Adherence to Hepatitis C Testing and Treatment Guidelines

Viral Hepatitis Summit
September 17, 2015

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Identifying Patients with Hepatitis C

- 4-5 million people in the US have hepatitis C virus (HCV) infection
- Most were infected in 1960's through 1980's
  - Up to 250,000 cases per year in 1980's
  - About 50% infected via IDU, rest from blood transfusions, sex, tattoos, medical procedures, and other factors
- Up to 75% of people have not been diagnosed
- Risk-based screening misses many people
  - Stigma associated with IDU, even if decades ago

Smith BD et al. MMWR. August 17, 2012/61(RR04);1-18. Armstrong GL et al. Ann Intern Med. 2006 May 16;144(10):705-14.
http://www.iom.edu/Reports/2010/Hepatitis-and-Liver-Cancer-A-National-Strategy-for-Prevention-and-Control-of-Hepatitis-B-and-C.aspx

Who Should Be Tested for HCV

CDC Recommendations

- Everyone born from 1945 through 1965 (one-time)
- Persons who ever injected illegal drugs
- Persons who received clotting factor concentrates produced before 1987
- Chronic (long-term) hemodialysis
- Persons with persistently abnormal ALT levels.
- Recipients of transfusions or organ transplants prior to 1992
- Persons with recognized occupational exposures
- Children born to HCV-positive women
- HIV positive persons

USPSTF Grade B Recs*

- Everyone born from 1945 through 1965 (one-time)
- Past or present injection drug use
- Sex with an IDU; other high-risk sex
- Blood transfusion prior to 1992
- Persons with hemophilia
- Long-term hemodialysis
- Born to an HCV-infected mother
- Incarceration
- Intranasal drug use
- Receiving an unregulated tattoo
- Occupational percutaneous exposure
- Surgery before implementation of universal precautions

*Only pertains to persons with normal liver enzymes; if elevated liver enzymes need HBV and HCV testing

Smith at al. Ann Intern Med 2012; 157:817-822. Moyer et al. Ann Intern Med epub 25 June 2013

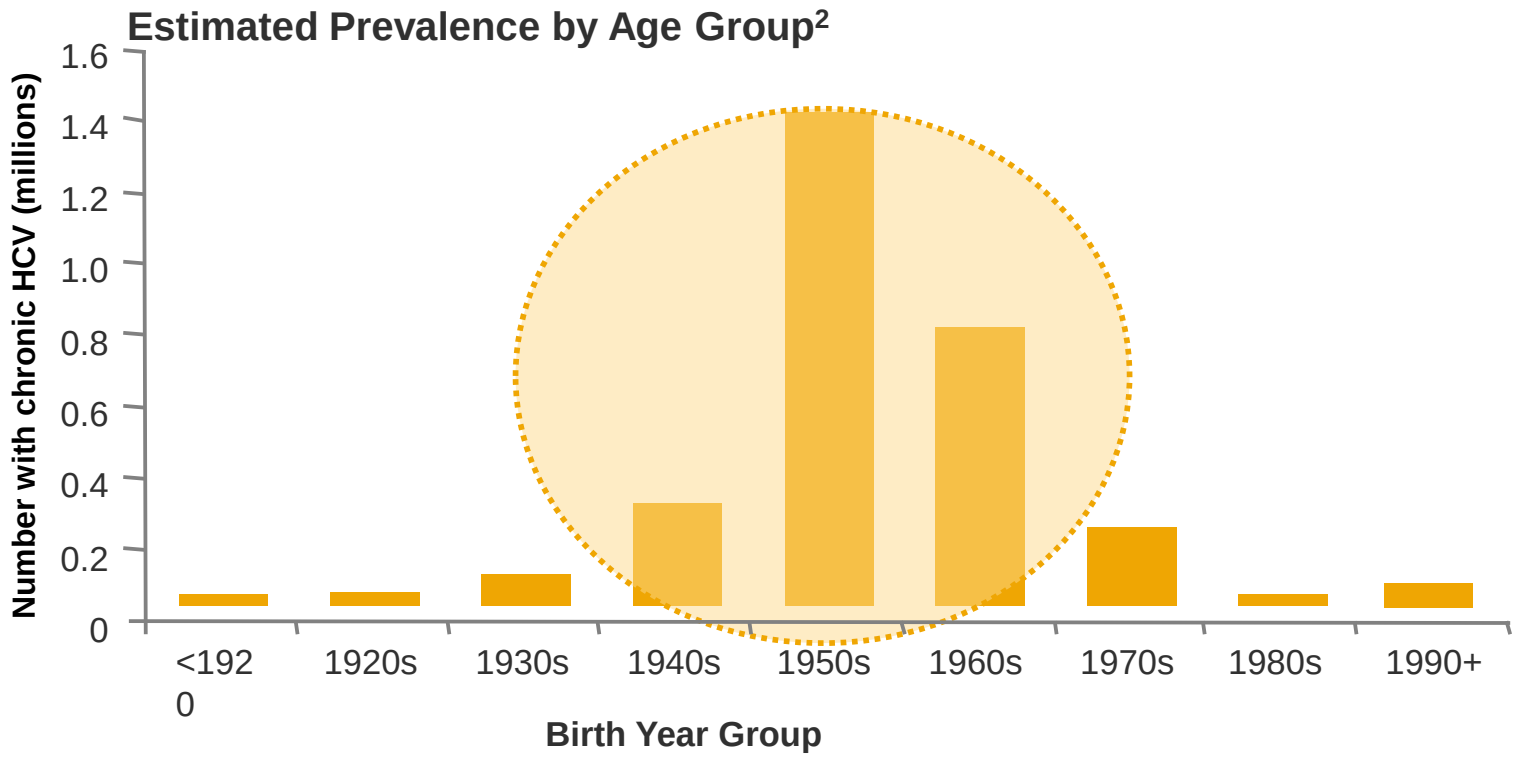
HCV Testing: Elevated Liver Enzymes?

Patients with at least 1 clinical encounter and no previous HCV diagnosis	865,659
Percent tested for HCV	13%
Percent of tested patients who were HCV positive	5.1%
Percent patients with ≥2 elevated ALT results tested for HCV	43.9%
Percent positive for HCV after ≥2 elevated ALT results	8.2%

Study included patients followed at Kaiser Permanente of Hawaii and Oregon, Henry Ford Health System, Detroit, and Geisinger Health System, PA

Spradling et al CID 2012; 55:1047-55.

Baby Boomers (Born in 1945–1965) Account for 76.5% of HCV in the US[1]



An estimated 35% of undiagnosed baby boomers with HCV currently have advanced fibrosis (F3-F4; bridging fibrosis to cirrhosis)[3]

1. Centers for Disease Control and Prevention. *MMWR*. 2012;61:1-32; Adapted from Pyenson B, et al. *Consequences of Hepatitis C Virus (HCV): Costs of a baby boomer Epidemic of Liver Disease*. New York, NY: Milliman, Inc; May 18, 2009. http://www.milliman.com/expertise/healthcare/publications/rr/consequences-hepatitis-c-virus-RR05-15-09.php Milliman report was commissioned by Vertex Pharmaceuticals; 3. McGarry LJ et al. *Hepatology.* 2012;55(5):1344-1355.

Initial Hepatitis C Testing and Evaluation

Who Should Be Tested for Hepatitis C?

New: Anyone born between 1945 and 1965 should be tested once, regardless of risk factors

In addition, patients with the following risk factors:

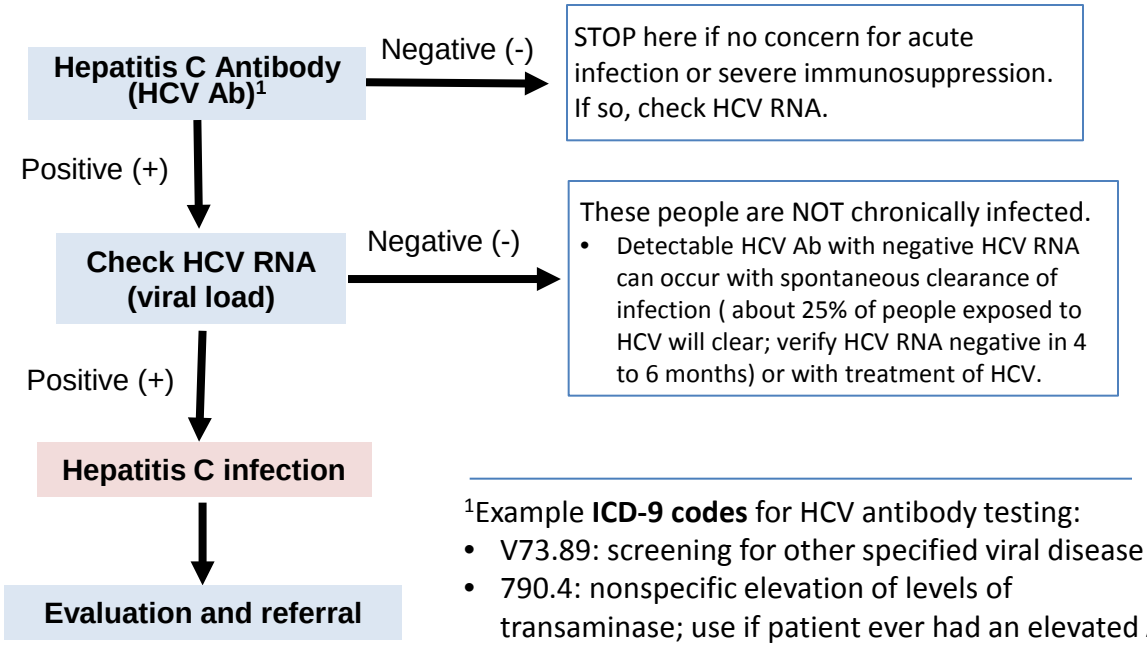
- Elevated ALT (even intermittently)
- A history of illicit injection drug use or intranasal cocaine use (even once)
- Needle stick or mucosal exposure to blood
- Current sexual partners of HCV infected persons
- Received blood/organs before 1992
- Received clotting factors made before 1987
- Chronic hemodialysis
- Infection with HIV
- Children born to HCV-infected mothers

Why Test People Born Between 1945-1965?

- 76% of the ~4 million people with HCV infection in the US are baby boomers
- In the 1945-1965 cohort:
  - All: 1 out of 30
  - Men: 1 out of 23
  - African American men: 1 out of 12
- Up to 75% do not know they have HCV
- 73% of HCV-related deaths are in baby boomers

What Can Happen to People with Hepatitis C?

- It is important to identify if patients have cirrhosis
- Patients with cirrhosis are at risk for liver cancer (HCC) and liver decompensation (ascites, variceal bleed, hepatic encephalopathy, jaundice)
- Hepatitis C is curable, and cure reduces the risk of severe complications, even with cirrhosis
- Refer patients to a specialist who has experience treating hepatitis C to see if they need treatment



[1]Example **ICD-9 codes** for HCV antibody testing:

- V73.89: screening for other specified viral disease
- 790.4: nonspecific elevation of levels of transaminase; use if patient ever had an elevated ALT

Counsel Patients with HCV Infection About Reducing Risk of Transmission

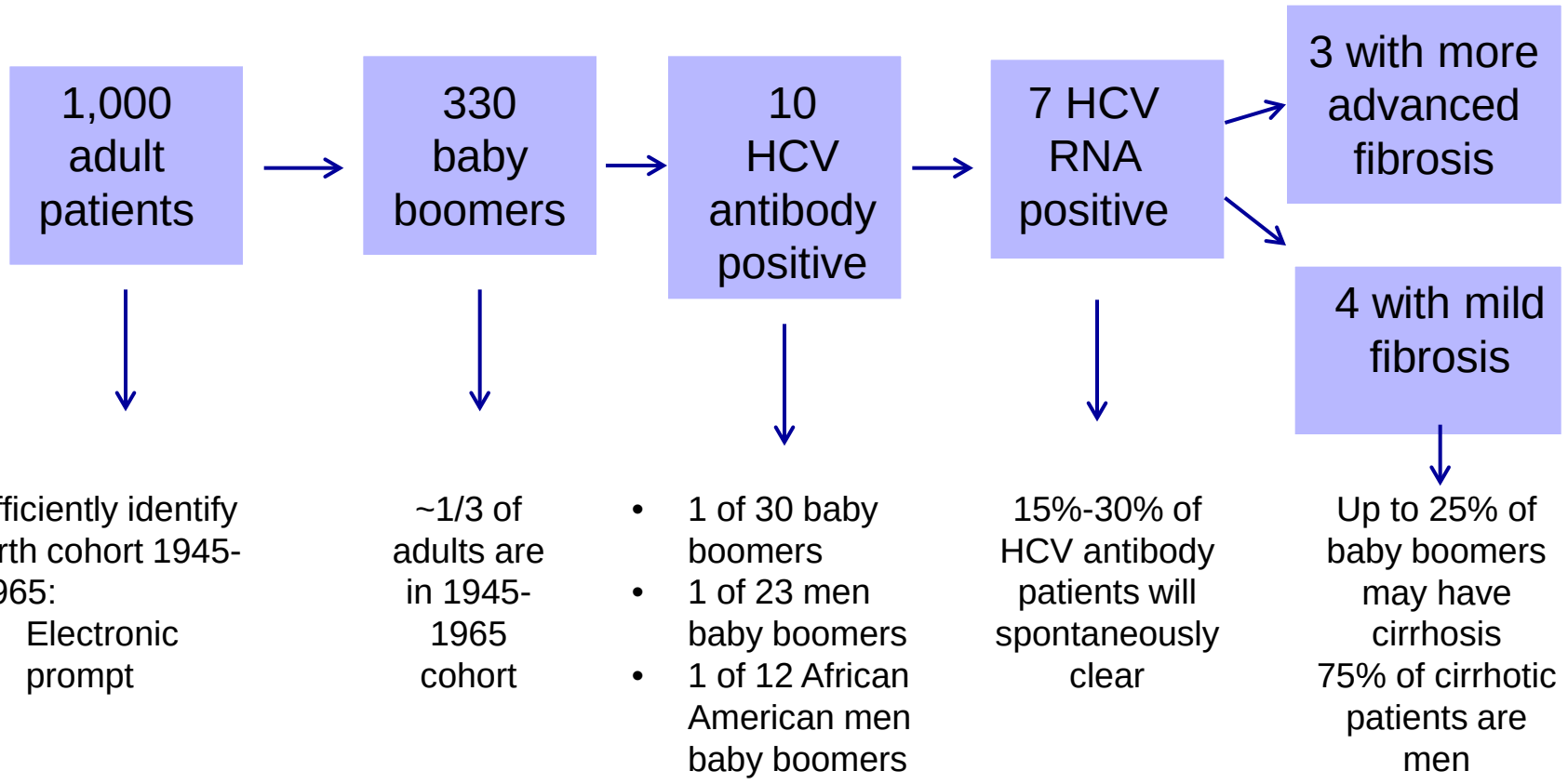
- Do not donate blood, body organs, other tissue, or semen
- Do not share personal items that might have small amounts of blood (toothbrushes, razors, nail-grooming equipment, needles) and cover cuts and wounds
- HCV is not spread by hugging, kissing, food or water, sharing utensils, or casual contact
- If in short term or multiple relationships, use latex condoms. No condom use is recommended for long-term monogamous couples (risk of transmission is very low)

Initial Management

- Evaluate alcohol use (CAGE, AUDIT-C) and recommend stopping use
- Vaccinate for hepatitis A and hepatitis B if not previously exposed
- Evaluate sources of support (social, emotional, financial) needed for HCV treatment

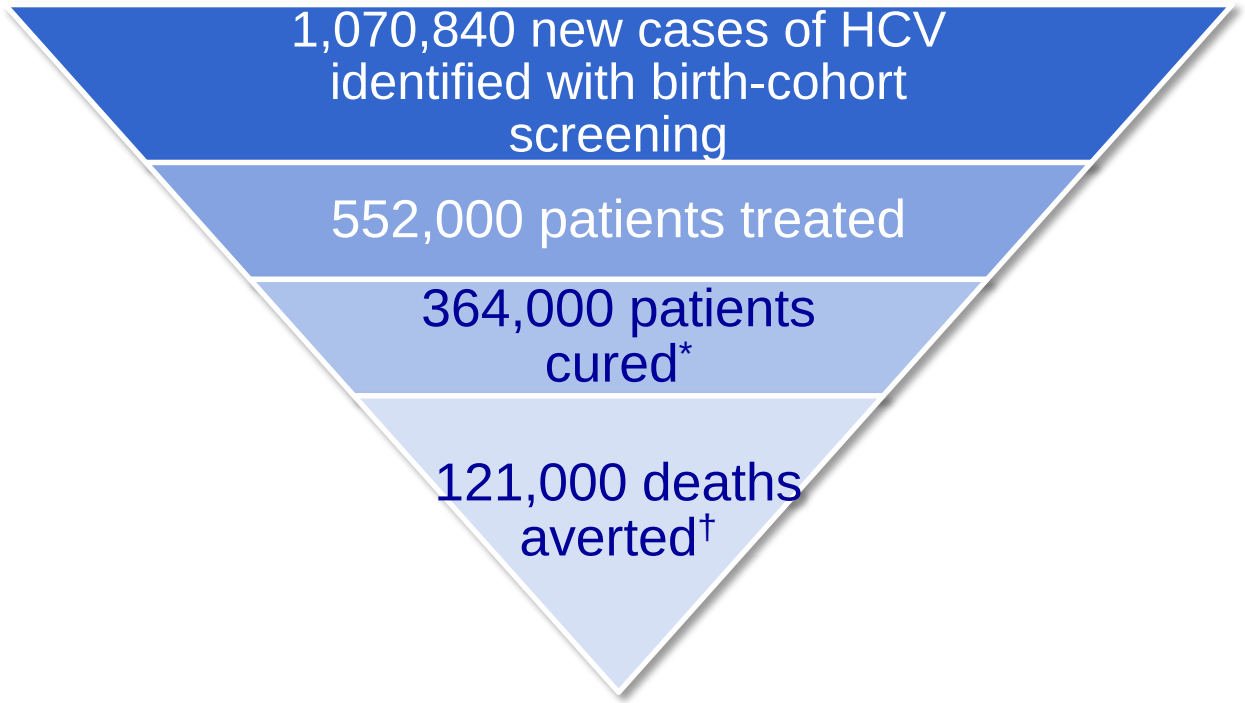
Smith BD et al. MMWR. August 17, 2012/61(RR04); 1-18. Adapted from Winston et al. Management of hepatitis C by the primary care provider: Monitoring guidelines; 2010; http://www.hcvadvocate.org/hepatitis/factsheets_pdf/PCP_web_10.pdf

PCP Education Example: Screening in Clinic



Davis, Gastro 2010; 138: 513

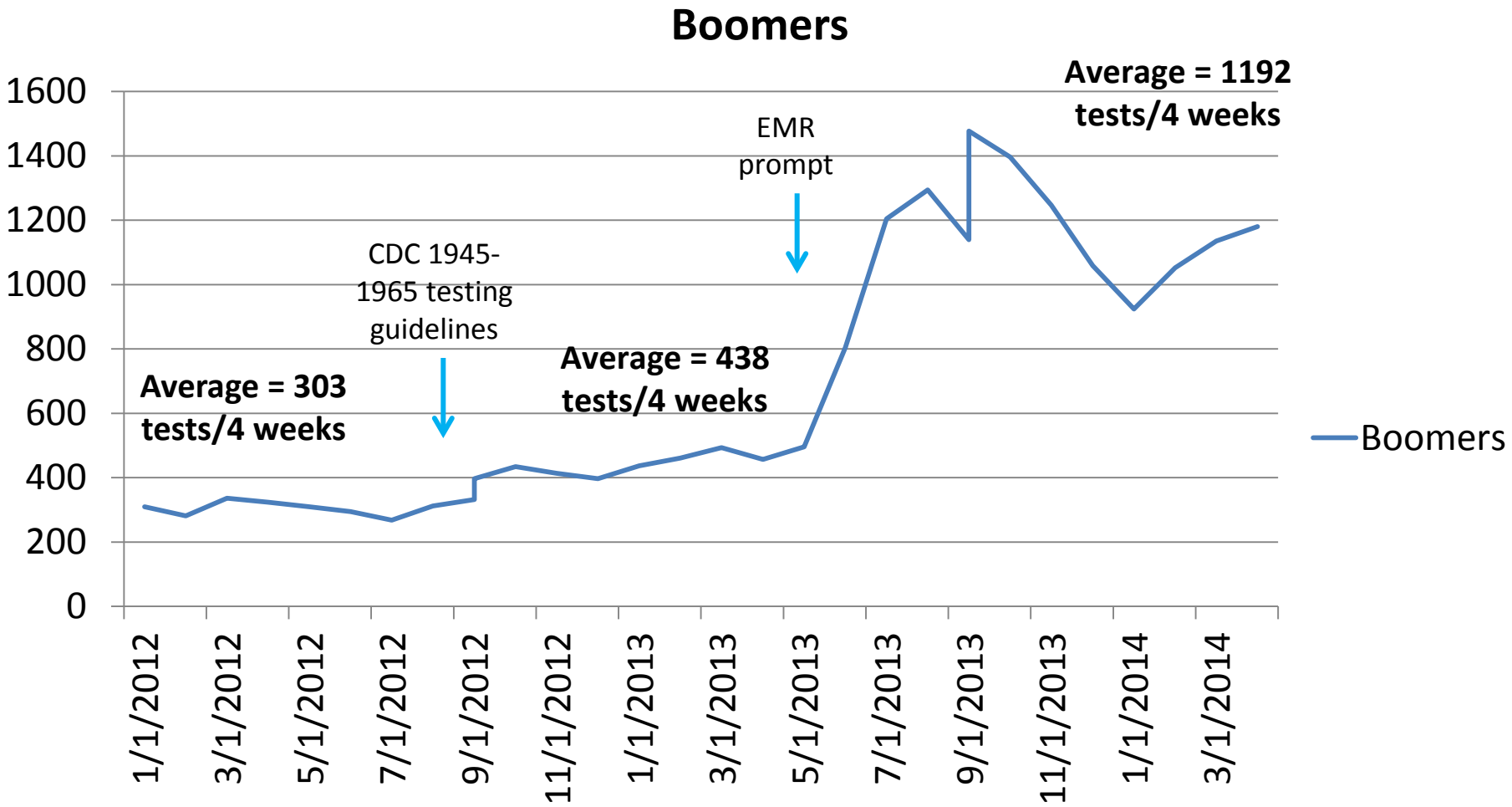
Screening of Baby Boomers May Prevent >120,000 Deaths Due to HCV Infection



- Birth-cohort screening in primary care would identify 86% of all undiagnosed cases in the birth cohort, compared with 21% under risk based screening[1]
- Cost effectiveness of HCV screening is comparable to cervical cancer or cholesterol screening (cost/QALY gained with protease inhibitor+IFN+RBV = $35,700)

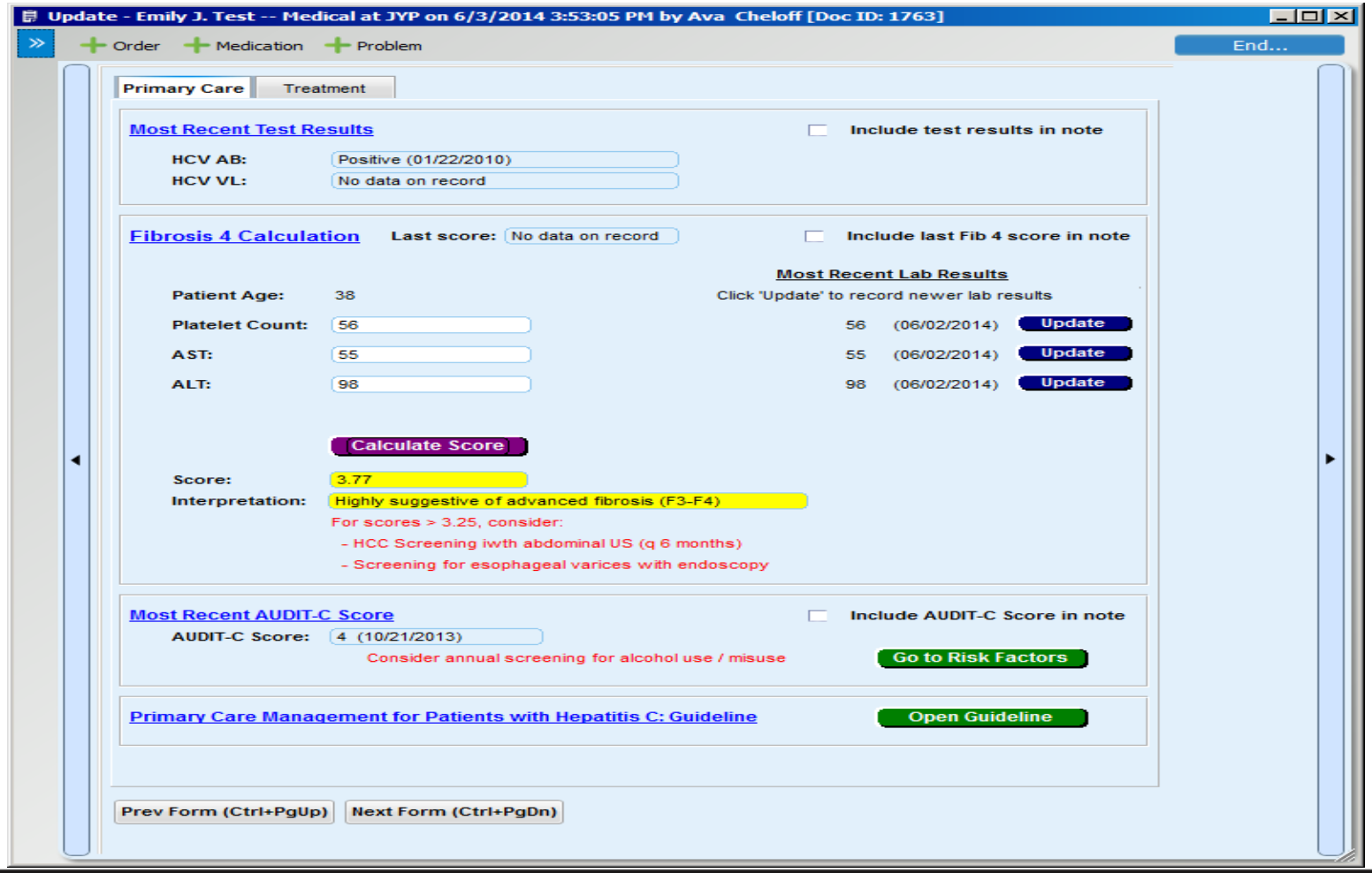
Markov chain Monte Carol simulation model of prevalence of hepatitis C antibody stratified by age, sex, race/ethnicity, history of injection drug use, and natural history of chronic hepatitis C.
*With pegylated interferon and ribavirin plus DAA treatment.
†Deaths due to decompensated cirrhosis or hepatocellular carcinoma within 1945-1965 birth cohort. 470,000 deaths under birth cohort screening vs 592,000 deaths under risk-based screening
1. Rein D et al. *Ann Intern Med.* 2012;156(4):263-270; 2. McGarry LJ et al. *Hepatology.* 2012;55(5):1344-1355.

HCV Antibody Test Volume Increased after EMR Prompt



Beth Israel Deaconess Medical Center, Boston, MA, Quality Outcomes Data, 6/5/14

FIB-4 Screening: - Centricity

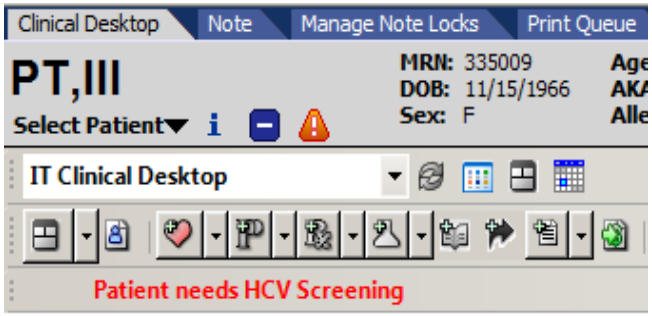


Courtesy of Maggie Beiser, BHCHP

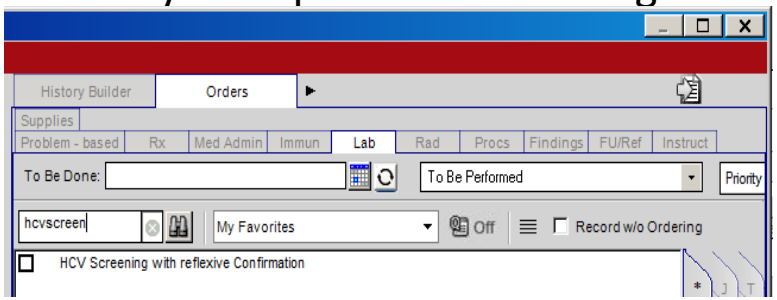
AllScripts Prompt

Drexel's "C a Difference" developed the following AllScripts alerts to help providers adhere to CDC Hepatitis C testing recommendations

1) All individuals who were born between 1945 and 1965 who have not been previously tested for HCV will have this alert in the chart:



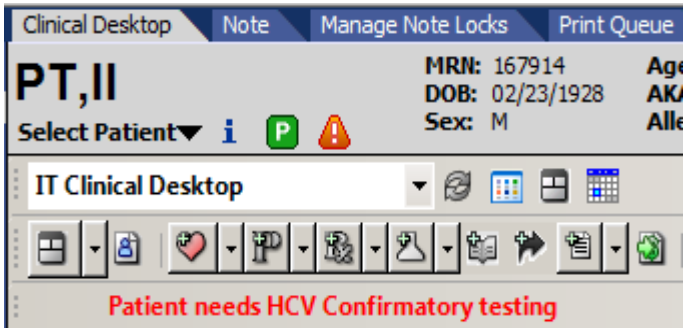
For these patients, type "hcvscreen" to order HCV antibody screening with reflex confirmatory PCR quantitative testing



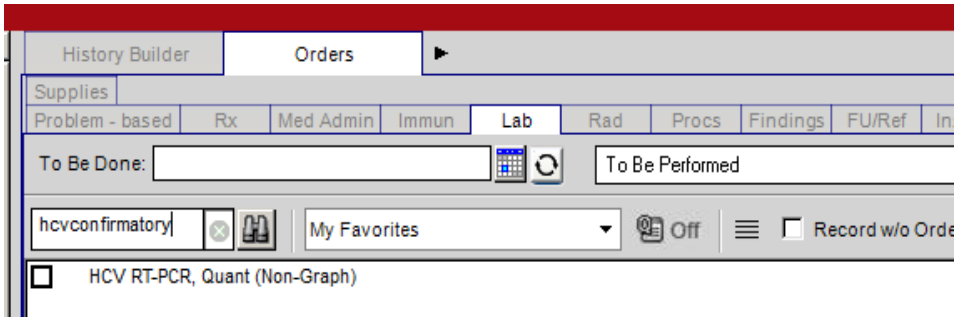
Courtesy of Stacey Trooskin, Drexel & HepCAP

AllScripts Prompt

2) All individuals who have had a reactive HCV antibody test or have an ICD-9 code consistent with chronic HCV infection, but have not had confirmatory PCR quantitative testing in the last 5 years will have this alert:



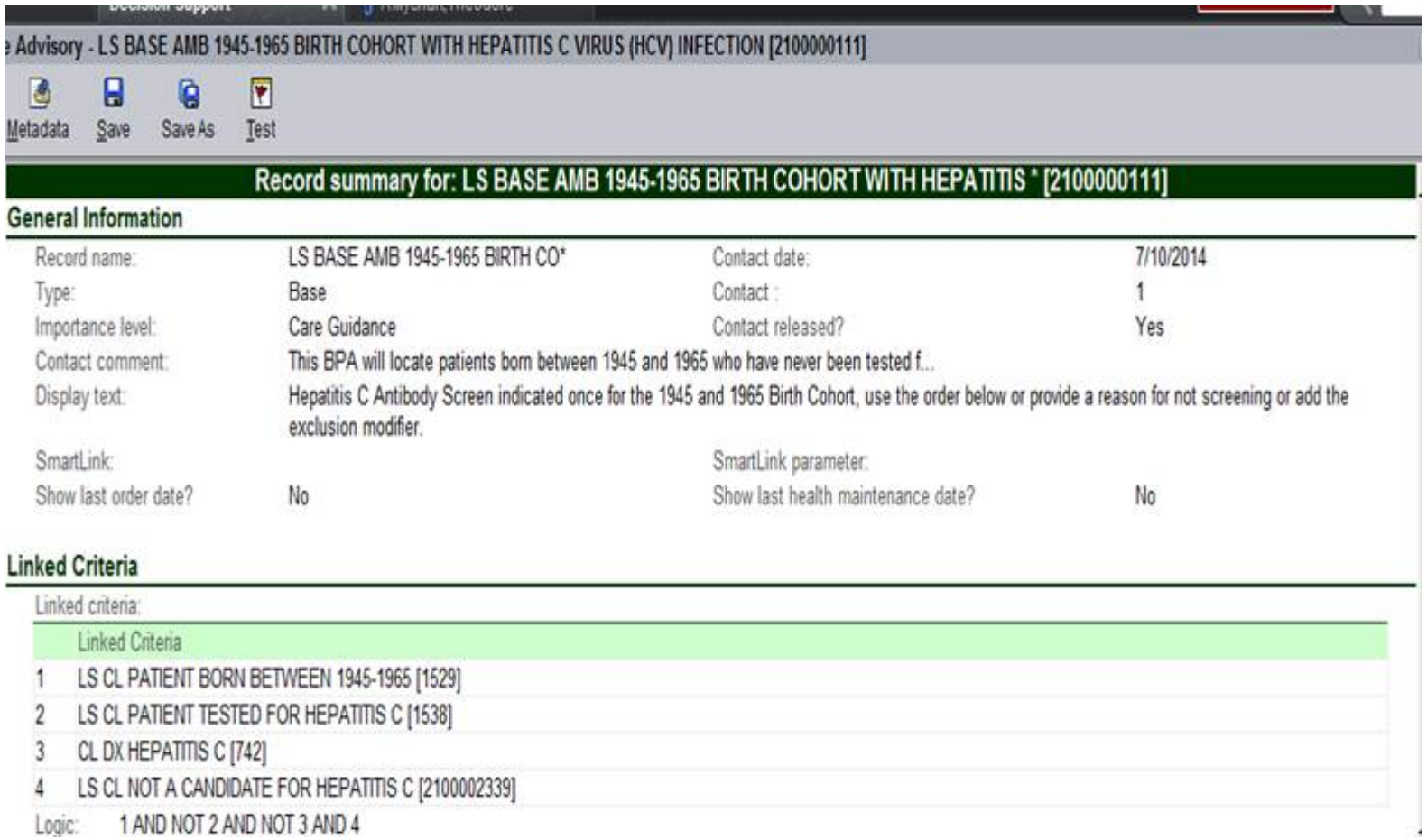
For these patients, type “hcvconfirmatory” or “hcvconfirm” to order HCV RNA PCR quantitative testing



Courtesy of Stacey Trooskin, Drexel & HepCAP

RI Birth Cohort prompt Epic

Lifespan
Delivering health with care.



Advisory - LS BASE AMB 1945-1965 BIRTH COHORT WITH HEPATITIS C VIRUS (HCV) INFECTION [2100000111]

Metadata | Save | Save As | Test

Record summary for: LS BASE AMB 1945-1965 BIRTH COHORT WITH HEPATITIS * [2100000111]

General Information

Record name:	LS BASE AMB 1945-1965 BIRTH CO*	Contact date:	7/10/2014
Type:	Base	Contact :	1
Importance level:	Care Guidance	Contact released?	Yes
Contact comment:	This BPA will locate patients born between 1945 and 1965 who have never been tested f...		
Display text:	Hepatitis C Antibody Screen indicated once for the 1945 and 1965 Birth Cohort, use the order below or provide a reason for not screening or add the exclusion modifier.		
SmartLink:		SmartLink parameter:	
Show last order date?	No	Show last health maintenance date?	No

Linked Criteria

Linked criteria:

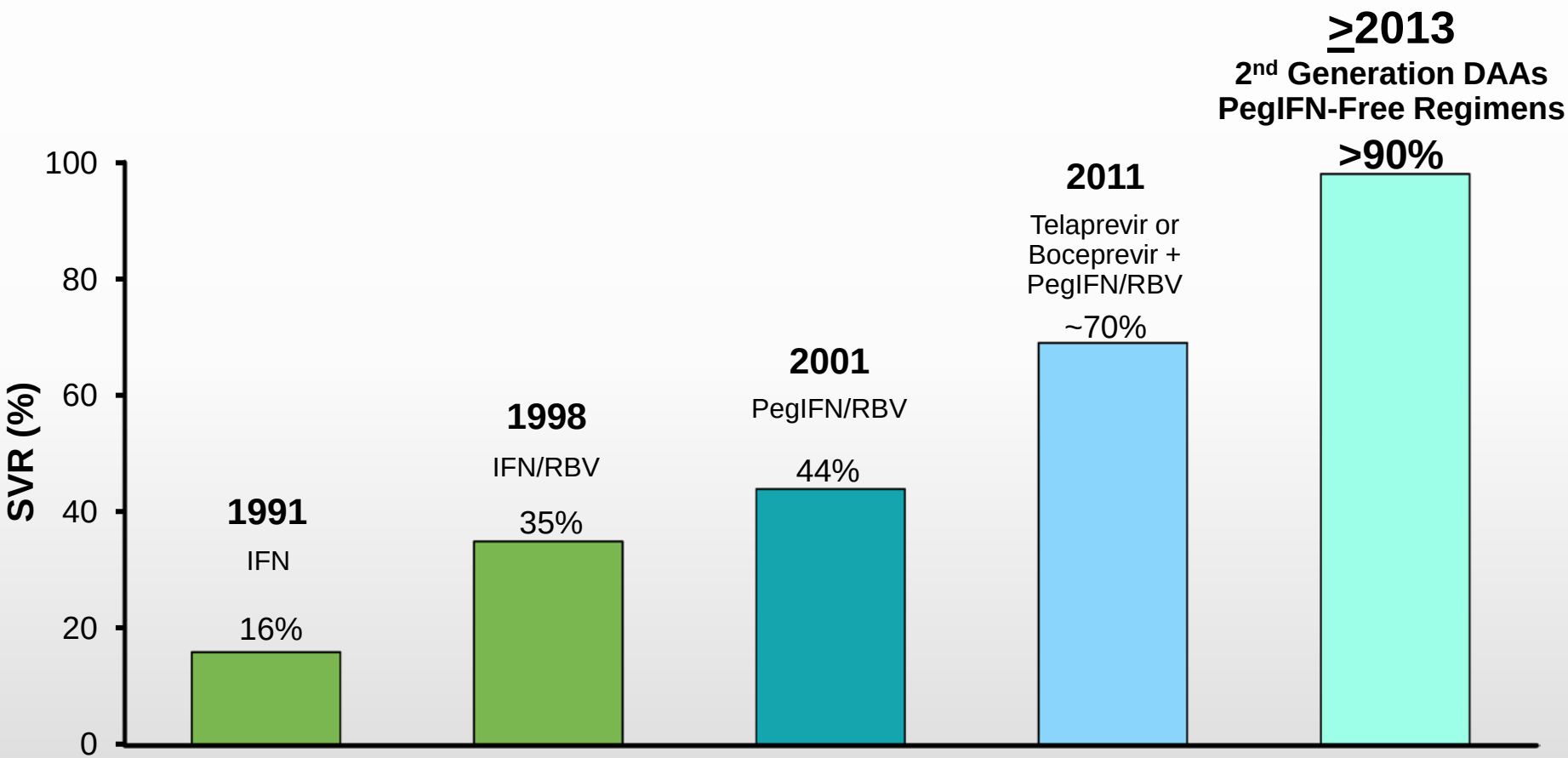
	Linked Criteria
1	LS CL PATIENT BORN BETWEEN 1945-1965 [1529]
2	LS CL PATIENT TESTED FOR HEPATITIS C [1538]
3	CL DX HEPATITIS C [742]
4	LS CL NOT A CANDIDATE FOR HEPATITIS C [2100002339]

Logic: 1 AND NOT 2 AND NOT 3 AND 4

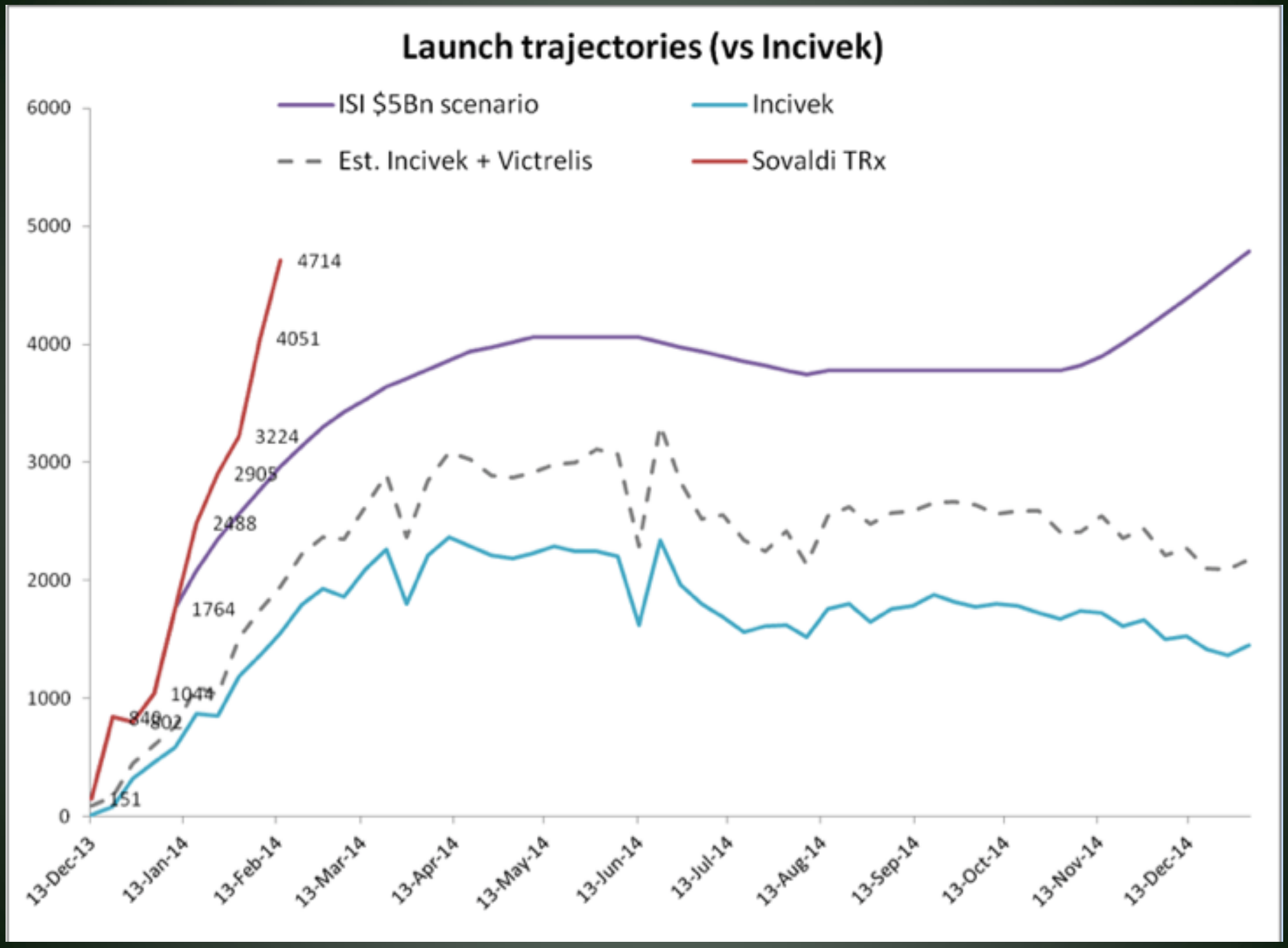
Courtesy of Lynn Taylor, Lifespan & RI Defeats Hep C

NVHR National Viral Hepatitis Roundtable

Chronic HCV Therapy: Advances in Raising Cure Rates



Schaefer EA, et al. *Gastroenterology.* 2012;142:1340-1350.
AASLD and IDSA. http://www.hcvguidelines.org/full-report-view. Version December 19, 2014.

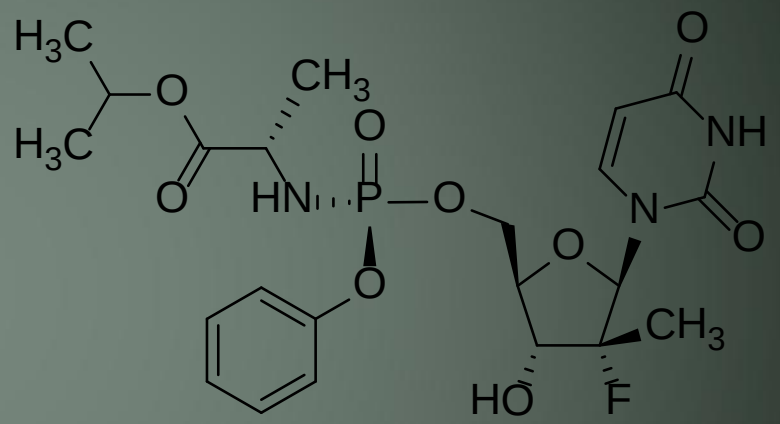

Launch trajectories (vs Incivek)
ISI $5Bn scenario
Incivek
Est. Incivek + Victrelis
Sovaldi TRx
6000
5000
4000
3000
2000
1000
0
4714
4051
3224
2905
2488
1764
1044
848
802
151
13-Dec-13
13-Jan-14
13-Feb-14
13-Mar-14
13-Apr-14
13-May-14
13-Jun-14
13-Jul-14
13-Aug-14
13-Sep-14
13-Oct-14
13-Nov-14
13-Dec-14

The “Ideal” HCV Antiviral

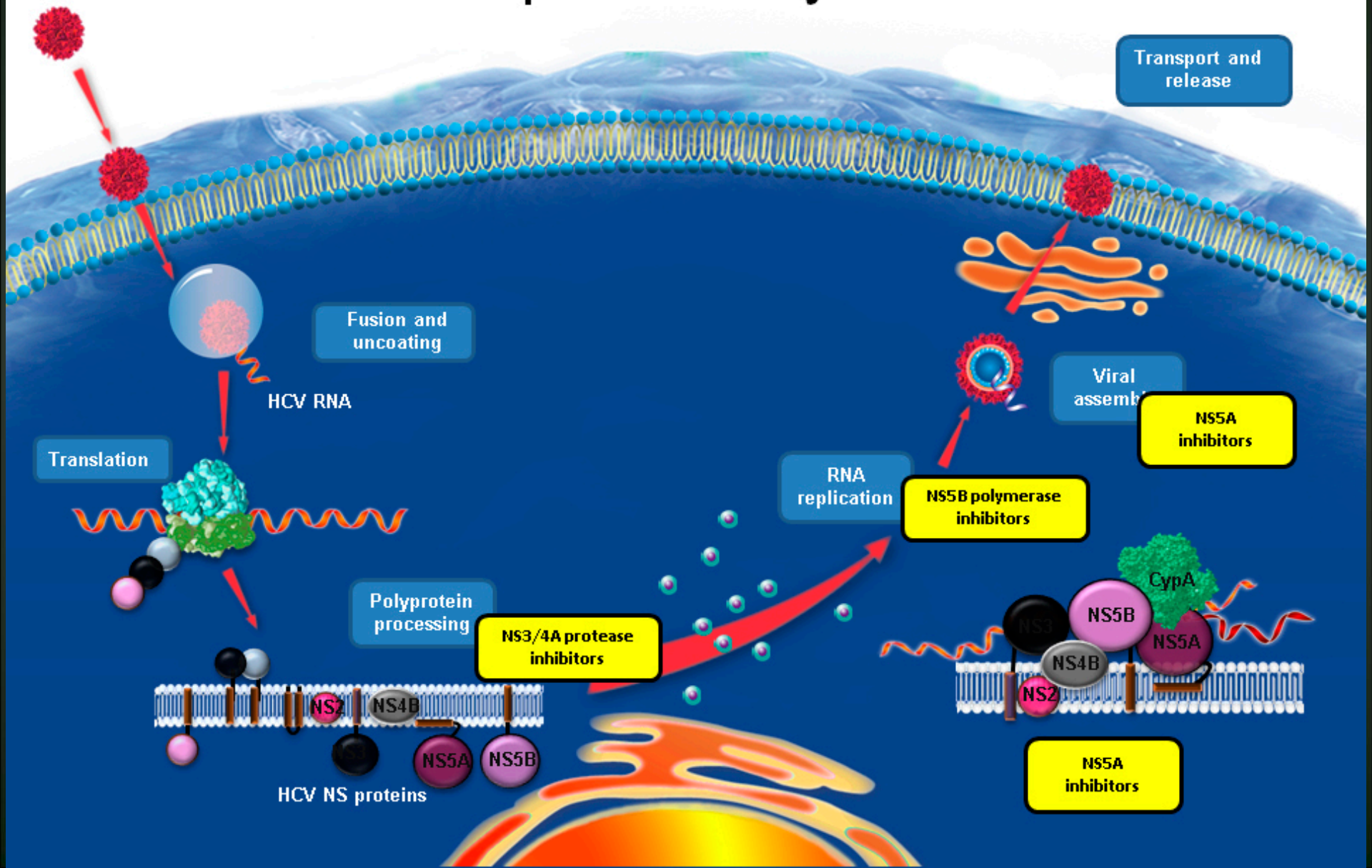
- High Antiviral Activity
- Activity against all genotypes
- High barrier to resistance
- Simple application (few pills, QD dosing)
- Highly favorable safety profile
- No Drug-Drug interactions
- Short and finite duration of therapy
- Efficacious in all patient populations
- Cure (very high SVR rates)
- High value

Sofosbuvir

- HCV-specific nucleotide polymerase inhibitor (chain terminator)
- Antiviral activity and clinical efficacy in HCV GT 1–6
- High barrier to resistance
- Once-daily, oral, 400-mg tablet
- Approved for use in combination with other agents for the treatment of chronic HCV
- Safety established in >3000 patients including patients with compensated cirrhosis



Potential Therapeutic Targets in the HCV Replication Cycle



DAAs Approved or in Late-Stage Clinical Development for Chronic HCV Infection

	NS3/4A Protease Inhibitors	Nucleotide NS5B Polymerase Inhibitors	Non-Nucleoside NS5B Polymerase Inhibitors	NS5A Replication Complex Inhibitors	Cyclophilin Inhibitors
Approved	**Simeprevir** **Boceprevir** **Telaprevir** **Paritaprevir/r**	**Sofosbuvir**	**Dasabuvir**	**Ledipasvir** **Ombitasvir** **Daclatasvir**	
Phase 3	Asunaprevir* Grazoprevir		Beclabuvir	† Elbasvir GS-5816	
Phase 2	GS-9256 GS-9451 ABT-493 Sovaprevir GS-9857	ACH-3422 MK-3682	ABT-072 GS-9669 TMC647055	ABT-530 ACH-3102 MK-8408 GSK2336805 PPI-668	SCY-635

*Approved in Japan.
†Approved in Europe.
Not all inclusive.

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AASLD / IDSA Hepatitis C Treatment Guidelines

- Panel of experts in hepatology and infectious disease
- HCVGuidelines.org
- AASLD.org
- Continuously updated
- May vary from FDA product information
- Represent Current Standard of Care
- Controversial

GENOTYPE 1A

Daily daclatasvir (60 mg*) and sofosbuvir (400 mg) for 12 weeks (no cirrhosis) or 24 weeks with or without weight-based RBV (1000 mg [<75 kg] to 1200 mg [>75 kg]) (cirrhosis) is recommended for treatment-naive patients with HCV genotype 1a infection.

Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) for 12 weeks is recommended for treatment-naive patients with HCV genotype 1a infection.

Daily fixed-dose combination of paritaprevir (150 mg)/ritonavir (100 mg)/ombitasvir (25 mg) plus twice-daily dosed dasabuvir (250 mg) and weight-based RBV for 12 weeks (no cirrhosis) or 24 weeks (cirrhosis) is recommended for treatment-naive patients with HCV genotype 1a infection.

Daily simeprevir (150 mg) and sofosbuvir (400 mg) for 12 weeks (no cirrhosis) or 24 weeks (cirrhosis without the Q80K polymorphism) with or without weight-based RBV is recommended for treatment-naive patients with HCV genotype 1a infection.

GENOTYPE 1B

- **Daily daclatasvir (60 mg*) and sofosbuvir (400 mg) for 12 weeks (no cirrhosis) or 24 weeks with or without weight-based RBV (cirrhosis) is recommended for treatment-naive patients with HCV genotype 1b infection.**
- **Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) for 12 weeks is recommended for treatment-naive patients with HCV genotype 1b infection.**
- **Daily fixed-dose combination of paritaprevir (150 mg)/ritonavir (100 mg)/ombitasvir (25 mg) plus twice-daily dosed dasabuvir (250 mg) for 12 weeks is recommended for treatment-naive patients with HCV genotype 1b infection.**
- **Daily simeprevir (150 mg) plus sofosbuvir (400 mg) for 12 weeks (no cirrhosis) or 24 weeks with or without weight-based RBV (cirrhosis) is recommended for treatment-naive patients with HCV genotype 1b infection.**

GENOTYPE 2

Daily daclatasvir (60 mg*) and sofosbuvir (400 mg) for 12 weeks is recommended for treatment-naive patients with HCV genotype 2 infection who cannot tolerate RBV.

Daily sofosbuvir (400 mg) and weight-based RBV for 12 weeks is recommended for treatment-naive patients with HCV genotype 2 infection.

Extending treatment to 16 weeks is recommended in patients with cirrhosis.

GENOTYPE 3

Daily daclatasvir (60 mg*) and sofosbuvir (400 mg) for 12 weeks (no cirrhosis) or 24 weeks with or without weight-based RBV (cirrhosis) is recommended for treatment-naive patients with HCV genotype 3 infection.

Daily sofosbuvir (400 mg) and weight-based RBV plus weekly PEG-IFN for 12 weeks is recommended for IFN-eligible, treatment-naive patients with HCV genotype 3 infection.

Alternative regimen for treatment-naive patients with HCV genotype 3 infection: **Daily sofosbuvir (400 mg) and weight-based RBV for 24 weeks is an alternative regimen for treatment-naive patients with HCV genotype 3 infection who are IFN-ineligible.**

Summary

- Active HCV infections with a detectable viral load are at increased risk of death due to hepatic and extrahepatic diseases
- Chronic HCV patients with active infection may benefit from antiviral treatment, once diagnosed, to reduce overall mortality
- HCV-related mortality among baby boomers prompted US health officials and the CDC to expand HCV testing to this entire age group
  - Stress the importance of testing and including an HCV RNA test for anti-HCV seropositives in clinical practice
  - HCV mortality may be reduced by increased treatment as a result of expanding screening to identify patients unaware of their infection

Lee M-H, et al. *J Infect Dis*. 2012;206:469-477.
Nelson KE. *J Infect Dis*. 2012;206:461-463.
Centers for Disease Control and Prevention. *MMWR*. 2012;61(RR-4):1-33.
AASLD and IDSA. http://www.hcvguidelines.org/full-report-view. Version December 19, 2014.

Summary

- Approval of newer, direct-acting, oral agents have high HCV cure rates, fewer adverse events, and negligible resistance compared with the first generation HCV Protease Inhibitors
  - IFN-free regimens are options for many patients
  - Interferon-based regimens are no longer recommended for treatment-naïve genotypes 1, 2, 3, 4, and 6s
  - Further research is needed on regimens based on newer, direct-acting, oral agents, especially for patients who failed previous HCV PI-based therapy
  - Role of viral resistance testing, especially in patients who fail current treatments, requires additional research
  - Cost issues continue to limit access to treatment for hundreds of thousands of patients
  - HCV could be eradicated in the US by year 2030 if current treatment rates can be sustained

PR: pegIFN + RBV.

Thank You

Richard.Manch@dignityhealth.org

What to know even more about HCV?

4th Annual Current Trends in Liver Disease

Hepatitis C From A to Z

CME Conference

Friday, October 9
11:30 a.m. – 5 p.m.

Sonntag Pavilion
St. Joseph's Hospital and Medical Center

Course Director:
Richard A. Manch, MD, FACP, FACG
Chief of Hepatology
St. Joseph's Hospital and Medical Center

Dignity Health™
St. Joseph's Hospital and Medical Center

A special CME conference focused on the latest developments in Hepatitis C management.

Target Audience:
Specialists (hepatology, gastroenterology, infectious disease), general practitioners, physician assistants, nurse practitioners, registered nurses, residents and others who manage patients with hepatitis C, including those with HCV/HIV coinfection.

Register today by calling the ResourceLInk at 1.877.602.4111

AMA PRA Category 1 Credit™ will be applied for through St. Joseph's Hospital and Medical Center.