A Pragmatic Guide for Primary Care Practitioners: The Diagnosis and Treatment of Patients with Hepatitis C Virus

Award ID - GM006263
Improving Diagnostic Accuracy for Hepatitis C with a Validated Teach/Improve Model: An Initiative to Enhance Clinical Judgement and Patient Health, and Reduce Patient and System-Level Risks

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Introduction

The Coverys Community Healthcare Foundation, Inc. generously funded a 2019 quality improvement proposal *"Improving Diagnostic Accuracy for Hepatitis C with a Validated Teach/Improve Model: An Initiative to Enhance Clinical Judgment and Patient Heath and Reduce Patient and System-Level Risks"* submitted by researchers and educators at the MedStar Institute for Quality and Safety, the MedStar Health Research Institute, and Med-IQ. The full project was adjusted due to COVID-19 challenges.

The goal: Improve the early diagnosis of hepatitis C virus (HCV) and the frequency with which patients diagnosed with HCV are treated in the primary care setting.

The evolving reality: In 2020 the U.S. Preventive Services Task Force, after years of consideration, broadened the guidelines for HCV testing which stimulated organizational, professional society and provider level support for routine, universal HCV testing in the primary care setting.[1]

In conjunction, the US Department of Health and Human Services and the World Health Organization shared a goal of eliminating viral hepatitis by 2030.[2,3]. To achieve this goal, we need more clinicians to identify and treat HCV. Primary care providers are well positioned to diagnose and cure HCV, for the vast majority of their patients, when presented with pragmatic information and insights on screening and testing, conducting the diagnostic workup, medication management, and post cure follow-up of HCV.

The funded program used a collaborative educational framework which allows for the movement of knowledge (not patients) and the development of highly effective care communities which minimize the risk to both patients and health systems. Project ECHO (Extension for Community Healthcare Outcomes) started in 2003 at the University of New Mexico School of Medicine[4] as a lifelong learning model that can provide best-practice specialty care and reduce health disparities using a team-based approach that allows patients to be evaluated and treated by the clinicians they know and trust and in the communities where they live and work. The ECHO model includes hub-and-spoke knowledge-sharing networks, led by expert teams (hubs) that use multi-point videoconferencing to conduct virtual clinics with community providers (spokes). Through Project ECHO, primary care clinicians become better equipped to provide excellent care to patients in their communities; patients receive more timely and accurate diagnoses, avoiding unnecessary visits with numerous specialists.

As our funded activities concluded, primary care providers who participated in the HCV ECHO sessions felt the knowledge gleaned during the initiative is important to share broadly, particularly because the risks of unidentified HCV are expanding in relationship with the current national opioid epidemic. The CDC reports a 21.8% increase in reported cases of acute HCV in just one year (2015 to 2016) with the highest increases in states (including Maryland, DC, and Virginia) with the opioid-related burdens.[5] According to data from the National Institute on Drug

Abuse, Maryland has the fourth highest opioid-related overdose death rate in 2018, and Washington, DC ranked seventh.[6]

The Need to Improve Diagnosis and Treatment in Healthcare

The 2015 National Academy of Medicine (NAM) Report *Improving Diagnosis in Health Care* suggested that each one of us is likely to experience a diagnostic error in our lifetime.[7] So great is the problem, the Emergency Care Research Institute (ECRI) named diagnostic errors as the number one patient safety concern for 2018.[8] A review of 23,527 cases in a malpractice database identified a diagnosis-related error in 20% of cases, more than half (57%) of which involved ambulatory care settings with an average payment of $422,000.[9]

The NAM report positioned patients at the center of the diagnostic team, depicted the diagnostic process as encompassing the continuum of care delivery, and acknowledged the many internal and external factors that influence the diagnostic process. The recommendations in the NAM report are far-reaching and many will likely require years of policy and curriculum reform, development and testing, and public awareness programs. At least one opportunity exists to reliably diagnose, treat, and mitigate a potentially life-threatening disease in the outpatient setting with relatively minor expense and patient inconvenience—hepatitis C viral infection. Tragically, it often goes unheeded.

Chronic HCV has been dubbed the 'silent killer' due to its largely asymptomatic nature until progression results in noticeable, often irreversible impact on the patient's health. For patients and health systems alike, HCV represents an under-appreciated and growing risk. Individuals with HCV have been shown to have a mean age of death that is 15 years younger than that of persons without HCV. [10] The risk for hepatocellular carcinoma, need for liver transplant, and premature death due to HCV are now preventable scenarios with the advent of direct-acting antiviral therapies which offer the opportunity to cure nearly all patients.[11] However, in order to cure patients, reduce transmission, and prevent the downstream morbidity and mortality associated with HCV, clinicians must appropriately screen, diagnose, and treat infected persons.

Why Hepatitis C?

An estimated 3.5 million people in the US are living with chronic HCV. For many years, chronic HCV has been known to be disproportionately prevalent among individuals born between 1945 and 1965—approximately 75% of those living with HCV are members of this cohort (also known as the "baby boomer" generation).[12] Among these individuals, the presence of HCV is independently associated with increased mortality and resource utilization.[13] Studies have repeatedly shown that substantial percentages (43%-85%) of this population are unaware of their HCV infection status[14-17] and 35% have advanced fibrosis at the time of diagnosis.[18] However, experts now recognize a bimodal distribution of newly identified infected patients.

New infections are nearly entirely related to the opioid crises; between 2004 and 2014 there was a 133% increase in acute HCV and a 93% increase in admissions for substance use disorder related to the use of injection opioids.[19] Unfortunately, despite the availability of therapies which can cure HCV and conceivably lead to the elimination of the virus, the incidence of HCV infection is increasing in the US.

Far too commonly, HCV infections are not identified until after notable disease progression. In fact, appropriate diagnosis of HCV is an unrecognized risk in health systems across the US. A review of more than 2 million patient records from 4 health systems found that only approximately one fifth (16,662 of an estimated 80,000 cases) of HCV-infected persons who died of their disease had a documented diagnosis of HCV.[10] Mortality related to HCV has steadily increased in the US; by 2007, deaths due to HCV outnumbered those due to human immunodeficiency virus (HIV), and in 2011 HCV mortality rates surpassed the combination of 60 other reportable infectious diseases.[20,21] Beyond an increased mortality, unrecognized HCV carries substantial other risks for healthcare systems and the health of the patients they serve. Failure to identify HCV infection early in the course of the disease allows for the potential development of numerous downstream sequelae related to advanced liver disease including liver failure requiring transplant and the development of hepatocellular carcinoma (HCC). Studies have demonstrated a 3.7-fold higher rate of all-cause hospitalizations among patients with HCV compared to those without[22], and patients with HCV account for more than one-third of those on liver transplant waitlists and those receiving transplants (32.2% and 35.1% respectively).[23]

Gap Analysis

The Centers for Disease Control and Prevention (CDC)[8], the US Preventive Services Task Force (USPSTF)[24], the World Health Organization (WHO)[25], and the Infectious Diseases Society of America and the American Association for the Study of Liver Diseases (IDSA/AASLD)[11] released guidelines in 2012 - 2013 supporting one-time testing among those within the baby boomer cohort regardless of the absence of traditional risk factors. Historically, data from the National Health and Nutrition Examination Survey (NHANES) has suggested that approximately one-half (54%) of persons infected with HCV are aware of their serostatus.[14] Published studies demonstrate significant disparities between clinical practice patterns and guideline-recommendations. Clinicians from NorthShore University Health System report that 11.2% of more than 100,000 baby boomer patients who presented for at least one outpatient visit have received recommended HCV-antibody testing.[26] Similarly, clinicians from the University of Kansas reported a historical birth cohort-based testing rate of 30% which improved to 55% with provider education over a 9-month period.[27] In 2020, the CDC, USPSTF and AASLD/IDSA all extended their guidelines to support one-time screening of all adults aged 18 to 79 regardless of identified risk factors; more frequent testing is recommended for individuals determined to be at higher risk.[1,11,28]

These data are particularly concerning in light of the fact that available direct-acting antiviral (DAA) therapies provide a cure for almost all patients within 8-12 weeks of oral therapy with minimal side effects. Moreover, HCV treatment is effectively delivered in the primary care setting, eliminating the need for specialist care unless the disease is unrecognized until the point of severe liver disease/failure.[29] Improving identification and facilitating treatment is an important public health concern and is critical for improving healthcare resource utilization and patient safety through earlier treatment and the reduction of unnecessary interventions.

Diagnosis of Hepatitis C

Screening and Testing

Pragmatic Information

One of the most important first steps in curing and eliminating hepatitis C (HCV) virus in all persons is to screen appropriately. It's become simpler in 2020 as all persons between 18 and 79 years are now supposed to be tested for HCV antibody, and RNA ordered if antibody reactive/positive. Additionally, all pregnant women should be tested at each pregnancy. Those with continued risk factors will need to be retested if negative at first or cured. This is recommended by major agencies, CDC, USPSTF, AASLD and IDSA. The most efficient test that one can order is the HCV antibody (Ab) test which should reflex to HCV RNA (if Ab positive). This initial reflex test will be a qualitative HCV NAA or RNA. Most electronic health records (e.g EPIC, Cerner) allow for alerts or prompts to be added for these patients and these should be implemented at your clinical site or system, when possible.

Summary of Recommendations for HCV Testing and Linkage to Care

Recommended Testing
Adults aged 18 to 79 years: Grade B

1. USPSTF update from March 2, 2020
2. High risk outside of age
3. Replaces recommendations based on birth year 1945-1965 and with risk factors

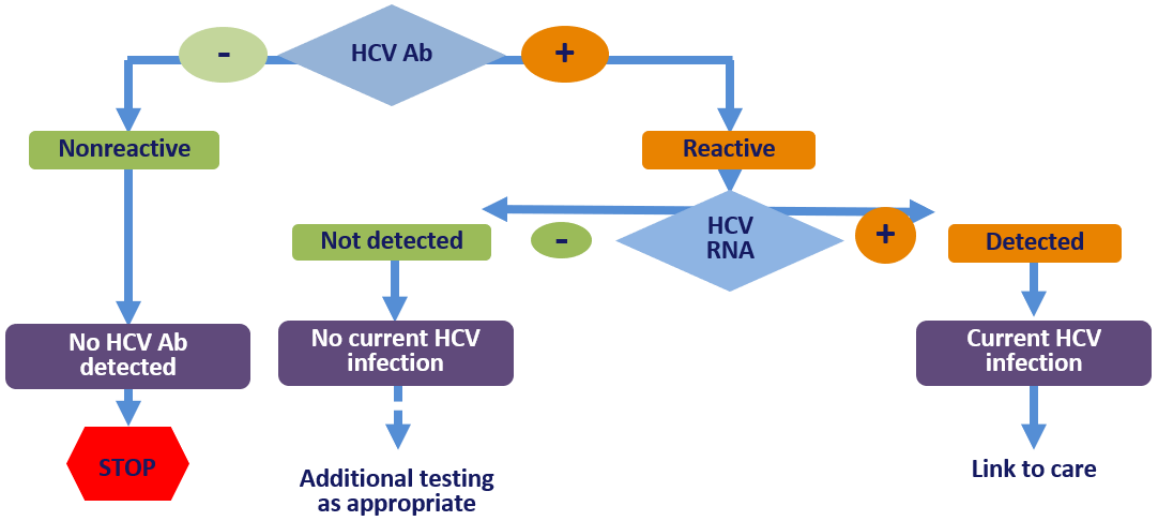
HCV Assays

Table 1: Interpretation of Results of HCV testing [30-31]

Anti-HCV	HCV RNA	Interpretation
+	+	**Acute or chronic HCV depending on the clinical context**
+	–	**False-positive HCV antibody** **Resolved infection** **Acute HCV infection during viremia**
–	+	**Early acute HCV infection** **Chronic HCV in setting of immunosuppressed state** **False-positive HCV RNA test**
–	–	**Absence of HCV infection**

HCV Diagnostic Process

Figure 1: Recommended Testing Sequence [32]



Positive Test Results for HCV

Pragmatic information: Once you know whether the patient is HCV Ab positive and/or NAA/RNA is detected then you can take the appropriate next steps (see Figure 1 above outlining the diagnostic process). If a patient is HCV Ab positive/reactive but the RNA is not detected then the patient has either (Table 1): (a) been infected but has spontaneously cleared the virus, (b) been infected but treated and cured or (c) a false positive antibody test. There is no current way to distinguish between (a) and (c) – patients need to be counseled on this and that they can be re-infected if they have continued risk factors for HCV acquisition.

If the patient's HCV RNA is detectable then they need to be counseled on the results and engaged in HCV specific care to discuss staging of disease and treatment. This may include a referral to Infectious Disease, Gastroenterology or Hepatology; however, Primary Care clinicians are capable of treating HCV themselves and patients may not need to be referred.[29] Additionally, it would be important to provide counseling on harm reduction and transmission, alcohol reduction and an overview of treatment. We can now safely say that treatment is short term (only 8-12 weeks in most instances), it's very well-tolerated and leads to cure in over 95% of cases.

Next Steps after a Positive HCV Test

1. Counsel patients on test results
2. Order HCV RNA, qualitative or quantitative (if not done as a reflex test)
3. Conduct additional screenings for other hepatitis viruses (hepatitis A and B), HIV, illicit drug use, alcohol use
4. Educate patients about disease transmission and harm reduction
5. If HCV RNA is *un*detectable, counsel on risk of reinfection

6. Initiate care and treatment as a primary care clinician, or refer patients to a specialist for treatment

Workup

Pragmatic Information

Once you know that a patient has HCV infection (with a detectable HCV RNA), then there are several initial tests to be ordered for liver disease staging and clinical decision making.[11] For their HCV, you will need to order:

- CBC, CMP, PT/INR
- HCV genotype, HCV quantitative RNA
- FibroSure or Fibrotest lab test (or other modality for staging like a FibroScan (transient elastography)
- calculation of an APRI and FIB-4, and
- screening for HCC, most likely with a liver ultrasound as the initial screen.

Patients are staged from Fibrosis F0 – F4; F3 and F4 signify advanced fibrosis or cirrhosis. If a patient has liver cirrhosis (F4), please calculate their Child-Turcotte-Pugh (CTP) score (https://www.hepatitisc.uw.edu/page/clinical-calculators/ctp) to determine if they are Child A, B or C. Patients with Child B and C are considered to have decompensated cirrhosis (see below). It is also important to test for HIV, hepatitis A and hepatitis B viral infections as each will need attention in the care of these patients (see below).

Additional Assessment after Diagnosis of HCV

1. HCV: genotype, viral load, stage for liver fibrosis, screen for hepatocellular carcinoma (above)
2. Hepatitis A (HAV): order the hepatitis A “total” or IgG; only order IgM if concerned for acute infection
3. Hepatitis B (HBV): order hep B surface antigen (HBsAg), core antibody IgG (HBcAb) and surface antibody (HBsAb); if concerned about acute hepatitis B then order the core IgM
4. HIV: HIV Ag/Ab 4th generation
5. Review medications- avoid potential hepatotoxins
6. Assess alcohol consumption
7. Assess for fatty liver – facilitate weight loss if markers for fatty liver in context of metabolic syndrome (overweight/obesity, DM, HTN, hyperlipidemia)
8. Counsel patients regarding HCV transmission and risks of reinfection
9. Hepatitis A and B vaccinations if not immune; pneumonia vaccination

Treatment

Pragmatic Information

Treatment is incredibly satisfying for both providers and patients, as patients most often want to be treated, and the treatment is short, well-tolerated and highly efficacious. How many chronic diseases are so easily cured with current therapeutics? We've gone from discovery of the virus in 1989 to an easy cure in 2013, only 24 years – this is revolutionary. Studies have shown that treating and curing these HCV patients may improve their patient experience and engagement in care for other chronic illnesses.

Most patients with HCV infection should be treated. Per the AASLD/IDSA guidelines: "Treatment is recommended for all patients with acute or chronic HCV infection, except those with a short life expectancy that cannot be remediated by HCV therapy, liver transplantation, or another directed therapy. Patients with a short life expectancy owing to liver disease should be managed in consultation with an expert."[33]

Selecting a Treatment

There are several treatments approved for HCV and please always refer to the updated guidelines at: https://www.hcvguidelines.org/.[11] Currently, the two most commonly used medications in the US are sofosbuvir/velpatasvir (Epclusa) and glecaprevir/pibrentasvir (Mavyret). The others that are currently used in the US include: sofosbuvir/ledipasvir (Harvoni), sofosbuvir/velpatasvir/voxilaprevir (Vosevi) and elbasvir/grazoprevir (Zepatier). When prescribing medication, it is important to know the following, as they all need to be considered in your shared decision making:

1. patient's prior HCV treatment experience and with which medications,
2. disease staging – fibrosis score (F0-F4), cirrhosis, decompensated cirrhosis,
3. concomitant medications due to potential drug-drug interactions,
4. other medical co-morbidities, including hepatocellular carcinoma (HCC),
5. renal dysfunction,
6. hepatitis B status,
7. HIV status,
8. patient preference for duration and pill burden,
9. possibly NS3/4A or NS5A resistance mutation testing, depending on drug choice and genotype, and
10. insurance preferred medication. Insurance preference should be considered early in the process as it often is the driver behind what is ultimately prescribed.

The AASLD/IDSA provides simplification guidelines for those with and without compensated cirrhosis (https://www.hcvguidelines.org/).[11] Always look at the most recent FDA package insert for each medication as the indications and Black Box Warnings are subject to change. Sustained viral response (SVR), a functional cure for HCV, is determined 12 weeks after

completion on the prescribed therapy. In long-term follow-up, SVR is considered a cure and the CDC and WHO have set elimination goals for 2030 due to individual cure rates.[34,35]

Post-Cure

Pragmatic Information

Now that you've cured your patient, how often do they need to be seen for their HCV? Once again the AASLD/IDSA guidelines are quite useful.[11] If a patient has early liver disease, stages 0-2, then they are usually discharged from care either 12- or 24-weeks post treatment and evidence of SVR. However, if they have advanced fibrosis or cirrhosis, then they need to remain in care and continue to be screened for liver disease progression or decompensation, and HCC, on a semi-annual basis.

Always keep in mind the following

1. A patient may become reinfected after they are cured, if they have ongoing risk factors,
2. Treatment does not lead to immunity,
3. HCV antibody levels will always remain detectable; however, antibodies do not cause ongoing liver damage nor lead to viral transmission – it is only the HCV virus that does this,
4. Once a patient has an SVR/cure, their HCV virus is gone and does not live in reservoirs
5. The American Red Cross has not yet amended their restriction on donating blood if one is HCV Ab positive, despite having been cured and HCV RNA is not detectable.
6. Patients and their primary care providers need to have continuing discussions if they are at risk.

More Complex Patients

Human Immunodeficiency Virus (HIV)

Patients with HIV need to be treated for their HCV; however, their HIV may need to be the first priority. They may often have opportunistic infections that also require more immediate attention. However, a low CD4 cell count or high HIV viral load does not preclude HCV treatment. It is very important to do a complete medicine reconciliation as there are often drug-drug interactions. If a patient is considered an HIV non-progressor or elite controller, they may be considered for HCV treatment prior to HIV treatment to avoid drug interactions. Decision making should be shared with the you, the patient, and their HIV provider.

Hepatitis B Virus (HBV)

There's a black box warning on HCV therapeutics that HBV infection can reactivate once patients are treated and cured of their HCV. It is important to check a patient's hepatitis B surface antigen (HBsAg) and hepatitis B core antibody (IgG; IgM for acute infection; HBcAb) to rule out chronic HCV infection; and hepatitis B surface antibody (HBsAb) to assess immunity. HBV DNA will need to be followed on- and after-treatment along with liver assessment tests if HBcAb or HBsAg are detected. Reactivation is more likely for patients with HBsAg positivity, and who are thus infected. It is still possible for those with hep B core Ab (likely signifying prior infection) to reactivate and also need to be followed. Patients with chronic hepatitis B infection (HBV; HBsAg) who meet criteria for treatment should be on stable therapy prior to going on HCV medications. Patients with chronic HBV infection (HBsAg) also need to be tested for hepatitis D, or Delta, with an antibody as this may result in more severe liver disease.

End-stage renal disease (ESRD)

Care for patients with ESRD used to be more complicated as only elbasvir/grazoprevir (Zepatier) and glecaprevir/pibrentasvir (Mavyret) were approved for use in patients with a GFR < 30 mL/min/1.73m^7, ESRD and ESRD on dialysis. The reasoning was that a toxic metabolite of sofosbuvir would build up and was not cleared by the kidney. However, with further studies, the FDA approvals for sofosbuvir/ledipasvir (Harvoni), sofosbuvir/velpatsavir (Epclusa) and sofosbuvir/velpatasvir/voxilaprevir (Vosevi) were amended (11/2019) such that no dosage adjustment is recommended in patients with any renal impairment or on dialysis. Patients may need to be monitored more closely for safety. If a patient is being considered for a renal transplant, please consult with the transplant nephrologist regarding the timing of HCV treatment as the patient may be considered earlier for transplant if they accept an HCV infected donor kidney.

Decompensated Cirrhosis

Patients with decompensated cirrhosis should be seen by a hepatologist for treatment, screening for esophageal varices, HCC screening and for liver transplant consideration. They may even be considered for liver transplant prior to HCV treatment; and may be considered earlier on the waitlist for a transplant if they are HCV infected and will accept an HCV positive liver, similar to renal transplant. Please keep in mind that neither glecapravir/pibrentasvir

(Mavyret) nor sofosbuvir/velpatasvir/voxilaprevir (Vosevi) can be prescribed for patients with severely decreased hepatic function or decompensated cirrhosis (Child Pugh B or C).

Medication Authorization Process

Pragmatic Information

1. Patient should be both seen in care and established as adherent with provider recommendations
2. Appropriate lab work should be ordered by the provider and completed by the patient

Steps in the process

Patient is notified of the HCV treatment/approval process before treatment begins:

1. Receives education and interventions for reducing progression of HCV and preventing transmission
2. Evaluation of fibrosis using a liver biopsy (rarely), Fibroscan, or Fibrosure/Fibrotest is recommended in order to determine the appropriate decision for HCV treatment strategy (most insurers will not accept an APRI or FIB-4 score alone for staging)
3. Vaccination against hepatitis A and hepatitis B is recommended for all persons with HCV infection who are not yet immune (this will not hold up approval)
4. Provider should flag/alert their treatment navigator to start prior authorization process (if your facility has navigators)
5. Some insurers may require patients and providers review and sign their medication commitment form (for example, DC Medicaid requires it)
6. Types of Assistance (see below)
    a. Patient Assistance Programs
    b. Grant funded co-pay assistance – usually for Medicare
    c. Manufacturer co-pay cards – does not cover patients with government insurance

Submitting a Prior Authorization

1. Send message to Pharmacy Navigator(s)* via EHR, email, or call (*if available in your setting) that you will treat this patient with [medication name] and duration.
2. Routes to submit a prior authorization
    a. Electronic via covermymeds.com
    b. Paper application and then fax in (Medicaid may require only a fax transmission)
    c. By phone with a representative
3. Some may need provider signature

Note: Requirements are always changing so it is important to check with the insurance provider.

Formularies

Table 2: Formularies by Insurer[a]

Insurance	Degree of Fibrosis by blood test	Fibroscan LSM cut-off	Drug Screen	Quantitative HCV RNA	Preferred drug for GT1	Preferred drug for non GT1
Aetna	Yes	Criteria not outlined	No	Within 6 months of PA submission	Mavyret	Mavyret
Blue-Cross (commercial)	Yes	Criteria not outlined	Yes, if pt has hx of ETOH and/or illicit drug abuse	Within 6 months	Varies, typically Harvoni	Varies, typically Epclusa
Cigna (commercial)	Yes	Criteria not outlined	Not typically required	Within 3 months	Varies, typically Harvoni	Varies, typically Epclusa
United (commercial)	Yes	Criteria not outlined	No, but must demonstrate treatment readiness	Within 3 months	Varies, typically Harvoni	Varies, typically Epclusa/Mavyret
Medicare D	Yes	Criteria not outlined	No	Usually within 6 months	Usually anything FDA approved and on-label	Usually anything FDA approved and on-label
Medicaid	Yes (though many have removed recently)	Criteria not outlined	No	Within 3 months	Mavyret	Mavyret

[a]These are subject to change and must be rechecked

Documentation to Submit:

1. Prior authorization form
2. Clinical note from the prescribing physician (treatment history and include readiness)
3. Form signed by patient and provider (if required by insurance)
4. Labs:
    a. HCV quantitative viral load (some plans may require viral loads separated by 6 months to prove chronicity) (sometimes within 90 days of PA)
    b. Genotype
    c. CBC/CMP/PT-INR (sometimes within 90 days of PA)
    d. HIV, HBV serology
    e. Negative drug/ETOH results (this is *not* required by many insurers)
    f. NS3/4 Resistance Test when applicable with GT 1a and using elbasvir/grazoprevir (Zepatier); or NS5A resistance test for GT 3 and using sofosbuvir/velpatasvir (Epclusa) (if cirrhotic or previously treated)
5. Liver fibrosis/cirrhosis
    a. Fibrosure/Fibrotest, Fibroscan or biopsy
6. Child Pugh Score (only calculated/required in patients with cirrhosis)
7. Submitting a complete submission packet will avoid delays and denials

Denied: Appeal

1. Received through fax or over the phone stating the reason of denial (denials currently occur much less often)
2. Patient also receives this denial – at times only the patient receives it
3. Read denial letter carefully to determine appeal process steps, including deadline, and the reason for the denial
4. Appeal letter submission information:
    a. Name
    b. D.O.B
    c. Insurance ID
    d. Prior auth. case number
    e. Original prior authorization paperwork
    f. Address reason for appeal and include clinical data and documentation
    g. Letter of medical necessity/ appeal letter (see Appendix for sample appeal letter)
    h. Denial letter

Support for Appeals

1. Appeal letter:
    a. Provide rationale for treatment selected
    b. Relevant guidelines, journal articles, clinical trial information, etc., included in letter or as attachment
    c. Restate request, should also add in a comment on patient's readiness for treatment if not previously in H & P note.
2. Utilize drug manufacturer websites for data, drug company info, and assistance with appeal letter drafting
3. Provider involvement: if you are a Primary Care provider one may need to justify experience, course involvement (ECHO, other HCV courses), and literature documenting HCV treatment efficacy with PCPs [29]
4. Identify drug interactions, if any
    a. https://hep-druginteractions.org/
5. Often other medical conditions will satisfy the appeal, including, heart disease, diabetes, HIV or HBV.
6. PubMed resources
    a. Reference and hyperlink PubMed articles

Appendices

Sample Appeal letter

Care provider LETTERHEAD

[Insert Date]
Case number: XXXXXX

Dear [Insurer] Medical Director:

Thank you for considering [drug] for [duration]. In this patient. I would like to appeal the denial.

She has hepatitis C infection and cirrhosis, with genotype 1a and 1b. She is treatment naïve. She has end stage renal disease and is on hemodialysis. Due to medical complexity including portal vein thrombosis and cardiac disease, I made the difficult decision with her last month to close her liver and kidney transplant evaluation. This was after nearly 2 years of testing. Transplant would have been preferred to allow her to live a normal life. Over the past 2 years, she has recovered significantly, and is now ambulatory, living independently and looking to get back to work.

Certainly, her cirrhosis by lab work is not Child-Turcotte-Pugh class A. However, on EGD [date], she did not have esophageal varices. She has no ascites on CT abdomen with contrast on [date] and US abdomen on [date]. She is gaining weight. Without these key decompensations, it is difficulty to clinically label her as decompensated cirrhosis. Sofosbuvir based regimens in the setting of end state renal disease have much less data on efficacy (reference: AASLD/IDSA Hepatitis C treatment Guidelines). However, [drug] can be used in cirrhosis (reference: Forns 2017 EXPEDITION-1 trial, and Rockstroh 2017, EXPEDITION-2 trial), and I would argue that this should be considered as she wants to do everything she can to do well and liver and kidney transplant is no longer an option for her.

Treating her hepatitis C would improve her liver function and lower her MELD score. It will have a major impact on reducing her hepatocellular carcinoma risk. She and her family are comfortable with any risks of using [drug] in her case.

I appreciate your time and consideration of this complex patient. I can speak in person to discuss her further as well.

Sincerely,

Care Provider signature and contact information

Example of Case Review from HCV Project ECHO Consultation

Case Study:

27-year-old female with Medicaid presents to clinic for a physical. Review of chart demonstrates that an HCV work up was done in 2019 and found patient to be HCV infected with genotype 1a. She has not been treated and there is no information about her liver health. Past medical history is positive for ADHD and morbid obesity. She reports injection and intranasal drug use within the last 12 months as well as use of benzodiazepines. Laboratory data is below. Her only current medication is Methadone 30 daily.

Laboratory Data:

Patient reports no history of depression or anxiety. There is no evidence of hepatitis A or B serology. The patient reports being erroneously told she is HCV negative by a previous provider. She learned of her infection when called by the department of health.

HCV RNA: 11,000	AST: 42H	Albumin: 3.7
Platelets: 239	T Bilirubin: 1.4H	BMI 35.8

Treatment considerations and suggestions from Project ECHO discussion:

1. The medical team should move forward with testing for HCV antibody because: (1) this may be acute HCV, as she has injected drugs within the last 12 months and she may spontaneously clear on her own; and, (2) it is important to always have documented HCV antibody test in the patient's chart.
2. Need to retest the HCV RNA as this could be acute HCV and patient may spontaneously clear.
3. The medical team should retest her liver assessment tests given the elevated total bilirubin and transaminases; and should include a direct bilirubin.
4. Please check for Hepatitis A and B – both acute and chronic serology given recent injection use (Hep A IgM and IgG total; Hep B s Ag, s Ab, core IgM and IgG total. If hep B surface Ag or core Ab is reactive, patient will need further testing and discussion.
5. Considering the patient is in an outpatient program designed to assist chemically dependent individuals, it may be helpful to coordinate HCV care and treatment with the center.
6. It appears the patient has a support system (the patient lives with her mother) but it may be helpful to reaffirm with the patient that compliance with treatment will not be a problem.
7. Methadone does not have a drug-drug interaction with any HCV treatment.
8. Mavyret will be the preferred drug from Maryland Managed Medicaid (Amerigroup).
9. Since this was a resident's case, it would be useful to provide them this summary and discuss the recommendations as a source of feedback.

Useful Websites

1. AASLD-IDSA HCV Guidelines: www.hcvguidelines.org
2. CDC Recommendations for Hepatitis C Screening Among Adults – United States, 2020 https://www.cdc.gov/mmwr/volumes/69/rr/rr6902a1.htm
3. US Preventive Services Taskforce: https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/hepatitis-c-screening
4. Simplified HCV Treatment for Treatment-Naïve Patients Without Cirrhosis: www.hcvguidelines.org/treatment-naive/simplified-treatment
5. Simplified HCV Treatment for Treatment-Naïve Patients With Cirrhosis: https://www.hcvguidelines.org/treatment-naive/simplified-treatment-compensated-cirrhosis
6. Hepatitis C Online: www.hepatitisc.uw.edu/go/evaluation-treatment/cost-access-medications/core-concept/all
7. FIB-4 Calculator: www.hepatitisc.uw.edu/page/clinical-calculators/fib-4
8. Project ECHO (Extension for Community Healthcare Outcomes): https://echo.unm.edu
9. National Viral Hepatitis Roundtable: www.nvhr.org
10. NVHR-CHLPI: Hepatitis C – State of Medicaid Access. https://stateofhepc.org/
11. HEP Drug Interactions: www.hep-druginteractions.org/checker
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