hepatitis C virus
HIV	human immunodeficiency virus
ICER	incremental cost-effectiveness ratio
IDU	injection-drug use
KQ	key questions
MSM	men who have sex with men
NAT	nucleic acid test
NHANES	National Health and Nutrition Examination Survey
NNDSS	National Notifiable Diseases Surveillance System
PWH	persons with HIV
PWID	persons who inject drugs
QALY	quality-adjusted life year
RNA	ribonucleic acid
STI	sexually transmitted infection
SVR	sustained virologic response

Figure 1. Rates of reported acute hepatitis C cases — United States, 2000-2017



Source: CDC, National Notifiable Disease Surveillance System

Figure 2. Chain of indirect evidence

How would universal screening for HCV affect the number (and composition) of people who screen positive for HCV? →	How many additional persons would be linked to care? →	Do desirable treatment effects outweigh undesirable effects?
K.Q.1.a. What is the prevalence of HCV infection in the U.S.? By: --general population --risk groups	K.Q.2.a. What is the diagnostic accuracy of HCV antibody testing?* K.Q.2.b. What are harms of HCV screening?† K.Q.2.c. What proportion of people who screen positive for HCV are linked to care?§,¶	K.Q.3.a. What is the effect of DAA treatment on HCV viral load?* K.Q.3.b. What is the effect of DAA treatment on morbidity (including cirrhosis, hepatocellular carcinoma)?* K.Q.3.c. What is the effect of DAA treatment on mortality (HCV-specific and all-cause)* K.Q.3.d. What are the adverse effects of DAA treatment?*

*Previously well-described and therefore not included in this review
†U.S. and non-U.S. studies included
§U.S. studies only included
¶For all adult review only

Figure 3. Search strategy for all adult literature review

Search Query: Does universal screening for hepatitis C virus infection among adults aged 18 years and older, compared to risk-based screening, reduce morbidity and mortality?

Search Strategy:

Database	Strategy	Run Date	Records
Medline **(OVID)** **1946-**	(exp Hepatitis C/ AND *Mass Screening/) OR ((Hepatitis C ADJ5 screen*) OR (hepC ADJ5 screen*) OR (HCV ADJ5 screen*) OR (Hepatitis C ADJ5 test*) OR (hepC ADJ5 test*) OR (HCV ADJ5 test*)).ti,ab. OR (*hepatitis C/ AND (screen* OR test*).ti) Limit 2010 - ; English	8/6/2018	3310
Embase **(OVID)** **1996-**	(exp Hepatitis C/ AND *Mass Screening/) OR ((Hepatitis C ADJ5 screen*) OR (hepC ADJ5 screen*) OR (HCV ADJ5 screen*) OR (Hepatitis C ADJ5 test*) OR (hepC ADJ5 test*) OR (HCV ADJ5 test*)).ti,ab. OR (*hepatitis C/ AND (screen* OR test*).ti) Limit 2010 -; English; Exclude Medline Journals	8/6/2018	559 -161 Duplicates* =398 unique items
CINAHL **(Ebsco)**	((MH "Hepatitis C"+) AND (MM "Mass Screening")) OR (("Hepatitis C" N5 screen*) OR (hepC N5 screen*) OR (HCV N5 screen*) OR ("Hepatitis C" N5 test*) OR (hepC N5 test*) OR (HCV N5 test*)) OR ((MM "hepatitis C") AND (TI (screen* OR test*))) 2010 - ; exclude Medline records ; English	8/6/2018	210 -128 Duplicates* =82 unique items
Scopus	TITLE-ABS-KEY(("Hepatitis C" W/5 screen*) OR (hepC W/5 screen*) OR (HCV W/5 screen*) OR ("Hepatitis C" W/5 test*) OR (hepC W/5 test*) OR (HCV W/5 test*)) AND NOT INDEX(medline) 2010 - ; English	8/6/2018	1769 -846 Duplicates*

			=923 unique items
Cochrane Library	(("Hepatitis C" NEAR/5 screen*) OR (hepC NEAR/5 screen*) OR (HCV NEAR/5 screen*) OR ("Hepatitis C" NEAR/5 test*) OR (hepC NEAR/5 test*) OR (HCV NEAR/5 test*)):ti,ab 2010 - ; English	8/6/2018	250 -96 Duplicates* =154 unique items

*Duplicates were identified using the Endnote automated "find duplicates" function with preference set to match on title, author and year, and removed from your Endnote library.

Figure 4. Search strategy for pregnancy literature review

Search Query: Does universal screening for hepatitis C virus infection among pregnant women, compared to risk-based screening, reduce morbidity and mortality among mothers and their children?

Search Strategy:

Database	Strategy	Run Date	Records
Medline **(OVID)** **1946-**	Hepatitis C OR hepC OR HCV AND Pregnanc* OR pregnant OR maternal AND Screen* OR test* 1998 - ;	7/2/2018	592
Embase **(OVID)** **1947-**	Hepatitis C OR hepC OR HCV AND Pregnanc* OR pregnant OR maternal AND Screen* OR test* 1998 - ;	7/2/2018	1226 -464 Duplicates* =762 unique items
CINAHL **(Ebsco)**	"Hepatitis C" OR hepC OR HCV AND Pregnanc* OR pregnant OR maternal AND Screen* OR test* 1998 - ; exclude Medline records	7/2/2018	38 -19 Duplicates* =19 unique items
Scopus	TITLE-ABS-KEY(("Hepatitis C" OR hepC OR HCV) AND (Pregnanc* OR pregnant OR maternal) AND (Screen* OR test*)) AND NOT INDEX(medline)	7/2/2018	333

			-216 Duplicates* =117 unique items
Cochrane Library	(("Hepatitis C" OR hepC OR HCV) AND (Pregnanc* OR pregnant OR maternal) AND (Screen* OR test*)):ti,ab	7/2/2018	23 -13 Duplicates* =10 unique items

*Duplicates were identified using the Endnote automated "find duplicates" function with preference set to match on title, author and year, and removed from your Endnote library.

Table 1. Summary of literature review: Hepatitis C prevalence by adult populations

Population	Number of studies included in table	Minimum and maximum anti-HCV positivity among tested	Range of RNA positivity among anti-HCV positive	Strongest estimate (based on sample size and generalizability)
Birth cohort (BC)	35	0% (0/13 and 0/16) - 19.8% (35/681)	20% (2/10) - 97.6% (41/42)	Jonas(90): 365/11200 (3.3%) anti-HCV positive
Emergency Department (ED) patients	8	1.6% (6/365) - 25.8% (40/155)	57.9% (292/504)	White(91): 525/6972 (7.5%) anti-HCV positive Torian(92): 372/4989 (7.5%; 95%CI: 6.7, 8.2) anti-HCV positive
General US population	9	1.2% (1/83) - 6.2% (352646/5651742)	46.9% (6383/13596) - 83% (292681/352646)	Hofmeister(9): 1.7% (95% CI: 1.4, 2.0) anti-HCV positive
Immigrant populations in the US	3	3.4% (11/326) - 7.5% (19/255)	81.8% (9/11)	
Others potentially at risk (e.g., low-income, homeless, etc.)	25	1.2% (4/326) - 27.4% (23/84)	45.5% (3449/7580) - 82.6% (19/23)	Ramirez(93) and Ward et al., 2016:
Persons with HIV (PWH)	5	8% - 19.3% (131/678)	No published data	
People who use drugs	25	1.6% (6/365) - 100% (63/63)	35.6% (1244/3495) - 82.6% (19/23)	Blackburn(94): 3495/15274 (22.9%) anti-HCV positive Platt(95): 83.5% (estimate from meta-analysis, 13 studies)
Pregnant women	26	0.09% - 67.0%	--	Clennon et al., 2017: 31,200/10,457,976 (0.3%)

Table 1. Summary of literature review: Hepatitis C prevalence by adult populations

Population	Number of studies included in table	Minimum and maximum anti-HCV positivity among tested	Range of RNA positivity among anti-HCV positive	Strongest estimate (based on sample size and generalizability)
				Ellington(96): 2008-2010: 2.13 per 1,000 pregnancy hospitalizations (numerator=28,567) Koneru(97): 0.32% Ly(98): 0.73% HCV-positive of 581,255 pregnant women

Table 2. Hepatitis C prevalence among adult populations

Study	Screening Guidelines/ Intervention	Design	Sample/Data Information	% Screened	Prevalence
Birth cohort					
Allison(99), 2016		Cross-sectional	Data from 2014-2015 Sample obtained using systematic random sampling in an urban ED Included BC patients presenting at the ED Excluded if presenting for MH problem, inability to interact w/phone interpreter (e.g., hearing difficulties), or in corrections 64% born outside US	383/427 (90%)	28/383 (7.3%) anti-HCV positive
Bourgi(100), 2016	Health system had employed EMR screening notifications for BC patients	Retrospective	Data from 2014-2015 Participants were patients at internal medicine clinics Excluded if given a previous HCV diagnosis	8657/40561 (21.3%)	109/8657 (1.3%) anti-HCV positive
Castrejon(101), 2017	Screening reminder added to EMR in August 2015	Interrupted time series	Data from 2014-2016 BC Patients in the UCLA health system with outpatient visit with HCV screening during study period	5676/19606 (29%) before intervention 13930/19606 (71%) after intervention	190/5676 (3.3%) anti-HCV positive pre-intervention 240/13930 (1.7%) anti-HCV positive post-intervention
Cornett(102), 2018	Opt-out screening for BC patients implemented in	Retrospective	Data from 2016 Study took place in a small-city ED with a socioeconomically		192/2928 (6.6%) anti-HCV positive 81/1048 (7.7%) Medicare BC

Study	Screening Guidelines/ Intervention	Design	Sample/Data Information	% Screened	Prevalence
	the ED 11am-7pm		diverse patient population Data were from EMR and included all screened BC patients in the ED during the study period Approximately of sample 56.7% were white, 18% black, 42% had private insurance, 35.8% Medicare, 13.6% Medicaid, and 8.5% were uninsured		patients were anti-HCV positive 49/397 (12.3%) Medicaid BC patients were anti-HCV positive 71/192 (37%) of anti-HCV positive were VL-positive
Donnelly(103), 2016	Opt-out HCV screening among BC and high-risk patients in the ED	Retrospective	Data from 2013-2015 Study conducted at the UAB ED 79% of tests conducted among BC patients		11.6% were anti-HCV positive
Falade-Nwulia(104), 2016	6/13 senior centers in Baltimore City randomly selected by BC Health Dept for testing events	Cross-sectional	Data from 2014 Testing sites (health department) were randomly selected (all located in Baltimore) 42% participants born before 1945; 71% female	All tested as part of study	14/149 (9.4%) anti-HCV positive 12/14 (86%) of those anti-HCV positive were RNA positive 78% of those with a history of IDU were positive
Federman(105), 2017	10 clusters were ID'd within the system and each cluster was randomly assigned to intervention (provider alert	Cluster RCT (primary outcome: screening)	Data from 2013-2014 Primary care practices of Mount Sinai Healthcare sys located in NYC and Long Island	2995/14825 (20.2%) of intervention visits 198/10795 (1.8%) of control visits	27/8713 (3.1%) of unique patients were anti-HCV positive in intervention group vs 6/5438 (1.1%) of unique patients in control group

Study	Screening Guidelines/ Intervention	Design	Sample/Data Information	% Screened	Prevalence
	in the EMR) or control (SOC)		Data are for visits (not individual patients) from BC patients not previously being treated for HCV		
Fitch(106), 2017	An automatic notification for BC screening was implemented in the EMR	Data reported in a letter to the editor	Data from 2015 Patients from hospital-based primary care clinic, serving primarily minorities and Medicaid patients (location not specified, authors from Wake Forest)	854/4355 (20%) before implementation 1220/4994 (24%) at implementation 1700/5578 (30%) after implementation	59/480 (12%) anti-HCV positive before implementation 218/1220 (18%) after implementation
Franco(107), 2016	Screening offered to ED BC patients unaware of their status	Retrospective	Data from 2013-2014 Study took place at UAB ED		473/4371 (10.8%) anti-HCV positive 332/473 (70.2%) of anti-HCV positive were RNA positive
Galbraith(108), 2015	Opt-out screening of BC patients presenting in the ED	Retrospective	Data from 2013 Study took place at UAB ED	1529/3170 (48.2%) of those completing pre-screening questionnaire	170/1529 (11.1%) anti-HCV positive 102/170 (60%) of anti-HCV positive were RNA positive
Geboy(109), 2016	HepTLC in DC at an urban primary care clinic BC patients with no history of HCV were screened	Prospective	Data from 2012-2013 Data are from HepTLC initiative in DC Study participants are from an urban primary care clinic that serves an area that is largely low-to-middle income and minority		99/1123 (8.8%) were anti-HCV positive

Study	Screening Guidelines/ Intervention	Design	Sample/Data Information	% Screened	Prevalence
Goel(110), 2017	HCV screening and LTC initiative	Prospective	Data from 2013-2015 Study conducted at Mt. Sinai Hospital primary care (Mt. Sinai serves a socioeconomically and racially diverse patient population) Record review conducted to examine rates pre-implementation (Nov 2013-Feb 2014), data collected post-implementation		147/4419 (3.3%) of those screened anti-HCV positive post-implementation (compared with 3.1% anti-HCV positive among screened in pre-implementation period) 84/134 (62.7%) of RNA tested were RNA positive post-implementation
Golden(111), 2017	EMR notification for screening of BC patients in primary care	Time series	Data from 2011-2015 Study conducted at a primary care clinic serving primarily low-income patients in Seattle Only BC patients without a record of HCV testing were included	681/3773 (18%) in pre-intervention period 1185/3336 (35.5%) in post-intervention period	35/681 (19.8%) anti-HCV positive in tested pre-intervention sample 123/1185 (10.4%) anti-HCV positive in tested post-intervention sample
Hossain(112), 2017	Extended BC was screened (age 40-75 years during the study period)	Cross-sectional (Case-control also reported on for research question related to risk factors for HCV)	Data from 2013-2015 Cases were in the age range 40-75 years (extended BC) and not known to have positive HCV status at outpatient gastro and hepatology clinics; controls were patients with known history of HCV or currently on treatment	All but 50 enrolled/consented participants agreed to testing	5/245 (2%) anti-HCV positive 2/5 (40%) of anti-HCV were RNA positive Among BC 4/188 (2.1%) were anti-HCV positive 1/4 (25%) of BC anti-HCV positive were RNA positive

Study	Screening Guidelines/ Intervention	Design	Sample/Data Information	% Screened	Prevalence
Isho(113), 2017	Community pharmacy screening program for BC clients	Pilot	NOTE: DATA COLLECTION DATES NOT SPECIFIED Community pharmacy based out of U of Illinois Hospital and Health Sciences System in Chicago Pharmacy serves hospital patients and patients from other clinics Of those screened, all but one were non-white, highest level of education for most was either a HS diploma or some college (no degree)	16/50 (32%) accepted screening	0/16 (0%) were anti-HCV positive
Jonas(90), 2016	An alert was added to the Kaiser EMR system to alert providers to screen BC patients without prior screening	Prospective	Data from 2014-2015 Study took place through KP Mid-Atlantic States (Maryland, Virginia, and DC)		365/11200 (3.3%) anti-HCV positive 277/365 (75.9%) of anti-HCV positive were RNA positive
Kugelmas(114), 2017	Screening program implemented at Walgreens in 9 major metro areas (5 stores per area); offered to adults in the BC or with CDC-defined risk factors for HCV	Prospective	Data from 2015-2016 Participants were recruited through advertising in the Walgreens stores 41% of sample was in BC, 7% had past or current IDU		103/1296 (7.9%) anti-HCV positive

Study	Screening Guidelines/ Intervention	Design	Sample/Data Information	% Screened	Prevalence
	Testing was performed 1 day per week				
Laufer(115), 2015	Program initiated to screen all US military retirees in BC presenting at an internal medicine clinic	Retrospective	Data from 2011-2014 BC military retirees screened as part of intervention compared with a comparison group of all BC retirees presenting at the clinic in the 16 months prior to intervention (when BC patients were screened if they had add'l risk factors)		10/478 (2.1%) in the intervention group were anti-HCV positive 2/10 (20%) of intervention group anti-HCV positive were RNA positive 5/221 (2.3%) in the comparison group (pre-intervention) were anti-HCV positive 4/5 (80%) of anti-HCV positive comparison group were RNA positive
MacLean(116), 2018	A prompt was added to the EMR to test BC patients	Retrospective	Data from 2012-2016 Subjects were patients at 9 family medicine or internal med practice sites at U of Vermont Med Center (8 urban, 1 rural) Subjects were in the BC and had at least one primary care visit in the last 3 years of the study period Almost all subjects were white (county is 91% white)		42/1059 (4.0%) anti-HCV positive pre-EMR prompt 41/42 (97.6%) of anti-HCV positive were RNA positive pre-EMR prompt 90/5552 (1.6%) anti-HCV positive following EMR prompt 39/90 (43.3%) of anti-HCV positive were RNA positive following EMR prompt

Study	Screening Guidelines/ Intervention	Design	Sample/Data Information	% Screened	Prevalence
Madhani(117), 2017	An educational intervention was implemented for residents Jan-Apr 2016	Retrospective	Data from 2013-2016 Participants were BC patients having at least 2 primary care visits in 2013 in the study setting (PC practice in Waterbury, Connecticut) Records for the pre-intervention and post-intervention period were reviewed 44% of study patients were on Medicaid	13/200 (6.5%) of participants pre-intervention completed testing 13/100 (13%) post-intervention completed testing	0 anti-HCV positive pre-intervention 1/13 (7.7%) anti-HCV post-intervention
Mera(118), 2016	Oct 2012 implemented tribal HCV testing policy, including EMR reminder for BC patients and HCV education to primary care clinicians; ECHO clinics; HCV registry, HCV outreach activities	Retrospective	Data from 2012-2015 Cherokee Nation Health Services patients with at least 1 medical visit in the last 3 years with no documented HCV test	16772/92012 (18.2%) of all patients at end of study period	715/16772 (4.3%) anti-HCV positive 388/16772 (2.3%) of all screened were RNA positive; 388/715 (54.3%) of anti-HCV positive were RNA positive
Miller(119), 2016	HepTLC initiative; Atlanta site at Grady IM residents received training as part of the initiative to screen BC patients; a prompt was included in the	Prospective	Data from 2012-2013 Patients were in the BC and seen at Grady Hospital in Atlanta (high-risk population)		201/2894 (6.9%) anti-HCV positive 124/201 (61.7%) of anti-HCV positive were RNA positive

Study	Screening Guidelines/ Intervention	Design	Sample/Data Information	% Screened	Prevalence
	EMR to test BC patients				
Morse(120), 2018 [Note: this article also included in the general population tables]		N/A	Data from 2013-2018 Numbers are derived from info available on health department websites, comparing rates among young adults (YA) to rates among BC Denominators obtained using Census data		Rates per 100,000 reported, broken down by state PA: 190 in YA; 150 in BC OH: 428 in YA, 237 in BC MA: 200 in YA, 190 in BC WV: 350 in YA, 200 in BC ME: 130 in YA, 100 in BC MI: 175 in YA and BC WI: 105 in YA, 110 in BC CT: 110 in YA and BC **Authors suggest universal screening based on the high rates of HCV in YA, higher than BC in some states and the increasing rates in many states**
Patel(121), 2016	Part of the HepTLC initiative (BC from all sites)	Prospective	Data from 2012-2014 HepTLC testing sites included EDs, FQHCs, comm. health clinics, STI clinics, and health depts.		2900/24966 (11.6%) anti-HCV positive 1497/2900 (51.6%) anti-HCV positive were RNA positive

Study	Screening Guidelines/ Intervention	Design	Sample/Data Information	% Screened	Prevalence
			This study included all BC participants from all HepTLC sites		
Patil(122), 2016 [Note: this article also included in PWUD table]	Screening was provided at local health units targeting IDUs and BC	Numbers reported via journal commentary	Data from 2014-2015 Data from the Arkansas Department of Health **Data include IDUs in addition to BC**		325/3544 (9.2%) anti-HCV positive
Ramirez(93), 2016 [Note: this article also included in PWUD table]	Part of the HepTLC initiative (all sites)	Retrospective	Data from 2012-2014 HepTLC initiative; testing sites included EDs, FQHCs, comm. health clinics, STI clinics, and health depts. **Data includes sites not focused on BC testing**		7580/57570 (13.2%) anti-HCV positive
Sears(123), 2013	Screening during colonoscopy appointments	Feasibility	Data from 2010-2011 Participants were patients presenting for a colonoscopy at a GI practice in Temple, TX Those born 1945-1960 (narrow BC) w/no known HBV or HCV scheduled for colonoscopy during the study period were invited to participate		4/346 (1.2%) anti-HCV positive 1/4 (25%) of anti-HCV positive were RNA positive
Shahnazarian(124), 2015	BPA for BC patients in the EMR was implemented	Retrospective	Data from 2013-2015 Study took place in NY Methodist Hospital primary care and outpatient clinics (no	9551/15965 (59.8%)	335/9551 (3.5%) anti-HCV positive

Study	Screening Guidelines/ Intervention	Design	Sample/Data Information	% Screened	Prevalence
			info provided on patient population)		
Sidlow(125), 2015	Prompt added to test BC patients included in the EMR beginning in May 2014	Retrospective	Data from 2014 Data are from all patients seen in primary care clinics of North Bronx Healthcare Network	Pre-implementation: 851/7764 (11%) Post-implementation: 3012/6577 (46%)	(only % reported in article) Pre-implementation: 2.5% (21/851) anti-HCV positive Postimplementation 0.86% (26/3012) anti-HCV positive
Taylor(126), 2016	BC screening program implemented An educational intervention was delivered to clinicians, testing orders were automatically sent for eligible patients, signs were placed around the hospital	Prospective	Data from 2012-2013 Data are from a study testing a BC patient screening program at University Hospital in San Antonio, which serves an indigent population 59% were Hispanic, 30% public insurance, 40% no insurance	2327/4813 (48.3%) Those excluded had prior HCV diagnosis or screening, psyc diagnosis, or poor diagnosis	192/2327 (8.3%) anti-HCV positive 108/192 (56.3%) of anti-HCV positive were RNA positive
Trinh(127), 2018	Quality improvement project implemented to increase screening Interventions included: distribution of guidance to providers, EMR prompt, rewards for	Retrospective	Data from 2013 Patients were seen at a Durham, NC-internal med-pediatric combined clinic during the study period Annual or new patient visit records among BC patients were examined	Screening rates were initially 24%; exceeded 90% after implementing a prompt in the EMR and providing physicians individualized feedback	Authors report 3.2% prevalence among patients at baseline

Study	Screening Guidelines/ Intervention	Design	Sample/Data Information	% Screened	Prevalence
	providers with highest screening rates				
Turner(128), 2015	Screening program implemented that included physician educational component and algorithm for ordering lab screening	Retrospective	Data from 2012-2014 Study took place at Texas hospital serving primarily low-income patients	4582/9037 (50.7%) 10.9% excluded due to previous HCV diagnosis; 32.7% excluded due to prior HCV test	316/4582 (6.9%) anti-HCV positive
Wong(129), 2017	Residents participated in an educational intervention to increase BC patient screening	Retrospective	Data from 2016 Data are from patients seen by the residents who participated in the study 99 residents participated from 3 hospitals in an urban teaching hospital system (in Baltimore, based on author affiliations)	Pre-intervention: 64/1023 (6%) 3 months post: 363/1026 (35%) 6 months post: 443/1070 (41%)	Pre-intervention: 5/64 (7.8%) anti-HCV pos, 2/5 (40%) RNA positive 3 months post: 6/363 (1.7%) anti-HCV pos, 2/6 (33.3%) RNA pos 6 months post: 3/443 (0.7%) anti-HCV pos, 2/3 (66.7%) RNA pos
Yartel(130), 2018	Three separate interventions targeting BC patients: mailings, BPA in the EMR, direct patient solicitation	RCT (examining screening rates as outcome)	Data from 2012-2014 This paper describes three separate RCTs conducted at primary care clinics testing three different interventions targeting BC patients for HCV testing: RCT1-mailings, RCT2-BPA in the EMR, and RCT3-direct patient solicitation	RCT1: 26.9% (n=805) in intervention, 1.4% (n=84) in control RCT2: 30.9% (n=2757) in intervention, 3.6% (n=197) in control RCT3: 63.5% (n=2736) in intervention, 2.0% (n=92) in control	Anti-HCV positivity: RCT1: 8/805 (1.0%) in intervention, 2/84 (2.4%) in control RCT2: 27/2757 (1.0%) in intervention, 6/197 (3.0%) in control RCT3: 34/2736 (1.2%) in

Study	Screening Guidelines/ Intervention	Design	Sample/Data Information	% Screened	Prevalence
			Clinics were part of academic medical centers (RCT1 - Henry Ford, RCT2 - Mt. Sinai, RCT3 - UAB)		intervention, 5/92 (5.4%) in control
Younossi(131), 2016	Pilot screening program	Pilot	Data from 2014-2015 Study conducted at 5 gastro practices in metro areas that had familiarity with preventative screening procedures English-speaking BC patients willing to consent were included Those with screening hx were excluded	All tested as part of study	10/2000 (0.5%) anti-HCV positive 4/10 (40%) of anti-HCV positive were RNA positive
Emergency Department (ED) patients					
Anderson(132), 2016	ED physicians and residents were encouraged to screen PWID	Prospective observational	Data from 2015	Anderson et al., 2016	ED physicians and residents were encouraged to screen PWID
Hsieh(133), 2016		Prevalence	Data from 2013 Conducted at Johns Hopkins Hospital ED Included all ED patients >17 yrs with excess blood specimens during study period 38% of study sample were in BC		652/4713 (13.8%) anti-HCV positive 204 (4.3% of full sample) had undocumented infection When adjusted for age, sex, race (comparing sample vs. ED pop) anti-HCV prevalence was 9.8%

Study	Screening Guidelines/ Intervention	Design	Sample/Data Information	% Screened	Prevalence
					25% of patients w/undocumented HCV would not be id'd with BC and risk-based screening alone (i.e., 25% of undoc'd inf were non-IDU, non-BC, HIV-)
Hsieh(134), 2018	Opt-out screening implemented in ED	Retrospective cohort	Data from 2016 Patients were participants of another study who had an ED visit ("index visit") between Dec 2015 and Jan 2016, were negative for HCV between 2003 and 2015, and had an HCV test after the index visit Conducted through Johns Hopkins		Incidence reported 6 patients seroconverted (6/299=2%); 3.5/1000 person-years
Merchant(135), 2014 [Note: this article also included under PWUD data tables]	Patients in ED waiting room 18-64 y/o reporting drug use were offered screening as part of study participation	Cross-sectional	Data from 2010-2012 Participants were part of the InVITED and BIDMED studies, which looked at screening ED patients in the Miriam Hospital and Rhode Island Hospital EDs **Participants were included in the study if they reported using drugs** and if their HCV status was negative or unknown		InVITED EMR screen: 129/1555 (8.3%) self-reported positivity InVITED study tested: 7/256 (2.7%) anti-HCV positive BIDMED study: 6/365 (1.6%) anti-HCV positive

Study	Screening Guidelines/ Intervention	Design	Sample/Data Information	% Screened	Prevalence
Schechter-Perkins(136), 2018	ED implemented an HCV screening program whereby all patients **>13 y/o** who were having blood drawn for any purpose were tested for HCV	Retrospective	Data from 2016-2017 Boston Medical Center serves a vulnerable pop (low income, minority, many with SUD) A BPA was fired for all patients meeting the criteria but large # were not tested likely b/c a resident who did not primarily serve the ED was seeing the patient	3808/19905 (19.1%) of all unique patient visits during the study period 7053 were not tested b/c no labs ordered, BPA fired for 9809 unique patient visits, test ordered for 3936, test completed for 3808	504/3808 (13.2%) anti-HCV positive 292/504 (57.9%) of anti-HCV positive were RNA positive **"Of those with active infection, 155 (53%) were outside the CDC birth cohort for increased risk for HCV including 46 (15.8%) who also did not report injection drug use."**
Torian(92), 2018	Serum samples taken from ED visit blood draws during the study period	Cross-sectional	Data from 2015 ED was in an academic hospital in the Bronx (high risk/low income/high unemployment/high foreign born) Serum or whole blood remaining from specimen draws were salvaged and tested 63.4% of ED visitors had a blood draw during the study period Blood draw population was similar to ED population overall 38% were in BC		372/4989 (7.5%; 95%CI: 6.7, 8.2) anti-HCV positive 167/4989 (3.3%; with imputation 3.9%, 95% CI: 2.8, 5.1) RNA positive 0.8% (95% CI: 0.3, 1.3) were undiagnosed infections based on comparison with HCV registry
White(91), 2018	Triage nurse screening program	Retrospective	Data from 2016-2017	2968/20975 (14.2%) in the	153/2968 (5.2%) anti-HCV positive in nurse-order

Study	Screening Guidelines/ Intervention	Design	Sample/Data Information	% Screened	Prevalence
	implemented (Mar-July 2016) followed by an automated alert program (Mar-July 2017) both targeting BC and PWID		Study was conducted at an urban ED in Oakland, CA with high number of low-income and minority patients Patients included in the study were those 18 to 75 yrs who completed triage and physician evaluation	nurse-order program 6972/19887 (35.1%) in the automated program Absolute difference 20.9 (95% CI: 20.1, 21.7)	program; 525/6972 (7.5%) in the automated program; Absolute diff of 2.3 (95% CI: 1.2, 3.3) 29/153 (19.0%) new diagnosis in nurse-order program; 101/525 (19.2%) new diagnosis in automated program; Absolute diff 0.2 (95% CI: -6.9, 7.3)
White(137), 2016	Triage nurse screening program implemented	Retrospective	Data from 2014 Same as study above but different dates	2028/26639 (7.6%) of patients were screened 7554/26639 (28.4%) were offered screening	185/2028 (9.1%) anti-HCV positive
General U.S. population					
Abara(43), 2019		Epi/surveillance	Data from 2010-2017 Data from the Organ Procurement and Transplantation Network (deceased organ donors)	All samples tested	3725/70414 (5.3%) of all donors anti-HCV positive 1306 (4.6%) of all donors were RNA positive 2400/12592 (19.1%) of "increased risk" donors were anti-HCV positive 1045 (14.9%) of "increased risk" donors were RNA positive

Study	Screening Guidelines/ Intervention	Design	Sample/Data Information	% Screened	Prevalence
Campbell(138), 2018	Screening not targeted, but aiming for patients in the BC and offered screening to those in USPSTF guidelines	Prospective observational	Data from 2015-2016 Adults presenting for an outpatient endoscopy 88% non-white, 60% in BC	502/1125 (44.6%) accepted 318/1125 (28.3%) completed	14/318 (4.4%) anti-HCV positive
Dodd(139), 2016 [Note: population in this article is blood donors]	Routine testing of blood supply	Surveillance	Data from 2011-2012 Red Cross, Blood Sys, Inc., and NY Blood Center supply, representing about 50% of US blood for transfusion	All samples tested	2.007/10000 donations (95% CI: 1.935, 2.079)
Dong(140), 2017	Pharmacists were trained to provide HCV POC rapid testing	Pilot	Data from 2016 Sample recruited using street outreach efforts in San Francisco near a community pharmacy Spanish primary language for 49% of participants; 65% in BC, 5% PWID	All screened as part of study	1/83 (1.2%) anti-HCV positive
Hofmeister(9), 2018		Prevalence	Data from 2013-2016 NHANES data, plus data for populations not represented in NHANES (**incarcerated**, homeless, active-duty military, nursing home residents)	N/A	1.5% (95% CI: 1.3, 1.8) anti-HCV positive (NHANES-only estimate) 0.9% (95% CI: 0.7, 1.0) RNA positive (NHANES-only estimate) 1.7% (95% CI: 1.4, 2.0) anti-HCV positive (combined estimate)

Study	Screening Guidelines/ Intervention	Design	Sample/Data Information	% Screened	Prevalence
					1.0% (95% CI: 0.8, 1.1) RNA positive from overall population (combined estimate)
Klevens(141), 2016 [Note: population in this article is people who were tested for HCV]		Cross-sectional	Data from 2010-2013 Quest Diagnostics lab data from all HCV tests with a patient ID and with both Ab and RNA results during the study period (i.e., individuals with only an antibody test or only an RNA test were excluded)		352646/5651742 (6.2%) anti-HCV positive 292681/352646 (83%) of anti-HCV positive were RNA positive
Morse(120), 2018 [Note: this article also included in the BC tables]		N/A	Data from 2013-2018 Numbers are derived from info available on health department websites, comparing rates among young adults (YA) to rates among BC Denominators obtained using Census data		Rates per 100,000 reported, broken down by state PA: 190 in YA; 150 in BC OH: 428 in YA, 237 in BC MA: 200 in YA, 190 in BC WV: 350 in YA, 200 in BC ME: 130 in YA, 100 in BC MI: 175 in YA and BC WI: 105 in YA, 110 in BC CT: 110 in YA and BC

Study	Screening Guidelines/ Intervention	Design	Sample/Data Information	% Screened	Prevalence
					Authors suggest universal screening based on the high rates of HCV in YA, higher than BC in some states and the increasing rates in many states
Rosenberg(8), 2018		Prevalence	Data from 2013-2016 Uses data from NHANES, ACS, and NVSS		0.84% (95% CI: 0.75, 0.96) RNA positive in non-institutionalized adult population (NHANES-only estimate) 0.93% RNA positive from overall population (combined estimate)
Viner(142), 2015		Epidemiologic	Data from 2010-2013 Study uses surveillance data from Philadelphia Dept of PH Population estimates used 2010 Census data for Philadelphia Co.		47525/1584848 (2.9%) of overall population anti-HCV positive (estimated) 6383/13596 (46.9%) of anti-HCV positive were RNA positive (of results obtained by DPH)
Woltmann(143), 2016		Epidemiologic	Data from 2010-2015 Data were from City of Cincinnati Health Dept for limited # counties		Incidence data provided; rate was 104/100000 in 2010 and 197/100000 in 2015 (an increase of 89%)
Immigrants					
Ma(144), 2015	HCV educational program	Prospective	Data from 2010-2011	255/309 (82.5%)	19/255 (7.5%) anti-HCV positive

Study	Screening Guidelines/ Intervention	Design	Sample/Data Information	% Screened	Prevalence
			Participants were recruited from **Vietnamese** CBOs in Pennsylvania and NJ		
Saab(145), 2018	Screening opportunity	Cross-sectional	Dates of data collection not reported Screening opportunity was advertised at houses of worship in S. CA where the researchers expected to find large numbers of **Egyptian** immigrants	All tested as part of study	11/326 (3.4%) anti-HCV positive 9/11 (81.8%) of anti-HCV positive were RNA positive
Strong(146), 2015	Free testing was offered	Cross-sectional	Data from 2011 Participants were offered testing at a **Vietnamese** health fair in the Baltimore-Washington metro area	All tested as part of study	29/617 (4.7%) anti-HCV positive
Others					
Coyle(147), 2015			Data from 2012-2014 Data are from the EMR at five CHCs in Philadelphia	4514 total screened for anti-HCV (denominator unreported) 550/595 (92.4%) received RNA testing	595/4514 (13.2%) anti-HCV positive 390/595 (65.5%) of anti-HCV positive were RNA positive
De la Torre(148), 2017	Risk assessment kiosk, patient navigator, and automated screening notification for BB EMR	Descriptive	Data from 2016 Data from urban Medicaid internal medicine clinic and a FQHC where a screening program was implemented		pre-kiosk: 13% of those tested were anti-HCV positive at IM clinic; 3.2% of those tested at FQHC post-kiosk: 24/254 (9.4%) of those

Study	Screening Guidelines/ Intervention	Design	Sample/Data Information	% Screened	Prevalence
					screened were anti-HCV positive
Falade-Nwulia(149), 2016		Cross-sectional	Data from 2013-2014 Sample was from 2 Baltimore City Health Dept STI clinics	testing was offered to 4399/6290 (70%) of patients who visited the clinic (not offered to patients enrolled in HIV care prog or those attending the clinic for nonclincal encounters) 2681/4399 (60.9%) of those offered testing were screened	189/2681 (7%) anti-HCV positive
Feldman(150), 2017	Free screening	Cross-sectional	Data from 2014-2015 Free screening program offered at a CHC in Miami, FL		21/357 (5.9%) of full sample RNA positive (anti-HCV results not reported)
Fill(151), 2018	Screening programs implemented at STI clinics (program varied by site); those tested within last 6 months or <=13 years were not screened	Case-control	Data from 2016 Health dept screening program in TN at STI/FP clinics, some clinics were opt-out and some were opt-in Data are from anyone tested at the test sites during the study period		397/4753 (8.4%) anti-HCV positive 294/397 (74.1%) of anti-HCV positive were RNA positive
Ford(152), 2018	Check Hep C program (targeted outreach, reflex RNA testing, LTC via patient navigators, medical	Prospective	Data from 2012-2013 Participants were from FQHCs and SEPs in NYC 49% of participants were Hispanic, 40% were black; 55% were		880/4751 (19%) anti-HCV positive 512/880 (58.2%) of anti-HCV positive were RNA positive

Study	Screening Guidelines/ Intervention	Design	Sample/Data Information	% Screened	Prevalence
	provider training)		born after 1965; 64% had Medicaid		
Irvin(153), 2016	People were tested as part of a community-academic partnership	Cross-sectional	Data from 2014-2015 Testing efforts were pursued through advertising at community block parties, intersections frequented by PWID, shelters, etc.		49/325 (15.1%) anti-HCV positive
Jewett(154), 2013	Patients were offered testing based on risk	Cross-sectional	Data from 2012 Data from patients at Denver Metro Health Clinic (STI and HIV testing facility)	876/926 (94.6%) 50 refused testing	33/876 (3.8%) of those tested were anti-HCV positive 21/33 (63.6%) of anti-HCV positive were RNA positive
Keys(155), 2014		Cross-sectional	Data from 2010 n is serum pools of 80 samples each from the state lab from people tested for HIV (due to risk) who were HIV-negative The sample comes from ~18,000 individuals seeking HIV testing in N. Carolina		Estimated 1.2% of samples with actively replicating HCV
McGonigle(156), 2017 [Note: article also included in the PWUD table]			Numbers in this article do not add up – need to review inclusion or contact authors		
Morano(157), 2014	Pilot study was initiated to	Prospective	Data from 2012-2013	438/1345 (32.6%)	27/438 (6.2%) anti-HCV positive

Study	Screening Guidelines/ Intervention	Design	Sample/Data Information	% Screened	Prevalence
	conduct POC testing in all patients presenting at the mobile health clinic; patients were allowed to self-select POC or standard testing (bundled with others)		Participants were patients seen through a mobile health clinic/van in New Haven, CT (poor community with high prevalence of HCV)		
Morse(158), 2017		Prospective	Data from 2012-2014 Convenience sample of women recently released from incarceration were recruited by a CHW who advertised and approached women in relevant locations, also community leaders and providers were made aware of the clinic; recruitment strategies varied over time	60/87 (69%) of those for whom screening was recommended	12/60 (20%) anti-HCV positive
Moss(159), 2014	No-cost, opt-in testing for syphilis, HCV, gonorrhea, chlamydia, and HIV offered to clients of the CBO	Retrospective	Data from 2011-2012 Data are from clients an AIDS CBO in Miami that caters to gay minority men	326/2988 (10.9%)	4/326 (1.2%) anti-HCV positive
Norton(160), 2014	Patient educational intervention:~15 min discussion of HCV w/Q & A session		Data from 2012 Participants were recruited from homeless shelters, drug rehab centers, and a "drop-in"		18% have been told they have HCV (SELF-REPORT)

Study	Screening Guidelines/ Intervention	Design	Sample/Data Information	% Screened	Prevalence
			community center in Raleigh, NC		
Pieper(161), 2018			Data from 2016 Patients were seeking wound care due to venous ulcers at an urban outpatient clinic Mean age of patients was 61.1, 41 were male, 51 were black, street drug use was common (38 reported IDU, 37 reported non-IDU)	39/58 (67.2%) reported being screened (SELF-REPORT)	31/58 (53.4%) of full sample had been told they were HCV infected (SELF-REPORT)
Ramirez(93), 2016 [Note: this article also included in BC and PWUD tables]	HepTLC initiative (screening programs at multiple sites targeting BC and risk-based screening) Includes all sites (screening guidelines varied by site)	Retrospective	Data from 2012-2014 This is from the HepTLC initiative, data are from all sites		7580/57570 (13.2%) anti-HCV positive 3449/7580 (45.5%) of anti-HCV positive were RNA positive
Raymond(162), 2012		Cross-sectional	Data from 2011 Samples were from the 2011 National HIV Behavioral Surveillance MSM3; men were in San Francisco	Screened as part of study	21/466 (4.5%) anti-HCV positive
Rhea(163), 2018	Part of HepTLC initiative (Durham Co., NC site; STI clinic)	Prospective	Data from 2012-2015 Data from all patients presenting at the STI clinic (Durham Co., NC	733/8431 (8.7%) of those presenting at the clinic	108/733 (14.7%) of those tested were anti-HCV positive

Study	Screening Guidelines/ Intervention	Design	Sample/Data Information	% Screened	Prevalence
	Patients reporting >=1 of these risk factors were offered testing: HIV-positive, IDU (ever), BC, ever received hemodialysis, received an organ transplant or blood transfusion before 1992, received an unregulated tattoo, ever incarcerated, sex with an ever-IDU; sex with an HCV-infected person, ever received a diagnosis of syphilis, ever exchanged sex for money or drugs, >3 sexual partners in the 60 days before HCV testing, and MSM		HepTLC site) during the study period were included		81/108 (75%) of anti-HCV positive were RNA positive
Robinson(164), 2018		Retrospective	Data from 2014-2015 Patients with cirrhosis at an urban safety net hospital	All study participants had been tested	47/157 (29.9%) of overall sample had chronic HCV

Study	Screening Guidelines/ Intervention	Design	Sample/Data Information	% Screened	Prevalence
Sena(165), 2016 [Note: this article also included in PWUD table]	Part of the HepTLC initiative Testing protocol varied by site	Prospective	Data from 2012-2014 Reporting on first year of HepTLC initiative in Durham Co., NC Testing was conducted at STI clinics, county jail, homeless shelters, SUD tx center	This article reports on all tested (2004 from all sites, including county jail)	STD clinic: 64/471 (13.6%) were anti-HCV positive, 47/64 (73.4%) of anti-HCV positive were RNA positive Community testing site: 150/741 (20.2%) were anti-HCV positive, 109/150 (72.7%) of anti-HCV positive were RNA positive Homeless health clinic: 23/84 (27.4%) were anti-HCV positive, 19/23 (82.6%) of anti-HCV positive were RNA positive
Takeuchi(166), 2015	Those screened had risk factors including IDU, unsterile tattoo/piercing, sex with HCV-infected person, blood transfusion pre-1992, other exposure to blood	Retrospective	Data from 2010-2013 Data are from Hawaii's health department program to expand screening to include HIV/AIDS early intervention program Screenings took place at community health sites across the state		508/8588 (5.9%) anti-HCV positive
Tieu(167), 2018		Cross-sectional	Data from 2010-2013 Participants were adult MSM (male at birth) residing in NYC	All tested as part of study	29/1028 (2.8%) anti-HCV positive
Trooskin(168), 2015	The Do One Thing program, a neighborhood-based screening	Prospective	Data from 2012-2014 Participants recruited through door-to-door		52/1301 (4%) anti-HCV positive

Study	Screening Guidelines/ Intervention	Design	Sample/Data Information	% Screened	Prevalence
	and LTC program in medically-underserved neighborhoods with high rates of infection (mobile medical unit)		and street outreach and community events Majority tested were African American (91%); 71% were not in BC		36/52 (69.2%) of anti-HCV positive were RNA positive
Ward(169), 2016	HepTLC initiative (all sites) Screening protocol varied by site	Prospective	Data from 2012-2014 Screening and LTC were promoted at sites across the US that serve people at risk for HCV	Report states 70% were screened; uncertain where the denominator comes from	7580/57570 (13.2%) anti-HCV positive 3449/64716 (5.3%) of all anti-HCV or RNA tested were RNA positive (some people were only RNA tested) 3449/4765 (72.4%) of those RNA tested were RNA positive
Zaller(170), 2016		Cross-sectional	Dates of data collection unspecified; project funded 2010 – 2014 Pilot study of screening program in two probation and parole offices in Rhode Island Inclusion criteria: probationer/parolee, at least 18 years, English-speaking, HCV status negative or unknown Probationers/parolees were: 42% white, 17% African American, 76% insured	All tested as part of study	12/130 (9.2%) anti-HCV positive 4 went back for RNA testing; 2/4 (50%) of those RNA tested were RNA positive

Study	Screening Guidelines/ Intervention	Design	Sample/Data Information	% Screened	Prevalence
Persons living with HIV					
Kalichman(171)., 2015		Cross-sectional	Data from 2012-2014 Recruitment conducted in waiting rooms of HIV service providers and infectious disease clinics in Atlanta as well as chain recruitment Participants were adult PLWH receiving ART	Screened as part of study	131/678 (19.3%) anti-HCV positive
Platt(95), 2016		Meta-analysis	Data from 2011-2012 Systematic review and meta-analysis of HCV prevalence in heterosexual or pregnant Persons with HIV individuals, PWID, and MSM HIV estimate for the US is based on 85 studies with estimates ranging from 3.8-29.4		Among heterosexual or pregnant Persons with HIV individuals: 8%
Raymond(162), 2012		Cross-sectional	Data from 2011 Samples were from the 2011 National HIV Behavioral Surveillance MSM3; men were in San Francisco	Screened as part of study	17/108 (15.7%) of HIV- infected MSM were anti-HCV positive Comparison: 4/358 (1.1%) of HIV-uninfected MSM were anti-HCV positive
Samandari(172), 2017		Prospective	Data from 2011-2013 Data are from the HIV Outpatient Study	Screened as part of study	Incidence reported:

Study	Screening Guidelines/ Intervention	Design	Sample/Data Information	% Screened	Prevalence
			(HOPS), following Persons with HIV adults from specialty HIV clinics since 1993		0.88 incidence rate per 100 py (95% CI: 0.50, 1.42)
Wurcel(173), 2017		Retrospective	Data from 2010-2013 Participants were seen in an HIV clinic; 57% white, 80% male, 74% of males were MSM	229/287 (79.8%)	Incidence reported: 3.1% incidence (7 new cases in 2 years); 1.57 new cases per 100 py
Persons who use drugs					
Aronson(174), 2017	Testing was offered following an educational intervention	Feasibility pilot study	Data from 2016 Included if client >= 18 y/o at SEP during study period Excluded if HIV or HCV positive or had HIV HCV testing in the last 2 months	10/31 (32.2% overall) 10/10 who were offered test based on participation in HCV module	2/10 (20% of those screened) Testing not specified but assumed to be antibody
Barocas(175), 2014	N/A	Cross-sectional	Data from 2012 Participants were PWID using a SEP in southern Wisconsin	384/520 (73.8%) SELF-REPORT DATA	41/384 (10.7% of those screened) – SELF-REPORT DATA
Blackburn(94), 2016	Part of HepTLC initiative Screening targeted to PWID	Prospective	Data from 2012-2014 Data are from all HepTLC sites targeting PWID	N/A	3495/15274 (22.9%) anti-HCV positive 1244/3495 (35.6%) of anti-HCV positive were RNA positive
Brown(176), 2017	N/A	Cross-sectional	Data from 2016 Participants receiving MAT at a clinic in the midwest	157/202 (77.8%) SELF-REPORT	67/202 (33.2%) SELF-REPORT

Study	Screening Guidelines/ Intervention	Design	Sample/Data Information	% Screened	Prevalence
Cedarbaum(177), 2016	N/A	Cross-sectional	Data from 2013 Participants from SEPs in Seattle-Kings County		38.9% SELF-REPORT
Des Jarlais(178), 2018		Cross-sectional	Data from 2011-2015 Sample from NYC drug detox (all patients in one ward were invited) and methadone maintenance programs (all patients admitted in the last month were invited) This study reports only on participants indicating IDU in the last 6 months	All screened as part of study	569/910 (62.5%) Anti-HCV positive
Grebely et al., 2013	N/A	Prospective	Data from 2011 Data are from the InC3 study of PWID Methodology varies by cohort Only US sample data are reported here (3 cohorts)	All screened as part of study	63/63 (100%) of Boston sample were HCV-infected 129/300 (43%) of Baltimore 144/414 (35%) of San Francisco
Hochstatter et al., 2017	N/A	Participants are from an RCT; this article describes the program and sample	Data from 2015 Participants were recruited from a community SEP in Wisconsin	N/A	72/235 (30.6%) 26 identified through surveillance system; 46 SELF-REPORTED
Jordan(179), 2015	N/A	Prospective	Data from 2010-2013 Participants were in either a detox	All screened as part of study	anti-HCV positivity: 2010: 106/161 (66%, detox)

Study	Screening Guidelines/ Intervention	Design	Sample/Data Information	% Screened	Prevalence
			program or a MMT program in NYC		2011: 90/144 (63% detox); 38/47 (81%, MMTP) 2012: 105/171 (61%, detox), 70/95 (74%, MMTP) 2013: 88/148 (59%, detox), 39/60 (65%, MMTP)
Lambdin(180), 2017	N/A	Cross-sectional	Data from 2011-2013 Study conducted in Oakland, CA in a cluster of ZIP codes having high community supervision Participants were adults reporting IDU or crack use in 6 mon prior to interview	N/A	31% SELF-REPORTED
McGonigle(156), 2017 [Note: article also included in the others at-risk table]			Numbers in this article do not add up – need to review inclusion or contact authors		
Merchant(181), 2014 [Note: this article also included under ED patients data tables]	Patients **in ED waiting room** 18-64 y/o reporting drug use were offered screening as part of study participation	Cross-sectional	Data from 2010-2012 Participants were part of the InVITED and BIDMED studies, which looked at screening ED patients in the Miriam Hospital and Rhode Island Hospital EDs Participants were included in the study		InVITED EMR screening: 129/1555 (8.3%) SELF-REPORT InVITED study tested: 7/256 (2.7%) Anti-HCV positive BIDMED study: 6/365 (1.6%) Anti-HCV positive

Study	Screening Guidelines/ Intervention	Design	Sample/Data Information	% Screened	Prevalence
			if they reported using drugs and if their HCV status was negative or unknown		5 InVITED positives and 5 BIDMED positives were confirmed new diagnoses, 5/10 would have met current CDC guidelines for screening based on BC or IDU
Neaigus(182), 2017	N/A	Cross-sectional	Data from 2012 National HIV Behavioral Surveillance study (NHBS); this article looked at NYC participants Active PWID were recruited using RDS		324/483 (67.1%) Anti-HCV positive
Norton(160), 2014	N/A	Single group pre-test post-test	Data from 2012 Participants were recruited from homeless shelters, drug rehab centers, and a "drop-in" community center in Raleigh, NC Sites were chosen due to high rates of PWID but IDU was not required for study inclusion	N/A 90% of participants reported that they would still want to be tested even if they were unable to receive HCV treatment	18% have been told they have HCV (SELF-REPORT)
Patil(122), 2016 [Note: this article also included in BC table]	Screening was provided at local health units targeting IDUs and BC	Numbers reported via journal commentary	Data from 2014-2015 Data from the Arkansas Department of Health		325/3544 (9.2%) anti-HCV positive

Study	Screening Guidelines/ Intervention	Design	Sample/Data Information	% Screened	Prevalence
Platt(95), 2016	N/A	Meta-analysis	Data from 2011-2012 Systematic review and meta-analysis of HCV prevalence in heterosexual or pregnant Persons with HIV individuals, PWID, and MSM PWID estimate for the US is based on 13 studies with estimates ranging from 8.0-94.7		83.5% (estimate from meta-analysis)
Ramirez(93), 2016 [Note: This study also included in BC table]	HepTLC initiative Includes non-PWID-targeted sites	Retrospective	Data from 2012-2014 This is from the HepTLC initiative, data are from all sites **(including non-PWID-targeted sites**)		7580/57570 (13.2%) anti-HCV positive
Raymond(162), 2012		Cross-sectional	Data from 2011 Samples were from the 2011 National HIV Behavioral Surveillance MSM3; men were in San Francisco	Screened as part of study	12/77 (15.6%) of MSM IDUs were anti-HCV positive 9/389 (2.3%) of MSM non-IDU were anti-HCV positive
Sena(165), 2016 [Note: this article also included in other at-risk table]	HepTLC initiative **Includes non-PWID-targeted sites**	Prospective	Data from 2012-2014 Reporting on first year of HepTLC initiative in Durham Co., NC Testing was conducted at STI clinics, county jail, homeless shelters, SUD tx center		Full sample (all Durham sites **including county jail**): 326/2004 (16.3%) were anti-HCV positive; 241/326 (73.9%) of anti-positive were RNA positive STD clinic: 64/471 (13.6%) anti-HCV positive; 47/64

Study	Screening Guidelines/ Intervention	Design	Sample/Data Information	% Screened	Prevalence
					(73.4%) were RNA positive Community testing site: 150/741 (20.2%) were anti-positive; 109/150 (72.7%) were RNA positive Homeless health clinic: 23/84 (27.4%) were anti-positive; 19/23 (82.6%) were RNA positive
Smith(183), 2017		Prospective	Timeframe of data collection uncertain (NIH project funded 2008-2012) Sample came from active drug users in a rural Appalachian County in KY participating in an HIV-related study		222/503 (44.1%) anti-HCV positive
Soipe(184), 2018	N/A	Cross-sectional	Data from 2015-2016 RAPiDS study; young adults (18-29) who are nonmedical Rx opioid (NMPO) users	154/196 (78.6%) SELF-REPORT	18/154 (11.7%) SELF-REPORT
Stockman(185), 2014	A rapid POC testing program was implemented at organizations for PWUD (all clients offered screening)	Pilot study	Data from 2012-2013 Participants from community-based organizations for PWUD in Wisconsin (details of organizations not provided)		246/1255 (19.6%) anti-HCV positive

Study	Screening Guidelines/ Intervention	Design	Sample/Data Information	% Screened	Prevalence
Talal(186), 2017	N/A	Prospective	Data from 2012-2013 Study participants were in an opioid agonist therapy program Mean participant age 54, 60% male, 70% African American, 60% had hx of IDU	Participants screened as part of study	65/109 (59.6%) were anti-HCV positive 48/65 (73.8%) of Anti-HCV positive were RNA positive
Tsui(187), 2018	N/A	Cross-sectional	Data from 2015 Nat'l HIV Beh Surveillance System among PWID in Seattle (NHBS-IDU4) Analyses included only those who reported any opioid use in the last year and who answered tx Qs	Number tested not reported (must be 472/486 given the percent seropositive)	325/? (article states percent as 68.9% but denominator not reported) anti-HCV positive
Zibbell(188), 2014	Screening was offered as part of study participation	Cross-sectional	Data from 2012 Sample consisted of PWID (last 12 mon), >=18 y/o, and residing in Cortland County, NY (rural) Participants were recruited from a community-based AIDS organization	100/123 (81.3%) The most common reason for refusing the test was reportedly already knowing their HCV status	34/100 (34%) anti-HCV positive
Pregnant women					
Abughali(189), 2014	1993-2011	Intervention to improve infant HCV testing	HCV positive moms, infants in Metro Health Medical Center, Case Western Reserve University, Cleveland OH; 73% of		280 infants born to moms with HCV/67,112 infants born ~0.4%

Study	Screening Guidelines/ Intervention	Design	Sample/Data Information	% Screened	Prevalence
			mothers with HCV report substance use; few with other risk factors documented, e.g., HIV 9/279 (3.2%)		
Berkley(190), 2008	2000-2006	Retrospective cohort- all pregnant women from Milagro Clinic identified thru database (351 pregnancies)	University of NM hospital-pregnant women from drug dependence and treatment program (Milagro Clinic); all enrolled in a drug dependence and treatment program	300/351 pregnancies (85%)	159/300 (53%) of pregnancies
Boudova(191), 2018	2016	Retrospective chart review	University of MD Medical Center, Baltimore 100/1426 (7%) of pregnancies were tested for HCV, 28 with risk factors; 50/78 (64.1%) total women with risks identified not tested	100/1426 (7%) pregnancies; 50/78 (64%) women with any risk factor were not tested	10/100 (10%)
Chappell(192), 2018	2006-2014	Retrospective cohort; infant records linked to HCV infected pregnant women	University of Pittsburgh Medical Center Magee Women's hospital-women who delivered classified as HCV-positive by billing codes; 68% of HCV positive have opiate use disorder; 11% other substance use; 0.5% of infected HIV+		1043/87924 (1.2%) pregnant women HCV-infected; increased 60% from 2006 to 2014
Chen(193), 2013	2003-2010	Surveillance	Nationwide Inpatient Sample (large survey of US hospitalizations); 72% of HCV-infected had		28,663/32,426,352 (0.09%) HCV-positive mothers

Study	Screening Guidelines/ Intervention	Design	Sample/Data Information	% Screened	Prevalence
			no traditional risk factors		
Choy(194), 2003	1993-1999	Intervention at clinic to obtain HCV testing from pregnant women with 1 or more STD	Prenatal clinic University Women's Health Center, New Jersey Medical School, Newark All were inner-city STD-infected obstetric patients		7/106 (6.6%) antibody positive (excluded patients with known HCV)
Clennon(195), 2017	2011-2013	Retrospective cohort	Nationwide data; did not report on HCV risk factors		31,200/10,457,976 (0.3%) singleton deliveries with HCV-infected mother
Ellington(96), 2015	2002-4; 2005-7; 2008-10	Hospital discharge data	Hospital Discharge data from Nationwide Inpatient Sample (HCUP); nationwide data; did not characterize HCV risk factors		2002-2004: 1.25 per 1,000 pregnancy hospitalizations (numerator=17,114) 2005-2007: 1.72 per 1,000 pregnancy hospitalizations (numerator=24,687) 2008-2010: 2.13 per 1,000 pregnancy hospitalizations (numerator=28,567)
Fernandez(196), 2016	2014-2015	Prospective cohort study	University of TN Medical Center-women from obstetric high risk clinic found to be HCV RNA positive in prenatal period; OB high risk clinic all HCV infected-72% used IV drugs, 94% snorted drugs; examined other HCV risks as well		127/189 (67%) HCV-positive pregnant women first told they had HCV after prenatal lab work obtained during routine prenatal care

Study	Screening Guidelines/ Intervention	Design	Sample/Data Information	% Screened	Prevalence
Holloman(197), 2016	2010-2013	Retrospective review of hospital deliveries	Orlando, FL-Winnie Palmer Hospital for Women and Babies/Orlando Health; reports HCV rates for people on methadone maintenance and those using cocaine/heroin		Enrolled in methadone program: 16% (denominator=55); Cocaine or heroin use but self-treatment/not in methadone program: 5% (denominator=19)
Jessop(198), 2005	2000-2001	Sample of mothers from Philadelphia birth cohort (n=550)	Philadelphia; represents Philadelphia births but HCV risk factors not reported		3/27 (11.1%)
Koneru(97), 2016	2011-2014	Data from large commercial lab and birth certificate data	KY and US KY: HCV-positive pregnant women 38% reported past/current injection drug use 2011-2014 US: nationwide commercial lab, does not have HCV risk factor data		From 2011 to 2014 KY: 0.71 to 1.59%; US 0.19 to 0.32% (calculated as infants born to HCV-infected women divided by total infants born)
Krans(72), 2016	2009-2012	Retrospective cohort	University of Pittsburgh Medical Center (tertiary care teaching hospital) pregnant women on opioid maintenance therapy; all women had opioid use disorder	611/791 (77.2%)	369/611 (60.4%)
Kuncio(199), 2016	2011-2013	HCV surveillance data matched to 2011-2013 birth certificates of	Philadelphia residents-500 women in hepatitis registry birthed 537 children; maternal HCV risk factors not reported		537/55623 (1%)

Study	Screening Guidelines/ Intervention	Design	Sample/Data Information	% Screened	Prevalence
		children ≥20 mo.			
Ly(98), 2017	2006-2014	Surveillance: National Notifiable Diseases Surveillance System and Quest Diagnostics Health Trends database	Nationwide data; does not report rates of HCV specific risk factors in pregnant women but overall, 5.4% of reproductive aged women used infection drugs; 92% unknown IDU status		0.73% HCV-positive of 581,255 pregnant women
Mast(200), 2005	1993-6 Houston and 1994-8 Honolulu	Cohort. Followed birth to ≥12 mo.	Houston TX and Honolulu Hawaii: 244 infants born to HCV-positive moms. In Houston offered anti HCV test to pregnant women attending prenatal public health clinics and women with no prenatal care, 2 county hospitals. In HI, all pregnant women who received prenatal testing on Oahu offered testing Of HCV-positive women, 52% history of injection drug use, 19.8% blood transfusion before donor screening, 61.6% had been incarcerated		567/75,909 (0.75%) anti-HCV positive
McDilda(201), 2018	2009-2014	Retrospective descriptive study (used ICD9 codes for HCV and pregnancy)	North Central Florida; of HCV-positive, 75% have history of injection drug use; cocaine use 37.5%,		275/17,081 (1.6%)

Study	Screening Guidelines/ Intervention	Design	Sample/Data Information	% Screened	Prevalence
			other risk factors reported		
O'Malley(202), 2018	2011-2015	Surveillance-birth records at National Center for Health Statistics	National American Indian/Alaskan Native mothers; AI/AN mothers; limited information on HCV risk factors.		500/43,647 HCV-positive increased from 0.58% in 2011 to 1.13% in 2015
Page(203), 2017			Prenatal care clinic women with substance use disorders, University of NM; all women had substance use disorders	178/190 (93.7%) tested for anti-HCV	95/178 (53.3%) anti- HCV-positive
Patrick(10), 2017	2009-2014	Surveillance data	National Vital Statistics System and Tennessee Department of Health Vital Records		3.4 per 1,000 live births in 2014
Rossi(204), 2018	2006-2015	Retrospective cohort	All livebirths in OH; limited maternal HCV risk factors reported		7,069/1,440,625 (0.5%) HCV infected; increased from 1.6 to 11.7 per 1,000 live births from 2006-15
Salemi(205), 2017	1998-2011	Cross sectional analysis of hospitalizations for liveborn singleton deliveries	Nationwide data; Nationwide Inpatient Sample, Healthcare Cost and Utilization Project; prevalence reported by risk group		118.6 per 100k deliveries; average 4,473 cases per year*; higher for drug users 3,931.2, HIV-positive 2,764.9, alcohol abusers 2,222.1, tobacco users 965.7, Medicaid/Medicare 213.8

Study	Screening Guidelines/ Intervention	Design	Sample/Data Information	% Screened	Prevalence
Salihu(206), 2011	1998-2007	Surveillance-hospital discharge data linked to birth records	All FL live births (1,700,734 singleton live births) 4.5% of HCV-positive mothers abused drugs; 4.4% HIV-positive		Peak in 2007 at 125.1 per 1,000 live births. Prevalence broken down by subgroups
Snodgrass(207), 2018	2015	Surveillance-birth certificate data that reports maternal HCV compared with state surveillance data	Oregon surveillance data, does not report HCV risk factors.		181/44,712 (0.4%) of women with live birth had HCV documented in registry; 2.91 moms with HCV per 1,000 live births in 2009 and 3.87 per 1,000 in 2014
Towers(208), 2018	2015-2016	Prospective database of mothers with positive HCV VL during pregnancy	University of TN Medical Center; 127 newborns of HCV VL positive mothers; does not report HCV risk factors		
Waruingi(44), 2015	2012		Metro Health Medical Center, Case Western Reserve University, Cleveland OH, pregnant women high risk inner city clinic admitted for delivery; high risk inner city clinic		4/37 (10.8%) in high risk group. Some were already infected in this group; prevalence 3/183 (1.6%) in low risk group, some of whom had risks
Watts(209), 2017	2011-2015	Surveillance-WI electronic disease surveillance system linked to WI Medicaid data for 2011-2015 births	Wisconsin HCV infected Medicaid population of pregnant women; limited maternal HCV risk factor information.		HCV infection evidence in 608/146267 (0.4%) WI Medicaid recipients with birth during 2011-2015; 2.7/1000 in 2011 to 5.2 per 1000 in 2015 (looked at % with HCV infection

Study	Screening Guidelines/ Intervention	Design	Sample/Data Information	% Screened	Prevalence
					before delivery date)

HCV, hepatitis C virus; VL, viral load, AI, American Indian; AN, Alaska Native; IDU, injection drug use; SUD, substance use disorder; PWID, persons who inject drugs; MSM, men who have sex with men; BC, birth cohort; ED, emergency department; IM, internal medicine; EMR, electronic medical record; MH, mental health

Table 3. Linkage-to-care (LTC) among adults

Study	Screening guidelines or LTC intervention (if any)	Study design	Population and sample information	% Anti-HCV and % RNA positive	% Attended follow-up appointment	% Treated (and % achieved SVR, if reported)
Allison(99), 2016		Cross-sectional	BC patients presenting to ED Recruited through systematic random sampling at a single urban ED		4/21 (19.0%)	1/4 (25%) treated
Anderson(210), 2017		Retrospective cohort	ED patients 2 urban EDs	301/435 (69%) of those RNA tested were RNA positive	97/158 (61.4%)	24/97 (24.7%) treated 19/24 (79.2%) SVR
Anderson(132), 2016		Prospective (Pilot)		40/155 (26%, 95% CI: 19, 33) anti-HCV positive 22/32 (69%) of those RNA tested were RNA positive	3/19 (15.8%)	1/3 (33.3%) treated
Assoumou(211), 2014		Retrospective cohort	Patients from an urban safety net hospital with reactive antibody tested Jan 2005-Dec 2010	5885/37828 (15.6%) anti-HCV positive		245 treated Additional note: 449 and 1,174 had HepA and HepB vaccination, respectively

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Assoumou(212), 2014		Retrospective cohort	Patients at a large safety net hospital with ≥2 outpatient visits, 6 mon follow-up time, current or past HCV infection	1,659/2,065 (80.3%) RNA tested were RNA positive		285/1659 (17.2%)
Blackburn(94), 2016	Part of HepTLC initiative	Prospective	PWID Participants had first testing visit between Oct 1, 2012 and June 28, 2014 at one of 84 testing sites included in the study	3,495/15,274 (22.7%) anti-HCV positive 1244/3495 (35.6%) of RNA tested were RNA positive	198/861 (23%)	
Bourgi(100), 2016		Retrospective cohort	BC patients Participants had at least one internal medicine visit from 21 clinics from an integrated health system in MI during the study period		51/109 (46.8%) were evaluated by a specialist	n=30 completed treatment
Campbell(138), 2018		Prospective Pilot Study	Patients at an urban safety net hospital All adults presenting for an outpatient endoscopy were recruited based on USPSTF guidelines	14/318 (4.4%) anti-HCV positive 6/11 (54.5%) RNA tested were RNA positive	6/6 (100%) patients linked to HCV clinic	
Castrejon(101), 2017	Screening reminder added to EMR in August 2015, care coordinator	Interrupted time series	BC Participants were BC patients who had a primary care visit between	Pre-intervention: 40/73 (54.8%) RNA tested were RNA positive Post-intervention: 49/124 (39.5%)	Pre-intervention: 35/40 (87.5%) of RNA positive linked to care	

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	added in Jan 2016		Aug 1, 2014 and July 31, 2016 seen at one of the outpatient clinics within UCLA Health and were tested for HCV	RNA tested were RNA positive	Post-intervention: 46/49 (93.9%) of RNA positive linked to care	
Coyle(213), universal group					106/277 (38.3%) of RNA positive attended appointment	
Coyle(213), risk group			BC or Risk group Participants were recruited from 5 FQHCs in Philadelphia		15/36 (41.7%) of RNA positive attended appointment	
Falade-Nwulia(149), 2016		Cross-sectional	Participants were 18-70 year old patients at STI clinics in Baltimore regardless of HCV testing history	189/3466 (5.5%) anti-HCV positive 155/185 (83.8%) RNA tested were RNA positive	81/155 (52.3%) of RNA positive attended appointment	n=37 were prescribed HCV meds
Falade-Nwulia(104), 2016			Seniors Participants were from 6 senior centers (randomly selected from 13 total senior centers)	14 (9.4%) anti-HCV positive; 9 were newly-diagnosed	3/12 (25%) of RNA positive **made** a follow-up appointment	Note: 6/12 visited clinic for HepB vaccination
Ford(152), 2018			Participants were from Check HepC funded sites in NYC (FQHCs, SEPs)	880/4751 (18.5%) anti-HCV positive 512/678 (76%) RNA tested were RNA positive	435/512 (85%)	n=14 (47 were treatment candidates) 29.8% of those eligible for treatment; 2.7% of those who

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						tested RNA positive 100% of patients who completed treatment (n=6) achieved SVR
Franco(107), 2016		Retrospective cohort	BC Participants were BC patients at UAB ED unaware of their HCV status	473/4371 (10.8%) anti-HCV positive 332/402 (82.6%) RNA tested were RNA positive	117/332 (35.2%)	
Galbraith(108), 2015		Cross-sectional	BC Participants were medically stable BC patients in an academic urban ED	170/1529 (11.1%) anti-HCV positive 102/150 (68%) RNA tested were RNA positive	21/102 (20.6%)	
Gade(214), 2018		Retrospective	Adults with congenital heart disease who underwent cardiac surgery before 1992	12/116 (10.3%) anti-HCV positive 11/12 (91.7%) RNA positive		5/11 (45.5%) treated 5/5 (100%) SVR
Geboy(109), 2016			BC Recruited from primary care clinic in DC	99/1123 (8.8%) anti-HCV positive 51/82 (62.2%) RNA tested were RNA positive	47/51 (92.2%)	14 scripts written, 5/51 (9.8%) treated 5/5 (100%) SVR
Goel(110), 2017	HCV screening and LTC initiative	Prospective	BC patients not HCV tested in the last two years Recruited from 2 NYC primary care practices	147/4419 (3.3%) anti-HCV positive post-implementation 84/134 (62.7%) of RNA tested were RNA positive	LTC rates: 43% in the medicine attending practice; 86% in the housestaff practice pre-implementation	32/60 (53.3%) started treatment

Table 3. Linkage-to-care (LTC) among adults

Study	Screening guidelines or LTC intervention (if any)	Study design	Population and sample information	% Anti-HCV and % RNA positive	% Attended follow-up appointment	% Treated (and % achieved SVR, if reported)
					60/84 (71.4%) were linked to care post-implementation	
Isenhour(215), 2018		Retrospective	NOTE: These are all who were tested Commercially insured individuals with at least 1 quantitative or qualitative HCV RNA result in the laboratory test results database; 18 year and older with prescription drug coverage and no claim for HCV treatment in the 6 months prior to HCV RNA index date; at least 6 months of continuous enrollment both before and after HCV RNA index date		n=5505 who engaged in care	n=2843 treated
Konerman(216), 2017	Prompt in the EMR		BC BC patients with at least 1 visit in prior 3 years at 1 of the primary care clinics in a health system; no documented testing	PRE-IMPLEMENTATION: 36/1705 (2.1%) anti-HCV positive 23/31 (74.2%) RNA tested were RNA positive POST-IMPLEMENTATION: 178/19847 (0.9%) anti-HCV positive	46/53 (86.8%)	DAA prescribed for 31 20/31 (64.5%) started treatment 9 completed treatment and confirmed SVR, 11 had

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Study	Screening guidelines or LTC intervention (if any)	Study design	Population and sample information	% Anti-HCV and % RNA positive	% Attended follow-up appointment	% Treated (and % achieved SVR, if reported)
				56/168 (33.3%) RNA tested were RNA positive (3 not confirmed on subsequent testing)		pending SVR labs
MacLean(116), 2018		Retrospective cohort	BC At least 1 primary care visit between Oct 2013 – July 2016; University of Vermont Medical Center serving urban and rural populations		164/182 (90.1%)	
McGonigle(156), 2017 Homeless Shelter nonwhite		Retrospective	Indigent populations in urban center in Southern US; homeless centers and residential substance abuse treatment centers in New Orleans	62/315 (19.7%) anti-HCV positive	14.52% of 62	Treatment started for 4.84% of 62
McGonigle(156), 2017 Homeless Shelter white				41/194 (21.1%) anti-HCV positive	4.88% of 41	Treatment started for 2.43% of 41
McGonigle(156), 2017 Substance Abuse Tx Center nonwhite				12/76 (15.8%) anti-HCV positive	8.33% of 12	Treatment started for 0% of 12
McGonigle(156), 2017 Substance Abuse Tx Center white				64/206 (31.1%) anti-HCV positive	6.25% of 64	Treatment started for 3.03% of 64
Mera(118), 2016	Oct 2012 implemented tribal HCV testing policy, including EMR reminder for BC patients		Cherokee Nation Health Services patients with at least 1 medical visit in the last 3 years with no documented HCV test	715/16772 (4.3%) anti-HCV positive 388/488 (79.5%) RNA tested were RNA positive		Treatment started for 223/388 (57.5%) 201/388 (51.8%)

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Study	Screening guidelines or LTC intervention (if any)	Study design	Population and sample information	% Anti-HCV and % RNA positive	% Attended follow-up appointment	% Treated (and % achieved SVR, if reported)
	and HCV education to primary care clinicians; ECHO clinics; HCV registry, HCV outreach activities					completed treatment 180/201 (89.6%) of those who completed treatment achieved SVR
Miller(119), 2016	Part of HepTLC initiative; EMR prompt, educational sessions, project coordinator	Prospective	BC Participants were BC patients at an urban safety net hospital in Atlanta who had not been tested previously for HCV	201/2894 (6.9%) anti-HCV positive 124/174 (71.2%) RNA tested were RNA positive	122 (98.3% of RNA positive) were referred to care 120/122 (98.4%) attended first appointment	
Morano(157), 2014	Mobile medical clinic		At-risk population Data reported from all mobile medical clinic clients in New Haven, CT	27/438 (6.2%) anti-HCV positive 27/27 (100%) RNA positive	17/27 (63.0%) linked to care	
Patel(121), 2016	Part of HepTLC initiative	Retrospective	BC Data are from all BC participants who were tested at 104 testing site in 21 US municipalities Patients seen in clinical settings such as: EDs, FQHCs, community health clinics, STD clinics, state health departments	2900/24966 (11.6%) anti-HCV positive 1497/2108 (71.0%) RNA positive	1201/1497 (80.2%) made follow-up appointment 938/1201 (78.1%) attended appointment	

Table 3. Linkage-to-care (LTC) among adults

Study	Screening guidelines or LTC intervention (if any)	Study design	Population and sample information	% Anti-HCV and % RNA positive	% Attended follow-up appointment	% Treated (and % achieved SVR, if reported)
			(HepTLC initiative)			
Pieper(161), 2018		Cross-sectional	Patients seen at an urban wound clinic (mean age 61, 71% male, 88% black, 66% previous IDU)		NOTE: ALL DATA ARE SELF-REPORTED 14/31 (45.2%) of those who self-reported being infected reported going to a clinic for care	11/31 (35.5%) of those who self-reported being infected reported undergoing treatment
Ramirez(93), 2016	HepTLC initiative	Retrospective	At-risk population All patients tested as part of the HepTLC initiative from 206 testing sites in 17 states Patients seen in clinical settings such as: EDs, FQHCs, community health clinics, STD clinics, state health; 23% were <=30 y/o; 31% Non-Hispanic White	7580/57570 (13.2%) anti-HCV positive 3449/4765 (72.4%) of RNA tested were RNA positive	2624/3449 (76.1%) made a follow-up appointment 1509/2624 (57.5%) attended the appointment	
Rhea(163), 2018	Part of HepTLC initiative An HCV bridge counselor provided test results and referrals (along with other	Retrospective	At-risk population Patients are from the Durham, NC HepTLC site (an STD clinic); patients reported at least 1 risk factor for HCV	108/733 (14.7%) anti-HCV positive 81/108 (75%) RNA positive	51/81 (63%) of patients were linked to care	

Table 3. Linkage-to-care (LTC) among adults

Study	Screening guidelines or LTC intervention (if any)	Study design	Population and sample information	% Anti-HCV and % RNA positive	% Attended follow-up appointment	% Treated (and % achieved SVR, if reported)
	services such as counseling, referrals for vaccinations, etc.)		Patients were 66% men, 69% black, 51% BC			
Schechter-Perkins(136), 2018	EMR prompt	Retrospective	ED patients All patients presenting to the ED at Boston Medical Center (urban safety net hospital serving a primarily indigent population) and having blood drawn were HCV screened	504/3808 (13.2%) anti-HCV positive 292/493 (59.2%) of RNA tested were RNA positive	102/292 (34.9%) made follow-up appointment 66/102 (64.7%) attended appointment	
Sears(123), 2013		Feasibility pilot study	BC Convenience sample of participants who were patients born 1945-1960 scheduled for an outpatient colonoscopy with Scott & White Healthcare in Temple, TX	4/346 (1.2%) anti-HCV positive 1/4 (25%) RNA positive	1/1 (100%)	1/1 (100%)
Sena(165), 2016	Part of the HepTLC initiative Bridge counselor or patient navigator	Prospective	At-risk population Patients were tested as part of the HepTLC initiative in Durham, NC; patients were seen at STI clinics, the county jail, homeless	Anti-HCV positivity: 326/2004 (16.3%) of full sample; STD clinic: 64/471 (13.6%); Comm testing site: 150/741 (20.2%); Homeless health clinic: 23/84 (27.4%) RNA-positivity:	123/134 (91.8%) of full sample	

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Study	Screening guidelines or LTC intervention (if any)	Study design	Population and sample information	% Anti-HCV and % RNA positive	% Attended follow-up appointment	% Treated (and % achieved SVR, if reported)
			shelters, a SUD tx center	241/326 (73.9%) of full sample; STD Clinic: 47/64 (73.4%); Comm testing site: 109/150 (72.7%); Homeless health clinic: 19/23 (82.6%)		
Soipe(184), 2018		Cross-sectional	Young PWUD (18-29 yrs) Participants were part of the RAPiDS study in Rhode Island; young adults (18-29 yrs) who are nonmedical Rx opioid users		NOTE: DATA ARE SELF-REPORTED 12/18 (66.7%) of those reporting to have tested positive reported receiving a referral for specialty care	
Taylor(126), 2016	Promotoras met with RNA-positive patients to help link them to care	Pilot study	BC BC patients receiving care at University Hospital in San Antonio (serving an indigent population; high proportion of Hispanic patients)	192/2327 (8.3%) anti-HCV positive 108/192 (56.3%) RNA positive	After 20 months, 94/108 (87%) were linked to care with PCP; 47/108 (43.5%) were linked to HCV specialty care	8/108 (7.4%)
Trooskin(168), 2015	Do One Thing program Testing provided in a mobile medical unit, patient navigators connected with those who test positive	Prospective	At-risk population Convenience sample of participants living in medically-underserved neighborhoods with high rates of infection	52/1301 (4%) anti-HCV positive 36/52 (69.2%) RNA positive	23/36 (63.9%) obtained a referral to specialty care 21/23 (91%) attended appointment	12/36 (33.3%)

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Study	Screening guidelines or LTC intervention (if any)	Study design	Population and sample information	% Anti-HCV and % RNA positive	% Attended follow-up appointment	% Treated (and % achieved SVR, if reported)
			91% African American; 71% were not in BC			
Turner(217), 2015	Promotoras met with RNA-positive patients to help link them to care	Retrospective	NOTE: SAME AS TAYLOR BC BC patients receiving care at University Hospital in San Antonio (serving an indigent population; high proportion of Hispanic patients)	240/3168 (7.6%) anti-HCV positive 134/240 (55.8%) RNA positive	108/134 (80.6%) received follow-up primary care; 52/134 (38.8%) received care from a hepatologist	5/134 (3.7%)
Viner(142), 2015		Epi/Surveillance (Modeling)	Estimates of prevalence and care cascade calculated for Philadelphia using data from NHANES, ACS, and Philadelphia Dept of PH	47525/1584848 (2.9%) estimated anti-HCV positive 6383/13596 (46.9%) RNA positive	1745/6383 (27.3%) estimated to be in care	956/6383 (15%)
Ward(169), 2016	HepTLC initiative LTC interventions varied by site	Prospective	At-risk population Data are from the HepTLC initiative; screening and LTC were promoted at sites across the US that serve people at risk for HCV; this report presents data from full initiative NOTE: See Ramirez article	7580/57570 (13.2%) anti-HCV positive 3449/64716 (5.3%) of all antibody or RNA tested were RNA positive	2624/3449 (76.1%) were referred to care, tx, and preventative services 1509/3449 (43.8%) attended appointment	
White(218), 2018		Prospective	ED patients	68/1217 (5.6%) anti-HCV positive	40/46 (87%) had referral	

Table 3. Linkage-to-care (LTC) among adults

Study	Screening guidelines or LTC intervention (if any)	Study design	Population and sample information	% Anti-HCV and % RNA positive	% Attended follow-up appointment	% Treated (and % achieved SVR, if reported)
			Participants were Level A and Level B trauma activations w/o a known prior HCV diagnosis		made or verification of ongoing outpatient care	
Younossi(131), 2016		Prospective	BC Participants were BC gastroenterology patients at 1 of 5 sites	10/2000 (0.5%) anti-HCV positive 4/10 (40%) RNA positive	4/4 (100%) made a follow-up appointment	
Zaller(170), 2016	Research assistant provided counseling and HCV prevention information; a brochure was given with info on local resources for primary care; RA scheduled the appointment for confirmatory testing; confirmatory testing was provided at no cost to participants	Cross-sectional	At-risk population Participants were adults currently on probation or parole with self-reported negative or unknown HCV status	12/130 (9.2%) anti-HCV positive 2/12 (16.7%) RNA positive	2/2 (100%) made a follow-up appointment 0/2 (0%) attended appointment	

LTC, linkage-to-care; SVR, sustained virologic response; ED, emergency department; BC, birth cohort; FQHC, federally qualified health center; SEP, syringe exchange program

Box 2. Persons recommended for hepatitis C testing

- Universal hepatitis C screening:
  - Hepatitis C screening at least once in a lifetime for all adults aged 18 years and older, except in settings where the prevalence of HCV infection (HCV RNA-positivity) is less than 0.1%
  - Hepatitis C screening for all pregnant women during each pregnancy, except in settings where the prevalence of HCV infection (HCV RNA-positivity) is less than 0.1%
- One-time hepatitis C testing regardless of age or setting prevalence, including among persons with recognized conditions or exposures:
  - Persons with HIV
  - Persons who ever injected drugs and shared needles, syringes, or other drug preparation equipment, including those who injected once or a few times many years ago
  - Persons with selected medical conditions, including:
    - persons who ever received maintenance hemodialysis
    - persons with persistently abnormal ALT levels
  - Prior recipients of transfusions or organ transplants, including;
    - persons who received clotting factor concentrates produced before 1987
    - persons who received a transfusion of blood or blood components before July 1992
    - persons who received an organ transplant before July 1992
    - persons who were notified that they received blood from a donor who later tested positive for HCV infection
  - Healthcare, emergency medical, and public safety personnel after needle sticks, sharps, or mucosal exposures to HCV-positive blood
  - Children born to mothers with HCV infection
- Routine periodic testing for persons with ongoing risk factors, while risk factors persist:

- Persons who currently inject drugs and share needles, syringes, or other drug preparation equipment

- Persons with selected medical conditions, including:
  - persons who ever received maintenance hemodialysis

- Any person who requests hepatitis C testing should receive it, regardless of disclosure of risk, because many persons may be reluctant to disclose stigmatizing risks

Box 3. Management of persons with HCV infection

- Medical evaluation (by either a primary-care clinician or specialist [e.g., in hepatology, gastroenterology, or infectious disease]) for chronic liver disease, including treatment and monitoring
- Hepatitis A and B vaccination
- Screening and brief intervention for alcohol consumption
- Avoiding new medicines, including over-the-counter and herbal agents, without first checking with their healthcare provider
- HIV risk assessment and testing
- Weight management or losing weight and following a healthy diet and staying physically active for persons who are overweight (BMI ≥25kg/m2) or obese (BMI ≥30kg/m2)
- Avoiding or stopping donating blood, tissue, or semen
- Refraining from sharing appliances that might come into contact with blood, such as toothbrushes, dental appliances, razors, and nail clippers.

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