HEPATITIS C

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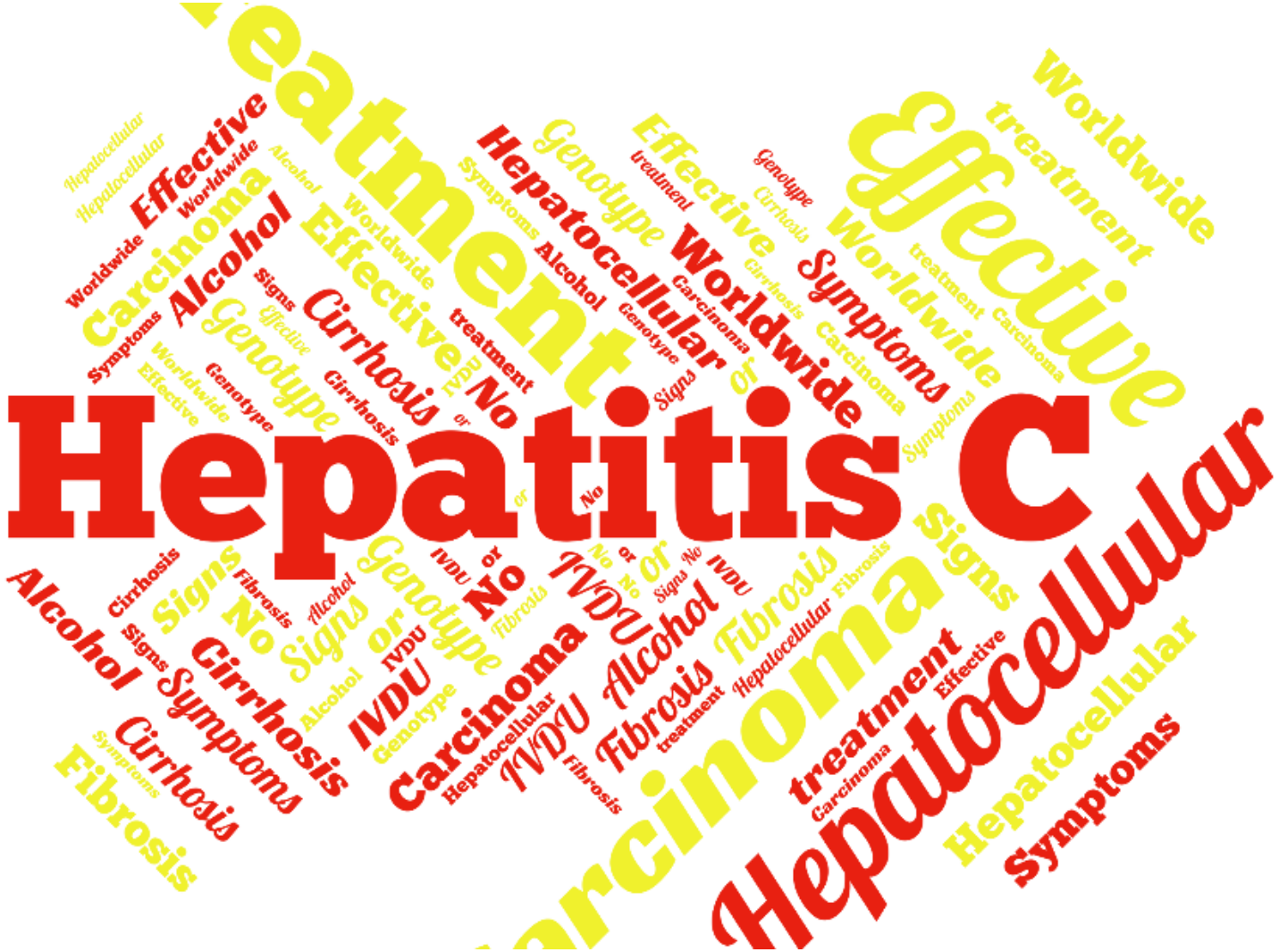
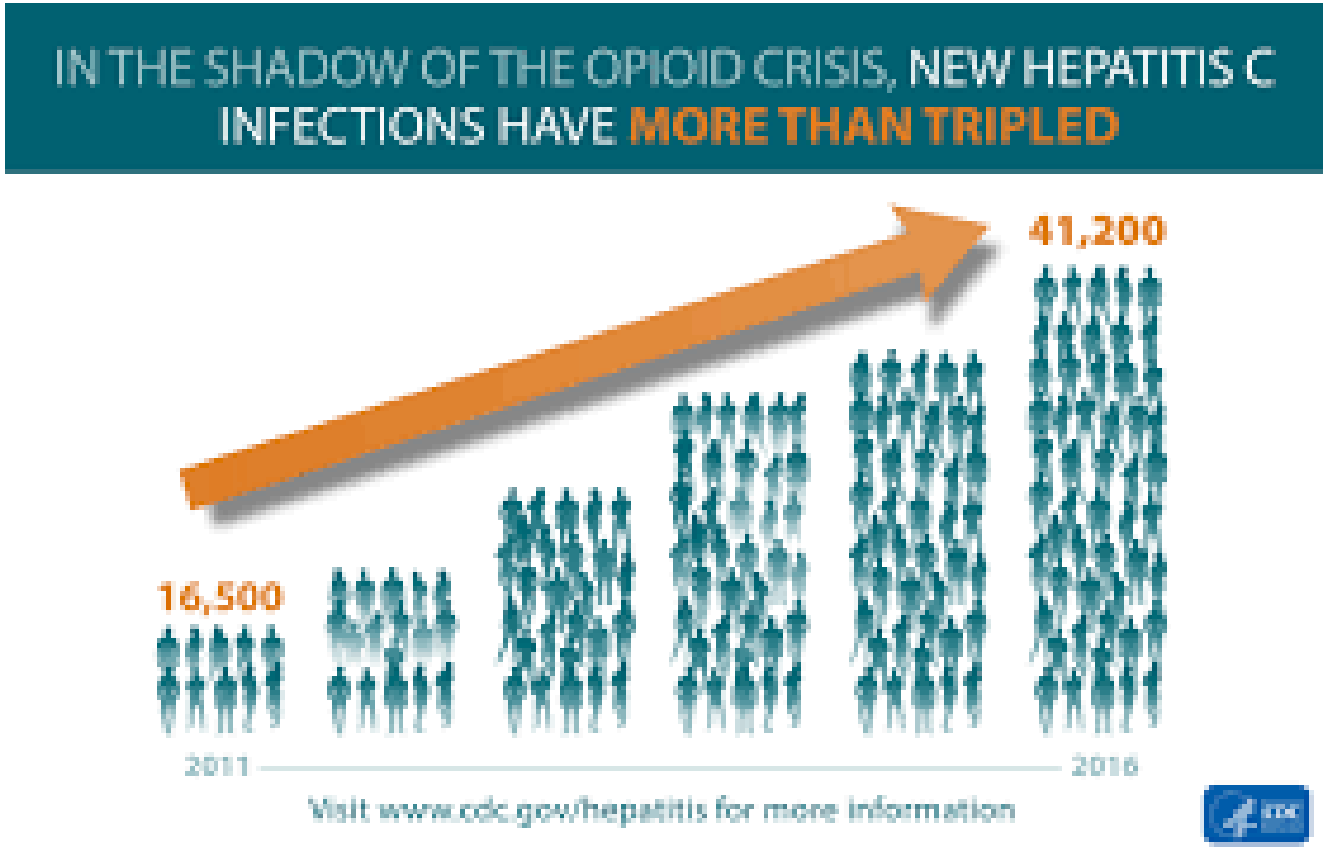
62ND ANNUAL FAMILY MEDICINE SEMINAR

RUIDOSO CONVENTION CENTER


Hepatitis C
Hepatocellular
Carcinoma
Treatment
Effective
Worldwide
Symptoms
Alcohol
Fibrosis
Cirrhosis
IVDU
Genotype
Signs
No
or

Introduction

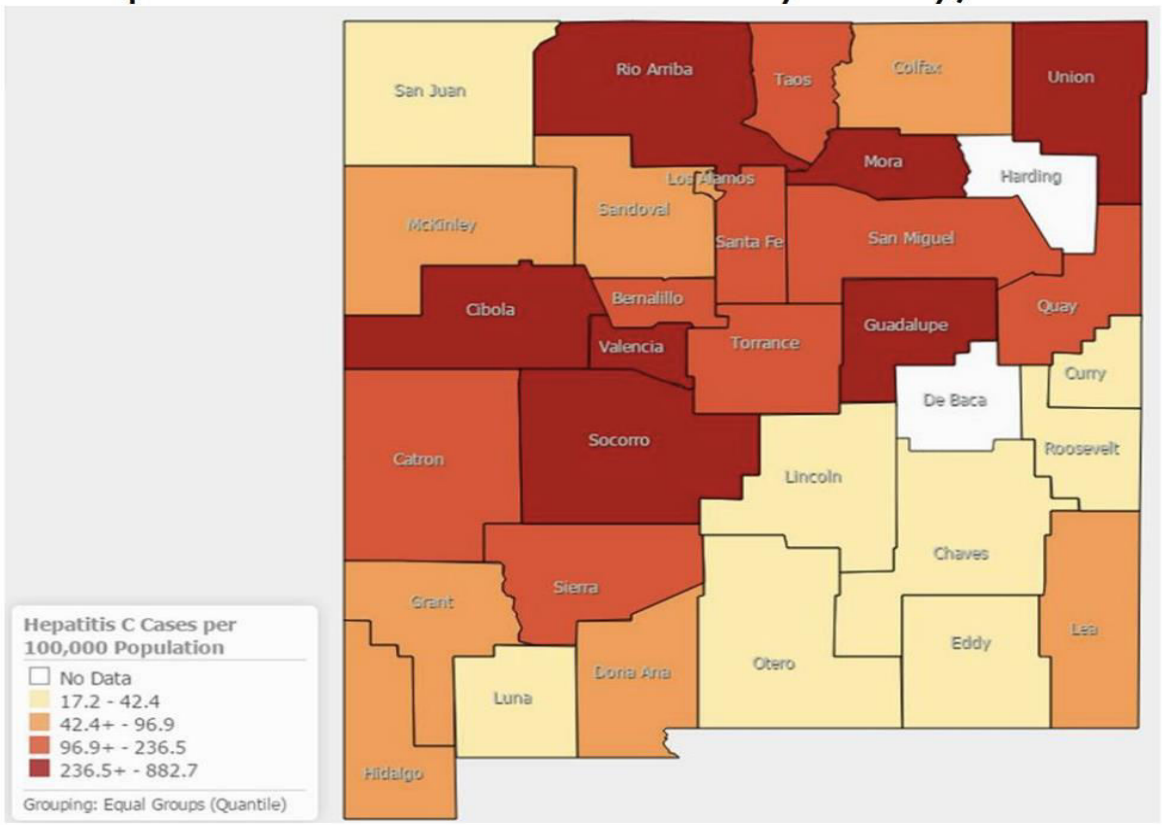
- Globally, an estimated **71 million people have** chronic **hepatitis C** infection
- 2.4million people in the US are **living with** Chronic Hepatitis C per the CDC (2016).
- Approximately 75-85% of **acute** Hepatitis C infections will become chronic.
- It is the **leading cause** of liver cancer, liver transplants and liver failure.
- Hepatitis C **kills** more Americans than any other infectious disease per the CDC.
- HCV infection rates are highest among baby boomers and injection drug users.
- There is **no vaccine** for Hepatitis C.
- Most are ***unaware*** of their diagnosis.
- It is estimated that **45,000** New Mexicans are living with chronic infections of hepatitis C virus (HCV). https://nmhealth.org/publication/view/plan/2219/



Epidemiology

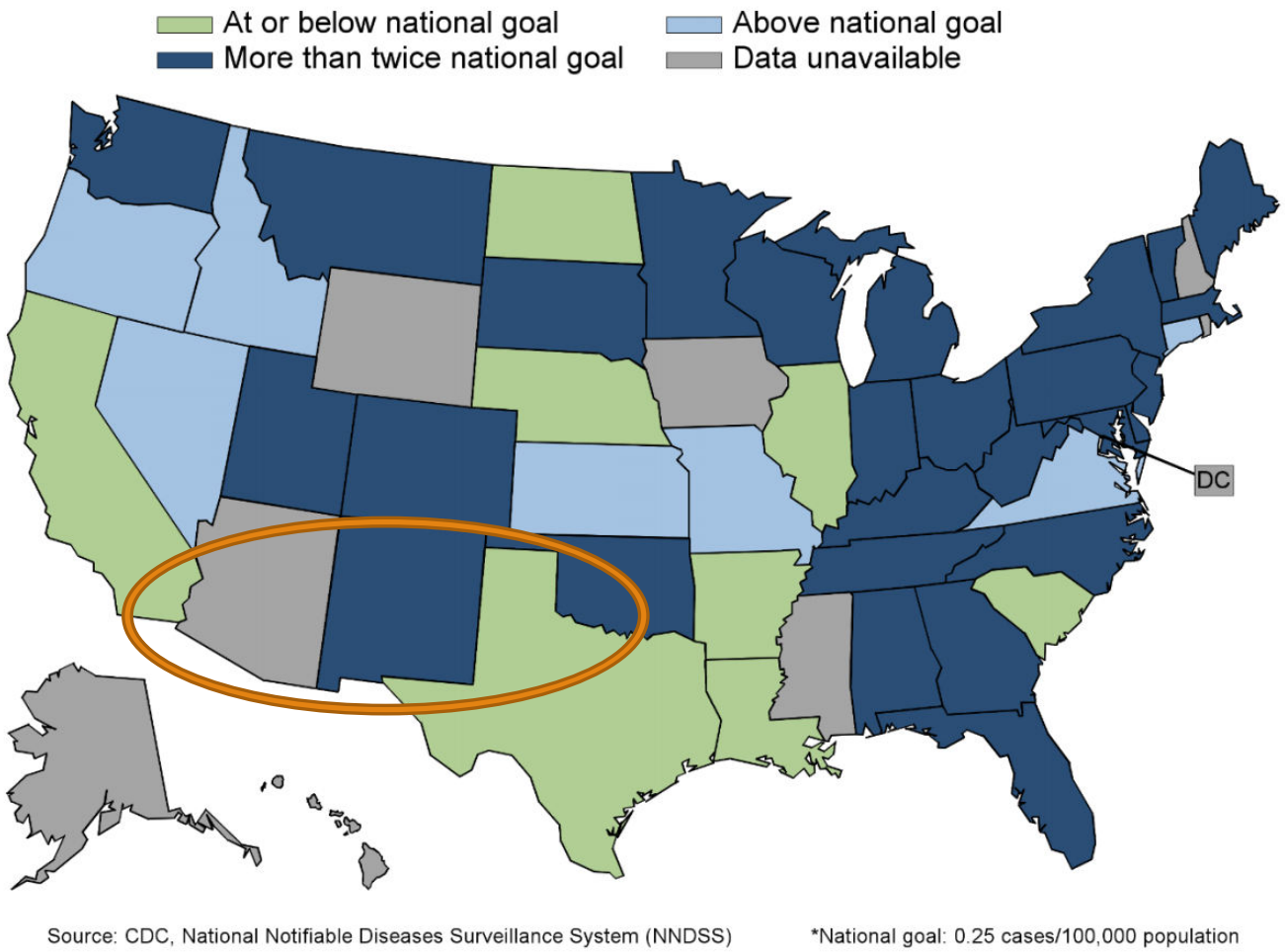
New Mexico Epidemiology

Hepatitis C Rates in New Mexico by County, 2015



Dates are from NM IBIS on 5/9/2016

Map 4.1 State Acute Hepatitis C Incidence Compared to Healthy People 2020 National Goal*
United States, 2016



Source: CDC, National Notifiable Diseases Surveillance System (NNDSS)

*National goal: 0.25 cases/100,000 population

New Mexico had rates of acute hepatitis C that were more than twice the national goal.

We’re Missing the Boat

Do you routinely screen for Hepatitis C at risk and those born between 1945-1965?

1. Yes
2. No

Why screen for Hepatitis C?

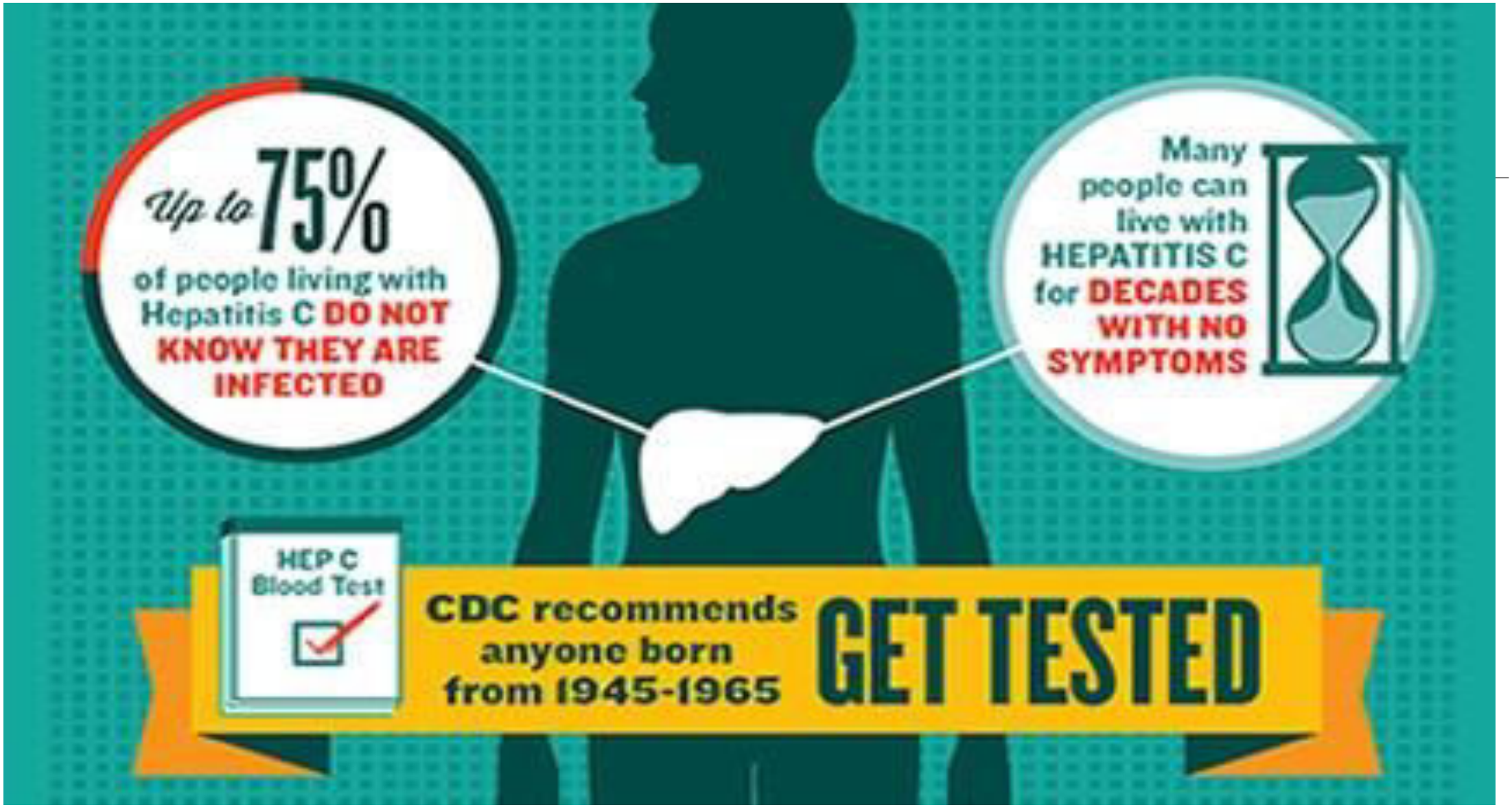
- Approximately 75% of people living with hepatitis C were born during 1945-1965.
- A high proportion of people with hepatitis C do not know that they are infected (estimates range from 45%-85%).
- Testing based solely on elevated ALT levels is estimated to miss 50% of chronic infections.
- For those who are chronically infected, clinical preventive services including regular medical monitoring, hepatitis A and B vaccination, and behavior changes like alcohol reduction/cessation and achieving and maintaining a healthy BMI can improve health outcomes for people with hepatitis C.
- New therapies, including interferon-free regimens, can halt disease progression, cure most infected with hepatitis C.
- **One-time testing of those born 1945-1965 is estimated to identify 800,000 infections and, with linkage to care and treatment, avert more than 120,000 HCV-related deaths. This strategy is estimated to save $1.5-$7.1 billion in liver disease-related costs.**

People Born 1945-1965 (Baby Boomers)

CDC Recommendation: Adults Born from 1945-1965 (Baby Boomers) get Tested for Hepatitis C

In addition to testing adults of all ages at risk for hepatitis C virus infection, CDC recommends:

- All adults born during 1945–1965 receive one-time testing for the hepatitis C virus (HCV).
- Testing should begin with anti-HCV. If the anti-HCV test is positive, or reactive, then a nucleic acid test (NAT) should follow.
- All persons identified with current HCV infection should receive a brief alcohol screening and intervention as clinically indicated, followed by referral to appropriate care and treatment services.


Up to 75%
of people living with Hepatitis C DO NOT KNOW THEY ARE INFECTED
Many people can live with HEPATITIS C for DECADES WITH NO SYMPTOMS
HEP C Blood Test
CDC recommends anyone born from 1945-1965
GET TESTED

USPTF Screening Recommendation

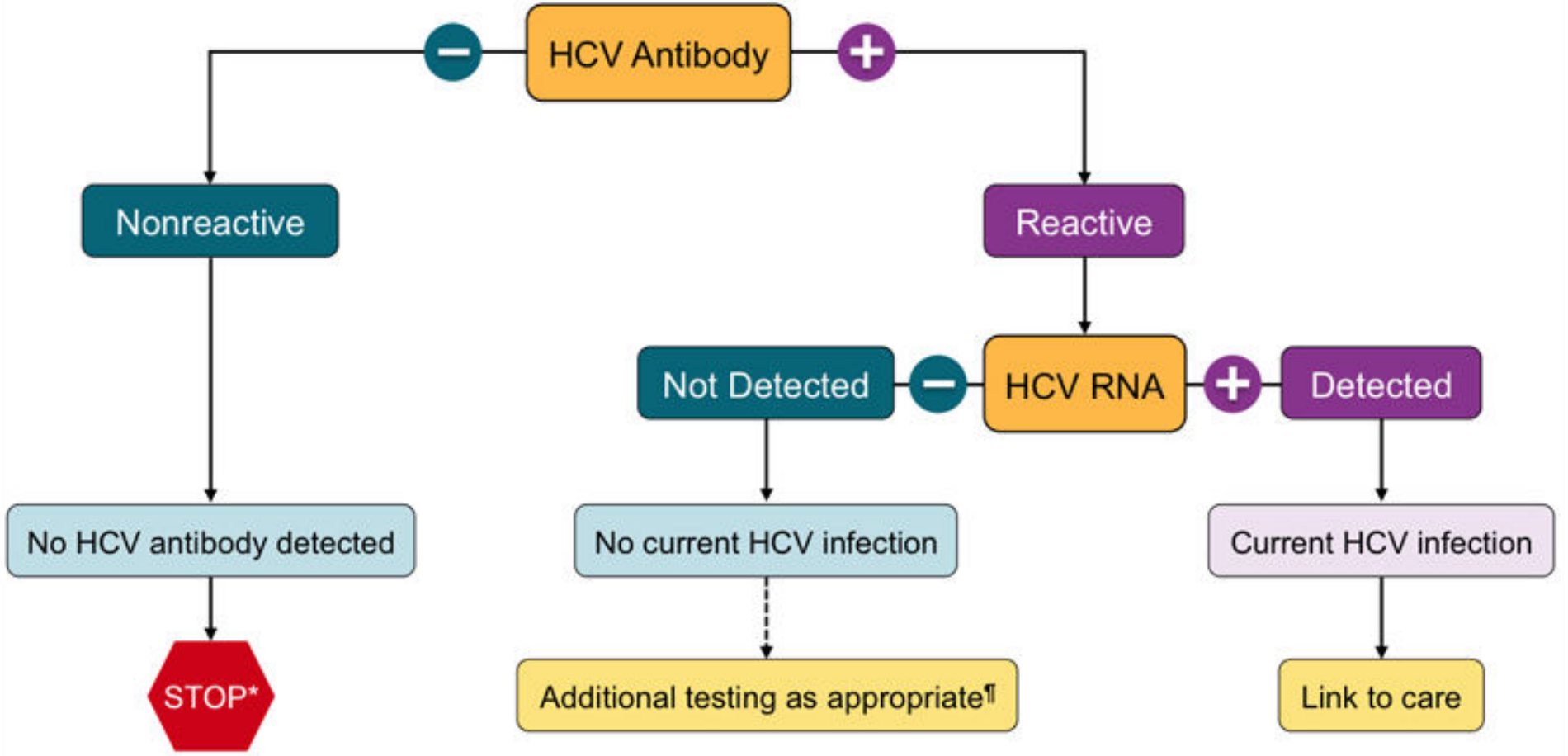
- The USPTF recommends screening for hepatitis C Virus (HCV) infection in persons at high risk for infection. The USPTF also recommends offering 1 time screening for HCV infection to adults born between 1945 and 1965.
  - Grade B recommendation

Point of Care Testing

- Linkage to care
- Expensive $39- $60
- Over the counter
- Oral Mucosal Transudate
- Sensitivity: 97.7 %
- Specificity : 98.8 %
- 20- 40 minutes

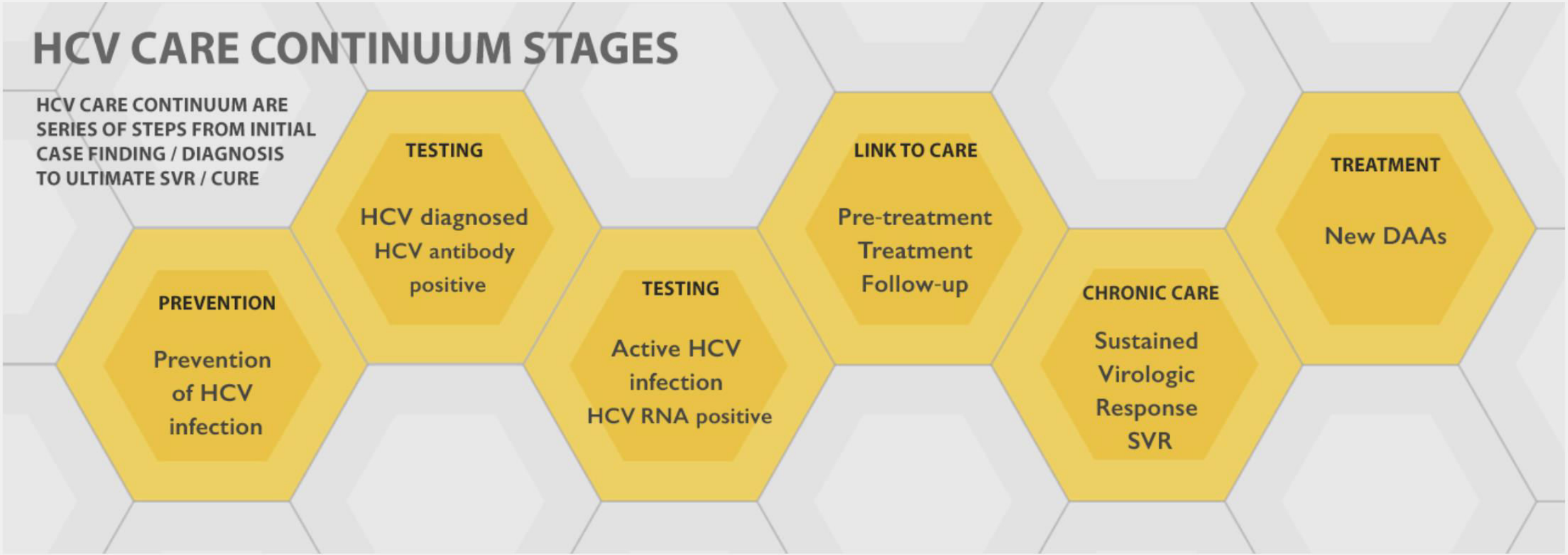
- ***If following screening recommendations primary care providers will see more individuals diagnosed with acute and chronic Hepatitis C.***

Recommended Testing Sequence for Identifying Current HCV Infection



* 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.

¶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.



HCV CARE CONTINUUM

HTTPS://WWW.INTECASI.COM/PRODUCTS/HCV-TEST

Acute Hepatitis C

- Acute Hepatitis C – signs and symptoms that occur within 6 months of presumed exposure.
- Approximately 20% to 50% spontaneous resolution.
- Hepatitis C RNA can be detected as early as 7 days after exposure.
- HCV Antibody test may be negative during the first 6 -8 weeks after exposure.
- ALT may or may not be elevated.
- HCV RNA may be transiently negative during acute HCV infection.
- Treat or not to treat?

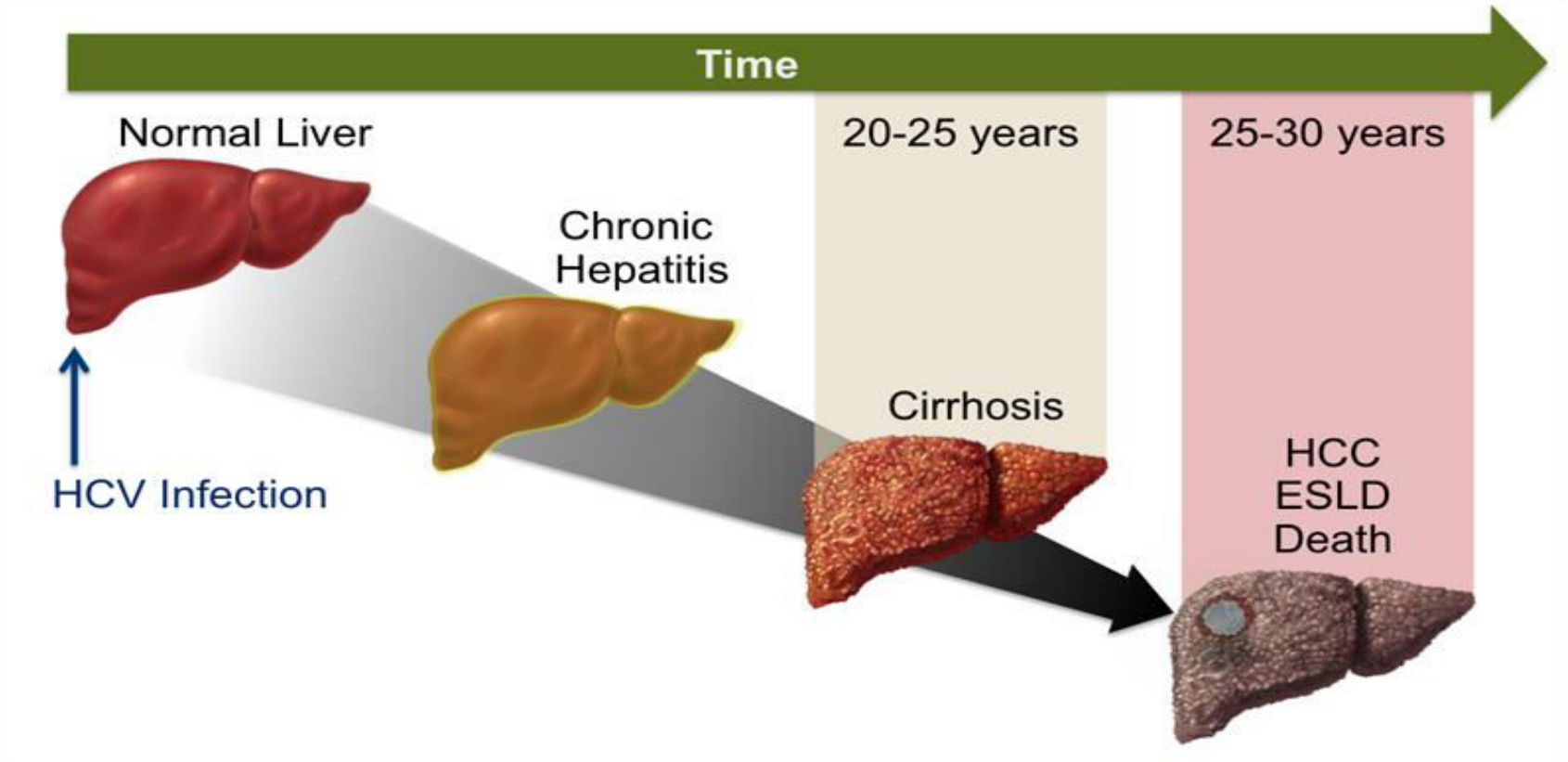
Chronic Hepatitis C

- Chronic hepatitis C is having the condition at least six months.
- Chronic hepatitis C can lead to liver damage - progression to cirrhosis and hepatocellular carcinoma. It is estimated that up to 25% of patients with chronic hepatitis C will develop cirrhosis within 20 years.
- Approximately 80% of patients with acute hepatitis C develop chronic infection.
- In many cases, there are no symptoms of the disease until liver problems have developed.
- Chronic Hepatitis C may be cause of B cell non-Hodgkin's lymphoma, role in RA and dermatomyositis

Symptoms of Hepatitis C

- Approximately 70%–80% of people with acute Hepatitis C do not have any symptoms. Some people, however, can have mild to severe symptoms soon after being infected, including:
  - Fever
  - Fatigue
  - Loss of appetite
  - Nausea
  - Vomiting
  - Abdominal pain
  - Dark urine
  - Clay-colored bowel movements
  - Joint pain
  - Jaundice (yellow color in the skin or eyes)

Progression of Hepatitis C



CASE

- John, a 45yo AA male presents to his PCP for follow up on his HTN and DM.
  - PMH: HTN,DM
  - SH: tobacco use , hx of IVDU, current alcohol use – drink 4 beers per day,smokes marijuana
  - Medication: Metformin 500mg bid ,Lisinopril 20 mg qd,omeprazole 20 mg qd

DO WE SCREEN HIM FOR HCV?

CASE

JOHN is found to have Positive HCV Antibody-

Note: 20% of patients with positive HCV spontaneously clear, need confirmation with RNA

HCV RNA – 7.3 MILLION

Now what?

- Pretreatment evaluation
- Follow up labs
- Treatment consideration
- Counseling

PRETREATMENT EVALUATION..

Pretreatment Evaluation:

- Achieve medical stability before HCV treatment
  - HCV treatment usually is not urgent; for ex. most experts prefer to control HIV infection, cardiac disease, asthma, etc. prior to HCV treatment
  - Waiting until the patient has no acute or unstable chronic conditions avoids confounding comorbid symptoms with treatment side effects
- Patient must be able to understand and adhere to care plan
  - HCV medications are expensive – use resources wisely by working aggressively to resolve barriers to success before treating

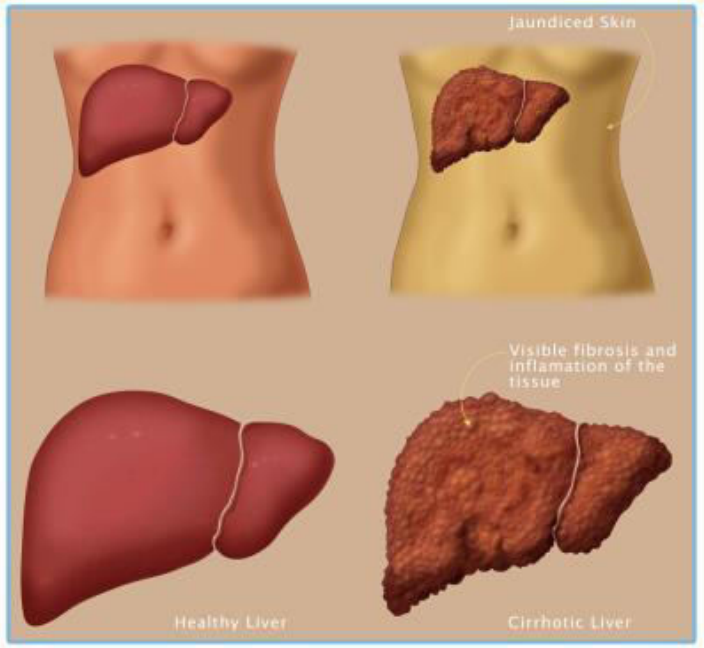
Pretreatment Evaluation:

- Approval for treatment varies by insurer. Factors may include:
  - Fibrosis stage
  - Sobriety requirements
  - Prescriber type: Hepatology, GI, ID, primary care
- Some states provide and require a certification process to prescribe HCV medications.
- Investigate your state's Medicaid HCV prior authorization process.

Pretreatment Evaluation – History and Physical Exam:

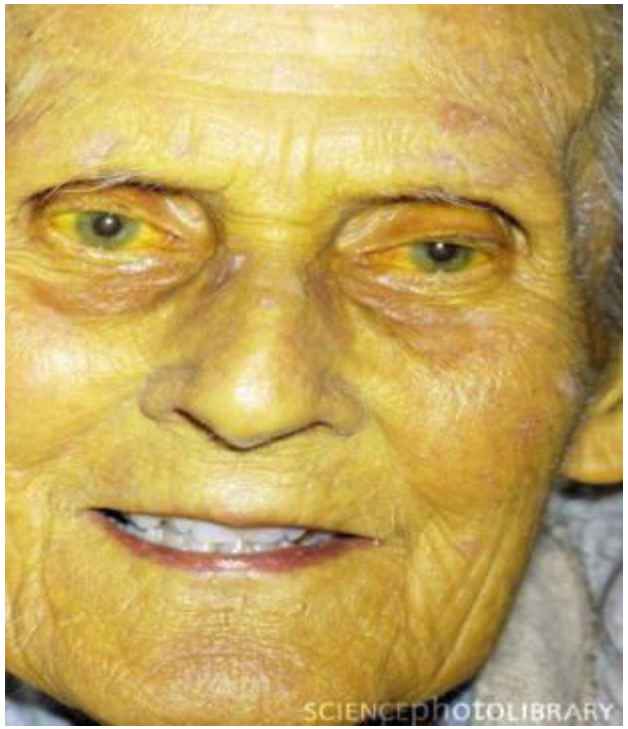
- Previous treatment history
- Evaluate symptoms and medical comorbidities.
- Ask about alcohol and drug use that may impact treatment.
- MENTAL HEALTH EVALUATION - ADHERENCE
- Elicit information about housing or food insecurity that may impact treatment.
- Reconcile medication list.
- Look for stigmata of liver disease – ***good physical exam***!

Healthy vs. Cirrhosis



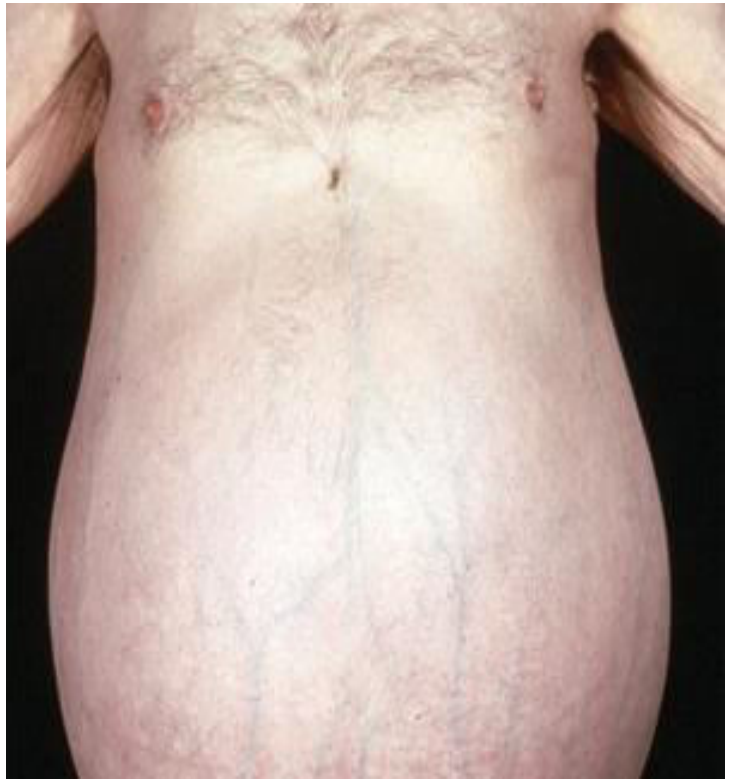
Signs of Cirrhosis

Jaundice

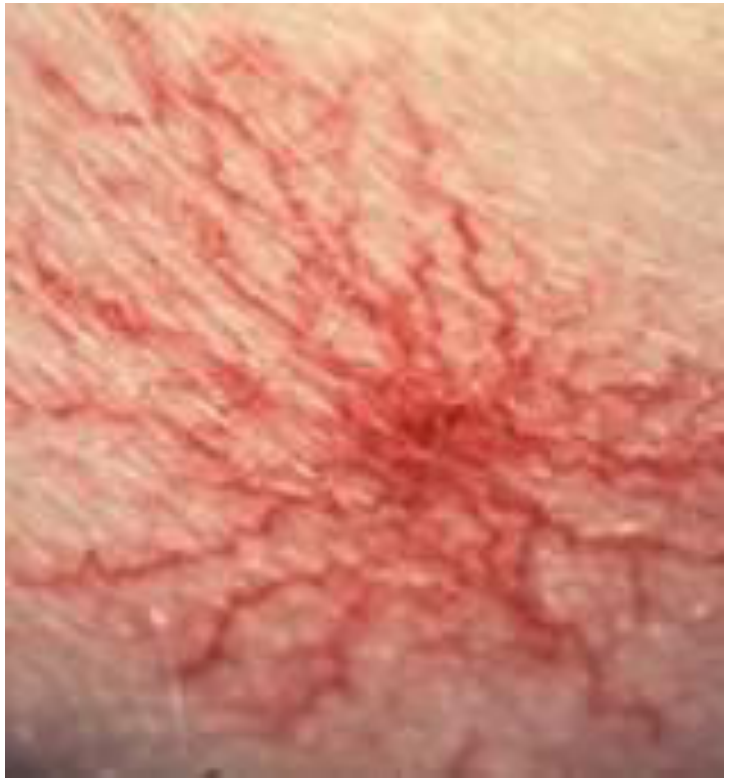


Signs of Cirrhosis

ASCITES

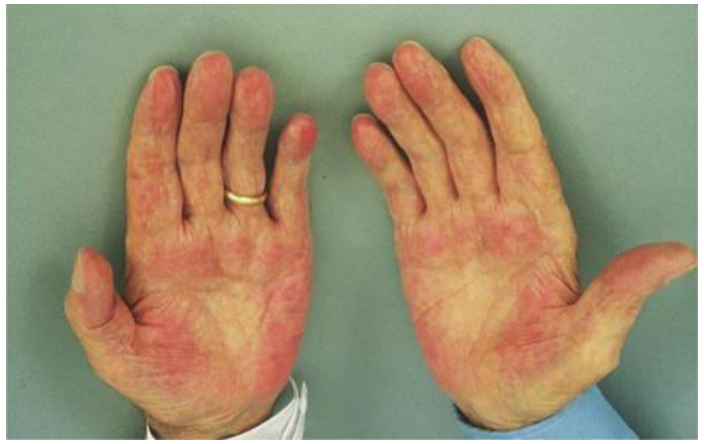


Spider angiomas

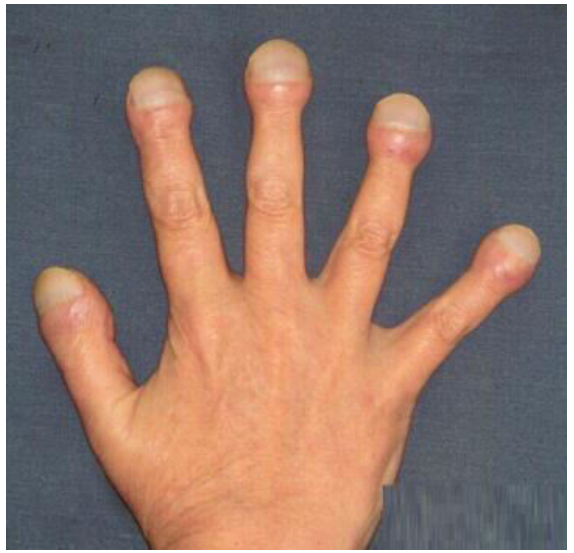


Signs of Cirrhosis

PALMER ERYTHEMA



Digital clubbing



Symptoms of Cirrhosis:

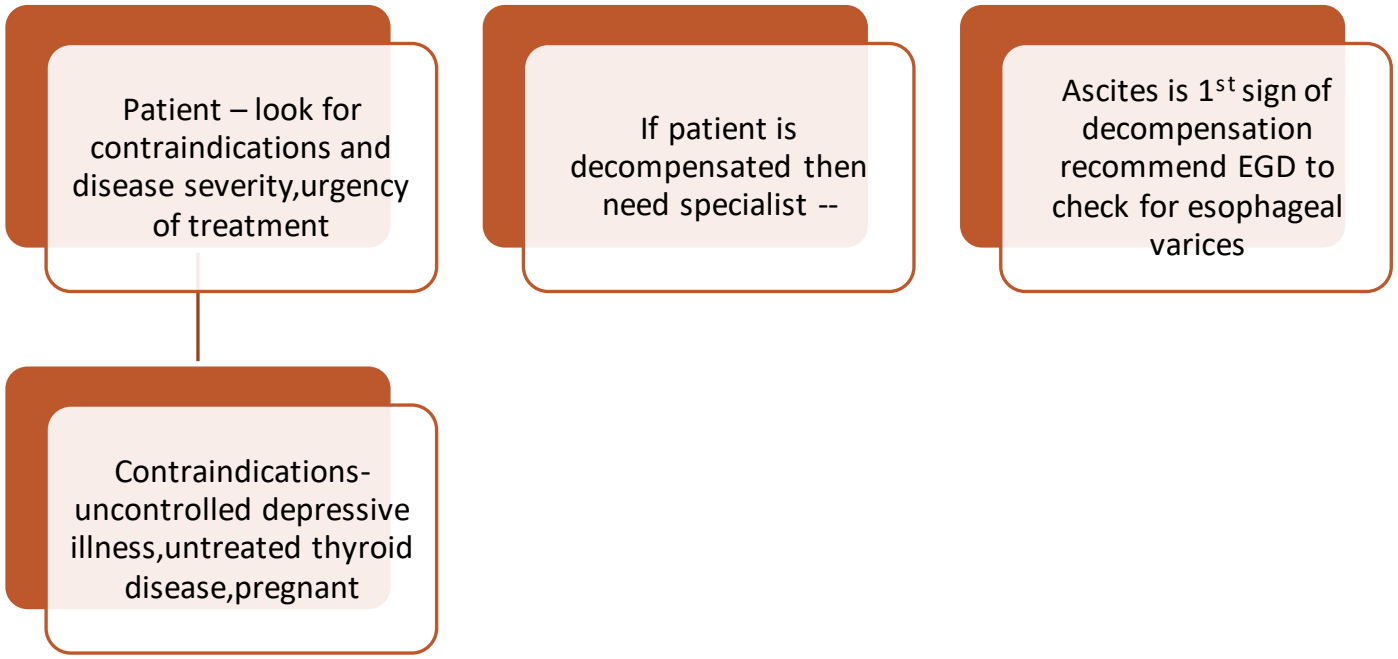
COMPENSATED

- fatigue
- nausea or abdominal pain
- loss of appetite and weight loss

DECOMPENSATED

- bleeding varices
- ascites
- jaundice
- encephalopathy

Consideration for treatment



Consideration for treatment:

Must treat patients with **COMPENSATED CIRRHOSIS.**

Determination of severity of liver disease: Childs –Turcotte-Pugh/MELD/MELD-Na

Prognosis in Cirrhotics

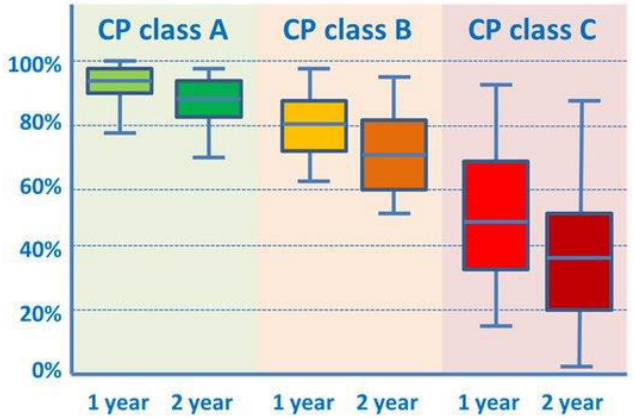
Child Pugh Score

Criteria	1	2	3
Encephalopathy	None	Mild	Severe
Ascites	None	Controlled	Uncontrolled
Bilirubin	≤ 33	34-50	≥ 51
Albumin	≥ 36	28-35	≤ 27
INR	≤ 1.6	1.7-2.2	≥ 2.3

Class	A = 5-6 pts	B = 7-9 pts	C = 10-15 pts

@kwburak

Survival by Child Pugh Class



Pooled analysis on prognosis from 118 studies (n=23,797)

Adapted from D'Amico G, et al. J Hepatol 2006; 44: 217-231.

MELD = Bilirubin & INR & Creatinine

MELD-Na = Bilirubin & INR & Creatinine & Sodium

5vMELD = Bilirubin & INR & Creatinine & Sodium & Albumin

NEXT STEPS – LABORATORY …

HCV Specific :

- HCV Genotype & subtype
- HCV RNA -VL
- HCV treatment history
- Liver staging
- Ultrasound – to r/o HCC in advanced cirrhosis
- Baseline Resistance testing – if needed

NEXT STEPS – LABORATORY….

- **Other Labs** (usually <12 weeks prior to treatment):
  - HIV – 4th-generation test preferred (if not HIV infected)
  - HAV Ab and HBV cAb, sAb, sAg (vaccinate if not immune)
    - If HBV cAb+/sAg-, consider checking HBV DNA, especially if patient is immunosuppressed, due to HBV reactivation risk with HCV treatment
  - LFTs, INR – needed to calculate Child-Turcotte-Pugh score
  - CBC (for platelets) and BMP creatinine/eGFR
  - Consider AFP if HCC risk higher (cirrhotic or HBV or HDV co-infected)
  - URINE TOXICOLOGY

Genotype (GT) :

- An important variable for all patients with chronic hepatitis C virus (HCV) is the "genotype" of HCV with which they are infected.
- This is the strain of the virus to which they were exposed when they were infected.
- Approximately 75% of Americans with HCV have genotype 1 of the virus (subtypes 1a or 1b);
- Small numbers of patients infected with genotypes 4, 5, or 6.

Genotype:

- Most patients with HCV are found to have only one principal genotype, rather than multiple genotypes.
- Genotype 4 is much more common in Africa than in many other parts of the world.
- Genotype 6 is common in Southeast Asia, and each area of the world has its own distribution of genotypes.
- Genotype 3 - leads to more HCC, more aggressive (leads to cirrhosis) so treated differently.

HCV Genotype

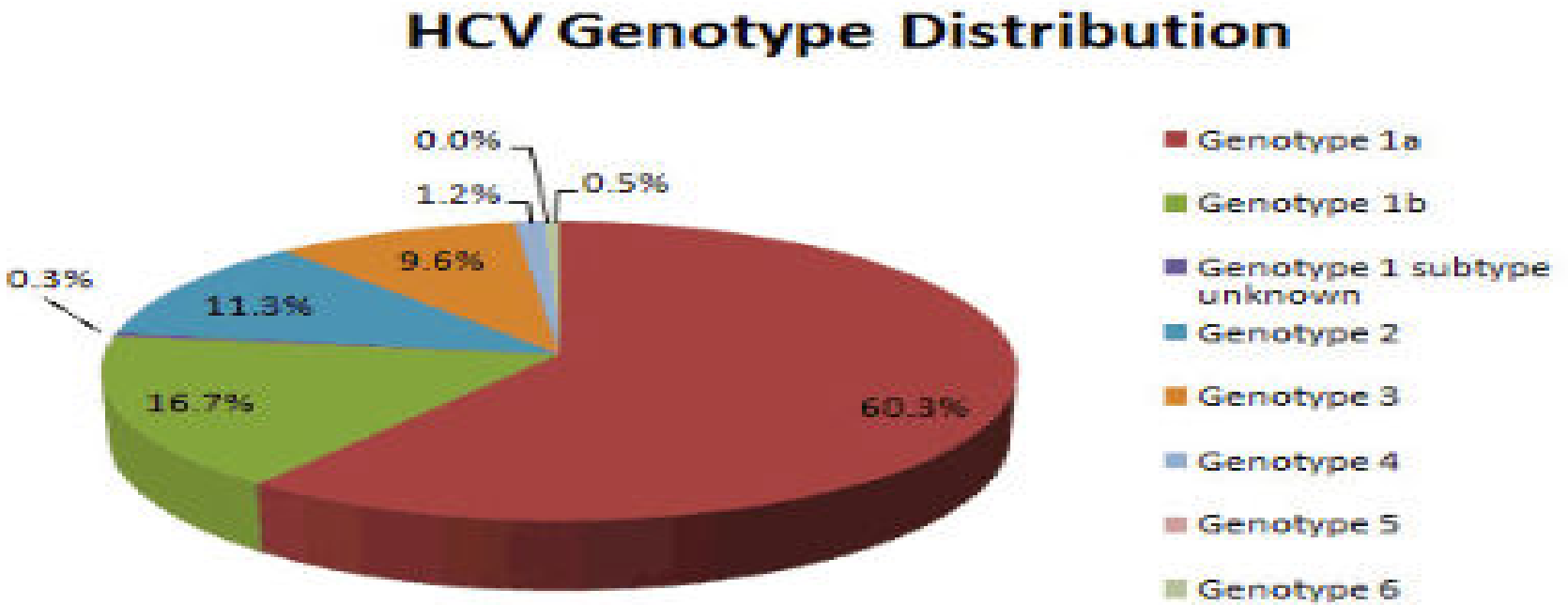


Figure 14. Distribution of HCV genotypes (1-6).

CASE:

JOHN:

Genotype – 1 b

LIVER STAGING…….

Staging:

- **Fibrosis staging**:
  - AASLD-IDSA recommends combining a **non-invasive serum biomarker assay** (such as FIB-4, FibroSURE, FIBROSpect II) and elastography (vibration-controlled transient liver elastography, MR elastography, acoustic radiation force impulse)
  - Liver biopsy is reserved for situations in which discordance between serum and elastography tests will impact clinical decisions
  - May also use the biomarker assay alone and reserve elastography or biopsy for intermediate results (i.e. F2-F3)
  - Individuals with clinically evident cirrhosis do not require additional staging (biopsy or noninvasive assessment)
- Liver ultrasound for most patients; consider CT scan/MRI if concern HCC

Staging:

- FO-F1 NO TO MINIMAL FIBROSIS
- F2 SIGNIFICANT FIBROSIS
- F3 SEVERE FIBROSIS
- F4 CIRRHOSIS

Fibroscan

Clinical Calculators

- CTP Calculator
- APRI Calculator
- BMI Calculator
- CrCl Calculator
- **FIB-4 Calculator**
- Glasgow Coma Scale
- GFR Calculator
- MELD Calculator
- SAAG Calculator

Fibrosis-4 (FIB-4) Calculator

Share

The Fibrosis-4 score helps to estimate the amount of scarring in the liver. Enter the required values to calculate the FIB-4 valu
It will appear in the oval on the far right (highlighted in yellow).

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

Interpretation:

Using a lower cutoff value of 1.45, a FIB-4 score <1.45 had a negative predictive value of 90% for advanced fibrosis (Ishak fibrosis score 4-6 which includes early bridging fibrosis to cirrhosis). In contrast, a FIB-4 >3.25 would have a 97% specificity and a positive predictive value of 65% for advanced fibrosis. In the patient cohort in which this formula was first validated, at least 70% patients had values <1.45 or >3.25. Authors argued that these individuals could potentially have avoided liver biopsy with an overall accuracy of 86%.

Clinical Calculators

- CTP Calculator
- APRI Calculator
- BMI Calculator
- CrCl Calculator
- FIB-4 Calculator
- Glasgow Coma Scale
- GFR Calculator
- MELD Calculator
- SAAG Calculator

AST to Platelet Ratio Index (APRI) Calculator

Share

This is an **A**ST to **P**latelet **R**atio **I**ndex (APRI) calculator tool. Enter the required values to calculate the APRI value. The APRI Score will appear in the oval on the far right (highlighted in yellow). Most experts recommend using 40 IU/L as the value for the AST upper limit of normal when calculating an APRI value.

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

Interpretation:

In a meta-analysis of 40 studies, investigators concluded that an APRI score greater than 1.0 had a sensitivity of 76% and specificity of 72% for predicting cirrhosis. In addition, they concluded that APRI score greater than 0.7 had a sensitivity of 77% and specificity of 72% for predicting significant hepatic fibrosis.[1]
For detection of cirrhosis, using an APRI cutoff score of 2.0 was more specific (91%) but less sensitive (46%). The

Summary – Staging:

- Need 2 different methods that measure things in different ways----
- Non invasive approaches
  - Serum markers
  - Elastography
- Need
  - Liver biopsy – rarely needed
  - Ultrasound, CT, MRI – more to determine liver cancer
  - Transient elastography – measures stiffness of the liver, looks at speed of travel through the liver

Case

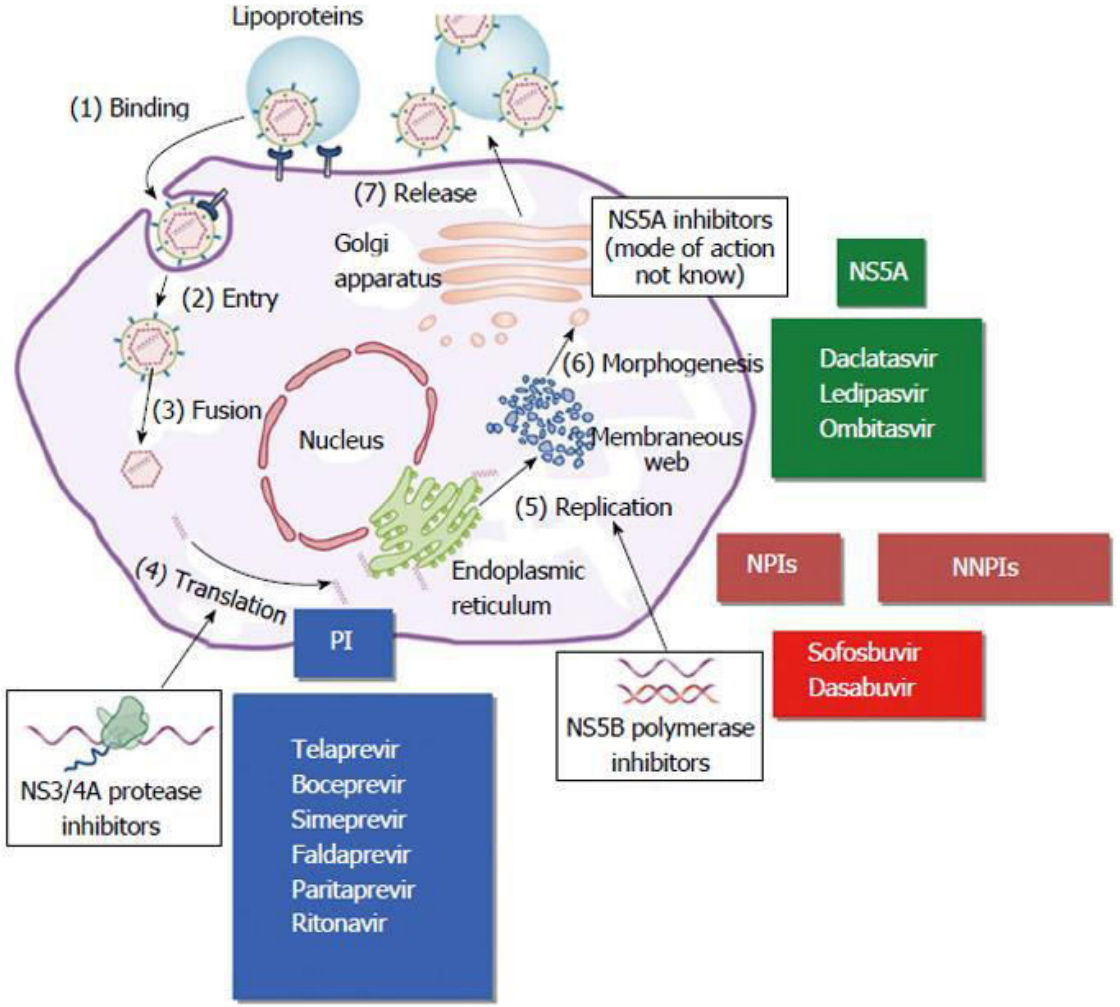
John:

- HCV VL 7.3million
- Genotype – 1b
- Treatment Naïve
- Fibrosure; F1 US- Negative
- No signs/symptoms of cirrhosis
- HIV – negative
- HBV C Ab – nonreactive sAb –negative sAg – negative HAV – total Ab positive
- ***Regimen: ?***

TREATMENT……..

Treatment:

- **Direct Acting Antivirals (DAAs)** are true antivirals that target critical steps of HCV replication, similar to antiretroviral inhibiting HIV, selection of resistant mutants is inevitable with monotherapy.
- Highly effective treatment (interferon free). Up to 100% cure – eradication!!
- Fewer side effects, more tolerable
- Shorter course of treatment
- Less treatment failures
- 3 Main Classes:
  - NS5A inhibitors
  - NS5B RNA polymerase
  - NS3/4 Protease inhibitors



HCV GENOME AND DRUG TARGETS

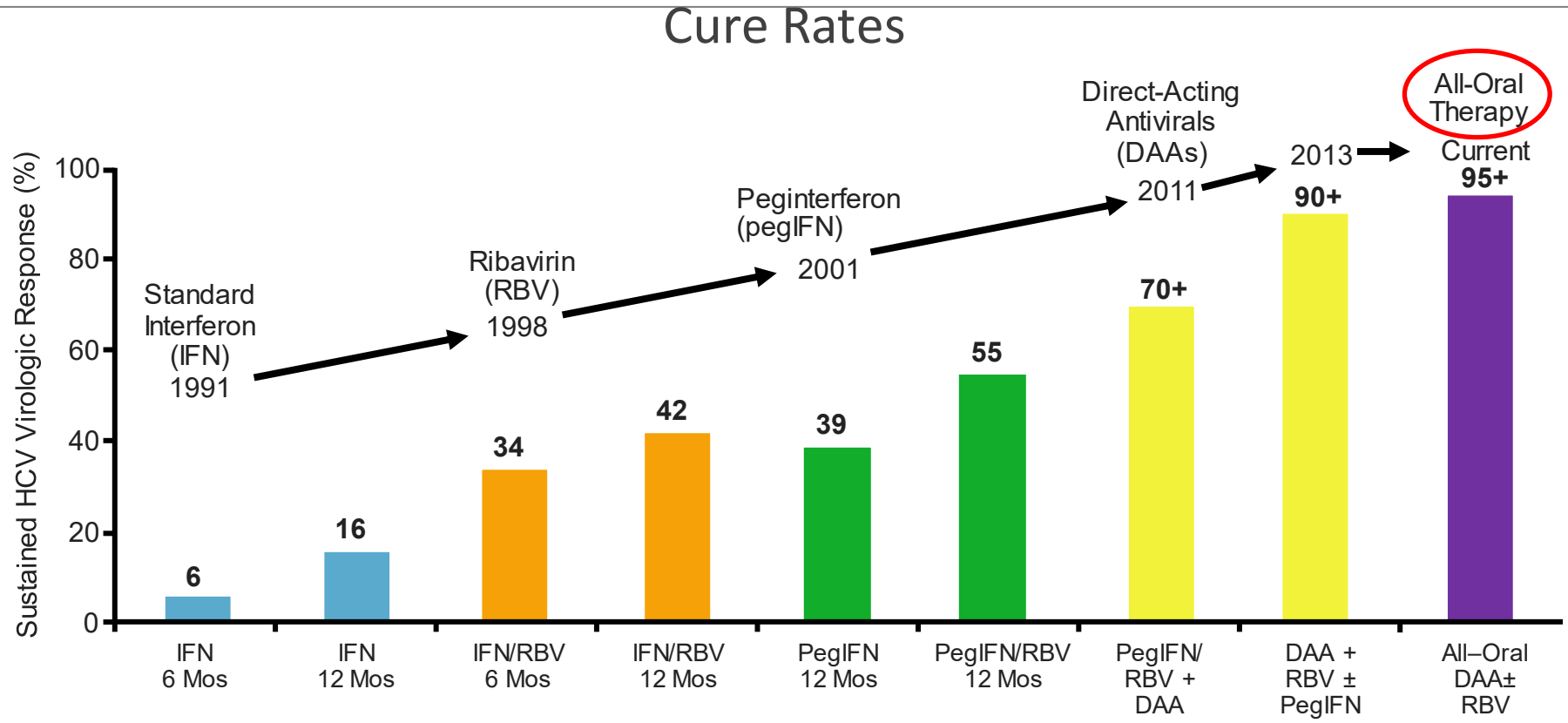
WORLD J HEPATOL. JAN 18, 2016; 8(2): 92-106
PUBLISHED ONLINE JAN 18, 2016. DOI: 10.4254/WJH.V8.I2.92

HCV Medication Classes:

- Co-formulated - usually two medication in one pill but sometimes three medications
  - **Protease inhibitors**: “previr”
    - e.g., glecaprevir, grazoprevir
  - **NS5A inhibitors**: “asvir”
    - e.g., ledipasvir, pibretasvir
  - **NS5B nucleotide polymerase inhibitors**: “buvir”
    - e.g., sofosbuvir, dasabuvir
- Ribavirin

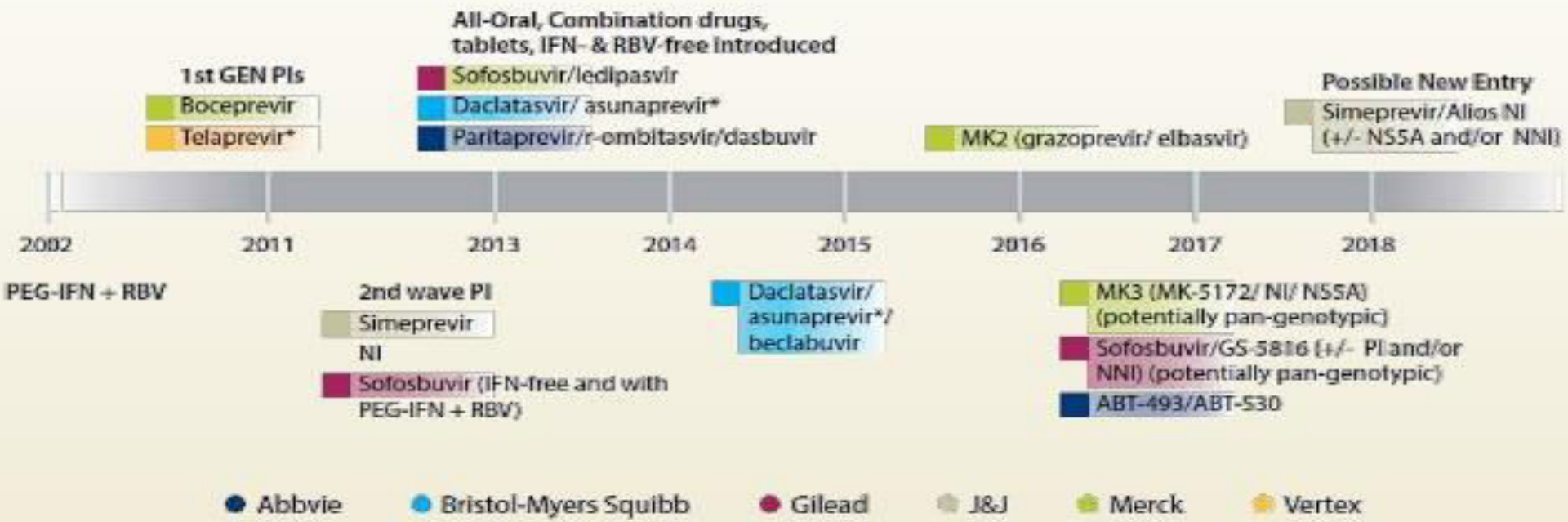
Current All-Oral Therapies

Highly effective, simple, well-tolerated



Box T, Clinical Care Options. 2017

Hepatitis C regimen roadmap



New Treatments/DAA Agents

Sofosbuvir/Ledipsavir(SOF/LDV)

- SOF (Nucleotide analog NS5B polymerase inhibitor) 400mg and LDV (NS5A inhibitor) 90mg
- One pill a day –without regards to food
- GT1, GT4, GT5, GT6
- Not if CrCl , 30 ml/min – due to sofosbuvir , also no amiodarone
- 8-24 weeks (12 weeks most common)
- Baseline VL < 6 million
- African American 12 weeks
- Generic now available
- Can be used with ribavirin if decompensated or liver transplant w/o cirrhosis
- Approved for children age 12 and older or weigh at least 35kg

Sofosbuvir/Velpatasvir (SOF/VEL)

- SOF- Nucleotide analog NS5B polymerase inhibitor) 400mg and VEL 100mg - NS5A inhibitor
- Take one pill per day with or without food
- Pangenotypic
- 12 weeks
- RAS testing if GT 3
- Sofosbuvir – problem with amiodarone,CrCl < 30
- Need to check for Y93 mutations if have then may not respond to therapy
- Generic now available

Glecaprevir /Pibrentasvir (GLE/PIB)

- Contains a Protease inhibitor – GLE (NS3/4A protease inhibitor 100mg per tab,PIB (NS5A inhibitor 40mg per tab)
- Pangenotypic
- 3 tablets per day (coformulated) with food
- Need to be taken with food – Protease
- Ok with low PPI
- Negligible renal excretion – ok with post renal transplant Ok in renal impairment
- Ok in HIV co-infection
- Missed dose – more forgiving
- Has questionable interaction with acid suppressing medications
- DO NOT USE IF DECOMPENSATED LIVER DISEASE

Grazoprevir/Elbasvir (GZR/EBR)

- GZR NS3/4A protease inhibitor 100mg,EBR 50mg
  NS5A inhibitor
- One pill per day with or without food
- GT1, GT 4
- Ok to use in end stage renal disease
- 12-16 weeks
- Had Protease – so not use if decompensated
- RAS testing
- NS5A if RAS at 28,30,31,93 may need to add Ribavirin at weight based dose and extend to 16 weeks
- No issue with PPI

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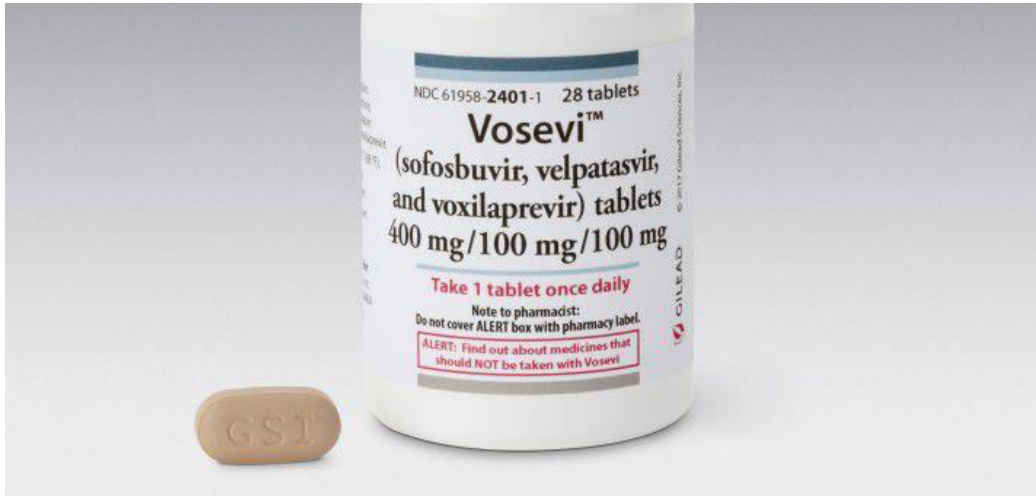
Sofosbuvir (NS3) Velpatasvir/Voxilaprevir (SOF/VEL/VOX)

- SOF- Nucleotide analog NS5B polymerase inhibitor) 400mg and VEL 100mg - NS5A inhibitor,VOX 100mg NS3/4A
- Salvage for NS5A failure (SOF/LDV, GLE/PIB,GZR/EBR)
- One pill a day with food
- Pangenotypic
- 12 weeks
- Nothing left if fail this
- Has a PI so contraindicated in decompensated LIVER DISEASE
- Velpatasavir issue with acid suppressing medication
- Contains PI

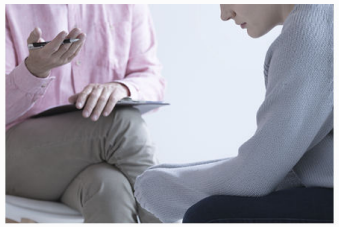


AASLD
AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES

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

IDSA
Infectious Diseases Society of America

ome | Test, Evaluate, Monitor | Treatment-Naive | Treatment-Experienced | Unique & Key Populations | About



New and updated:

HCV and People Who Inject Drugs
Injection drug use is the most common risk factor for HCV infection in the US and Europe, with an HCV seroprevalence of 10% to 70%, depending on geographic location and duration of exposure to injection drug use.

Search the Guidance

Enter your keywor | Search

Start Here: Choose a patient profile from the menu above. ×

Welcome to HCVGuidelines.org

The AASLD and IDSA in partnership with the panel have created an updated web experience to facilitate easier and faster access to this important resource. Please select a patient profile from the menu above, click on a guidance section below, or use the search box to begin.

+ **Contents and Introduction** - *Select a Page*

+ **Testing, Evaluation, and Monitoring of Hepatitis C** - *Browse Topics*

+ **Initial Treatment of HCV Infection** - *Choose Patient Genotype*

+ **Retreatment of Persons in Whom Prior Therapy Has Failed** - *Choose Patient Genotype*

Treatment-Influences on HCV Regimen Selection

- Prior treatment history, whether with IFN or DAAs
- HCV genotype
- Presence or absence of cirrhosis
- If cirrhotic: compensated vs. decompensated
- Renal impairment
- Other comorbid conditions and **medication interactions**

Recommended and alternative regimens listed by evidence level and alphabetically for:

Treatment-Naive Patients Genotype 1b Without Cirrhosis

RECOMMENDED	DURATION	RATING
Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg)	12 weeks	I, A
Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg)[a]	8 weeks	I, A
Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg)	12 weeks	I, A
Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) for patients who are non-black, HIV-uninfected, and whose HCV RNA level is <6 million IU/mL	8 weeks	I, B
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)	12 weeks	I, A
ALTERNATIVE	**DURATION**	**RATING**
Daily fixed-dose combination of paritaprevir (150 mg)/ritonavir (100 mg)/ombitasvir (25 mg) with dasabuvir (600 mg) as part of an extended-release regimen or plus twice-daily dosed dasabuvir (250 mg)	12 weeks	I, A
Daily simeprevir (150 mg) plus sofosbuvir (400 mg)	12 weeks	I, A
Daily daclatasvir (60 mg)[b] plus sofosbuvir (400 mg)	12 weeks	I, B

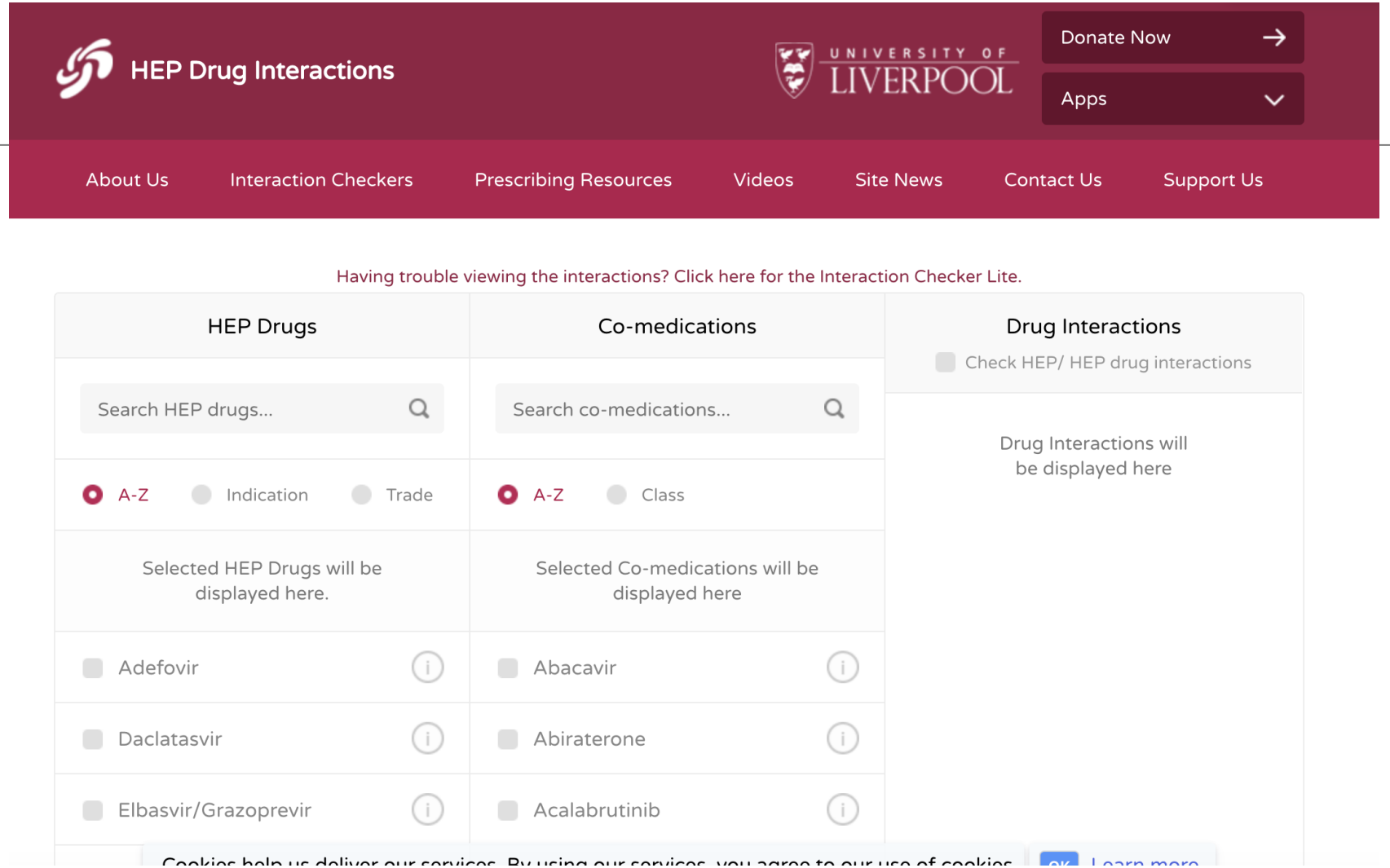
[a] This is a 3-tablet formulation. Please refer to the prescribing information

CASE:

John:

Treatment Request: GZR/EBR 12 weeks, GLE/PIB 8 weeks or SOF/LDV 12 weeks

DRUG INTERACTIONS: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Abiraterone
Elbasvir/Grazoprevir
Acalabrutinib
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Learn more

Drug-drug Interactions:

- Newer medications can have many drug-drug interactions
- With PPI's, tamsulosin, some statins, St. John's Wort,topiramate, colchicine, phenytoin,estradiol,amlodipine

Case: John

SOF/LDV – potential interaction with omeprazole 20mg

GLE/PIB – weak interaction with omeprazole 20mg

ELB/GRA – no interaction with omeprazole 20mg

Laboratory Monitoring During Treatment:

- 4-week HCV VL, eGFR, LFTs for all regimens
  - Plus other labs for some specific regimens – see guidelines
  - HCV VL check is recommended by AASLD-IDSA and required by some insurers, but treatment should **not be stopped** if the HCV VL is not done
  - Consult guidelines for stopping treatment based on side effects or lab abnormalities
- If 4-week HCV VL undetectable, continue treatment and consider rechecking at end of treatment (recommendations are not firm)
- If 4-week HCV VL detectable, recheck at 6 weeks
  - Consider stopping treatment if 6-week HCV VL has increased, particularly if 10-fold increase from 4-week level
  - Consultation with an HCV expert or clinical resource

Summary: Monitoring after Treatment:

- 12-week post-treatment HCV VL:
  - if undetectable = SVR = 99% chance of durable cure!
- 24-week post-treatment HCV VL is optional; order if risk is higher, such as:
  - Viremia present on 4-week HCV VL check.
  - Adherence problems identified.
  - Patients who have received a liver transplant.
- If viremia reappears at 12 or 24 weeks, consider rechecking HCV genotype to see if patient may have been dually infected with a different minority genotype.

Additional Monitoring Post-treatment:

- HCC screening with every 6-month liver ultrasound if F3-F4 fibrosis or cirrhosis
- Also includes:
  - Counseling to prevent reinfection
  - Screening for reinfection
  - Behavior modifications

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Goal of Treatment	
RECOMMENDED	RATING
The goal of treatment of HCV-infected persons is to reduce all-cause mortality and liver-related health adverse consequences, including end-stage liver disease and hepatocellular carcinoma, by the achievement of virologic cure as evidenced by a sustained virologic response.	I, A

Recommendation for When and in Whom to Initiate Treatment	
RECOMMENDED	RATING
Treatment is recommended for all patients with 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

Summary - Treatment Considerations:

- Although the AASLD/IDSA guideline recommend that everyone with chronic hepatitis C be considered for treatment – **challenges exist –**
  - High cost of therapy.
  - Lack of enough specialists to treat everyone living with the disease.
  - Restrictions (insurance/access) such as fibrosis score and sobriety requirements prevent patients from receiving treatment that complies with this standard of care. These restrictions are motivated by financial, not medical concerns.
  - Lack of enough syringe exchange programs, MAT (harm reduction programs).

Summary – Starting Treatment:

- Genotype
- Stage – fibrosis/cirrhosis
- Prior treatment experience
- Drug interactions
- Resistance testing
- Barriers to Adherence

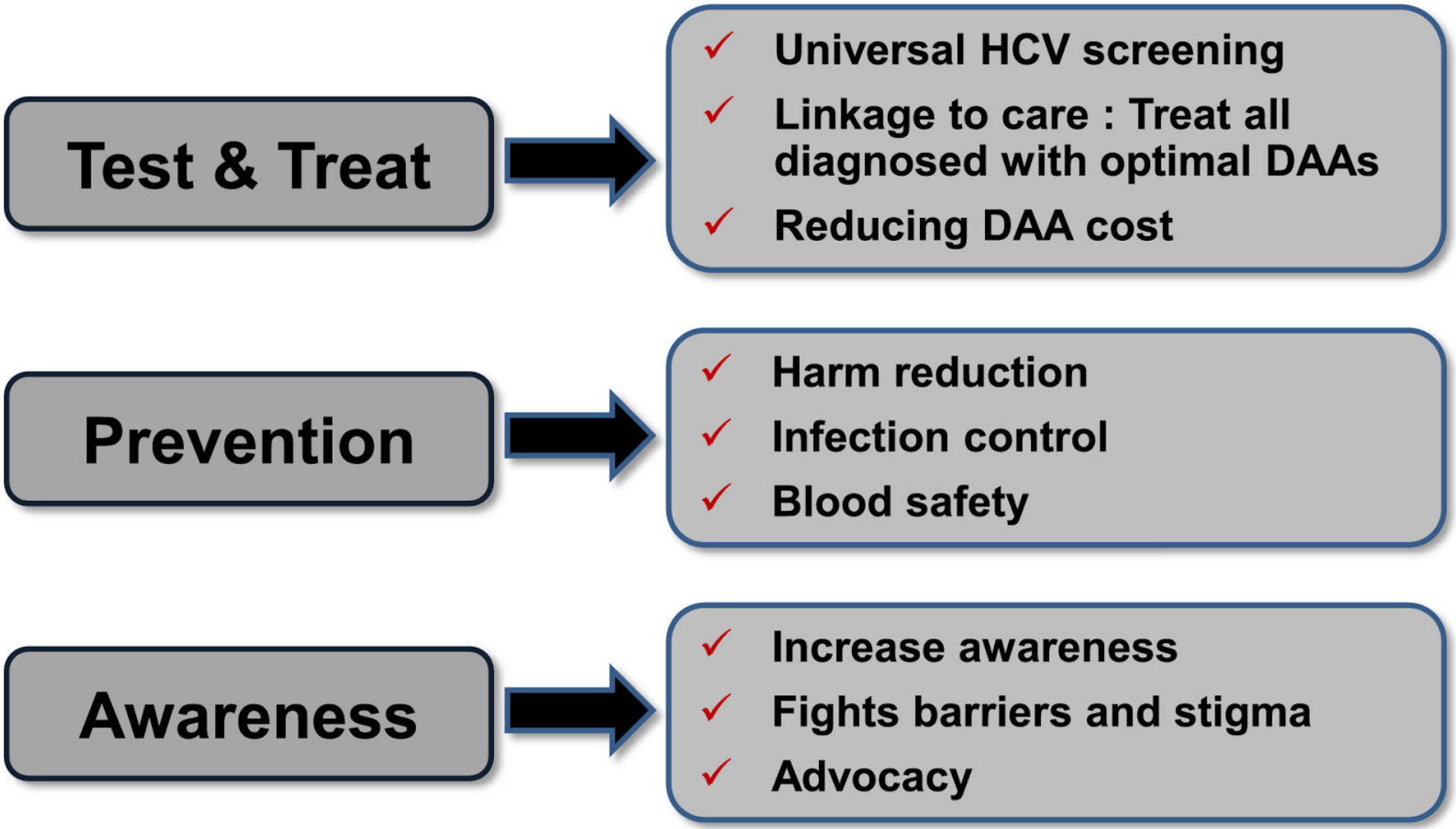
Treatment Goals:

- Goal – sustained virological response (SVR) which is defined as no detectable RNA –HCV 24 months after treatment.
- Treatment to lower risk of progression to end stage liver disease or hepatocellular carcinoma.
- Studies have found that SVR is linked with a 30% - 50% decrease in all cause mortality.

Summary Case:

John:

- Treatment recommendation: ELB/GRA for 12 weeks
  - Drug Interactions – look at PPI (Omeprazole 20mg)-OK
  - Need Hepatitis B Series
- Counseling
  - Tobacco use, alcohol use, marijuana


Test & Treat
✓ Universal HCV screening
✓ Linkage to care : Treat all diagnosed with optimal DAAs
✓ Reducing DAA cost
Prevention
✓ Harm reduction
✓ Infection control
✓ Blood safety
Awareness
✓ Increase awareness
✓ Fights barriers and stigma
✓ Advocacy

SPECIAL CONSIDERATIONS:

Chronic HBV/HCV Co-infected Patients Require Extra Monitoring:

- HCV can suppress HBV in vivo, so HBV may flare when HCV is treated
  - Risk is much lower in HIV co-infected patients who are on tenofovir, lamivudine, or emtricitabine.
- Stage chronic HBV patients with eAg/eAb/ALT/VL before treatment for HCV (along with the fibrosis assessment), then check ALT and HBV VL during and immediately after HCV treatment.
- Treat if HBV treatment criteria are met.

HCV Treatment in Pregnancy and Breastfeeding:

- **No DAAs are approved for use during pregnancy or breastfeeding.**
- Ribavirin is highly teratogenic.
  - Women of childbearing age need dependable contraception when taking ribavirin and for 6 months thereafter.
  - Men taking ribavirin should avoid close contact with pregnant women during treatment and for 6 months thereafter.
  - Best to treat before pregnancy until we have data from ongoing trials in pregnancy.
  - Providers can however prepare patients for treatment after completion of pregnancy and breastfeeding.

Other Special Populations: Treatment Consideration

- Decompensated cirrhosis
- Renal failure
- Failure of treatment with new DAA
- Chemotherapy
- Liver transplant

Resistance:

- There is no cross-resistance between classes.
- AASLD/IDSA HCV medication recommendations tell you when to screen for resistance prior to treatment in special circumstances.
- These guidelines should be consulted each time a treatment regimen is selected:
  - For example: treatment-naïve, non-cirrhotic genotype 1a patients require NS5A resistance testing prior to treatment with elbasvir/grazoprevir
- For a full review of HCV resistance, please see https://www.hcvguidelines.org/evaluate/resistance

If Treatment Is Deferred:

- Annual assessment of fibrosis progression – labs and vibration-controlled transient elastography or equivalent testing
- HCC screening with liver ultrasound every 6 months in patients with advanced fibrosis (METAVIR F3 or F4)
- Work to resolve barriers to treatment!!!!

When Treatment Fails:

- DAA resistance and re-treatment strategies are areas of ongoing research; consult AASLD-IDSA guidelines.
- General approach – do two of the following:
  - Switch regimen
  - Add ribavirin
  - Lengthen treatment
  - Consider NS5A resistance testing
- With all patients, assess adherence and work to resolve adherence barriers.
- May also wait for new therapies if re-treatment is not urgent.

Cost of Treatment:

Real Cost of Treatment

- With limited discounts , coverage ranges approx. $50,000 per patient with a 90% cure rate and more tolerable . Usually only need one course of treatment.
- Older regimens had low success rates of cure and often had to be repeated were estimated to have cost $250,000 per cure achieved.
- Generic available (SOF/LEP,SOF/VEL).
- Cost of liver transplant for patients that had resultant liver failure - > $300,000.
- **Summary – Newer therapy cost effective!!!!**


hepatitis

Key Points

- **Family Physicians can and should provide HCV treatment to confront the HCV epidemic.**
- The **AASLD-IDSA HCV Guideline website** is the definitive source for treatment recommendations.
- Other websites provide helpful clinical tools and opportunity to practice and reinforce knowledge. ECHO projects are increasing available.
- The main challenge in HIV/HCV co-infection treatment is managing drug interactions.

References

- AASLD-IDSA. When and in whom to initiate HCV therapy. Recommendations for testing, managing, and treating http://www.hcvguidelines.org/full-report/when-and-whom-initiate-hcv-therapy.
- Hepatitis C Update for Primary Care. Clinical Care Options. February 21, 2017. http://review.clinicaloptions.com/Hepatitis/Treatment%20Updates/Primary%20Care.aspx
- Presentation - Philip J. Bolduc, MD (New England AETC) for the AETC National Coordinating Resource Center in July 2017 and updated December 2018.
- www.hcvguidelines.org
- www.aasld.org/publications/practice-guidelines
- www.medscape.com- AASLD Update Hepatitis C
- www.hepatitisc.uw.edu

FIB-4 Calculator/APRI Calculator:

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

Resources

- Hepatitis C Online: Module 5: Treatment of Chronic Hepatitis C Infection.
  - Slide presentations
    http://www.hepatitisc.uw.edu/browse/all/lectures
  - Case studies
    http://www.hepatitisc.uw.edu/go/treatment-infection
- Hepatitis C Online: Child-Turcotte-Pugh Calculator http://www.hepatitisc.uw.edu/page/clinical-calculators/ctp
- https://www.seaetc.com/state-partner-information/south-carolina-aetc/
- Live expert support: National Clinicians Consultation Center http://nccc.ucsf.edu/ or call (844) HEP-INFO or (844) 437-4636
  Monday – Friday, 9 a.m. – 8 p.m. ET

THANK YOU!!!!