Primary Care Approach to Diagnosis and Management of Chronic Hepatitis C

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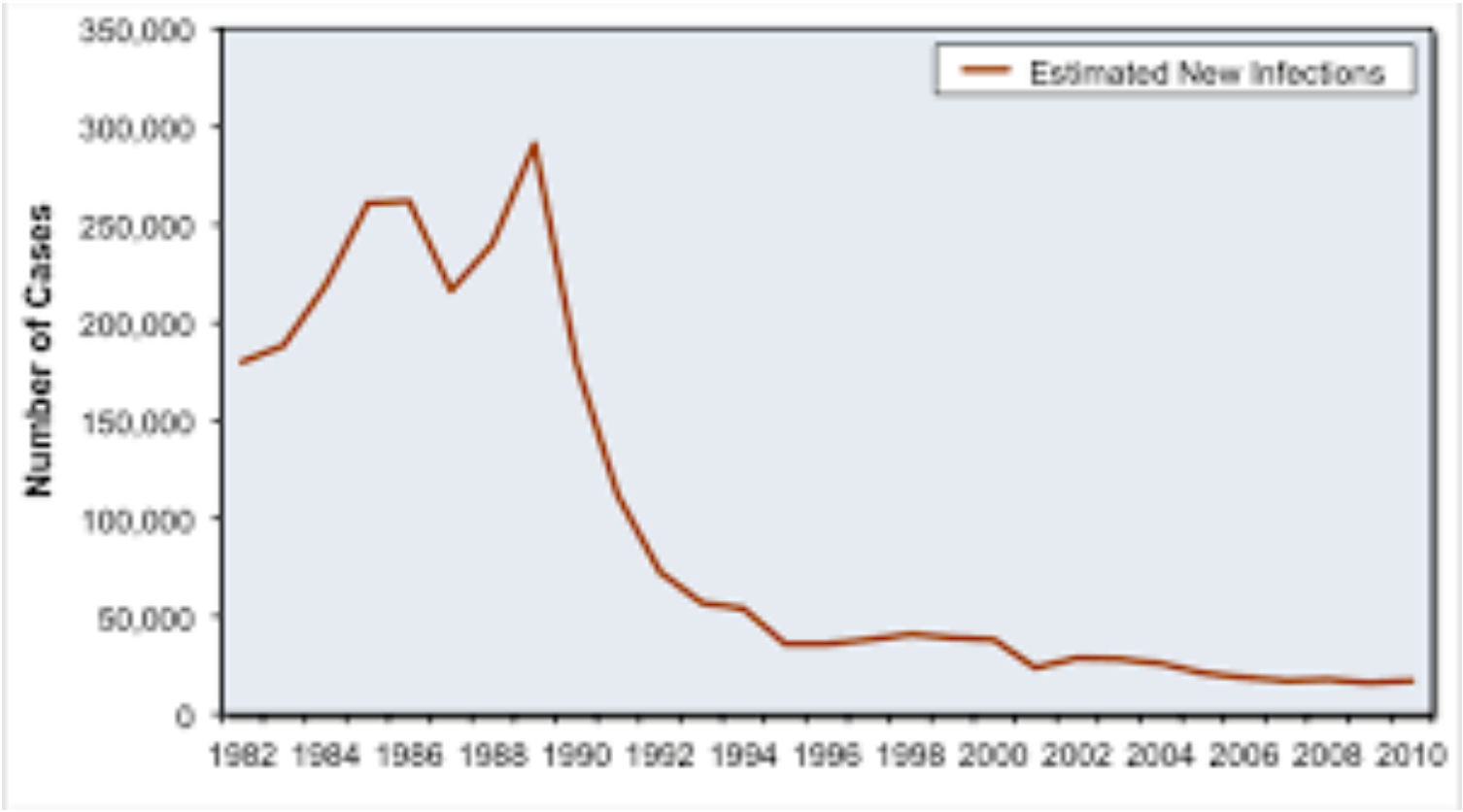
Objectives

- Epidemiology of chronic hepatitis C
- CDC guidelines on screening or hepatitis C
- Diagnosing hepatitis C
- New treatments and application in certain patient populations

Hepatitis C- epidemiology

- CDC recommends that an average 17,000 new cases of chronic hepatitis C are diagnosed yearly in the United States
  - Most common bloodborne infection
- Prevalence- 5.2 million people in the United States are chronically infected with hepatitis C
  - 2% of the population
  - 75% of those people were born between 1945 and 1965

Incidence by year



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Hepatitis C- epidemiology (cont.)

- 40-85% of patient's infected with HCV are unaware

- In the United States, approximately 70% of chronic HCV infections are caused by hepatitis C genotype 1, 15 to 20% by genotype 2, 10 to 12% genotype 3, 1% genotype 4, and less than 1% genotype 5 or 6.

Hepatitis C- risk factors

- IVDA (intranasal cocaine as well)
- Blood transfusion prior to 1992
- Solid organ transplantation
- Hemophilia- receipt of factor concentrates prior to 1987
- MSWM
- Tattoos
- Unknown

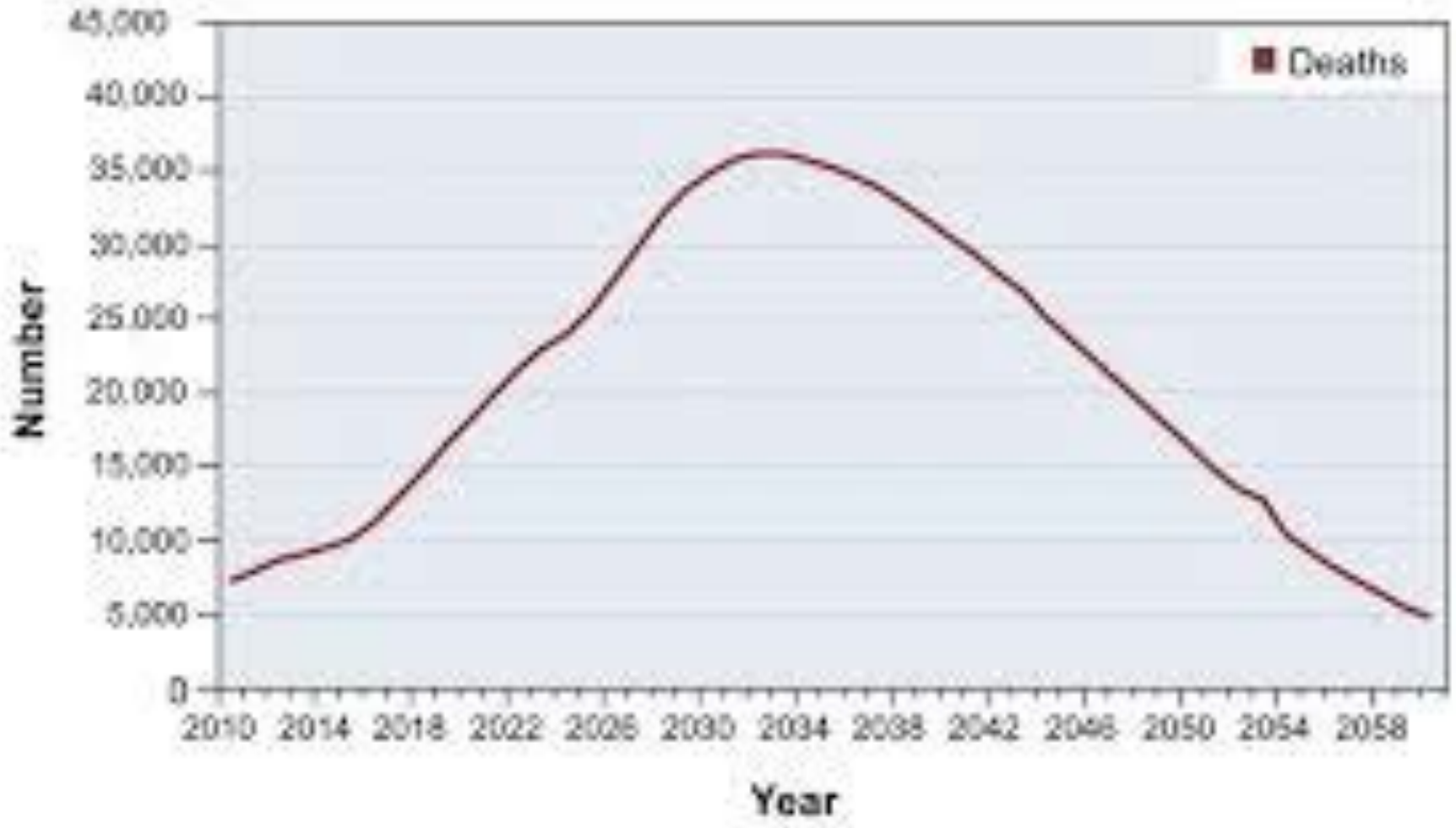
Hepatitis C- Special circumstances

- Perinatal- 5% will transmit HCV to child
  - Risk factor→ elevated viral load at birth
    - Increased risk in co-infected patients
  - No increased risk with breastfeeding
- Sexual exposure- controversial
  - Most accurate study- 0.07% per year (1/190,000)
  - Higher in MSWM

Hepatitis C- Disease burden

- Infected patients all-cause mortality >2 times that of HCV-negative patients
- 20% of HCV infected patient will develop cirrhosis after 20 years of infection if left untreated
- Number 1 reason for liver transplantation
  - THIS WILL BE CHANGING SOON
- Number one cause of hepatocellular carcinoma (50%)

Forecasted annual deaths- HCV



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CDC screening guidelines- HCV

- Adults born from 1945-1965
- IVDA
- Clotting factor prior to 1987
- Long-term hemodialysis
- Persistently elevated transaminases
- HIV
- Transfusions prior to 1992
- Exposure in healthcare professional

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HCV- diagnosis

- Initial screening test is Hepatitis C IgG
- A reactive antibody should be followed by HCV RNA testing
  - If positive, diagnosis is confirmed
  - If negative -> past HCV infection vs false positive
- Once diagnosis is established, genotype should be tested along with metavir score

Metavir score

- Knowledge of fibrosis stage guides treatment
  - FOR THE INSURANCE COMPANY
- Can be assessed indirectly through H/P, labs, or other non-invasive tests
  - FibroSure
  - FibroScan
- Liver biopsy

Differential Diagnosis

- NASH- US + exclude other causes
- Hepatitis B- serology (core and surface)
- Hemochromatosis- iron studies, genetic test
- Autoimmune hepatitis- ASMA, ANA
- Primary biliary cirrhosis- AMA
- DILI- careful history + exclude other causes
- Wilson's disease- Ceruloplasmin, eye exam

Hepatitis C- Treatment

- Many advances over last 20 years
- First available treatment was interferon
- Then pegylated interferon + ribavirin
  - SVR obtained in 10-40% of cases
  - Treatment for 52 weeks and terrible side effects
- Then protease inhibitors boceprevir and telepravir
  - Again bad side effects an lots of monitoring
  - Increased SVR rates to 60-75

Hepatitis C- Specific treatments

- Many new medicines over last several years
- Most are specific for particular genotypes
- Goal is pan-genotypic, low side effects, one pill once daily with little laboratory monitoring
  - In addition, use in cirrhotic (compensated and decompensated), transplant, co-infected, renal failure and few drug interactions

Harvoni (ledipasvir/sofosbuvir)

- Genotype 1a or 1b- NO RESISTANCE TESTING
  - 12 weeks of 1 pill daily with minimal side effects
  - Treatment naïve, experienced, cirrhosis
    - If decompensated, add ribavirin (same with transplant patients)
- No drug or lab monitoring during treatment
- Drug interactions
  - Requires acidic environment- Stop PPI therapy and H2RA therapy or alter timing
  - Amiodarone- contraindicated due to risk of bradycardia

Harvoni (ledipasvir/sofosbuvir)

	Patient Population	Treatment Regimen and Duration
Genotype 1	Treatment-naïve without cirrhosis or with compensated cirrhosis (Child-Pugh A)	HARVONI 12 weeks
	Treatment-experienced¨ without cirrhosis	HARVONI 12 weeks
	Treatment-experienced¨ with compensated cirrhosis (Child-Pugh A)	HARVONI 24 weeks
	Treatment-naïve and treatment-experienced¨ with decompensated cirrhosis (Child-Pugh B or C)	HARVONI + ribavirin 12 weeks
Genotype 1 or 4	Treatment-naïve and treatment-experienced¨ liver transplant recipients without cirrhosis, or with compensated cirrhosis (Child-Pugh A)	HARVONI + ribavirin 12 weeks
Genotype 4, 5 or 6	Treatment-naïve and treatment-experienced**, without cirrhosis or with compensated cirrhosis (Child-Pugh A)	HARVONI 12 weeks

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Sofosbuvir/velpatasvir- Epclusa

- Fixed-dose combination of sofosbuvir, a hepatitis C virus (HCV) nucleotide analog NS5B polymerase inhibitor, and velpatasvir, an HCV NS5A inhibitor, and is indicated for the treatment of adult patients with chronic HCV genotype 1, 2, 3, 4, 5, or 6 infection
- No drug or lab monitoring
- Drug interactions- Same as Harvoni due to sofosbuvir component

Sofosbuvir/velpatasvir- Epclusa

Table 1 Recommended Treatment Regimen in Patients with Genotype 1, 2, 3, 4, 5, or 6 HCV

Patient Population	Treatment Regimen and Duration
Patients without cirrhosis and patients with compensated cirrhosis (Child-Pugh A)	EPCLUSA 12 weeks
Patients with decompensated cirrhosis (Child-Pugh B or C)	EPCLUSA + ribavirin[a] 12 weeks

a. When administered with EPCLUSA, the recommended dosage of ribavirin is based on weight (administered with food): 1000 mg per day for patients less than 75 kg and 1200 mg for those weighing at least 75 kg, divided and administered twice daily. The starting dosage and on-treatment dosage of ribavirin can be decreased based on hemoglobin and creatinine clearance. For ribavirin dosage modifications, refer to the ribavirin prescribing information.

Elbasvir/grazoprevir-Zepatier

- Combo nucleoside and protease inhibitor
- Testing for the presence of virus with NS5A resistance-associated polymorphisms is recommended
- If present, treat for 16 weeks with ribavirin
- No renal impairment dose adjustments
- Perform hepatic laboratory testing prior to therapy, at treatment week 8, and as clinically indicated. For patients receiving 16 weeks of therapy, perform additional hepatic laboratory testing at treatment week 12. For ALT elevations on ZEPATIER, follow recommendations in full prescribing information.

Elbasvir/grazoprevir-Zepatier

Dosage Regimens and Durations for ZEPATIER in Patients with Genotype 1 or 4 HCV with or without Cirrhosis

Patient Population	Treatment	Duration
Genotype 1a: Treatment-naïve or PegIFN/RBV-experienced* without baseline NS5A polymorphisms†	ZEPATIER	12 weeks
Genotype 1a: Treatment-naïve or PegIFN/RBV-experienced* with baseline NS5A polymorphisms†	ZEPATIER + ribavirin	16 weeks
Genotype 1b: Treatment-naïve or PegIFN/RBV-experienced*	ZEPATIER	12 weeks
Genotype 1a or 1b: PegIFN/RBV/PI-experienced‡	ZEPATIER + ribavirin	12 weeks
Genotype 4: Treatment-naïve	ZEPATIER	12 weeks
Genotype 4: PegIFN/RBV-experienced*	ZEPATIER + ribavirin	16 weeks

*Peginterferon alfa + ribavirin.
†Polymorphisms at amino acid positions 28, 30, 31, or 93.
‡Peginterferon alfa + ribavirin + HCV NS3/4A protease inhibitor.

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Paritaprevir/ritonavir/ombitasvir \dasabuvir + ribavirin (Veikira)

- 12 week regimen for Genotype 1
- Not to be used in Child B or worse cirrhotics due to risk of decompensation
- Increased risk of drug interactions
- Many side effects with ribavirin

Veikira Pak

Treatment Regimen and Duration by Patient Population

Patient Population	Treatment*	Duration
Genotype 1a, without cirrhosis	VIEKIRA PAK + ribavirin	12 weeks
Genotype 1a, with cirrhosis	VIEKIRA PAK + ribavirin	24 weeks**
Genotype 1b, without cirrhosis	VIEKIRA PAK	12 weeks
Genotype 1b, with cirrhosis	VIEKIRA PAK + ribavirin	12 weeks
*Note: Follow the genotype 1a dosing recommendations in patients with an unknown genotype 1 subtype or with mixed genotype 1 infection. **VIEKIRA PAK administered with ribavirin for 12 weeks may be considered for some patients based on prior treatment history *[See Clinical Studies (14.3)]*.		

- HCV/HIV-1 co-infection: For patients with HCV/HIV-1 co-infection, follow the dosage recommendations in the table above. (2.1)
- Liver Transplant Recipients: In liver transplant recipients with normal hepatic function and mild fibrosis (Metavir fibrosis score ≤2), the recommended duration of VIEKIRA PAK with ribavirin is 24 weeks. (2.2)

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Simeprevir / sofosbuvir

- Indicated for Genotype 1 and 4
- Screening for the presence of virus with the NS3 Q80K polymorphism is strongly recommended and alternative therapy should be considered if Q80K is detected.
- 12 weeks in non-cirrhotic patients
- 24 weeks in compensated cirrhotic patients

Daclatasvir + sofosbuvir

- Indicated for genotype 1 and genotype 3
- Treat for 12 weeks
  - If cirrhosis present- add ribavirin

- Dose modifications based on drug interactions make this a confusing regimen

What can you as a primary care physician take from this info?

- Knowing initial blood work and diagnostic testing to guide treatment plan
- Once genotype and fibrosis status are established choosing a treatment regimen you are comfortable with

My recommendations…

- Decide which patient's you are willing to treat comfortably
  - What genotypes?
  - Cirrhosis
  - Co-infected?
- Pick a treatment plan that works for you and only treat that type of patient
- Consult your look gastroenterologist or ID for remainder

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Cirrhosis

- There are certain things that need monitored in cirrhosis
  - HCC status- US +/- AFP q 6 months
  - Esophageal variceal screening- EGD q 1-2 years
    - Banding +/- non-selective Beta blocker
  - Fluid management- ascites
  - Encephalopathy- psychometric evaluation

Thank you…

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