

The American College of Preventive Medicine Position Statement on Hepatitis C Virus Infection



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The American College of Preventive Medicine Prevention Practice Committee contributes to policy guidelines and recommendations on preventive health topics for clinicians and public health decision makers. After review of the currently available evidence, the College is providing a consensus-based set of recommendations designed to increase screening for and prevention of hepatitis C virus infection, increase linkage to care, improve access to treatment, and encourage development of hepatitis C virus–related quality measures.

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Introduction

An estimated 185 million people have been infected with hepatitis C virus (HCV) globally,¹ and chronic HCV infection is a major cause of liver cirrhosis and hepatocellular carcinoma.² Approximately 1,778 acute HCV infections were reported in the U.S. in 2012, an increase of 75% from 2010.³ After adjusting for asymptomatic infections and under-reporting, CDC estimates 21,870 new HCV infections occurred in 2012.³ Of the 3.6 million individuals in the U.S. with HCV antibody, approximately 2.7 million are thought to be chronically infected, though this likely represents a significant underestimation.^{4–6} Between 75% and 85% of those infected with HCV are expected to progress to chronic disease, with varying rates in selected subgroups.^{7–10} Disease burden is

also disproportionate in people who are uninsured or have publically funded insurance.¹¹ Further, an estimated 22% of the chronic HCV cases occur in African Americans, even though African Americans represent only 12% of the U.S. population.¹¹ HCV-related mortality is highest among individuals aged 55–64 years (25.2 deaths/100,000 population in 2013), American Indians/Alaska Natives (12.2 deaths/100,000 population), and men (approximately 2.6 times the rate for women).¹² New outbreaks of HCV infection have been observed among young adult injection drug users in predominantly suburban and rural areas and have been linked to opioid abuse.^{13–16}

Infection with HCV is the leading cause of advanced liver disease and the leading indication for liver transplant, and was the underlying or contributing cause of death in 19,368 people in the U.S. in 2013.¹⁷ A major challenge is that most infected individuals are asymptomatic or unaware of their illness.

Screening for Hepatitis C Virus Infection

“Baby boomers,” defined as people born between 1945 and 1965, are estimated to account for 75% of individuals infected with HCV and are, on average, five times more likely to be infected than any other age group in the overall U.S. population.¹⁸ In 2012 and 2013, CDC and U.S. Preventive Services Task Force (USPSTF) addressed the high prevalence of HCV infection in the baby boomer population by recommending a one-time screening for the virus in people born between 1945 and 1965, regardless of their history of

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risk factors for infection.^{14,17,19} In addition to age-cohort-based screening, CDC and USPSTF recommended screening in people at high risk for HCV infection, including those with HIV infection.²⁰ Risk factors for HCV infection include injection or intranasal drug use, receiving a blood transfusion before 1992, long-term hemodialysis, being born to an HCV-infected mother, incarceration, receiving an unregulated tattoo, and other percutaneous exposures. In addition, the following groups may be considered high risk on a case by case basis and warrant HCV screening: recipients of transplanted tissue (e.g., corneal, musculoskeletal, skin, ova, and sperm), people with a history of noninjected illegal drug use, individuals with a history of tattooing or body piercing, people with a history of multiple sex partners or sexually transmitted diseases, and long-term steady sex partners of HCV-positive individuals.

Special Populations

Young Prescription Opioid Abusers Who Transition to IV Drug Use

Analysis of data from the general U.S. population has shown an HCV prevalence higher in men than women, in non-Hispanic blacks than non-Hispanic whites, and among people born from 1945 to 1965.²¹ However, a new and growing epidemic of HCV infection has been recognized recently among adolescent and young adult people who inject drugs and live primarily in suburban and rural communities.^{13–16} Further, these young adults often initiated drug use with oral prescription opioids (without a doctor's prescription) before transitioning to IV drug use.^{13,22} In fact, this new epidemic of HCV infection overlaps temporally and geographically with the ongoing epidemic of prescription drug abuse in the U.S.²³

HIV/Hepatitis C Virus Co-infection Among Men Who Have Sex With Men

Co-infection with HIV/HCV is a global public health problem in men who have sex with men (MSM), where the prevalence of co-infection surpassed 90% prior to effective HIV/AIDS outreach programs and interventions, and has more recently been estimated to be 16% in the U.S.^{24–26} A 2012 systematic review found that HIV-positive MSM had a 4.1 times higher risk of acquiring HCV infection than HIV-negative MSM.²⁵ Since 2000, evidence has accumulated for permucosal transmission of HCV among HIV-infected MSM in Europe, Australia, the U.S., and Asia.²⁷ The Multicenter AIDS Cohort Study prospectively followed 5,310 HCV antibody (anti-HCV)-negative MSM from 1984 to 2011 for anti-HCV seroconversion.²⁸ HIV infection and unprotected receptive anal intercourse with more than one male partner were

independent significant risk factors for HCV seroconversion.²⁸ The HCV incidence rate was inversely proportional up to a CD4 T-cell count of 500 cells/mm³ and there was no association with highly active antiretroviral therapy.²⁸

Specific sexual practices, such as unprotected anal intercourse, manual insertion of fingers into the rectum (“fisting”), and other traumatic sexual practices, may potentiate HCV transmission because trauma to the mucosal lining frequently results in bleeding.^{29,30} Certain drugs, such as crystal methamphetamine, are nasally or rectally used by some subpopulations of HIV-positive MSMs. These drugs may cause behavioral disinhibition and increased pain threshold, thus enhancing risk-taking behavior involving traumatic sexual practices that last longer and are more intense, with potential for significant mucosal inflammation and bleeding.³¹ A 2007–2008 cross-sectional survey among MSM attending a large sexually transmitted infection clinic found that HIV infection, IV drug use, fisting, and gamma hydroxybutyrate use were significantly associated with HCV infection among MSM.³²

Linkage to Care

Recent advances in oral therapies for HCV treatment have presented an opportunity to link individuals to effective care, reduce community viral load, and also reduce transmission rates. With only 32%–38% of all HCV-infected people receiving follow-up hepatitis care, and only 5%–6% successfully treated, effective linkage to care and treatment is critical to improve outcomes.³³

Improved utilization of primary care systems, including Federally Qualified Health Centers and patient-centered medical homes, and utilization of inpatient settings and emergency departments, could increase screening rates, counseling to prevent infection, transmission and progression, access to care, and treatment opportunities.^{34,35} New resources for guidelines, such as those from American Association for the Study of Liver Diseases/Infectious Disease Society of America/International Antiviral Society-USA, are available to inform both primary care and specialist physicians.³⁶

Barriers to care for patients with HCV infection include treatment contraindications, competing treatment priorities, loss to follow-up, treatment duration, adverse effects, lack of access to treatment, high price, and lack of practitioner expertise. These barriers can be addressed through multiple approaches. Population-based strategies include the use of a case management model, such as with HIV; directly observed therapy; collocation of primary care with drug treatment programs; and other services, such as needle exchange programs,

assurance of coverage for HCV-infected people through the Patient Protection and Affordable Care Act, and optimal use of Pharmaceutical Patient Assistance Programs.³⁶ New Mexico is trying to improve access in rural communities through use of telemedicine with Project ECHO at the University of New Mexico to increase provider training and support for treatment.³⁷

Once linked to care, behavioral counseling and education are critical components for improved HCV disease outcomes. Counseling should include avoidance of alcohol and other hepatotoxins; behavior modifications to reduce blood transfer, such as sharing toothbrushes and dental or shaving equipment, illicit drug use, and needle sharing; donation of blood or organs; and the use of barrier precautions to reduce the risk of sexual transmission by patients with HIV infection or those with multiple sex partners.

Access to Treatment

The most recent direct and indirect cost estimates of HCV infection for the U.S. were \$694–\$1,660 million and \$1,780 million per year, respectively.^{38,39} The cost of care for patients who develop cirrhosis from HCV infection is driven by complications such as decompensated cirrhosis, variceal hemorrhage, refractory ascites, liver transplant, and hepatocellular carcinoma.⁴⁰ The reduction in HCV-related complications with treatment and cure has the potential to markedly decrease these costs.

There has been considerable concern raised about the price of direct-acting antiviral agents (DAAs) approved for use in the last 2 years. However, the actual prices paid, specifically the prices paid after negotiations between pharmaceutical companies and pharmacy benefit managers, private insurance companies, or Medicaid plans, are rarely known. This is because negotiated prices are confidential business contracts, with the exception of mandated rebates given to federal government agencies.⁴¹ It is well recognized that the high prices of DAAs and subsequent restrictions on DAA reimbursement have reduced patient access to treatment.^{42–44} For example, 31 of 42 (75%) states with known Medicaid reimbursement criteria for sofosbuvir limit access to this drug to patients with advanced fibrosis, 37 (88%) states have requirements related to substance abuse, and 14 (33%) states have prescriber-type restrictions.⁴² A disproportionate number of people with chronic HCV infection in the U.S. live on incomes near the poverty level, and are therefore disproportionately impacted by HCV treatment restrictions.⁴² These restrictions, and thus limitations to access, are not consistent with current recommendations from professional medical organizations.³⁶

Until recently, HCV treatments consisted of a combination of a DAA with peginterferon and ribavirin.^{45,46} A new class of DAA has significantly improved the treatment of HCV infection and includes sofosbuvir, ledipasvir, paritaprevir, ombitasvir, dasabuvir, daclatasvir, simeprevir, elbasvir, and grazoprevir.⁴⁷ Newer, all-oral, interferon-free DAAs have minimal side effects, cure rates >90% for all genotypes except in select patient populations, and evidence has amassed in the past year that they are cost effective in the U.S.^{48–53} The societal willingness-to-pay threshold is typically considered to range from about \$50,000 to \$100,000 per quality-adjusted life year.⁴⁴ Compared with the interferon-based old standard of care, the incremental cost-effectiveness ratios per quality-adjusted life year ranged from \$12,825 to <\$100,000, with higher incremental cost-effectiveness ratios in people with less severe fibrosis.^{48–53} However, significant improvement in long-term survival with treatment at earlier stages of fibrosis has been observed in recent studies, strongly supporting treatment of people with less severe fibrosis.^{54,55} It is important to note that no cost-effectiveness analysis to date has included the added potential benefit of treatment to reduce HCV transmission.

Guided by the cumulative evidence, professional medical organizations have recently updated their guidelines in August 2015 and now recommend treatment for all patients with chronic HCV infection, except those with short life expectancies owing to comorbid conditions³⁶ (Table 1). Despite robust evidence and recommendations supporting treatment, there is a current access-to-care crisis. It is important to note that the high prices and coverage restrictions causing this crisis are not the result of immutable conditions, but the consequence of decisions made by pharmaceutical companies, pharmacy benefit managers, and private and public insurers. Efforts of all stakeholders should be coordinated to better ensure that policy and decision making around treatment are equitable, evidence-based, and maximize the public health benefit to society.

Quality Measures

The development and use of HCV quality measures have the potential to improve HCV screening and linkage to care. There are three main performance measure sets:

1. ORYX[®] measures used by The Joint Commission as part of the hospital accreditation process;
2. the Healthcare Effectiveness Data and Information Set consisting of 80 measures across five domains of outpatient care and currently used by >90% of healthcare plans to measure performance; and
3. the Physician Quality Reporting System, a required pay-for-performance program for eligible professionals who treat Medicare patients.^{59–61}

Table 1. Recommendations on Hepatitis C Virus Screening, Transfer of Care, and Treatment by Professional Organization

Agency or organization	Recommendation (screening, transfer of care, treatment), evidence grading, ^a year of recommendation
USPSTF ^{19,20}	Screening: Screening for HCV infection in persons at high risk for infection (B recommendation, 2013). Offering one-time screening for HCV infection to adults born between 1945 and 1965 (B recommendation, 2013).
CDC ¹⁸	Screening: One-time testing without prior ascertainment of HCV risk for persons born during 1945–1965 (strong recommendation, moderate quality of evidence, 2012). Transfer of care: Early detection and treatment of asymptomatic individuals. Treatment decisions should be made by the patient and provider after several factors are considered, including stage of disease, hepatitis C genotype, comorbidities, therapy-related adverse events, and benefits of treatment.
ALF ⁵⁶	Screening: HCV testing at least once for persons born between 1945 and 1965. Rating: Class I, Level B (2014). Other persons should be screened for risk factors for HCV infection, and one-time testing should be performed for all persons with behaviors, exposures, and conditions associated with an increased risk of HCV infection. Rating: Class I, Level B (2014).
IOM ⁵⁷	Screening: Risk factor screening for hepatitis C should be included as a core component of preventive care (2010).
Canadian Liver Foundation ⁵⁸	Screening: All adults born between 1945 and 1975 undergo a test for hepatitis C (2014).
AASLD/IDSA/IAS-USA ³⁶	Screening (2014): HCV testing at least once for persons born between 1945 and 1965 without ascertainment of risk. Rating: Class I, level B. Other persons should be screened for risk factors for HCV infection, and one-time testing should be performed for all persons with behaviors, exposures, and conditions associated with an increased risk of HCV infection. Rating: Class I, level B. Annual HCV testing for persons who inject drugs and for HIV-seropositive men who have unprotected sex with men. Periodic testing should be offered to other persons with ongoing risk factors for exposure to HCV. Rating: Class IIA, Level C. Transfer of care (2014): Evaluation by a practitioner who is prepared to provide comprehensive management, including consideration of antiviral therapy, is recommended for all persons with current (active) HCV infection. Rating: Class IIa, level C. Persons with current (active) HCV infection should receive education and interventions aimed at reducing progression of liver disease and preventing transmission of HCV. Rating: Class IIa, Level B. Treatment (2015): Treatment for all patients with chronic HCV infection is recommended, except those with short life expectancies that cannot be remediated by treating HCV, by transplantation, or by other directed therapy. Rating: Class I, Level A. 2. Pretreatment assessment of a patient’s understanding of treatment goals and provision of education on adherence and follow-up are essential. A well-established therapeutic relationship between practitioner and patient remains crucial for optimal outcomes with new direct-acting antiviral therapies.

^aSee citations for how each agency or organization defined evidence grade.
AASLD/IDSA/IAS-USA, American Association for the Study of Liver Diseases/Infectious Disease Society of America/International Antiviral Society-USA; ALF, American Liver Foundation; HCV, hepatitis C virus; USPSTF, U.S. Preventive Services Task Force.

The use of quality measures has been associated with improvements in clinical performance in non–hepatitis-related areas. For example, national programs that publicly report quality data have shown significant improvements in process measures and lower mortality rates for heart attacks, heart failure, and pneumonia.^{62,63} Also, although few peer-reviewed published studies exist, some found that every 10% increase in adherence to a quality measure was associated with a 10% improvement in outcomes.⁶⁴

Currently, there are no ORYX[®] or Healthcare Effectiveness Data and Information Set measures related to HCV. In the Physician Quality Reporting System, there are eight measures related to HCV. None are related to HCV screening recommendations or to linkage to care.⁶⁵ This represents a missed opportunity for setting benchmarks and improving HCV care.

In February 2014, the Office of HIV/AIDS and Infectious Disease Policy, Office of the Assistant

Secretary for Health, DHHS published the “Action Plan for the Prevention, Care, and Treatment of Viral Hepatitis,” updated for 2014–2016.⁶⁶ This plan presented 155 specific actions that 14 agencies or offices from across four federal departments will implement, including seven progress measures. The plan includes specific goals to increase the proportion of individuals who are aware of their HCV infection and to reduce the number of new HCV infections. Priority areas identified in the plan include educating providers and communities to reduce health disparities and improving testing, care, and treatment to prevent liver disease and cancer. Evidence-based strategies outlined by the DHHS action plan could well be used as a starting point for development of HCV quality measures.

Recommendations From Other Professional Organizations

Recommendations on HCV screening, transfer of care, and treatment prioritization by professional organizations along with the level of evidence and date of each are presented in [Table 1](#).

Recommendations From the American College of Preventive Medicine

The American College of Preventive Medicine (ACPM) is the medical specialty society that addresses population health. The following is a list of ACPM population-based recommendations for HCV screening, prevention, linkage to care, and access to treatment developed by a review of the current scientific literature, including the evidence-based guidelines of other professional organizations. These recommendations were developed in a consensus-based manner in the ACPM Prevention Practice Committee and endorsed by the ACPM Board of Regents.

Recommendations for Screening

1. Screening for HCV infection at least once for people born between 1945 and 1965 and in certain high-risk populations to include individuals with HIV and those who use or have used IV drugs. Targeted screening of young (aged <30 years) oral opioid prescription abusers and people who use IV drugs living in rural and suburban areas should be considered. USPSTF and CDC should evaluate the expansion of screening recommendations to high HCV prevalence secondary care venues, such as inpatient, emergency departments, and behavioral health settings.
2. The National Committee for Quality Assurance, The Joint Commission, and the Centers for Medicare and Medicaid Services consider the development of quality

and accountability measures for HCV screening based on the age guidelines recommended by CDC and USPSTF.

Recommendations for Prevention

1. Counseling on behavior modifications to reduce blood transfer, such as avoiding sharing toothbrushes and dental or shaving equipment, illicit drug use, and needle sharing; improved access to evidence-based drug abuse treatment programs; continuing HCV screening prior to donation of blood or organs; and using barrier precautions to reduce the risk of sexual transmission by patients with HIV infection or those with multiple sex partners.
2. Research into the efficacy of DAA usage as pre- and post-exposure prophylaxis for HCV infection.
3. Research for development of an HCV vaccine.
4. Comparative effectiveness research of drug abuse treatment interventions, such as pharmacotherapy and needle exchange programs.

Recommendations for Linkage to Care

1. The National Committee for Quality Assurance, The Joint Commission, and the Centers for Medicare and Medicaid Services consider the development of quality and accountability measures for linkage to HCV disease care.
2. The DHHS Office of HIV/AIDS and Infectious Disease Policy Action Plan for the Prevention, Care, and Treatment of Viral Hepatitis should be adopted by nonfederal HCV stakeholders to include state and local health departments and healthcare plans.
3. Asymptomatic individuals who screen positive for current (active) infection should receive early confirmation, be provided quantitative HCV RNA and genotyping, and evaluated for treatment.
4. Behavioral counseling should be provided to decrease the risk of HCV transmission and infection. Providers should serve as patient advocates and assist with linkage to drug treatment programs.
5. Treatment decisions should be made by the patient and provider after several factors are considered, including stage of disease, HCV genotype, comorbidities, therapy-related adverse events, and benefits and harms of treatment.

Recommendations for Access to Treatment

1. A coordinated and multifaceted approach with all stakeholders is needed to optimize access to new direct-acting antiviral therapy for HCV and to ensure policy and decision making around treatment are equitable, evidence-based, and maximize the public

health benefit to society. The impacts of restrictions on treatment access should be measured and publicly shared to direct decision-making processes.

2. Other opportunities to improve access should be used, including case management models such as with HIV, directly observed therapy, use of telemedicine to enable providers to access specialty support, co-location of primary care with drug treatment programs and other services, assurance of coverage for HCV-infected people through the Patient Protection and Affordable Care Act, and optimal use of Pharmaceutical Patient Assistance Programs.

Conclusions

This article briefly reviewed the literature regarding the public health implications of the HCV epidemic. The burden of disease related to HCV infection is expanding. Fortunately, new treatment options are proving to be highly effective on an individual and a population basis. The ACPM policy statements presented here are consistent with recommendations from other federal agencies and professional organizations. Critical areas for development of healthcare policy, improvement of public health practices, and continued research are highlighted. Only through a coordinated and multifaceted approach with multiple stakeholders can the goal of reduced morbidity, mortality, and the associated personal and societal costs be realized.

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