HCV TREATMENT AND ITS APPLICATION IN A RURAL TRIBAL HEALTH PROGRAM

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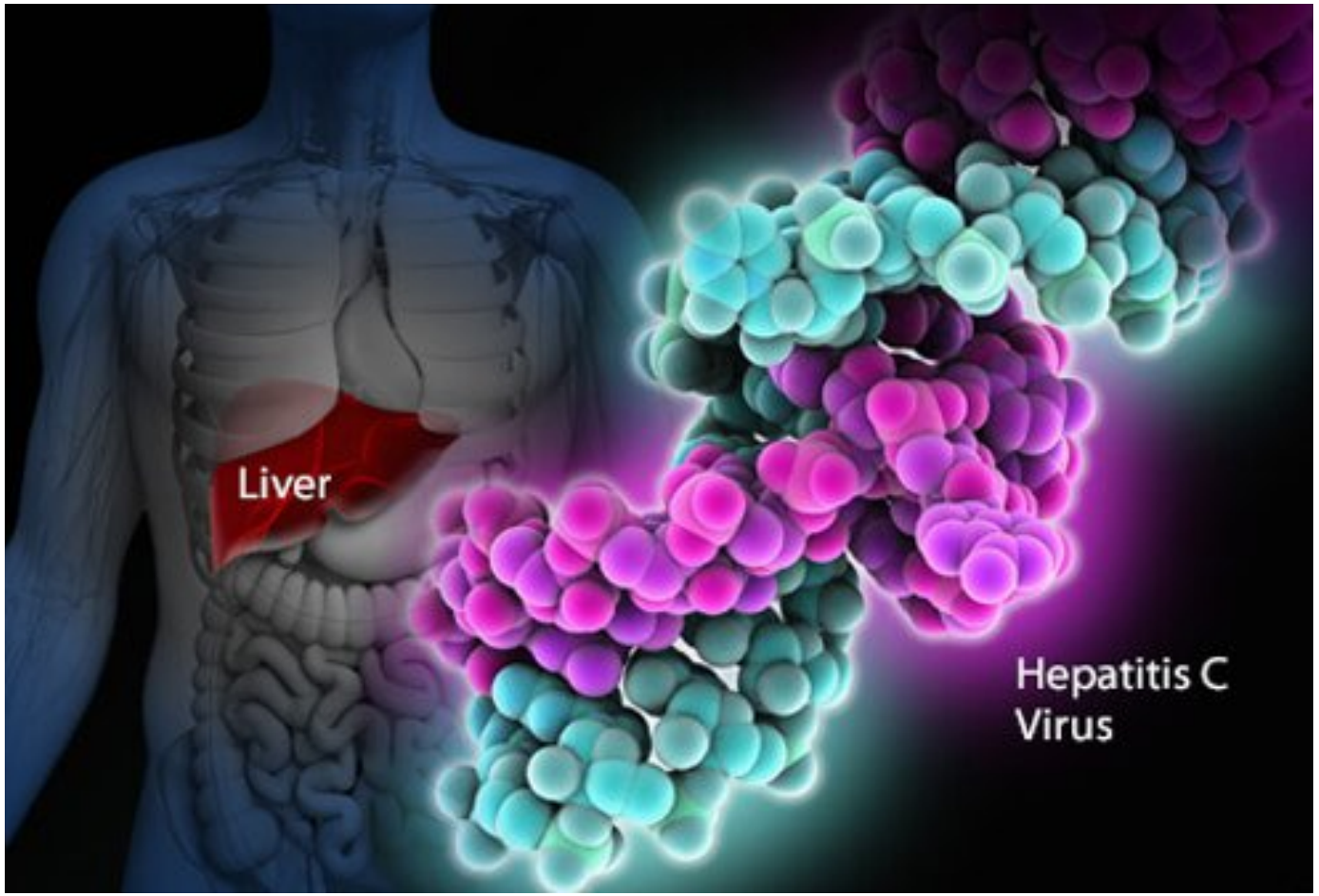
UNITED INDIAN HEALTH SERVICES



DISCLOSURES

- No financial relationships to disclose
- Thanks to Dr. Cleveland for slide deck
- Thanks to UCSF ECHO, Clinical Consultation Center and Gilead for the donation of slides towards this presentation.

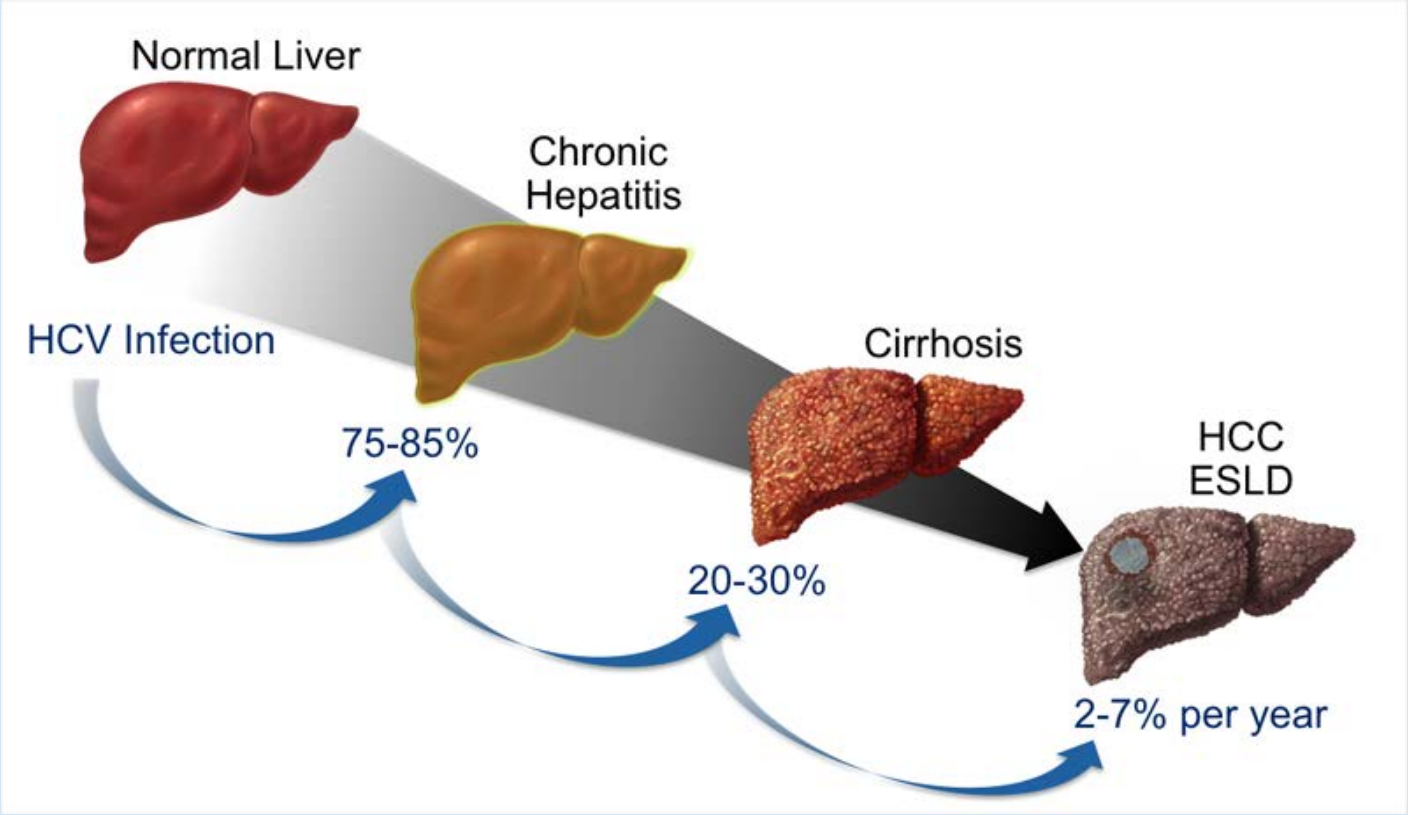
About our practice

- United Indian Health Services ~10,000 patients, rural north coast
- Joined UCSF HCV project ECHO group January 2016
- First patient initiated treatment July 2016
- 84 patients started on treatment, 55 with confirmed SVR 12
- Our team: MD, nurse, pharmacy technician
- ½ day per week HCV clinic

GOALS

- Review HCV screening guidelines
- Overview of HCV treatment – it isn’t hard
- Review cases
- Share eradication implementation strategies

Natural History



Not so fun HCV facts…

Leading cause of infectious disease death in US

2013 cost of HCV infection in US $6.5 billion

~3.5 million people in the US have HCV

~ Half in US are aware of HCV infection

Leading cause of Liver Cancer

Most common reason for Transplants

~ 70 million with HCV worldwide

Increases risk of DM by 70%

AI/AN with highest HCV rate in 2014

Mortality rates among AI/AN highest in US

Federal IHS sites have screened ~50% boomers

No HCV medications on IHS formulary

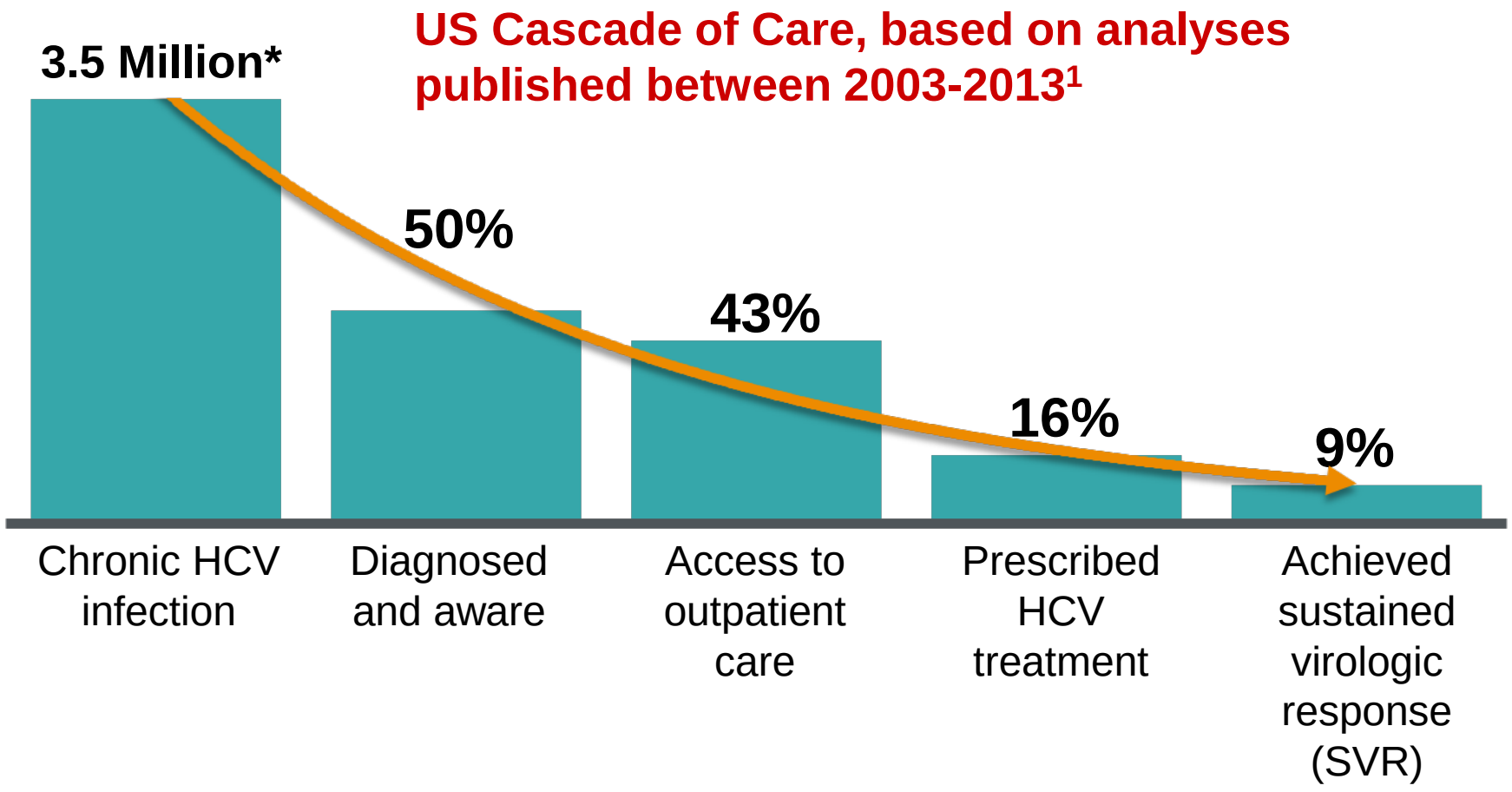
CDC, JAMA MAY 10, 2016, VOLUME 315, NUMBER 15, WHO

Byrd KK, et al Pub Hlth Rep 2011

NUWhite DL, et al. Hepatitis C infection and risk of diabetes: a systematic review and meta-analysis. Hepatol. 2008;49(5):831.

Holmberg S, et al. "Continued Rising Mortality from Hepatitis C Virus in the United States, 2003-2013"Presented at ID Week 2015, October 10, 2015, San Diego, CA

Population Studies Show a Significant Gap in HCV Care in the United States



*Including populations excluded from NHANES (e.g., the incarcerated, homeless, institutionalized, and those living on Native American reservations) brings the total estimate to 4.6 million[3]

1 Yehia BR, et al. *PLoS One*. 2014;9:e101554
2 Zein NN, et al. *Ann Intern Med*. 1996;125:634-639
3 Edlin BR, et al. *Hepatology*. 2015;62:1353-1363.

Potential Benefits of SVR (Virologic Cure)

- Reduced medical costs when compared with patients who do not achieve SVR[1,a]
- Reductions in HCC, liver-related mortality or transplantation, and all-cause mortality[2,a]
- Lowering the incidence of HCV-related comorbidities
- Improving relevant aspects of attention and neurocognitive performance[7,a]
- Certain improved quality-of-life measurements in a real-world cross-sectional study[8,a]
- Regression of cirrhosis and fibrosis are frequently observed in patients with cirrhosis who achieve long-term SVR (median period of 61 months)[9]

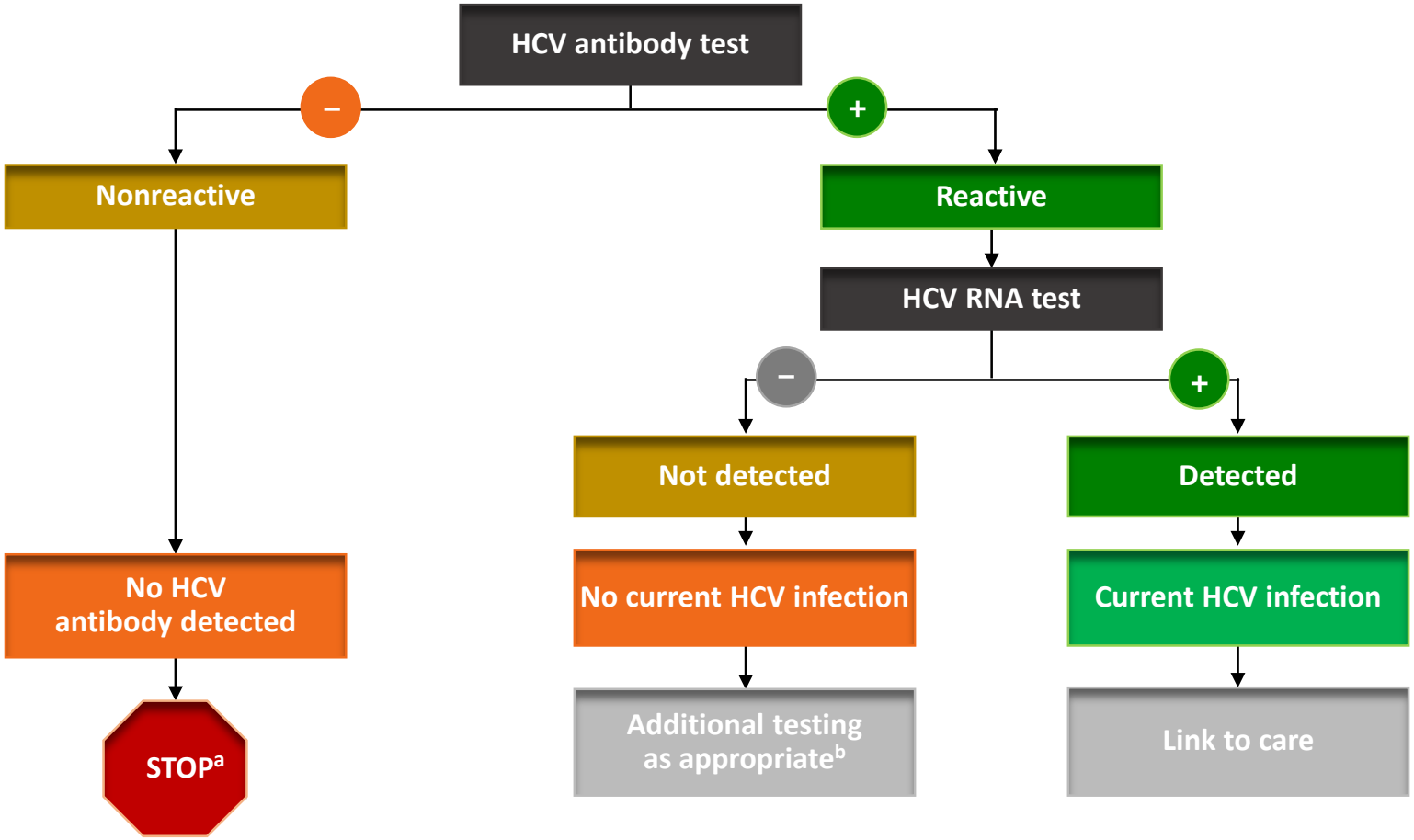
1. Manos MM, et al. *J Managed Care Pharmacy.* 2013;19:438-447.
2. van der Meer AJ, et al. *JAMA.* 2012;308:2584-2593.
3. Arase Y, et al. *Hepatology.* 2009;49:739-744.
4. Arase Y, et al. *J Med Virol.* 2014;86:169-175.
5. Arcaini L, et al. *Ann Oncol.* 2014;25:1404-1410.
6. Hsu YC, et al. *Hepatology.* 2014;59:1293-1302.
7. Kraus MR, et al. *Hepatology.* 2013;58:497-504.
8. John-Baptiste AJ, et al. *Am J Gastroenterol.* 2009;104:2439-2448.
9. D'Ambrosio R, et al. *Hepatology.* 2012;56:532-543.

TREATING HCV IS NOT DIFFICULT!!!!

- 70-80% Can be treated with once a day medication for 8-12 weeks
- Easier than managing many chronic conditions
- Cure rate with new medications 90-99%

Screening

Recommended Testing Sequence for HCV Screening and Diagnosis*

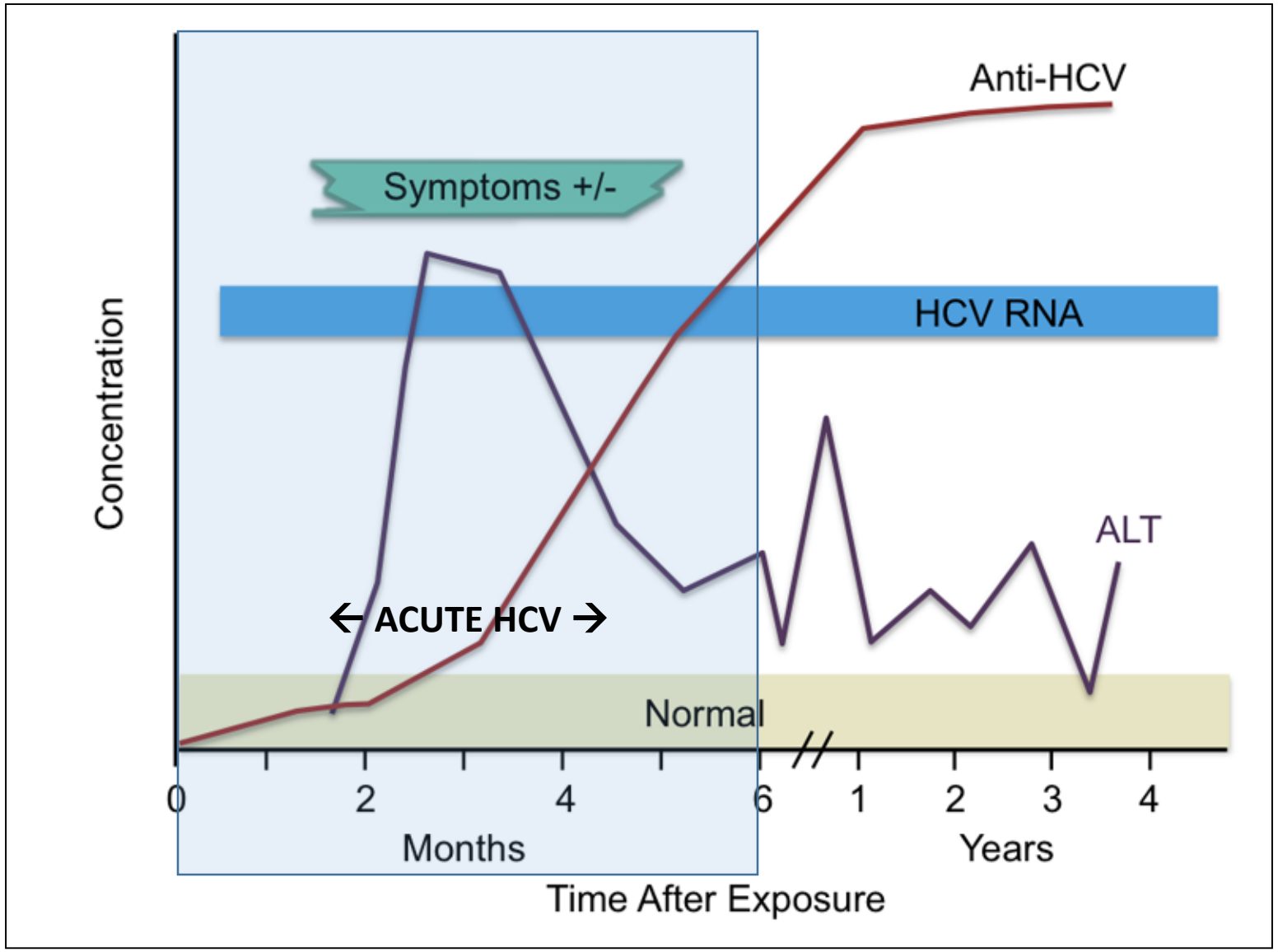


[a]For persons who might have been exposed to HCV within the past 6 months, testing for HCV RNA or follow-up testing for HCV antibody is recommended. For persons who are immunocompromised, testing for HCV RNA can be considered.

[b]To differentiate past, resolved HCV infection from biologic false positivity for HCV antibody, testing with another HCV antibody assay can be considered. Repeat HCV RNA testing if the person tested is suspected to have had HCV exposure within the past 6 months or has clinical evidence of HCV disease, or if there is concern regarding the handling or storage of the test specimen.

Adapted from CDC. MMWR. 2013;62:1-4.

Timing of Lab Marker Appearance

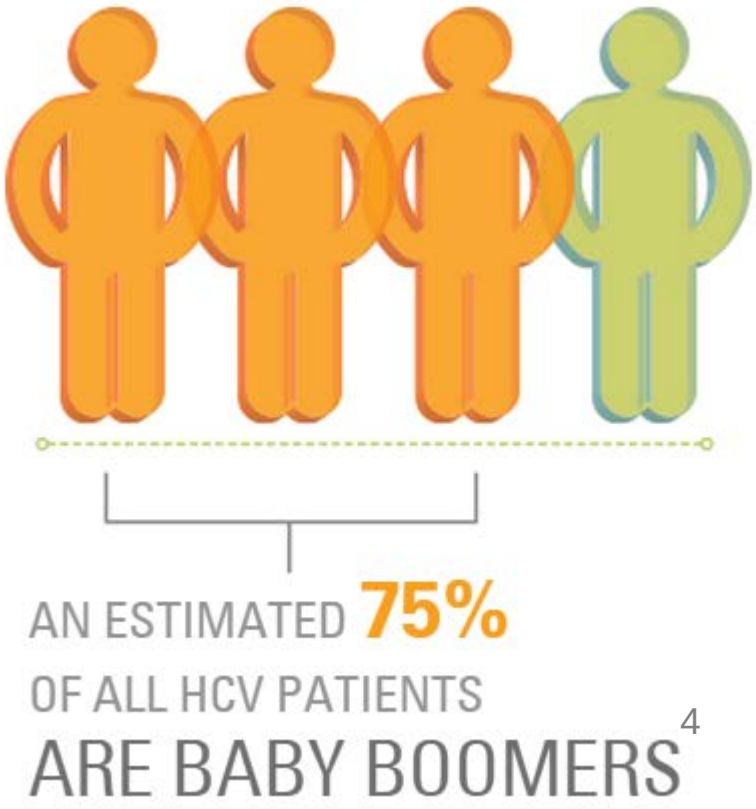


Acute HCV: 20-30% develop symptoms

[CDC]

CDC, USPSTF, and AASLD HCV Screening Recommendations in Baby Boomers

Screen all baby boomers (born between 1945 and 1965) regardless of the presence of risk factors[1, 2, 3]



Baby boomers account for 73% of HCV-related mortality and are at greatest risk for liver cancer and other liver-related complications[1]

1. Smith BD et al. *MMWR Recomm Rep*. 2012;61(RR-4):1-32.
2. USPSTF. http://www.uspreventiveservicestaskforce.org/uspstf12/hepc/hepcfinalrs.htm. Accessed October 12, 2016.
3. AASLD, IDSA, IAS-USA. Recommendations for testing, managing, and treating hepatitis C.http://www.hcvguidelines.org. Accessed January 19, 2017
4. CDC. http://www.cdc.gov/nchhstp/newsroom/docs/HCV-TestingFactSheetNoEmbargo508.pdf. Accessed October 12, 2016.

Regardless of Any Symptoms, Screen Patients Who Have Any of These Risk Factors[1-3]

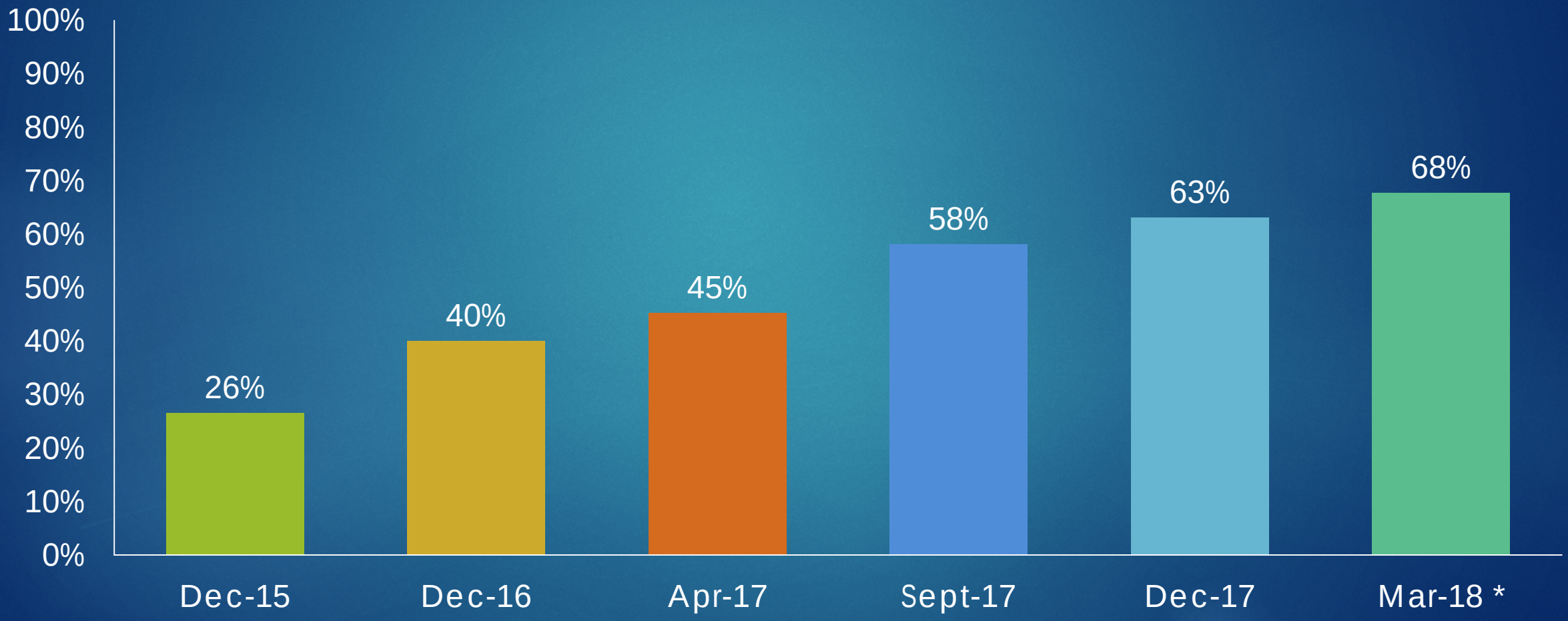
	Persons who ever injected illegal drugs
	HIV-infected patients
	Persons who have received tattoos from unlicensed or unregulated environ
	Those with certain medical conditions, including: • Persons who received clotting factor concentrates produced before 1987 • Persons who were ever on long-term hemodialysis • Persons with persistently abnormal alanine transaminase levels
	Prior recipients of transfusions or organ transplants, including: • Persons who were notified that they received blood from a donor who late positive for HCV infection • Persons who received a blood transfusion, blood components, or an organ before July 1992
	Healthcare, emergency medical, and public safety workers after needlesticks or mucosal exposures to HCV-positive blood
	Children born to an HCV-positive mother

- 1. Smith BD et al. *MMWR Recomm Rep.* 2012;61(RR-4):1-32.
- 2. USPSTF. http://www.uspreventiveservicestaskforce.org/uspstf12/hepc/hepcfinalrs.htm. Accessed December 7, 2015.
- 3. AASLD, IDSA, IAS-USA. Recommendations for testing, managing, and treating hepatitis C. http://www.hcvguidelines.org. Accessed December 7, 2015

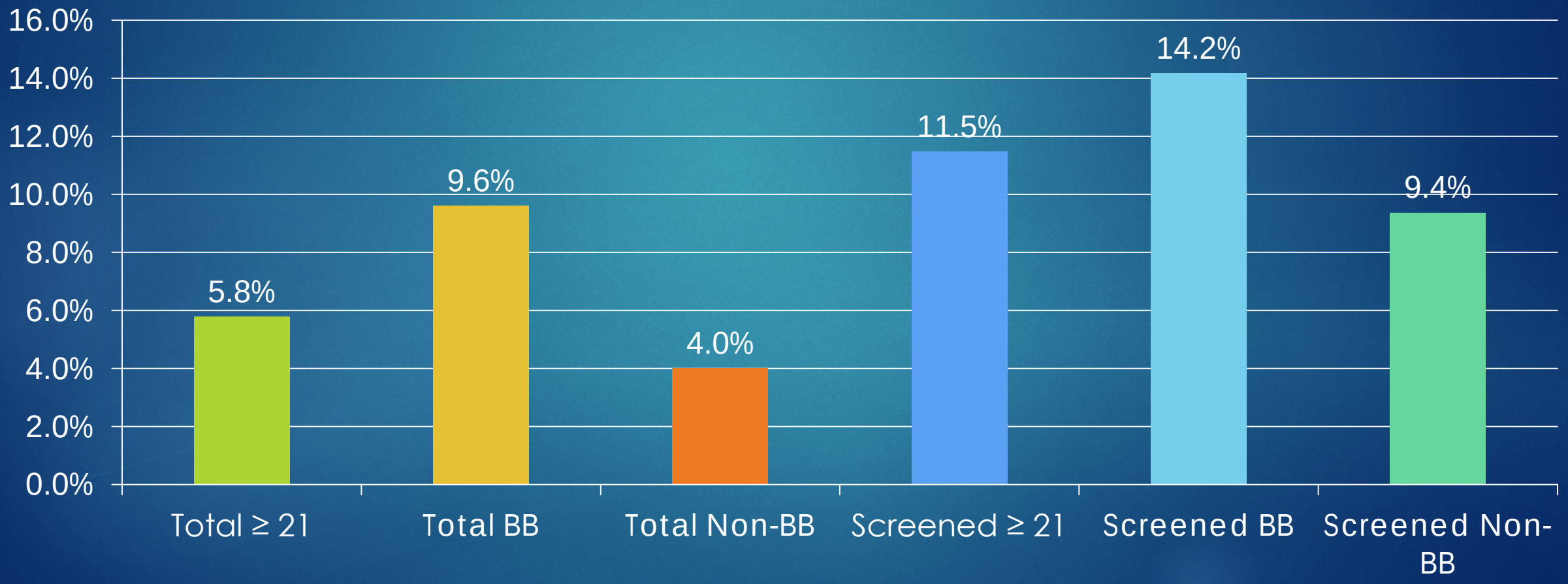
HCV Screening at UIHS

- Pregnant women
  - Universal screening since ~ 2005
  - Included in pre-natal laboratory panel
- High risk screening
  - Offered annually since ~2013
  - Opt-In for testing via questionnaire (dropped 11/2016)
- Baby boomers
  - Opt out - EMR prompt added in 11/2016
  - Age 50-75, one time screening ordered by MA per protocol
- Universal screening
  - Opt-out, one time screen all 21 years and older
  - Added 3/19/18

HCV Screening 50-75 year olds/1945-1965*



Prevalence - UIHS



Treatment

Guidelines

AASLD – IDSA (American Association for the Study of Liver Diseases and Infectious Disease Society of America)

www.HCVguidelines.org

Who to Treat

AASLD recommends:

- Treatment for **ALL** patients with chronic HCV infection

Except:

- Those with a short life expectancy (generally considered less than 12 months) that cannot be remediated by HCV therapy, liver transplantation or another directed therapy

Decompensated cirrhosis should be treated by or in close consultation with a hepatologist connected to a transplant center

EVERYONE ELSE GETS TREATED!

DO NOT hold treatment for those who are…

- *Actively drinking*
- *Smoking*
- *Doing drugs – IV or otherwise*

Treatment Comparison

Toenail Fungus

- Consultation visit
- Provide education, risks/benefits
- Send nail for culture
- Draw pre-treatment labs
- Return visit for prescription
- Check for medication interactions
- +/- Complete prior authorization
- Return visit for monitoring labs
- Return visit to assess for cure

Hepatitis C

- Consultation visit
- Provide education, risks/benefits
- Order ultrasound (if needed)
- Draw pre-treatment labs
- Return visit for prescription
- Check for medication interactions
- Complete prior authorization
- Return visit for monitoring labs
- Return visit to assess for cure

What is Project ECHO?

(Extension for Community Healthcare Outcomes)

Project ECHO empowers front-line primary care professionals to provide the right care, in the right place, at the right time.

Using a model of telementoring, collaborative medical education and care management, UCSF HCV experts are able to partner with community providers to extend Hepatitis C treatment expertise.

Training Opportunities and Support

UCSF ECHO

400 Parnassus Ave,
Ste. 331, SF, CA 94143

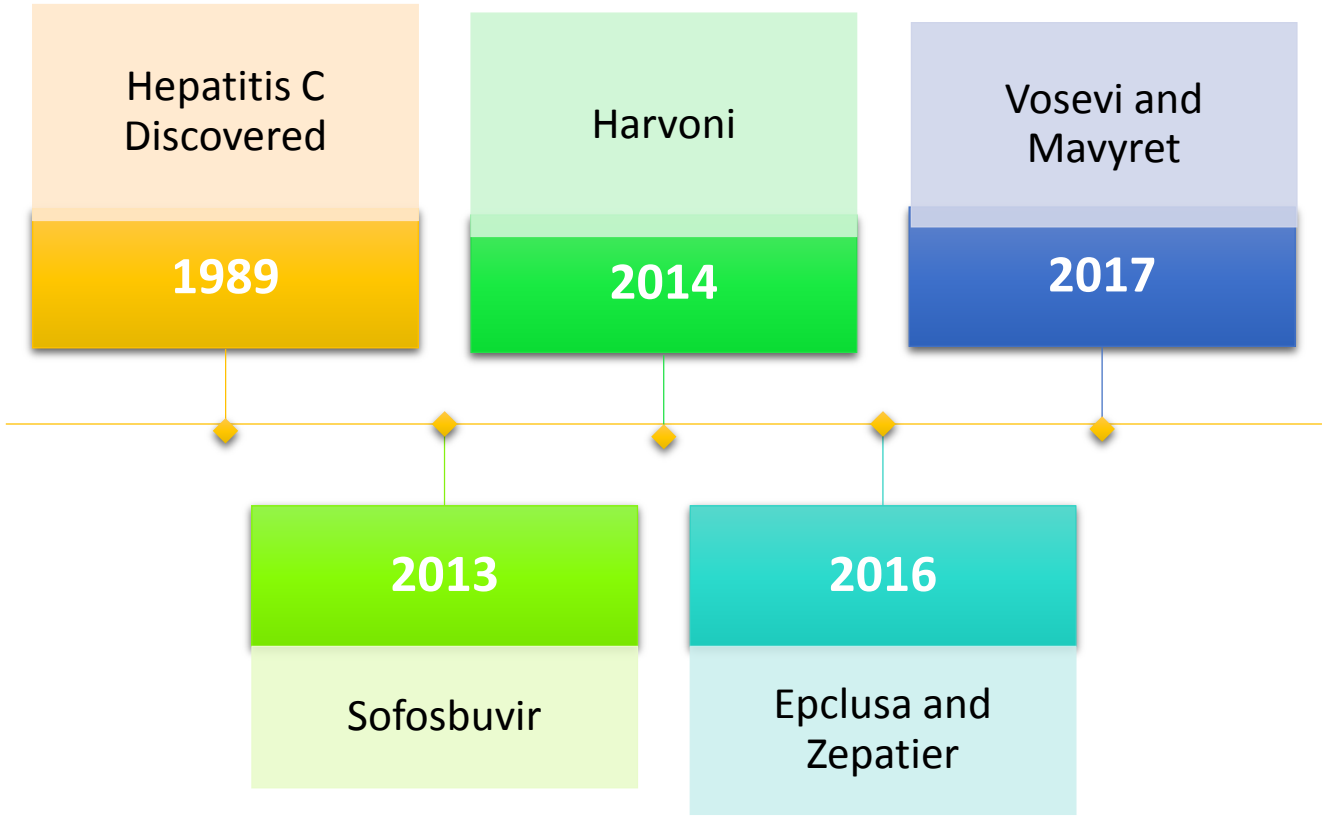
- Ph. (415) 353-4994
- Fax (415) 353-2562
- hcvecho@ucsf.edu

UNM ECHO

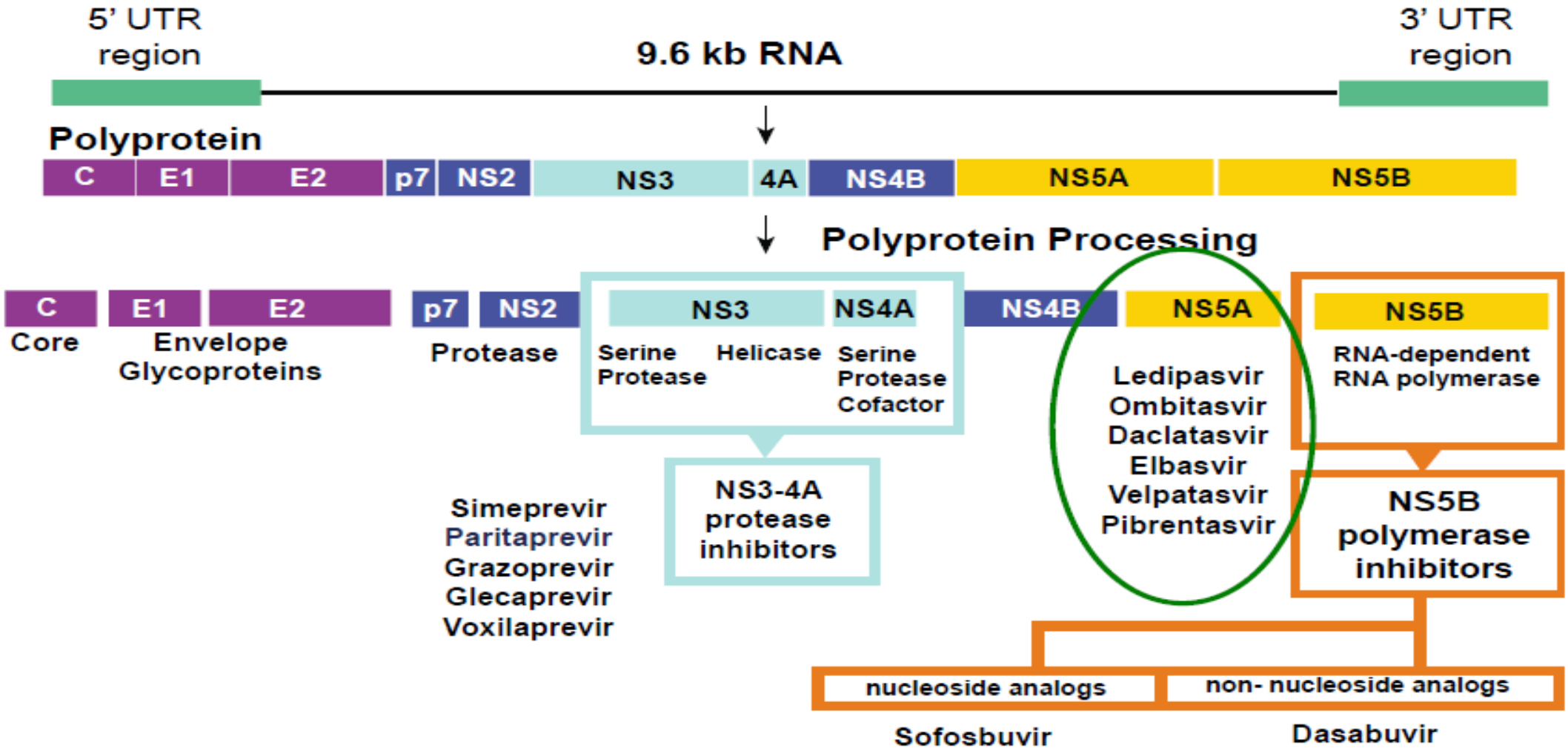
Albuquerque, NM

- (505) 272-5811
- http://echo.unm.edu
- Contact Person: Amy Armistad

Quick History of ARV Development of Primary Medications to Treat Hepatitis C



Multi-targeted Approach for Treatment: Approved Protease, Polymerase and NS5A Inhibitors



Adapted from McGovern B, Abu Dayyeh B, and Chung RT. *Hepatology*. 2008; 48:1700-12

HCV Treatment Options (Rough Overview)

Generic names	Brand name (Manufacturer)	FDA indication(s) (NOT 100% COMPLETE)
Glecaprevir (NS3/4A protease inhibitor) + Pibrentasvir (NS5A inhibitor)	Mavyret (AbbVie)	GT 1, 2, 3, 4, 5, or 6 • w/o cirrhosis or compensated cirrhosis (CP-A) • Okay in patient with CKD and HD • 8 week regimen if no cirrhosis
Sofosbuvir (NS5B polymerase inhibitor) + Velpatasvir (NS5A inhibitor)	Epclusa (Gilead)	• GT 1, 2, 3, 4, 5, or 6 w/o cirrhosis or compensated cirrhosis decompensated cirrhosis (in combination with RBV)
Sofosbuvir (NS5B polymerase inhibitor) + Velpatasvir (NS5A inhibitor) + Voxilaprevir (NS3/4A protease inhibitor)	Vosevi (Gilead)	GT 1, 2, 3, 4, 5, or 6 • previously treated with NS5A inhibitor-containing regimen
Elbasvir (NS5A inhibitor) + Grazoprevir (NS3/4A protease inhibitor)	Zepatier (Merck)	GT 1 or 4 *Breakthrough designation: use in ESRD/HD
Ledipasvir (NS5A inhibitor) + Sofosbuvir (NS5B polymerase inhibitor)	Harvoni (Gilead)	GT1, 4, 5, 6 • w/o cirrhosis or compensated cirrhosis • 8 week regimen for 1a w/VL < 6 million * Also approved for some children/adolescents 12yo+

Partnership HealthPlan of California Hepatitis C Treatment regimens – Naïve to prior treatment and IFN/RBV experienced, effective 10/1/2017

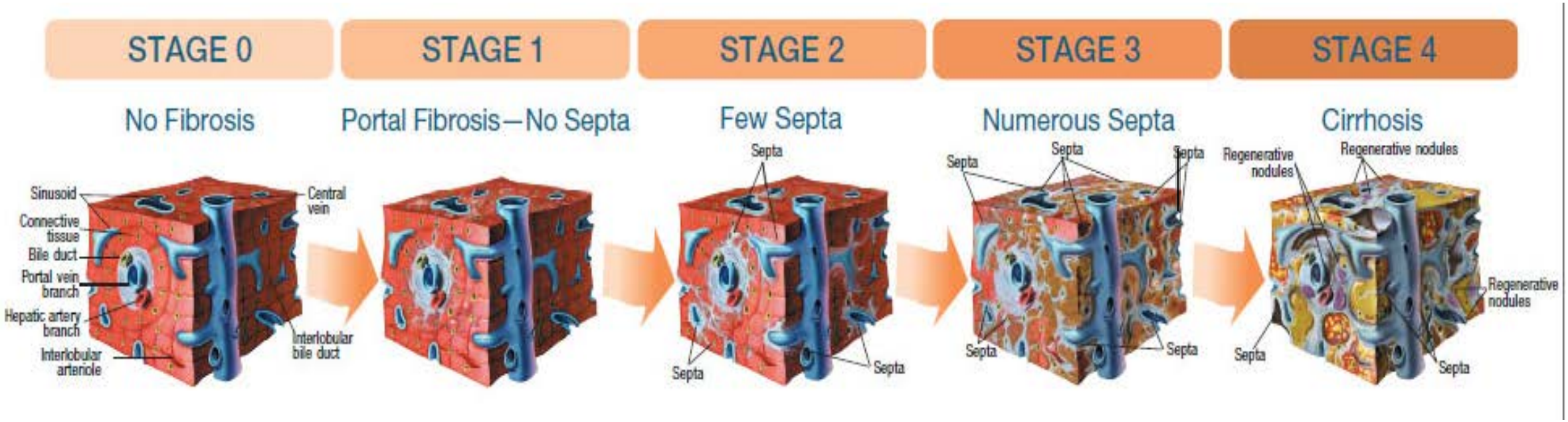
Genotype	Stage 0-1	Stage 2-4, unconfirmed cirrhosis		Cirrhosis -definitive (bx, US, FibroSure/Test ≥ 0.75, findings of portal HTN, ascites, varices, encephalopathy)			
				CTP A (Score 5-6)		CTP B (7-9) / C (10-15)	
		Naïve	IFN/RBV experienced	Naïve	IFN/RBV experienced	Naïve	IFN/RBV experienced
GT 1a, mixed a/b or indeterminate GT 1	Treatment eligible only under special circumstances defined by the State of California Medi-Cal benefit. Stages 0-1 criteria with special circumstances, the preferred treatment will follow that specified for stages 2-4 at right	**Mavyret x 8 weeks**		**Mavyret x 12 weeks**		**Epclusa / RBV WB X 12 weeks**	**Epclusa / RBV WB x 24 wks* OR Harvoni / RBV LD x 12 wks**
		Zepatier (no baseline NS5A RAVs) x 12 wks				Harvoni / RBV LD x 12 wks	
		Harvoni x 8 wks (HCV VL <6 million, non-black, HIV-uninfected)	Epclusa x 12 wks*	Epclusa x 12 wks	Epclusa x 12 wks*	Epclusa x 24 wks* if RBV intolerant	
		Epclusa x 12 wks		Harvoni x 12 wks		Harvoni x 24 wks* if RBV intolerant	
GT 1b		**Mavyret x 8 weeks**		**Mavyret x 12 weeks**		**Epclusa / RBV WB x 12 weeks**	**Epclusa / RBV WB x 24 wks* OR Harvoni / RBV LD x 12 wks**
		Zepatier x 12 wks				Harvoni / RBV LD x 12 wks	
		Harvoni x 8 wks (HCV VL <6 million, non-black, HIV-uninfected)	Epclusa x 12 wks*	Epclusa x 12 wks	Epclusa x 12 wks*	Epclusa x 24 wks* if RBV intolerant	
		Epclusa x 12 wks		Harvoni x 12 wks		Harvoni x 24 wks* if RBV intolerant	
GT 2		**Mavyret x 8 weeks**		**Mavyret x 12 weeks**		**Epclusa / RBV WB x 12 weeks**	**Epclusa / RBV WB x 24 wks***
		Epclusa x 12 wks	Epclusa x 12 wks*	Epclusa x 12 wks	Epclusa x 12 wks*	Dac / Sof / RBV LD x 12 wks	
						Epclusa x 24 wks* if RBV intolerant	
GT 3		**Mavyret x 8 weeks**	**Epclusa x 12 weeks* (RAS testing for Y93H required)**	**Mavyret x 12 weeks**	**Vosevi x 12 weeks***	**Epclusa / RBV WB x 12 weeks**	**Epclusa / RBV WB x 24 wks***
		Epclusa x 12 wks	*Mavyret x 16 wks*	Epclusa x 12 wks (RAS testing for Y93H required)	Zepatier / Sovaldi x 12 wks*	Dac / Sof / RBV LD x 12 wks	
			Vosevi x 12 wks (when Y93H present)	*Vosevi x 12 wks (when Y93H present)*	*Mavyret x 16 wks**	Epclusa x 24 wks* if RBV intolerant	
					*Epclusa / RBV WB x 12 wks**		
GT 4		**Mavyret x 8 weeks**		**Mavyret x 12 weeks**		**Epclusa / RBV WB X 12 weeks**	**Epclusa / RBV WB x 24 wks***
		Zepatier x 12 wks	Zepatier x 12 wks* (virologic relapse after prior interferon/ribavirin therapy)	Zepatier x 12 wks	Zepatier x 12 wks* (virologic relapse after prior interferon/ribavirin therapy)	Harvoni / RBV LD x 12 wks	
		Epclusa x 12 wks	Epclusa x 12 wks*	Epclusa x 12 wks	Epclusa x 12 wks*	Epclusa x 24 wks* if RBV intolerant	
						Harvoni x 24 wks* if RBV intolerant	
GT 5,6		**Mavyret x 8 weeks**		**Mavyret x 12 weeks**		**Epclusa / RBV WB X 12 weeks**	**Epclusa / RBV WB x 24 wks***
		Epclusa x 12 wks				Harvoni / RBV LD x 12 wks	
		Harvoni x 12 wks				Epclusa x 24 wks* if RBV	
						Harvoni x 24 wks* if RBV	
Pre/Post Liver Transplant		**Case by Case Review, Transplant Specialist Referral Required**					

Cases

Case 1

- 46 year old female with active HCV, HTN, GERD
- H/O IVDU in 20's no current DOA
- No history of prior HCV treatment
- Genotype 3 with viral load of ~ 4 million
- Medications – Prilosec 20mg QD, enalapril
- Labs – Hgb 11.2, Plt 210,000, Alt 54 U/L, AST 45 U/L, Bili/Cr/albumin/INR normal, HBV cAb/sAg negative/sAb positive, HIV neg
- Ultrasound normal
- Physical exam normal
- Blue Cross

Liver Fibrosis Progression Diagram



*As this cascade of processes continues, fibrous tissue bands (**septa**) separate hepatocyte nodules, which eventually replace the entire **liver** architecture, leading to decreased blood flow throughout (Wikipedia)*

Razavi H, et al. *Hepatology*. 57(6):2164-2170

*An assessment of liver fibrosis using either non-invasive testing **OR** direct tissue examination is recommended by AASLD/IDSA[1]**

Non-Invasive Options[2]

Imaging and Elastography

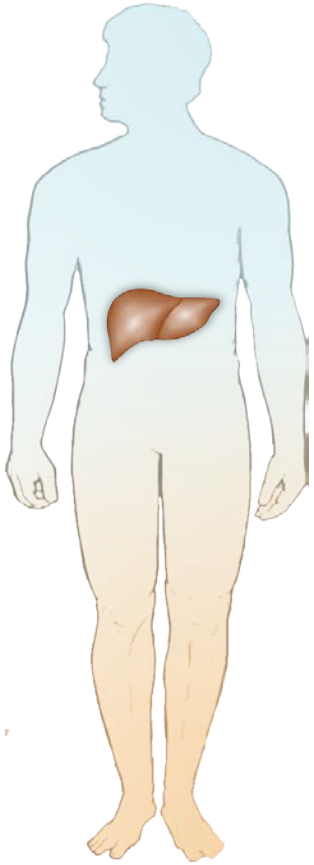
- Ultrasound (nodular liver, signs of portal HTN)
- Transient elastography (FibroScan®)
- Magnetic resonance elastography

Biomarkers

- FibroSURE™ (based on 6 serum biomarkers)
- FIB-4 (based on age, ALT, AST, and platelet count)
- APRI (based on AST and platelet count)

Physical Signs and Labs

- CHEMISTRY TESTS (Elevated Liver Enzymes, Bilirubin, and INR, or low Platelets, Albumin)
- PHYSICAL SIGNS (i.e. Spider Angioma, Telangiectasia, Palmar Erythema, Varices on EGD)



Direct Tissue Examination[3]

Biopsy

- Allows for direct examination of liver tissue for evidence of fibrosis
- Prone to sampling error
- Potential complications include pain and bleeding

ALT = alanine aminotransferase; AST = aspartate aminotransferase; APRI = AST to Platelet Ratio Index.

1. AASLD/IDSA. Recommendations for Testing, Managing, and Treating Hepatitis C. http://www.hcvguidelines.org. Accessed August 18, 2015.
2. Martinez SM, et al. *Hepatology*. 2011;53:325-335. 3. Rockey DC, et al. *Hepatology*. 2009;49:1017-1044.

APRI

- APRI (Aspartate Aminotransferase-to-Platelet ratio index)
- > 0.7 suggests significant fibrosis
- > 1.0 suggests cirrhosis (76% sens, 72% spec)
- > 2 more specific for cirrhosis (91%) but less sens (46%)

$$\textbf{APRI} = \frac{\dfrac{\text{AST Level}}{\text{AST (Upper Limit of Normal)}}}{\text{Platelet Count } (10^9/\text{L})} \times 100$$

http://www.hepatitisc.uw.edu/page/clinical-calculators/apri

Wai CT, et al. Hepatology 2003;38:518-26

FIB-4

- FIB-4 (Fibrosis-4 score uses age, AST, platelets and ALT)
- < 1.45 suggests advanced fibrosis NOT present
- > 3.25 suggests advanced fibrosis is present

$$\text{FIB-4} = \frac{\text{Age (years)} \times \text{AST (U/L)}}{\text{Platelet Count } (10^9/\text{L}) \times \sqrt{\text{ALT (U/L)}}}$$

http://www.hepatitisc.uw.edu/page/clinical-calculators/fib-4

Vallet-Pichard A, Mallet V, Nalpas B, et al. FIB-4: an inexpensive and accurate marker of fibrosis in HCV infection. comparison with liver biopsy and fibrotest. Hepatology. 2007;46:32-6.

Case 1

- 46 year old female with active HCV, HTN, GERD
- APRI 0.536
- Fib-4 1.34
- Ultrasound normal
- Physical exam normal
- Blue Cross

Partnership HealthPlan of California Hepatitis C Treatment regimens – Naïve to prior treatment and IFN/RBV experienced, effective 10/1/2017

Genotype	Stage 0-1	Stage 2-4, unconfirmed cirrhosis		Cirrhosis -definitive (bx, US, FibroSure/Test ≥ 0.75, findings of portal HTN, ascites, varices, encephalopathy)			
				CTP A (Score 5-6)		CTP B (7-9) / C (10-15)	
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		Zepatier (no baseline NS5A RAVs) x 12 wks				Harvoni / RBV LD x 12 wks	
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		Epclusa x 12 wks		Harvoni x 12 wks		Harvoni x 24 wks* if RBV intolerant	
GT 1b		**Mavyret x 8 weeks**		**Mavyret x 12 weeks**		**Epclusa / RBV WB x 12 weeks**	**Epclusa / RBV WB x 24 wks* OR Harvoni / RBV LD x 12 wks**
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		Epclusa x 12 wks		Harvoni x 12 wks		Harvoni x 24 wks* if RBV intolerant	
GT 2		**Mavyret x 8 weeks**		**Mavyret x 12 weeks**		**Epclusa / RBV WB x 12 weeks**	**Epclusa / RBV WB x 24 wks***
		Epclusa x 12 wks	Epclusa x 12 wks*	Epclusa x 12 wks	Epclusa x 12 wks*	Dac / Sof / RBV LD x 12 wks	
						Epclusa x 24 wks* if RBV intolerant	
GT 3		**Mavyret x 8 weeks**	**Epclusa x 12 weeks* (RAS testing for Y93H required)**	**Mavyret x 12 weeks**	**Vosevi x 12 weeks***	**Epclusa / RBV WB x 12 weeks**	**Epclusa / RBV WB x 24 wks***
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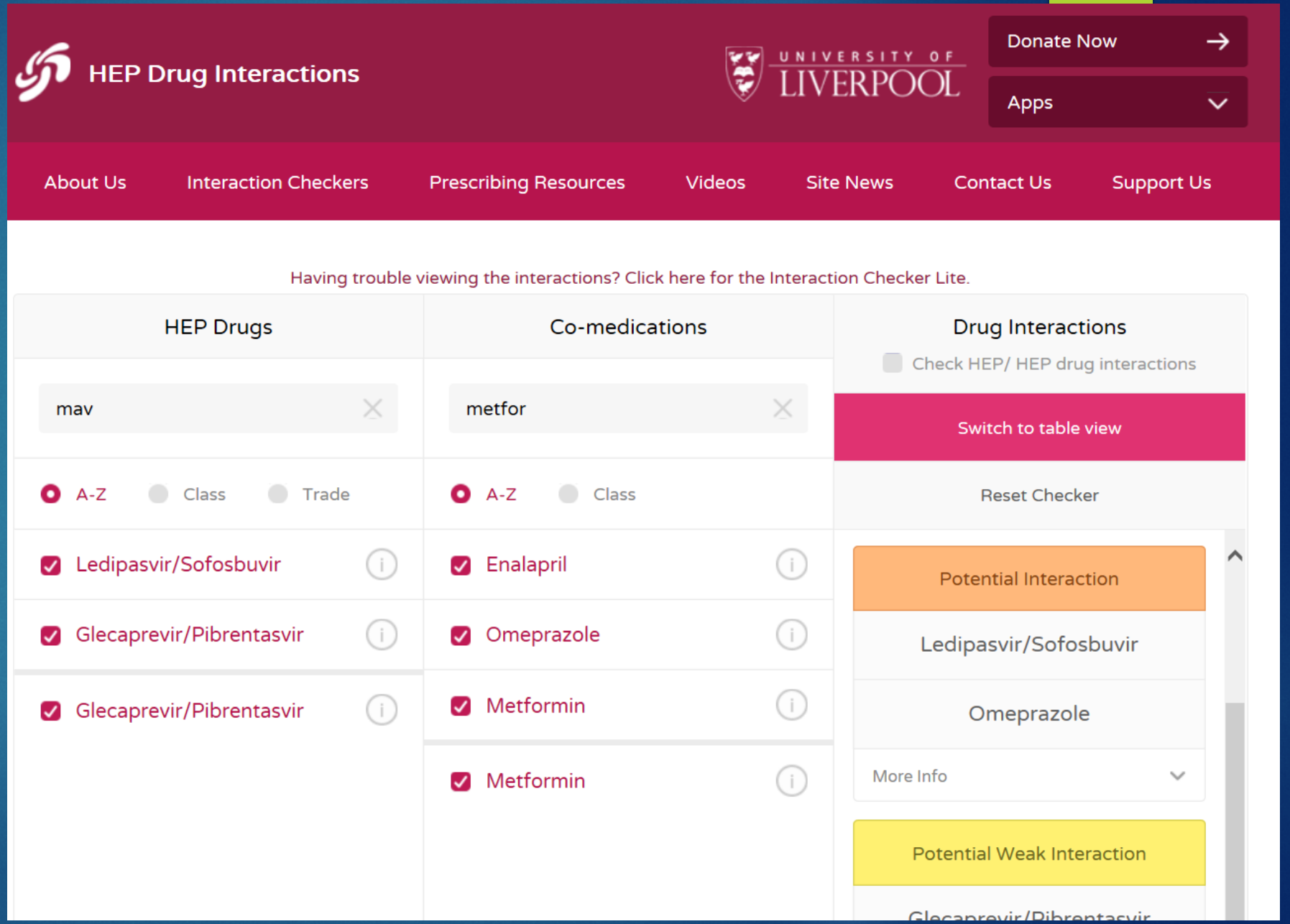
		Harvoni x 12 wks				Epclusa x 24 wks* if RBV	
						Harvoni x 24 wks* if RBV	
Pre/Post Liver Transplant		**Case by Case Review, Transplant Specialist Referral Required**					

Medication Interactions

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



SUMMARY ACID BLOCKER AND TIMING (UCSF)

Much to do about something
Acid Blockers

	How to take	Daily PPI‡	BID PPI	H2-Blocker*
Sofosbuvir + Daclatasvir	±			
Sofosbuvir/ledipasvir (Harvoni)	±	Harvoni + PPI (empty stomach)	NO	Harvoni + H2-Blocker
Sofosbuvir/velpatasvir (Epclusa)	±	Epclusa (food) PPI 4h later	NO	Epclusa + H2-Blocker
Sofosbuvir/velpatasvir/ Voxilaprevir (Vosevi)	With food	Vosevi (food) +PPI	??	Vosevi (food)
Elbasvir/grazoprevir (Zepatier)	±			
Glecaprevir/pibrentasvir (Mavyret)	With food		NO¥	

‡Not to exceed omeprazole 20mg/day
*Give *with* or 12h apart at a dose not to exceed famotidine 40mg BID
¥Yu G. *Lancet* 2017;17:1239.

Refer to PDR for detailed Acid Blocker Interactions with DAA's Regimens

Summary Drug-Drug Interactions (UCSF)

Summary of Selected Drug-Drug Interactions with DAAs

Concomitant Medication	Sofosbuvir + Daclatasvir	Sofosbuvir / Ledipasvir	Sofosbuvir / Ledipasvir	PrOD	Elbasvir / Grazoprevir	Sofosbuvir/ Velpatasvir/ Voxilaprevir	Glecaprevir/ Pibrentasvir
Acid reducing agents*		X	X	X		X	
Amiodarone	X	X	X	X		X	
Anticonvulsants*	X	X	X	X	X	X	X
Azole antifungals*	X#			X	X		
Ca^{2+} channel blockers*	X			X			
Digoxin	X	X	X			X	
Ergot derivatives				X			
Ethinyl estradiol prod.				X			X
Glucocorticoids*	X#			X			
Dabigatran (Pradaxa)						X	X
St. John's wort	X	X	X	X	X	X	X
Macrolide antibiotics*	X#						
Phosphodiesterase-5 inhibitors*				X			
Rifamycins*	X	X	X	X	X	X	X
Statins*	X	X	X	X	X	X	X

*Some interactions are not class specific. Refer to specific prescribing information, #May require daclatasvir dose adjustment

Case 2

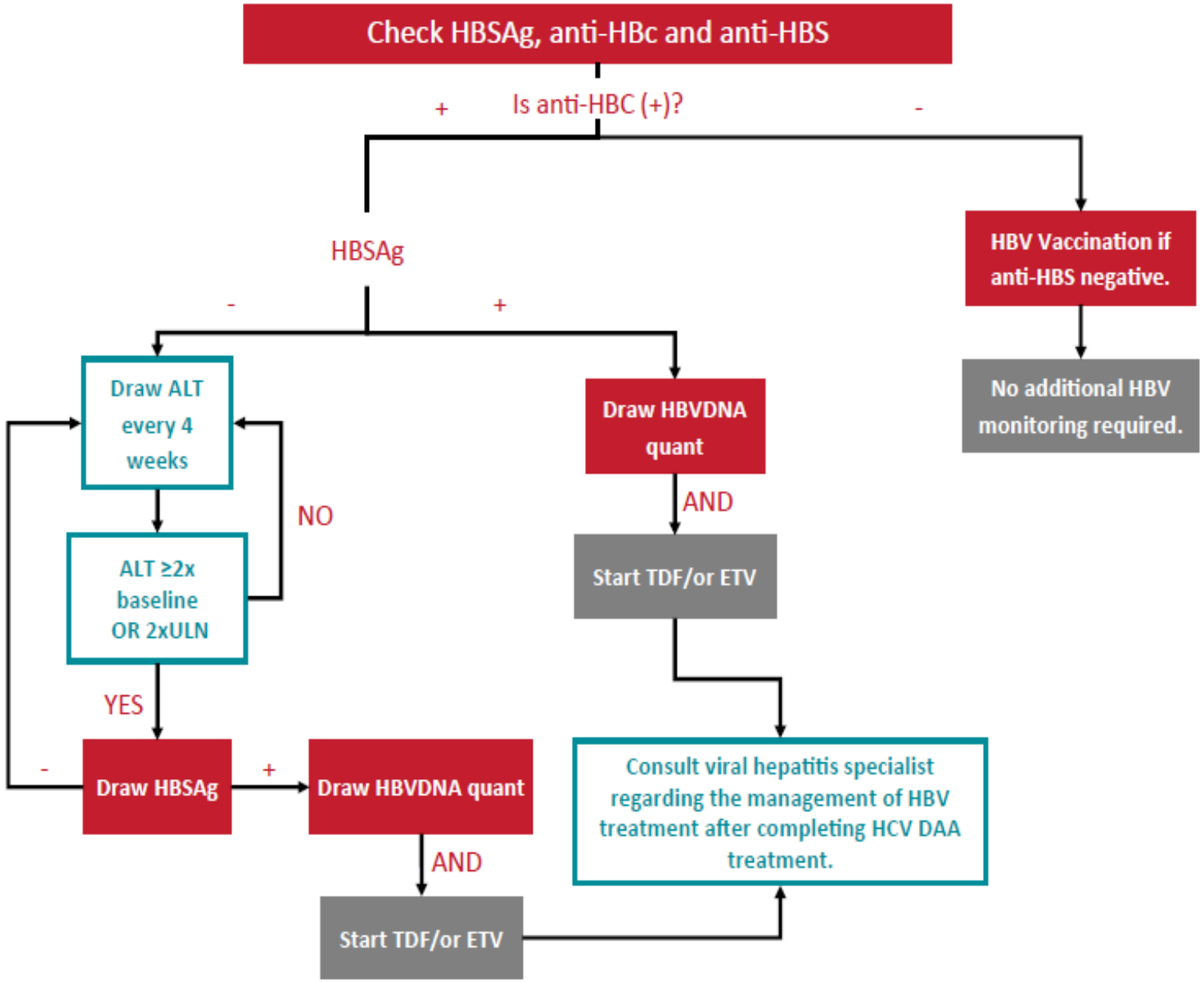
- 54 year old male with active HCV, chronic pain
- Prior IVDU, current ETOH up to a pint a day
- Interferon/ribavirin when incarcerated
- Genotype 2 with viral load of ~ 6 million
- Medications – occasional OTC ibuprofen
- Labs – Hgb 15, Plt 246,000, Alt 84 IU/L, AST 96 IU/L, Bili/Cr/albumin/INR normal, **HBcAb positive,** HBsAg/sAb negative, HIV neg
- APRI 0.976, FIB-4 2.30, Fibrosure 0.61 (stage 3)
- Ultrasound moderate hepatomegaly with fatty changes
- Physical palpable liver edge 2cm below ribs, otherwise exam WNL
- Medi-Cal (PHP)

Partnership HealthPlan of California Hepatitis C Treatment regimens – Naïve to prior treatment and IFN/RBV experienced, effective 10/1/2017

Genotype	Stage 0-1	Stage 2-4, unconfirmed cirrhosis		Cirrhosis -definitive (bx, US, FibroSure/Test ≥ 0.75, findings of portal HTN, ascites, varices, encephalopathy)			
				CTP A (Score 5-6)		CTP B (7-9) / C (10-15)	
		Naïve	IFN/RBV experienced	Naïve	IFN/RBV experienced	Naïve	IFN/RBV experienced
GT 1a, mixed a/b or indeterminate GT 1	Treatment eligible only under special circumstances defined by the State of California Medi-Cal benefit. Stages 0-1 criteria with special circumstances, the preferred treatment will follow that specified for stages 2-4 at right	**Mavyret x 8 weeks**		**Mavyret x 12 weeks**		**Epclusa / RBV WB X 12 weeks**	**Epclusa / RBV WB x 24 wks* OR Harvoni / RBV LD x 12 wks**
		Zepatier (no baseline NS5A RAVs) x 12 wks				Harvoni / RBV LD x 12 wks	
		Harvoni x 8 wks (HCV VL <6 million, non-black, HIV-uninfected)	Epclusa x 12 wks*	Epclusa x 12 wks	Epclusa x 12 wks*	Epclusa x 24 wks* if RBV intolerant	
		Epclusa x 12 wks		Harvoni x 12 wks		Harvoni x 24 wks* if RBV intolerant	
GT 1b		**Mavyret x 8 weeks**		**Mavyret x 12 weeks**		**Epclusa / RBV WB x 12 weeks**	**Epclusa / RBV WB x 24 wks* OR Harvoni / RBV LD x 12 wks**
		Zepatier x 12 wks				Harvoni / RBV LD x 12 wks	
		Harvoni x 8 wks (HCV VL <6 million, non-black, HIV-uninfected)	Epclusa x 12 wks*	Epclusa x 12 wks	Epclusa x 12 wks*	Epclusa x 24 wks* if RBV intolerant	
		Epclusa x 12 wks		Harvoni x 12 wks		Harvoni x 24 wks* if RBV intolerant	
GT 2		**Mavyret x 8 weeks**		**Mavyret x 12 weeks**		**Epclusa / RBV WB x 12 weeks**	**Epclusa / RBV WB x 24 wks***
		Epclusa x 12 wks	Epclusa x 12 wks*	Epclusa x 12 wks	Epclusa x 12 wks*	Dac / Sof / RBV LD x 12 wks	
						Epclusa x 24 wks* if RBV intolerant	
GT 3		**Mavyret x 8 weeks**	**Epclusa x 12 weeks* (RAS testing for Y93H required)**	**Mavyret x 12 weeks**	**Vosevi x 12 weeks***	**Epclusa / RBV WB x 12 weeks**	**Epclusa / RBV WB x 24 wks***
		Epclusa x 12 wks	*Mavyret x 16 wks*	Epclusa x 12 wks (RAS testing for Y93H required)	Zepatier / Sovaldi x 12 wks*	Dac / Sof / RBV LD x 12 wks	
			Vosevi x 12 wks (when Y93H present)	*Vosevi x 12 wks (when Y93H present)*	*Mavyret x 16 wks**	Epclusa x 24 wks* if RBV intolerant	
					*Epclusa / RBV WB x 12 wks**		
GT 4		**Mavyret x 8 weeks**		**Mavyret x 12 weeks**		**Epclusa / RBV WB X 12 weeks**	**Epclusa / RBV WB x 24 wks***
		Zepatier x 12 wks	Zepatier x 12 wks* (virologic relapse after prior interferon/ribavirin therapy)	Zepatier x 12 wks	Zepatier x 12 wks* (virologic relapse after prior interferon/ribavirin therapy)	Harvoni / RBV LD x 12 wks	
		Epclusa x 12 wks	Epclusa x 12 wks*	Epclusa x 12 wks	Epclusa x 12 wks*	Epclusa x 24 wks* if RBV intolerant	
						Harvoni x 24 wks* if RBV intolerant	
GT 5,6		**Mavyret x 8 weeks**		**Mavyret x 12 weeks**		**Epclusa / RBV WB X 12 weeks**	**Epclusa / RBV WB x 24 wks***
		Epclusa x 12 wks				Harvoni / RBV LD x 12 wks	
		Harvoni x 12 wks				Epclusa x 24 wks* if RBV	
						Harvoni x 24 wks* if RBV	
Pre/Post Liver Transplant		**Case by Case Review, Transplant Specialist Referral Required**					

Version: 10/24/2016

Project ECHO HBV Monitoring for Patients on HCV Treatment



Surveillance Stage 3-4 Fibrosis

Varices:

- At diagnosis
- Q 2-3 years if no varices
- Q 1-2 years if small varices
- Q year if decompensated cirrhosis
- OK to initiate HCV treatment prior to EGD

Hepatocellular Carcinoma:

- US (or quad-phase CT or MRI) q 6 months
- AFP q 6-12 months

Case 3

- 74 year old male with active HCV, Cirrhosis, chronic pain
- Tattooing currently sober
- No prior treatment
- Genotype 1a with viral load of ~ 1 million
- Medications – Voltaren gel, baclofen, norco
- Labs – Hgb 15, Plt 99,000, Alt 96 IU/L, AST 140 IU/L, Bili 2.0, Cr 0.67, albumin 4.2, INR 1.4, HBcAb/sAg Negative, HBsAb positive, HIV neg
- Liver Bx 2009 stage 4 fibrosis
- Ultrasound nodular liver, normal spleen, no ascites
- Telangectasias, otherwise exam WNL
- MediCare

Child-Turcotte-Pugh Classification for Severity of Cirrhosis			
	Points*		
	1	2	3
Encephalopathy	None	Grade 1-2 (or precipitant induced)	Grade 3-4 (or chronic)
Ascites	None	Mild to moderate (diuretic responsive)	Severe (diuretic refractory)
Bilirubin (mg/dL)	< 2	2-3	>3
Albumin (g/dL)	> 3.5	2.8-3.5	<2.8
INR	<1.7	1.7-2.3	>2.3
*Child-Turcotte-Pugh Class obtained by adding score for each parameter (total points)			
Class A = 5 to 6 points (least severe liver disease)			
Class B = 7 to 9 points (moderately severe liver disease)			
Class C = 10 to 15 points (most severe liver disease)			

MELD Score

The Model for End Stage Liver Disease (MELD) predicts 3 month survival for patients with advanced liver disease based on:

- Serum Bilirubin *(mg/dL)*
- INR (International Normalized Ratio)
- Serum Creatinine *(mg/dL)*
- Dialysis status

http://www.hepatitisc.uw.edu/page/clinical-calculators/meld

PLEASE REFER TO/CONSULT WITH HEPATOLOGY IF MELD SCORE IS:

➢ 15 or > 10 with Sign and Symptoms of Decompensation

Source: *Kamath PS, Kim WR; Advanced Liver Disease Study Group. The model for end-stage liver disease (MELD). Hepatology. 2007; 45:797-805.*

Partnership HealthPlan of California Hepatitis C Treatment regimens – Naïve to prior treatment and IFN/RBV experienced, effective 10/1/2017

Genotype	Stage 0-1	Stage 2-4, unconfirmed cirrhosis		Cirrhosis -definitive (bx, US, FibroSure/Test ≥ 0.75, findings of portal HTN, ascites, varices, encephalopathy)			
				CTP A (Score 5-6)		CTP B (7-9) / C (10-15)	
		Naïve	IFN/RBV experienced	Naïve	IFN/RBV experienced	Naïve	IFN/RBV experienced
GT 1a, mixed a/b or indeterminate GT 1	Treatment eligible only under special circumstances defined by the State of California Medi-Cal benefit. Stages 0-1 criteria with special circumstances, the preferred treatment will follow that specified for stages 2-4 at right	**Mavyret x 8 weeks**		**Mavyret x 12 weeks**		**Epclusa / RBV WB X 12 weeks**	**Epclusa / RBV WB x 24 wks* OR Harvoni / RBV LD x 12 wks**
		Zepatier (no baseline NS5A RAVs) x 12 wks				Harvoni / RBV LD x 12 wks	
		Harvoni x 8 wks (HCV VL <6 million, non-black, HIV-uninfected)	Epclusa x 12 wks*	Epclusa x 12 wks	Epclusa x 12 wks*	Epclusa x 24 wks* if RBV intolerant	
		Epclusa x 12 wks		Harvoni x 12 wks		Harvoni x 24 wks* if RBV intolerant	
GT 1b		**Mavyret x 8 weeks**		**Mavyret x 12 weeks**		**Epclusa / RBV WB x 12 weeks**	**Epclusa / RBV WB x 24 wks* OR Harvoni / RBV LD x 12 wks**
		Zepatier x 12 wks				Harvoni / RBV LD x 12 wks	
		Harvoni x 8 wks (HCV VL <6 million, non-black, HIV-uninfected)	Epclusa x 12 wks*	Epclusa x 12 wks	Epclusa x 12 wks*	Epclusa x 24 wks* if RBV intolerant	
		Epclusa x 12 wks		Harvoni x 12 wks		Harvoni x 24 wks* if RBV intolerant	
GT 2		**Mavyret x 8 weeks**		**Mavyret x 12 weeks**		**Epclusa / RBV WB x 12 weeks**	**Epclusa / RBV WB x 24 wks***
		Epclusa x 12 wks	Epclusa x 12 wks*	Epclusa x 12 wks	Epclusa x 12 wks*	Dac / Sof / RBV LD x 12 wks	
						Epclusa x 24 wks* if RBV intolerant	
GT 3		**Mavyret x 8 weeks**	**Epclusa x 12 weeks* (RAS testing for Y93H required)**	**Mavyret x 12 weeks**	**Vosevi x 12 weeks***	**Epclusa / RBV WB x 12 weeks**	**Epclusa / RBV WB x 24 wks***
		Epclusa x 12 wks	*Mavyret x 16 wks*	Epclusa x 12 wks (RAS testing for Y93H required)	Zepatier / Sovaldi x 12 wks*	Dac / Sof / RBV LD x 12 wks	
			Vosevi x 12 wks (when Y93H present)	*Vosevi x 12 wks (when Y93H present)*	*Mavyret x 16 wks**	Epclusa x 24 wks* if RBV intolerant	
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GT 4		**Mavyret x 8 weeks**		**Mavyret x 12 weeks**		**Epclusa / RBV WB X 12 weeks**	**Epclusa / RBV WB x 24 wks***
		Zepatier x 12 wks	Zepatier x 12 wks* (virologic relapse after prior interferon/ribavirin therapy)	Zepatier x 12 wks	Zepatier x 12 wks* (virologic relapse after prior interferon/ribavirin therapy)	Harvoni / RBV LD x 12 wks	
		Epclusa x 12 wks	Epclusa x 12 wks*	Epclusa x 12 wks	Epclusa x 12 wks*	Epclusa x 24 wks* if RBV intolerant	
						Harvoni x 24 wks* if RBV intolerant	
GT 5,6		**Mavyret x 8 weeks**		**Mavyret x 12 weeks**		**Epclusa / RBV WB X 12 weeks**	**Epclusa / RBV WB x 24 wks***
		Epclusa x 12 wks				Harvoni / RBV LD x 12 wks	
		Harvoni x 12 wks				Epclusa x 24 wks* if RBV	
						Harvoni x 24 wks* if RBV	
Pre/Post Liver Transplant		**Case by Case Review, Transplant Specialist Referral Required**					

Summary Renal/Hepatic Impairment (UCSF)

Use in Renal/Hepatic Impairment

Drug	Renal Impairment				Hepatic Impairment			
	Mild	Moderate	Severe	Dialysis	Mild (CP A)	Moderate (CP B)	Severe (CP C)	Decompensated Cirrhosis
Simeprevir	Yes	Yes	Yes	Yes	Yes	No	No	No
Sofosbuvir	Yes	Yes	No	No	Yes	Yes	Yes	Yes
Daclatasvir	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Sofosbuvir/Ledipasvir	Yes	Yes	No	No	Yes	Yes	Yes	Yes
Sofosbuvir/Velpatasvir	Yes	Yes	No	No	Yes	Yes	Yes	Yes
Paritaprevir/Ombitasvir +ritonavir±Dasabuvir	Yes	Yes	Yes	Yes	Yes	No	No	No
Elbasvir/Grazoprevir	Yes	Yes	Yes	Yes	Yes	No	No	No
Sofosbuvir/Velpatasvir/ Voxilaprevir	Yes	Yes	No	No	Yes	No	No	No
Glecaprevir/Pibrentasvir	Yes	Yes	Yes	Yes	Yes	No	No	No
Ribavirin	Yes (dose reduction)				Yes	Yes	Yes	Yes

[1] Table information based on prescribing information for each product as of 8/28/17; Yes = use in recommended; No = use is contraindicated; CP = Child Pugh class

Sofosbuvir prescribing information (8/2015); http://www.gilead.com/~/media/Files/pdfs/medicines/liver-disease/sovaldi/sovaldi_pi.pdf; Simeprevir prescribing information (10/2015); https://www.olysio.com/shared/product/olysio/prescribing-information.pdf; Ledipasvir/Sofosbuvir prescribing information (11/2015); http://www.gilead.com/~/media/Files/pdfs/medicines/liver-disease/harvoni/harvoni_pi.pdf ; Daclatasvir prescribing information (7/2015); http://packageinserts.bms.com/pi/pi_daklinza.pdf; Paritaprevir/ritonavir/ombitasvir and dasabuvir prescribing information (10/2015); http://www.rxabbvie.com/pdf/viekirapak_pi.pdf ; Elbasvir/grazoprevir prescribing information (1/2016); http://www.merck.com/product/usa/pi_circulars/z/zepatier/zepatier_pi.pdf Vosevi prescribing information (8/2017): https://www.gilead.com/~/media/files/pdfs/medicines/liver-disease/vosevi/vosevi_pi.pdf?la=en; Mavyred prescribing information (8/2017): http://www.rxabbvie.com/pdf/mavyret_pi.pdf

Monitoring

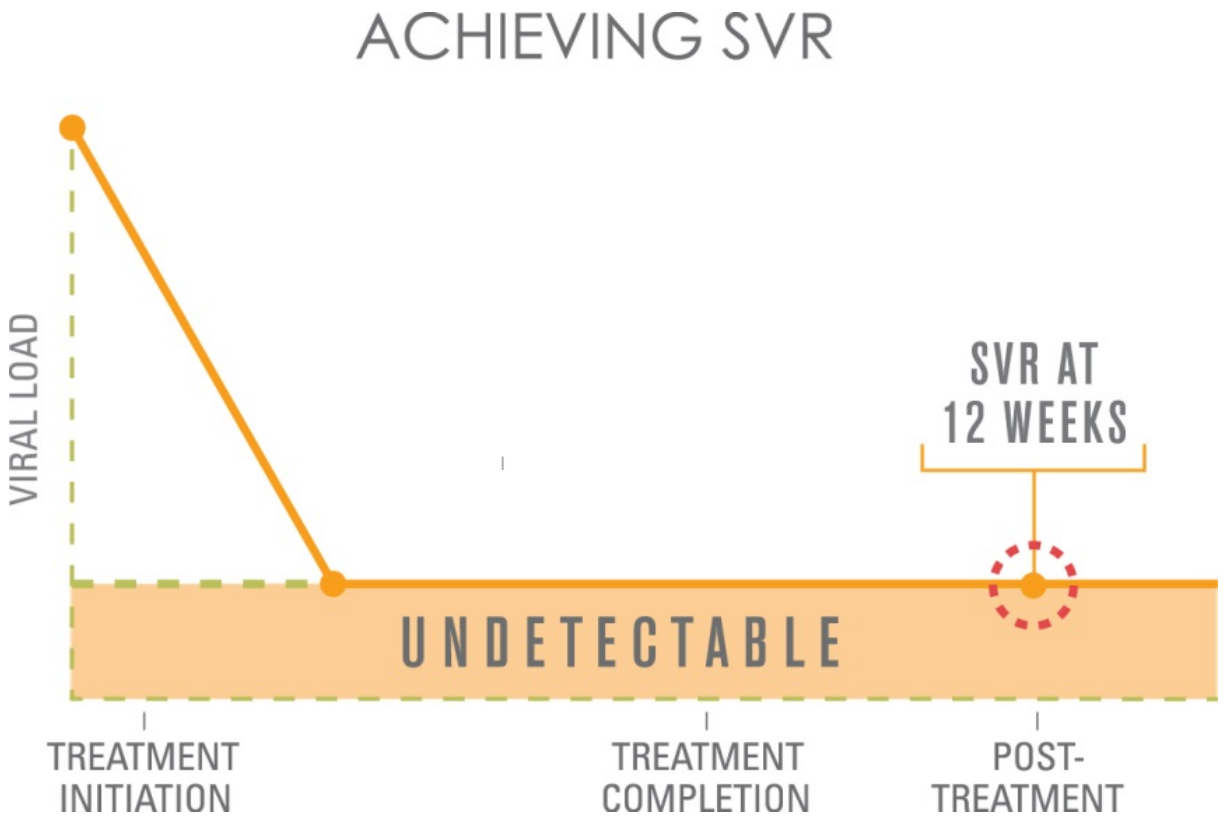
During Treatment (non-ribavirin):

- CBC/CBP q 4 weeks
- VL at 4 weeks

After Treatment:

CBC/CMP/VL 12 weeks after last dose

What Defines HCV Cure?

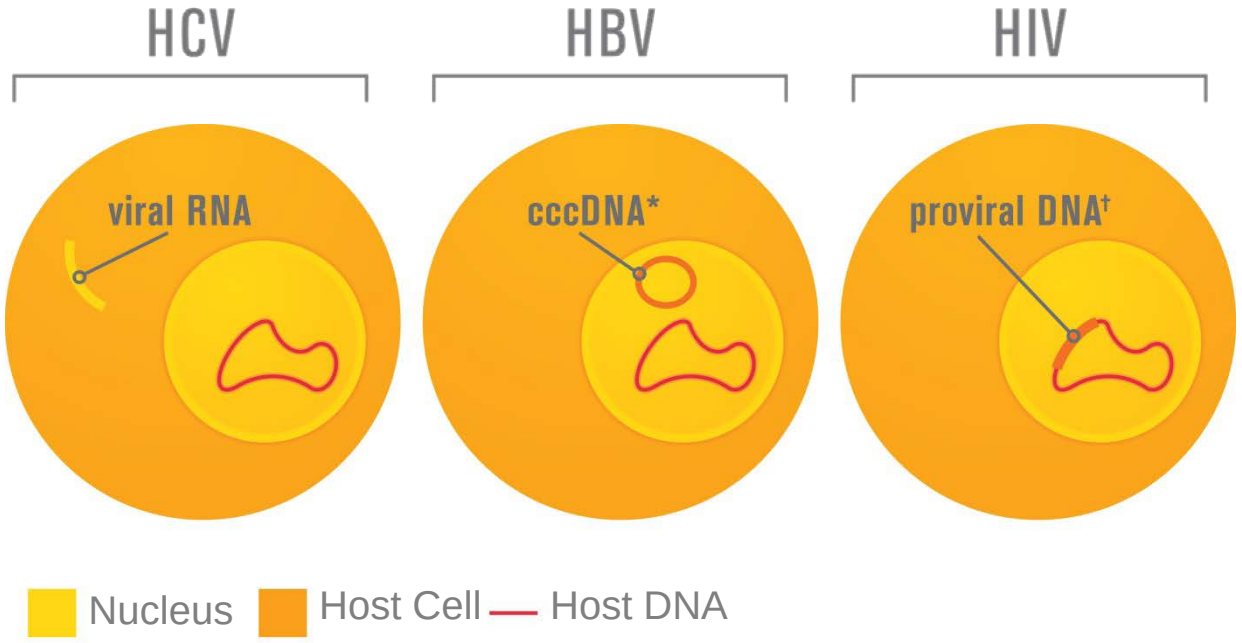


Cure, also known as sustained virologic response (SVR), is defined as no detectable HCV in the blood at 12 or more weeks after therapy is complete[1,2]

1. US Department of Health and Human Services, Center for Drug Evaluation and Research. Draft Guidance for Industry. Chronic Hepatitis C Virus Infection: Developing Direct-Acting Antiviral Drugs for Treatment. October 2013.
2. AASLD, IDSA, IAS-USA. Recommendations for testing, managing, and treating hepatitis C. http://www.hcvguidelines.org. Accessed October 22,, 2016.
3. Swain MG et al. *Gastroenterology.* 2010;139(5):1593-1601.

Why Is Cure Possible?

- HCV does not integrate into the nuclei of infected cells, while HBV and HIV DNA are incorporated into the nucleus of the cell[1]



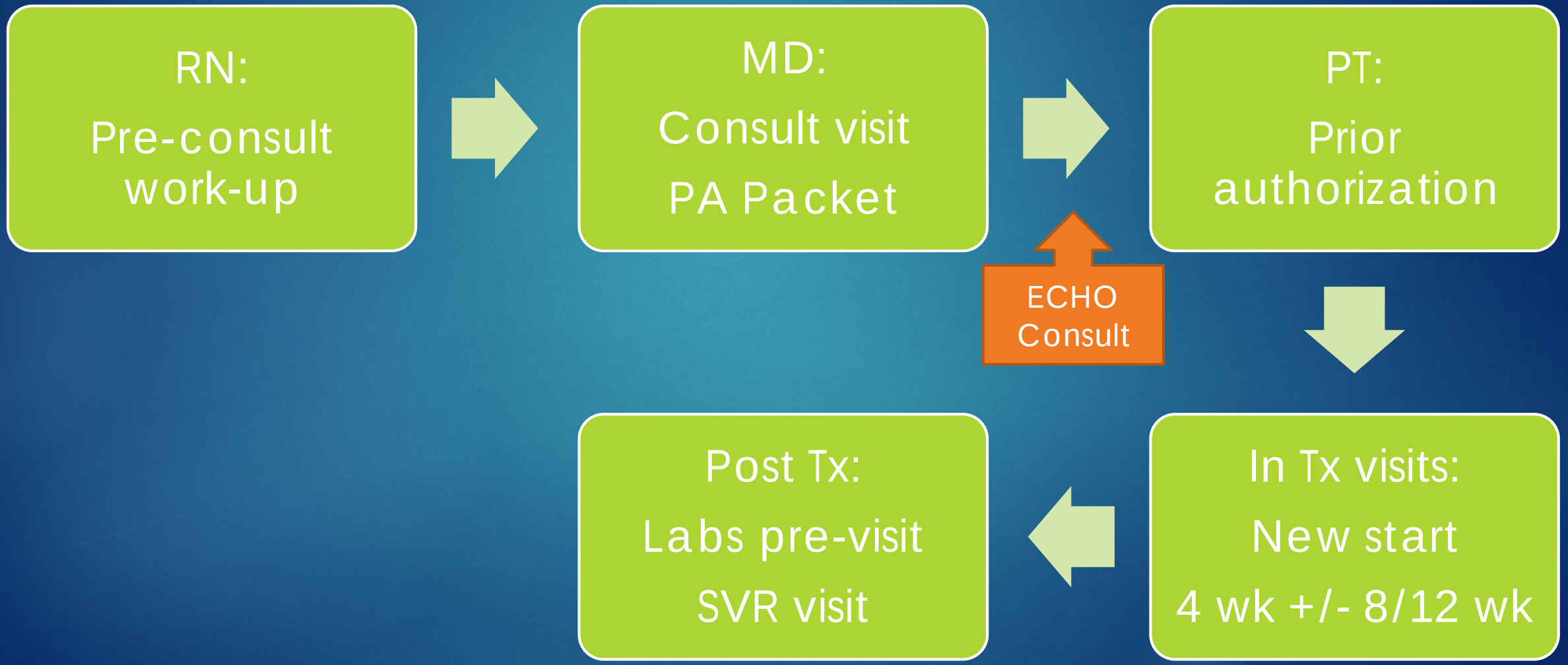
*HBV cccDNA (covalently closed circular DNA): accumulates in hepatocyte nuclei, acting as a template for viral messenger RNA transcription.
†HIV proviral DNA: integrates into the chromatin of infected cells, acting as the template for the transcription of viral genes.

1. Soriano V et al. *J Antimicrob Chemother.* 2008;62(1):1-4.

Eradication Project

UIHS EXPERIENCE

UIHS Workflow



Data is Critical (we use NextGen)

Find all HCV patients in system

- Problem/diagnosis list reports
  - all with “hepatitis”
- Lab module data
  - Positive HCV Ab screens
  - Any HCV RNA test
- Confidential Morbidity Reports

Clarify diagnoses in a way you can track

History of Hepatitis C

- Spontaneous cure or treated with SVR 12

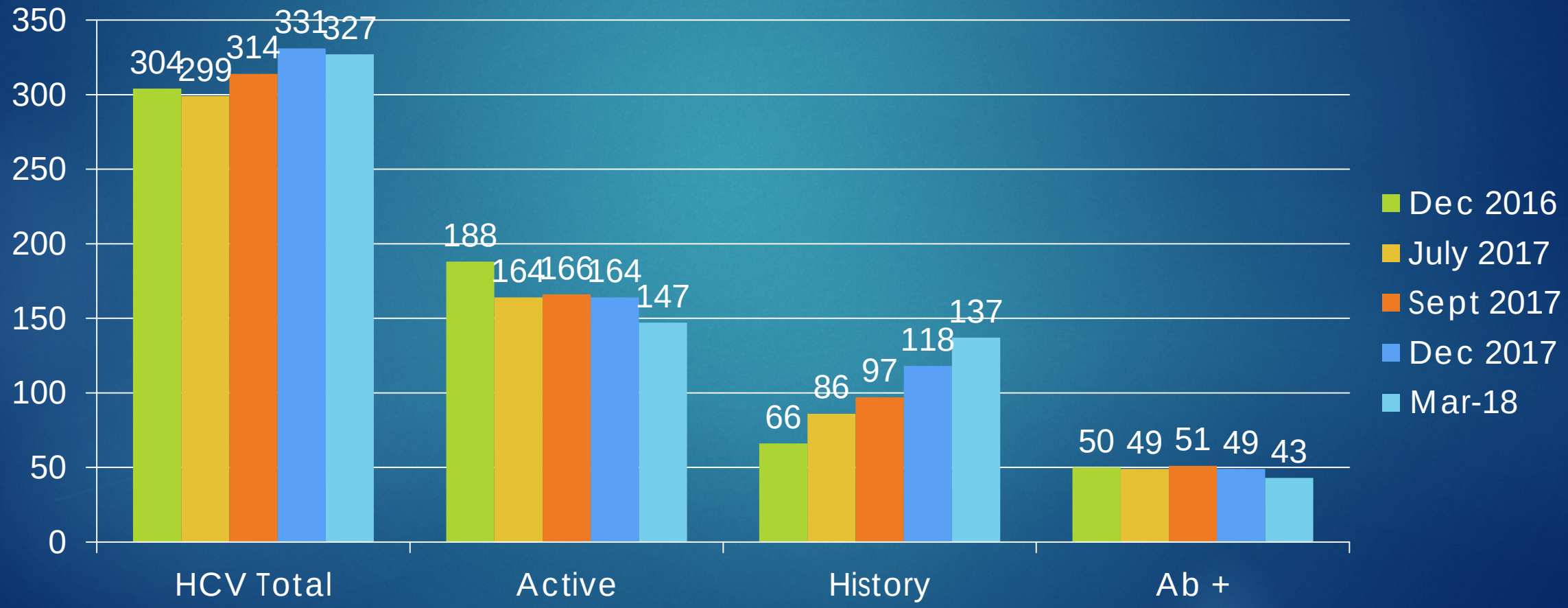
Hepatitis C Antibody Positive

- Missing RNA testing
- Put in future order for HCV RNA test

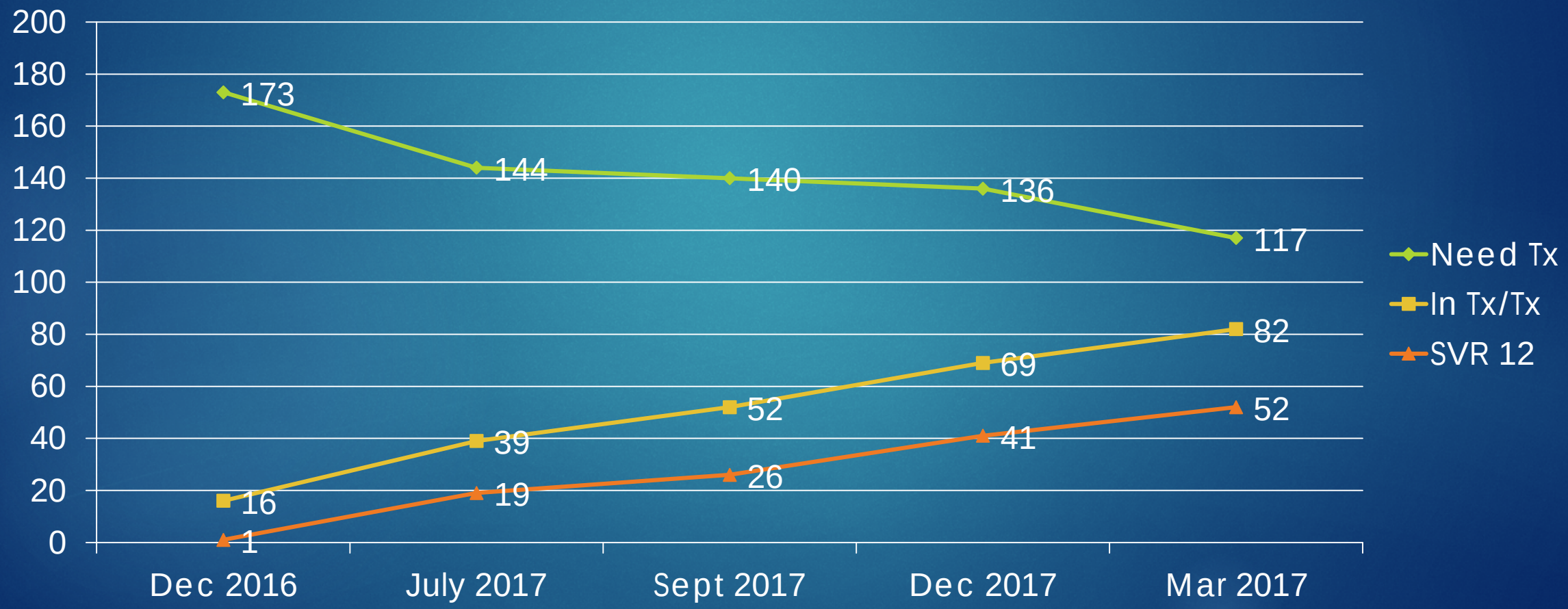
Chronic Viral Hepatitis C

- Positive RNA

UIHS HCV Statistics



UIHS HCV Treatment Data



Challenges

#1 Prior Auths

- Medication Adherence
  - Not as much of an issue as feared
  - Lost/stolen medications – police report
  - Bubble packing
- Active Addiction
  - Case worker as reminder and delivery location
  - Medication delivery to clinic
- No phone and/or transportation
  - Weekly visits to clinic
  - Outreach worker assistance
  - Minimize unnecessary clinic visits
  - Phone visits at remote clinic locations

Prevention

- Needle-syringe exchange
  - Humboldt County Public Health – active exchange
  - Weitchpec Clinic
  - Del Norte County Public Health – no active exchange
  - Klamath Clinic
- Suboxone program
  - Prevention and adherence

Contact Information

- Katie.cassel@crihb.org

Resources

Hepatitis C Consultation Services
(844) 437-4636 | 6AM-5PM PST, M-F
nccc.ucsf.edu

The Clinician Consultation Center (CCC) provides up-to-date expert advice to support clinicians managing patients with hepatitis C (HCV) and co-morbidities such as substance use, hepatitis B, or HIV. Guidance is based on established treatment guidelines, current scientific findings, and best clinical practices.

Consultation topics include:

- HCV transmission & prevention
- HCV screening & diagnostic testing
- Chronic HCV evaluation & monitoring
- Pre-treatment evaluation & counseling
- Initial regimen selection, re-treatment strategies
- Co-infection (HCV-HIV, HCV-HBV)
- HCV and special populations (kidney disease, cirrhosis/ESLD, pregnancy/breastfeeding)

This project is supported by the Health Resources and Services Administration (HRSA) of the U.S. Department of Health and Human Services (HHS) under grant number U1OHA30039-01-00 (AIDS Education and Training Centers National Clinician Consultation Center) awarded to the University of California, San Francisco. (updated 10/24/17)

CLINICIAN CONSULTATION CENTER
Translating science into care

The Clinician Consultation Center is a free telephone advice service for clinicians by clinicians. Receive expert clinical advice on HIV, hepatitis C, substance use, PrEP, PEP, and perinatal HIV.

See nccc.ucsf.edu for more information.

HIV/AIDS Warmline 800-933-3413
HIV treatment, ARV decisions, complications, and co-morbidities

Perinatal HIV Hotline 888-448-8765
Pregnant women with HIV or at-risk for HIV & their infants

Hepatitis C Warmline 844-HEP-INFO 844-437-4636
HCV testing, staging, monitoring, treatment

PrEPline 855-HIV-PrEP
Pre-exposure prophylaxis for persons at risk for HIV

Substance Use Warmline 855-300-3595
Substance use evaluation and management

PEPline 888-448-4911
Occupational & non-occupational exposure management

Patient/Copay Assistance Programs

Contact Information

- AbbVie 844-277-6233
- Johnson & Johnson (Simeprevir) 800-652-6227 or www.jjpaf.org
- Gilead Sciences (Sofosbuvir, Harvoni) 855-769-7284 or www.MySupportPath.com

May requires documentation of a denial of coverage for insured patients.

Guidelines, Advocacy News (Helpful Links)

- Treatment Guidelines
  - AASLD and IDSA guidelines www.hcvguidelines.org
  - University of Washington online study moduleshttp://www.hepatitisc.uw.edu/browse/all/lectures
  - VA HCV Guidelines http://www.hepatitis.va.gov/pdf/treatment-considerations-2015-02.pdf
- Hepatitis C news and conference proceedings
  - www.natap.org
  - www.hivandhepatitis.com
- Advocacy and patient education
  - Project Inform http://www.projectinform.org/category/hepc/
  - HepMag www.hepmag.com
  - Hcvadvocate.org
  - National Viral Hepatitis Roundtable www.nvhr.org

Harvoni (UCSF)

Indications and Usage:

- HARVONI is indicated for the treatment of chronic hepatitis C virus (HCV) genotype (GT) 1, 4, 5, or 6 infection in patients at least 12 years of age (or ≥35 kg) without cirrhosis or with compensated cirrhosis.
- HARVONI is used with ribavirin (RBV) in GT 1 adults with decompensated cirrhosis and in GT 1 or 4 adult liver transplant recipients without cirrhosis or with compensated cirrhosis.
- For Treatment-Naïve, patients and a viral load < 6 million units/ml and without Cirrhosis, treatment duration is generally 8 weeks.

Direct Acting Agents

Sofosbuvir/Ledipasvir (Harvoni)

- **Pharmacology:**
  - Sofosbuvir: NS5B inhibitor
  - Ledipasvir: NS5A inhibitor
  - Inhibit viral replication
  - Approved genotypes 1 & 4-6
- **Pharmacokinetics**
  - Eliminated by kidneys
  - Do NOT use if eGFR is <30mL/min/1.73m^2
- **Dosing:**
  - 1 tablet PO daily
  - With or without food
  - ± Ribavirin
- **Drug-drug interactions§:**
  - Acid reducing agents:
    - Proton pump inhibitors (PPI
    - H2-Blockers
    - Antacids
  - Anticonvulsants:
    - Carbamazepine/oxcarbazep
    - Phenytoin/phenobarbital
  - Rifampin
  - St. John's wort
- **Adverse effects:**
  - Fatigue
  - Headache
  - Nausea
  - Bradycardia (with amio

§Partial list of drug-drug interactions

Harvoni [package insert]. Foster City, Ca: Gilead Sciences; February 2016.

Epclusa (UCSF)

Indications and Usage:

EPCLUSA is indicated for the treatment of adult patients with chronic HCV GT 1, 2, 3, 4, 5, or 6 infection:

- without cirrhosis or with compensated cirrhosis
- with decompensated cirrhosis for use in combination with RBV

Direct Acting Agents

Sofosbuvir/Velpatasvir (Epclusa)

- **Pharmacology:**
  - Sofosbuvir: NS5B inhibitor
  - Velpatasvir: NS5A inhibitor
  - Inhibit viral replication
  - Approved genotypes 1-6
- **Pharmacokinetics**
  - Eliminated by kidneys
  - Do NOT use if eGFR is <30mL/min/1.73m^2
- **Dosing:**
  - 1 tablet PO daily
  - With or without food
  - ± Ribavirin
- **Drug-drug interactions[§]:**
  - Acid reducing agents:
    - Proton pump inhibitors (AVOID)
    - H2-Blockers
    - Antacids
  - Anticonvulsants:
    - Carbamazepine/oxcarbazepine
    - Phenytoin/phenobarbital
  - Rifampin
  - St. John's wort
- **Adverse effects:**
  - Fatigue
  - Headache
  - Nausea
  - Bradycardia (with amiodarone)

[§]Partial list of drug-drug interactions

Epclusa [package insert]. Foster City, Ca: Gilead Sciences; June 2016.

Zepatier (UCSF)

Indications and Usage:

-Indicated for the treatment of Chronic HCV Genotype 1 or 4 infection in adults.

-Okay to use with Amiodarone

-Okay to use in Renal Failure

Direct Acting Agents

Grazoprevir/Elbasvir (Zepatier)

- **Pharmacology:**
  - Grazoprevir: NS3/4A Inhibitor
  - Elbasvir: NS5A inhibitor
  - Inhibit viral replication/assembly
  - Approved genotypes 1&4
- **Pharmacokinetics**
  - Substrate of:
    Cytochrome P450 (CYP450)
    P-glycoprotein (PGP)
- **Dosing:**
  - 1 tablet PO daily
  - With or without food
  - ± Ribavirin
- **Drug-drug interactions[§]:**
  - Rifampin
  - Phenytoin/carbamazepine
  - Efavirenz
  - Statins
- **Adverse effects:**
  - Fatigue
  - Headache
  - Nausea
  - Elevated bilirubin/ALT levels
  - Do NOT use in decompensated cirrhosis (Child class B or C)

[§]Partial list of drug-drug interactions

Zepatier [package insert]. Whitehouse Station: Merck & Co. Inc.; 2016.

Mavyret (UCSF)

Indications and Usage:

- Treatment-naïve patients with HCV genotypes 1-6 in without cirrhosis and with compensated cirrhosis (Child-Pugh A)

- HCV genotype 1 previously treated with a regimen containing an HCV NS5A inhibitor or an NS3/4A protease inhibitor, but not both *(NEXT SLIDE)*

-Treatment Naïve: 8 weeks No Cirrhosis, 12 weeks Cirrhosis, across all Genotypes

Direct Acting Agents

Glecaprevir/Pibrentasvir (Mavyret)

- **Pharmacology:**
  - Glecaprevir: NS3/4A Inhibitor
  - Pibrentasvir: NS5A inhibitor
  - Inhibit viral replication/assembly
- **Pharmacokinetics**
  - Cytochrome P450 (CYP3A)
  - NO renal elimination (OK in patients w/CKD and HD)
- **Dosing:**
  - 3 tablets PO daily
  - With food
- **Drug-drug interactions[§]:**
  - Rifampin
  - Phenytoin/carbamazepine
  - Efavirenz
  - Statins
- **Adverse effects:**
  - Fatigue
  - Headache
  - Nausea
  - Diarrhea
  - NOT recommended in decompensated cirrhosis (Child class B), and is contraindicated in Child class C)

[§]Partial list of drug-drug interactions

Mavyret [package insert]. North Chicago, IL: Abbvie Inc.; 2017.

Vosevi (UCSF)

Indications and Usage:

- Genotype 1,2, 3, 4, 5 or 6 infection and have previously been treated with an HCV regimen containing an NS5A inhibitor:

-Genotype 1a or 3 infection and have previously been treated with an HCV regimen containing Sofosbuvir without an NS5A inhibitor:

Prior NS5A Regimens:

Sofosbuvir/Ledipasvir
Elbasvir/Grazoprevir
Sofosbuvir/Daclatasvir
Paritaprevir/Ritonavir/Ombitasvir/Dasabuvir

- Three Drug Fixed Dose Combinations (FDC): NS5B (Sofosbuvir), NS5A (Velpatasvir), NS3/4A Protease Inhibitor (Voxilaprevir) **(Vosevi)**

Direct Acting Agents

Sofosbuvir/Velpatasvir/**Voxilaprevir (Vosevi)**

- **Pharmacology:**
  - Sofosbuvir: NS5B inhibitor
  - Velpatasvir: NS5A inhibitor
  - Voxilaprevir:NS3/4A inhibitor
- **Pharmacokinetics**
  - Sofosbuvir eliminated by kidneys
  - Do NOT use if eGFR is <30mL/min/1.73m^2
  - Velpatasvir/Voxilaprevir eliminated by biliary excretion
- **Dosing:**
  - 1 tablet PO daily
  - With food
- **Drug-drug interactions[§]:**
  - Acid reducing agents:
    OK to give WITH PPI[‡] or H2-Blocker
    Space antacids 4h apart
  - Anticonvulsants:
    Carbamazepine/oxcarbazepine
    Phenytoin/phenobarbital
  - Rifampin/Rifabutin
- **Adverse effects:**
  - Fatigue
  - Headache
  - Nausea
  - Diarrhea
  - Bradycardia (with amiodarone)
  - Do NOT use in decompensated cirrhosis (Child class B or C)

[§]Partial list of drug-drug interactions, [‡] Omeprazole 20mg/day

Vosevi [package insert]. Foster City, Ca: Gilead Sciences; 2017.