3rd Paris NASH Symposium

French-US Meetings

July 6 & 7, 2017

Institut Pasteur - Paris

Organized by

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AFEF Société Française d'Hépatologie

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3rd Paris Nash Symposium, July 6 & 7 2017

Is NASH responsible for disease progression after SVR in subjects with HCV?

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Circulation, metabolism, nutrition

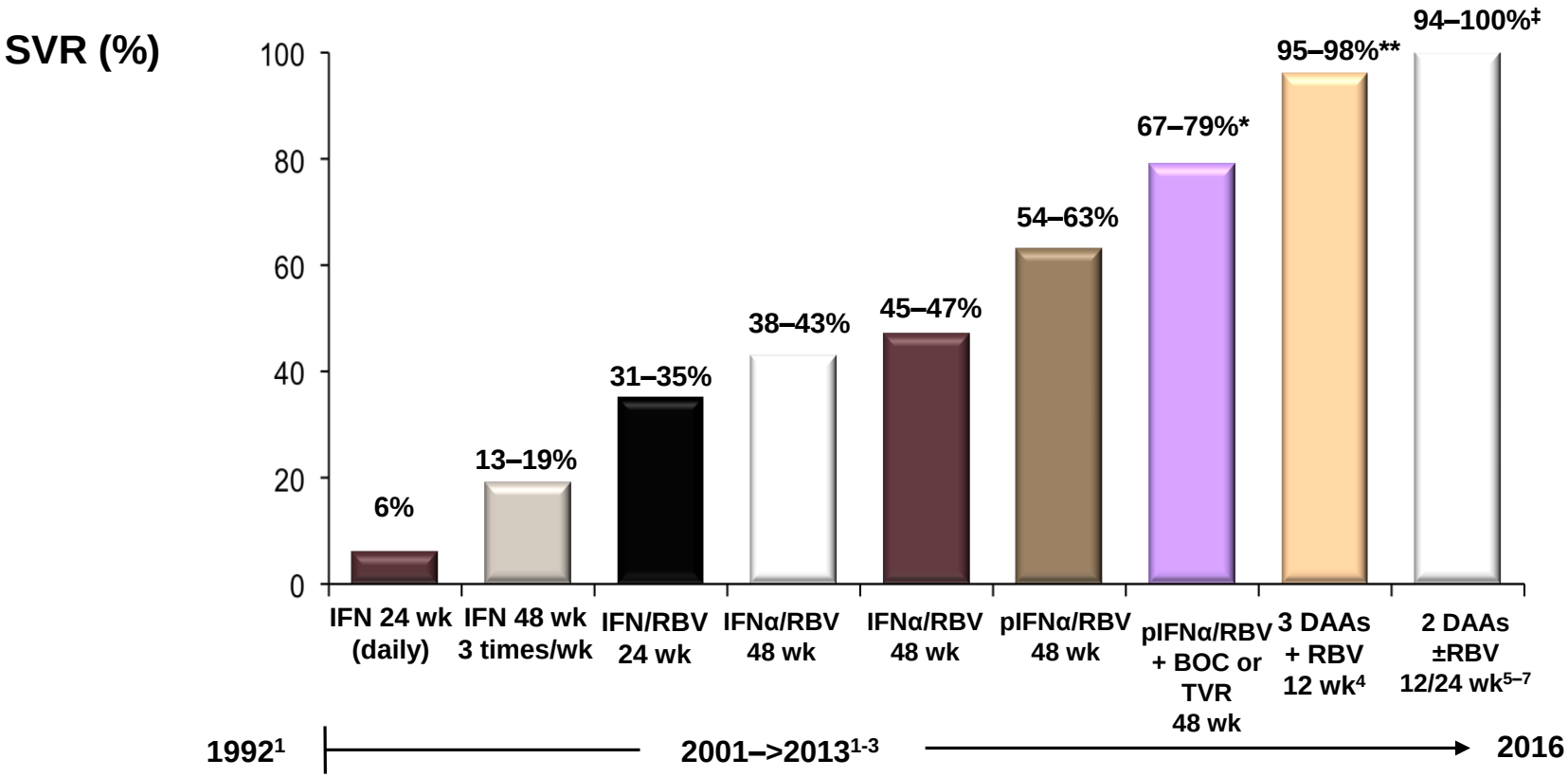
Inserm

French Institute of Health and Medical Research

Disclosures

- Consulting, advisory committees or review panel
  - Abbvie, Allergan, Bristol-Myers Squibb, Gilead, Intercept, Janssen, Merck Sharp & Dohme
- Speaking and teaching
  - Abbvie, Aptalis, Bristol-Myers Squibb, Gilead, Janssen, Merck Sharp & Dohme, Roche

New all-oral regimens are transforming the HCV treatment landscape



*In patients with HCV genotype 1 only; ** In treatment-naïve patients; ‡Includes treatment-naïve and -experienced patients

BOC, boceprevir; IFN, interferon; RBV, ribavirin; SVR, sustained virologic response; TVR, telaprevir

1. Adapted from Manns MP, et al. *Gut* 2006;55:1350–9. 2. Tran TT. *Am J Manag Care* 2012;18(14 Suppl.):S340–9. 3. Goralczyk AD, et al. BMC *Gastroenterology* 2013;13:148. 4. Feld JJ, et al. *N Engl J Med.* 2014;370:1594-603. 5. Sulkowski M, et al. *N Engl J Med*. 2014;370(3):211-21. 6. Afdhal N, et al. *N Engl J Med.* 2014;370:1889–98. 7. Afdhal N, et al. *N Engl J Med.* 2014;370:1483-93.

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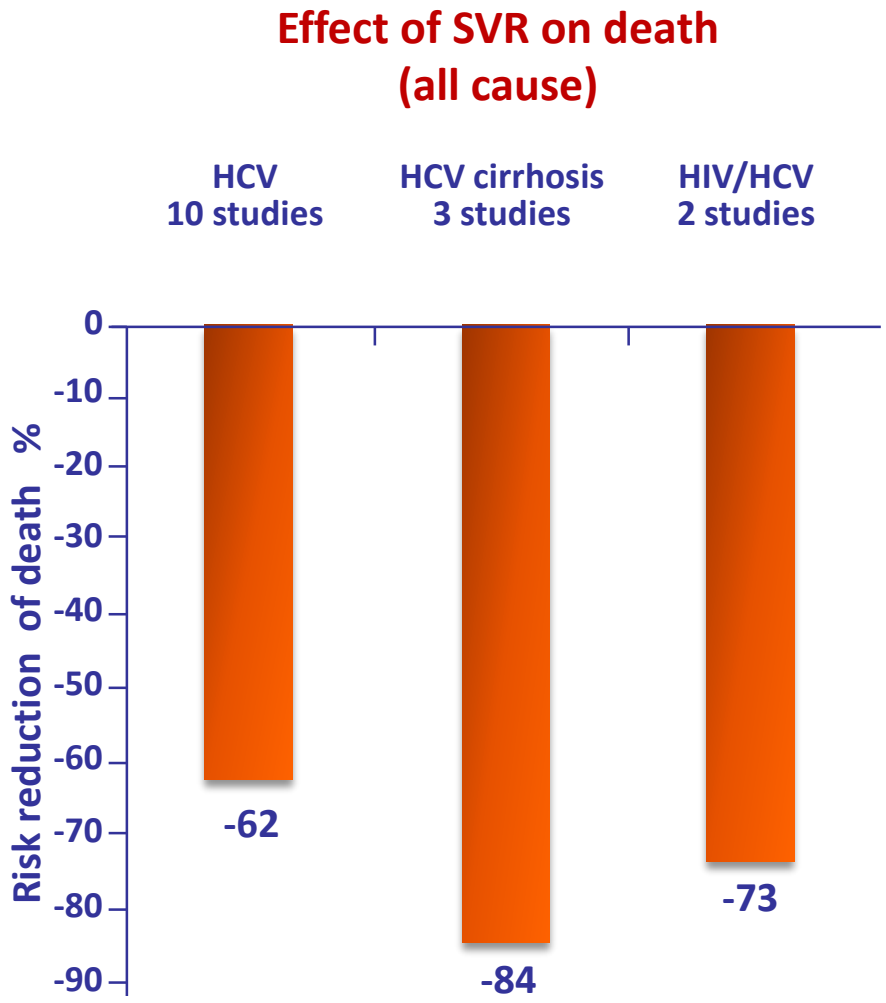
SVR is associated with improvement of survival *(meta-analysis n=34 563)*



Simmons B, et al. Clin Infec Dis 2015

Liver disease outcome in SVR patients

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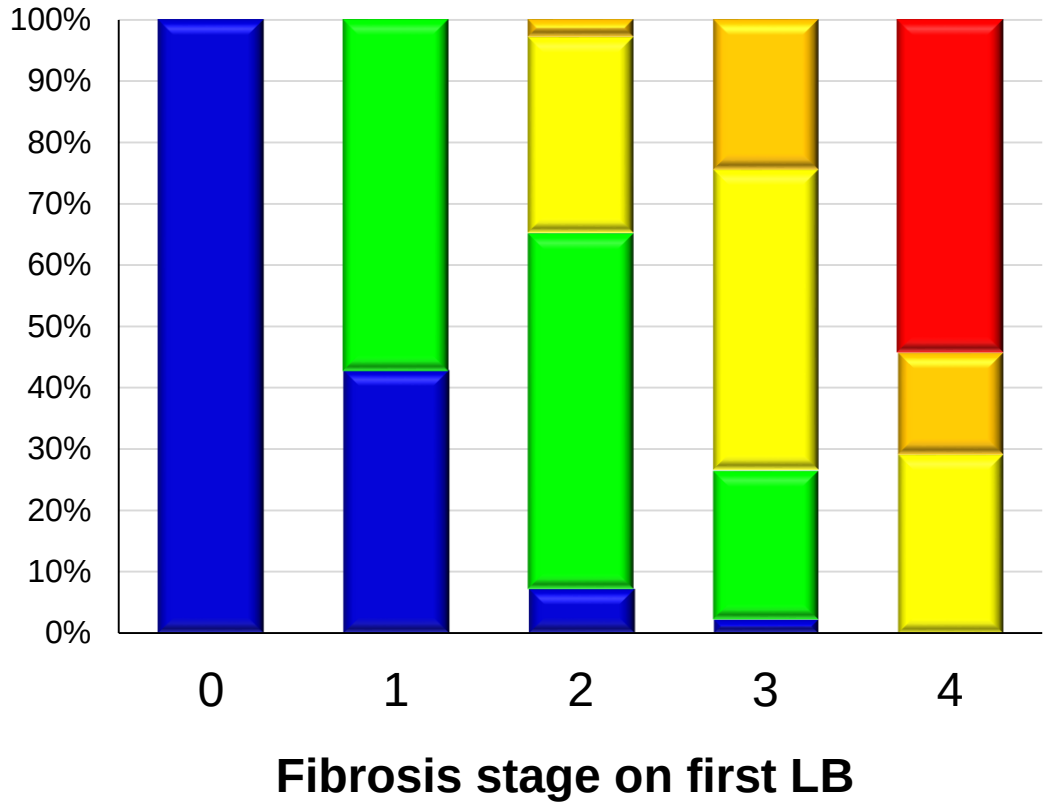
Regression of fibrosis in SVR patients is slow

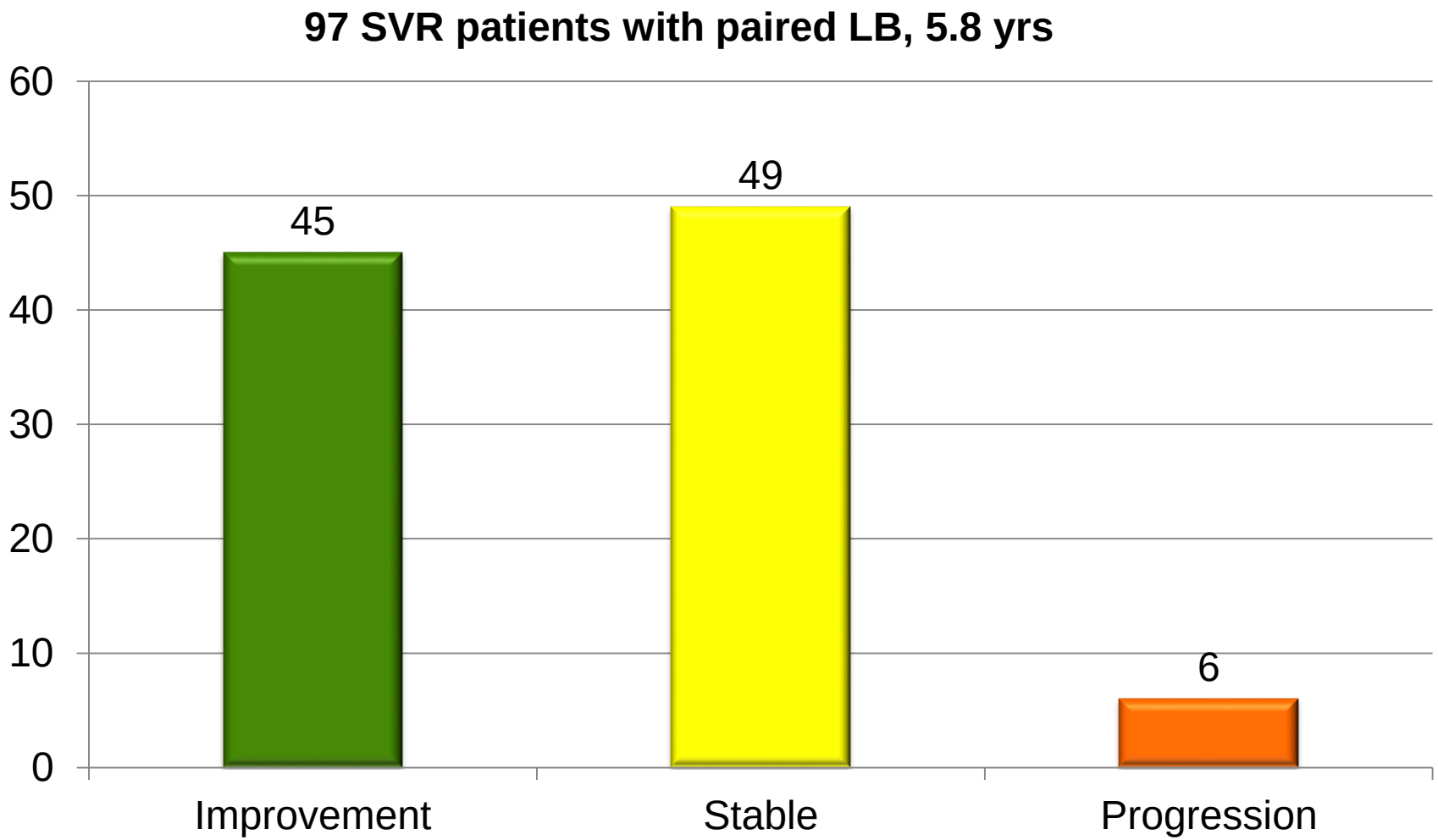
183 HCV patients with SVR
2nd liver biopsy at 3.7 yrs



Mean rate of fibrosis regression: 0.28±0.03 unit/yr

Shiratori Y, et al. Ann Intern Med 2000

Regression of fibrosis in SVR patients is slow



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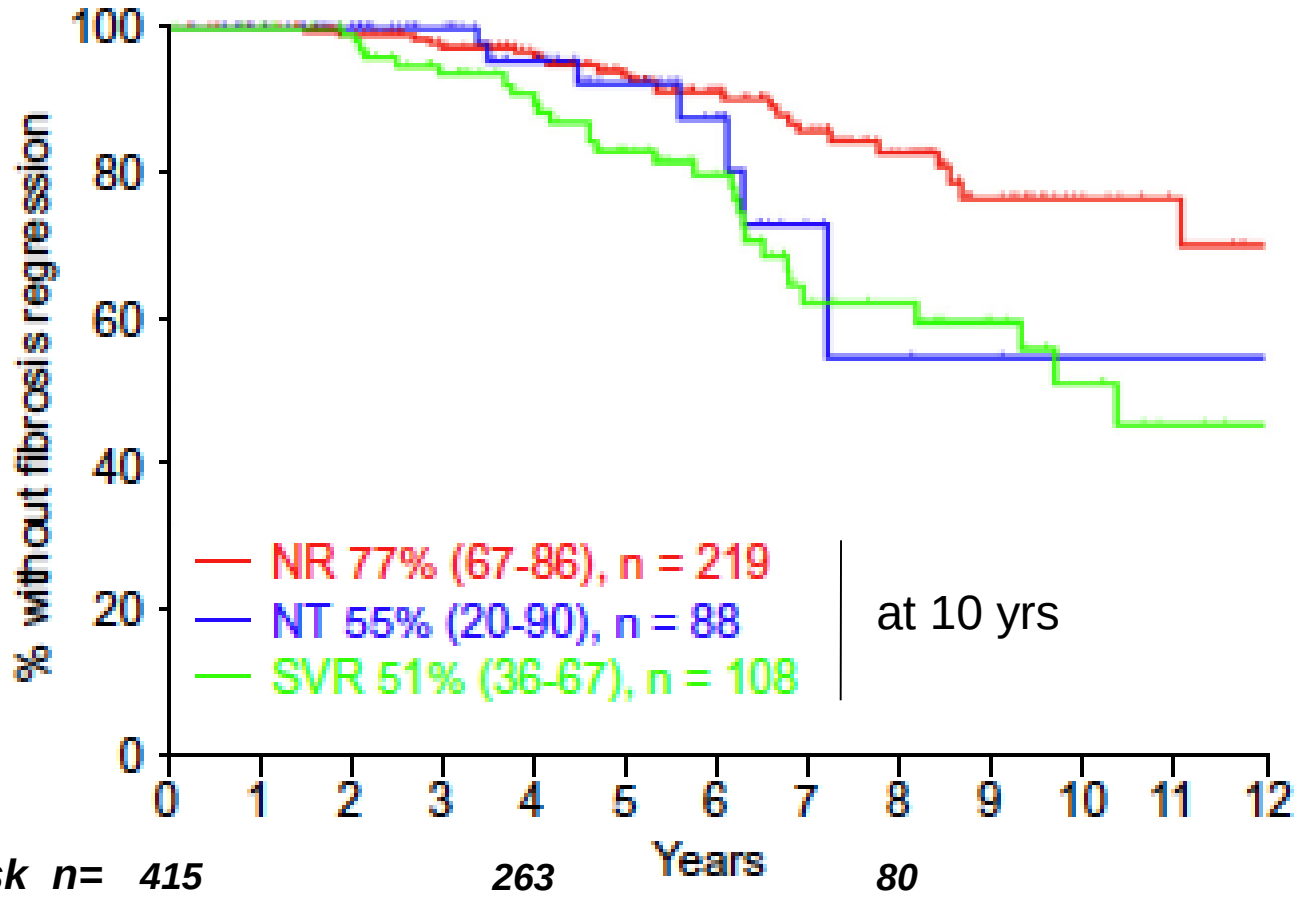
Tachi Y, et al. Hepatol Res 2015; 45: 238–46.

Long term fibrosis outcomes in SVR patients according to non invasive markers

933 HCV patients with paired Fibrotest™, median FU 5.3 yrs

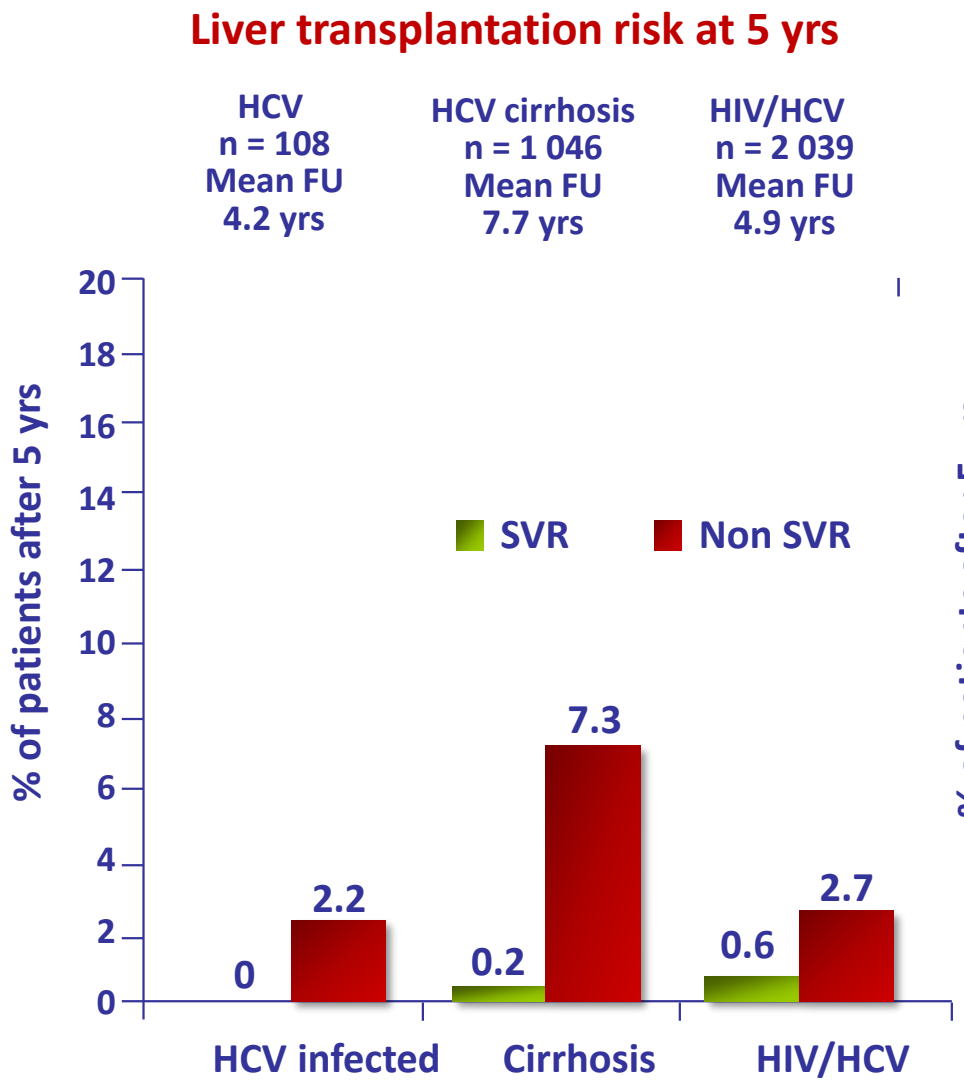
↓

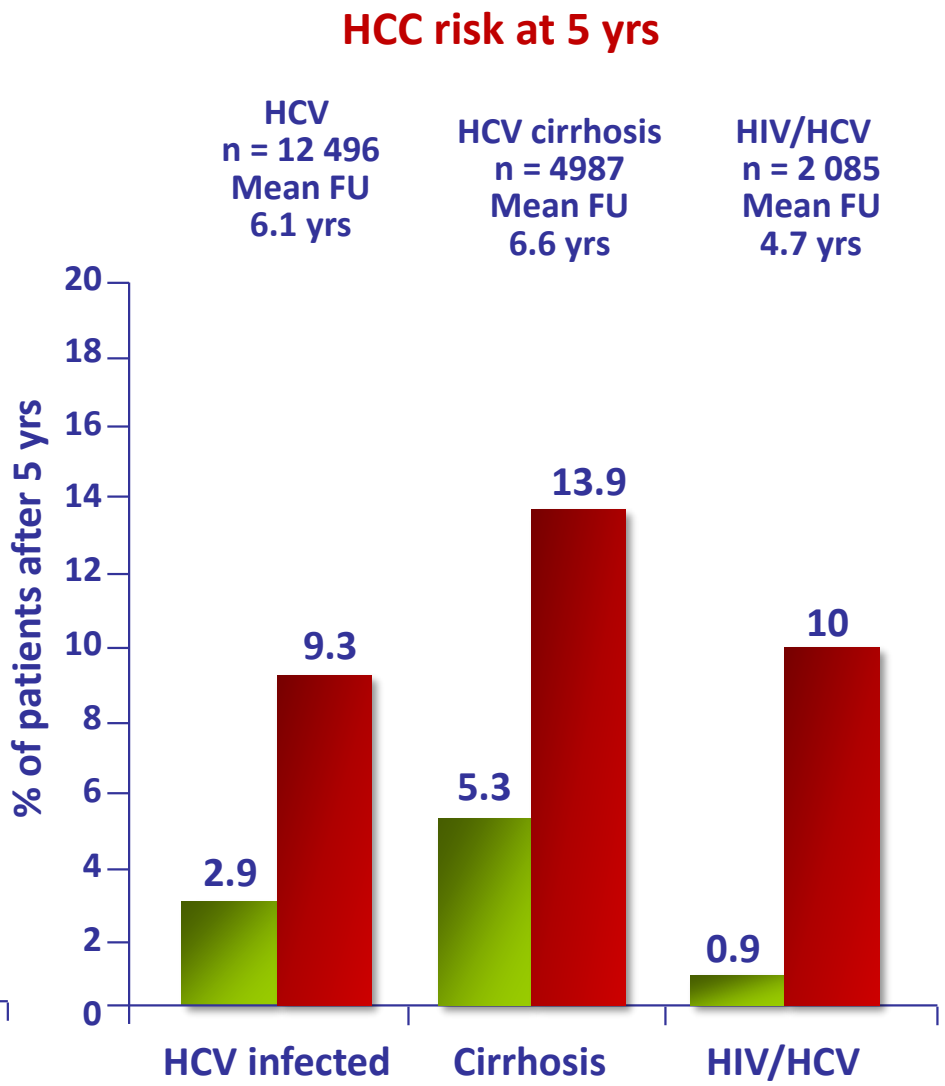
415 patients with advanced fibrosis



Poynard T, et al. J Hepatol 2013

The risk of liver transplantation or HCC according to SVR *(meta-analysis n=34 563)*

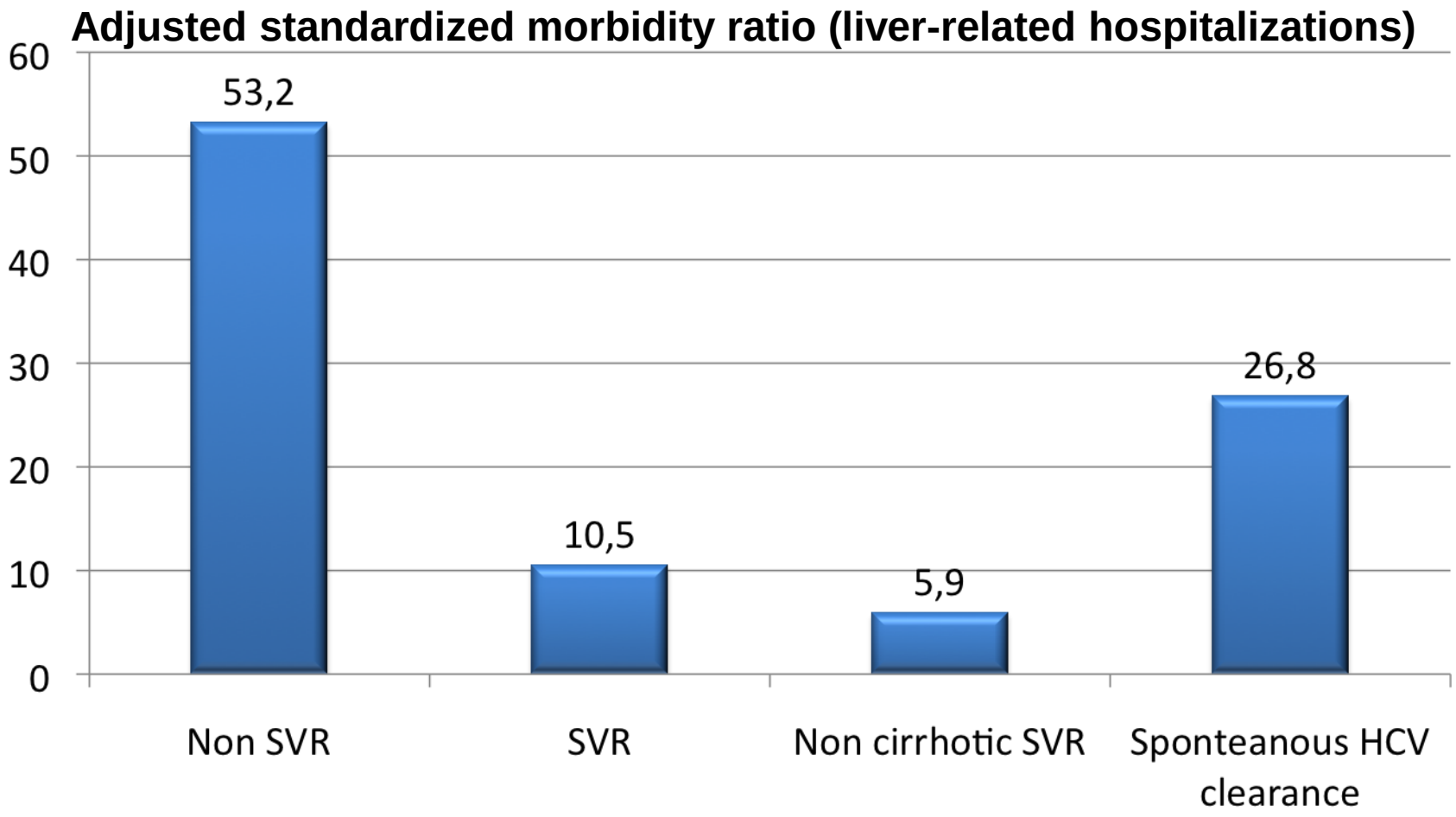




Simmons B, et al. Clin Infec Dis 2015

Excess liver-related morbidity following discharge of SVR patients

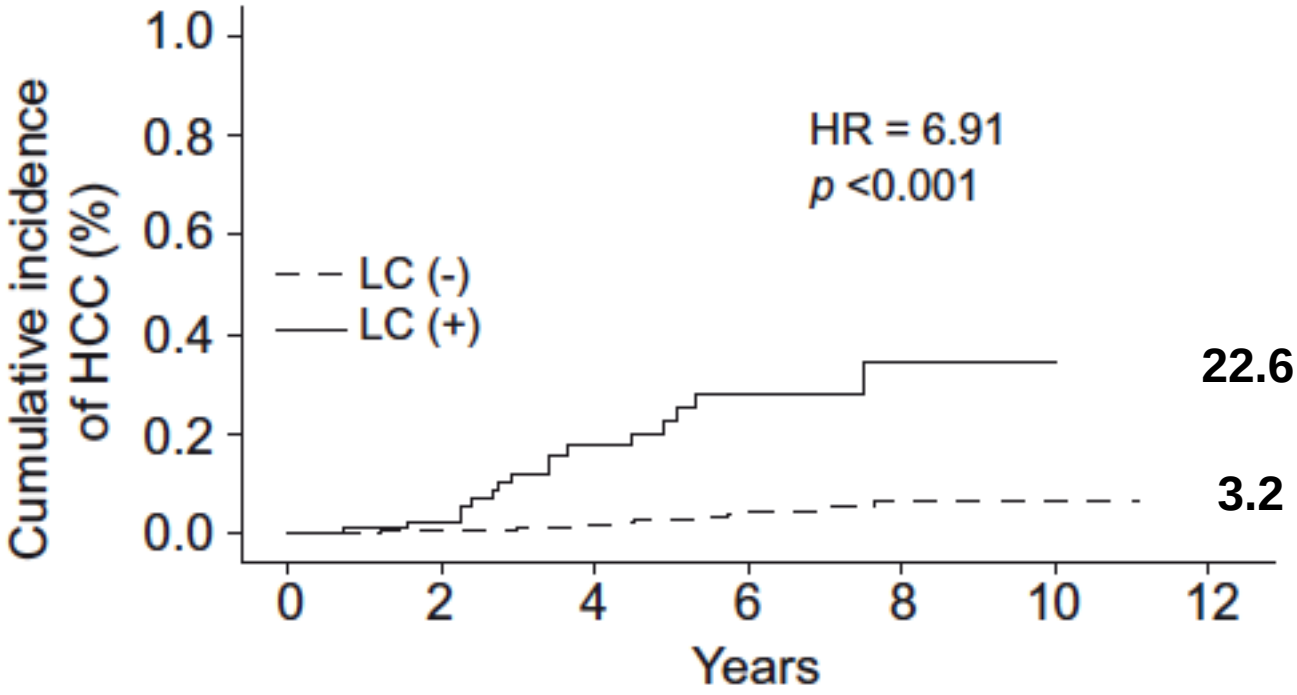
1215 HCV patients treated between 1996-2007, follow-up 5.3 yrs



Innes HA, et al. Hepatology 2011

Risk of HCC in cirrhotic and non cirrhotic patients following HCV eradication *(Far East)*

642 SVR patients followed 53 mo: 86 cirrhotics, 556 non-cirrhotics



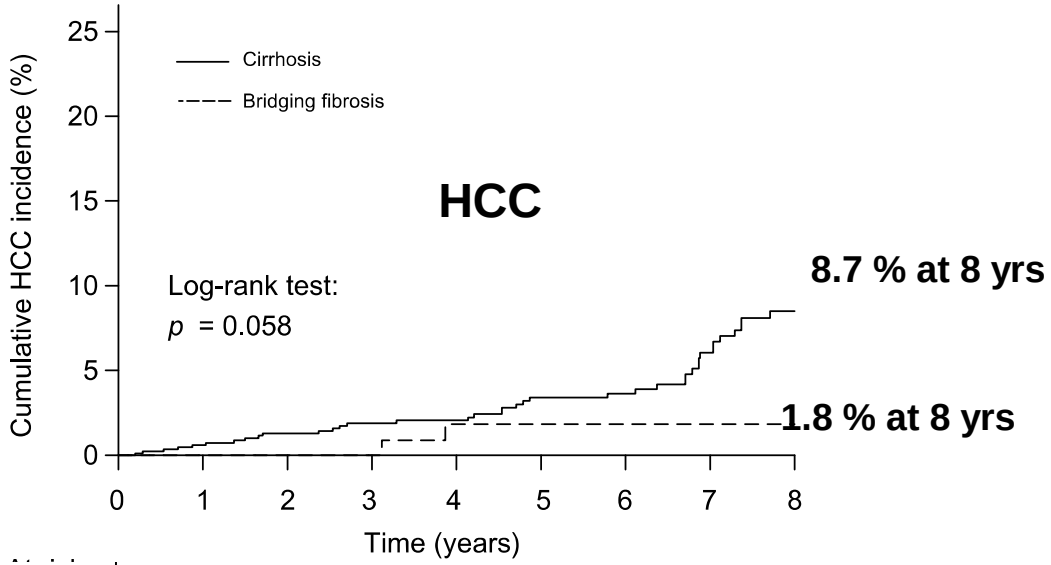
22.6 % at 5 yrs

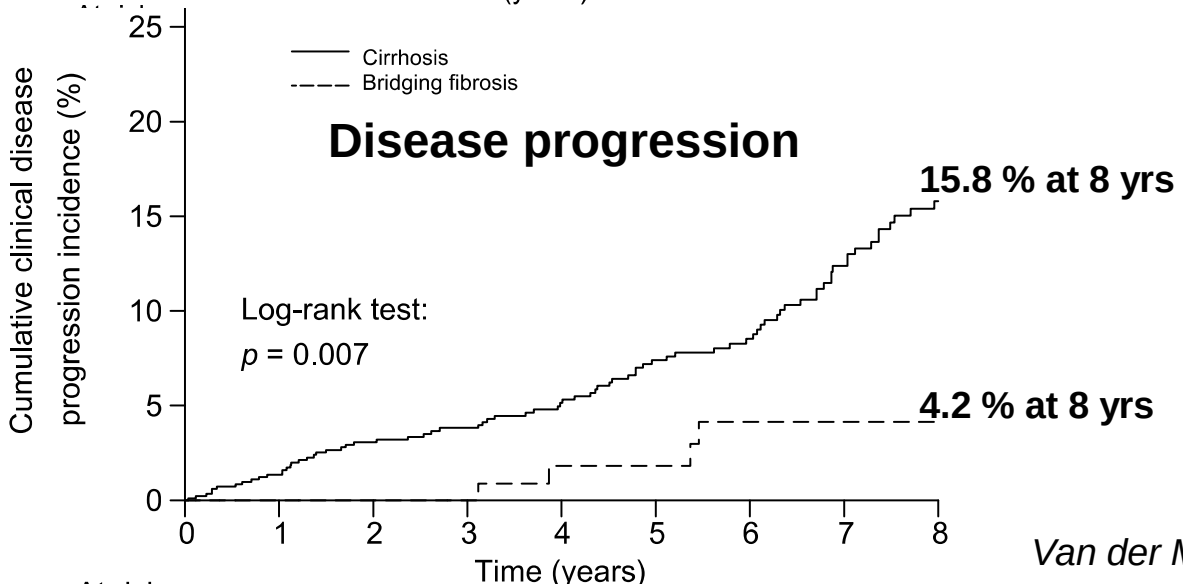
3.2 % at 5 yrs

Huang CF, et al. J Hepatol 2014

Risk of HCC in cirrhotic and bridging fibrosis patients following SVR *(western countries)*

1000 SVR patients followed 5.7 yrs: 842 cirrhotics,158 bridging fibrosis





Van der Meer AJ, et al. J Hepatol 2016

Predictors of liver disease progression in SVR patients

The role of NAFLD ?

Circulation, metabolism, nutrition

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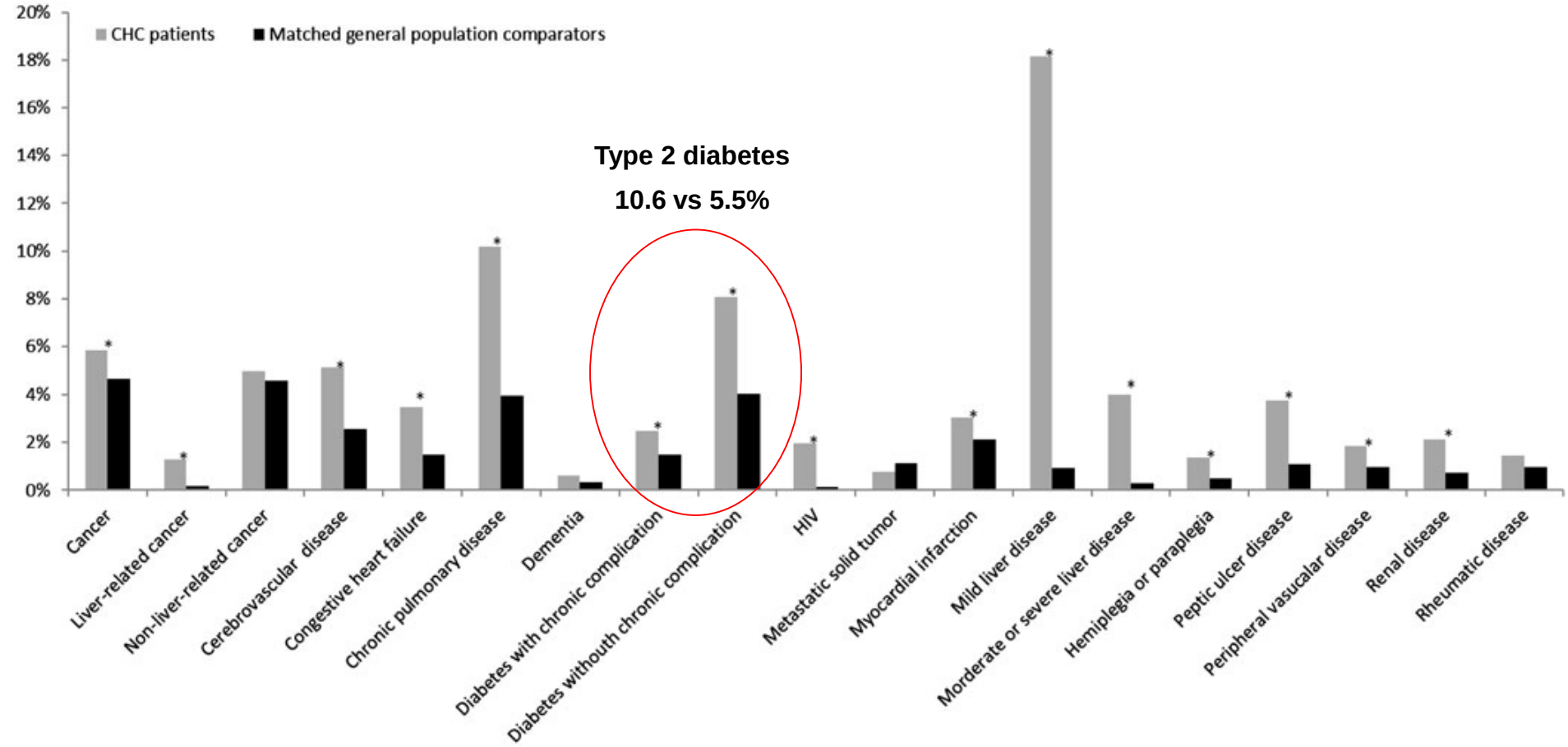
High prevalence of comorbidities in HCV patients

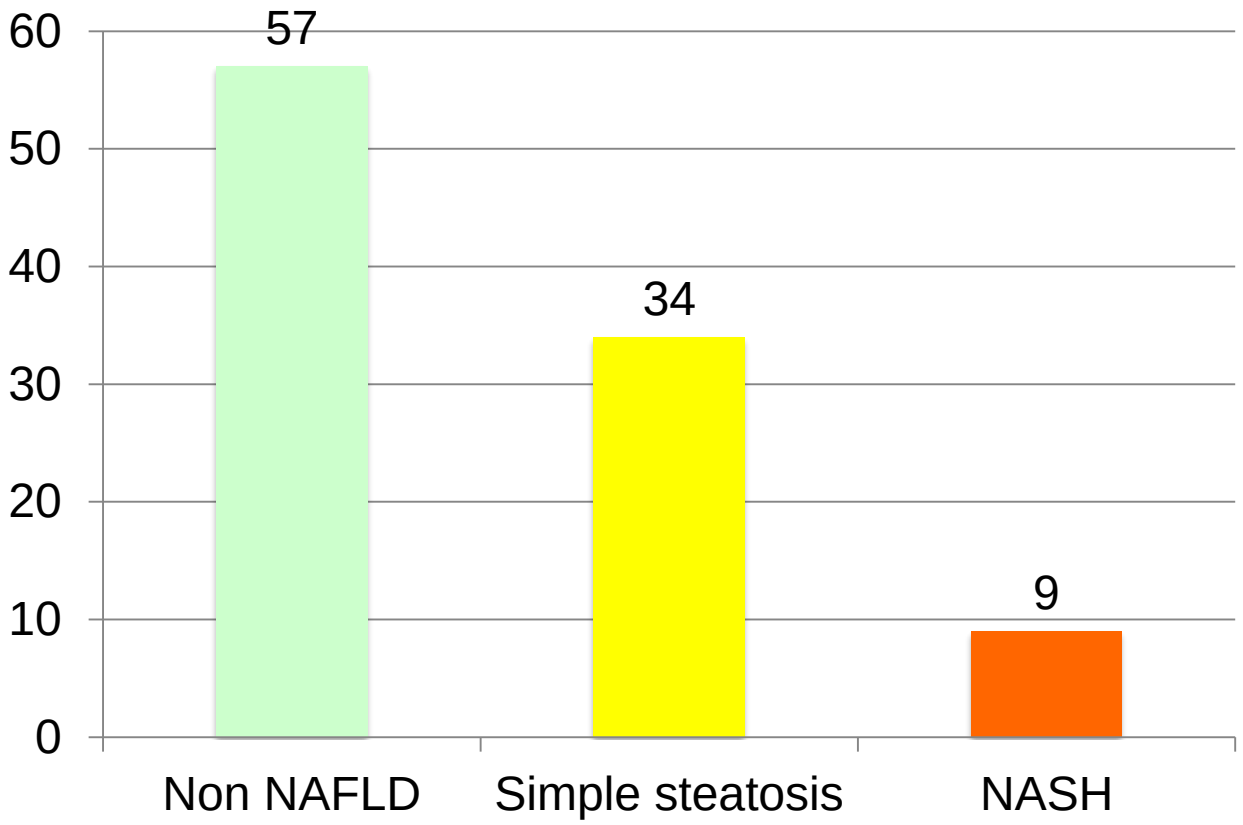
Nationwide population-based register study in Sweeden



Büsch K, et al. Scand J Gastroenterol 2017

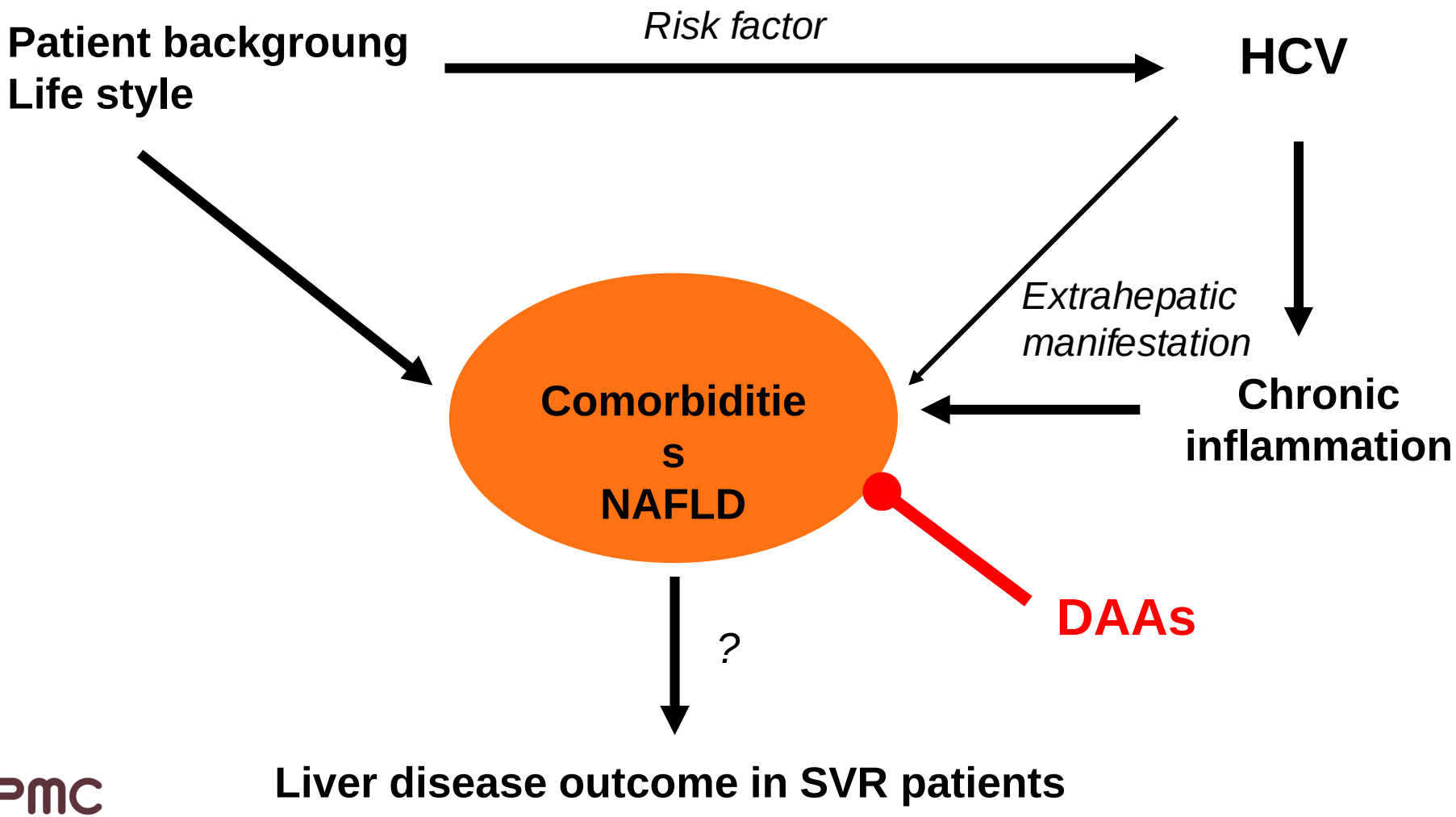
High prevalence of NAFLD in HCV patients

278 consecutive patients with biopsy proven hepatitis C

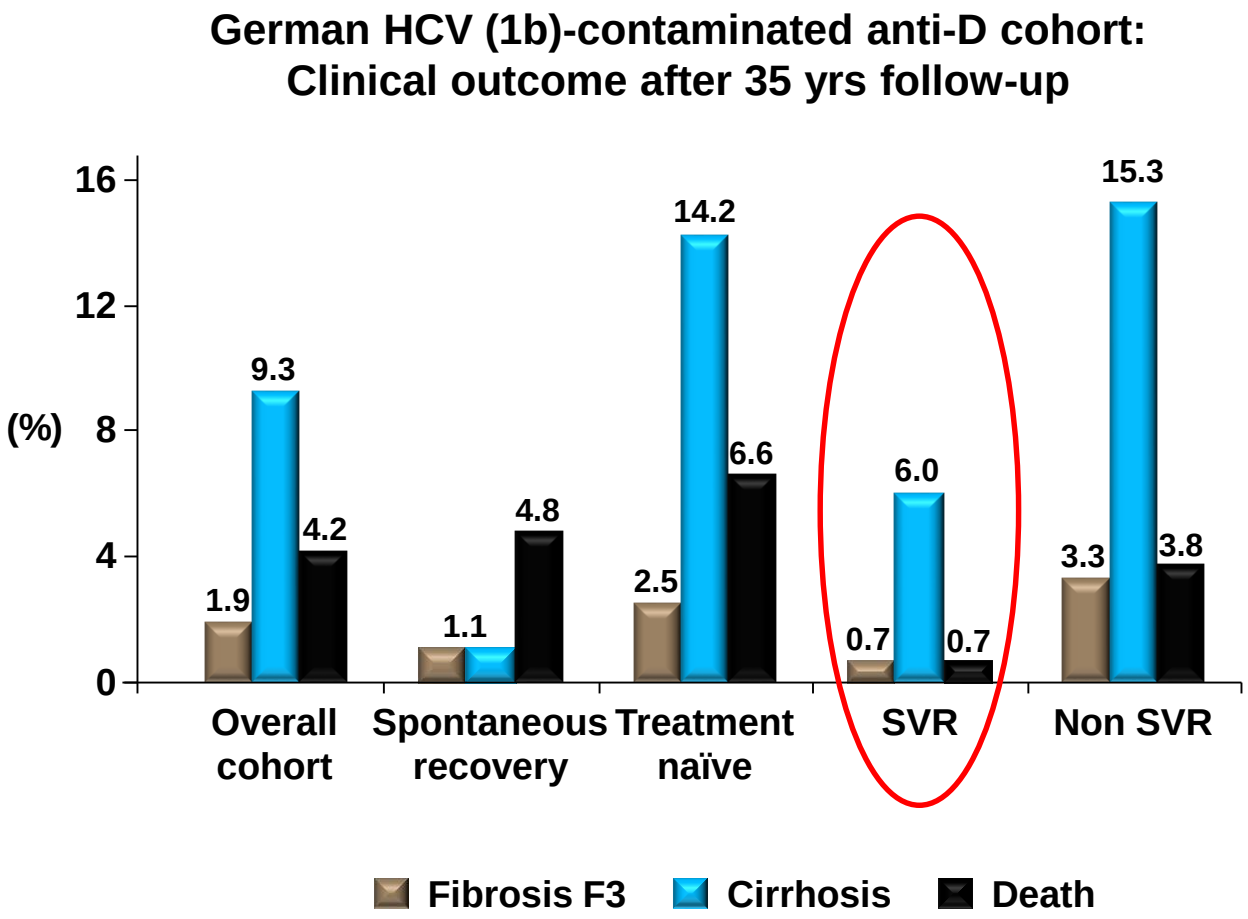


Bedossa P et al, Hepatology 2007

Comorbidities in HCV patients



Overweight is a risk factor of cirrhosis occurrence in SVR patients



- Overall survival was significantly enhanced after SVR, compared to treatment-naïve patients or non-SVR (p=0.027)
- Independent factors associated with cirrhosis
  - No response to treatment
  - No spontaneous recovery
  - BMI >25 kg/m^2 (RR: 1.125)

Wiese M, et al. Hepatology 2014 ;59:49–57.

Risk factors of HCC following SVR

1000 SVR patients followed 5.7 yrs: 842 cirrhotics,158 bridging fibrosis

	Hepatocellular carcinoma								
	Univariable analyses			Multivariable analyses (n = 630)[#]			Imputation analyses (n = 1000)[#]		
	HR	95% CI	*p* value	HR	95% CI	*p* value	HR	95% CI	*p* value
Age									
<45 years	1.00	Ref.	Ref.	1.00	Ref.	Ref.	1.00	Ref.	Ref.
45–60 years	5.13	1.57–16.79	0.007	8.54	1.13–64.64	0.038	9.68	1.28–72.95	0.028
>60 years	6.95	2.03–23.76	0.002	8.91	1.12–70.79	0.039	9.76	1.23–77.77	0.031
Males	1.28	0.69–2.38	0.426	-	-	-	-	-	-
BMI, per 1.0 kg/m^2	1.03	0.96–1.13	0.314	-	-	-	-	-	-
Cirrhosis	2.94	0.91–9.42	0.071	-	-	-	-	-	-
Laboratory markers of liver disease severity									
Platelet count, per 10 × 10^9/L	0.93	0.88–0.98	0.005	0.94	0.87–1.00	0.048	0.93	0.87–0.99	0.029
Bilirubin, per mmol/L	1.01	0.99–1.04	0.233	-	-	-	-	-	-
Albumin, per g/L	0.97	0.91–1.04	0.428	-	-	-	-	-	-
AST/ALT ratio, per 0.1	1.04	1.00–1.08	0.046	1.04	1.00–1.09	0.084	1.04	1.00–1.09	0.068
gGT, per 10 IU/L	1.02	0.99–1.04	0.143	-	-	-	-	-	-
Treatment naïve	0.39	0.22–0.71	0.002	-	-	-	-	-	-
Diabetes mellitus	1.90	0.91–4.00	0.090	2.36	1.02–5.42	0.044	2.27	0.98–5.29	0.057
History of severe alcohol use	0.89	0.40–1.97	0.774	-	-	-	-	-	-
Anti-HBc positive	1.16	0.60–2.25	0.655	-	-	-	-	-	-

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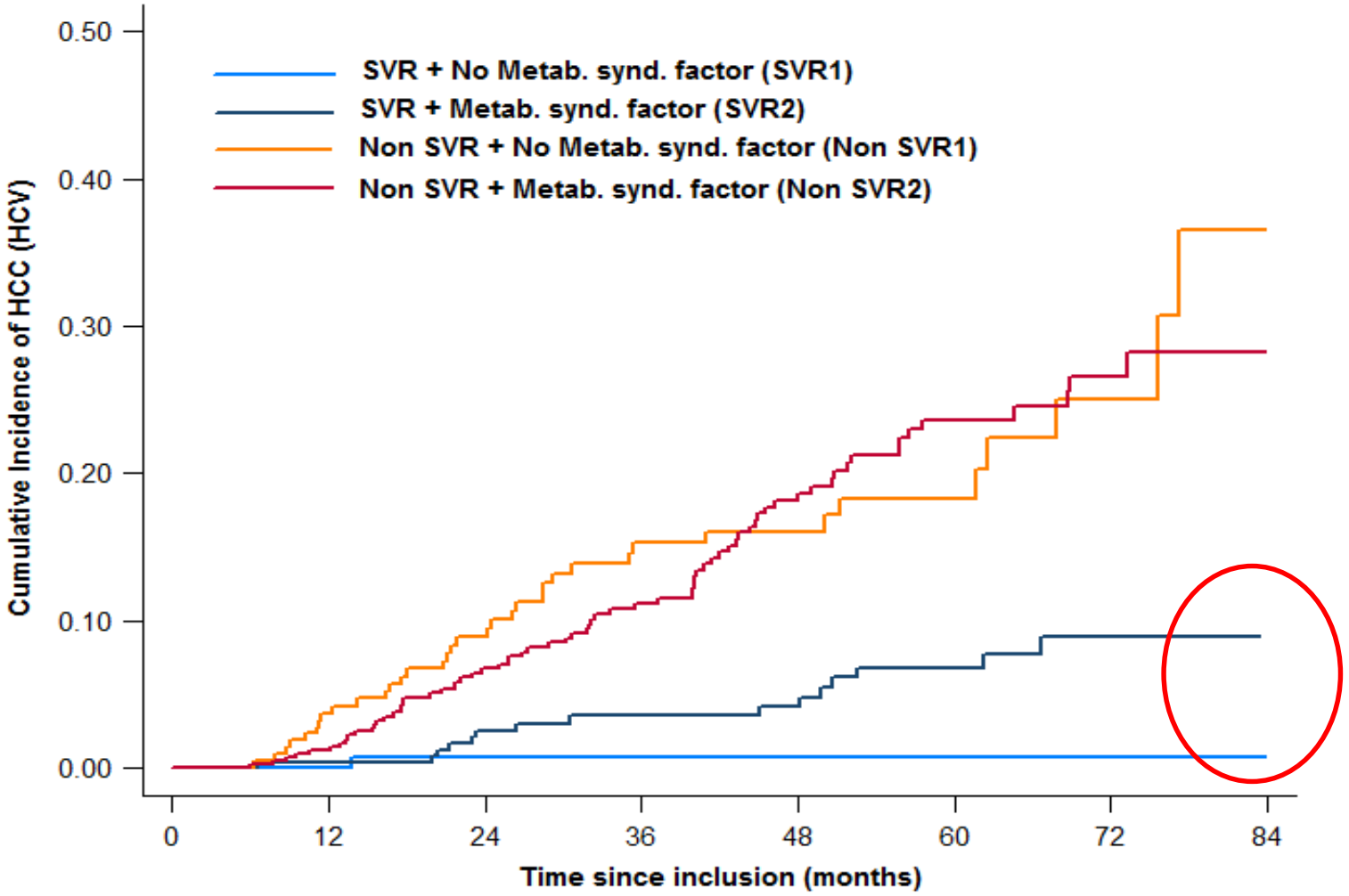
Van der Meer AJ, et al. J Hepatol 2016

Metabolic syndrome and risk of HCC in cirrhotic patients with SVR

Risk of HCC according to SVR and Met S

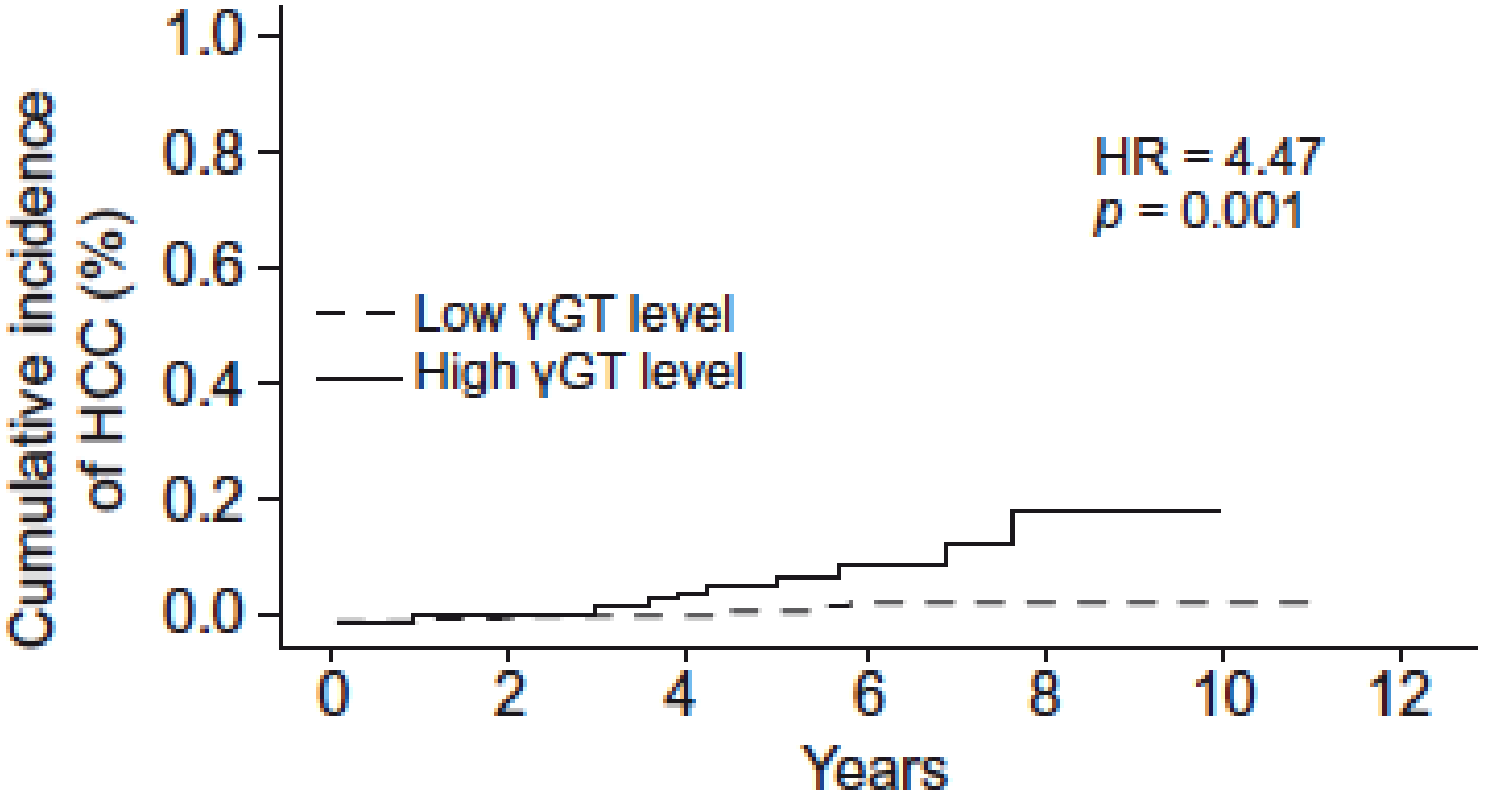


Ganne-Carrie N et al, Hepatology 2016

Risk factors of HCC following SVR in non-cirrhotic patients

556 non-cirrhotic patients with SVR

Predictive factors of HCC **:** age, **GGT, type 2 diabetes** and APRI



Huang CF, et al. J Hepatol 2014

Conclusion

- After the cure of HCV infection, regression of fibrosis varies and the risk of liver-related complications remains, even in the absence of cirrhosis.
- Comorbidities, such as diabetes or NAFLD, are common in HCV patients, mainly as HCV-associated condition but also as HCV-driven in some cases.
- Metabolic disorders in SVR patients are associated with progression of liver disease.
- Risk stratification for NASH should be performed in SVR patients with persistent metabolic disorders.
- Screening for HCC after SVR is recommended in patients with extensive fibrosis and metabolic risk factors.