Clinical Pearls on Chronic C Infection: Special Consideration and Current Treatments

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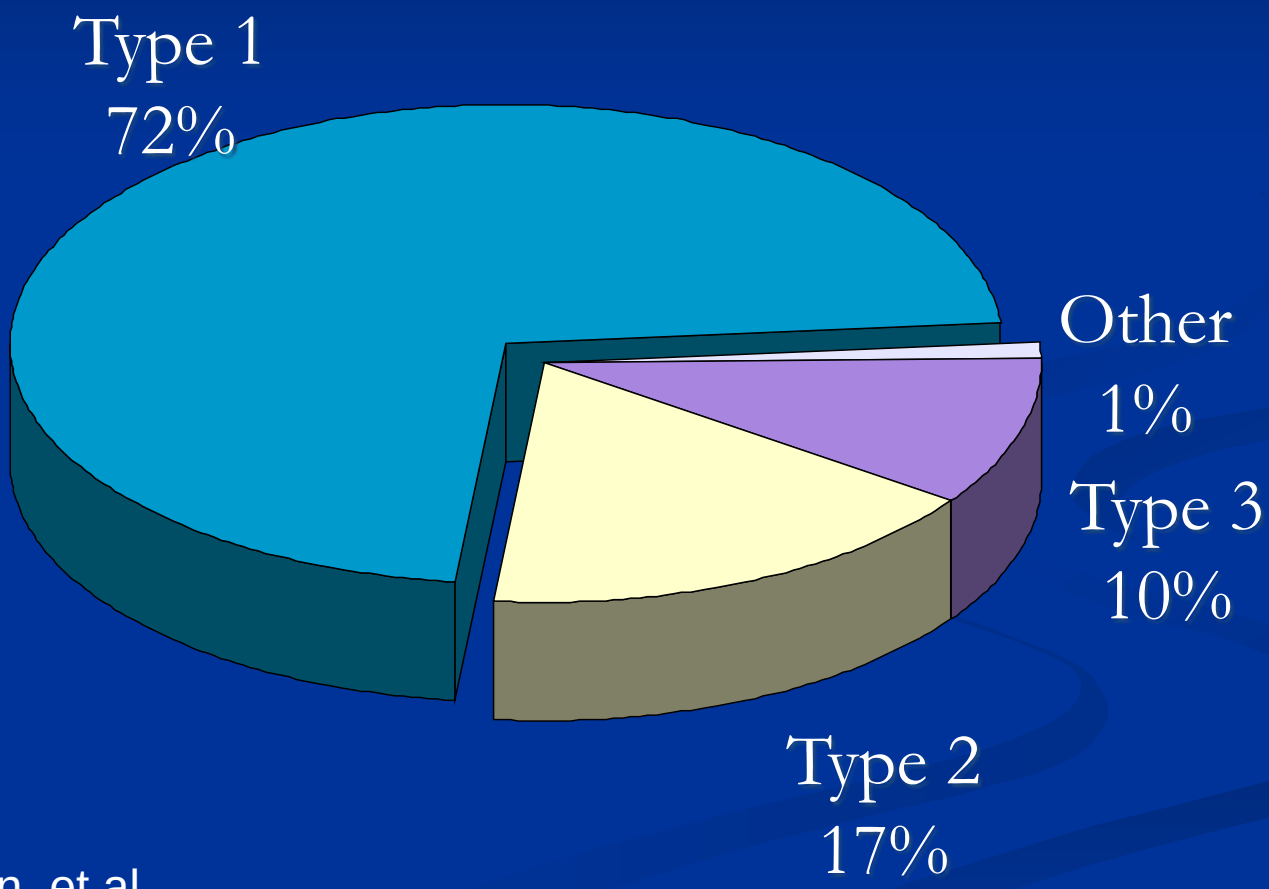
Learning Objectives

- Recognize the important steps in the evaluation of patient with hepatitis C antibody positivity
- Recognize strategies to best stage patient's liver disease prior to initiation of hepatitis C treatment
- Identify medications and duration for chronic hepatitis C treatment

Case 1: A New Referral

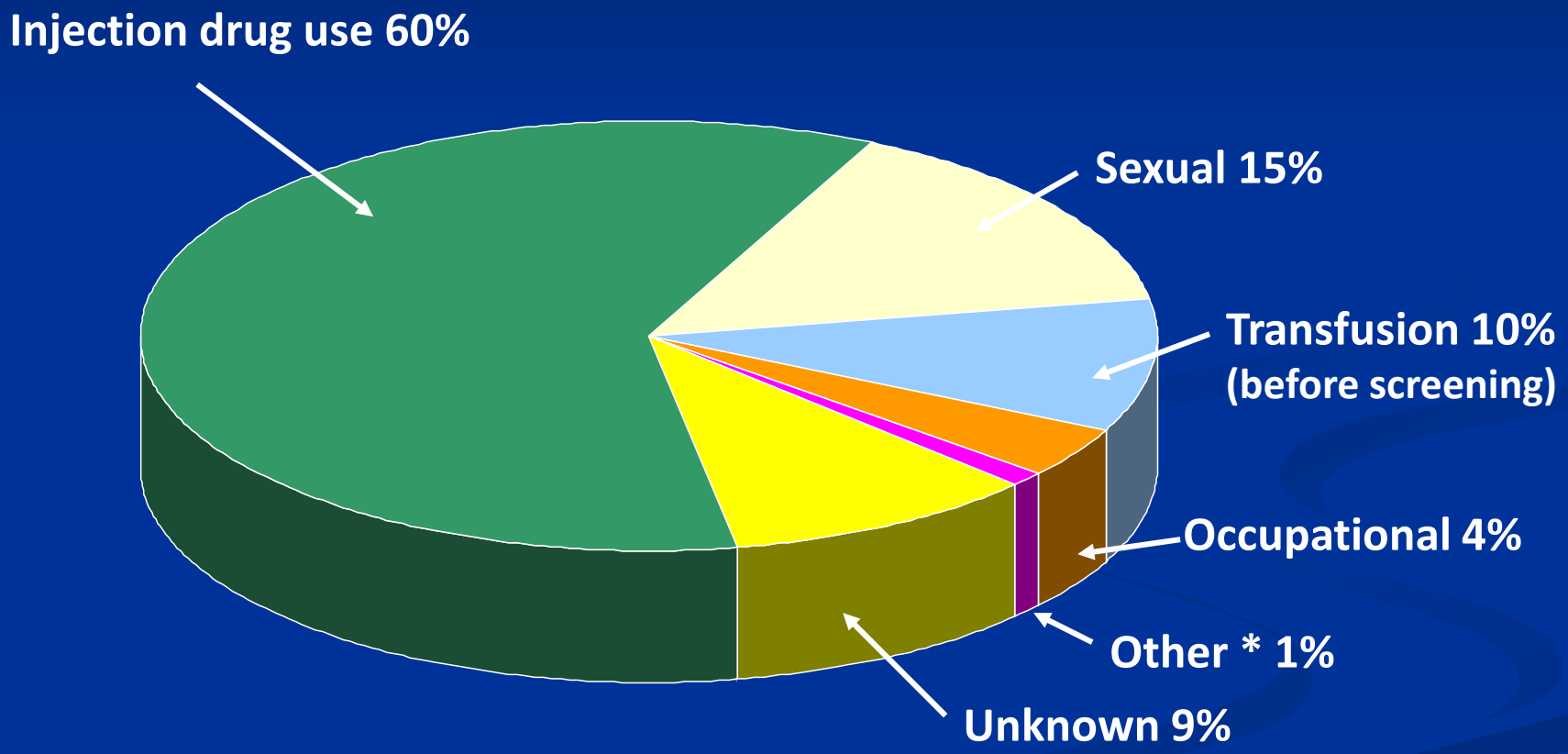
- 22 year old male with history of cocaine abuse who is currently in a drug rehabilitation program who presents to the clinic for evaluation of hepatitis C Ab positivity. What are the next steps to consider in the management of patient?

Hepatitis C Genotypes in U.S.



JG McHutchison, et al.
NEJM 1998;339:1485-1492.

Sources of Infection for Persons with Hepatitis C: USA



*Nosocomial; iatrogenic; Perinatal

Adapted from CDC Hepatitis Slide Kit http://www.cdc.gov/ncidod/diseases/hepatitis/slideset

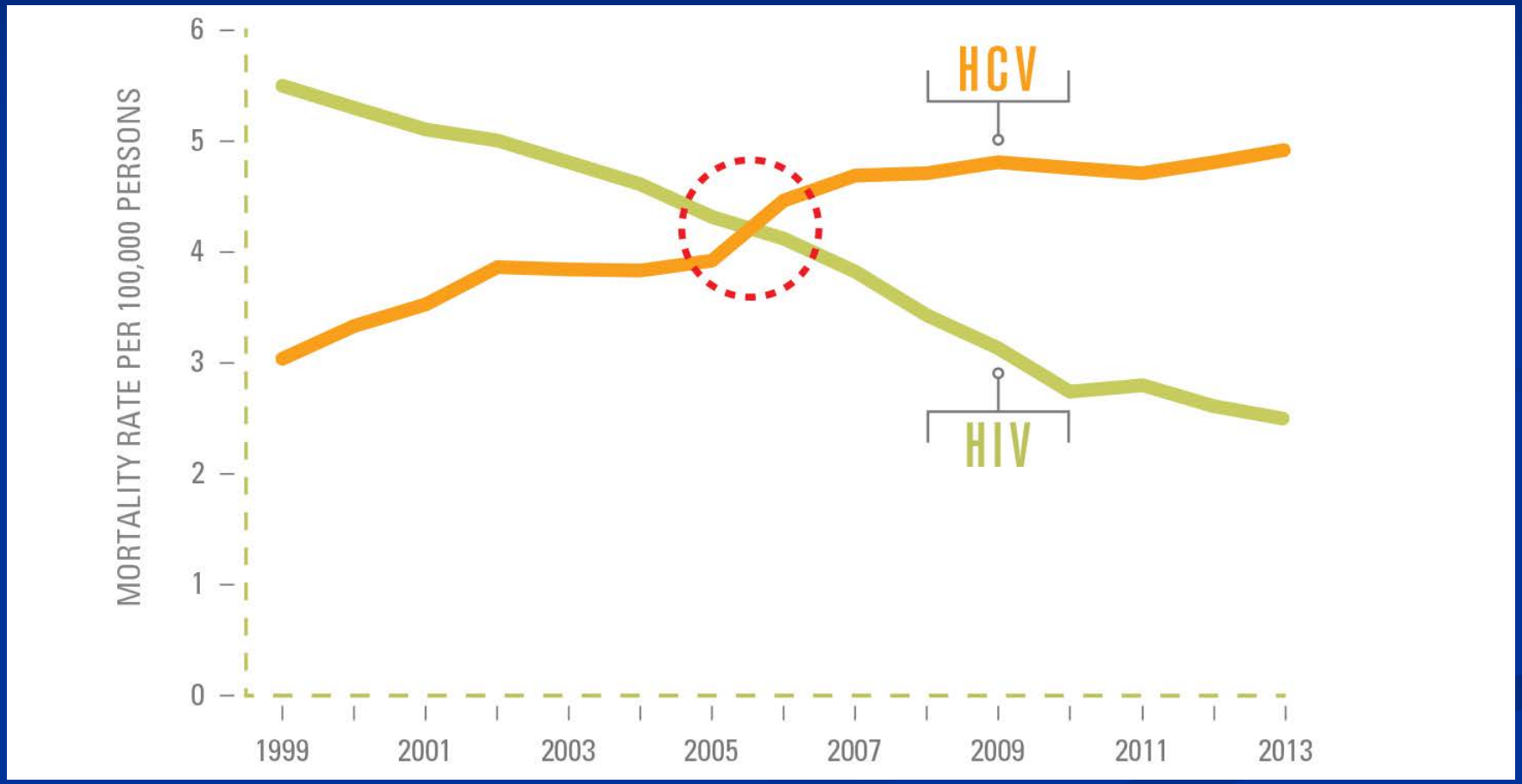
Who Should You Screen?

	Persons who ever injected illegal drugs
	HIV-infected patients
	Persons who have received tattoos from unlicensed or unregulated environments
	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 later tested positive for HCV infection • Persons who received a blood transfusion, blood components, or an organ transplant before July 1992
	Healthcare, emergency medical, and public safety workers after needlesticks, sharps, or mucosal exposures to HCV-positive blood
	Children born to an HCV-positive mother

Age Cohort Screening for Hepatitis C

	Birth 1945 - 1965
US Population (millions)	78.8
Anti-HCV Prevalence	3.29%
Percent anti-HCV identified	74.5%
Gender	
Male	4.35%
Female	2.23%
Race/Ethnicity	
White	2.93
Black	6.31
Hispanic	3.92

Mortality Risk with Hepatitis C



1. Ly KN et al. *Ann Intern Med.* 2012;156(4):271-278.
2. Holmberg S, Ly KN, Xing J, Moorman AC. Rising mortality from hepatitis C virus in the United States, 2002-2013. Paper presented at: American College of Gastroenterology Annual Scientific Meeting and Postgraduate Course; October 16-21, 2015; Honolulu, HI.

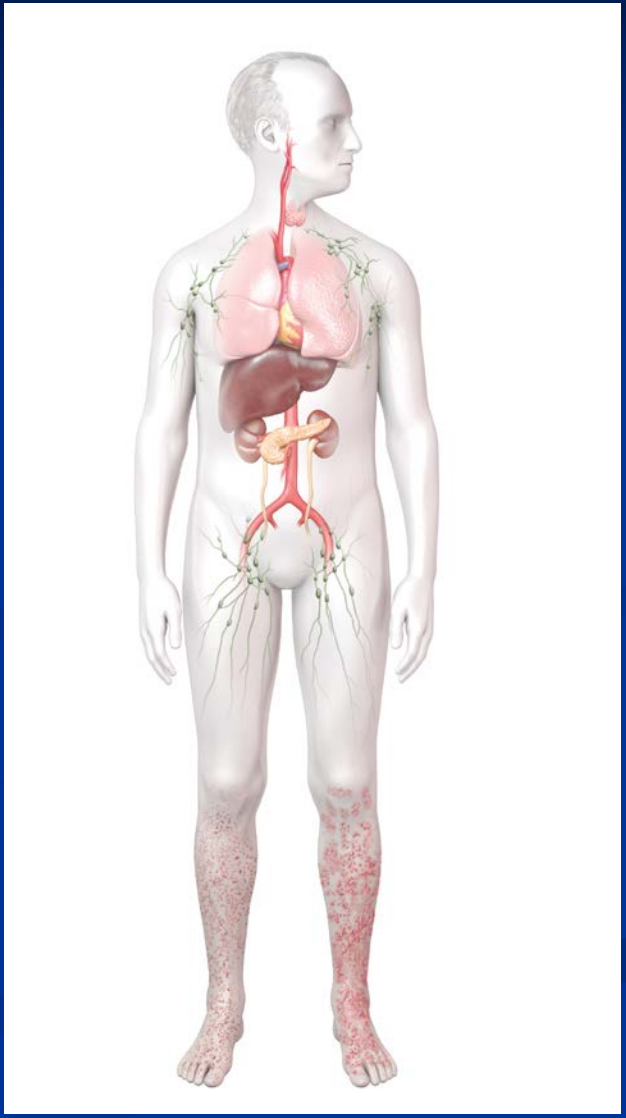
Hepatitis C: A Systemic Illness

INCREASED RISK FOR:

- Depression
- Carotid atherosclerosis/atherothrombosis
- Type 2 diabetes mellitus
- Hypertension
- Congestive heart failure
- Chronic kidney disease
- End-stage renal disease
- Kidney cancer
- Other renal manifestations (*eg, glomerulonephritis, proteinuria*)[a]
- Low bone mineral density (BMD)
- Rheumatologic manifestations (*eg, polyarthralgia, polyarthritis*)[a]
- Fatigue

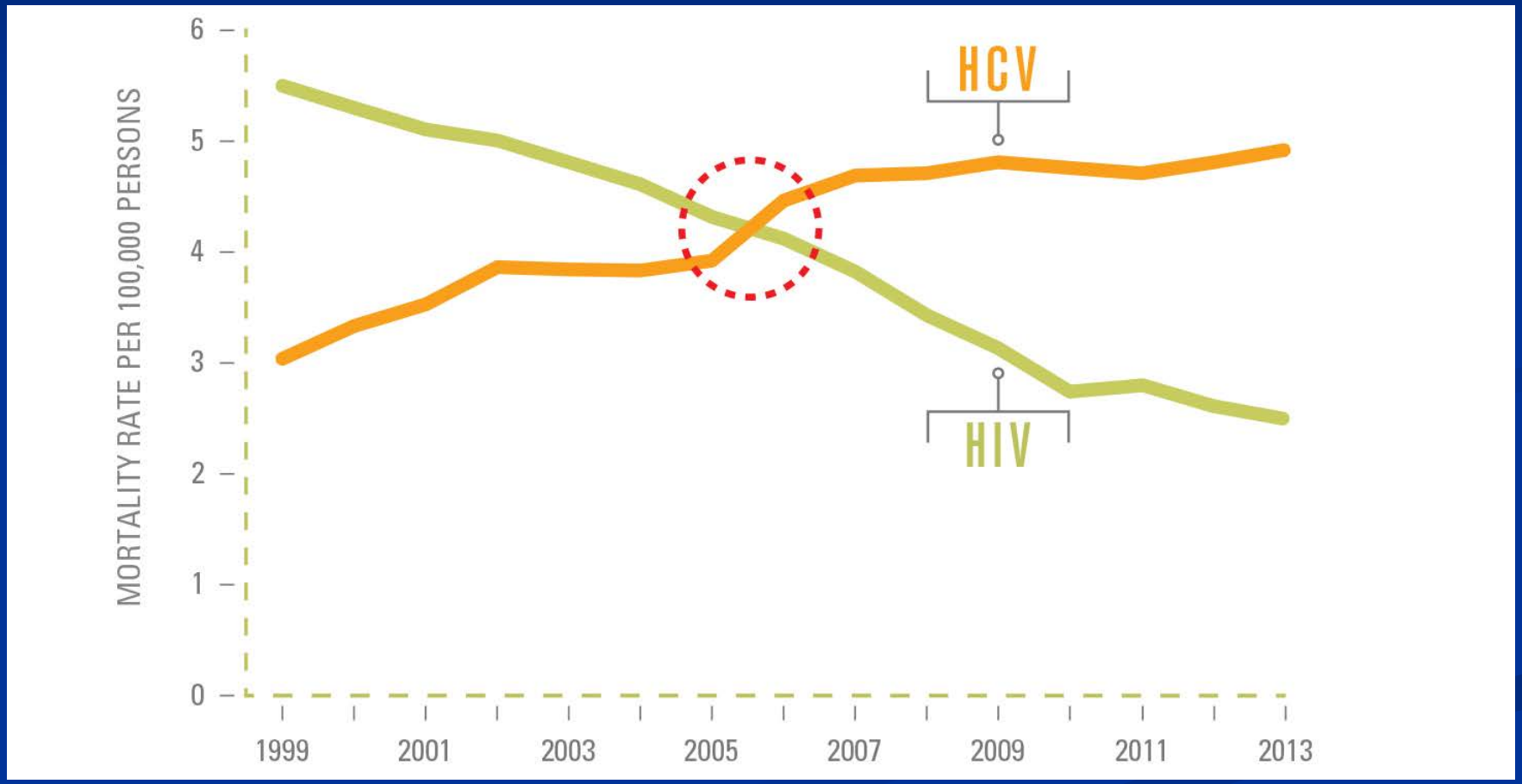
POSSIBLE INCREASED RISK FOR:

- Neurologic impairment/disorders
- Stroke
- Coronary artery disease/ischemic heart disease



AASLD, IDSA, IAS-USA. Recommendations for testing, managing, and treating hepatitis C. http://www.hcvguidelines.org. Accessed December 7, 2015. 2. Jacobson IM et al. *Clin Gastroenterol Hepatol.* 2010;8(12):1017-1029.

Mortality: HCV vs HIV



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Clinical Pearl #1

- Among patients with hepatitis C antibody positivity, follow-up hepatitis C RNA quantitative and hepatitis C genotype should be sent to confirm chronic hepatitis C infection

Clinical Pearl #2

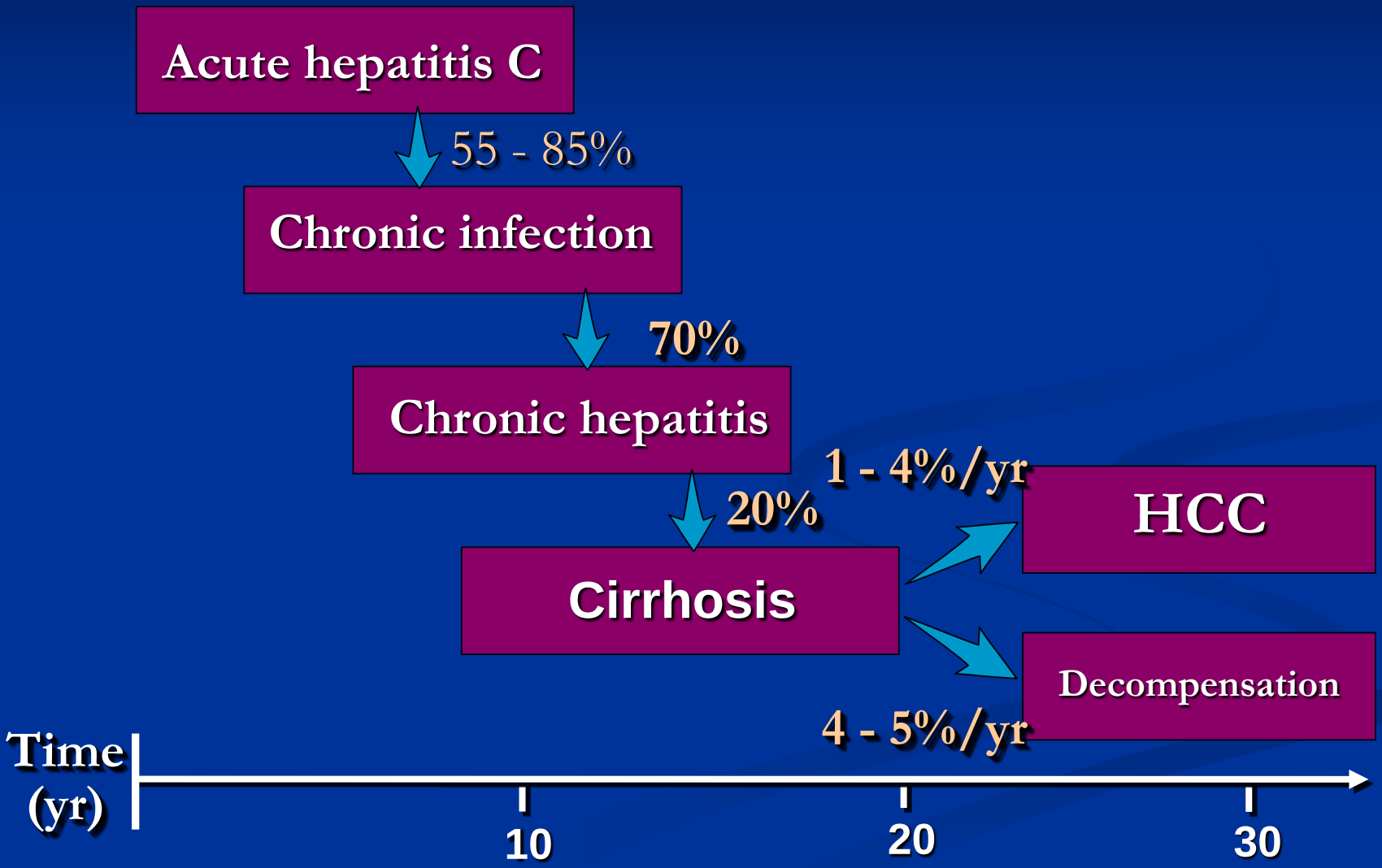
- Due to similar mode of transmission of hepatitis C, hepatitis B, and HIV, it is important to send for:
  - Hepatitis B sAg, Hepatitis B sAb, Hepatitis B cAb total
  - HIV screening

Case #2: Staging of Liver Disease

- 48 year old male with a history of chornic hepatitis C infection. Patient is treatment naïve.
- His lab results are as follows:
  - CBC—Hgb 13.0. WBC 5.0, platelet count 120,000
  - Hepatitis BsAg, BcAb, BsAb all negative
  - Hepatitis C Ab was positive
  - HCV RNA 4,000,000 IU/ml
  - HCV genotype 1a

- **What are your next considerations prior to offering patient treatment for hepatitis C?**

Outcome Following Hepatitis C Infection

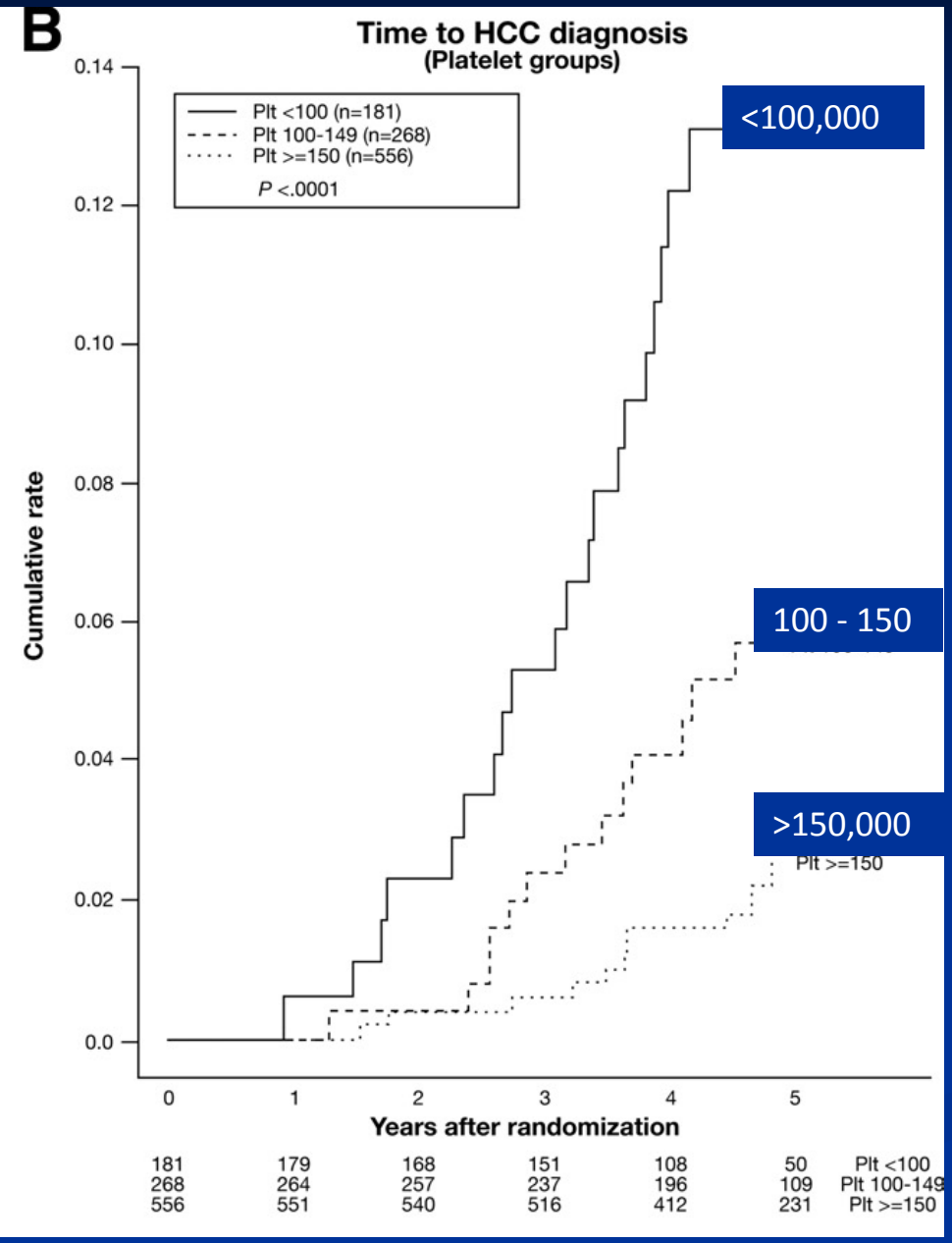


Staging of Liver Disease

- FIB-4
- AST to platelet ratio index (APRI)
- Fibrosure
- Ultrasound with dopplers
- Ultrasound-based transient hepatic elastography
- Upper endoscopy
- Liver Biopsy

Klibansky DA, J Viral Hepat, 2012

Risk of Hepatocellular Carcinoma: Platelet Count < 150,000



Screening for HCC

Risk factor:

Cirrhosis

(Platelet count < 150,000/mm^3)

Ultrasound of liver

every 6-12 months

Clinical Pearl #3

- It is important to stage patient's liver disease prior to initiation of hepatitis C treatment because it affects treatment duration and post-treatment monitoring

- If you are using a non-invasive marker to determine cirrhotic liver disease, it is important to use at least 2 markers to rule out existing advanced fibrosis or cirrhosis.

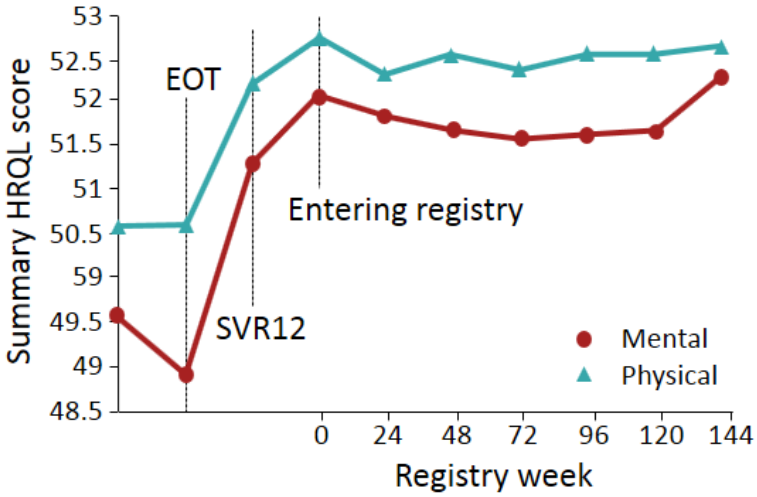
Case #3: Treatment Decisions

- A 55 year old male with a history of prior IV drug use who presents to the clinic for evaluation of abnormal liver function testing. He underwent extensive work-up which included:
  - CBC—Hgb 13.0. WBC 5.0, platelet count 120,000
  - Hepatitis BsAg, BcAb, BsAb all negative
  - Hepatitis C Ab was positive
  - HCV RNA 4,000,000 IU/ml
  - HCV genotype 1a
  - Liver biopsy shows: Grade 3, Stage 3 disease
- **What are additional history to considered prior to recommendation of treatment of hepatitis C?**

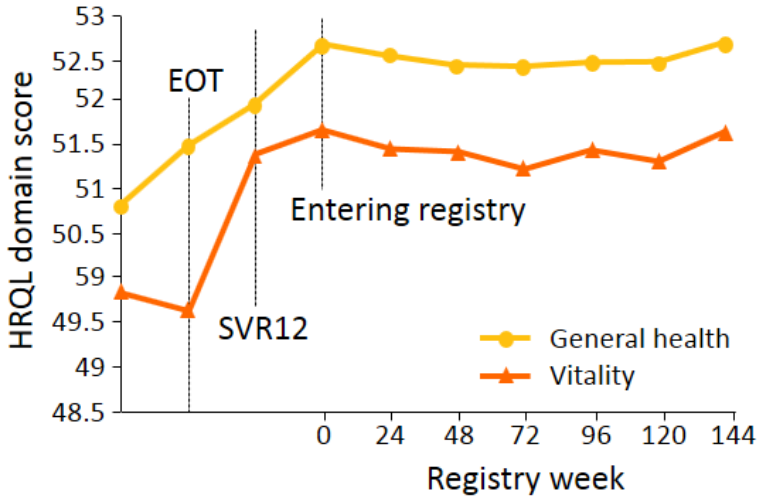
Qualify of Life After SVR12

HRQL outcomes in 3486 patients with SVR12

SF-36 summary scores



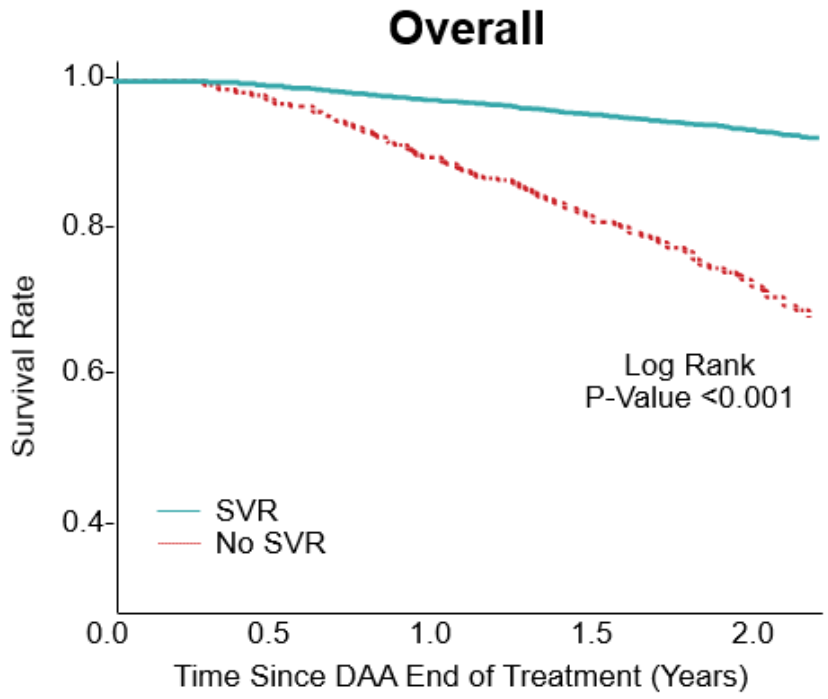
Greatest HRQL gains consistently observed General Health and Vitality domains



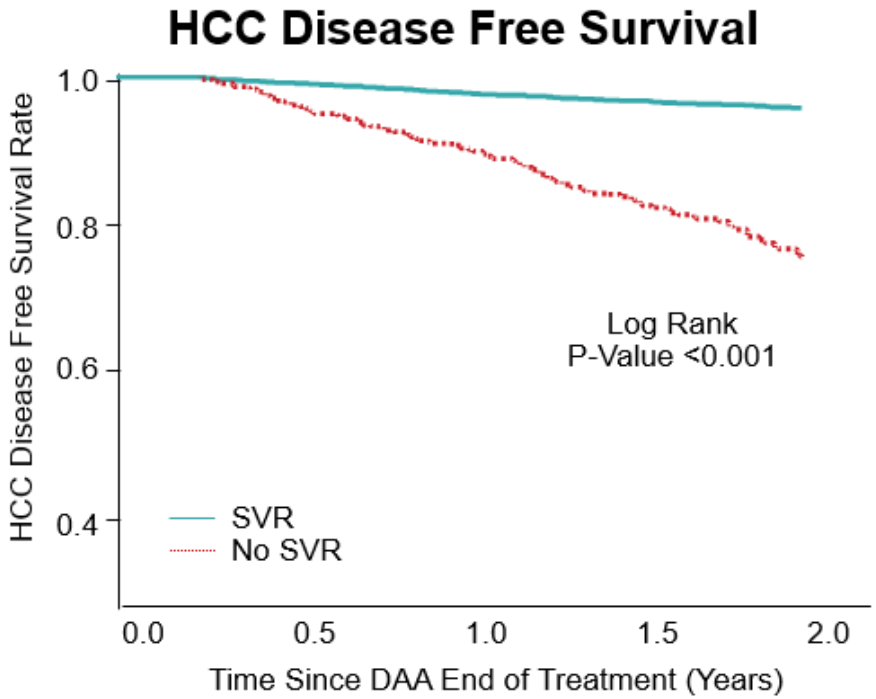
Improvement in HRQL after achieving SVR is maintained in the long-term follow up

Younossi ZM et al AASLD 2017, Ab 64

Survival Curves for CLD Patients With and Without SVR



No SVR	1067	923	650	326	105
SVR	13992	12939	9521	5437	1875



No SVR	871	844	650	425	181
SVR	13153	13070	10759	7482	3588

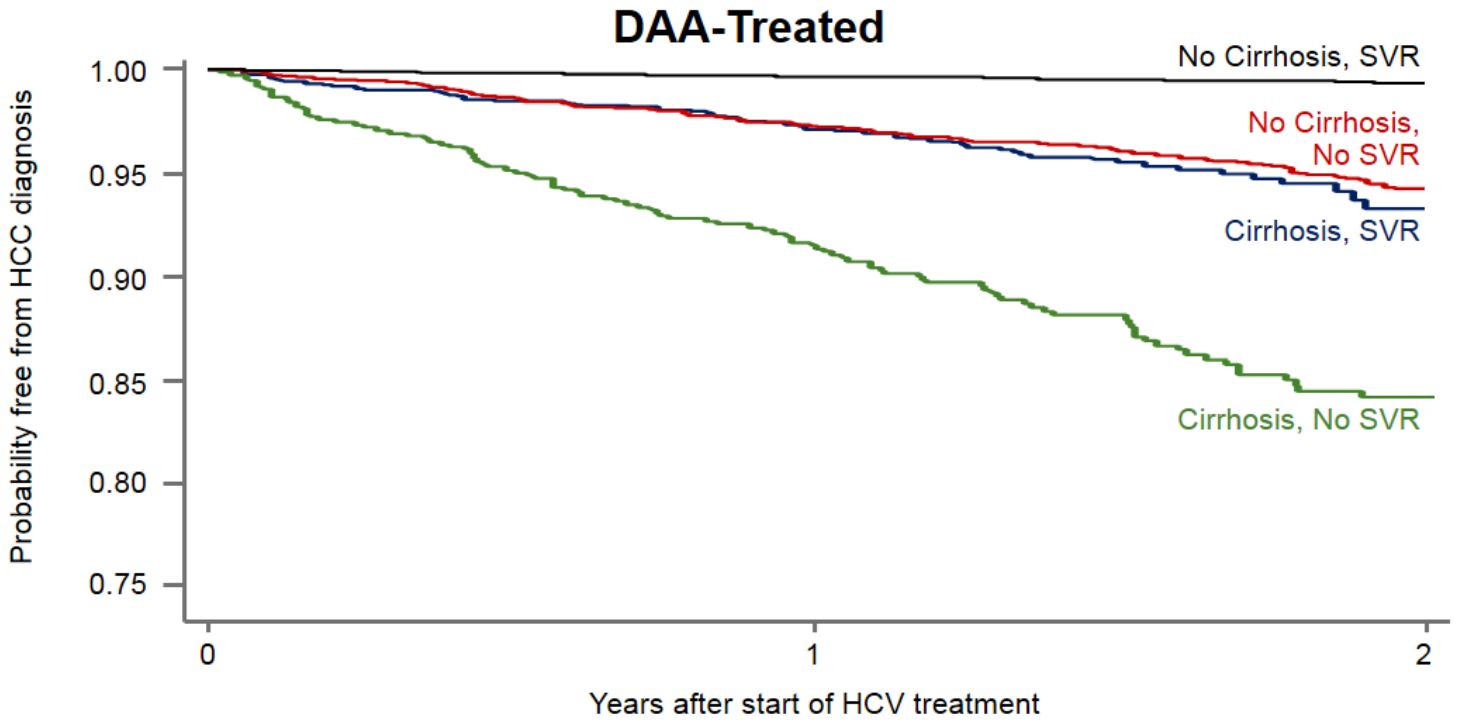
Increasing access to DAAs for ACLD patients should result in fewer overall deaths

Veterans Affairs HCV Clinical Case Registry

Backus, AASLD, 2017, oral 78

HCC Risk with SVR12

Retrospective study in 167 medical centers including 35,871 IFN-only regimens, 4,535 DAA+IFN and 21,948 DAA-only (80% SOF-based regimens); mean f/u of 6.1 years (range: 2-18); incident HCCs=3,271



DAA-induced SVR is associated with 71% reduction in HCC risk

Veterans Affairs HCV Registry

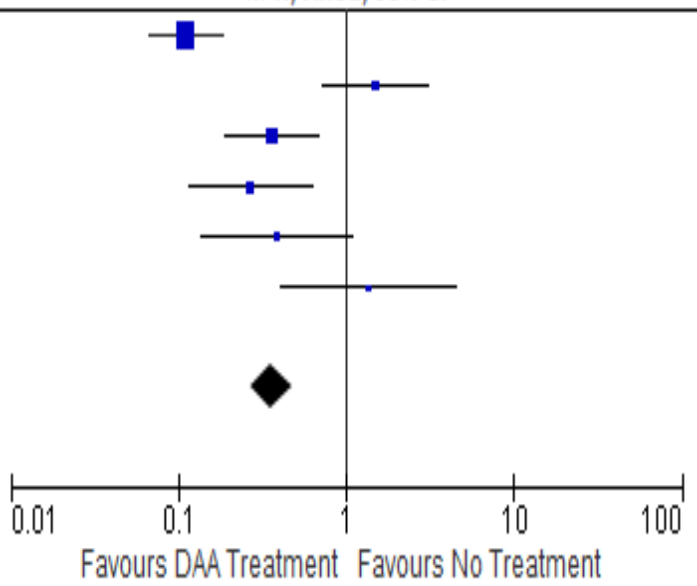
Ioannou et al, AASLD, 2017, oral 142

HCC Recurrence after DAA Treatment

Study or Subgroup	With DAA Treatment Events	Total	Without Treatment Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI
ANRS Collaborative Study	32	516	47	125	46.3%	0.11 [0.07, 0.18]
Cheung et al 2016	25	406	11	261	8.2%	1.49 [0.72, 3.08]
Ikeda et al 2017	21	89	41	89	20.4%	0.36 [0.19, 0.69]
Minami et al 2016	8	27	525	861	14.6%	0.27 [0.12, 0.62]
Virlogeux et al 2017	10	23	30	45	7.5%	0.38 [0.14, 1.08]
Vukotic et al 2017	8	16	14	33	3.0%	1.36 [0.41, 4.50]
Total (95% CI)		**1077**		**1414**	**100.0%**	**0.36 [0.27, 0.47]**
Total events	104		668			

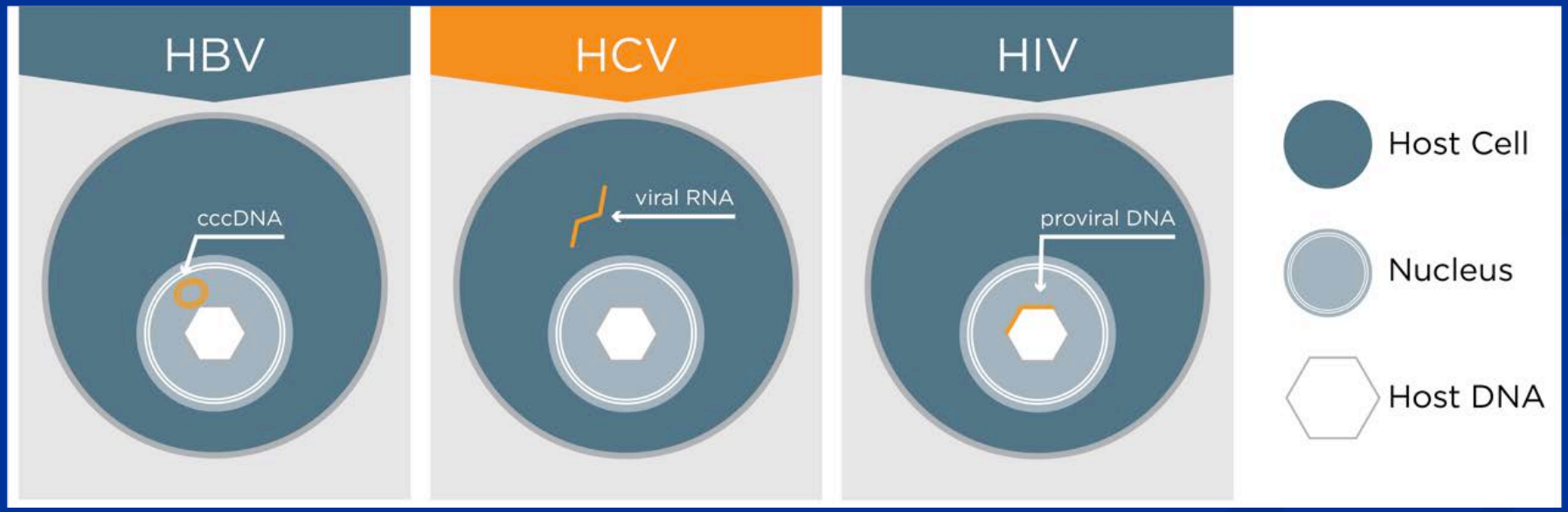
Heterogeneity: $Chi^2 = 40.69$, $df = 5$ ($P < 0.00001$); $I^2 = 88\%$

Test for overall effect: $Z = 7.13$ ($P < 0.00001$)

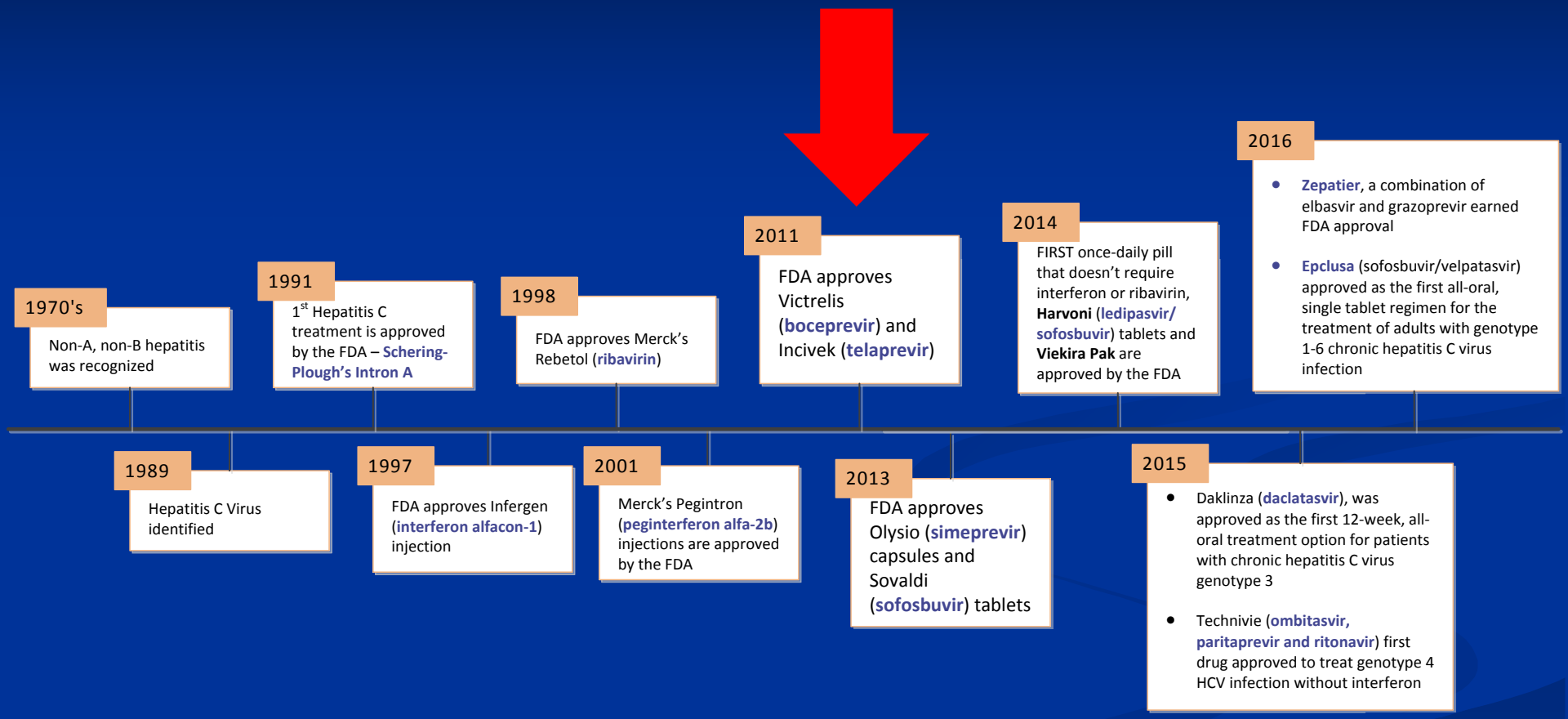


Nguyen DL et al, ACG 2018

Why is Hep C Curable?



Hepatitis C Treatment Evolution

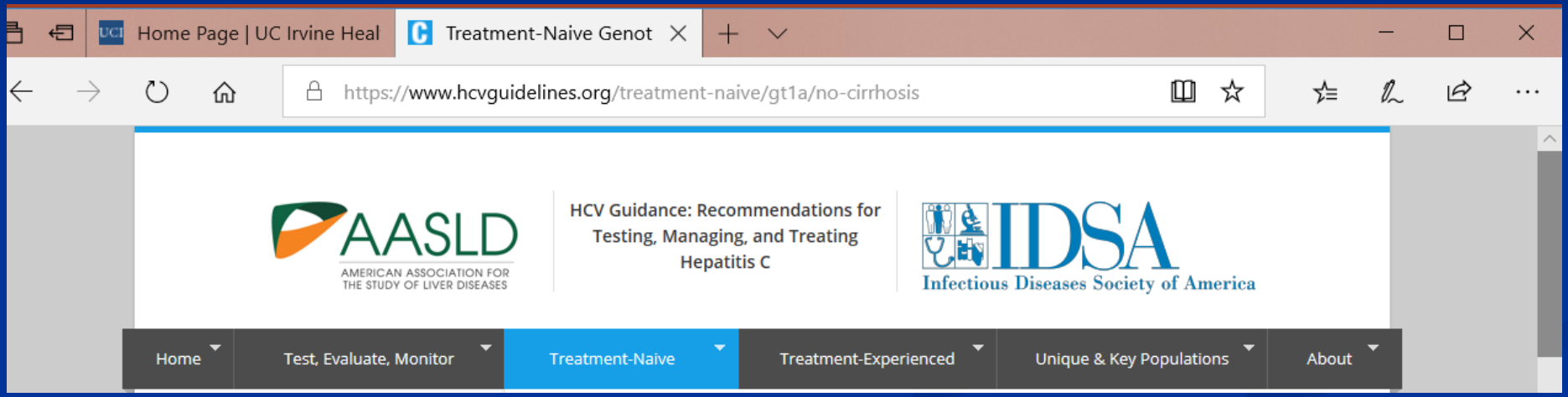


Important Initial Treatment Considerations

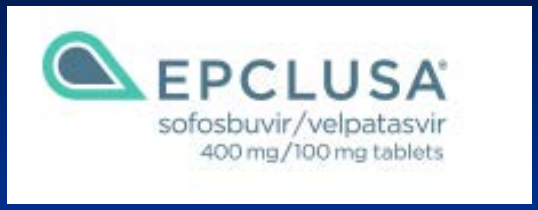
- Treatment status
  - Treatment naïve vs. treatment experienced
  - Prior failure of DDA
  - Prior failure of interferon-based therapy
- Hepatitis C genotype
- Hepatitis C baseline viral load
- Co-existing advanced renal disease
- Stage of liver disease
  - Non-cirrhotic, compensated cirrhosis, decompensated cirrhosis

Nguyen DL et al, Open Medicine, 2016

HCV Treatment Guidelines

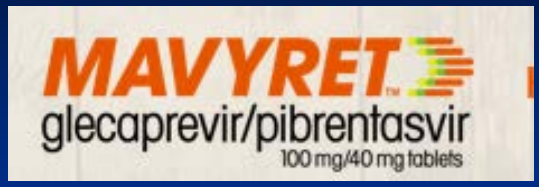


Pan-Genotypic Regimens



1. **12-week regimen for all genotypes**
2. Decompensated cirrhosis add in RBV for 12-weeks. If RBV ineligible, then 24-weeks
3. Decompensated cirrhosis with prior failure of sofosbuvir or NS5A-based treatments, 24 weeks with RBV

12-week salvage regimen for prior treatment failures of NS5A and sofosbuvir failures. Not for decompensated cirrhotics



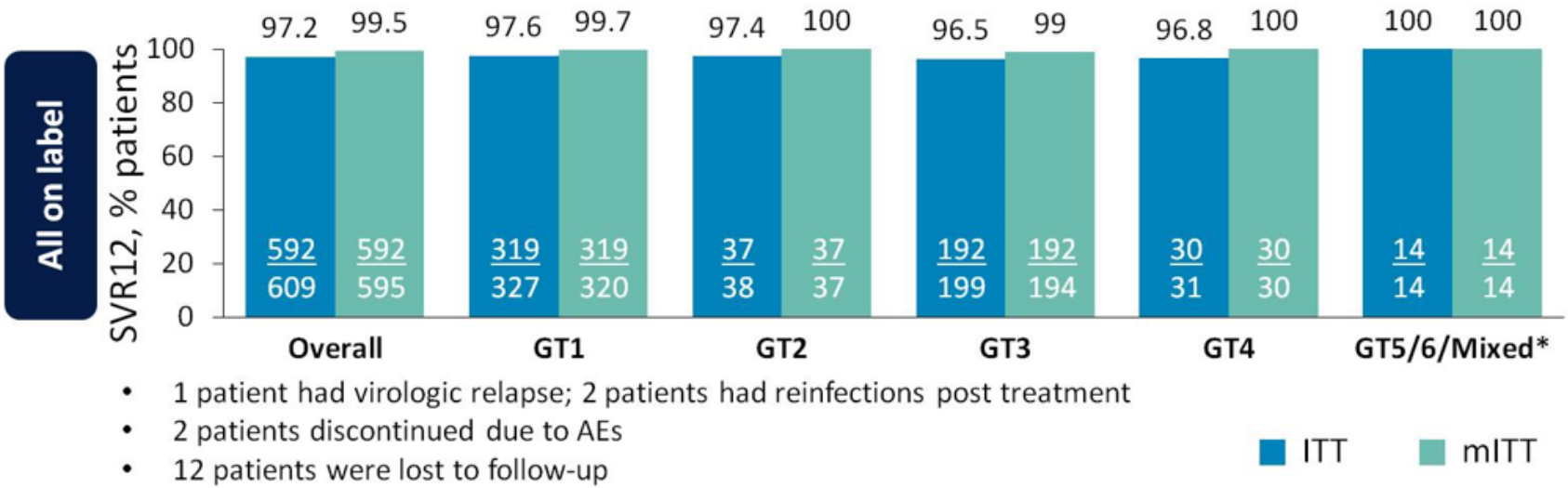
1. **8-week Treatment-naïve, non-cirrhotic**
2. 12-week Treatment naiive, compensated cirrhotic
3. ***Not indicated for decompensated cirrhosis***
4. Treatment experienced:

GT 1—NS5A w/o NS3/4A: 16 weeks
—NS3/4A w/o NS5A: 12 weeks (non-cirrhotic); 16 weeks (cirrhotic)

GT 1,2,4,5,6 PRS– 8 weeks (non-cirrhotic); 12 weeks cirrhotic

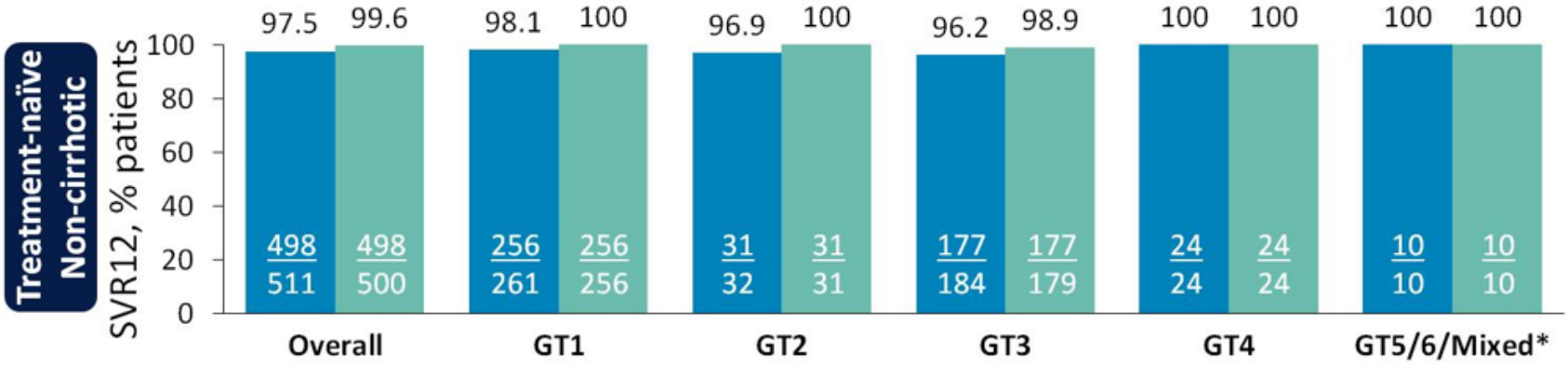
GT 3 PRS— 16 weeks (non-cirrhotic, compensated cirrhotic)

G/P Real World Data: German Hepatitis Registry



- 1 patient had virologic relapse; 2 patients had reinfections post treatment
- 2 patients discontinued due to AEs
- 12 patients were lost to follow-up

ITT mITT

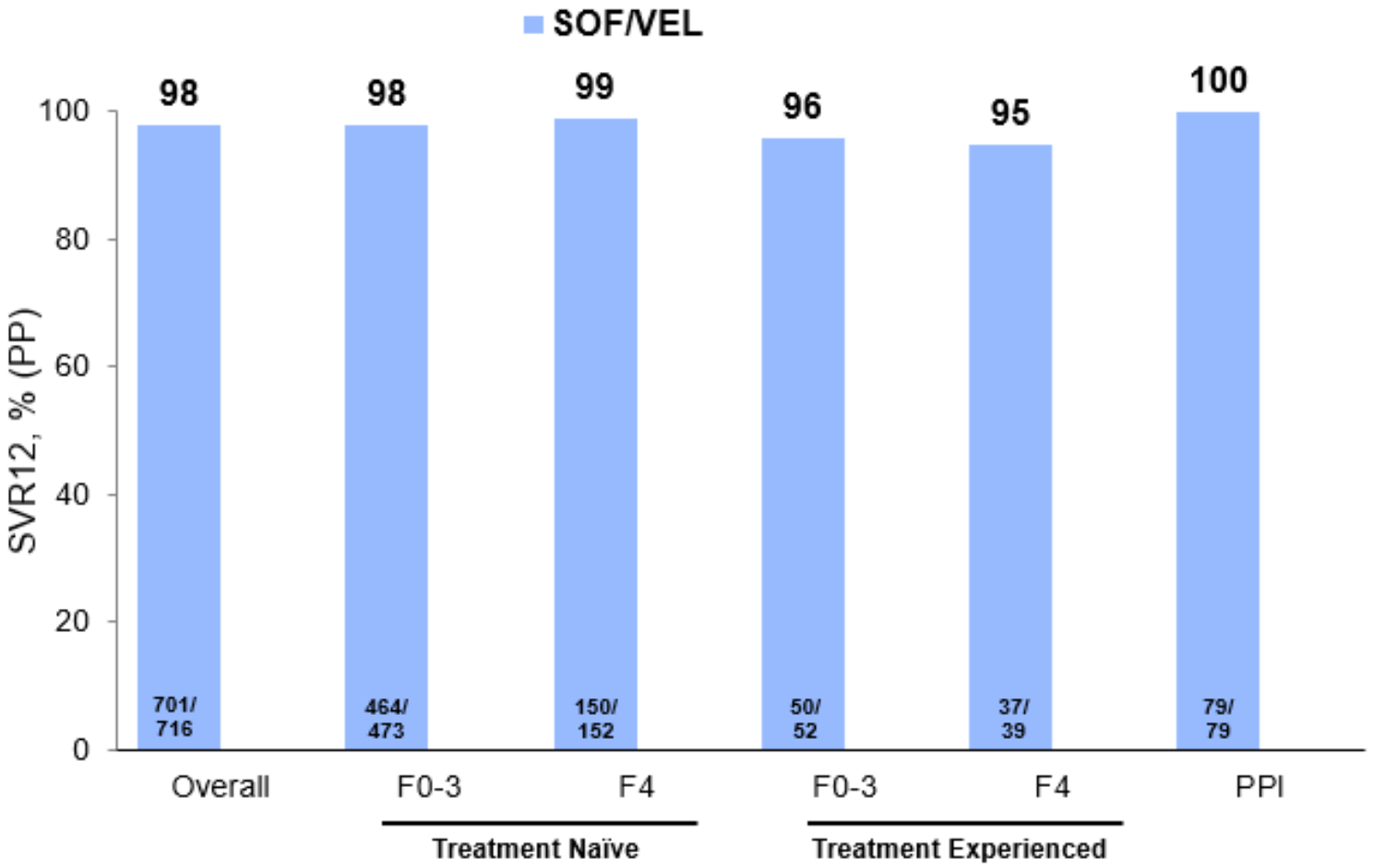


- 1 patient had virologic relapse; 1 patients had reinfection post treatment

*Includes unknown GTs and mixed GT populations (GT1 + GT2 and GT1 + GT3)
AE, adverse event; d/c, discontinuation; ITT, intent-to-treat; mITT, modified intent-to-treat.

Wiegand J, AASLD 2018 Poster Presentation #611.

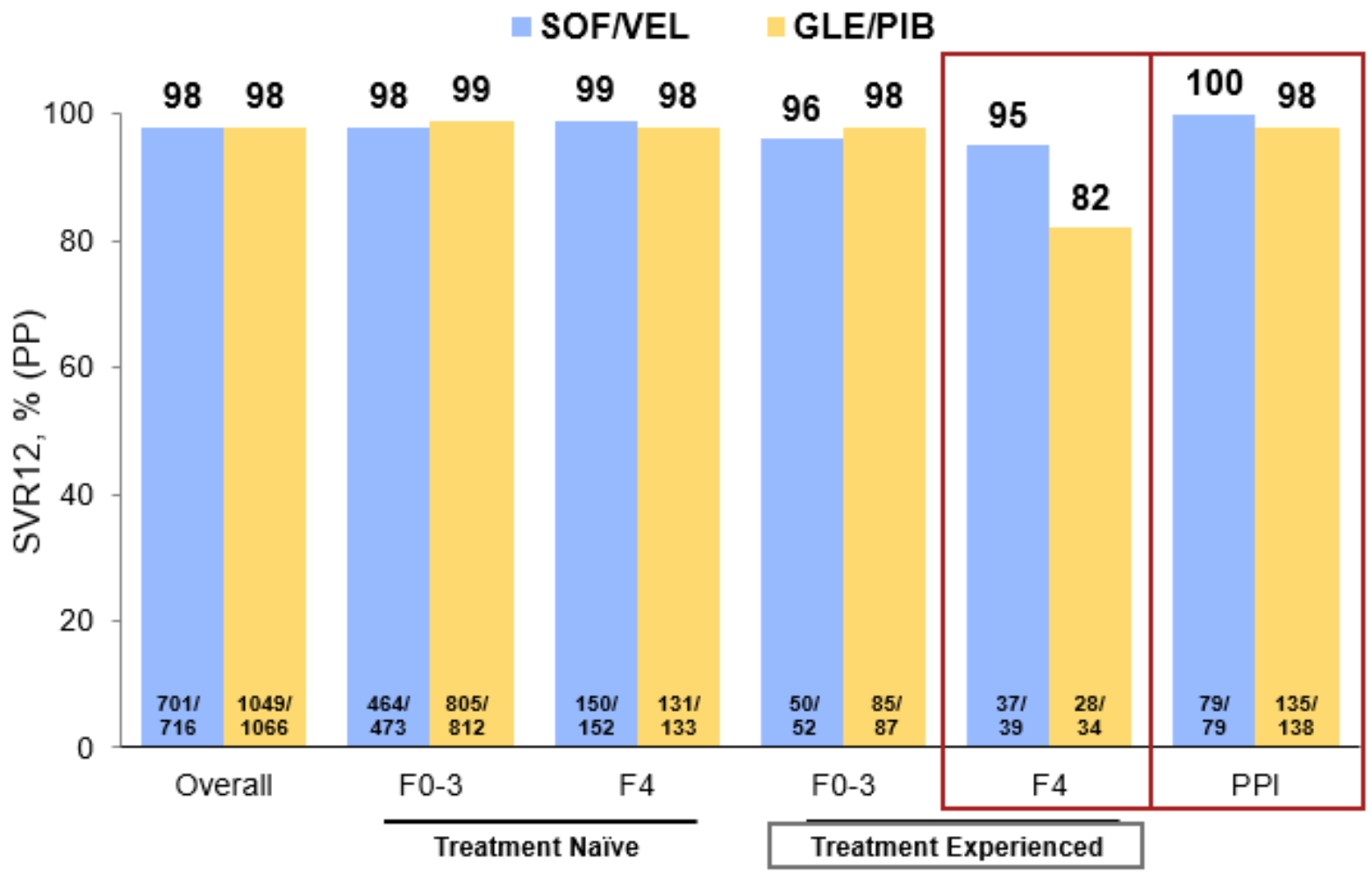
TRIO Real World Cohorts for HCV Patients with GT 1-6



LDV/SOF data is excluded from this slide

Curry, AASLD 2018, 678

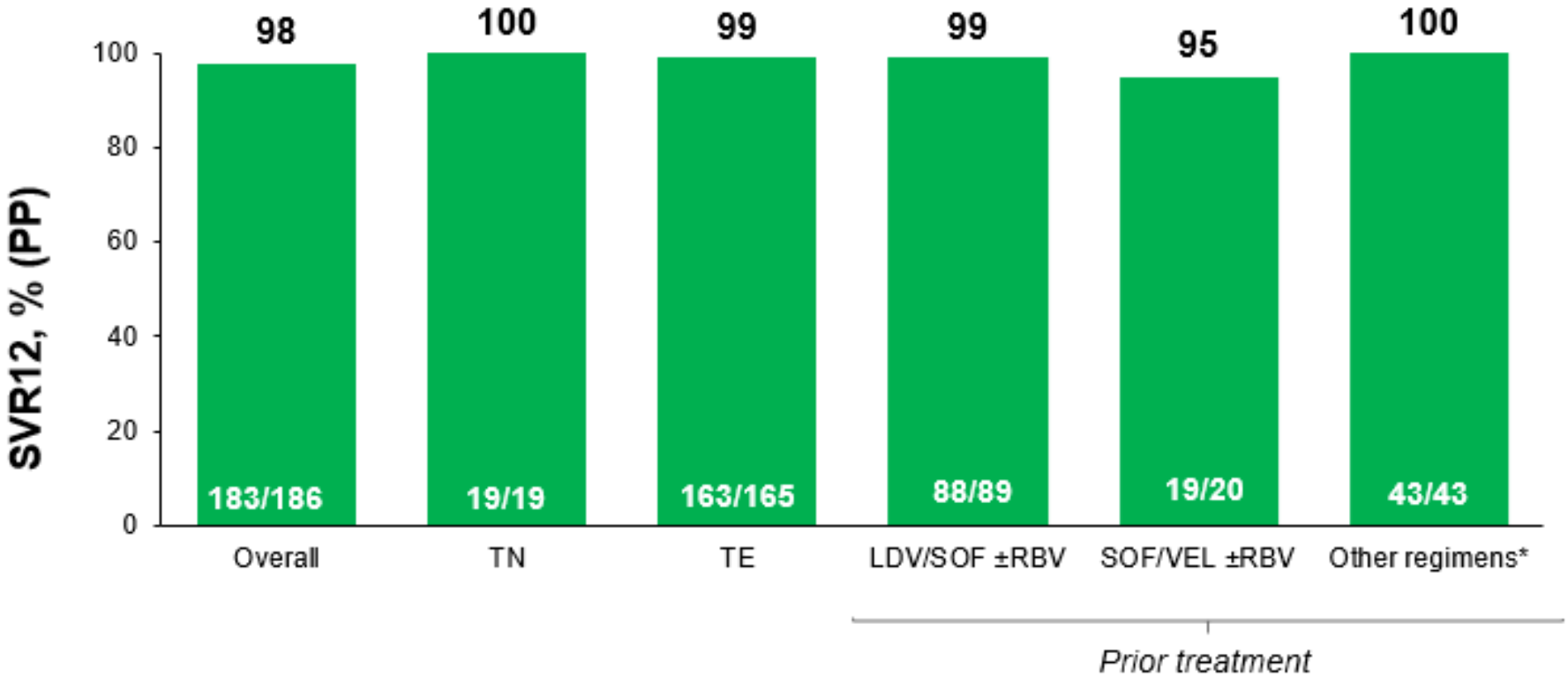
TRIO Real World Data for GT 1-6



LDV/SOF data is excluded from this slide

Curry, AASLD 2018, 678

TRIO Real World Data for SOF-VEL-VOX

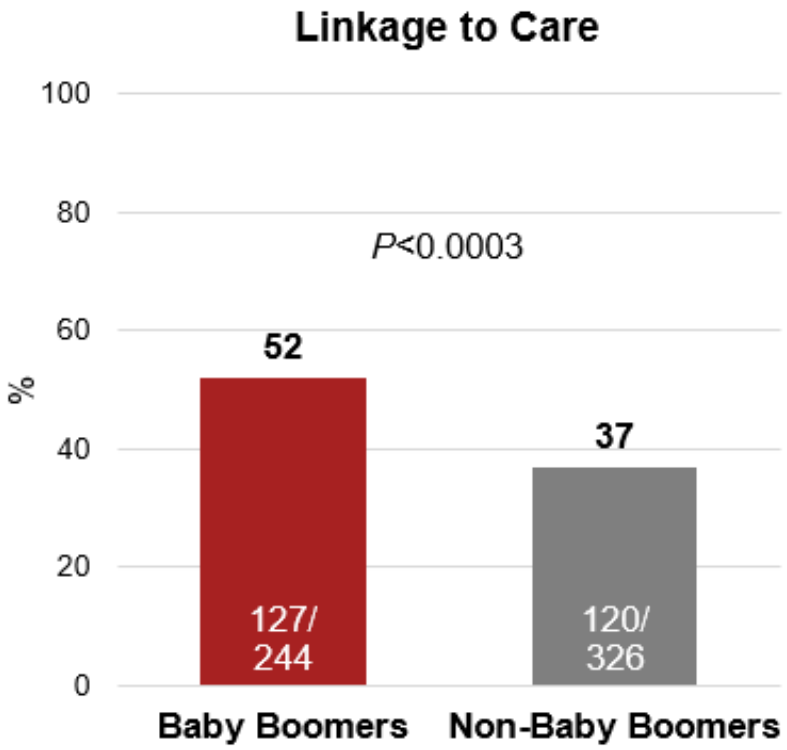


SOF/VEL/VOX for 12 weeks resulted in high real world efficacy, irrespective of genotype and prior treatment regimen

Bacon AASLD 2018, #706

Linkage to Care

Differences in linkage to care with HCV specialists at health center (2016 – 1Q/2017)



Multivariate Analysis for Association with Linkage

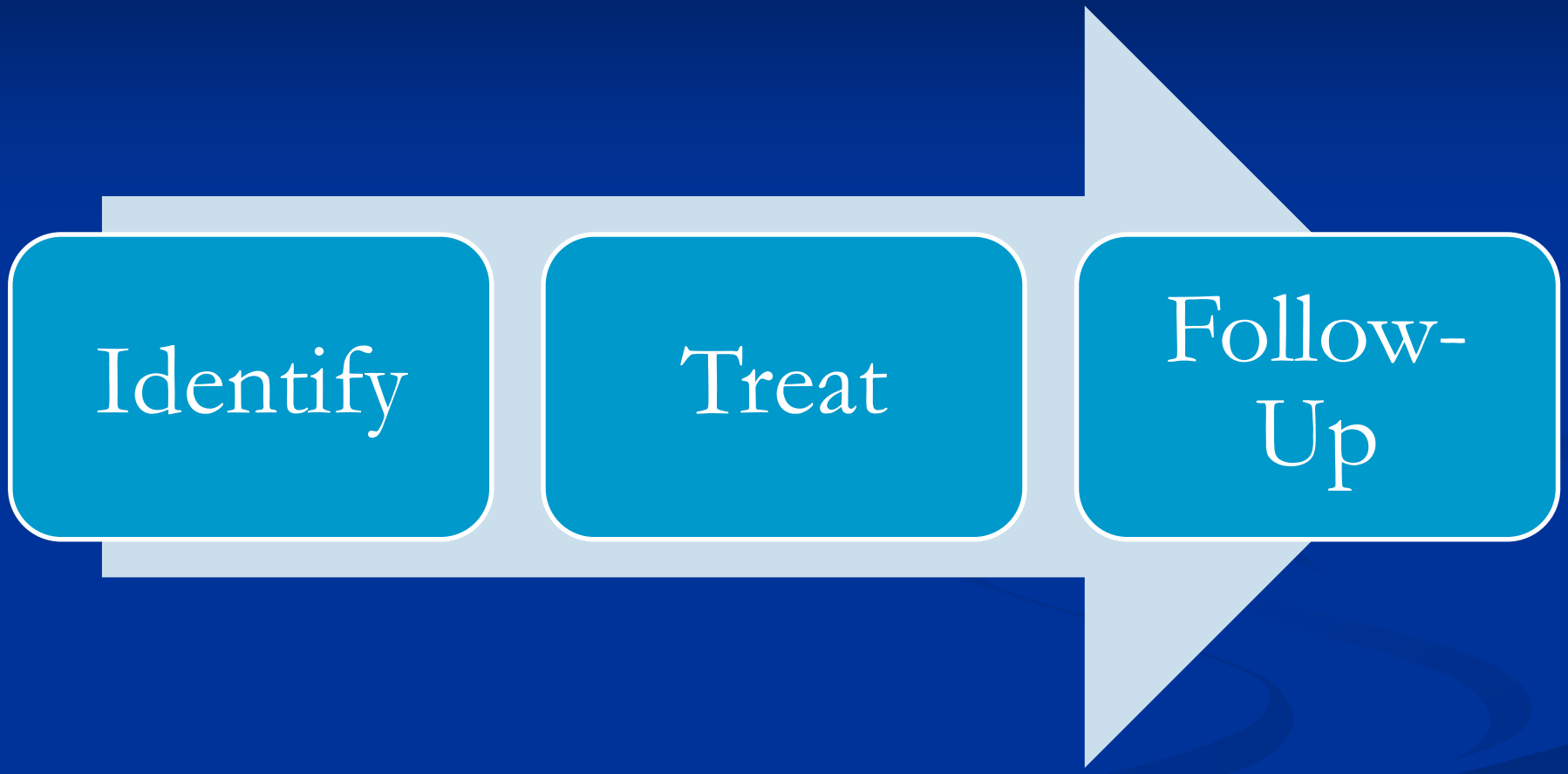
	aOR (95% CI)	*p*-value
Birth cohort	2.3 (1.4–3.7)	0.0008
Clinical Site		
Outpatient	1.0	Ref
ED	0.7 (0.3–1.4)	0.3162
Inpatient	0.5 (0.3–0.8)	0.009
Jail	0.4 (0.04–3.9)	0.430
Risk Factor		
Other	1.0	Ref
Active IVDU	0.4 (0.2–0.7)	0.0005
Remote IVDU	1.0 (0.6–1.7)	0.9364
Psychiatric Illness	0.8 (0.5–1.1)	0.1831

Overall, only 43% of patients were linked to care with HCV specialists

METROHEALTH CLEVELAND, OH

Pham, AASLD 2017, Oral 23

CONCLUSIONS



Questions?