DISCLOSURES

This activity is jointly provided by Northwest Portland Area Indian Health Board and Cardea

Cardea Services is approved as a provider of continuing nursing education by Montana Nurses Association, an accredited approver with distinction by the American Nurses Credentialing Center's Commission on Accreditation.

This activity has been planned and implemented in accordance with the accreditation requirements and policies of the Institute for Medical Quality/California Medical Association (IMQ/CMA) through the joint providership of Cardea and Northwest Portland Area Indian Health Board. Cardea is accredited by the IMQ/CMA to provide continuing medical education for physicians.

Cardea designates this in-person training for a maximum of 7 *AMA PRA Category 1 Credit(s)™*. Physicians should claim credit commensurate with the extent of their participation in the activity.

NPAIHB
Indian Leadership for Indian Health

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DISCLOSURES

COMPLETING THIS ACTIVITY

Upon successful completion of this activity 7 contact hours will be awarded

Successful completion of this continuing education activity includes the following:

- Attending the entire CE activity;
- Completing the online evaluation;
- Submitting an online CE request.

Your certificate will be sent via email

If you have any questions about this CE activity, contact Michelle Daugherty at mdaugherty@cardeaservices.org or (206) 447-9538

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CONFLICT OF INTEREST

None of the planners or presenters of this CE activity have any relevant financial relationships with any commercial entities pertaining to this activity.

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Acknowledgement

This event is funded in part by:

The Indian Health Service HIV Program
and
The Secretary's Minority AIDS Initiative Fund

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Objectives

By the end of this learning event participants will be able to:

- Describe the rationale and goals of universal HCV treatment
- Discuss the use of screening and treatment policies to implement universal HCV treatment.

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HCV Screening, Management, & Treatment Guidelines

Justin Iwasaki MD MPH

Executive Medical Director

Lummi Tribal Health Center

No Disclosures

Thank You to Dr. Jorge Mera for Slide Info

Should primary care providers treat chronic hepatitis C?

Diagnosis
Does my patient have chronic hepatitis C?

Management + Treatment
How do I treat chronic hepatitis C?

“A clinician with a panel size of 2500 patients would have to spend 18 hours per day to provide excellent chronic and preventative care and would require even more hours for acute care and care coordination.”

Ghorob and Bodenheimer. N Engl J Med 2012; 366:1955-1957 DOI: 10.1056/NEJMp1202775

Completed Family Medicine Residency at the University of Washington 2014

No Training in Treating Chronic Hepatitis C During Residency

Lummi Tribal Health Health Center: In 2015 Referred All Patients with Chronic HCV to Hepatology/GI (ARNP & PA's)

We Have Two Family Medicine Physicians Trained at Lummi (Myself and Dr. Ron Battle)

Cured >70 patients with chronic HCV

Treating Diabetes is More Complicated than Treating Chronic Hepatitis C

Why Should Primary Care Providers Treat Chronic HCV?

When we cure 30 patients with HCV we will prevent

12 cases of HCV related cirrhosis

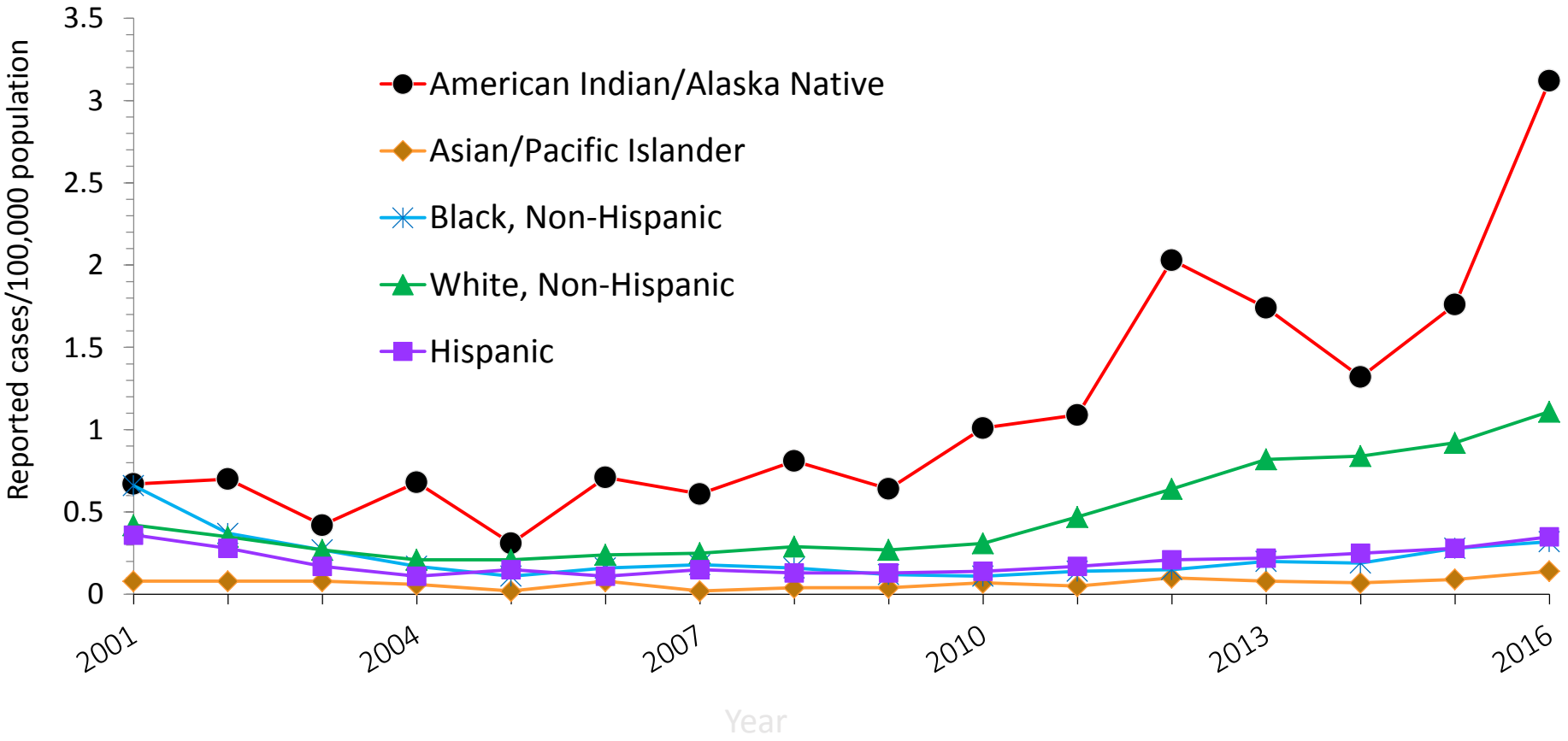
2 cases of HCV related hepatocellular carcinoma (HCC)

If we treat 104 patients with high cholesterol with statins for 5 years, we will prevent

1 first time heart attack

¾ of a stroke

Incidence of Acute Hepatitis C by Race/Ethnicity (USA)



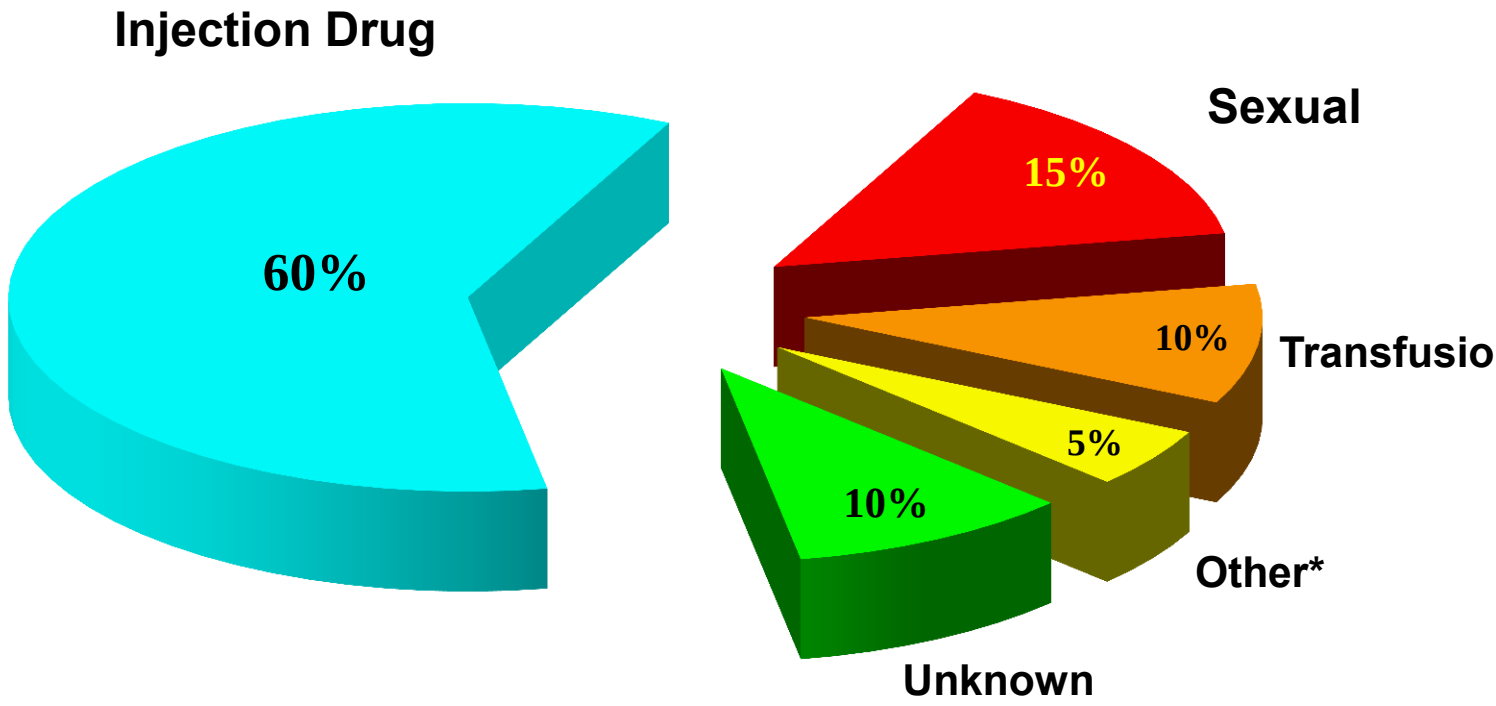
Source: National Notifiable Diseases Surveillance System (NNDSS)

HCV Transmission (USA)*Limited Data*

Blood
- IVDU is the leading cause in the United States
  - Snorting
- Percutaneous injuries
- Dental
- Non Professional Tattoo
- Blood transfusion (Before 1992)

Sexual contact
- Rare in heterosexual
- More frequent in HIV + MSM

Mother-to-child
- The rate is 1.7% - 4.3 %

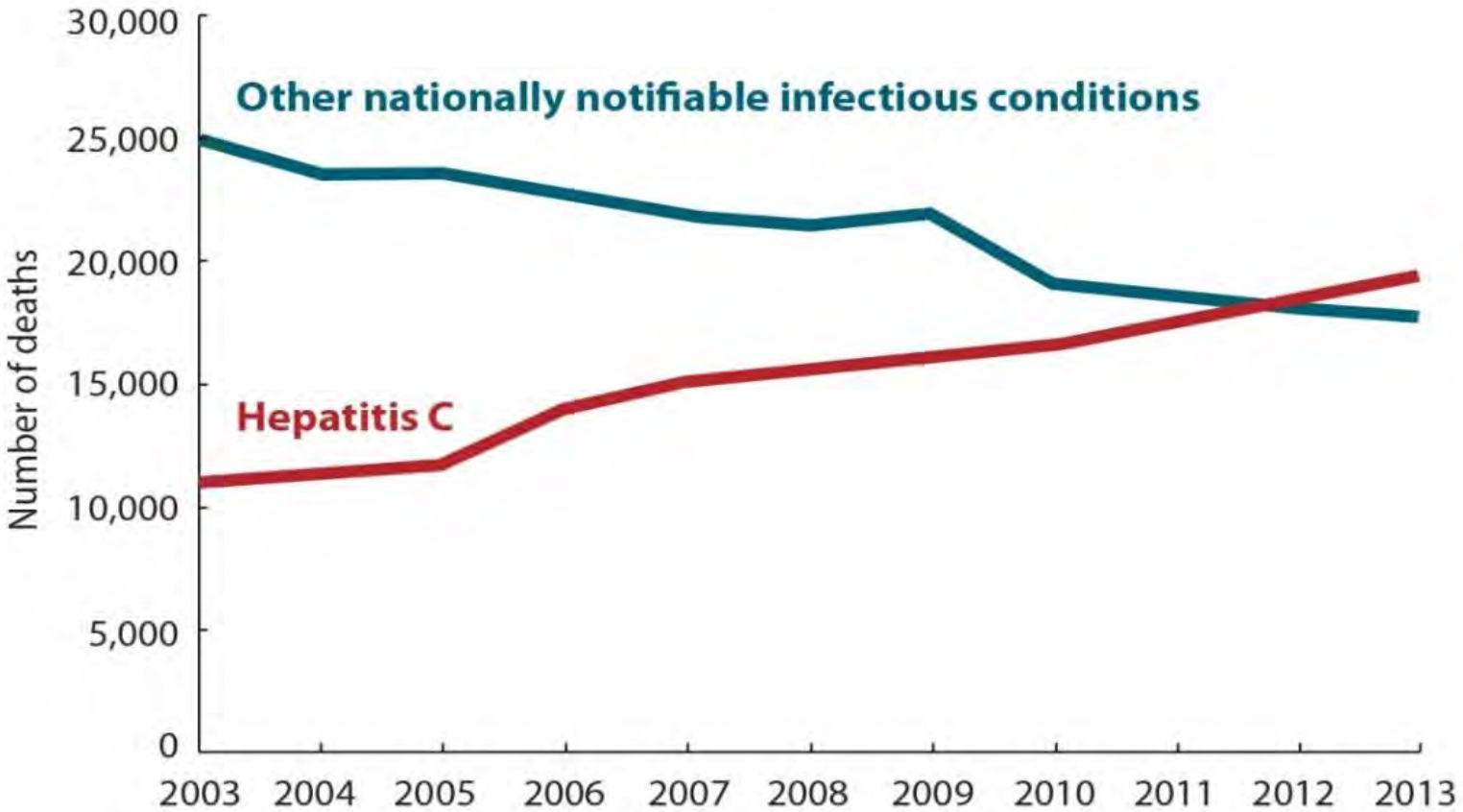


CDC, National Notifiable Diseases Surveillance System (NNDSS)

Today Over 80% of HCV Transmission Occurs in People Who Inject Drugs (PWID)

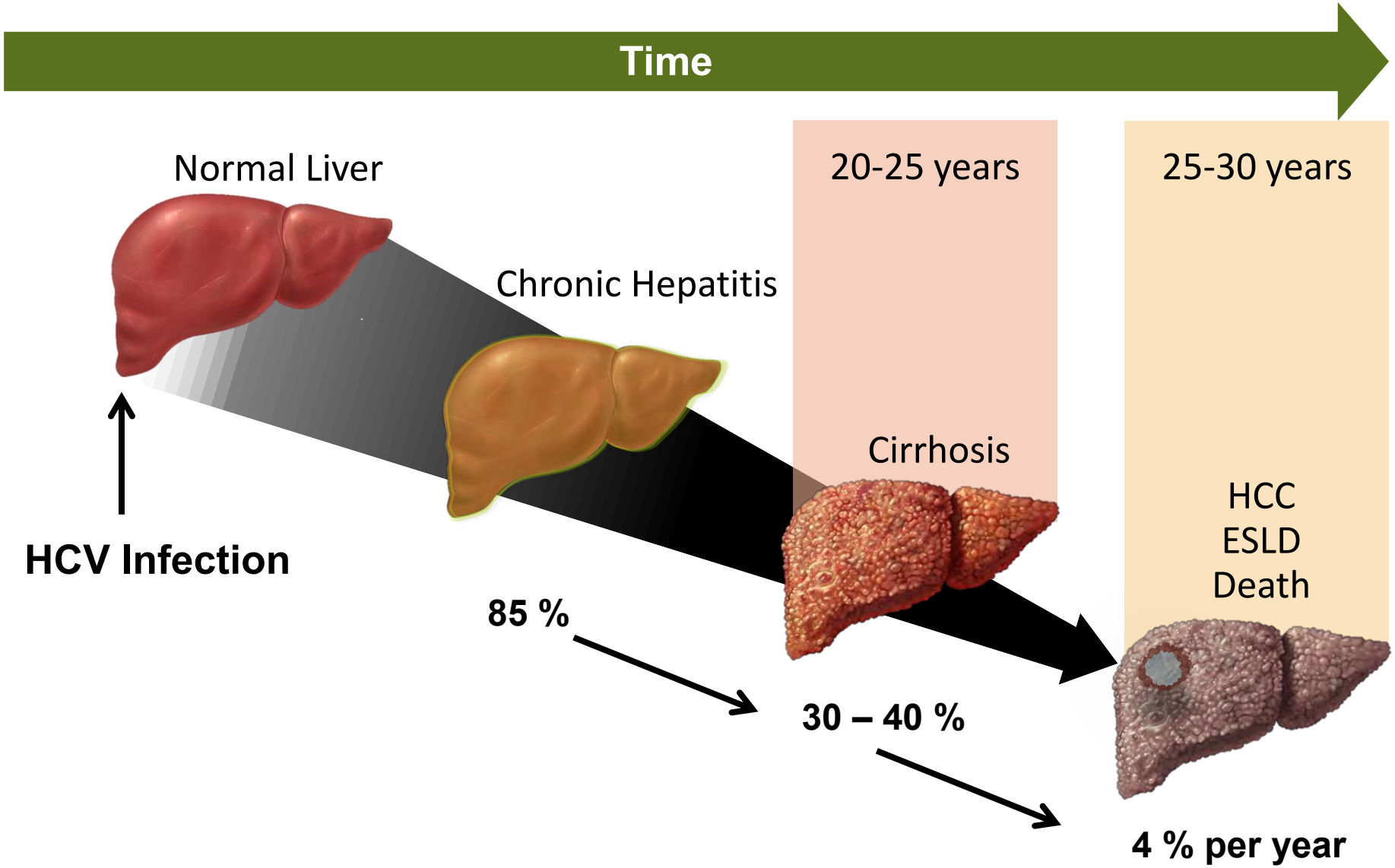
More People Are Dying of HCV Than All 60 Other Nationally Notifiable Infectious Diseases Combined.

Annual number of hepatitis C-related deaths vs. other nationally notifiable infectious conditions in the US, 2003-2013



Source: Centers for Disease Control and Prevention

Progression of Liver Disease Due to Chronic HCV



Natural History of Cirrhosis

Compensated Cirrhosis → Decompensated Cirrhosis → Death

Median Survival ~12 Years

Median Survival ~2 Years

Bleeding Varices
Ascites
Encephalopathy
Jaundice

D'Amico G, Garcia-Tsao G, Pagliaro L. Natural history and prognostic indicators of survival in cirrhosis: a systematic review of 118 studies J Hepatol. 2006;44:217-231.

Curing HCV is Associated With

50% Reduction in All-Cause Mortality
70% Reduction of Hepatocellular Carcinoma
90% Reduction in Liver Failure

Lok A. NEJM 2012; Ghany M. Hepatology 2009; Van der Meer AJ. JAMA 2012

Chronic HCV is Not Just A Liver Disease

Extrahepatic Manifestations of Chronic HCV

Immune Mediated
Chronic Inflammation

Approximately 40% of Chronic HCV Patients Will Develop at Least One Extrahepatic Manifestation

Often Not Clinically Recognized

Cirrhosis and Liver Disease Not Required

Common Symptoms and Illnesses

Insulin Resistance/Diabetes

Peripheral Neuropathy

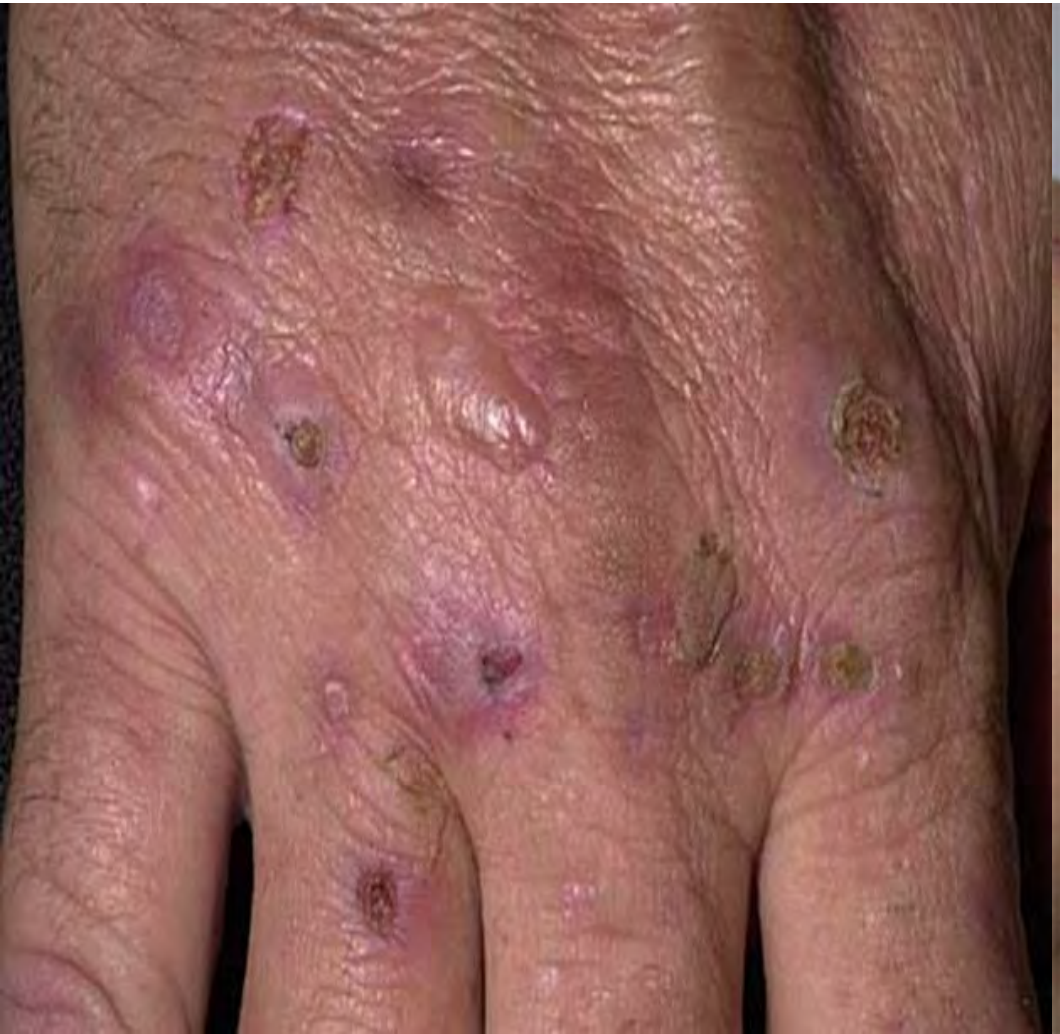
Renal Disease

Lymphoproliferative Disease: Cryoglobulinemia and B-Non Hodgkin Lymphoma

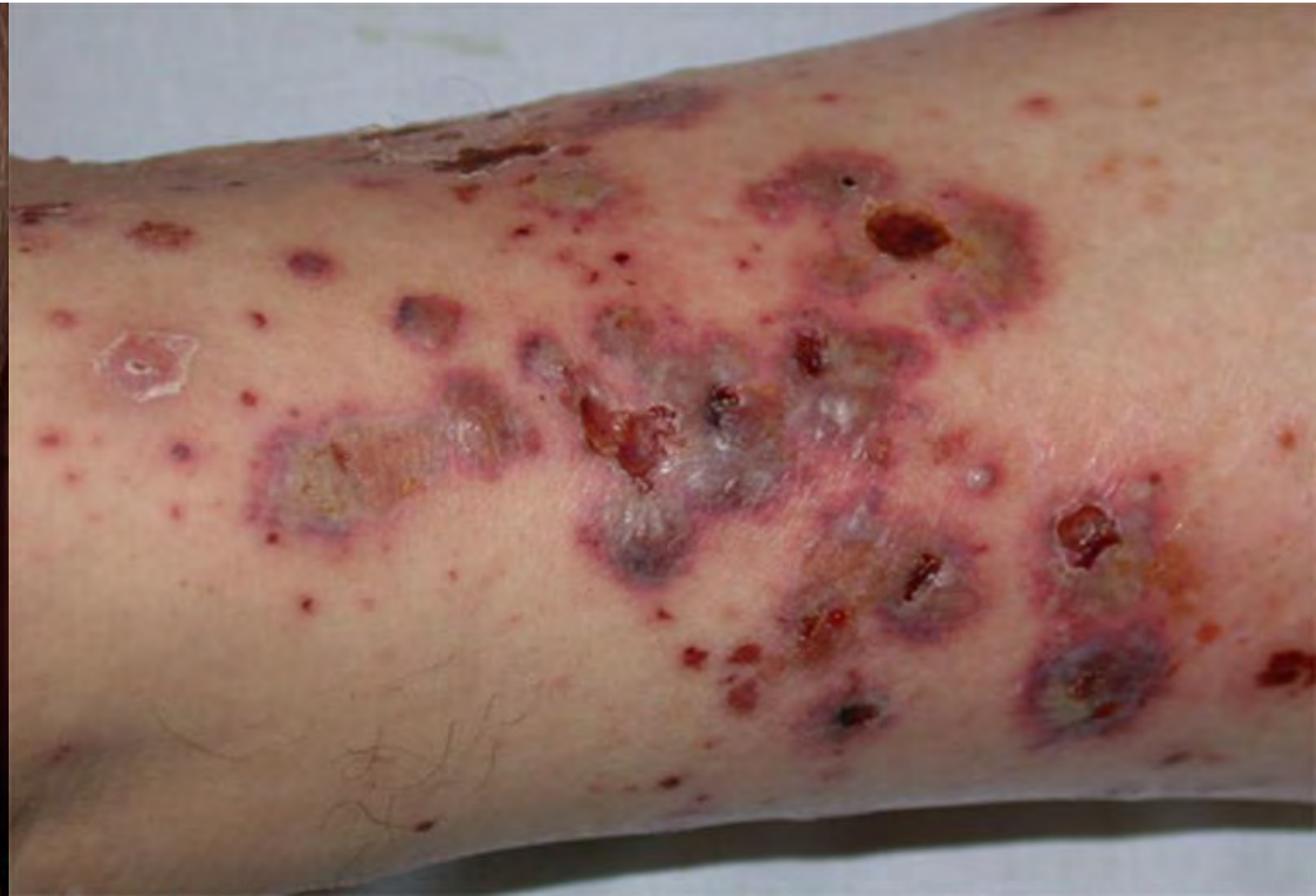
Arthralgias Often Misdiagnosed as Rheumatoid Arthritis

Dermatologic Manifestations

Porphyria Cutanea Tarda



Leukocytoclastic Vasculitis



Why Should Primary Care Providers Treat Chronic HCV?

Offer A Life Saving Cure

Treatment as Prevention for People Who Inject Drugs

Build Trust and Improve Access to Care for Community Members Who Inject Drugs

Does my patient have chronic hepatitis C?

Diagnosis

Positive HCV Ab = Previous Exposure

Once Positive-Always Positive.

No Need to Recheck.

Positive HCV RNA = Hepatitis C Virus Present

Diagnosis

15-30% Patients Will Spontaneously Clear the Hepatitis C Virus. HCV RNA ”Undetectable”

Of Those Who Will Clear

>95% Will Clear the Virus in 3 Months

Remainder Clear Virus in 6 Months

1. Positive HCV Ab (January 1)
   Negative HCV RNA (June 30)
   = Exposed to HCV and Spontaneously Cleared

2. Positive HCV Ab (January 1)
   Positive HCV RNA (June 30)
   = The Patient Has Chronic HCV

Diagnosis

3. Positive HCV Ab (January 1)
   Positive HCV RNA (January 30)
   = Patient May Clear Virus.
   Recheck HCV RNA at 6 months (June 30)
   (*review exposure history)

4. Positive HCV Ab (January 1)
   Positive HCV RNA (January 30)
   Negative HCV RNA (March 1)
   = The Patient Does Not Have Chronic HCV Spontaneously Cleared. (*review exposure history).

Diagnosis

5. Positive HCV RNA (January 1)
   Positive HCV RNA (June 30)
   =The Patient Has Chronic HCV

Diagnosis

Washington Medicaid Hepatitis C Policy January 2018

A Patient has a chronic HCV infection defined by:

1. Fibrosis Score ≥ F1 and HCV RNA (>15 IU/mL) within the last 12 months; OR
2. **Normal Liver (<F1); AND**

    1. **Positive HCV Ab at least 6 months old AND HCV RNA (15 IU/mL) presents 6 months after positive HCV Ab; OR**

    2. **Two HCV RNA (>15 IU/mL) at least 6 months apart.**

Diagnosis

https://www.hca.wa.gov/assets/billers-and-providers/WA-Apple-Health-Hepati
Clinical-Policy.pdf

Break?

Management + Treatment
How do I treat chronic hepatitis C?

We Offer Treatment to All Patients Except

Co-Occurring HIV + HCV

Decompensated Cirrhosis

(Bleeding Varices, Hepatic Encephalopathy, Ascites, Jaundice)

Follow the Algorithms. Participate in ECHO.

Treatment

Essential Information for WA Medicaid

- Does the patient have chronic HCV?
- What is the genotype?
- Does the patient have cirrhosis?
  - Compensated or Decompensated cirrhosis?
- Has the patient been treated before?

Treatment

All the Information You Need (nearly) to Treat HCV in One Sentence:

“35 yo male with chronic HCV, genotype 1a, non-cirrhotic, treatment naïve patient presents to discuss treatment for HCV.”

“35 yo male with chronic HCV, genotype 1a, non-cirrhotic, treatment naïve patient presents to discuss treatment for HCV.”

Genotype?
Cirrhosis vs Non-Cirrhotic?
Previous Treatment?

Treatment

What is the genotype? (may not matter soon…)

Order the HCV Genotype

Likely Results

Genotype 1
Genotype 2
Genotype 3

Treatment

Follow the Algorithms.

Treatment

Does the Patient Have Cirrhosis?

Treatment

Multiple Accepted Methods to Determine if a Patient Has Cirrhosis

HCA-accepted diagnostic tests and scores to stage liver fibrosis

Metavir Score	Biopsy	Fibroscan	Elastography (ARFI/PSWE)	FibroSure	APRI	Other Imaging
F4	F4	≥ 12.5 kPa	≥ 2.34 m/s	≥ 0.75	≥ 2.0	Cirrhosis
F3	F3	9.6 – 12.4 kPa	2.01 – 2.33 m/s	0.58 – 0.74	1.5 – 1.9	
F2	F2	7.1 – 9.5 kPa	1.38 – 2.0 m/s	0.49 – 0.57	1.0 – 1.4	
F1	F1	≤ 7.0 kPa	≤ 1.37 m/s	0.23 - 0.48	≤ 0.9	
F0	F0			≤ 0.22		

Treatment

HCA-accepted diagnostic tests and scores to stage liver fibrosis

Metavir Score	Biopsy	Fibroscan	Elastography (ARFI/PSWE)	FibroSure	APRI	Other Imaging
F4	F4	≥ 12.5 kPa	≥ 2.34 m/s	≥ 0.75	≥ 2.0	Cirrhosis
F3	F3	9.6 – 12.4 kPa	2.01 – 2.33 m/s	0.58 – 0.74	1.5 – 1.9	
F2	F2	7.1 – 9.5 kPa	1.38 – 2.0 m/s	0.49 – 0.57	1.0 – 1.4	
F1	F1	≤ 7.0 kPa	≤ 1.37 m/s	0.23 - 0.48	≤ 0.9	
F0	F0			≤ 0.22		

F0 No fibrosis

F1 Scattered portal fibrosis

F2 Diffuse periportal fibrosis

F3 Bridging fibrosis

F4 Cirrhosis

- Compensated
- Decompensated (Ascites, Bleeding Varices, Jaundice, Hepatic Encephalopathy)

Multiple Accepted Methods to Determine if a Patient Has Cirrhosis

Liver Ultrasound

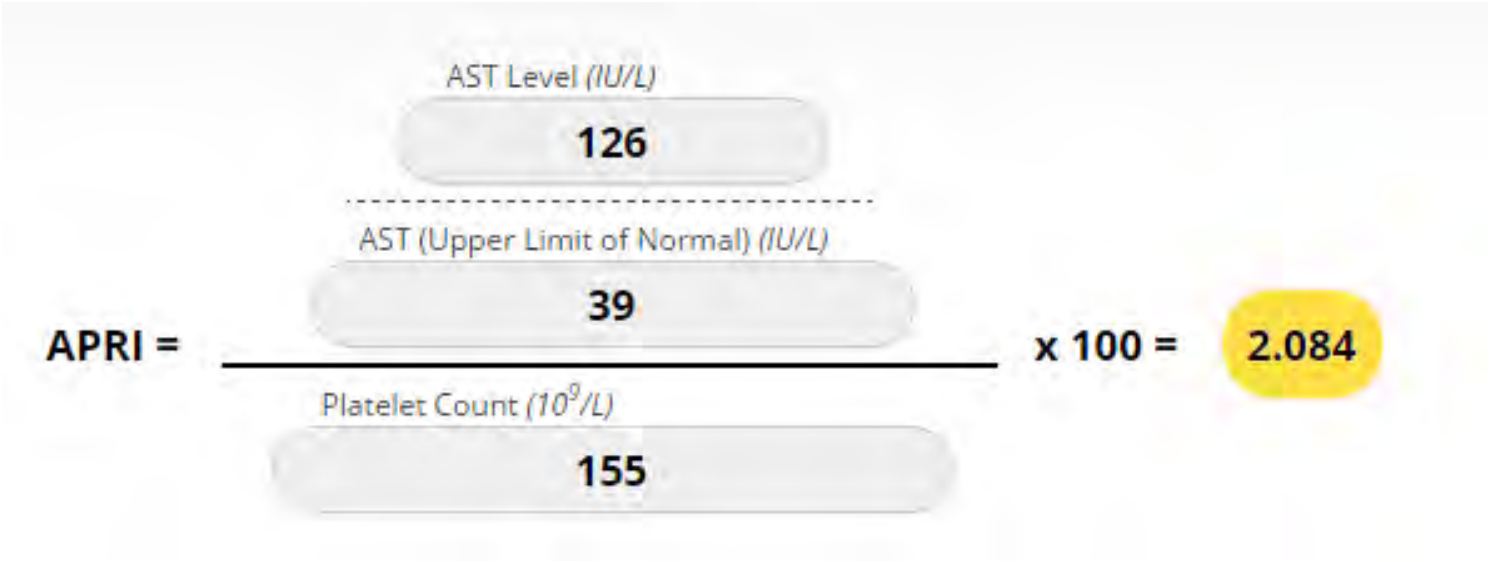
FibroSure: Blood Test. Check Your Local Lab.

Liver Biopsy: Rarely Needed.

Treatment

Multiple Accepted Methods to Determine if a Patient Has Cirrhosis

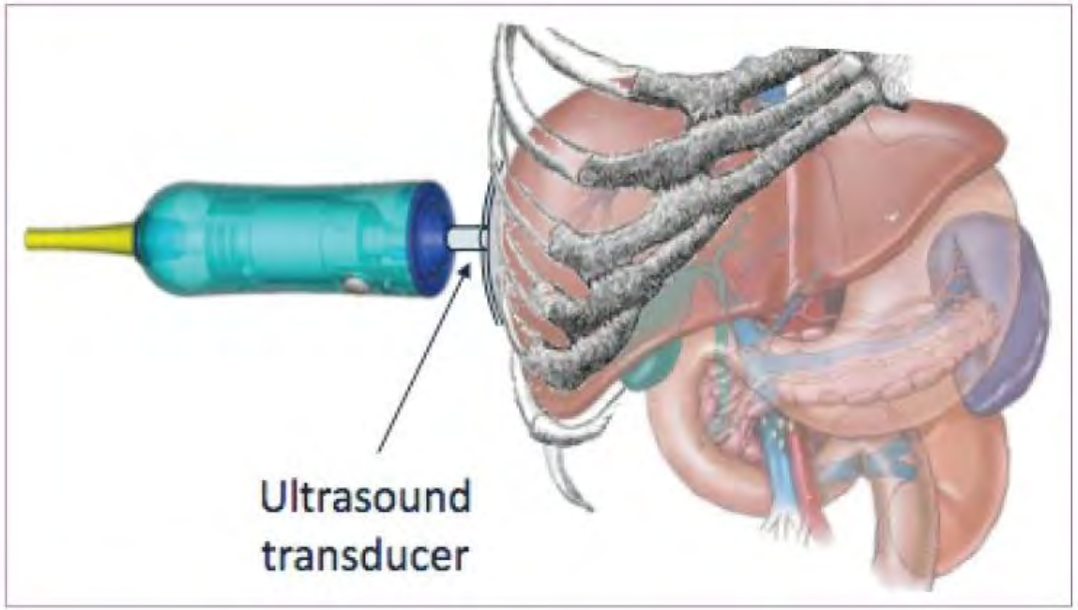
APRI: AST to Platelet Ratio Index (UW online Calculator)

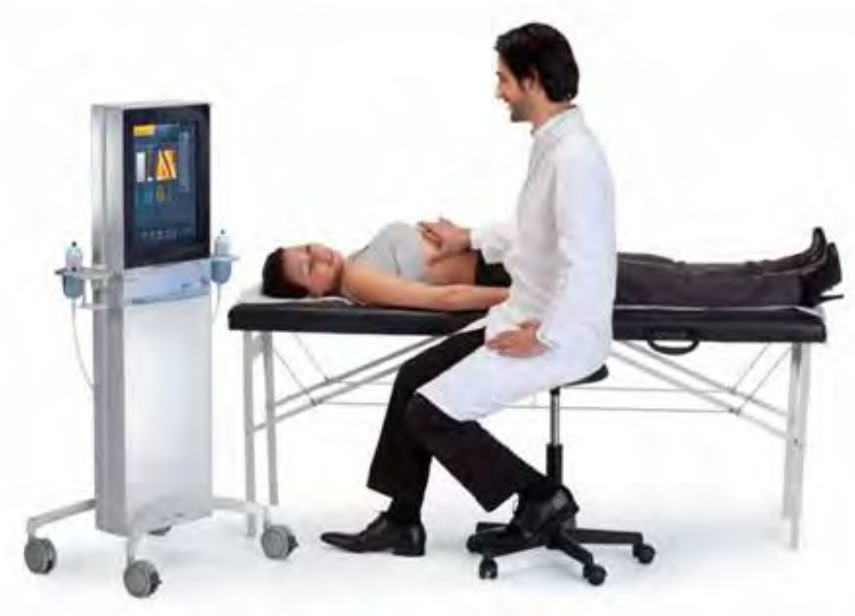


Treatment

Multiple Accepted Methods to Determine if a Patient Has Cirrhosis

Fibroscan: calculates liver stiffness based on sound wave. Non-invasive. (UW, VM, Lummi)





Treatment

Has the Patient Been Previously Treated for HCV?

Ask Them!

35 yo male with chronic HCV, genotype 1a, non-cirrhotic, treatment naïve patient presents to discuss treatment for HCV.

In Washington, as of January 2018, the first option for Medicaid Patients is MAVYRET (Glecaprevir/Pibrentasvir)

Treatment

https://www.hca.wa.gov/assets/billers-and-providers/WA-Apple-Health-HepatitisC-Clinical-Policy.pdf

glecaprevir/pibrentasvir (Mavyret®)

100mg/40mg tablet

Take 3 tablets once daily with food

glecaprevir

NS3/4A protease inhibitor

pibrentasvir

NS5A inhibitor

Pan-genotypic

Genotypes 1,2,3,4,5,6

Approved for some treatment failures

No dosage adjustment in patients with mild, moderate, or severe renal impairment, including dialysis

- FDA Approval August 3, 2017

Treatment

glecaprevir/pibrentasvir (Mavyret®)

All Genotypes, Non-Cirrhotic = 8 Weeks of Treatment

All Genotypes, Compensated Cirrhosis = 12 Weeks of Treatment

Treatment

glecaprevir/pibrentasvir (Mavyret®)

Most common adverse effects (~10%)
Headache
Fatigue
Child-Pugh Class B- Not Recommended
Child-Pugh Class C- Contraindicated
No additional monitoring parameters provided in package insert

glecaprevir/pibrentasvir (Mavyret®)

HMG-CoA Reductase Inhibitors

- Levels of statin drugs are increased; doses should be adjusted per package insert

Omeprazole

- Package insert states no dose adjustments required
  - 40mg daily is highest dose studied
  - 20mg: Coadminister with GLE/PIB
  - 40mg: Give one hour before GLE/PIB

No interaction with antacids or H2 blockers

Ethinyl estradiol-containing products

- Coadministration of Mavyret may increase the risk of ALT elevations and is not recommended (Mirena, Paraguard, Nexplanon, Mini-pill)

glecaprevir/pibrentasvir (Mavyret®)

Other Considerations

Check HBV Status to Monitor for Reactivation

If positive HBsAg or anti-HBc, FOLLOW ALGORITHM for Hep B Reactivation

Pregnancy Risk

Check for Medication Interactions: HEP Drug Interactions

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

Start 8 Week Treatment With Mavyret

Baseline Labs

Serum Creatinine, Hepatic Function Panel: Albumin, Total Bilirubin, Direct Bilirubin, ALT, AST, Alk Phos, CBC, INR, HBsAg, anti-HB core, and anti-HBs

Return at 4 Weeks

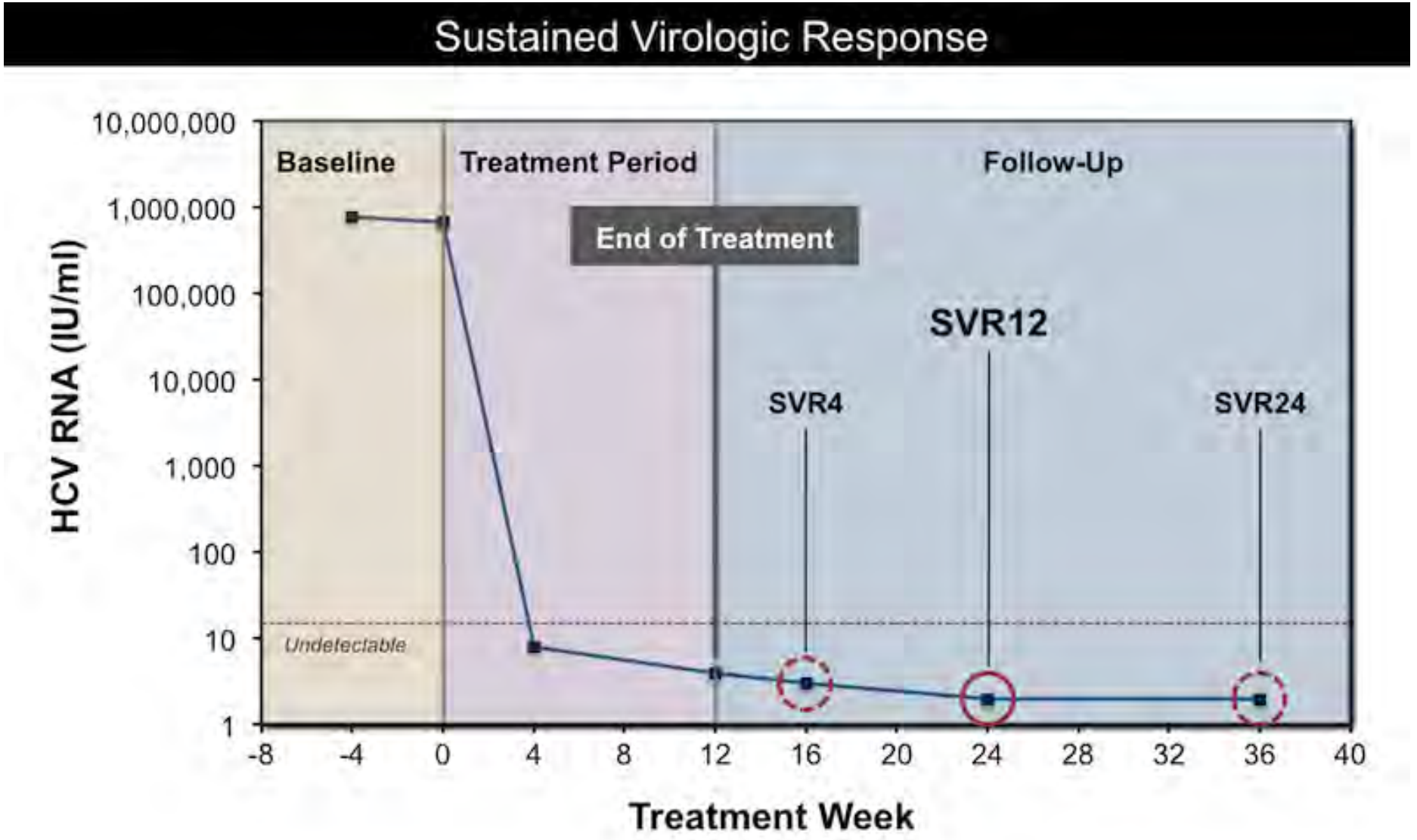
HCV RNA- Should be Undetectable

Serum Creatinine, Hepatic Function Panel, CBC

Return at 8 Weeks

HCV RNA- Should be Undetectable

Treatment



SVR = Sustained Virologic Response = Cure

Treatment

Approach When HCV RNA Detectable at Treatment Week 4

Recheck HCV RNA Week 6. If 10-fold increase, stop treatment/consult expert. If persistent low level viremia, continue treatment. Consult.

https://www.hepatitisc.uw.edu/go/treatment-infection

Management of Abnormal ALT at Week 4 of Therapy

If 10-fold or Greater Increase in ALT- STOP Treatment

If Less than 10-fold increase but symptomatic hepatitis (weakness, jaundice, nausea, vomiting_- STOP Treatment

If Less than 10-fold and asymptomatic, recheck ALT 6 and 8 weeks. Consult.

https://www.hepatitisc.uw.edu/go/treatment-infection

35 yo male with chronic HCV, genotype 1a, non-cirrhotic, treatment naïve patient presents to discuss treatment for HCV.

Completed 8 Weeks of Mavyret

Sustained Virologic Response (SVR) at 12 Weeks After Completing Therapy

The Patient is Cured

https://www.hepatitisc.uw.edu/go/treatment-infection

Continuing Education

Learn About Harvoni, Epclusa and Vosevi (used for treatment failures)

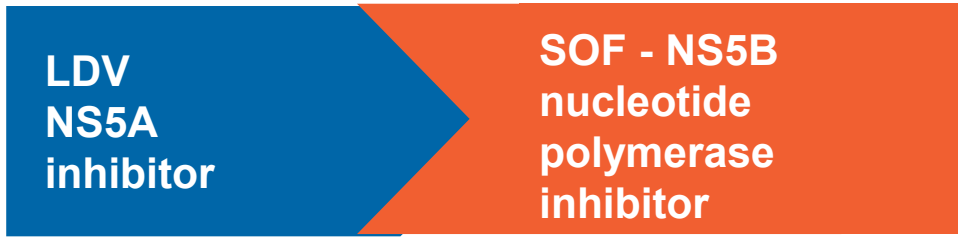
Harvoni- no longer preferred by WA Medicaid

UW Hepatitis C Online Course
www.hepatitisc.uw.edu

Thank You and Questions

ledipasvir/sofosbuvir (Harvoni®)

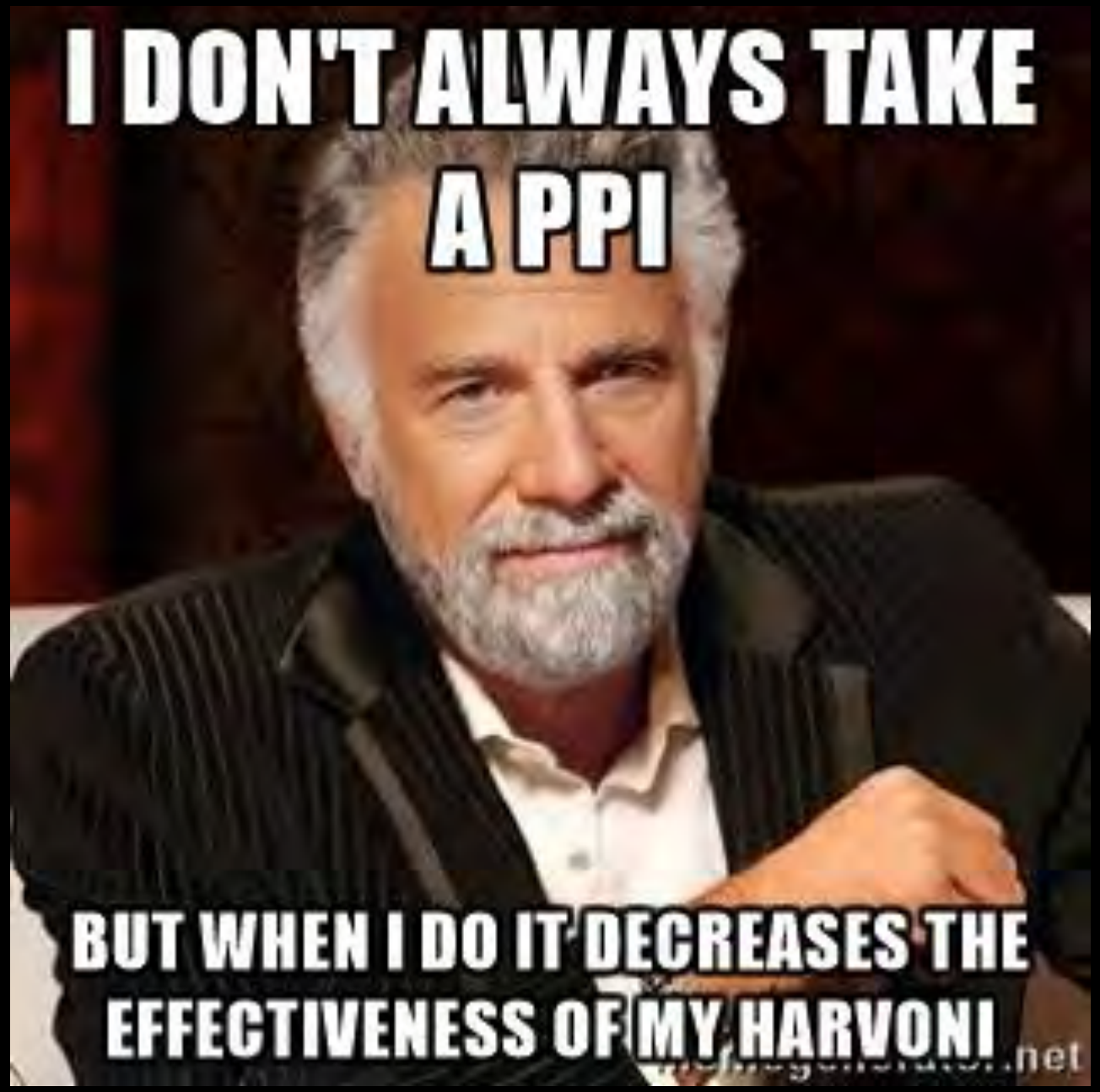
- Once daily single oral tablet
- Genotype 1 and 4
- Minimal DDIs, no food effect
- 8 week treatment available
  - Naïve/Non cirrhotic/VL < 6 million
- **Do not use in patients with GFR < 30**
- Avoid use with anti acids
  - May use with 20 mg of omeprazole ***if necessary***



Approved: Oct 10, 2014

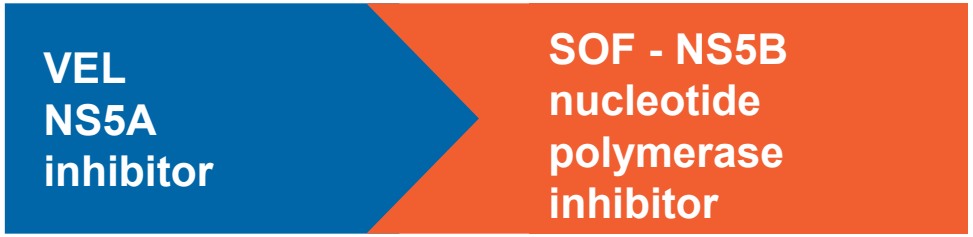
DDI: Drug-Drug Interactions

Harvoni® [package insert]. Gilead Sciences, Foster City, CA


I DON'T ALWAYS TAKE A PPI
BUT WHEN I DO IT DECREASES THE EFFECTIVENESS OF MY HARVONI

velpatasvir/sofosbuvir (Epclusa®)

- Once Daily Single Oral Tablet
- Minimal DDIs, no food effect
- **Genotype 1,2,3,4**
- Do not co-administer with PPI
  - *If medically necessary, take Epclusa with food 4 hours before omeprazole 20 mg andOnly doses ≤ omeprazole 20 mg*
- Do not use in patients with GFR < 30



Approved: June 28, 2016

Epclusa® [package insert]. Gilead Sciences, Foster City, CA