AAVBC

AMERICAN ACADEMY OF VALUE BASED CARE

Hepatitis C Medication

Quick Reference Guide

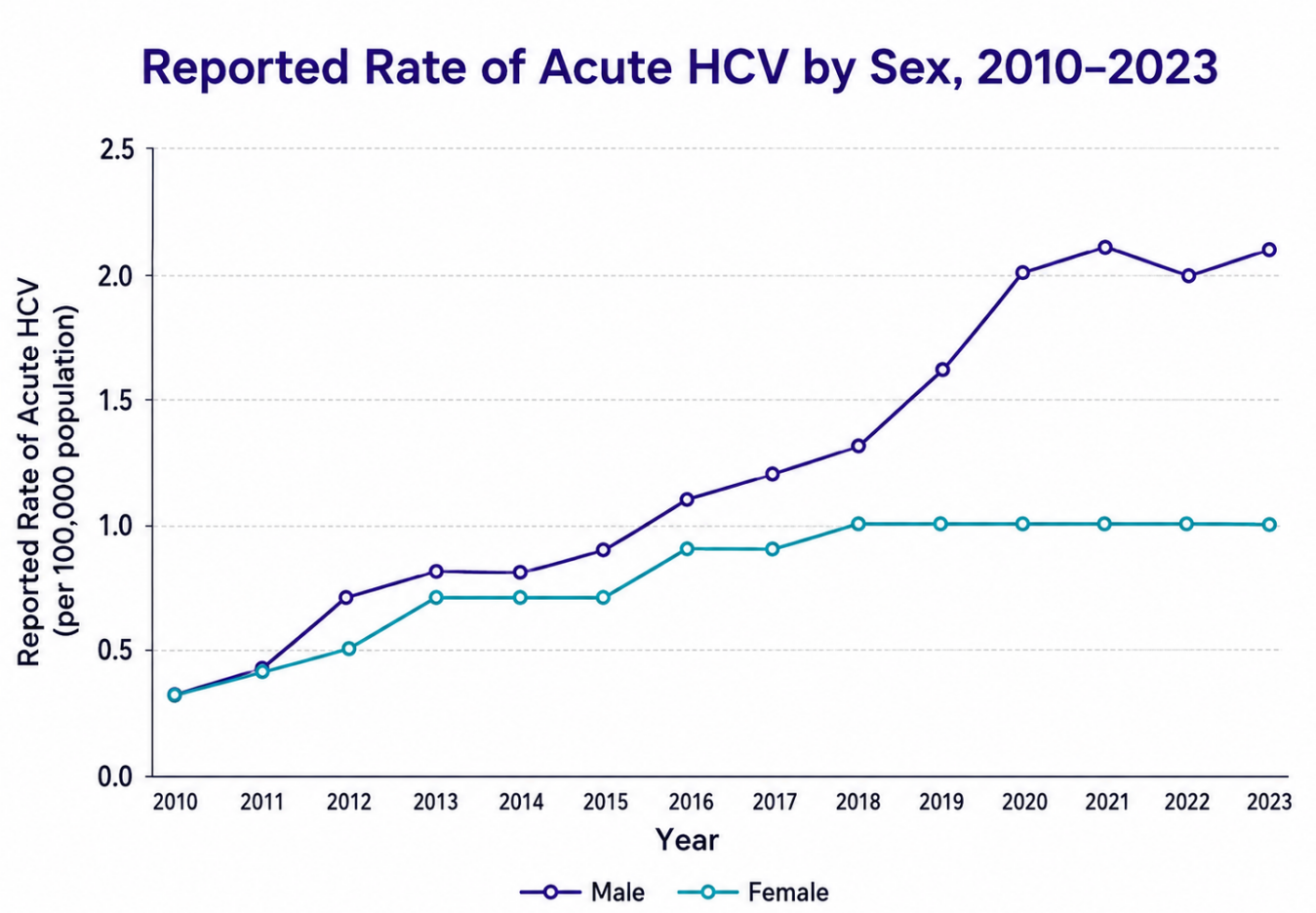
2026

Table of Contents

LANDSCAPE OF HEP C MEDICATIONS IN VBC

Direct-acting antiviral (DAA) therapies are curative, short-course oral medications used to treat chronic hepatitis C virus (HCV) infection. Their greatest and most well-established benefit is achieving **sustained virologic response** (**SVR**), defined as **undetectable HCV RNA** 12 weeks after treatment completion, which is considered a **virologic cure**.[1,2] SVR is associated with a **>70%** reduction in the risk of **hepatocellular carcinoma** (**HCC**), a **90%** reduction in the risk of liver-related mortality and liver transplantation, reduced all-cause mortality, and improvements in extrahepatic manifestations including cryoglobulinemic vasculitis, quality of life, and physical functioning.[3,4]

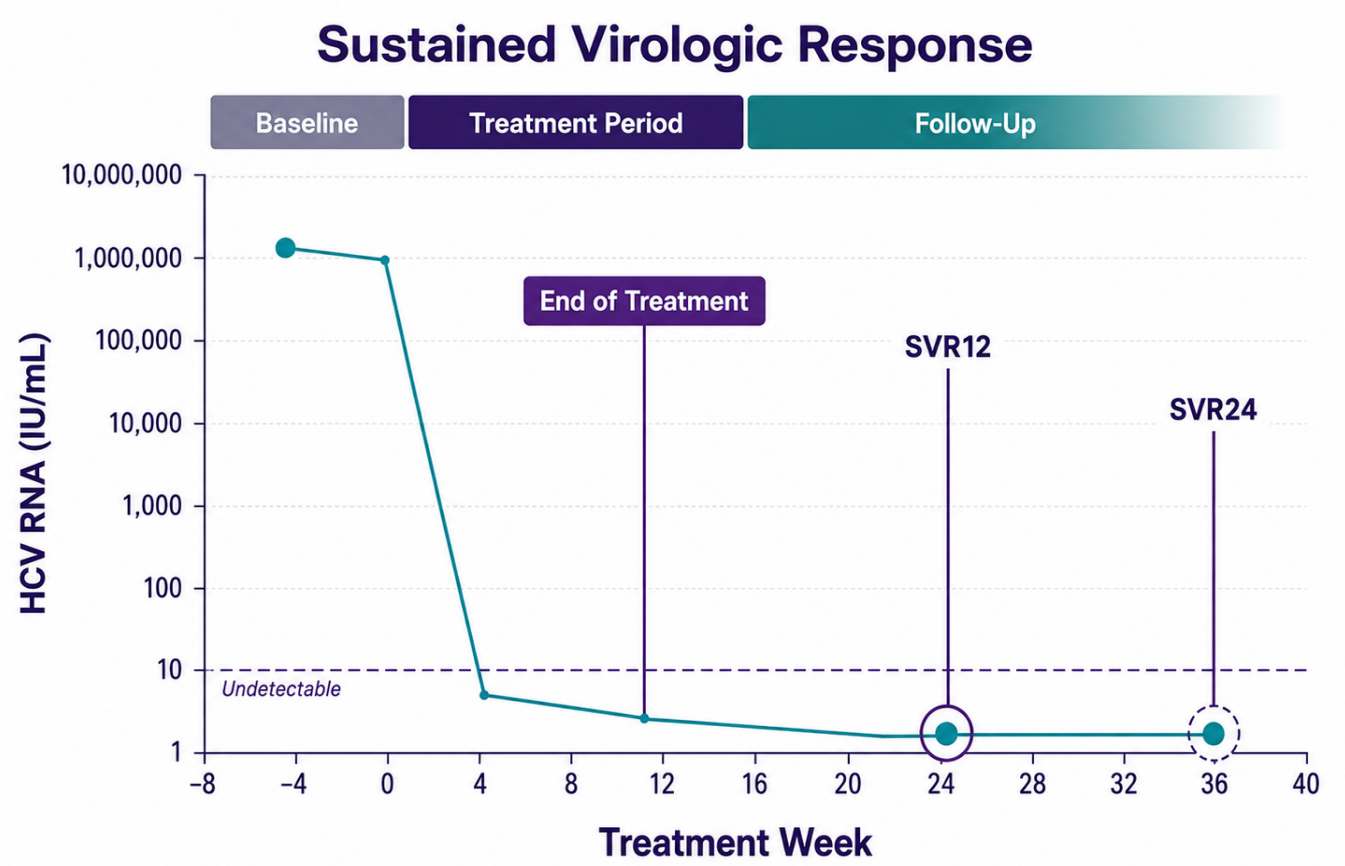
HCV infection is the **most commonly reported chronic bloodborne infection** in the United States and a leading cause of complications from chronic liver disease.[5–7] An estimated **2.4 to 4 million** adults in the United States have current HCV infection (**~1.0–1.6%** prevalence), with approximately **44,700** new infections occurring annually, driven in large part by the ongoing opioid and injection drug use epidemic.[1,5,7]



Source: CDC *Viral Hepatitis Surveillance Report—United States, 2023.*

HCV-associated morbidity is sizable: approximately **20–30%** of chronically infected individuals progress to cirrhosis, and HCV remains a leading indication for liver transplantation.

Annual direct healthcare costs associated with chronic HCV infection are substantial, with costs **escalating dramatically with disease progression**—from approximately **$4,483 per patient per month** for chronic hepatitis C to **$19,021** for hepatocellular carcinoma (HCC) and **$27,836** at the liver transplant stage.[8] Medicare Part D spending on HCV DAA therapies has also been substantial, reaching **$4.5 billion** in 2014 following the initial launch of sofosbuvir-based regimens, though **spending has moderated** as drug prices have declined and the treated population has shifted.[9,10] **Key agents covered under Part D include** glecaprevir/pibrentasvir (Mavyret), sofosbuvir/velpatasvir (Epclusa), ledipasvir/sofosbuvir (Harvoni and authorized generics), and sofosbuvir/velpatasvir/voxilaprevir (Vosevi).[4] These figures likely **underestimate the full economic impact of untreated HCV**, as the projected total lifetime medical cost burden for the current US cohort with chronic hepatitis C is estimated at **$200 billion** if all are treated with DAAs, compared with **$347 billion** if left untreated.[11]



The American Academy of Value-Based Care (AAVBC) supports the appropriate and timely use of DAA therapies to **achieve virologic cure**, **prevent progression** to advanced liver disease, and **reduce downstream healthcare utilization** including hospitalizations for decompensated cirrhosis, HCC, and liver transplantation. **Within a value-based care framework**, HCV treatment emphasizes universal screening, expedited screening for high-risk individuals, prompt linkage to care, simplified treatment algorithms, and removal of unnecessary treatment restrictions.

High-value care in this setting includes **prioritizing pangenotypic regimens that simplify treatment** (eliminating the need for **HCV genotype testing** in most patients), selecting lower-cost **generic drug regimens** when clinically appropriate, utilizing simplified treatment pathways that **enable non-specialist prescribers** to treat uncomplicated cases, and ensuring treatment access regardless of fibrosis stage or substance use history.[3,13] Several **pre-treatment**

assessments are essential **PCP-level value-based interventions**: calculating **FIB-4** (age-adjusted cutoff ≥2.0 for patients ≥65) to stratify **cirrhosis status** and determine PCP-managed versus specialist-referral tracks; checking **eGFR** to guide regimen selection (GLE/PIB preferred if <30 mL/min); testing **HBV serologies** (HBsAg, anti-HBc, anti-HBs) to prevent potentially fatal HBV reactivation (FDA Boxed Warning on all DAAs); and performing **DDI screening** (hep-druginteractions.org) to identify necessary medication holds before initiating therapy. These approaches support better patient outcomes while **reducing avoidable downstream complications** and **unnecessary healthcare utilization**.

AAVBC PERSPECTIVE

*A key component of high-value HCV care is ensuring **universal screening** and removing barriers to treatment initiation. The **USPSTF** and **CDC** recommend **one-time HCV screening for all adults aged 18 years and older**, with screening during each pregnancy and periodic testing for individuals with ongoing risk factors.[3,7] When HCV infection is identified, prompt treatment with a **pangenotypic DAA regimen**—either glecaprevir/pibrentasvir (8 weeks for most patients) or sofosbuvir/velpatasvir (12 weeks)—achieves cure rates **exceeding 95% across all genotypes**, with minimal adverse effects.[3,14] DAA treatment has been consistently demonstrated to be cost-effective across all genotypes and fibrosis stages, with incremental cost-effectiveness ratios well below **$100,000 per quality-adjusted life-year**.[15,16] **Prioritizing simplified treatment algorithms** that can be delivered by primary care and non-specialist providers, removing prior authorization barriers based on fibrosis stage or sobriety requirements, and selecting **lower-cost generic formulations** when available supports broader access to cure while **reducing preventable complications** and long-term healthcare costs.[3]*

↔ MAKING CONNECTIONS

For additional context on **chronic hepatitis**, please consult the **AAVBC Chronic Hepatitis QRG**

Prevalence and Clinical Context - DAA Therapies in Older Adults

CLINICAL SCENARIO	CLINICAL SIGNIFICANCE IN OLDER ADULTS[3,7,17–19]	KEY PCP CONSIDERATIONS*[3,18,20–22]
Chronic HCV, treatment-naive, no cirrhosis	Baby Boomers (1945–1965) have **~5× higher** HCV prevalence → **many undiagnosed**; universal screening recommended **≥18 years**	**Pangenotypic DAAs** (GLE/PIB 8 wk or SOF/VEL 12 wk) **prescribed by PCPs** without specialist referral → SVR ≥95–98% **regardless of age**

CLINICAL SCENARIO	CLINICAL SIGNIFICANCE IN OLDER ADULTS[3,7,17–19]	KEY PCP CONSIDERATIONS*[3,18,20–22]
Compensated cirrhosis (Child-Pugh A)	Older adults more likely to present with **cirrhosis** (53% vs 40%); **HCC risk 2.4x higher** in ages 65–85 (8.4 vs 2.6 per 1,000 PY).	GLE/PIB 8 wk (**EXPEDITION-8**: **98%** SVR12) or SOF/VEL 12 wk; **lifelong HCC surveillance** (US ± AFP q6 months) required post-SVR
Decompensated cirrhosis (Child-Pugh B/C)	**Higher morbidity/mortality**; protease inhibitor–containing regimens (e.g., GLE/PIB) **contraindicated**	**Specialist referral required**; SOF/VEL ± ribavirin 12 wk; consider **liver transplant evaluation**
CKD (eGFR <30) or dialysis	Common in older adults; **HCV accelerates CKD** and causes **MPGN**	**GLE/PIB preferred** (no dose adjustment; **EXPEDITION-4**: 100% SVR12); SOF-based regimens have expanded CKD labeling but **require monitoring**
Polypharmacy/ drug-drug interactions	**80%** of patients ≥75 years have **clinically significant DDIs**; **common culprits**: statins, PPIs, CCBs, anticoagulants	**Mandatory pre-treatment DDI check** (hep-druginteractions.org); **statins most common** contraindicated co-med (10.2%); **temporary hold** during DAA course is safe
Extrahepatic manifestations (diabetes, CVD, CKD, cryoglobulinemia, lymphoma)	Up to **74%** develop extrahepatic disease; HCV confers **23% increased CKD risk** and **60% increased lymphoma risk**	**SVR reduces**: CVD events, insulin resistance, diabetes, cryoglobulinemia, and lymphoma → may be primary treatment indication **even without significant liver disease**
Prior DAA treatment failure	**Uncommon** (<5%) but may occur in patients who received **earlier regimens**	SOF/VEL/VOX (Vosevi) 12 wk **for NS5A failures** = specialist consultation required
Older age/frailty/ limited life expectancy	Age alone is **not** a contraindication → treat all except those with **short life expectancy** not remediable by HCV therapy	**SVR 97.9%** in ≥65 years, comparable to younger adults; prefer **ribavirin-free regimens** (ribavirin increases serious AEs **1.9-fold** in elderly)

ABBREVIATIONS: PCP = primary care physician; HCV = hepatitis C virus; DAA = direct-acting antiviral; GLE/PIB = glecaprevir/pibrentasvir; wk = weeks; SVR = sustained virologic response; Child-Pugh = Child-Pugh classification; HCC = hepatocellular carcinoma; PY = person-years; US = ultrasound; AFP = alpha-fetoprotein; q6 months = every 6 months; SOF/VEL = sofosbuvir/velpatasvir; e.g. = for example; CKD = chronic kidney disease; eGFR = estimated glomerular filtration rate; MPGN = membranoproliferative glomerulonephritis; DDI = drug-drug interaction; PPI = proton pump inhibitor; CCB = calcium channel blocker; co-med = concomitant medication; CVD = cardiovascular disease; NS5A = nonstructural protein 5A; SOF/VEL/VOX = sofosbuvir/velpatasvir/voxilaprevir; AE = adverse event; FDA = US Food and Drug Administration

***Consult FDA labels for the most up-to-date dosage information, contraindications, and drug-drug interactions**

Burden of Male vs Female Acute HCV Infection Rates in the USA

Data source: Lewis *et al.* (2023) *Clin. Infect. Dis.* 77[23]

Cost Estimate Snapshot - HCV DAA Regimens

REGIMEN	ESTIMATED COST[4,24–26]	DURATION*	WHAT IT REPRESENTS*[4,24–26]
SOF/VEL (Epclusa) — brand	**~$75,000**	12 wk	WAC, **pangenotypic first-line** = 1 tab daily; **GT 1–6**, including **decompensated cirrhosis**
SOF/VEL (Epclusa) — authorized generic	**~$20,100 - $21,000**	12 wk	Authorized generic cash price (**~72% below brand WAC**); identical active ingredients and formulation; Medicare Part D formulary **coverage varies**
LDV/SOF (Harvoni) — brand	**~$94,500**	8–12 wk	WAC; GT1,4,5,6; **selected treatment-naive GT1 patients** may qualify for 8-week therapy
LDV/SOF (Harvoni) — authorized generic	**~$30,000-$37,000**	8–12 wk	Authorized generic WAC substantially below brand (**~60%-70% lower**); limited Medicare Part D formulary coverage
GLE/PIB (Mavyret) — brand	**~$26,400** (8 wk) to **~$39,600** (12 wk)	8–12 wk	Current WAC pricing (**$13,200** per 4-week supply as of 2025-2026); **pangenotypic first-line regimen** (GT1-6); 3 tablets daily with food; appropriate in CKD/ESRD; lowest-cost branded pangenotypic regimen
SOF/VEL/VOX (Vosevi)	**~$74,760**	12 wk	WAC, salvage regimen for **DAA/NS5A failures**; **GT 1–6**; **not first-line**
EBR/GZR (Zepatier)	**WITHDRAWN from US market**	N/A	Voluntarily withdrawn for **commercial reasons** (not safety-related); no longer available in the United States
Federal/VA acquisition	SOF/VEL: **~$24,000**; GLE/PIB: **~$20,000–$30,000**	As above	Federal pricing substantially lower; relevant for **dual-eligible Medicare/VA patients**

REGIMEN	ESTIMATED COST[4,24–26]	DURATION*	WHAT IT REPRESENTS*[4,24–26]

ABBREVIATIONS: SOF/VEL = sofosbuvir/velpatasvir; WAC = wholesale acquisition cost; GT = genotype; tab = tablet; wk = week(s); LDV/SOF = ledipasvir/sofosbuvir; GLE/PIB = glecaprevir/pibrentasvir; CKD = chronic kidney disease; ESRD = end-stage renal disease; SOF/VEL/VOX = sofosbuvir/velpatasvir/voxilaprevir; DAA = direct-acting antiviral; NS5A = nonstructural protein 5A; EBR/GZR = elbasvir/grazoprevir; VA = Veterans Affairs; FDA = US Food and Drug Administration

Estimated costs reflect approximate 2024–2026 US wholesale acquisition cost (WAC) or out-of-pocket ranges and do not account for insurance coverage, copay assistance, or negotiated rates.

***Consult FDA labels for the most up-to-date dosage and duration information, contraindications, and drug-drug interactions**

CLINICAL PEARL: COST-OPTIMIZATION MUST INTEGRATE COVERAGE CONSIDERATIONS

DAA prices have declined substantially since sofosbuvir launched at $84,000/course in 2013, driven by market competition and authorized generics.[26,27] **For Medicare Part D beneficiaries**, out-of-pocket costs for authorized generic SOF/VEL are approximately **$3,494** vs **$6,035** for brand; authorized generic LDV/VEL approximately **$4,103** vs **$7,077** for brand.[26] However, most Part D plans still **preferentially cover brand products** due to manufacturer rebate structures.[26]

The one-time curative DAA cost should be weighed against the **substantial lifetime medical cost burden of untreated HCV**. A 2026 CDC study using claims data and Markov modeling estimated that the overall per-person lifetime medical cost is **$90,089** for DAA-treated patients versus **$155,930** for untreated patients, a **$65,841** per-person savings with treatment.[28] Lifetime costs for untreated patients escalate dramatically by disease stage: $**150,669 for non-cirrhosis**, **$197,469 for cirrhosis**, **$208,646 for decompensated cirrhosis**, and **$113,975 for HCC**.[28] At the population level, treating the estimated 2.228 million US adults with chronic HCV would cost **$200 billion** versus **$347 billion** if untreated — representing **$147 billion** in projected savings nationally.[28] DAA treatment is cost-effective **across all genotypes** and **fibrosis stages**, with ICERs consistently below **$100,000/QALY**.[3] These data reinforce that **early screening and treatment** generate net healthcare savings while preventing progression to high-cost advanced liver disease.[8,28]

Direct Savings and Value Impact Matrix

VALUE LEVER	CLINICAL STRATEGY	FINANCIAL MECHANISM AND IMPACT[29–32]
Site of Care Optimization	Shift non-complex management from specialty clinics **to PCPs**	Lowers overall cost per treatment initiation by **up to 35%**
Simplified Diagnostics	Substitute manual imaging scans with **automated FIB-4 baseline scoring**	Eradicates **unnecessary imaging spend** and accelerates initiation

VALUE LEVER	CLINICAL STRATEGY	FINANCIAL MECHANISM AND IMPACT[29–32]
Waste Elimination	Utilize digital adherence tracking to **prevent uncompleted treatment cycles**	Avoids write-offs of mid-therapy medications (**$20K+ per occurrence**)
Downstream Risk Reduction	Attain high SVR12 rates across the attributed risk pool	Yields an **89% drop in liver mortality** and drastically cuts **future transplant risk**

ABBREVIATIONS: PCP = primary care provider; FIB-4 = Fibrosis-4 Index; SVR12 = sustained virologic response at 12 weeks

INDICATIONS AND CONTRAINDICATIONS

FDA Approved Indications for HCV Antivirals

This Quick Reference Guide applies primarily to **older adults** (>65) with **chronic HCV infection receiving curative DAA therapy** for one of the following primary indications:

A. Chronic HCV Infection — Treatment-Naive, No Cirrhosis

The most common treatment scenario. Baby Boomers (born 1945–1965) have ~5x higher HCV prevalence than other adults; many remain undiagnosed.[3,7,13] PCPs can prescribe pangenotypic DAAs **without specialist referral** using the AASLD-IDSA **simplified treatment algorithm**.[3]

Recommended first-line regimens (pangenotypic, ribavirin-free):

- **Glecaprevir/pibrentasvir** (Mavyret): 3 tablets once daily with food × 8 weeks[3]
- **Sofosbuvir/velpatasvir** (Epclusa): 1 tablet once daily × 12 weeks[20]

Both achieve SVR12 ≥95% **across all genotypes** (1–6) regardless of age.[3,18] **No genotype testing** required for simplified pathway.[3] **Pre-treatment workup**: HCV RNA, CBC, CMP (including eGFR), hepatic fibrosis assessment (FIB-4), HIV/HBV testing, DDI review.[3]

B. Chronic HCV with Compensated Cirrhosis (Child-Pugh A)

Older adults more likely to present **with cirrhosis** (53% vs 40% in younger patients); HCC risk 2.4x higher in ages 65–85.[33]

Recommended regimens:

- **Glecaprevir/pibrentasvir**: 3 tablets daily × 8 weeks (**EXPEDITION-8**: 98-99% SVR12)[3]
- **Sofosbuvir/velpatasvir**: 1 tablet daily × 12 weeks (genotype testing recommended if GT3 suspected)[3,34,35]

Lifelong HCC surveillance (ultrasound ± AFP every 6 months) **required even after SVR**.[17]

C. Decompensated Cirrhosis (Child-Pugh B/C)

Protease inhibitor–containing regimens (GLE/PIB, Vosevi) are contraindicated due to **hepatotoxicity risk** from increased drug exposure.[3]

Recommended regimen:

- **Sofosbuvir/velpatasvir ± ribavirin** × 12 weeks[3,36]

SVR rates **>80%** but lower than in compensated cirrhosis; **risk of further decompensation** if albumin <3.5 g/dL or MELD >14.[36] Requires specialist referral. Consider liver transplant evaluation.[3]

D. Chronic Kidney Disease (eGFR <30 mL/min) or Dialysis

Common comorbidity in older adults. **HCV accelerates CKD progression**.[3]

Recommended regimen:

- **Glecaprevir/pibrentasvir**: preferred — no dose adjustment needed (**EXPEDITION-4**: 98% SVR12 in CKD G4–G5D)[21,37]
- **Sofosbuvir-based regimens** now have expanded FDA labeling for severe CKD but require monitoring.[37]

KDIGO recommends DAA evaluation **for all CKD patients with HCV** (Grade 1A).[37]

E. Prior DAA Treatment Failure

Uncommon (<5%) but may occur in patients who received earlier, less effective regimens.[3]

Recommended salvage regimen:

- **Sofosbuvir/velpatasvir/voxilaprevir** (Vosevi): 12 weeks for most prior DAA failures (SVR ~96%)[3,38]
- **Add ribavirin** for GT3 with cirrhosis; extend to 16–24 weeks for multiple DAA failures[3]

Requires specialist consultation.

F. Special Considerations in Older Adults

CONSIDERATION	KEY POINTS*[3,17,18,22,39]
Age/frailty	Age alone is **not a contraindication**: SVR 97.9% in ≥65 years; treat all except those with short life expectancy not remediable by HCV therapy
Ribavirin avoidance	**Ribavirin increases serious AEs 1.9-fold** in elderly (primarily anemia) → prefer ribavirin-free regimens when possible
Polypharmacy/ DDIs	**80%** of patients ≥75 have clinically significant DDIs; **statins most common** contraindicated co-med (**10.2%**) → **mandatory DDI check**
HBV coinfection screening	**HBV reactivation risk during DAA therapy** → test HBsAg, anti-HBc, anti-HBs **before treatment**; monitor LFTs if prior HBV markers present

CONSIDERATION	KEY POINTS*[3,17,18,22,39]
Post-SVR follow-up	**Patients with cirrhosis**: lifelong HCC surveillance; **no cirrhosis + SVR**: can be discharged if no comorbidities; **reinfection monitoring if ongoing risk factors**

ABBREVIATIONS: SVR = sustained virologic response; HCV = hepatitis C virus; AE = adverse event(s); DDI = drug-drug interaction(s); HBV = hepatitis B virus; DAA = direct-acting antiviral; HBsAg = hepatitis B surface antigen; anti-HBc = antibody to hepatitis B core antigen; anti-HBs = antibody to hepatitis B surface antigen; LFT = liver function test(s); HCC = hepatocellular carcinoma; FDA = US Food and Drug Administration
***Consult FDA labels for the most up-to-date dosage information, contraindications, and drug-drug interactions**

Contraindications

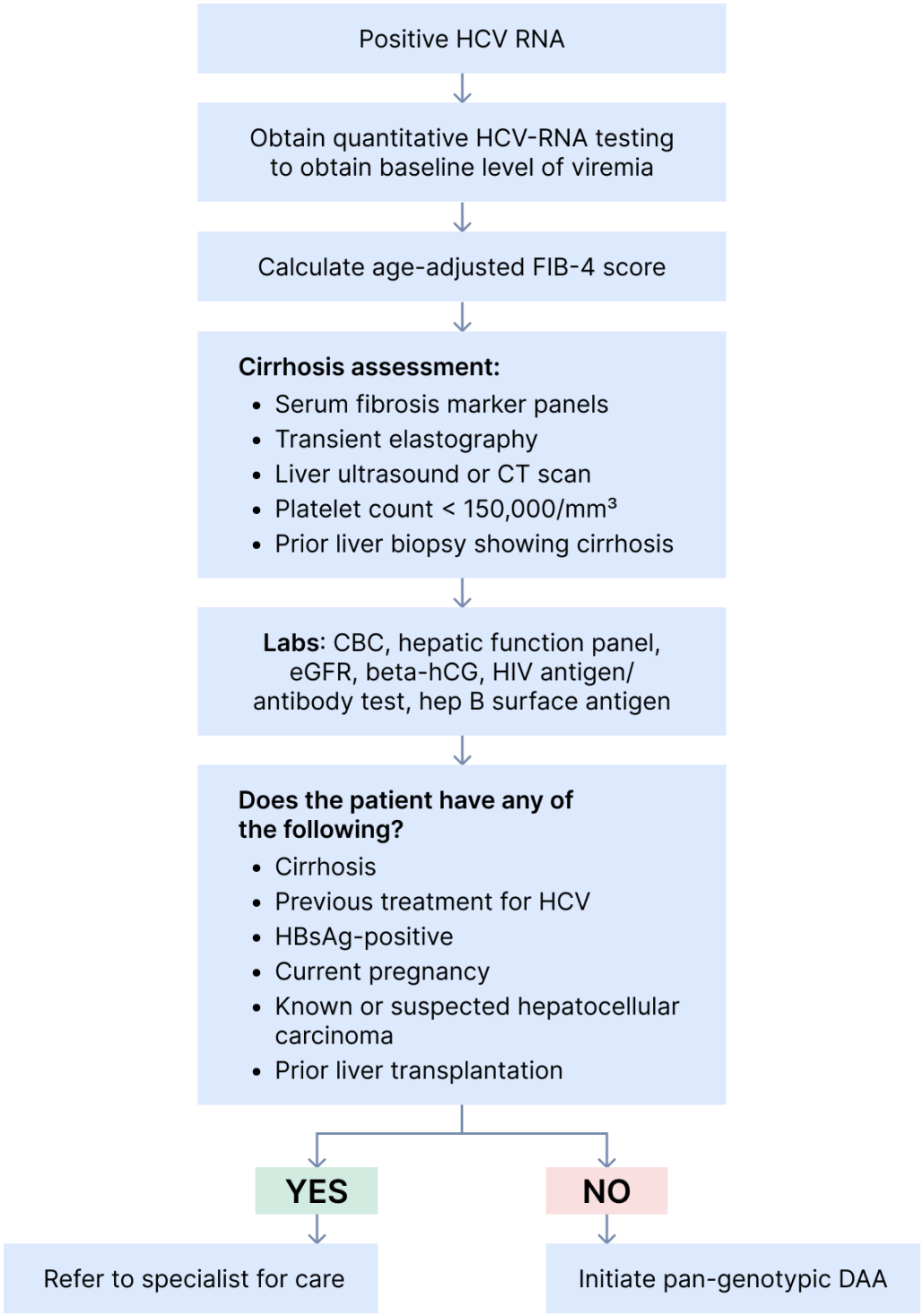
The vast majority of older adults with chronic HCV are **eligible for curative DAA therapy**, including those with advanced age, frailty, CKD, and multiple comorbidities.[3,18] **True absolute contraindications to DAA therapy are few**.[3] However, specific clinical scenarios require either selection of an alternative regimen, pre-treatment management, or specialist referral **before initiating therapy**.[3] The table below outlines the key contraindications and precautions organized by category, with the applicable DAA regimen(s) indicated.

CATEGORY	CONTRAINDICATION/ PRECAUTION	APPLIES TO*	CLINICAL RATIONALE*[3,39–42]
Decompensated cirrhosis (Child-Pugh B/C)	Moderate-severe hepatic impairment or prior decompensation	GLE/PIB (Mavyret), SOF/VEL/VOX (Vosevi)	**PI-containing DAAs contraindicated**; glecaprevir exposure ↑ up to 11x in Child-Pugh C; use SOF/VEL ± ribavirin; refer to specialist
Concomitant amiodarone	Coadministration with amiodarone	**All SOF-containing regimens** (SOF/VEL, SOF/VEL/VOX, LDV/SOF)	Serious **bradycardia** and **fatal cardiac arrest** reported; onset hours to 2 wk; if unavoidable, **inpatient cardiac monitoring** × 48 hr
Concomitant atazanavir	Coadministration with atazanavir	GLE/PIB (Mavyret)	**Contraindicated**; significantly ↑ glecaprevir exposure via **OATP1B1/3 inhibition**
Concomitant rifampin	Coadministration with rifampin	GLE/PIB (Mavyret), SOF/VEL (Epclusa)	**Potent P-gp/CYP inducer**; significantly ↓ DAA levels → **treatment failure**
Strong P-gp/CYP inducers	Carbamazepine, phenytoin, phenobarbital, St John's wort	SOF/VEL (Epclusa), GLE/PIB (Mavyret)	Significantly ↓ DAA concentrations; risk of **virologic failure**; coadmin not recommended

CATEGORY	CONTRAINDICATION/ PRECAUTION	APPLIES TO*	CLINICAL RATIONALE*[3,39–42]
HBV coinfection (HBsAg+)	Active HBV without concurrent suppressive therapy	**All DAA regimens** (FDA Boxed Warning)	**HBV reactivation risk ~24%**; test HBsAg/anti-HBc/anti-HBs pre-tx; **start HBV therapy if indicated** or monitor HBV DNA q4 wk
PPIs	Concurrent PPI use	SOF/VEL (Epclusa)	Velpatasvir absorption pH-dependent; **PPIs ↓ levels**; if necessary, SOF/VEL with food 4 hr before omeprazole ≤20 mg; consider GLE/PIB instead
Statin interactions	Atorvastatin, rosuvastatin, simvastatin at standard doses	GLE/PIB (Mavyret), SOF/VEL (Epclusa)	↑ Statin levels → **myopathy risk**; most common contraindicated co-med (**~10%**); **temp hold or dose ↓** during 8–12 wk DAA course
Drug hypersensitivity	Known hypersensitivity to active ingredient or excipient	**All DAA regimens**	**Standard contraindication**; re-exposure may provoke allergic reaction
Pregnancy (ribavirin)	Pregnancy or male partners of pregnant women when ribavirin used	SOF/VEL + ribavirin (**decompensated cirrhosis regimen**)	**Ribavirin is Category X** (teratogenic); DAAs without ribavirin not contraindicated by FDA labeling

ABBREVIATIONS: GLE/PIB = glecaprevir/pibrentasvir; SOF/VEL/VOX = sofosbuvir/velpatasvir/voxilaprevir; PI = protease inhibitor; DAA = direct-acting antiviral; SOF/VEL = sofosbuvir/velpatasvir; LDV/SOF = ledipasvir/sofosbuvir; wk = week(s); hr = hour(s); OATP1B1/3 = organic anion transporting polypeptide 1B1/3; P-gp = P-glycoprotein; CYP = cytochrome P450; HBV = hepatitis B virus; HBsAg = hepatitis B surface antigen; anti-HBc = antibody to hepatitis B core antigen; anti-HBs = antibody to hepatitis B surface antigen; FDA = US Food and Drug Administration; tx = treatment; DNA = deoxyribonucleic acid; q4 wk = every 4 weeks; PPI = proton pump inhibitor(s)
***Consult FDA labels for the most up-to-date dosage and duration information, contraindications, and drug-drug interactions**

Essential PCP Pretreatment Checks Before DAA Initiation



CLINICAL PEARL: PRE-DAA LABS DETERMINE TREATMENT TRACK

Pre-treatment labs stratify patients into **PCP-managed versus specialist-referral pathways**:

- **FIB-4 score** (AST, ALT, platelets, age): ≤1.45 + platelets ≥150K → PCP simplified track; >3.25 (or >2.0 if ≥65 y) → presume cirrhosis, confirm with VCTE or refer to hepatology; indeterminate → confirmatory testing before regimen selection[34,43]
- **HBV serologies** (HBsAg, anti-HBc, anti-HBs): required per FDA Boxed Warning; HBsAg+ → start HBV suppression before DAA initiation[3,44]
- **eGFR**: <30 mL/min → GLE/PIB preferred; SOF-based regimens require caution[37,44]
- **Signs of decompensation** (ascites, encephalopathy, variceal history): if present → **specialist referral required**; GLE/PIB contraindicated[45]

Bottom line: FIB-4 + HBV serologies + eGFR + decompensation assessment = four data points that determine whether the patient stays on the **PCP-managed simplified track** or requires **hepatology referral**.

Common DDI Management Before DAA Therapy Initiation

DRUG CLASS	ISSUE*[3,41,46,47]	PCP STRATEGY*[3,41,47,48]
Statins (atorvastatin, simvastatin, lovastatin)	**Most common contraindicated co-med** (~10%); GLE/PIB ↑ statin levels → **myopathy/ rhabdomyolysis risk**	**Temporarily hold for 8–12 wk**; safe to resume post-treatment; **if statin essential**; switch to SOF/VEL (low-dose atorvastatin or rosuvastatin acceptable)
PPIs (omeprazole, pantoprazole)	↓ Velpatasvir absorption (pH-dependent) with SOF/VEL	**If using SOF/VE**L: take with food 4 hr before omeprazole ≤20 mg; or **switch to GLE/PIB** (no PPI interaction); or substitute H2RA
Amiodarone	**Life-threatening bradycardia/cardiac arrest** with all SOF-containing regimens; onset hours to 2 wk	Contraindicated with SOF/VEL; **use GLE/PIB instead**; if amiodarone cannot be stopped and GLE/PIB not suitable → **inpatient cardiac monitoring ×48 hr**
Anticonvulsants (carbamazepine, phenytoin, phenobarbital)	**Potent CYP/P-gp inducers** → ↓ DAA levels → virologic failure	Not recommended with either GLE/PIB or SOF/VEL; consult neurology for **temporary switch to non-inducing agent** (e.g., levetiracetam) for treatment duration
Rifampin	**Potent inducer** → contraindicated with GLE/PIB and SOF/VEL	**Contraindicated**; coordinate with infectious disease for alternative (rifabutin may be acceptable with some regimens → verify at hep-druginteractions.org)

DRUG CLASS	ISSUE*[3,41,46,47]	PCP STRATEGY*[3,41,47,48]
Warfarin	DAA-mediated changes in hepatic metabolism may **alter INR**	**Monitor INR more frequently** during and 2–4 wk after DAA course; dose adjustments may be needed

ABBREVIATIONS: GLE/PIB = glecaprevir/pibrentasvir; wk = week(s); SOF/VEL = sofosbuvir/velpatasvir; PPI = proton pump inhibitor(s); hr = hour(s); H2RA = histamine-2 receptor antagonist; SOF = sofosbuvir; CYP = cytochrome P450; P-gp = P-glycoprotein; DAA = direct-acting antiviral; INR = international normalized ratio; PCP = primary care provider; FDA = US Food and Drug Administration
***Consult FDA labels for the most up-to-date dosage and duration information, contraindications, and drug-drug interactions**

DOSE AND DURATION RECOMMENDATIONS

Dose Escalation and Treatment Intensification Criteria

TRIGGER[17,49–52]	ACTION*[3,17,49,51,52]
Positive HCV antibody on universal or risk-based screening	**Reflex HCV RNA quantitative** (CPT 87521); if detectable → code **B18.2**; **calculate FIB-4** (age-adjusted cutoff ≥2.0 for patients ≥65 y); initiate **simplified DAA treatment pathway** or refer within 12 weeks of diagnosis
Treatment-naïve, no cirrhosis	**Glecaprevir/pibrentasvir 8 wk** or **sofosbuvir/velpatasvir 12 wk** per AASLD simplified algorithm; medication reconciliation + drug-drug interaction check required before initiation; minimal on-treatment monitoring is safe and effective
Treatment-naïve, compensated cirrhosis (Child-Pugh A)	Same DAA regimens as above (glecaprevir/pibrentasvir 8 wk or sofosbuvir/velpatasvir 12 wk); obtain **liver ultrasound within 6 months before DAA initiation** to exclude HCC and subclinical ascites; enroll in **semiannual HCC surveillance** (US + AFP q6 months)
FIB-4 indeterminate (2.0–2.67 in ≥65 y) or elevated (>3.25)	**Confirm fibrosis stage with VCTE** (preferred) or ELF; if VCTE ≥12.5 kPa → presume cirrhosis → treat as **compensated cirrhosis pathway**; if discordant results → consider **hepatology referral**
Decompensated cirrhosis (Child-Pugh B/C)	**Do NOT use protease inhibitor–containing regimens** (glecaprevir/pibrentasvir contraindicated); **refer to hepatology** for sofosbuvir/velpatasvir ± ribavirin; evaluate for **transplant if MELD ≥15**

TRIGGER[17,49–52]	ACTION*[3,17,49,51,52]
DAA treatment failure (detectable HCV RNA at SVR12)	**Refer to hepatology**; retreatment options include sofosbuvir/velpatasvir/voxilaprevir 12 wk (first-line for sofosbuvir-based failures) or glecaprevir/pibrentasvir + sofosbuvir ± ribavirin 16 wk; **resistance testing** may guide regimen selection in **GT3** or **multiply-failed patients**
Post-SVR with cirrhosis	Continue **semiannual HCC surveillance** (US + AFP q6 months) indefinitely → **HCC risk persists ≥10 years** post-SVR; **endoscopic variceal surveillance** per AASLD guidance; annual HCV RNA if **ongoing reinfection risk**
Post-SVR without cirrhosis	Routine HCC surveillance **NOT recommended** (annual HCC incidence below cost-effectiveness threshold); recheck HCV RNA if **new aminotransferase elevation** or ongoing risk behaviors

ABBREVIATIONS: HCV = hepatitis C virus; RNA = ribonucleic acid; CPT = current procedural terminology; FIB-4 = Fibrosis-4 index; y = year(s); DAA = direct-acting antiviral; wk = week(s); AASLD = American Association for the Study of Liver Diseases; HCC = hepatocellular carcinoma; US = ultrasound; AFP = alpha-fetoprotein; q6 = every 6; VCTE = vibration-controlled transient elastography; ELF = Enhanced Liver Fibrosis test; kPa = kilopascal; MELD = Model for End-Stage Liver Disease; SVR12 = sustained virologic response at 12 weeks; GT3 = genotype 3; FDA = US Food and Drug Administration

***Consult FDA labels for the most up-to-date dosage information, contraindications, and drug-drug interactions**

CLINICAL PEARL: AGING SILENTLY RESHAPES HCV DISEASE IN OLDER ADULTS

Older adults with chronic HCV present **unique clinical challenges** despite the high efficacy of DAA therapy **across all age groups** (SVR rates 97–98% in patients ≥65 years, comparable to younger populations).[33,53] Three **clinically actionable consequences** of aging in HCV warrant PCP attention:

- **Fibrosis is more advanced at presentation**. Older adults present with significantly higher rates of **advanced fibrosis** (53% vs 40% in younger patients), reflecting decades of subclinical disease progression.[33] **FIB-4 requires age-adjusted thresholds** (lower cutoff ≥2.0 for patients ≥65 y) to avoid false-positive fibrosis staging[34,54]
- **HCC risk persists longer after cure**. Aging is an independent unfavorable factor for fibrosis regression and HCC development **even after SVR** — immune senescence impairs clearance of pre-malignant hepatocytes.[55] Patients with cirrhosis at time of SVR remain at **elevated HCC risk for at least 10 years** and require indefinite semiannual surveillance[56]
- **Treatment should not be withheld based on age alone**. DAA safety and tolerability are comparable across age groups, **including patients ≥75 years**.[33,53] AASLD recommends DAA treatment for **all patients with chronic HCV** except those with **short life expectancy** that cannot be remediated by treatment or transplantation[3]

Bottom line: Older HCV patients **present later** with more fibrosis, face **persistent post-cure HCC risk**, yet **respond equally well** to DAA therapy — making early identification and treatment a high-value PCP intervention.

Duration of DAA Therapies

DAA treatment for chronic HCV is a **finite, curative course**, **not chronic maintenance therapy**.[3] Treatment duration is determined by **three factors**: the specific DAA regimen, cirrhosis status, and prior treatment history. The **AASLD-IDSA simplified treatment algorithm** enables PCPs to select the appropriate duration for the **majority of older adult patients without specialist consultation**.[3]

First-Line Treatment-Naïve Patients

CLINICAL SCENARIO[3,44]	REGIMEN*	DURATION*[3,14,20]	SVR RATE[14,20,35,57]
No cirrhosis (any genotype)	Glecaprevir/pibrentasvir (Mavyret)	8 weeks	>97%
No cirrhosis (any genotype)	Sofosbuvir/velpatasvir (Epclusa)	12 weeks	>95%

CLINICAL SCENARIO[3,44]	REGIMEN*	DURATION*[3,14,20]	SVR RATE[14,20,35,57]
Compensated cirrhosis, Child-Pugh A (any genotype)	Glecaprevir/pibrentasvir (Mavyret)	8 weeks	98%
Compensated cirrhosis, Child-Pugh A (any genotype)	Sofosbuvir/velpatasvir (Epclusa)	12 weeks	95–96%
Decompensated cirrhosis, Child-Pugh B/C	Sofosbuvir/velpatasvir ± ribavirin (hepatology-managed)	12 weeks	83–95%

ABBREVIATIONS: SVR = sustained virologic response; FDA = US Food and Drug Administration
***Consult FDA labels for the most up-to-date dosage and duration information, contraindications, and drug-drug interactions**

Key duration principles for PCPs:

- **Generic sofosbuvir/velpatasvir** (Epclusa) 12 weeks is the recommended **cost-effective curative course** for treatment-naïve patients with or without compensated cirrhosis across all genotypes, with SVR12 >95–99% and a 2026 WAC approximately **~72% below brand** (~$20,000 vs ~$75,000 per course); glecaprevir/pibrentasvir 8 weeks remains an alternative with the **shortest treatment duration** (SVR12 98%)[3,20]
- **No dose titration or escalation** is required: DAAs are prescribed at fixed doses for the full treatment course. Unlike many chronic disease medications, there is **no** "**starting dose**" **or gradual uptitration**[3]
- **Protease inhibitor–containing regimens** (glecaprevir/pibrentasvir) are **contraindicated** in **decompensated cirrhosis** (Child-Pugh B/C) → these patients require **sofosbuvir-based regimens** managed by hepatology

Retreatment After DAA Failure

Retreatment scenarios are **uncommon** (<3–5% of treated patients) and should be **managed in consultation with hepatology**.[3]

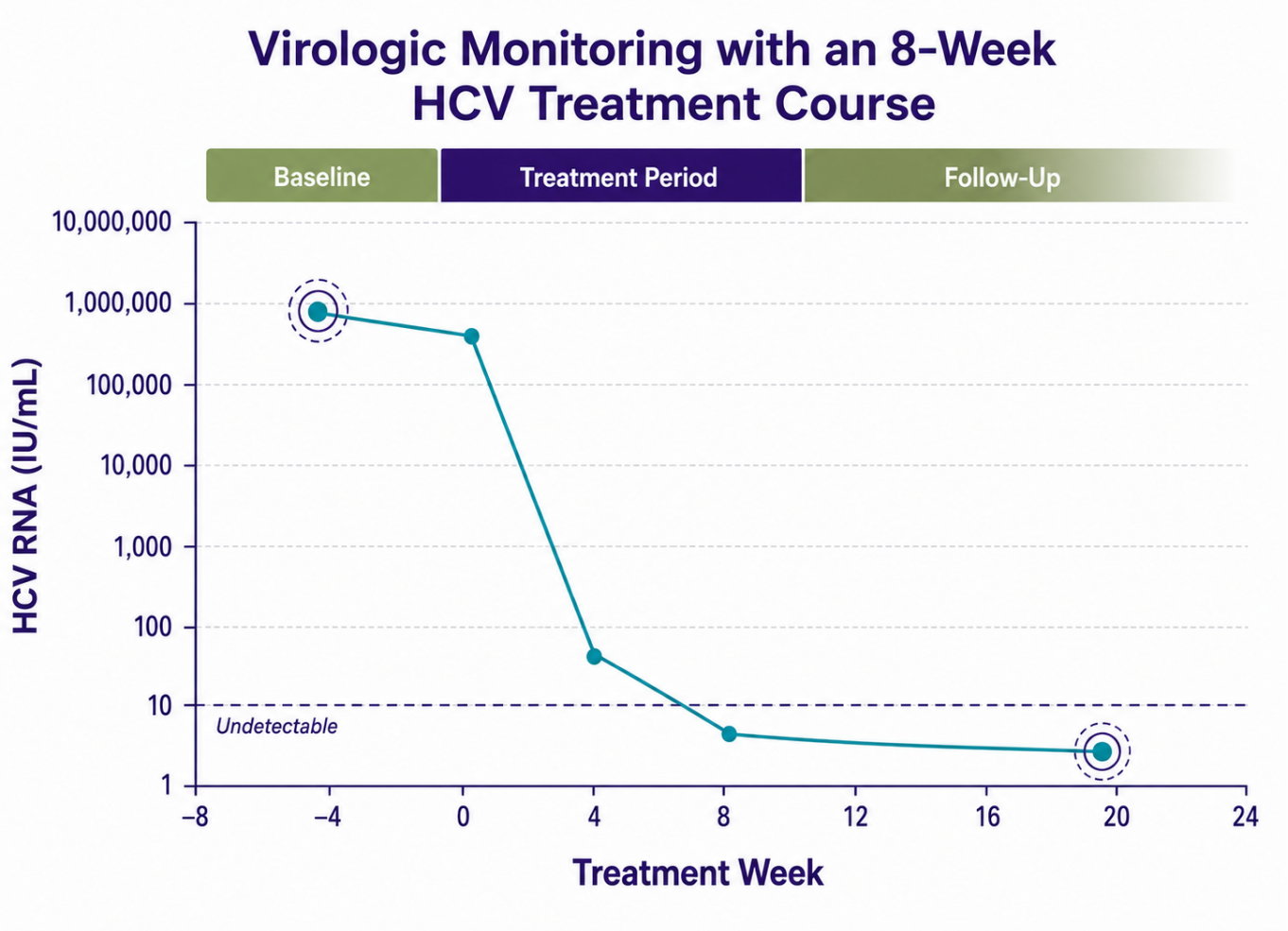
PRIOR FAILURE[3,58]	RETREATMENT REGIMEN*[3,38,59]	DURATION*
Sofosbuvir-based regimen failure	Sofosbuvir/velpatasvir/voxilaprevir (Vosevi)	12 weeks
Glecaprevir/pibrentasvir failure	Sofosbuvir/velpatasvir/voxilaprevir OR glecaprevir/pibrentasvir + sofosbuvir + ribavirin	12–16 weeks
Multiple DAA failures	Glecaprevir/pibrentasvir + sofosbuvir + ribavirin (specialist-managed)	16–24 weeks

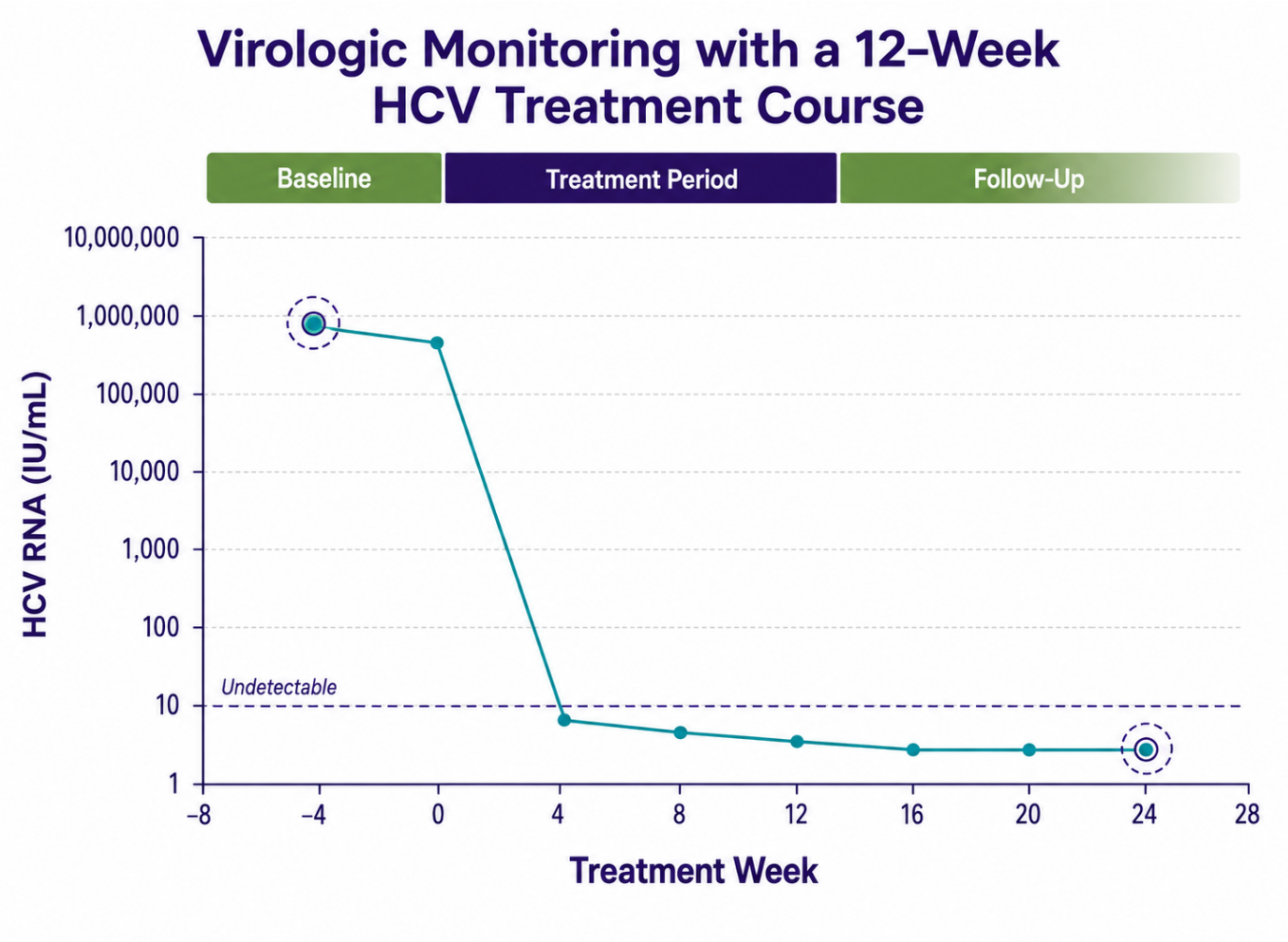
PRIOR FAILURE[3,58]	RETREATMENT REGIMEN*[3,38,59]	DURATION*

ABBREVIATIONS: DAA = direct-acting antiviral; FDA = US Food and Drug Administration
***Consult FDA labels for the most up-to-date dosage and duration information, contraindications, and drug-drug interactions**

On-Treatment Monitoring and SVR Confirmation

The **AASLD simplified algorithm** supports minimal on-treatment monitoring for treatment-naïve patients; the **MINMON trial** demonstrated that dispensing the entire treatment course at initiation with no scheduled on-treatment visits achieved **SVR rates comparable to standard monitoring** (95%, n=399).[3,60] Routine on-treatment HCV RNA testing is not recommended unless **ALT fails to decline or adherence concerns arise**.[3] SVR is confirmed by **undetectable HCV RNA at 12 weeks post-treatment completion** (**SVR12**), which is consistent with virologic cure — SVR12 durability **approaches 100%** over 4+ years of follow-up.[61]




Virologic Monitoring with a 12-Week HCV Treatment Course
Baseline
Treatment Period
Follow-Up
HCV RNA (IU/mL)
10,000,000
1,000,000
100,000
10,000
1,000
100
10
1
Undetectable
−8
−4
0
4
8
12
16
20
24
28
Treatment Week

CLINICAL PEARL: OLDER ADULT HCV PATIENT DAA DURATION CONSIDERATIONS

DAA regimens achieve **equivalent cure rates across all age groups**, but **older adults require attention to** ribavirin avoidance, renal dosing, and drug-drug interactions.

- **No age-based dose or duration adjustments are needed**. Pooled data from nine phase 2/3 trials confirm **equivalent SVR rates** (97.9%) and **comparable safety** in **patients ≥65 years** versus younger patients[53]
- **Ribavirin-free regimens are preferred in older adults**: ribavirin increases adverse events (particularly anemia) in elderly patients (OR 1.90 for dose reduction), while ribavirin-free regimens show **no significant difference in adverse event rates** between age groups[18]
- **Severe renal impairment** (eGFR <30 mL/min): **Glecaprevir/pibrentasvir is preferred** (no dose adjustment needed; SVR ~99% in CKD stages 4–5). Sofosbuvir-based regimens are **not recommended in eGFR <30** due to accumulation of the GS-331007 metabolite, though recent FDA labeling updates have expanded use in some settings[37,44]
- **Drug-drug interaction review is essential** before initiating therapy, particularly given polypharmacy prevalence in older adults. The University of Liverpool **HEP Drug Interactions Checker** (hep-druginteractions.org) is the standard resource[22]

Drug-Drug Interaction (DDI) Checks

Reconcile all medications, OTC drugs, and supplements before and during therapy using hep-druginteractions.org.[4,40,41] **Key interactions in older adults**: amiodarone (contraindicated with all SOF-containing regimens — fatal bradycardia reported); **statins** (most common contraindicated co-med at ~10% — temporarily hold during 8–12 week course); **PPIs** (reduce velpatasvir absorption — if unavoidable, take SOF/VEL with food 4 hours before omeprazole ≤20 mg or switch to GLE/PIB); **strong CYP/P-gp inducers** such as carbamazepine, phenytoin, and rifampin (significantly reduce DAA levels → **virologic failure**).[4,40,41]

Hepatic Function Tests

Routine on-treatment LFT monitoring is **not required for most patients on the simplified pathway**.[3] Check hepatic function if **clinically indicated** (new jaundice, ascites, severe nausea, or worsening fatigue). Discontinue DAA therapy and **urgently evaluate if ALT rises ≥10×** ULN or is accompanied by signs of **hepatic decompensation**.[3]

Hepatitis B (HBV) Reactivation

All patients must have **pre-treatment HBV serologies** (HBsAg, anti-HBc, anti-HBs) per FDA Boxed Warning on all DAA labels.[3,44] **HBsAg-positive patients**: initiate or continue HBV suppressive therapy (entecavir or TAF) **before starting DAAs** and monitor HBV DNA and LFTs **every 4 weeks** during and for 12 weeks after DAA completion.[3] **Patients with isolated anti-HBc positivity** (resolved HBV): monitor LFTs during treatment; check HBV DNA if ALT flare occurs.[62]

HCV DAA UTILIZATION FRAMEWORK IN VALUE-BASED CARE

A Closed Loop DAA VBC Pathway for PCPs

Step 1: Automated Identification

- **Trigger**: EHR notification alerts care teams for all adults aged 18–79 who **lack a documented HCV screening history**[7,13]

Step 2: Single-Visit Confirmation

- **Protocol**: Order a **HCV antibody test** with **automatic reflex to HCV RNA** to bypass secondary testing barriers and speed up time-to-treatment[3]

Step 3: Low-Cost Severity Stratification

- **Calculation**: Generate an automated **baseline FIB-4 score** using standard routine labs (AST, ALT, platelets, and age)
- **Triage Rule**: Use **age-adjusted cutoffs** for patients **≥65 years** (low ≥2.0; high ≥2.67) to reduce false-positive fibrosis staging; standard cutoffs (<1.45; >3.25) apply for patients <65. **Below the low cutoff** → **PCP-led** simplified track; **above** the high cutoff → **specialist evaluation**; indeterminate → confirmatory VCTE or ELF before triage[34,43]

Step 4: Evidence-Based Treatment Selection

- **Formulary**: Limit prescribing strictly to plan-preferred, **cost-negotiated pangenotypic option** like 12 weeks of **sofosbuvir/velpatasvir**

Step 5: Adherence and Value Realization

- **Monitoring**: Deploy text-based virtual check-ins during **weeks 2 and 4** to verify medication possession and prevent costly **mid-cycle product waste**[29]
- **Closure**: Order an HCV RNA blood test **at least 12 weeks post-therapy**; SVR12 confirmation officially flags the patient as **cured** in the value-based registry[3]

PCP vs Specialist Responsibilities

Primary Care Providers (PCPs)

- **Adopt Simplified Regimens**: Manage non-complex, treatment-naive patients **in-house** using **pangenotypic 8-week or 12-week** regimens rather than referring out[29]

- **Deploy Digital Screening Triggers**: Integrate automated Electronic Health Record (EHR) reminders for **universal adult screening** to capture infections **before advanced disease** develops[13]
- **Utilize Biomarker Staging**: Employ the low-cost **FIB-4** index rather than expensive transient elastography (FibroScan) or liver biopsies for baseline staging[3,4]
- **Deploy Clinical Pharmacists**: Leverage embedded or plan-provided clinical pharmacists to handle **DDI checks** and adherence monitoring[41]

Specialists (Hepatologists/Infectious Disease)

- **Offload Non-Complex Caseloads**: Transition uncomplicated HCV cases back to primary care, freeing up specialized clinical bandwidth for complex pathologies[29]
- **Manage Advanced Disease Only**: Anchor care specifically on patients with **decompensated cirrhosis**, **treatment failure**, or **severe renal impairment**[3,4]
- **Lead e-Consult Networks**: Provide asynchronous electronic consultation (e.g., **Project ECHO** models) to mentor PCPs, earning alternative value-based infrastructure revenue[63,64]
- **Audit Value-Based Pathways**: Act as clinical governance leaders to **update organizational guidelines**, ensuring rapid adoption of cost-effective therapies[3]

CLINICAL PEARL: DECENTRALIZED HCV CARE REMOVES BOTTLENECKS FOR OLDER ADULTS

Shifting DAA prescribing **from subspecialty clinics into primary care**, community health centers, and substance use programs removes barriers that disproportionately affect older adults — including transportation, specialist wait times, and fragmented coordination.[29,65]

- **PCP-led treatment achieves equivalent cure rates**.[29,65] Meta-analysis shows no significant SVR12 difference between decentralized and specialist settings (RR 1.05; 95% CI 0.98–1.1); PCPs achieved **86.9% SVR** after brief training, with **loss to follow-up**, **not treatment failure**, as the primary driver of non-SVR[29,65]
- **Simplified algorithms enable non-specialist prescribing**. The AASLD-IDSA simplified pathway allows PCPs to treat **treatment-naïve patients ± compensated cirrhosis** without genotype testing or specialist referral[3,4]
- **Older adult–specific checks apply in any setting**. **Age-adjusted FIB-4**, HBV serologies, DDI screening, ribavirin avoidance, and renal-appropriate regimen selection remain essential regardless of prescriber type[3]

Actionable Cost Optimization Strategies

Chronic HCV is **curable with a short DAA course** (8–12 weeks), representing a **one-time treatment investment** that can eliminate downstream costs of progressive liver disease, cirrhosis management, and transplantation.[3,66] **Delaying treatment increases long-term costs** — Medicare beneficiaries treated within one year of diagnosis demonstrate larger sustained reductions in liver-related and total medical expenditures.[66]

Several cost levers are available to PCPs: the Inflation Reduction Act **$2,000 annual OOP cap** limits Medicare Part D beneficiary exposure;[67] authorized **generic sofosbuvir/velpatasvir** offers **~72% lower list price**;[26] and **340B-eligible sites** can acquire DAAs at **steeply discounted prices for uninsured patients**.[27] The following table summarizes estimated costs and high-value prescribing strategies:

BRAND (EST. COST)*[24,68–71]	GENERIC/ ALTERNATIVE (EST. COST)*[70–74]	EST. SAVINGS + COST-SMART TIP*[67,69,72,75,76]
Glecaprevir/ pibrentasvir (Mavyret) 8-wk HCV course ~$26,400 WAC	**No generic available**	**Only branded options available; 8-wk course** (vs. 12-wk SOF/VEL) saves **~33% on drug cost** with equivalent SVR >98% in treatment-naïve patients including compensated cirrhosis; Part D covered with IRA **$2,000 annual OOP cap**; AbbVie Patient Foundation for **qualifying uninsured patients**
Sofosbuvir/velpatasvir (Epclusa) 12-wk HCV course ~$74,760 WAC	**Authorized generic** sofosbuvir/velpatasvir **~$25,000/course** (67% lower list price)	**~$50,000 per course; Substantial cost savings with generic;** specify authorized generic on prescription; only **~3%** of Medicare beneficiaries are in plans covering authorized generic alone → **verify formulary**; **340B-eligible sites** can acquire at steeply discounted prices for uninsured patients
Chronic management of decompensated cirrhosis (~$15,000–$30,000/yr including monitoring)	**Transplant evaluation** when **MELD ≥15**; curative intent reduces long-term costs	**Variable: transplant is cost-effective long-term; Refer to transplant center early**; do not delay evaluation while managing decompensation; for patients not transplant-eligible, **align care intensity with goals** → palliative care consultation reduces unnecessary hospitalizations and improves quality of life

ABBREVIATIONS: WAC = wholesale acquisition cost; HCV = hepatitis C virus; wk = week(s); SOF/VEL = sofosbuvir/velpatasvir; SVR = sustained virologic response; OOP = out-of-pocket; IRA = Inflation Reduction Act; MELD = Model for End-Stage Liver Disease; 340B = federal drug pricing program; FDA = US Food and Drug Administration
Estimated costs reflect approximate 2024–2025 US wholesale acquisition cost (WAC) or out-of-pocket ranges and do not account for insurance coverage, copay assistance, or negotiated rates.
***Consult FDA labels for the most up-to-date dosage and duration information, contraindications, and drug-drug interactions**

Non-Pharmacological Intervention Strategies

INTERVENTION	TARGET/ RECOMMENDATION[77–82]	NOTES[83–86]
Complete alcohol abstinence	**All chronic hepatitis etiologies**	Alcohol **accelerates fibrosis**; **AUDIT-C at every visit**; brief intervention or MAT referral for alcohol use disorder
Weight loss and Mediterranean-style diet	Caloric reduction of **500–1,000 kcal/day**	**Reduces hepatic fat and inflammation**; **consider dietitian referral**; elderly with mobility limits → chair aerobics, water aerobics, tai chi
Metabolic optimization	Target **BMI <30**; **HbA1c <7%** in diabetics; manage dyslipidemia per guidelines	**MASLD/MASH** coexists in **~30–55%** of HCV patients; SVR alone **may not resolve steatosis**; uncontrolled metabolic syndrome accelerates **residual fibrosis post-SVR**; coordinate with endocrinology if T2DM uncontrolled
Abnormal lab follow-up	Evaluate persistently elevated ALT **>6 months post-SVR**	SVR eliminates HCV as cause → **investigate alternative etiologies**: MASLD/MASH, iron overload (ferritin + TSAT), drug/supplement hepatotoxicity, alcohol, autoimmune hepatitis; **do not attribute persistent ALT elevation to prior HCV**
Physical activity/ exercise	**≥150 minutes/week** moderate-intensity aerobic exercise per AASLD MASLD guidance	**Adapt for frailty and mobility**: walking, chair-based programs, PT referral for deconditioned elderly; exercise alone has **metabolic benefit** independent of weight loss
Avoid hepatotoxic supplements	**Counsel against**: kava, high-dose green tea extract, germander, pennyroyal, high-dose vitamin A, raw seafood (Vibrio risk in cirrhosis)	Document in medication reconciliation **at every visit**; patients often do not consider OTC/ supplements as 'medications'

ABBREVIATIONS: AUDIT-C = Alcohol Use Disorders Identification Test – Consumption; MAT = medication for addiction treatment; kcal = kilocalorie(s); BMI = body mass index; HbA1c = hemoglobin A1c; MASLD = metabolic dysfunction-associated steatotic liver disease; MASH = metabolic dysfunction-associated steatohepatitis; HCV = hepatitis C virus; SVR = sustained virologic response; T2DM = type 2 diabetes mellitus; ALT = alanine aminotransferase; TSAT = transferrin saturation; AASLD = American Association for the Study of Liver Diseases; PT = physical therapy; OTC = over-the-counter

Patient-Centered Conversation Framework

Document the following education topics, the patient and caregiver(s) present, materials provided, and patient understanding (**teach-back method**):

- **Diagnosis in plain language**: Hepatitis C is a viral liver infection usually **found through a blood test**, not symptoms; most people **feel well even with liver damage**; early treatment can cure the virus and prevent serious liver disease[3,4]
- **Warning symptoms → ED**: **Vomiting blood or black stools**; confusion or unusual drowsiness; new yellowing of skin/eyes with fever; rapid belly swelling[43,85]
- **Why screening matters**: Adults born **1945–1965** have **sixfold higher** hepatitis C rates; a one-time blood test can find curable infection before permanent liver damage occurs[3,7]
- **Treatment expectations**: Hepatitis C is **cured with 8–12 weeks of oral pills** taken once or twice daily; **cure rates exceed 95%**; most patients experience few or no side effects; no injections are needed[86]
- **Medication adherence**: Missing doses can **reduce cure rates**; set a daily reminder; **do not stop early even if feeling well**; bring all current medications (including supplements) to every visit so the care team can check for interactions[3]
- **Post-cure follow-up**: A blood test **12 weeks after finishing treatment** confirms cure; patients with significant liver scarring **still need liver cancer screening** (ultrasound every 6 months) even after cure[3]
- **Geriatric considerations**: Age alone **does not prevent treatment**; overall health and personal goals guide the plan; kidney function and other medications may affect which pill is chosen but do not rule out a cure[51,76]
- **Reinfection prevention**: Cure does not create immunity; **reinfection can occur** through shared needles, unsterile tattoo equipment, or other blood-to-blood contact; discuss individual risk factors openly and without judgment[3]
- **Advance care planning**: For patients with advanced liver disease, document a **healthcare proxy**, code status, and care goals early — **before complications** make these conversations harder; revisit at each major health change[85]
- **Caregiver assessment**: Screen for caregiver burden **at each visit**; refer to social work if strain is identified; support resources should begin early, **not only at advanced disease stages**[76,85]

HCC and Quality Alignment

Accurate ICD-10 coding for HCV encounters is **essential for appropriate risk adjustment**, **care coordination**, and **ensuring continuity** across the treatment cascade; from diagnosis through

DAA therapy and post-SVR surveillance. **PCPs should document**: the specific HCV disease stage, treatment status, and presence or absence of cirrhosis at each encounter, as this directly impacts hierarchical condition category (HCC) mapping and downstream care planning.[87,88] Comprehensive coding also **supports identification of patients who remain untreated** or **require ongoing HCC surveillance post-cure**.[3]

↔ MAKING CONNECTIONS

For additional context on **HCV and chronic hepatitis coding**, please consult the **AAVBC Chronic Hepatitis QRG**

Key HEDIS/MIPs/PQA Measures

No HCV-specific HEDIS measures exist in MY2026. However, **several HCV-specific MIPS measures** and the **PQA HCV Medication Adherence Measure are directly reportable by PCPs**:

- **MIPS #387**: Annual HCV Screening for Active Injection Drug Users
- **MIPS #400**: One-Time Screening for HCV and Treatment Initiation
- **MIPS #516**: HCV Sustained Virological Response (SVR)
- **PQA HCV**: Treatment of Chronic Hepatitis C: Completion of Therapy

MEASURE	STANDARD	HCV APPLICABILITY*[3,34,89,90]
MIPS #387: Annual HCV Screening for Active Injection Drug Users	**Denominator**: patients ≥18 y seen twice in reporting year with at least one preventive visit + active injection drug user; **Numerator**: patients with HCV antibody test performed during the measurement year; **Exclusions**: chronic HCV diagnosis; HCC diagnosis	Captures ongoing-risk rescreening in PWID; IDU accounts for **~70% of new HCV infections**; annual testing recommended by AASLD-IDSA **regardless of prior negative results**; relevant to **K70.1** and **K71.x** patients with concurrent IDU
MIPS #400: One-Time Screening for HCV and Treatment Initiation	**Denominator**: patients ≥18 y seen twice in reporting year with at least one preventive visit **Numerator**: patients screened for HCV and treatment initiated within three months if positive **Exclusions**: diagnosed with chronic HCV	Directly identifies the **screening-to-treatment cascade** for the Baby Boomer cohort; aligns with USPSTF 2020 Grade B recommendation; PCP-reportable measure that incentivizes reflex RNA testing and **expedited DAA referral within 30 days of positive antibody**

MEASURE	STANDARD	HCV APPLICABILITY*[3,34,89,90]
MIPS #516: HCV Sustained Virological Response (SVR)	**Denominator**: patients ≥18 y with chronic HCV (**B18.2**) who completed a course of DAA therapy during the measurement period or 12 months prior; **Numerator**: patients with documented SVR12 (HCV RNA undetectable ≥12 weeks post-treatment completion); **Exclusions**: hospice; palliative care; HCC diagnosis	The only national quality measure tracking **HCV cure**; **SVR12** is the accepted clinical cure endpoint (PPV >99% for SVR24); only **~34%** of persons with initial HCV infection have evidence of viral clearance nationally, highlighting the **treatment gap** this measure addresses
PQA HCV: Treatment of Chronic Hepatitis C: Completion of Therapy	Percentage of individuals who **initiated antiviral therapy** for treatment of chronic hepatitis C, and who **completed the minimum intended duration of therapy** with no significant gap(s) in therapy	**Measures DAA adherence and course completion** → premature discontinuation or gaps >7 days reduce SVR rates; pharmacy-level measure used by Medicare Part D plan star ratings; relevant to PCP adherence counseling **at initiation and mid-course**; aligns with **MINMON** evidence that simplified monitoring still requires full course completion

ABBREVIATIONS: MIPS = Merit-based Incentive Payment System; HCV = hepatitis C virus; y = year(s); PWID = persons who inject drugs; IDU = injection drug use; AASLD = American Association for the Study of Liver Diseases; IDSA = Infectious Diseases Society of America; USPSTF = United States Preventive Services Task Force; PCP = primary care provider; RNA = ribonucleic acid; DAA = direct-acting antiviral; SVR = sustained virologic response; SVR12 = sustained virologic response at 12 weeks; SVR24 = sustained virologic response at 24 weeks; PPV = positive predictive value; HCC = hepatocellular carcinoma; PQA = Pharmacy Quality Alliance; MINMON = Minimal Monitoring; FDA = US Food and Drug Administration
***Consult FDA labels for the most up-to-date dosage information, contraindications, and drug-drug interactions**

TEN KEY TAKEAWAYS FOR HCV DAA THERAPIES

1 HCV is curable

An 8–12 week oral DAA course achieves SVR (virologic cure) in **>95%** of patients across all genotypes, ages, and fibrosis stages — including older adults ≥65 years with equivalent efficacy and safety.[3]

2 Screen universally, treat promptly

USPSTF and CDC recommend **one-time HCV screening for all adults ≥18 years**. Delayed treatment increases lifetime medical costs by **~$66,000 per patient** and allows preventable progression to cirrhosis and HCC.[7,28]

3 PCPs can treat most patients without specialist referral

The AASLD-IDSA simplified treatment algorithm enables **non-specialist prescribing for treatment-naïve patients** with or without compensated cirrhosis — refer only decompensated cirrhosis, DAA failures, and complex DDI scenarios.[3,29]

4 Pre-treatment checks are essential VBC interventions

FIB-4 (age-adjusted cutoff ≥2.0 for patients ≥65) stratifies cirrhosis status and determines **PCP-managed versus specialist-referral tracks**; **eGFR** guides regimen selection (GLE/PIB preferred if <30 mL/min); **HBV serologies** (HBsAg, anti-HBc, anti-HBs) are required per FDA Boxed Warning to prevent fatal reactivation; and **DDI screening** (hep-druginteractions.org) identifies necessary medication holds **before initiating therapy**.[3,91]

5 Choose the right regimen, not simply the shortest one

Generic sofosbuvir/velpatasvir (12 weeks) is a cost-effective, **pangenotypic first-line option** across genotypes and fibrosis stages, while glecaprevir/pibrentasvir offers an 8-week alternative for appropriate patients. **Regimen selection should integrate** clinical factors, drug-drug interactions, renal function, formulary coverage, and **total treatment cost** rather than duration alone.[3,20]

6 Manage drug interactions, do not defer cure

Polypharmacy affects **80%** of patients ≥75 years; statins, PPIs, amiodarone, and anticonvulsants are the most common DDI concerns. Most can be managed with **temporary holds during the short treatment course** → use hep-druginteractions.org **before every initiation**.[22]

7 Cirrhosis requires lifelong post-cure surveillance

SVR does not eliminate HCC risk in patients with cirrhosis at treatment: semiannual ultrasound ± AFP **must continue indefinitely**. Patients **without cirrhosis who achieve SVR** can be discharged from hepatology follow-up.[3,56]

8 Leverage cost optimization levers

The IRA $2,000 annual OOP cap **limits Medicare Part D beneficiary exposure**; authorized generic SOF/VEL offers **~67%** lower list price; **340B pricing** and **manufacturer patient assistance programs** further reduce barriers for uninsured patients.[67,72]

9 Treating HCV generates net healthcare savings

The lifetime medical cost burden is **$90,089** per treated patient versus **$155,930** per untreated patient — a **$65,841** per-person savings.[28,66] At the population level, universal treatment would save an estimated **$147 billion** nationally.[28,66]

10 Accurate coding drives care coordination and risk adjustment

Document **B18.2** (chronic HCV) with treatment status and cirrhosis stage at every encounter; this maps to **HCC 65** (RAF 0.185) and supports quality measure reporting (**MIPS #400**, **#516**) that **directly incentivizes the screening-to-cure cascade**.[87,88,92]

AAVBC SUMMARY AND CONCLUSION

Chronic HCV is among the highest-value treatment targets in medicine: a short, well-tolerated oral course cures >95% of patients, prevents progression to cirrhosis and HCC, and generates substantial lifetime cost savings.[28]

The AAVBC recommends that PCPs integrate universal HCV screening into routine care, utilize **simplified DAA treatment pathways** to initiate therapy without specialist referral for uncomplicated cases, and complete essential **pre-treatment assessments** (FIB-4 and HBV serologies) to ensure safe, effective treatment. Accurate ICD-10 documentation, quality measure alignment, and cost-conscious regimen selection further reinforce the value proposition. **Every cured patient** represents preventable morbidity, avoided downstream costs, and a measurable step toward national HCV elimination.[66]

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