Medi-Cal Rx

Screening, Diagnosis, and Treatment of Chronic Hepatitis C Virus Infection

September 17, 2024

Disclaimer: This article was published by the Medi-Cal Drug Use Review (DUR) Program and is not an official policy of the Department of Health Care Services (DHCS).

Learning Objectives

- Review the updated guidance from the American Association for the Study of Liver Diseases and the Infectious Diseases Society of America (AASLD/ISDA) for testing, managing, and treating hepatitis C virus (HCV) infection.
- Discuss strategies to improve treatment initiation rates after a diagnosis of chronic HCV infection.
- Assess the status of chronic HCV screening, diagnosis, and treatment initiation among Medi-Cal members.

Key Points

- Numerous studies have reported a sharp decline in HCV screening, diagnosis, and treatment amidst the Coronavirus disease 2019 (COVID-19) pandemic. Interventions to improve treatment initiation among individuals who receive a diagnosis of chronic HCV are needed.
- In order to improve case identification, current AASLD/ISDA guidance recommends universal HCV screening for all adults aged 18 years or older. For initial testing, AASLD/ISDA suggests HCV antibody screening with reflex (automatic) HCV RNA testing to establish the presence of active infection (as opposed to spontaneous or treatment-induced viral clearance).
- Universal direct-acting antiviral (DAA) treatment continues to be strongly recommended for all people with chronic HCV infection, except those with a short life expectancy (<12 months) that cannot be remediated by HCV therapy, liver transplantation, or another directed therapy. Most HCV treatments are 95% effective when given once daily for 8-12 weeks, with limited side effects.
- AASLD/IDSA have created simplified treatment algorithms that can be utilized to select an appropriate DAA therapy for treatment-naïve adults with and without cirrhosis. There is also a new algorithm for incomplete treatment adherence for persons who have missed greater than or equal to seven days of DAA therapy.
- Today, in the United States, the majority of persons become infected with HCV by sharing needles or other equipment used to inject drugs. Injection drug use does not alter treatment success and should not delay treatment initiation.

- Despite improvements in HCV screening, the treatment rate for HCV infection among Medi-Cal members continues to remain relatively stagnant. However, among members newly diagnosed with chronic HCV in 2023, treatment rates in 2023 did appear higher (35.0%) than among all members diagnosed with chronic HCV (15.4%).

Background

As of 2018, an estimated 318,900 people are chronically infected with HCV in California.[1] Chronic HCV infection is associated with increased rates of mortality and development of severe complications including cirrhosis, end-stage liver disease, liver transplantation, and hepatocellular carcinoma (HCC).[2] With the development of effective DAA medications and the removal of treatment restrictions for individuals covered under Medi-Cal, timely initiation of therapy for HCV is now both an accessible and critical component of improving health outcomes and preventing further transmission in the community.[3, 4]

The COVID-19 pandemic further exacerbated existing barriers to HCV testing and treatment across the United States.[5-8] A national retrospective study in the United States found only 23% of people on Medicaid with a positive HCV RNA test between January 30, 2019, and October 31, 2020, initiated DAA treatment.[8] Recent studies revealed that important disparities exist in HCV treatment across the US, reporting the lowest treatment rates were among young adults and Medicaid recipients. Within Medicaid, treatment was even less likely to be initiated for Black individuals and in states with treatment restrictions.[9,10] More than half of patients with a history of injection drug use received DAA treatment and those with HCC or decompensated cirrhosis were 30% less likely to receive treatment, despite finding the cure rate was over 95% in these groups when treated.[11]

Injection drug use is the leading risk factor for HCV infection and is present in more than half of all new HCV infections.[12] Because of the high prevalence of HCV among people who inject drugs (PWID), interventions that aim to improve treatment rates in this population are especially important. Common barriers that prevent PWID from seeking HCV treatment after receiving a positive test result include lack of information about where to seek HCV medical care, current use of drugs and alcohol, and experiences of stigma and discrimination.[13]

Statewide Efforts to Improve HCV Screening, Diagnosis, and Treatment in California

In December 2021, DHCS updated the Treatment Policy for the Management of Chronic Hepatitis C. The policy urges providers to follow AASLD/IDSA guidance regarding HCV treatment which recommends treatment for all patients with chronic HCV infection except in the case of short life expectancy that cannot be improved with HCV therapy, liver transplantation, or another directed therapy.

As serologic testing is the primary means for identifying people with hepatitis C infection, recent California legislation has been passed to improve hepatitis screening rates in concordance with updated HCV screening recommendations from U.S. Preventive Services Task Force (USPSTF), Centers for Disease Control (CDC), and AASLD/IDSA. Effective January 1, 2022,

Assembly Bill (AB) 789 (Low, Chapter 470, Statutes of 2021) required that adult patients receiving primary care services are offered a screening test for hepatitis C, except under specified circumstances. If the patient accepts the offer to test and the test is positive, the provider must also offer follow-up care or refer the patient to a health care professional who can provide follow up care. For initial testing, AASLD/ISDA suggests HCV antibody screening with reflex HCV RNA testing to establish the presence of active infection (as opposed to spontaneous or treatment-induced viral clearance).[14,15]

In August 2023, the California Department of Public Health (CDPH) published an updated Viral Hepatitis Guide for Primary Care Providers, which includes guidance for clinicians to effectively screen individuals for HCV and complete appropriate follow-up in the case of a positive test result.[14] The guide also includes a *Patient Self-Assessment for Viral Hepatitis* form to identify patients who may need testing for hepatitis.[14] In general, HCV screening should be offered to all adults, to people of any age at risk for infection, and to all pregnant persons during *each* pregnancy. Routine periodic testing is also recommended for patients with ongoing risk factors, including people who currently inject drugs and share needles, syringes, or other drug preparation equipment and those with selected medical conditions.[14,15]

Effective March 1, 2024, the diagnosis restriction was removed for all HCV treatment drugs on the *Medi-Cal Rx Contract Drugs List*, removing another treatment barrier for members.

Medi-Cal also offers transportation to and from appointments for services covered by Medi-Cal. This includes transportation to medical, dental, mental health, or substance use disorder appointments, and to pick up prescriptions and medical supplies. For more information about transportation services, please see Transportation Services, located on the DHCS website.

Simplified Treatment Strategy for Adults with Chronic HCV Infection

The AASLD/IDSA continues to publish updated and comprehensive HCV guidance, most recently the Hepatitis C Guidance 2023 Update: AASLD-IDSA Recommendations for Testing, Managing, and Treating Hepatitis C Virus Infection, which includes guidance on the detection and management of HCV infection with important considerations for pediatric patients, HIV/HCV coinfection, severe renal and liver impairment, and treatment after a liver or kidney transplant.[15]

Pretreatment clinical evaluation is an essential component of selecting an effective treatment regimen. However, given pangenotypic DAA regimens now available, evaluation is more simplified and may even be promptly initiated in Emergency Departments, further reducing barriers for patients who atypically access health care.

In addition, on June 27, 2024, the U.S. Food and Drug Administration (FDA) announced they have granted marketing authorization for a point-of-care HCV RNA test. Rather than requiring a sample to be sent to a central lab for testing, the test detects HCV RNA and delivers results in about an hour using a blood sample from the fingertip. A test-to-treat approach for HCV is

now possible, where a person can be tested for HCV, and if positive for HCV RNA, be linked to care and potentially receive treatment during the same health care visit.

For full treatment recommendation details, providers should refer to the AASLD/IDSA guidance on pretreatment evaluation and treatment monitoring,[15] which includes assessment of liver function, viral load, HCV genotyping for certain individuals, vaccination history, pregnancy status, medication reconciliation, and screening for drug-drug interactions (see HEP Drug Interaction Checker by the University of Liverpool).

Providers should screen for presence of cirrhosis and refer to the appropriate simplified treatment algorithm linked below from the AASLD/IDSA HCV guidance webpage:

- Simplified HCV Treatment Algorithm for Treatment-Naive Adults Without Cirrhosis
- Simplified HCV Treatment Algorithm for Treatment-Naive Adults With Compensated Cirrhosis

While the preferred treatment regimen may be appropriate for the vast majority of patients, refer to the full treatment guidelines for patient-specific recommendations and considerations for special populations, including genotypes. As of October 2023, HIV has been removed as a contraindication to the simplified treatment approach.

First line antiviral therapy for chronic HCV available on the *Medi-Cal Rx Contract Drugs List* at the time of publication of this article are listed in **Table 1**.

Table 1. First-line Chronic HCV Treatment Options on the Medi-Cal Rx Contract Drugs List *

	Drug Regimen	Genotype	Duration/ Frequency	Total Doses	Oral Dose
Preferred	Glecapravir/pibrentasavir	All 1, 2, 3, 4, 5, 6	8 weeks/ 1 x daily	56	300 mg/ 120 mg
	Sofosbuvir/velpatasvir	All 1, 2, 3, 4, 5, 6	12 weeks/ 1 x daily	84	400 mg/ 100 mg
Alternative	Elbasvir/grazoprevir	Select 1, 4	12 weeks/ 1 x daily	84	50 mg/ 100 mg
	Ledipasvir/sofosbuvir	Select 1, 4, 5, 6	12 weeks/ 1 x daily	84	90 mg/ 400 mg

* For current information on covered products, check the Medi-Cal Rx Contract Drugs List page on the Medi-Cal Rx Web Portal.

Treatment Monitoring

During DAA treatment, individuals should be followed at clinically appropriate intervals to ensure medication adherence, assess adverse events and potential drug-drug interactions, and monitor blood test results necessary for patient safety. Recent data suggest that a minimal monitoring approach is safe and could achieve sustained virologic response (SVR) at a rate

comparable to that with standard monitoring.[14] Minimal monitoring involved: 1) no pre-treatment genotyping; 2) dispensing the entire treatment course (56 or 84 tablets) at entry; 3) no scheduled visits or laboratory monitoring; and 4) remote contact at week 4 to assess DAA adherence and at week 22 to schedule SVR assessment at week 24.[16]

The most common adverse effects of DAAs are headache and fatigue. A greater than or equal to 10-fold increase in ALT values from baseline at any time during treatment should prompt discontinuation of DAA therapy (especially with signs or symptoms of liver inflammation or increasing conjugated bilirubin, alkaline phosphatase, or INR). Quantitative HCV viral load testing is recommended 12 or more weeks after completion of therapy to document SVR, which is consistent with cure of chronic HCV infection.

Importantly, the AASLD/IDSA guidance now includes algorithms for incomplete treatment adherence for persons who have missed greater than or equal to seven days of DAA therapy, either during the first 28 days of DAA therapy or after receiving at least 28 days of DAA therapy.[15] All patients with incomplete adherence should be asked about contributing factors and counseled regarding the importance of adherence.[15]

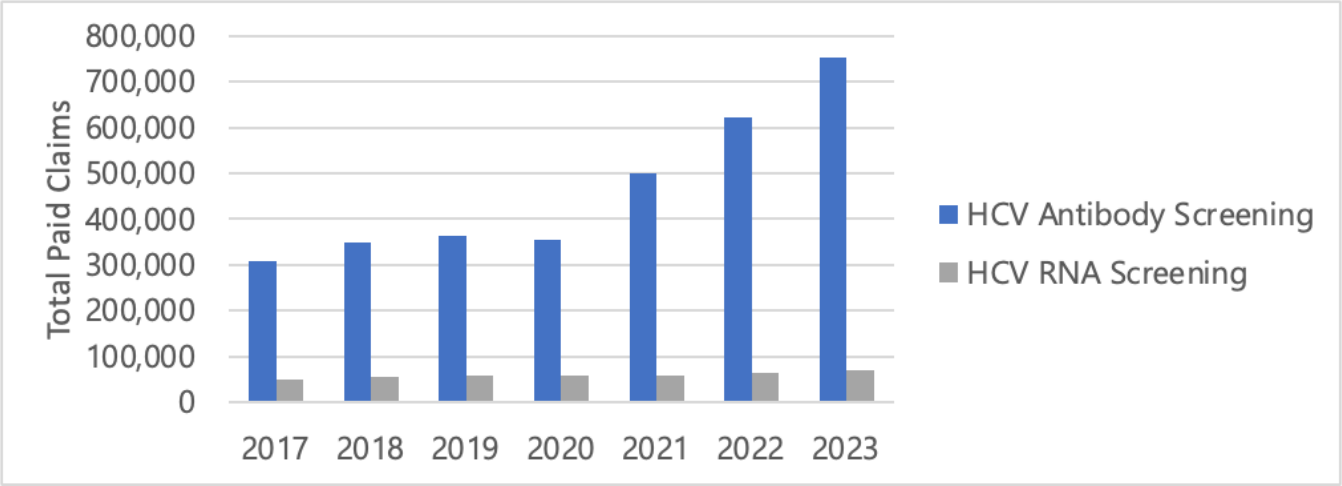
Screening, Diagnosis, and Treatment of Chronic HCV in the Medi-Cal Population

A retrospective cohort study was conducted to evaluate annual trends in screening, diagnosis, and treatment of chronic HCV in the Medi-Cal population between January 1, 2017, and December 31, 2023. Pharmacy claims and encounter data were reviewed for all certified-eligible Medi-Cal members, including CPT codes for HCV antibody screening (G0472, 86803, and 86804) and HCV RNA diagnostic tests (87520, 87521, and 87522), ICD-10 codes for diagnosis of chronic HCV (B18.2), and paid pharmacy claims for HCV treatment medications. Members with a diagnosis for acute HCV infection only and those members who were dually eligible for Medicare were excluded.

Results

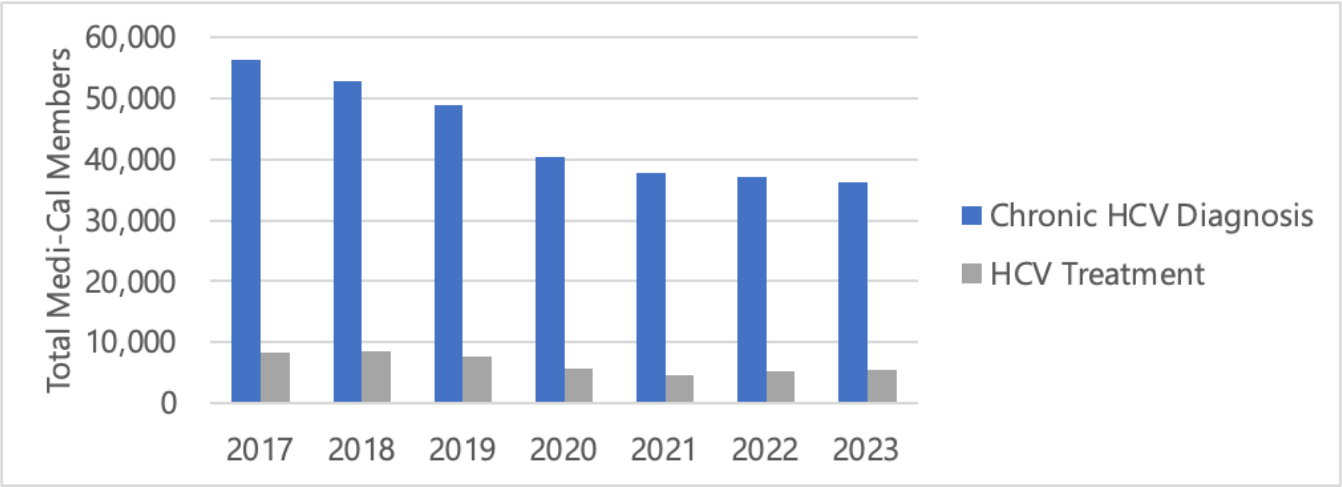
As shown in **Figure 1**, between 2017 and 2023, paid claims for HCV antibody screening tests increased by 143% and HCV RNA diagnostic tests increased by 41%. Paid claims for both tests increased each year since 2020, after a presumed pandemic-related dip.

Figure 1. HCV Screening Tests in the Medi-Cal Population, 2017 – 2023



Presumably, legislative updates in California (such as AB 789) and clinical guidance by all organizations recommending the expanded HCV screening among adults have been contributory factors in the increased testing. However, increased testing has not led to a subsequent increase in the diagnosis or treatment of chronic HCV in the Medi-Cal population. As shown in **Figure 2**, between 2017 and 2023 there was a 35% decrease in members with a diagnosis of chronic HCV and a 34% decrease in members with a paid claim for HCV treatment.

Figure 2. HCV Diagnosis and Treatment in the Medi-Cal Population, 2017 – 2023



Of note, there are limitations with the diagnostic data, as a diagnosis of chronic HCV had to be present as either a primary or secondary diagnosis in the claims encounter data in order to be counted.

Overall treatment rate was calculated by dividing the number of members in each calendar year with a paid medical claim indicating a primary or secondary diagnosis of chronic HCV by the number of members with at least one paid claim for an HCV treatment medication in during that calendar year. For 2023, treatment rates among were up slightly from 2017, going from 15.0% in 2017 to 15.4% in 2023.

For 2023, among a subset of members (n = 15,942) in the claims database who had their first recorded primary or secondary diagnosis code for chronic HCV indicated on a paid medical claim during 2023, a total of 5,581 of these members had at least one paid claim for an HCV treatment medication in 2023. For these presumed newly diagnosed members, the treatment rate was much improved within this group at 35.3%.

Conclusion/Discussion

The findings from this retrospective review add to the growing body of literature that shows a decline in HCV screening and treatment as a result of the COVID-19 pandemic. Although screening rates have since recovered and now surpass pre-pandemic levels, treatment initiation rates remain low. Even when state pharmacy policy improves access, barriers to widespread adoption of DAA treatment for chronic HCV infection remain.

The Viral Hepatitis National Strategic Plan for the United States provides a framework and an opportunity to dramatically expand access to HCV treatment, substantially reducing HCV-related morbidity and mortality. while also decreasing overall healthcare spending within ten years. A June 2024 report by the Congressional Budget Office focused on policies to increase national HCV treatment rates among Medicaid enrollees found that savings from health care costs that would be avoided by increased HCV treatment would more than offset direct spending on HCV treatment. With timely initiation of treatment critical to reducing HCV mortality, disparities, and transmission, effective interventions linking diagnosis and treatment should be a priority for all health care providers. The recent approval by the FDA of a point-of-care HCV RNA test provides an opportunity for providers to move towards a test-to-treat model, improving critical access to HCV treatment.

Clinical Recommendations

- One-time HCV screening should be offered to all adults, to people of any age at risk for infection, and during each pregnancy. Routine periodic testing is recommended for patients with ongoing risk factors, including people who currently inject drugs and share needles, syringes, or other drug preparation equipment and those with selected medical conditions.
- If a patient is newly diagnosed with chronic HCV, refer to recommendations from AASLD/IDSA for guidance on pretreatment clinical evaluation and appropriate treatment selection.
- Patient education should include comprehensive counseling on DAA medications, as well as methods to reduce liver disease progression and prevent HCV transmission:
  - Recommend patients with HCV infection reduce or eliminate intake of alcohol and other liver toxins.
  - Counsel patients with HCV infection to avoid sharing personal items that may have blood on them including razors, needles, clippers, toothbrushes, and tattoo and piercing equipment.
  - For patients who inject drugs, provide information on safer injection strategies, HIV pre-exposure prophylaxis, local harm reduction services, and options for substance use

disorder treatment if desired. For more information on syringe services programs and nonprescription sales of syringes in pharmacies, see the Syringe Services Programs in California website.
  - Evaluate all patients with active HCV infection for other conditions that may accelerate liver fibrosis, including hepatitis B and HIV infections.
  - Evaluate all patients with active HCV infection for advanced hepatic fibrosis using noninvasive tests (serum panels, elastography) or liver biopsy, if required.
  - Vaccinate all eligible patients with HCV infection against hepatitis A and hepatitis B. All vaccinations recommended by the USPSTF must be provided to Medi-Cal members without cost-sharing.
  - Vaccinate all eligible patients with cirrhosis against pneumococcal infection.
- Additional tools and resources for both providers and patients can be found on the following websites:
  - CDC Hepatitis C Frequently Asked Questions for Health Professionals
  - Free educational modules developed by the University of Washington Infectious Diseases Education & Assessment (IDEA) program are available at Hepatitis C Online (includes free CME for providers).
  - The National Clinician Consultation Center (NCCC) offers clinician-to-clinician advice on HCV and co-infection management.
  - Video-conferencing-based training for primary care providers in California, available at UCSF Project ECHO Liver Care and USC Hepatitis C Project ECHO.
  - The CDPH Office of Viral Hepatitis Prevention provides viral hepatitis prevention information and resources, including CDPH Hepatitis C Patient Education Materials, which are available in both English and Spanish.
  - The Resource Center page on the American Liver Foundation website has educational materials and information specific for caregivers.
  - The National Harm Reduction Coalition created Hepatitis C Basics for People Who Use Drugs (PWUD) to help patients learn about HCV and harm reduction strategies.
  - World Hepatitis Day includes materials available to download in a range of languages, as well as customizable posters and social media graphic tools to create materials in any language not currently available.

References

1. Rosenberg ES, Rosenthal EM, Hall EW, et al. Prevalence of Hepatitis C Virus Infection in US States and the District of Columbia, 2013 to 2016. *JAMA Netw Open*. 2018;1(8):e186371. Available at: https://doi.org/10.1001/jamanetworkopen.2018.6371. Accessed: September 12, 2024.
2. Van Der Meer AJ, Veldt BJ, Feld JJ, et al. Association between sustained virological response and all-cause mortality among patients with chronic hepatitis C and advanced hepatic fibrosis. *JAMA*. 2012, 308, 2584–2593. Available at: https://doi.org/10.1001/jama.2012.144878. Accessed: September 12, 2024.
3. California Department of Health Care Services (DHCS). Treatment Policy for the Management of Chronic Hepatitis C. Published December 9, 2021. Available at: https://www.dhcs.ca.gov/Documents/Revised-Treatment-Policy-for-the-Management-of-Chronic-Hepatitis-C-12921.pdf. Accessed: September 12, 2024.
4. Wester C, Osinubi A, Kaufman HW, et al. Hepatitis C virus clearance cascade — United States, 2013–2022. *MMWR*. 2023;72:716–720. Available at: https://dx.doi.org/10.15585/mmwr.mm7226a3. Accessed: September 12, 2024.
5. Kondili LA, Buti M, Riveiro-Barciela M, et al. Impact of the COVID-19 pandemic on hepatitis B and C elimination: An EASL survey. *JHEP Rep*. 2022;4(9):100531. Available at: https://doi.org/10.1016/j.jhepr.2022.100531. Accessed: September 12, 2024.
6. Hoenigl M, Abramovitz D, Flores Ortega RE, et al. Sustained impact of the Coronavirus disease 2019 pandemic on hepatitis C virus treatment initiations in the United States. *Clin Infect Dis*. 2022 Aug 24;75(1):e955-e961. https://doi.org/10.1093/cid/ciac175. Accessed: September 12, 2024.
7. Levengood TW, Aronsohn AI, Chua KP, Conti RM. Dispensing of HIV and Hepatitis C Antivirals During COVID-19: An Interrupted Time-Series Analysis of U.S. National Data. *Am J Prev Med*. 2022;63(4):532-542. Available at: https://doi.org/10.1016/j.amepre.2022.04.024. Accessed: September 12, 2024.
8. Thompson WW, Symum H, Sandul A, et al. *Vital Signs:* Hepatitis C Treatment Among Insured Adults — United States, 2019–2020. *MMWR Morb Mortal Wkly Rep*. 2022;71:1011-1017. Available at: http://dx.doi.org/10.15585/mmwr.mm7132e1. Accessed: September 12, 2024.
9. Sirpal S, Chandok N. Barriers to hepatitis C diagnosis and treatment in the DAA era: Preliminary results of a community-based survey of primary care practitioners. *Can Liver J*. 2022;5(1):96-100. Available at: https://doi.org/10.3138/canlivj-2021-0032. Accessed: September 12, 2024.
10. Jiang X, Song HJ, Chang CY, et al. Disparities in Access to Hepatitis C Treatment Among Arizona Medicaid Beneficiaries With Chronic Hepatitis C. *Med Care*. 2023;61(2):81-86. Available at: https://doi.org/10.1097/MLR.0000000000001801. Accessed: September 12, 2024.
11. Teshale EH, Roberts H, Gupta N, Jiles R. Characteristics of Persons Treated for Hepatitis C Using National Pharmacy Claims Data, United States, 2014-2020. *Clin Infect Dis*.

2022;75(6):1078-1080. Available at: https://doi.org/10.1093/cid/ciac139. Accessed: September 12, 2024.
12. Centers for Disease Control and Prevention. Viral Hepatitis Surveillance Report – United States, 2022. https://www.cdc.gov/hepatitis/statistics/2022surveillance/index.htm. Published April 2024. Accessed: September 12, 2024.
13. Degenhardt L, Peacock A, Colledge S, et al. Global prevalence of injecting drug use and sociodemographic characteristics and prevalence of HIV, HBV, and HCV in people who inject drugs: a multistage systematic review. *Lancet Global Health*. 2017;5(12):e1192-e1207. Available at: https://doi.org/10.1016/S2214-109X(17)30375-3. Accessed: September 12, 2024.
14. California Department of Public Health (CDPH). Viral Hepatitis Guide for Primary Care Providers Screening, Vaccination, and Billing. August 2023. Available at: https://www.cdph.ca.gov/Programs/CID/DCDC/CDPH Document Library/HepatitisBandCScreeningToolkitforPrimaryCare.pdf. Accessed: September 12, 2024.
15. AASLD-IDSA. Recommendations for testing, managing, and treating hepatitis C. Available at: http://www.hcvguidelines.org. Accessed: September 12, 2024.
16. Solomon SS, Wagner-Cardoso S, Smeaton L, Smeaton L. A minimal monitoring approach for the treatment of hepatitis C virus infection (ACTG A5360 [MINMON]): a phase 4, open-label, single-arm trial. *Lancet Gastroenterol Hepatol*. 2022;7(4):307-317. Available at: https://doi.org/10.1016/S2468-1253(21)00397-6. Accessed: September 12, 2004.