JAMA Clinical Guidelines Synopsis

Screening for Hepatitis C Virus

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GUIDELINE TITLE HCV Guidance: Recommendations for Testing, Managing, and Treating Hepatitis C

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DEVELOPER AND FUNDING SOURCE American Association for the Study of Liver Diseases (AASLD) and Infectious Diseases Society of America (IDSA)

TARGET POPULATION All individuals residing in the US

MAJOR RECOMMENDATIONS AND RATINGS

- One-time hepatitis C virus (HCV) screening is recommended for all individuals aged 18 years or older (strength of recommendation: I [evidence and/or general agreement regarding benefit, usefulness, and effectiveness]; level of evidence: B [data from a single randomized trial, nonrandomized studies, or equivalent]).
- Annual HCV testing is recommended for all individuals who inject drugs and for men who are infected with HIV, have sex with men without condom use, or have sex with men and are taking preexposure prophylaxis (PrEP) for HIV (strength: IIa [weight of evidence and/or opinion favors usefulness and efficacy]; evidence: C [consensus opinion of experts or case studies]).
- Interval repeat HCV testing is recommended for all individuals with activities, exposures, and conditions or circumstances associated with increased risk of HCV infection (strength: IIa; evidence: C).
- One-time HCV screening is recommended for all individuals younger than 18 years with increased risk of HCV exposure (strength: I; evidence: B).
- Prenatal HCV testing is recommended with each pregnancy (strength: I; evidence: B).

Summary of the Clinical Problem

Based on data from 2013 to 2016, an estimated 4.1 million adults in the US had past or current HCV infection.[1] During the 21st century, the incidence of acute HCV infection has substantially increased among individuals aged 20 to 49 years.[2-4] Hepatitis C virus infection is commonly asymptomatic and associated with no clinical signs of active disease in its early stages. Oral non–interferon-based therapeutics result in undetectable HCV levels (ie, virologic cure) for most patients treated with these well-tolerated, short-term regimens. Untreated HCV infection progresses to a chronic state in more than 50% of individuals with viremia,[2] and chronic HCV infection is a leading etiology for both chronic liver disease and liver transplantation in the US. Screening and treatment for HCV infection in the US population are key to mitigating morbidity and mortality.[5]

Characteristics of the Guideline Source

This guideline was developed by the AASLD and the IDSA (**Table**)[6] without support by commercial entities. Grants from the Centers for Disease Control and Prevention (CDC) were used in the acquisition and review of HCV evidence. Hepatology and infectious diseases specialists and HCV community representatives comprised a guidance panel of HCV experts. All panel members were vetted and appointed by their respective societies and volunteered their time. Specific commercial relationships were proscribed among panel members while other disclosures required reporting but did not determine exclusion from the panel. The panel offers regular updates to the guideline based on emerging data, with major revisions approximately once yearly. Hepatitis C virus screening recommendations published in 2019 have not been modified with subsequent guideline updates in 2020 and 2021.

Evidence Base

The guideline recommends 1-time, opt-out HCV testing for all individuals aged 18 years or older regardless of risk factors (strength: I; evidence: B). This recommendation further broadens screening criteria for persons at high risk of HCV exposure, as first endorsed by the CDC in 1998 and the US Preventive Services Task Force (USPSTF) in 2004.[3,4] National disease surveillance data, efficacious HCV therapeutics, and cost-effectiveness analyses support this testing strategy vs risk factor–based screening approaches now recognized to be poorly effective.[2,7,8]

Based on epidemiologic data, annual HCV testing is suggested for all persons who currently inject or have previously injected drugs (unchanged since the last AASLD/IDSA update; strength: IIa; evidence: C).[1,2] Annual HCV testing is also recommended for men who have sex with men and who are infected with HIV or are taking PrEP for HIV (strength: IIa; evidence: C). This recommendation stems from the common modes of transmission for these infections and existing literature that identifies heightened incident HCV infections among men who have sex with men and who engage in sexual practices that may cause trauma to rectal mucosa or pass on sexually transmitted infections.[6]

Table. Guideline Rating

Standard	Rating
Establishing transparency	Good
Management of conflict of interest in the guideline development group	Good
Guideline development group composition	Good
Clinical practice guideline–systematic review intersection	Fair
Establishing evidence foundations and rating strength for each of the guideline recommendations	Fair
Articulation of recommendations	Good
External review	Good
Updating	Good
Implementation issues	Good

The AASLD and the IDSA also continue to recommend periodic repeat HCV testing using a risk-based strategy for individuals with activities, exposures, and conditions or circumstances associated with increased risk of HCV infection (strength: IIa; evidence: C). Principal goals are early identification and treatment to reduce viral transmission. Risks include injection or intranasal drug use, sexual or drug-use practices among men who have sex with men, long-term hemodialysis, birth by a parent with HCV infection, percutaneous or parenteral exposures in health care and unregulated settings, past or present incarceration, HIV infection, evaluation for PrEP, chronic liver disease or hepatitis, unexplained liver enzyme derangements, and donation or receipt of any solid organ transplant. Limited evidence exists to support the optimal periodicity for HCV testing after initial screening, and the guideline recommends that repeat testing be based on risk of ongoing exposure or, if previously infected with HCV, reexposure.[6]

The AASLD and the IDSA continue to recommend 1-time screening for all individuals younger than 18 years with increased risk of HCV exposure (strength: I; evidence: B) due to the known prevalence of HCV infection in this population and prevailing data in support of a risk-based testing strategy.[2,6] Risks are defined as activities, exposures, and conditions or circumstances associated with an increased risk of HCV infection, as outlined above. As first recommended in 2018, prenatal HCV testing is also recommended with each pregnancy (strength: I; evidence: B) to account for the rise in incident HCV infection among persons of childbearing age and to augment linkage to care for pregnant persons and perinatally exposed children.[6]

Benefits and Harms

Application of this guideline will increase diagnosis of acute and chronic HCV infection in the US. Given the current state of HCV therapeutics and assuming patients receive treatment after HCV diagnosis, universal screening could markedly reduce late-term complications of chronic infection and reduce its spread. Possible harms of expansive screening include testing costs, patient effects of HCV diagnosis (eg, anxiety, stigma), and disease identification among patients who do not have access to treatment or who would not benefit from treatment.[8]

Discussion

The 2019 AASLD/IDSA guidance update reflects the present epidemiology of HCV infection in the US and will bolster local, regional, and national goals for disease elimination.[5,9] The USPSTF and the CDC have also endorsed universal HCV screening for adults and testing for pregnant persons and those with specific risk factors. The AASLD/IDSA guidance and that of the USPSTF and the CDC diverge in important respects.[3,4] Screening is not suggested by the USPSTF after age 79 years, the CDC does not recommend screening if disease prevalence is less than 0.1% within a specific region or population, and neither entity encourages periodic repeat testing in relation to sexual behaviors. With accessible clinical resources, such as the Project ECHO program and the AASLD/IDSA guideline, comprehensive prevention, diagnosis, and treatment of HCV can be realized in primary care settings irrespective of preexisting clinician training and expertise.[6,10]

Areas in Need of Future Study or Ongoing Research

There is a paucity of outcome data to support universal HCV screening for the adult US population. This guidance update is contingent on assumptions of accurate screening tests gathered by an opt-out approach as well as unrestricted access to effective therapy for HCV infection. Because trials are unlikely to be conducted to demonstrate the absolute benefit of HCV screening, observational and implementation studies that estimate real-world effectiveness, cost burdens and savings, and patient-centered outcomes will further corroborate a universal testing strategy. Person-first and gender-expansive language needs to be adopted in AASLD/IDSA and other society-sponsored HCV recommendations to champion dignity in relation to a stigmatizing disease and inclusivity across the gender spectrum. Disparities in HCV transmission across racial, political, and cultural identities (eg, markedly high disease incidence among American Indian and Alaska Native persons) merit further attention to identify subpopulation-specific risk exposures and implement germane harm reduction practices.[2]

Related guidelines and other resources

US Preventive Services Task Force

Centers for Disease Control and Prevention

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