FROM DIAGNOSIS TO TREATMENT:
How to Build an HCV Clinical Toolkit

Part 2 for Music City PrEP

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August 2024

AETC AIDS Education & Training Center Program Southeast

Objectives

At the end of this training, the learner will be able to:

- Select hepatitis C virus (HCV) therapy based on clinical criteria using evidence-based tools;
- Evaluate the impact of comorbid conditions on HCV management and care, including:
  - Drug-drug interactions;
  - Hepatitis B virus (HBV);
  - Human immunodeficiency virus (HIV);
  - Medication access and adherence;
  - Substance misuse.

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Drug-drug Interactions

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Where Do I Check For Drug Interactions?

https://www.hep-druginteractions.org/checker

HEP Drug Interactions

UNIVERSITY OF LIVERPOOL

Interaction Checker

Apps

HEP Drugs	Co-medications	Drug Interactions
Search HEP drugs...	Search co-medications...	Check HEP/HEP drug interactions
A-Z Indication Trade	A-Z Class	Drug Interactions will be displayed here
Selected HEP Drugs will be displayed here.	Selected Co-medications will be displayed here.	
Adefovir	Abacavir	
Daclatasvir	Abiraterone	
Elbasvir/Grazoprevir	Acalabrutinib	
Entecavir	Acamprosate	

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Drug Interactions

Type the drug name (brand or generic) in the search field. Selec

Enter search term:

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Interactions

Southeast

Requirements Prior to Initiation of HCV Therapy

"Prior to starting treatment, **patients should be evaluated for potential drug-drug interactions** with selected antiviral medications by consulting the prescribing information and using other resources."

Pretreatment and On-Treatment Monitoring

Recommended Assessments Prior to Starting DAA Therapy	
RECOMMENDED	RATING
Staging of hepatic fibrosis is essential prior to HCV treatment (see Testing and Linkage to Care and see When and in Whom to Treat). Assessment of potential drug-drug interactions with concomitant medications is recommended prior to starting DAA therapy and, when possible, an interacting co-medication should be stopped or switched to an alternative with less risk for potential interaction during HCV treatment. (See Table of Drug Interactions with Direct-Acting Antivirals and Selected Concomitant Medications below or use an online resource such as University of Liverpool interaction checker.)	

Recommended Monitoring During Antiviral Therapy	
RECOMMENDED	RATING
Clinic visits or telephone contact are recommended as clinically indicated during treatment to ensure medication adherence and monitor for adverse events and potential drug-drug interactions (see table of Drug Interactions with Direct-Acting Antivirals and Selected Concomitant Medications below), especially with newly prescribed medications.	I, B

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Drug-Drug Interaction Terminology

- **Drug metabolizing enzymes and drug transporters**
  - Cytochrome P450 (CYP enzymes, i.e., CYP3A4, CYP2D6)
  - P-glycoprotein (P-gp)
  - Breast cancer resistance protein (BCRP)
  - Organic anion transporting polypeptide (OATP)

- **Substrate** – substance on which an enzyme acts
- **Inducer** – "increases" enzyme activity (speeds up metabolism)
- **Inhibitor** – "blocks" enzyme activity (slows down metabolism)

Drug-Drug Interaction Mechanisms

	Substrate		Inhibitor		Other
Medication name	**CYP3A4**	**P-gp**	**CYP3A4**	**P-gp**	
glecaprevir/pibrentasvir	X	X	X	X	BCRP, OATP
sofosbuvir	X		X		BCRP
ledipasvir		X		X	
velpatasvir	X	X		X	BCRP, OATP
voxilaprevir	X	X		X	BCRP, OATP
elbasvir/grazoprevir	X		X		OATP

Red Flag Medication Classes

Antacids, H2RAs, PPIs	**Amiodarone/dronedarone**	**Anticonvulsants** [namely oxcarbazepine, phenytoin, carbamazepine), quetiapine (G/P only)]	**Statins**
ART regimens containing protease inhibitors, cobicistat, ritonavir, or efavirenz	**Oral anticoagulants** (namely rivaroxaban, warfarin)	**Hormone therapies** (namely combined oral contraceptives containing estrogen, hormone replacement therapy)	**Herbal medications/supplements**

Green Flag Medication Classes

Pain and sedating medications (oxycodone, hydrocodone, tramadol), benzodiazepines	**SSRIs, SNRIs, mirtazapine**	**MAT** (buprenorphine, naloxone)
Diabetes medications*	**Blood pressure medications***	**Antibiotics** used for STIs, uncomplicated URIs, or SSTIs

P-gp Interaction Considerations

- All HCV direct acting antiviral agents are substrates of the drug transporter p-gp.

P-gp Inducers Contraindicated	P-gp Inhibitors Contraindicated vs. Redose vs. Monitor
Antiepileptics (e.g., carbamazepine; oxcarbazepine, phenobarbitol, phenytoin)	Azole antifungals
Rifamycins	Verapamil
St. John's wort	HIV protease inhibitors
Modafanil, armodafanil	Amiodarone
	Cyclosporine

DAAs and Statins

	Rosuvastatin	Atorvastatin	Pravastatin	Lovastatin	Simvastatin	Pitavastatin
Ledipasvir	↑ rosuva- **Not rec.**	↑ atorva- Lowest dose, Monitor	↑ prava- Lowest dose, Monitor	↑ lova- Lowest dose, Monitor	↑ simva- Lowest dose, Monitor	↑ pitava- Lowest dose, Monitor
Velpatasvir	↑ rosuva- **Max 10mg**	↑ atorva- Lowest dose, Monitor	OK	↑ lova- Monitor	↑ simva- Lowest dose, Monitor	↑ pitava- Lowest dose, Monitor
Pibrentasvir/ glecaprevir	↑ rosuva- **Max 10mg**	↑ atorva- **Not rec.**	↑ prava- **Max 20mg** **Reduce 50%**	↑ lova- **Not rec.**	↑ simva- **Not rec.**	↑ pitava- Monitor
Elbasvir/ grazoprevir	↑ rosuva- **Max 10mg**	↑ atorva- **Max 20mg**	OK	↑ lova- **Max 20mg**	↑ simva- **Max 20mg**	OK
Velpatasvir/ Voxilaprevir/ Sofosbuvir	↑ rosuva- **Not rec.**	↑ atorva- Lowest dose, Monitor	↑ prava- **Max 40mg**	↑ lova- Lowest dose, Monitor	↑ simva- Lowest dose, Monitor	↑ pitava- **Not rec.**

DAAs and Acid-Reducing Agents

	PPI	H2RA	Antacids
LDV/SOF	Doses equivalent to pantoprazole 40 mg daily administered simultaneously on an empty stomach	Coadministration of famotidine (40 mg single dose) simultaneously with or 12 hours prior to DAA	Separate administration by 4 hours
SOF/VEL	Not recommended; doses equivalent to omeprazole 20 mg daily administered 4 hours before DAA	Coadministration of famotidine (40 mg BID) simultaneously with or 12 hours apart	Separate administration by 4 hours
GLE/PIB	Doses equivalent to omeprazole 20 mg daily administered simultaneously with food	Levels may decrease, no dose adjustment needed	N/A
SOF/VEL/VOX	Doses equivalent to omeprazole 20 mg daily administered simultaneously with food	Co-administration of famotidine (40 mg BID) simultaneously or 12 hours apart	Separate administration by 4 hours

PPI = proton pump inhibitor
H2RA = histamine-2 receptor antagonists

Hepatitis B Co-Infection

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HBV Serology Interpretations

State	sAg	cAb	sAb
Naïve	-	-	-
Immune due to immunization	-	-	+
Immune due to natural infection	-	+	+
Active infection	+	+	-
Multiple Options: -Occult infection -Lost sAb -Window period -False positive	-	+	-

Interpreting HBV Serologies

Seromarker	Result	Interpretation: Status
HBsAg HBcAb HBsAb	Negative Negative Negative	Susceptible
HBsAg HBcAb HBsAb	Negative Positive Positive	Immune due to natural infection
HBsAg HBcAb HBsAb	Negative Negative Positive	Immune due to HBV vaccination
HBsAg HBcAb HBsAb	Positive Positive Negative	Active infection
HBsAg HBcAb HBsAb	Negative Positive Negative	Immune due to natural infection (w/ “lost” sAb) Occult HBV infection (low level DNA) False positive Recent acute hepatitis B (i.e., “window period”)

HBV/HCV-coinfected individuals are susceptible to a process called viral interference wherein one virus may interfere with the replication of the other virus. Thus, when treating one or both viruses with antiviral drugs, periodic retesting of HBV DNA and HCV RNA levels during and after therapy is prudent, particularly if only one of the viruses is being treated at a time. Treatment of HCV infection in such cases utilizes the same genotype-specific regimens as are recommended for HCV monoinfection (see Initial Treatment of HCV Infection). HBV infection in such cases should be treated as recommended for HBV monoinfection (Lok, 2009).

WARNING: RISK OF HEPATITIS B VIRUS REACTIVATION IN PATIENTS COINFECTED WITH HCV AND HBV

See full prescribing information for complete boxed warning.

Hepatitis B virus (HBV) reactivation has been reported, in some cases resulting in fulminant hepatitis, hepatic failure, and death.

(Package insert for glecaprevir/pibrentasvir and sofosbuvir/velpatasvir)

ORIGINAL RESEARCH

Annals of Internal Medicine

Hepatitis B Virus Reactivation Associated With Direct-Acting Antiviral Therapy for Chronic Hepatitis C Virus: A Review of Cases Reported to the U.S. Food and Drug Administration Adverse Event Reporting System

Susan J. Bersoff-Matcha, MD; Kelly Cao, PharmD; Mihaela Jason, PharmD; Adebola Ajao, PhD; S. Christopher Jones, PharmD, MS, MPH; Tamra Meyer, PhD, MPH; and Allen Brinker, MD, MS

Published June 6, 2017

Case Series

- 29 cases reported from 11/2013 – 10/2016
  - 13 occurred in patients with positive sAg
  - 4 occurred in patients with negative sAg
  - 12 occurred with unknown baseline sAg status
- 2 deaths and 1 liver transplant
- Resulted in boxed warning with all DAA therapies

THE LANCET
Gastroenterology & Hepatology

Articles

Hepatitis B virus reactivation during direct-acting antiviral therapy for hepatitis C: a systematic review and meta-analysis

Marcus M Mücke, MD, Lisa I Backus, MD, Victoria T Mücke, MD, Nicola Coppola, MD, Carmen M Preda, MD, Ming-Lun Yeh, MD, Lydia S Y Tang, MBChB, Pamela S Belperio, PharmD, Eleanor M Wilson, MD, Prof Ming-Lung Yu, MD, Prof Stefan Zeuzem, MD, Prof Eva Herrmann, PhD, Johannes Vermehren, MD

Published: 19 January 2018

Meta-Analysis

- 17 observational trials

- 1621 patients treated with DAAs for HCV
  - 242 with chronic HBV (i.e., sAg positive)
  - 1379 with resolved HBV (i.e., cAb positive)

- HBV reactivation rates variable
  - 24% among patients with chronic HBV
  - 1.4% among patients with resolved HBV

- Clinically significant events variable
  - 9% of chronic HBV patients with HBV-reactivation-related hepatitis
  - 1 liver decompensation, 2 with liver failure (one requiring liver transplant)
  - **No clinically significant events among those with resolved HBV infection**

Approaching HCV In Setting of HBV

- Treat chronic HBV based on guideline recommendations
- Do not withhold HCV therapy if HBV not treated but monitor closely
- Consider treatment of chronic HBV prior to or during HCV therapy, particularly among those with measurable HBV DNA
- Consider closer monitoring of HBV and associated liver disease in those with resolved HBV infection while on DAA therapy

HIV Co-infection

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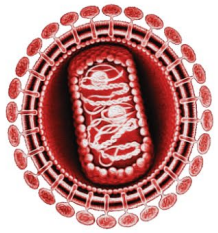
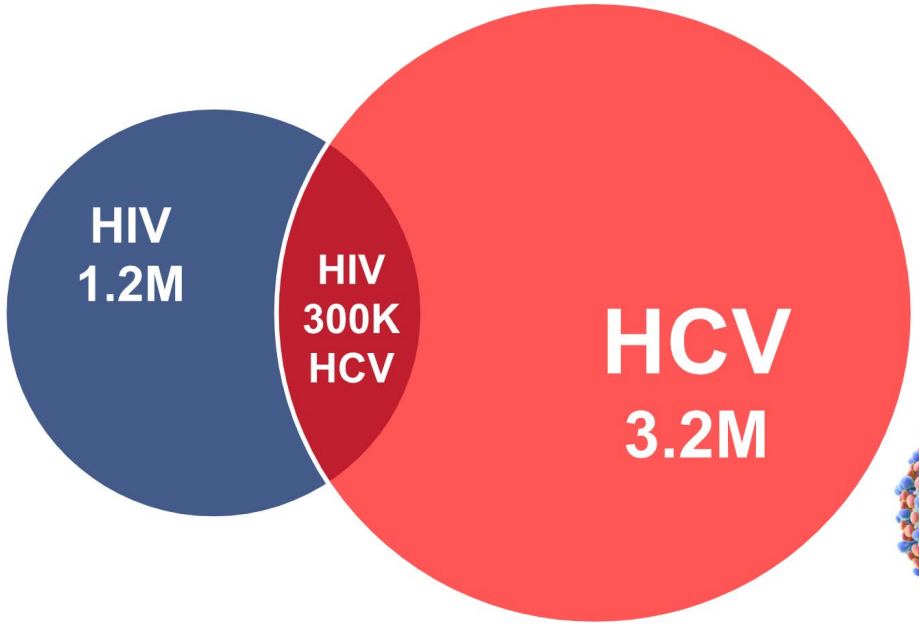
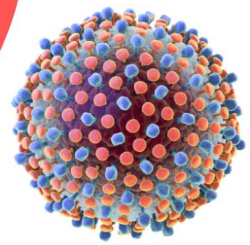
About 25% of PLWH in the U.S. also Have HCV Infection[17,21]







HIV/HCV Co-infection: An AETC National Curriculum

17. Hall HI, Song R, Rhodes P, et al. Estimation of HIV Incidence in the United States. JAMA: the journal of the American Medical Association. 2008;300(5):520-529. PMCID: PMC2919237.

21. Division of HIV/AIDS Prevention, National Center for HIV/AIDS, Viral Hepatitis, Sexual Transmitted Diseases and Tuberculosis Prevention, Centers for Disease Control and Prevention. HIV Mortality (through 2014). Accessed 6/16/2017.

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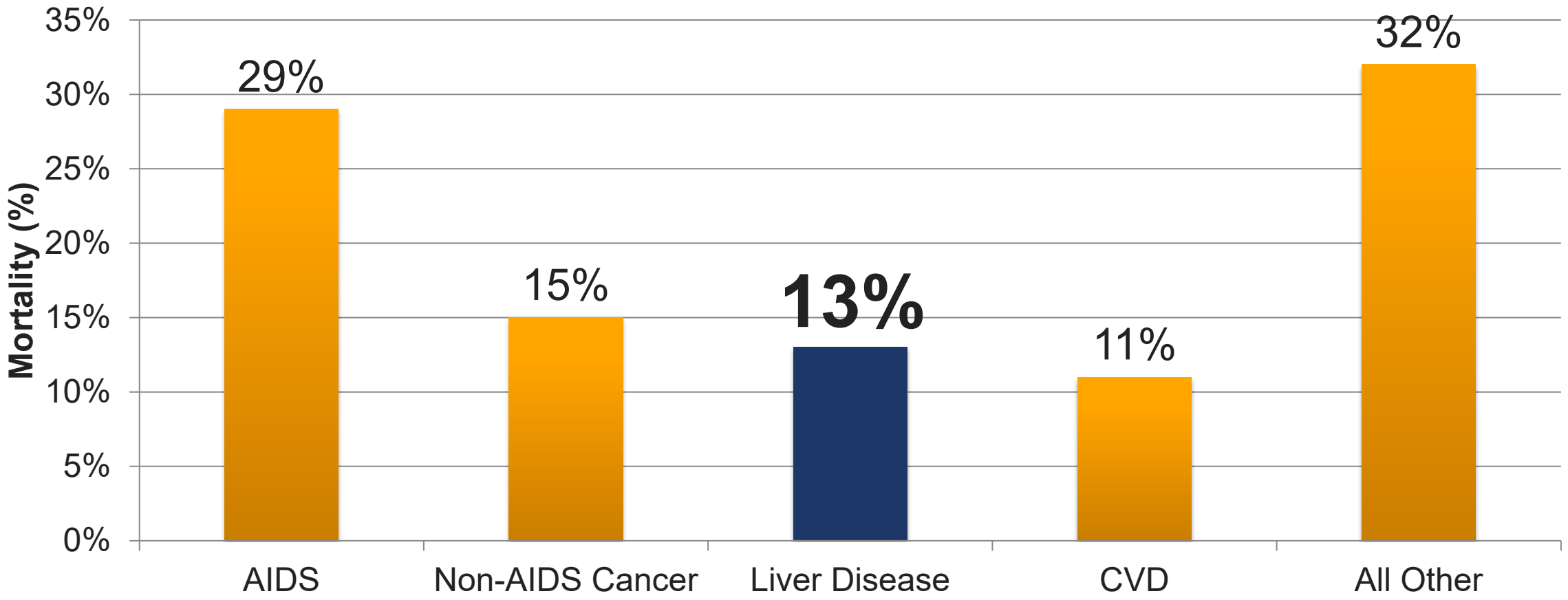
Cause of Death in D:A:D Cohort



Smith CJ et al. *Lancet* 2014.

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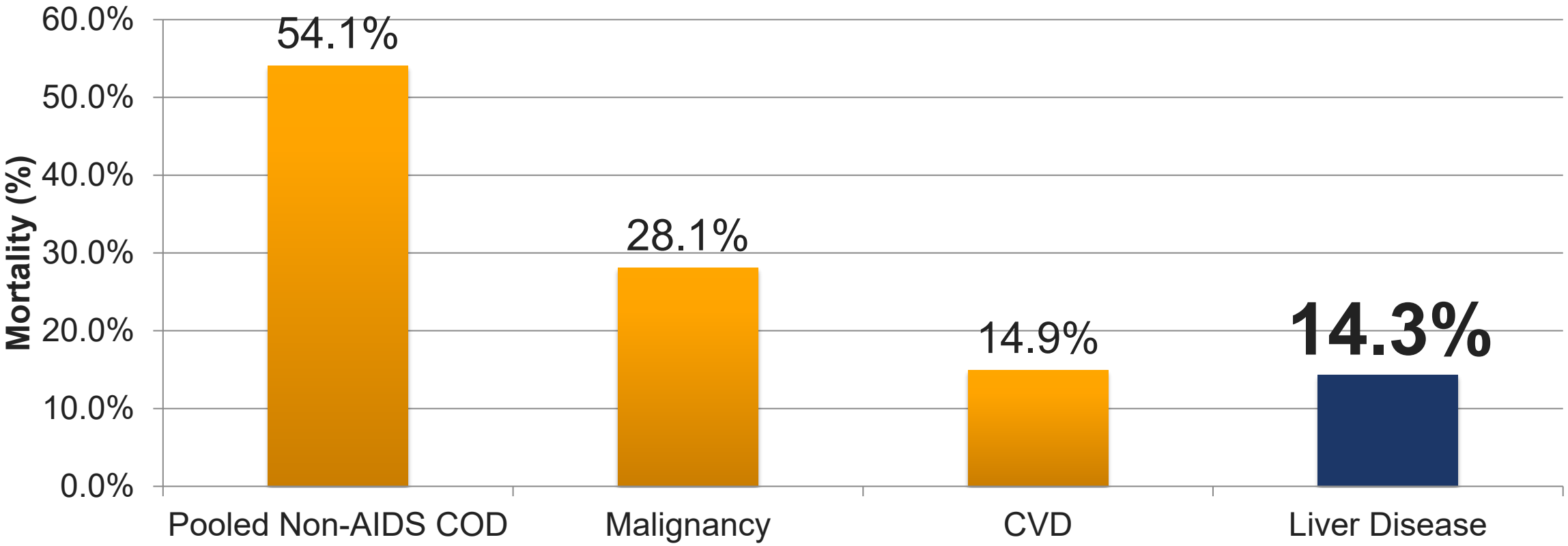
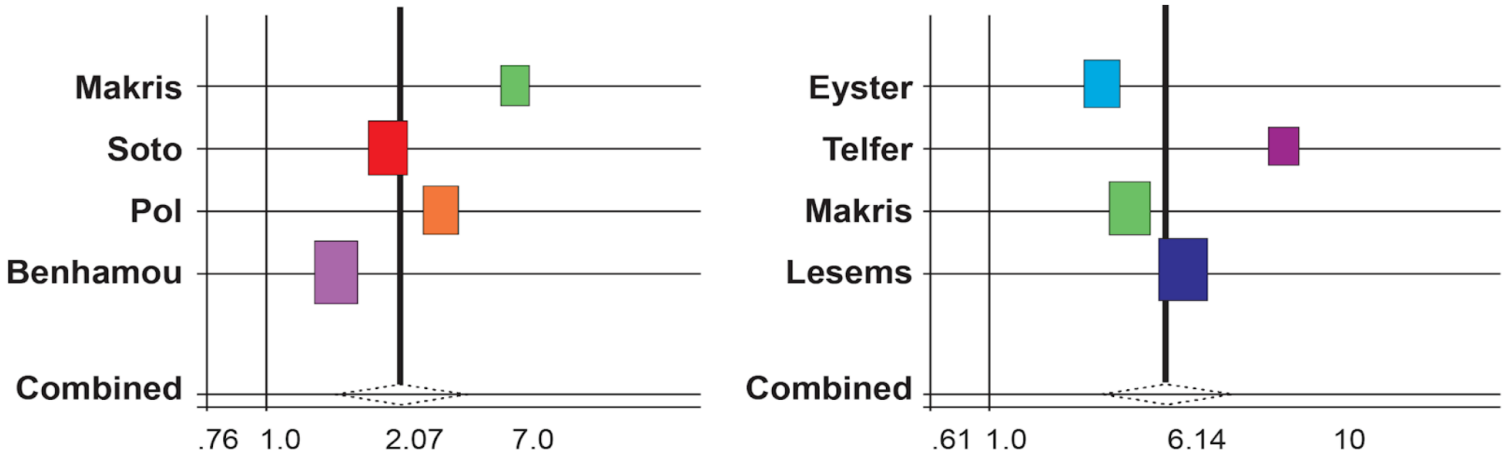
Non-HIV Cause of Death Among PWH In High Income Countries in PWH



Farahani M et al. *Int J STD AIDS* 2016.

Meta-analysis of the Impact of HIV Infection on the Natural History of Untreated HCV Infection[4]



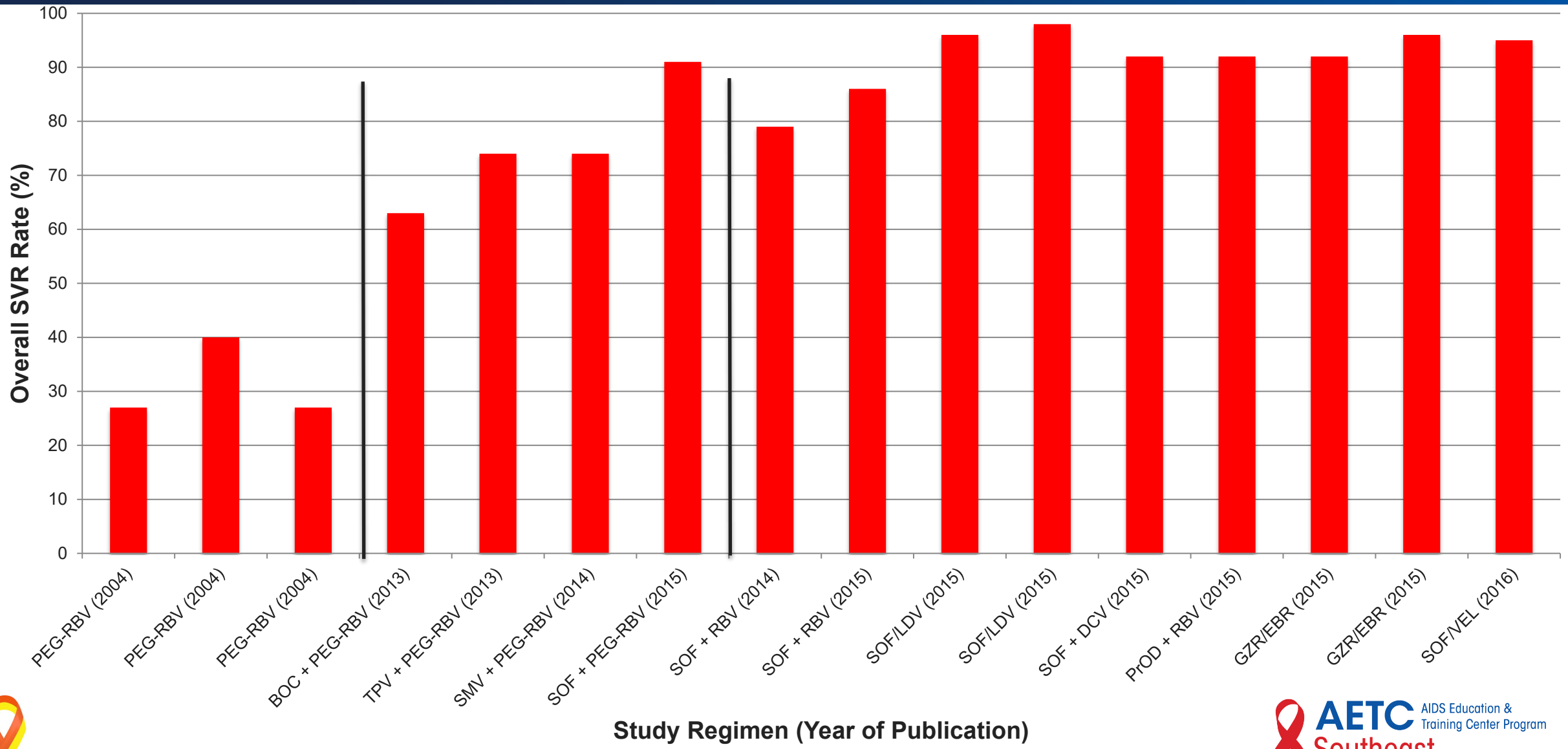
3. Fierer DS, Dieterich DT, Fiel MI, et al. Rapid progression to decompensated cirrhosis, liver transplant, and death in HIV-infected men after primary hepatitis C virus infection. Clin Infect Dis. 2013 Apr;56(7):1038-43. PubMed PMID: 23264364.
4. Graham CS, Baden LR, Yu E, et al. Influence of human immunodeficiency virus infection on the course of hepatitis C virus infection: a meta-analysis. Clin Infect Dis. 2001 Aug 15;33(4):562-9. PubMed PMID: 11462196.

Factors Associated with Fibrosis Progression in HIV/HCV Co-infected Persons

- Older age
- Higher BMI
- More alcohol use
- Higher HCV viral load
- Higher HIV viral load
- Lower CD4 count nadir

Kirk GD et al. *Ann Int Med* 2013.

Sustained Virologic Response in HIV/HCV Co-infection Trials



Adapted from Bagwell A and Chastain CA. *Curr Treat Options Infect Dis* 2016.

Treatment Recommendations for Patients With HIV/HCV Coinfection

RECOMMENDED	RATING
HIV/HCV-coinfected persons should be treated and retreated the same as persons without HIV infection, after recognizing and managing interactions with antiretroviral medications (see Initial Treatment of HCV Infection and Retreatment of Persons in Whom Prior Therapy Has Failed).	I, B

HCV GUIDANCE: RECOMMENDATIONS FOR TESTING, MANAGING, AND TREATING HEPATITIS C

Simplified HCV Treatment* for Treatment-Naive Patients Without Cirrhosis

WHO IS ELIGIBLE FOR SIMPLIFIED TREATMENT

Patients with chronic hepatitis C
who do not have cirrhosis and
have not previously received
hepatitis C treatment

WHO IS *NOT* ELIGIBLE

Patients who have any of the following characteristics:

- Prior hepatitis C treatment
- Cirrhosis
- Prior liver transplant
- HIV or HBsAg positive
- End-stage renal disease (ie, eGFR <30 mL/min/m^2)
- Currently pregnant

Drug Interactions Between DAAs and ARV Drugs—Recommended Regimens

Green indicates coadministration is safe; yellow indicates dose change or additional monitoring is warranted; pink indicates combination should be avoided.

	Ledipasvir/ Sofosbuvir (LDV/SOF)	Sofosbuvir/ Velpatasvir (SOF/VEL)	Elbasvir/ Grazoprevir (ELB/GRZ)	Glecaprevir/ Pibrentasvir (GLE/PIB)	Sofosbuvir/Velpatasvir/ Voxilaprevir (SOF/VEL/VOX)
Ritonavir-boosted atazanavir (ATZ)	▲ LDV ▲ ATZ[a]	▲ VEL ▲ ATZ[a]	▲ ELB ▲ GRZ ▲ ATZ	▲ GLE ▲ PIB ▲ ATZ	▲ VOX ▲ ATZ
Ritonavir-boosted darunavir (DRV)	▲ LDV ◄► DRV[a]	◄► VEL ◄► DRV[a]	▲ ELB ▲ GRZ ◄► DRV	▲ GLE ◄► PIB ▲ DRV	▲ VOX ▼ DRV
Ritonavir-boosted lopinavir (LPV)	No data[a]	◄► VEL ◄► LPV[a]	▲ ELB ▲ GRZ ◄► LPV	▲ GLE ▲ PIB ▲ LPV	No data
Ritonavir-boosted tipranavir (TPV/r)	No data	No data	No data	No data	No data
Efavirenz (EFV)	▼ LDV ▼ EFV[a]	▼ VEL ▼ EFV	▼ ELB ▼ GRZ ▼ EFV	No data	No data
Rilpivirine (RPV)	◄► LDV ◄► RPV	◄► VEL ◄► RPV	◄►ELB ◄►GRZ ◄►RPV	◄► GLE ◄► PIB ▲ RPV	◄► VOX ▼ RPV
Etravirine (ETV)	No data	No data	No data	No data	No data
Raltegravir (RAL)	◄► LDV ◄► RAL	◄► VEL ◄► RAL	◄► ELB ◄► GRZ ▲ RAL	◄► GLE ◄► PIB ▲ RAL	No data
Cobicistat-boosted elvitegravir (COB)	▲ LDV ▲ COB[a]	▲ VEL ▲ COB[a]	▲ ELB ▲ GRZ ▲ COB	▲ GLE ▲ PIB ▲ COB	▲ VOX ▲ COB[a]
Dolutegravir (DTG)	◄► LDV ◄► DTG	◄► VEL ◄► DTG	◄► ELB ◄► GRZ ▲ DTG	▼ GLE ▼ PIB ▲ DTG	No data
Tenofovir Alafenamide (TAF) / Emtricitabine (FTC) /Bictegravir (BIC)	▼ LDV ◄► BIC	No data	No data	No data	◄► VOX ▲ BIC
Maraviroc (MVC)	No data	No data	No data	No data	No data
Tenofovir (TFV) disoproxil fumarate	◄► LDV ▲ TFV[c]	◄► VEL ▲ TFV[b]	◄► ELB ◄► GRZ ▲ TFV	▲ TFV	▲ TFV[b]
Tenofovir (TFV) alafenamide	◄► LDV ▲ TFV[d]	◄► VEL ▲ TFV[d]	No data	◄► TFV	▲ TFV[b]

[a] Caution only with tenofovir disoproxil fumarate. [b] Increase in tenofovir depends on which additional concomitant antiretroviral agents are administered. [c] Avoid tenofovir disoproxil fumarate in patients with an eGFR <60 mL/min; tenofovir concentrations may exceed those with established renal safety data in individuals on ritonavir- or cobicistat-containing regimens. [d] Studied as part of fixed-dose combinations with ledipasvir/sofosbuvir or sofosbuvir/velpatasvir plus TAF, emtricitabine, elvitegravir, and cobicistat.

ART and DAA Drug-Drug Interactions (DDI)

- HIV protease inhibitors, ritonavir and cobicistat
  - Cause frequent interactions
- Tenofovir disoproxil fumarate (TDF)
  - Impacted by some HIV and HCV antiviral medications
  - May warrant additional renal function monitoring
- Older ART not studied with DAA therapy
  - Opportunity to update ART

Access

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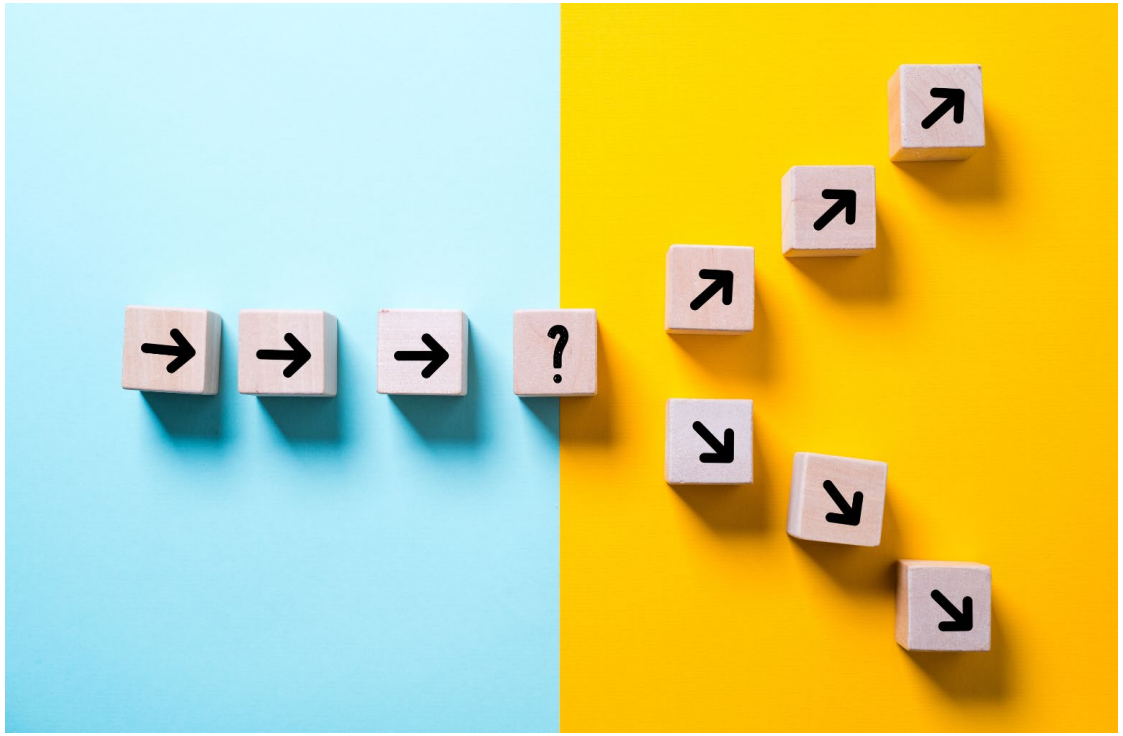
Accessing Treatment

- Insurance Status = Uninsured
- What pathway would be utilized?
- How do we effectively advocate?

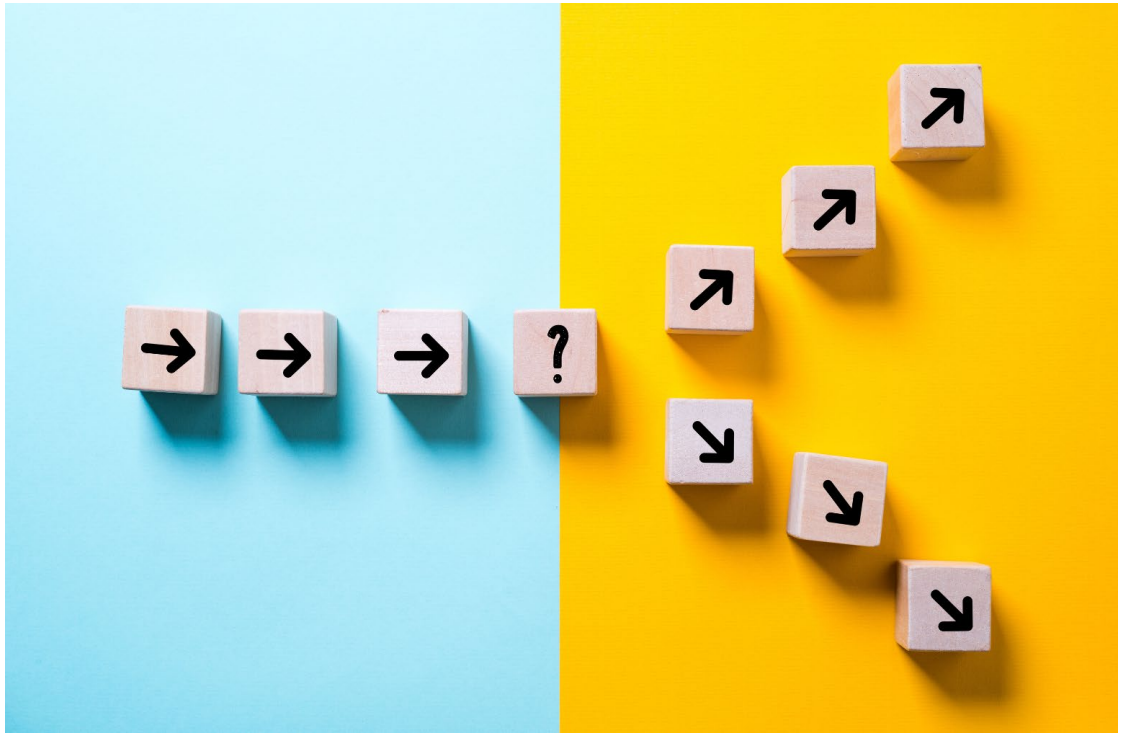


Requirements for PAP Forms

- **Proof of income*** (*must include anyone included in household size)
  - Tax return
  - Copy of disability letter
  - Social security income statement
  - Retirement and/or pension statement
  - Pay stub
  - Letter (if no other option available)
- **Proof of residency**
  - Letter of residency or state-issued ID
- **Household size***
- **Clinical information**

Accessing Treatment

- Insurance Status = Private Insurance
- What pathway would be utilized?
- What barriers are anticipated?



Coverage for Insured Patients

- **ALL** HCV medications typically require a prior authorization (PA)
- Can be completed:
  - Electronically (covermymeds.com)
    - Supporting documents collected/attached electronically
    - Approval/denial informed via fax
  - Paper
    - Call insurance and/or obtain form online
    - Paperwork and supporting documents submitted via fax to PA department
    - Approval/denial informed via fax
  - Phone (primarily used for PA extensions)

I submitted the PA form… now what?

- PA responses usually take 24-72 hours to return

PA approval

- Pharmacy should run a test claim to ensure approval and determine co-pay
- Determine if patient qualifies for co-pay assistance
  - Medicaid → $0-$1.50 co-pay (total per fill)
  - Medicare → cannot use co-pay cards, consider foundation/grant assistance
  - Private → obtain co-pay card

PA denial

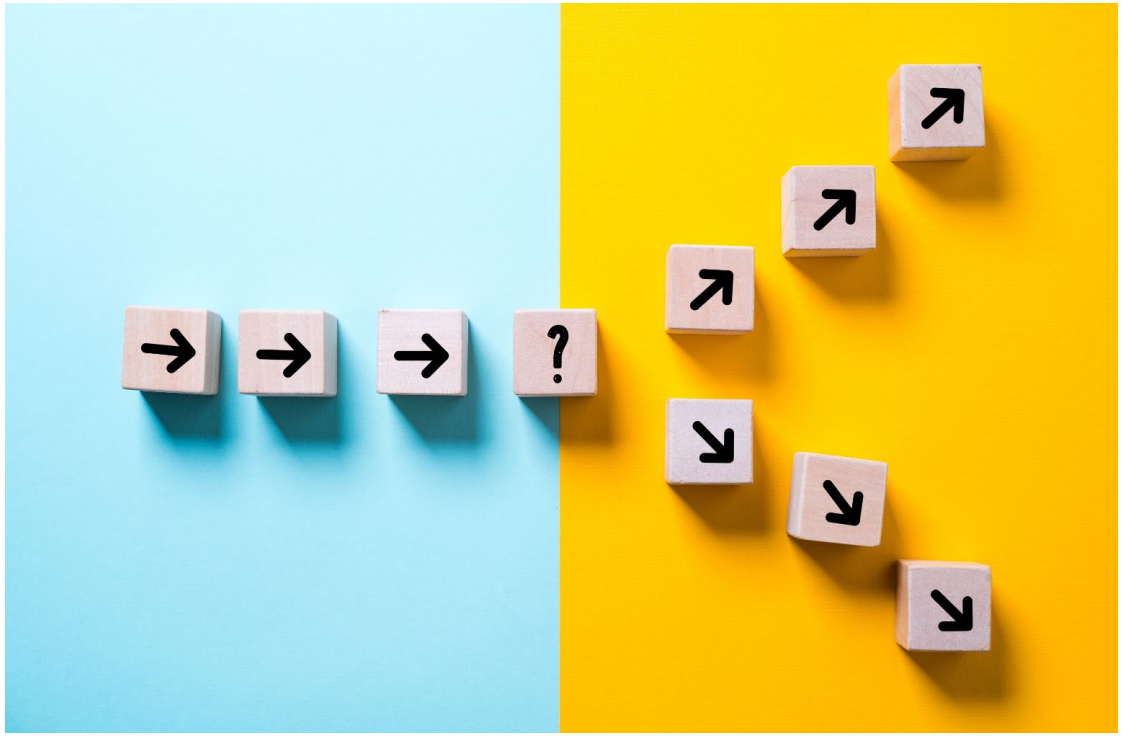
- If not stated on fax, call insurance to inquire about reason for denial (i.e. preferred agent, additional information needed)
- Verify next steps (e.g. appeal letter, peer-to-peer review, external review, etc.).
- Draft appeal letter with supporting documentation to submit
  - Include original PA paperwork, supporting documentation (AASLD/IDSA guidelines, clinical trial data, drug-interaction analysis, etc.)

Hepatitis C Medication Co-pay Cards

Drug	Co-pay	Copay Card Information	Card Details	Eligibility
Ledipasvir/sofosbuvir	$5	https://www.harvoni.com/support-and-savings/co-pay-coupon-registration	-Co-pay card will pay up to a maximum of 25% of the catalog price of 12 weeks of medication -Valid for 6 months from 1st redemption	-Resident of US, PR, or US territories -No state or federally funded programs -Age ≥18 years old
Sofosbuvir/velpatasvir (brand)	$5	http://www.epclusainfo.com/support-and-savings/co-pay-coupon-registration		
Authorized generic of ledipasvir/sofosbuvir and sofosbuvir/velpatasvir	$5	https://qv.trialcard.com/Asegua#/app/layout/home Contact: 1-855-769-7284		
Glecaprevir/pibrentasvir	$5	https://www.mavyret.com/savings-card Contact: 1-877-628-9738	-Co-pay card will pay up to a maximum of 25% of the catalog price of 8weeks of medication -Valid for 12 uses -Expires 12 months from 1st redemption	-Resident of US -No state or federally funded programs

Accessing Treatment

- Insurance Status = TennCare
- What pathway would be utilized?
- What barriers are anticipated?



A Note about Medicaid

- State Medicaid programs vary on sobriety requirements for HCV treatment approval
- **TennCare *no longer* has sobriety restrictions,** but has required:
  - Genotype, cirrhosis status, treatment naïve vs experienced, hepatitis B and HIV status, reason for selecting one agent over another, etc.
  - Prescription written in consultation with an ID or GI specialist
  - Clinical documentation/drug interaction screening

Example TennCare PA Form

1. What is the diagnosis and duration of therapy for which this drug is being requested? ☐ Chronic Hepatitis C, genotype 1 ☐ Chronic Hepatitis C, genotype 2 ☐ Chronic Hepatitis C, genotype 3 ☐ Chronic Hepatitis C, genotype 4 ☐ Chronic Hepatitis C, genotype 5 ☐ Chronic Hepatitis C, genotype 6 ☐ Other:_____ Requested Duration of Therapy: _____		
2. Does the patient have a diagnosis of compensated cirrhosis?	☐ Yes	☐ No
3. Is the patient post liver transplant?	☐ Yes	☐ No
4. Is the patient taking concomitantly with ribavirin?	☐ Yes	☐ No
5. Does the patient have any of the following: (if yes to any, go to question 6, if no, go to question 7)		
a. decompensated cirrhosis, defined as a Child-Pugh score of greater than 6 (Class B or C)?	☐ Yes	☐ No
b. history of HIV?	☐ Yes	☐ No
c. co-infection with Hepatitis B Virus	☐ Yes	☐ No
d. prior history with direct acting hepatitis C antiviral?	☐ Yes	☐ No

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Underinsured Patients

- Patients may require additional assistance after PA denial and/or inadequate financial coverage coverage

- Consider application to patient assistance program (PAP)
  - If denied, can be reviewed by an exception committee
  - Must contact supervisor at PAP to discuss

Adherence

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Adherence during HCV Therapy

- Limited data available in patients who have incomplete adherence that may impact achievement of sustained virologic response (SVR12)

- Adherence is critical while taking direct acting antiviral therapy to:
  - Ensure success of treatment
  - Prevent treatment failures
  - Avoid development of resistance

- IDSA/AASLD guidelines emphasize importance of adherence as part of **pre-treatment assessment, initial counseling, and ongoing monitoring**

Pretreatment and On-Treatment Monitoring

Recommended Assessments Prior to Starting DAA Therapy
Patients should be educated about the proper administration of DAA medications (eg, dose, frequency of medicines, food effects, missed doses, adverse events, etc), the crucial importance of adherence, and the need to inform the healthcare provider about any changes to their medication regimen.

Available Data Regarding Incomplete Adherence in HCV Treatment Courses

- Subgroup analysis from the **SIMPLIFY** trial
  - Investigated adherence among people with recent injection drug use taking SOF/VEL (n=103)
  - Medications administered via 1-week electronic bluster pack with sensors monitoring when doses were taken
  - Results:
    - Most common episodes of non-adherence lasted 1-2 days (61% of episodes) and 11% of episodes lasted ≥7 days; 35% of participants missed 1-4 doses
    - **All participants achieved SVR12+**
- Retrospective data collected from patient database of those who prematurely discontinued HCV treatment (n=365)
  - Results:
    - Majority of patients were being treated with SOF/VEL (24.7%), but variety of regimens represented
    - In patients **without** cirrhosis, SVR rates were lower in patients treated for less than 4 weeks (50% vs **99.1%**) than those treated ≥4 weeks
    - In patients **with** cirrhosis, SVR rates were lower in patients treated for less than 8 weeks (**83.3**% vs **94.6%**) than those treated ≥8 weeks

Cunningham EB, Amin J, Feld JJ, et al. *Int J Drug Policy.* 2018;62:14-23.
Fabbiani M, Lombardi A, Colaneri M, et al. *J Viral Hepat.* 2021;28(3):558-568.

Strategies to promote adherence

- Patient education
- Follow-up assessments while on treatment (telemedicine, phone, or in person) performed by pharmacist, technician, or support staff
- Cognitive/behavioral and lifestyle interventions
- Medication blister packs/adherence packaging
- Directly observed therapy
- Prompt management of adverse effects
- Technology based adherence reminders (i.e., alarms, apps on phone, reminders from pharmacy)

Grebely J, Oser M, Taylor LE, , et al. *J Infect Dis.* 2013;207(S1):S19-25.
Zuckerman A, Carver C, Chastain CA, et al. *Curr Treat Opt Infect Dis.* 2018;10(4):431-446.

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

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- When and in Whom
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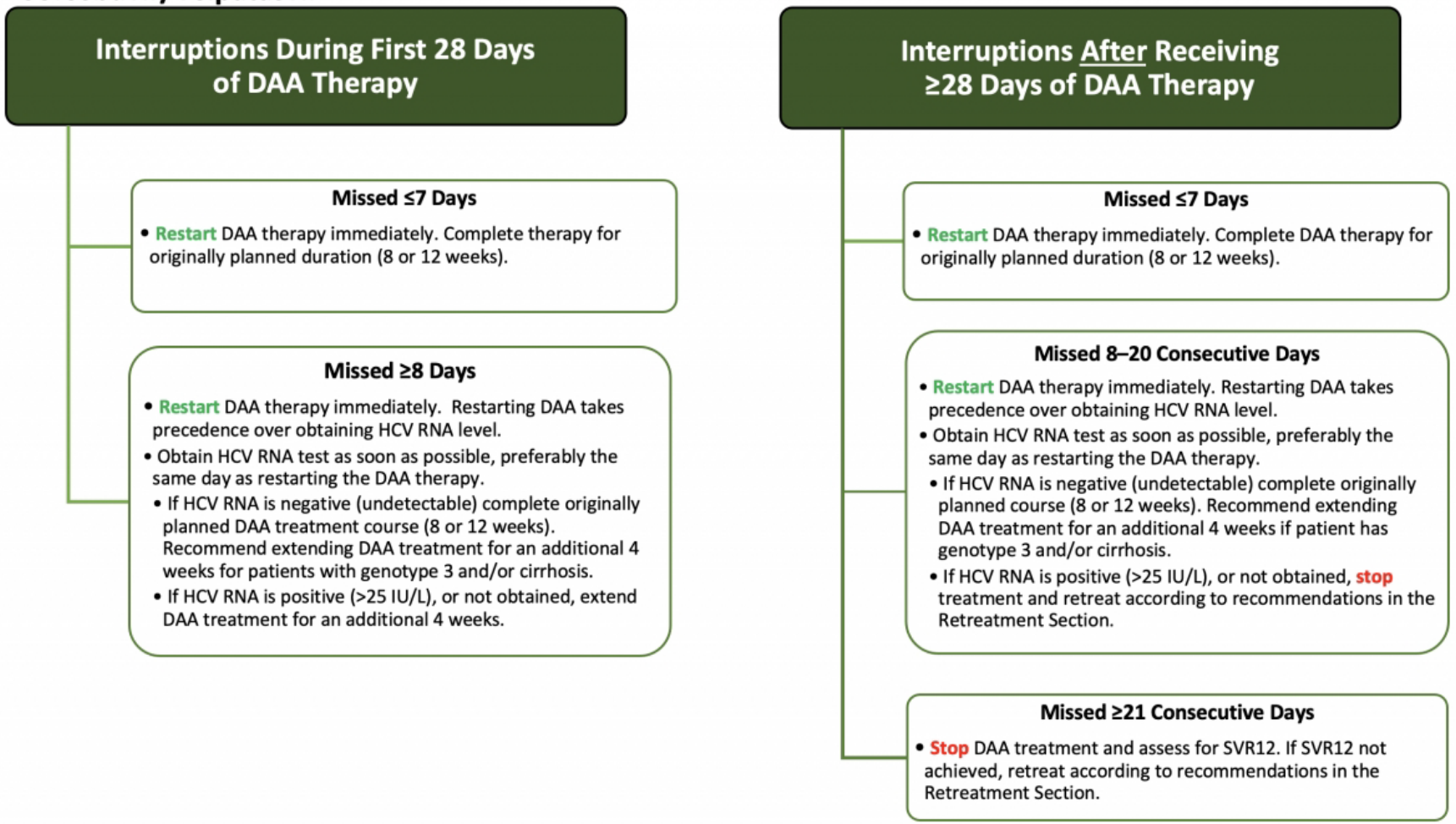
Figure 1. Recommended Management of DAA Treatment Interruptions for Treatment-Naive Patients, Without Cirrhosis or With Compensated Cirrhosis, Receiving Glecaprevir/Pibrentasvir or Sofosbuvir/Velpatasvir



DAA, direct-acting antiviral; HCV RNA, hepatitis C virus ribonucleic acid; SVR12, sustained virologic response 12 weeks after end of treatment.

General Approach to Nonadherence Per AASLD-IDSA HCV Treatment Guidance Panel

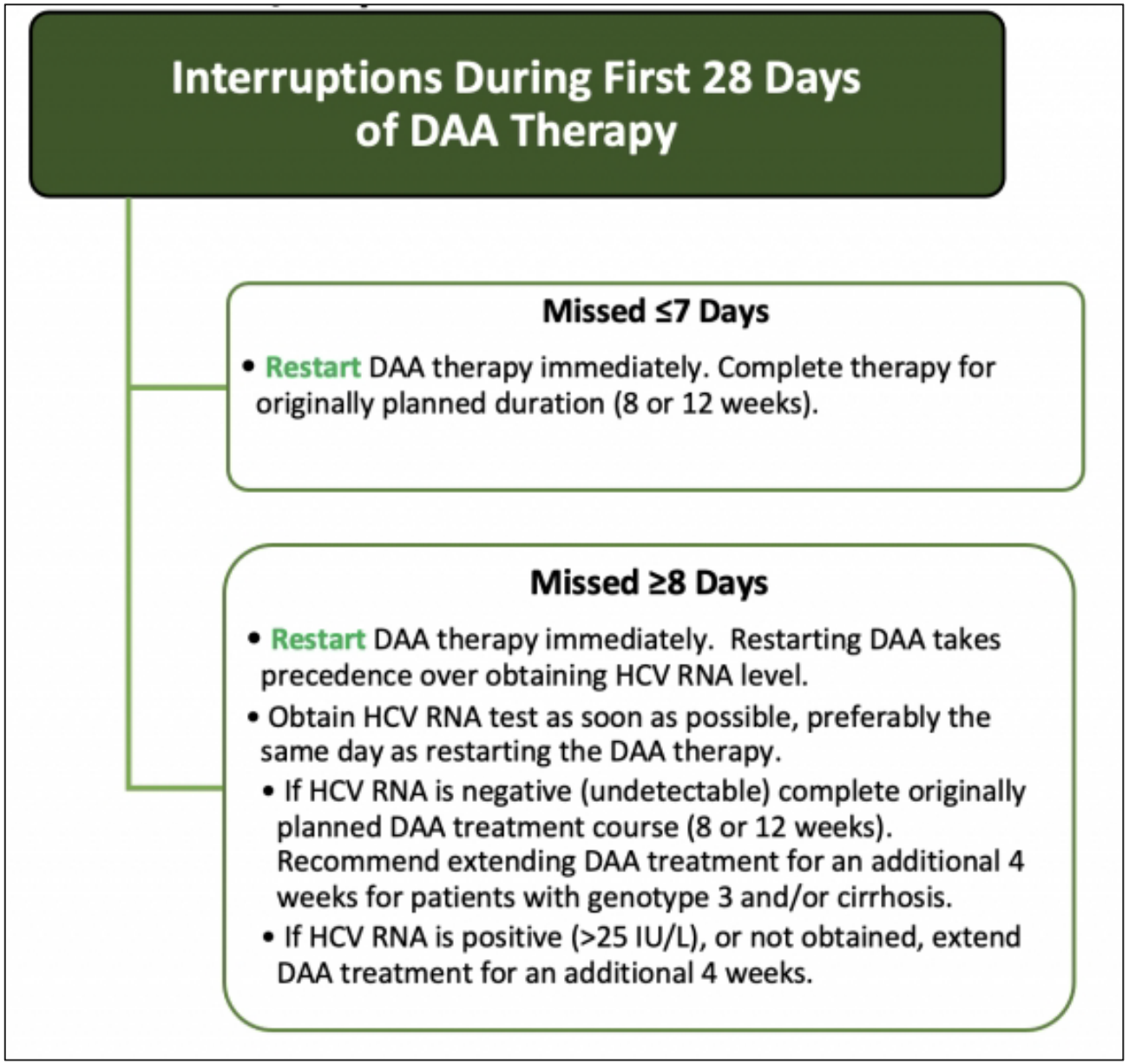
- Ask about factors contributing to nonadherence
- Counseling to optimize adherence
- Treatment interruptions <7 days unlikely to impact SVR12

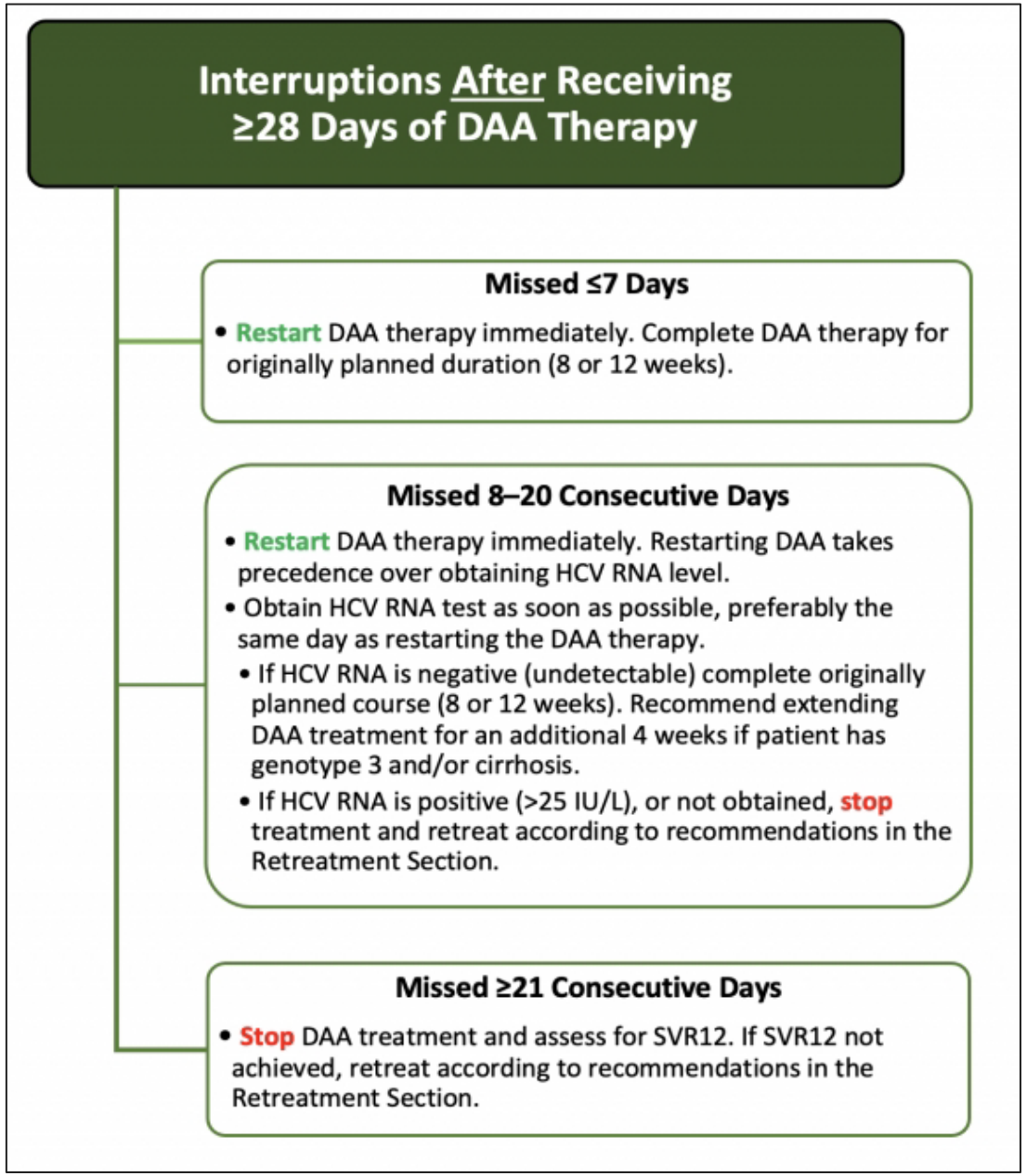
Caveats for Guidelines on DAA Treatment Interruptions

- Recommendations based on opinion of AASLD-IDSA HCV Treatment Guidance Panel

- Applicable to:
  - Treatment-naïve
  - Acute or chronic HCV
  - Without cirrhosis or with compensated cirrhosis
  - Receiving either GLE/PIB or SOF/VEL

- Not applicable to:
  - Prior DAA treatment
  - Receiving other DAA treatment regimens
  - Other populations (e.g., decompensated cirrhosis, post-transplant)


Interruptions During First 28 Days of DAA Therapy
Missed ≤7 Days
• Restart DAA therapy immediately. Complete therapy for originally planned duration (8 or 12 weeks).
Missed ≥8 Days
• Restart DAA therapy immediately. Restarting DAA takes precedence over obtaining HCV RNA level.
• Obtain HCV RNA test as soon as possible, preferably the same day as restarting the DAA therapy.
• If HCV RNA is negative (undetectable) complete originally planned DAA treatment course (8 or 12 weeks). Recommend extending DAA treatment for an additional 4 weeks for patients with genotype 3 and/or cirrhosis.
• If HCV RNA is positive (>25 IU/L), or not obtained, extend DAA treatment for an additional 4 weeks.


Interruptions After Receiving ≥28 Days of DAA Therapy
Missed ≤7 Days
• Restart DAA therapy immediately. Complete DAA therapy for originally planned duration (8 or 12 weeks).
Missed 8–20 Consecutive Days
• Restart DAA therapy immediately. Restarting DAA takes precedence over obtaining HCV RNA level.
• Obtain HCV RNA test as soon as possible, preferably the same day as restarting the DAA therapy.
• If HCV RNA is negative (undetectable) complete originally planned course (8 or 12 weeks). Recommend extending DAA treatment for an additional 4 weeks if patient has genotype 3 and/or cirrhosis.
• If HCV RNA is positive (>25 IU/L), or not obtained, stop treatment and retreat according to recommendations in the Retreatment Section.
Missed ≥21 Consecutive Days
• Stop DAA treatment and assess for SVR12. If SVR12 not achieved, retreat according to recommendations in the Retreatment Section.

Substance Use and HCV

AETC AIDS Education & Training Center Program Southeast

How does alcohol and substance use factor into HCV treatment?

AASLD/IDSA Guidance Re: HCV Treatment and Substance Use

Recommendation for When and in Whom to Initiate Treatment	
RECOMMENDED	RATING
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.	I, A

Recommendations for Screening and Treatment of HCV Infection in People Who Inject Drugs (PWID)	
RECOMMENDED	RATING
Annual HCV testing is recommended for PWID with no prior testing, or past negative testing and subsequent injection drug use. Depending on the level of risk, more frequent testing may be indicated.	IIa, C
Substance use disorder treatment programs and needle/syringe exchange programs should offer routine, opt-out HCV-antibody testing with reflexive or immediate confirmatory HCV-RNA testing and linkage to care for those who are infected.	IIa, C
PWID should be counseled about measures to reduce the risk of HCV transmission to others.	I, C
PWID should be offered linkage to harm reduction services including intranasal naloxone, needle/syringe service programs, medications for opioid use disorder, and other substance use disorder treatment programs.	I, B
Active or recent drug use or a concern for reinfection is not a contraindication to HCV treatment.	IIa, B

HCV and Alcohol Use

- Alcohol may contribute to liver disease independently of HCV
- Treatment of HCV may or may not mitigate progressive liver disease due to alcohol use
- Alcohol use is not a contraindication for HCV treatment
- Alcohol use may be considered a reason for denial by payers
- Patients should be counseled to abstain from alcohol use to eliminate impact on liver disease.
- Providers should use discretion when weighing risks/benefits of HCV therapy in these settings.

HCV and Substance Use

- Substance use is unlikely to contribute to liver disease independent of HCV
- Substance use (including injection drug use) is not a contraindication for HCV treatment
- Substance use may be considered a reason for denial by payers
- Patients should be counseled to abstain from drug use for general health.
- Abstinence and/or engagement in rehab may be required by payers.