
HCC
connect
POWERED BY COR2ED

IS THERE A DIFFERENCE IN LIVER CANCER RATES IN PATIENTS WHO RECEIVE TREATMENT FOR HEPATITIS?

Dr. Sammy Saab
David Geffen School of Medicine,
Los Angeles, USA

April 2018

DISCLAIMER

HCC connect
POWERED BY COR2ED

Please note:

The views expressed within this presentation are the personal opinion of the author. They do not necessarily represent the views of the author's academic institution or the rest of the HCC CONNECT group

HEPATOCELLULAR CARCINOMA (HCC)

HCC connect
POWERED BY COR2ED

- Fifth most common solid tumor in the world[1]
  - Second most common cause of death from cancer worldwide[2]
  - Estimated to be responsible for nearly 746,000 deaths in 2012[2]

- Hepatobiliary cancer is the fifth most common cause of cancer-related death in the United States among males[3]
  - In 2017, it was estimated that there would be 40,710 new cases of liver and intrahepatic bile duct cancer and an estimated 28,920 people would die of this disease[4]

1. Thomas MB et al. *J Clin Oncol* 2005; 23: 2892-2898; 2. GLOBOCAN 2012 http://www.iarc.fr 3. Siegel RL. *CA Cancer J Clin* 2016; 66: 7-30; 4. National Institute of Health https://seer.cancer.gov/statfacts/html/livibd.html

CIRRHOTIC LIVER DISEASE: MAJOR RISK FACTOR FOR HCC

HCC connect
POWERED BY COR2ED

Major risk factors in the US for developing HCC[1]:

- Hepatitis C virus
  - Based on CDC estimates, at least 3.5 million persons are living with HCV infection in the United States[2]
- Hepatitis B virus
  - There are 850,000 HBV-infected persons in the US[3]
  - Non-Hispanic Asians have 10-fold greater prevalence than the general population[3]
- Alcoholic cirrhosis, NASH

1. El-Serag HB et al. *Gastroenterol* 2007; 132: 2557-76; 2. Edlin BR et al. *Hepatology* 2015 Nov; 62(5): 1353-63; 3. Roberts H. *Hepatology* 2016; 63(2): 388-97
CDC, Centers for Disease Control and Prevention; HCC, HepatoCellular Carcinoma; HBV, Hepatitis B Virus; NASH, NonAlcoholic SteatoHepatitis

NATURAL HISTORY OF COMPENSATED HCV CIRRHOSIS: A 17-YEAR COHORT STUDY (N=214)

HCC connect
POWERED BY COR2ED

Complication	Total %	Annual rate %
Death	35	4.0
HCC*	32	3.9
Ascites	23	2.9
Jaundice	17	2.0
GI bleed	6	0.7
Encephalopathy	1	0.1

*HCC was the main cause of death (44% of deaths) and the first complication to develop (27% of patients)

Sangiovanni A et al. *Hepatology* 2006; 43: 1303-1310

HCV, Hepatitis C Virus; HCC, HepatoCellular Carcinoma; GI, GastroIntestinal

POOR PROGNOSIS FOR PATIENTS WITH HCC

HCC connect
POWERED BY COR2ED

- Usually slow growing tumor with long latency[1]
  - Usually diagnosed at advanced stage

- Limited medical therapies[1]
  - Surgical resection, liver transplantation, local ablation
  - Systemic chemotherapy

5-year survival rates by stage at diagnosis, 1996-2002[2]				
Liver cancer	All stages	Local	Regional	Distant
	10.5%	21.9%	7.2%	3.3%

1. Thomas MB et al. *J Clin Oncol* 2005; 23: 2892-2898; 2. American Cancer Society. Cancer Facts and Figures 2007. Atlanta: American Cancer Society; 2007
HCC, HepatoCellular Carcinoma

EARLY DIAGNOSIS OF HCC

HCC connect
POWERED BY COR2ED

- Surveillance with ultrasound every 6 months for detection of early HCC is recommended in cirrhotic patients and other specific risk groups

- Accurate diagnosis of small liver nodules is of paramount importance
  - Dynamic radiological behavior (contrast up-take in arterial phase, rapid wash out in venous/late phase) utilized in early HCC in cirrhotic patients
  - Pathological diagnosis of small nodules is challenging even in expert hands — tissue markers might standardize diagnosis

Llovet JM et al. *J Hepatol* 2008; 48: S20-37
HCC, HepatoCellular Carcinoma

TARGETED SURVEILLANCE FOR HCC

HCC connect
POWERED BY COR2ED

Hepatitis B carriers

- Asian males ⩾ age 40
- Asian females ⩾ age 50
- Patients with cirrhosis
- Family history of HCC
- Africans > age 20
- High HBV DNA

Non-hepatitis B cirrhosis

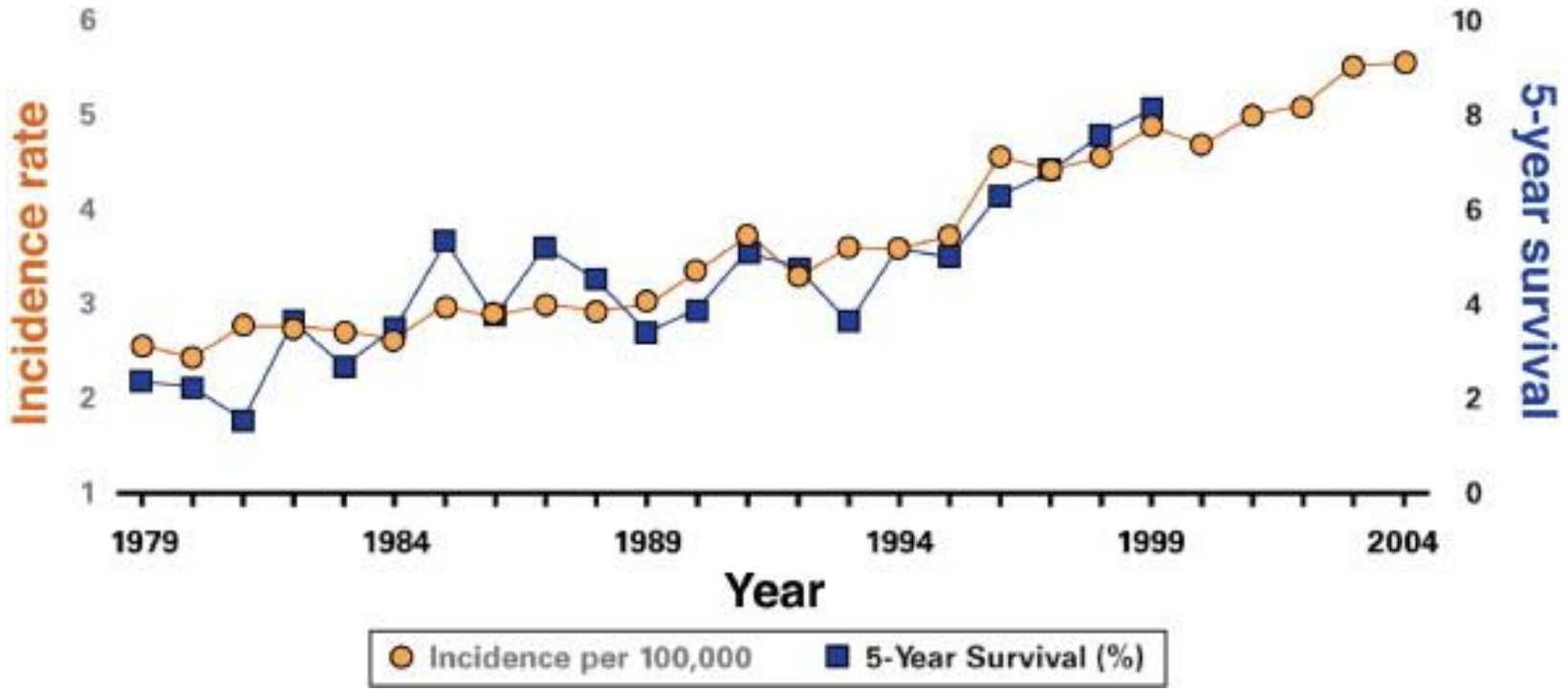
- Hepatitis C
- Alcoholic cirrhosis
- Genetic hemochromatosis
- Primary biliary cirrhosis
- Other (? efficacy)
  - A1AT deficiency
  - NAFLD
  - Autoimmune hepatitis

- Surveillance for HCC should be with ultrasound at 6 to 12 month intervals; AFP is not adequate

Bruix J et al. *Hepatology* 2005; 42: 1208-36

HCC, HepatoCellular Carcinoma; HBV, Hepatitis B Virus; DNA, deoxyribonucleic acid; A1AT, alpha-1-antitrypsin; NAFLD, NonAlcoholic Fatty Liver Disease; AFP, Alpha-FetoProtein

PRIMARY LIVER CANCER: AGE-ADJUSTED INCIDENCE RATES AND 5-YEAR SURVIVAL RATES, 1979–2004

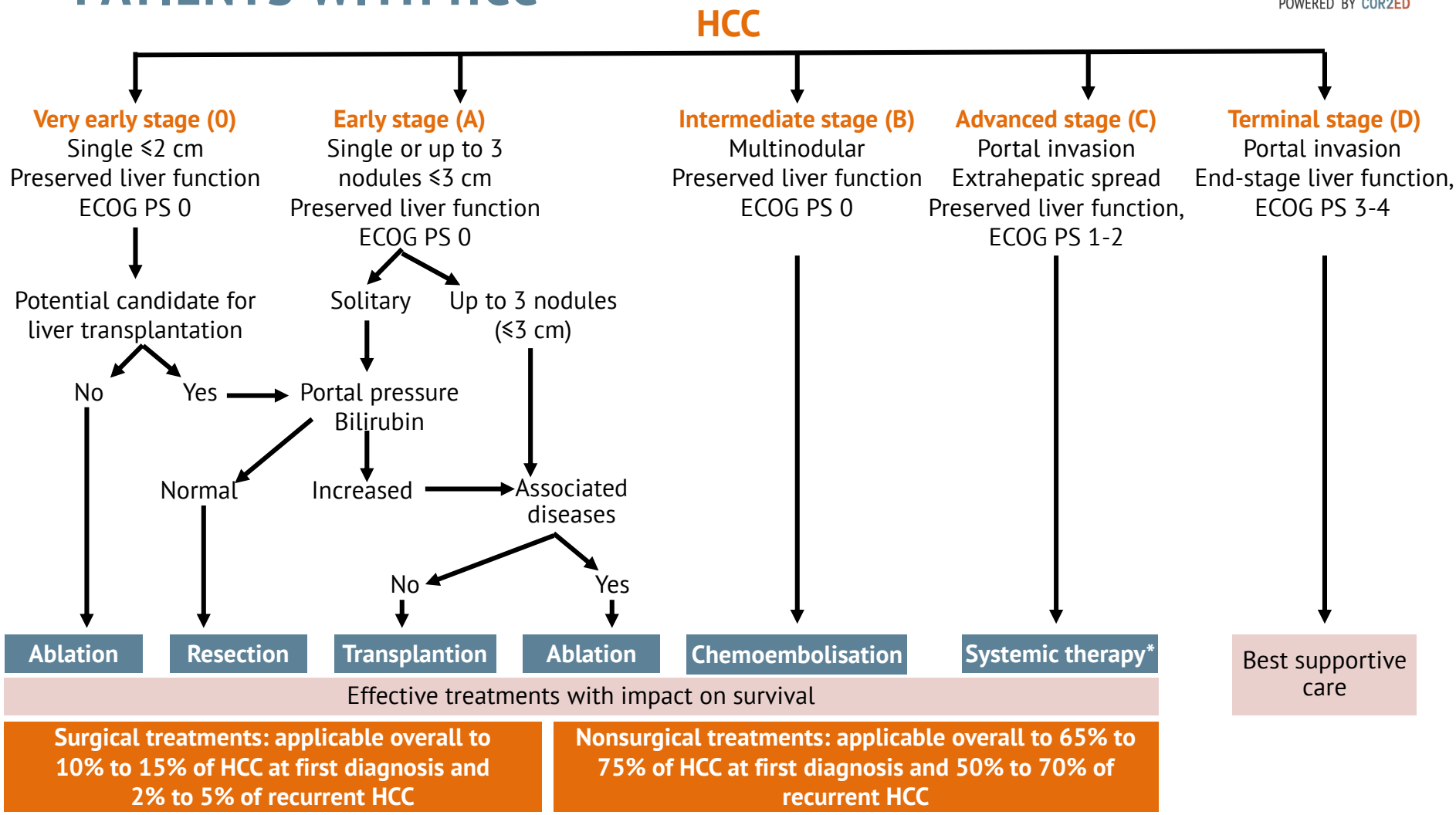


(Source: Surveillance, Epidemiology, and End Results [SEER] Program.)

Everhart JE et al. *Gastroenterol* 2009; 136: 1134-44

STAGING STRATEGY AND TREATMENT FOR PATIENTS WITH HCC

HCC connect
POWERED BY COR2ED



*Currently, sorafenib followed by regorafenib has been shown to be effective. Lenvatinib has been shown to be non- inferior to sorafenib, but no 2nd-line option after lenvatinib has been explored. HCC, HepatoCellular Carcinoma; PEI/RF, Percutaneous Ethanol Injection/RadioFrequency Ablation; PST, Performance Status Test; RCT, Randomized Clinical Rrial; TACE, TransCatheter Arterial Chemoembolization. Forner A et al. *Lancet* 2018; January 4, 2018 http://dx.doi.org/10.1016/S0140-6736(18)30010-2

HCC SCREENING AND SURVEILLANCE: IT'S NOT WORKING

HCC connect
POWERED BY COR2ED

- Rates of surveillance remain dismally low
  - Less than 30% nationwide in patients with cirrhosis
  - Better among patients followed by specialists, but only 20-40% of cirrhotics are followed by GI/Hepatology

- Most liver cancers are still diagnosed at advanced stage

- Diagnosis of cirrhosis is poor: nearly 40% of those diagnosed with HCC did not have previously recognized liver disease

Singal AG et al. *Clin Gastroenterol Hepatol* 2013; 11: 472-477
HCC, HepatoCellular Carcinoma; GI, GastroIntestinal

WHY THE LACK OF ADHERENCE TO SURVEILLANCE?

HCC connect
POWERED BY COR2ED

Among Providers?[1,2]

- Inadequate knowledge
- Provider forgetfulness
- Time constraints in clinic
- Provider fatigue
- Lack of financial incentive
- Competing health problems
- Mistrust in ultrasound imaging
- Patient fatigue

Among Patients?[3]

- This doesn't seem to be a big problem right now – >95% of patients complete HCC screening once ordered by their provider
- Lower screening rates associated with younger age, minority race, lower socioeconomic status
  - Is this due to lack of access?
  - Non-adherence?

1. Orlandi MA. *Prev Med.* 1987; 16: 119-130; 2. Pommerenke FA et al. *J Fam Pract* 1992; 34: 92-7; 3. Del Poggio P et al. *Clin Gastroenterol Hepatol.* 2014; 12: 1927-1933.e2

KNOW WHO TO SCREEN AND SURVEY WHO IS AT RISK?

HCC connect
POWERED BY COR2ED

High-risk groups for HCC in whom surveillance might be indicated.*	
Cirrhosis	**HCC risk per year**
• Hepatitis C (HCV)	2–7%
• Hepatitis B (HBV)	3–5%
• Genetic hemochromatosis	NA
• Primary biliary cirrhosis (PBC)	2–3%
• Non-alcoholic steatohepatitis (NASH)	NA
• Alpha-1 antitrypsin deficiency, autoimmune hepatitis	NA
HBV without cirrhosis	
• Asian males >40 years of age	0.4–0.6
• Asian females >50 years of age	0.3–0.6
• Africans >20 years of age	NA
• Family history of HCC	NA

*Estimates of the annual HCC risk are also provided where reliable data are available

El-Serag HB, et al. *Ther Adv Gastroenterol* 2011; 4: 5-10
NA, Not Available

SURVEILLANCE GUIDELINES FOR HIGH-RISK PATIENTS

HCC connect
POWERED BY COR2ED

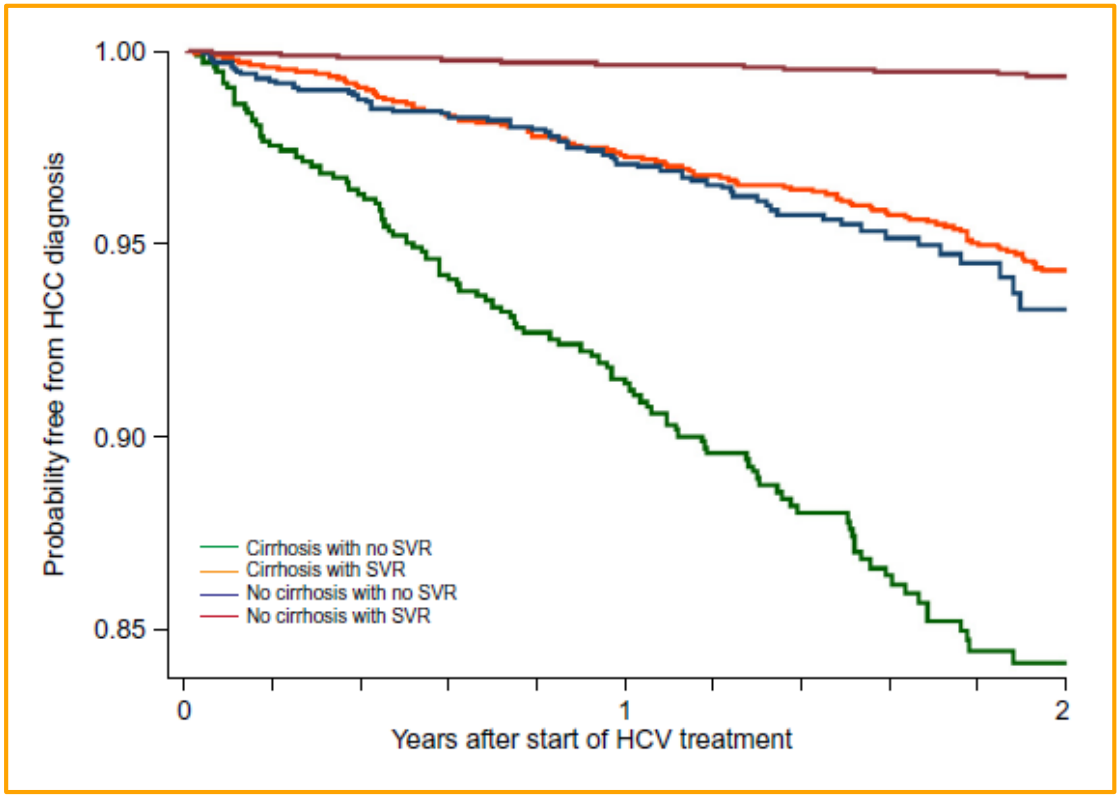
Society/institution	Guidelines
AASLD[1] American Association for the Study of Liver Diseases	US every 6 months
EASL[2] European Association for the Study of the Liver	US every 6 months
APASL[3] Asian-Pacific Association for the Study of the Liver	AFP + US every 6 months
NCCN[4] National Comprehensive Cancer Network	US +/- AFP every 6 months
VA[5] United States Department of Veterans Affairs	AFP + US every 6-12 months

1. Heimbach et al. *Hepatology* 2018; 67(1): 358-380; 2. EASL, EORTC. *J Hepatol* 2012; 56: 908-943; 3. Omata M et al. *Hepatol Int* 2017; 11(4): 317-370; 4. National Comprehensive Cancer Network . Available at: https://www.nccn.org/professionals/physician_gls/pdf/hepatobiliary.pdf 5. US Dept of Veterans Affairs. Available at: http://www.hepatitis.va.gov/pdf/2009HCC-guidelines.pdf. Accessed September 23, 2015.
AFP, alpha-fetoprotein; US, ultrasound

KAPLAN-MEIER CURVES OF SURVIVAL FREE OF HCC BY CIRRHOSIS AND SVR STATUS AFTER DAA-ONLY ANTIVIRAL TREATMENT

HCC connect
POWERED BY COR2ED

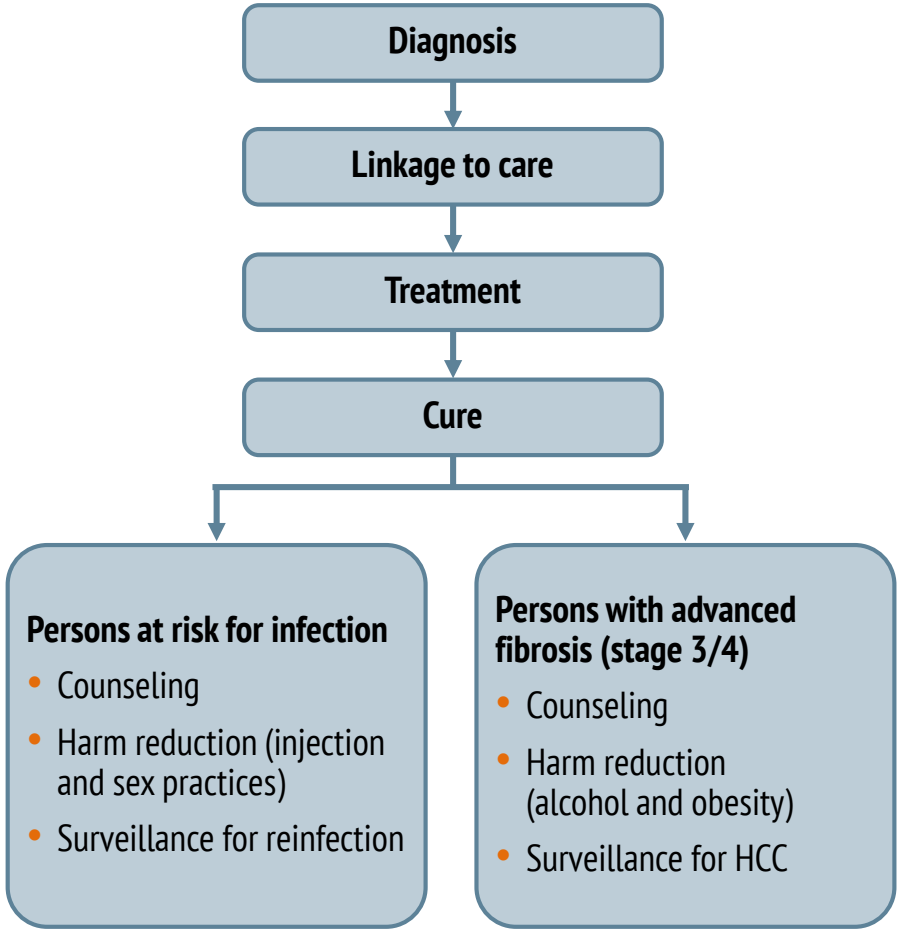
- DAA-induced SVR is associated with a 71% reduction in HCC risk
- SVR is associated with a similar reduction in HCC risk no matter what regimen is used to achieve it
- Treatment with DAAs is not associated with increased HCC risk compared with interferon



Ioannou GN et al. *J Hepatol* 2017 Sep 5 [Epub ahead of print]
HCC, HepatoCellular Carcinoma; SVR, Sustained Virologic Response; DAA, Direct-Acting Antiviral

EXTENDED HEPATITIS C CARE CONTINUUM

HCC connect
POWERED BY COR2ED



Falade-Nwulia O et al. *J Hepatol* 2017; 66: 267-269
HCC, HepatoCellular Carcinoma

HCC CONNECT
Bodenackerstrasse 17
4103 Bottmingen
SWITZERLAND

Dr. Antoine Lacombe
Pharm D, MBA
Phone: +41 79 529 42 79
antoine.lacombe@cor2ed.co

Dr. Froukje Sosef
MD
Phone: +31 6 2324 3636
froukje.sosef@cor2ed.com