

Natural history of chronic viral hepatitis in Germany

Prof. Dr. Michael P. Manns

Vorstandsvorsitzender Deutsche Leberstiftung / Chairman German Liver Foundation

in Kooperation mit Prof. Dr. Markus Cornberg

Strategietreffen: „Virushepatitis in Deutschland eliminieren

Strategy Meeting: „Elimination of Viral Hepatitis In Germany“

Berlin, 30 November 2016

Hepatitis Viruses

Hepatitis A	Feinstone	1973	RNA
Hepatitis B	Blumberg	1965	DNA
Hepatitis C	Houghton	1988	RNA
Hepatitis D	Rizzetto	1977	RNA
Hepatitis E	Balayan	1980	RNA

Viral hepatitis was accountable for 1,454,000 deaths in 2013. The majority of mortality is due to liver cancer and cirrhosis

1990

1. Ischemic heart disease
2. Cerebrovascular disease
3. Lower respiratory infections
4. Diarrheal disease
5. COPD
6. Tuberculosis
7. Neonatal preterm birth
8. Road injuries
9. Lung cancer
- 10. Viral hepatitis**

2013

1. Ischemic heart disease
2. Cerebrovascular disease
3. COPD
4. Lower respiratory infections
5. Alzheimer's disease
6. Lung cancer
- 7. Viral hepatitis**
8. Road injuries
9. AIDS
10. Diabetes



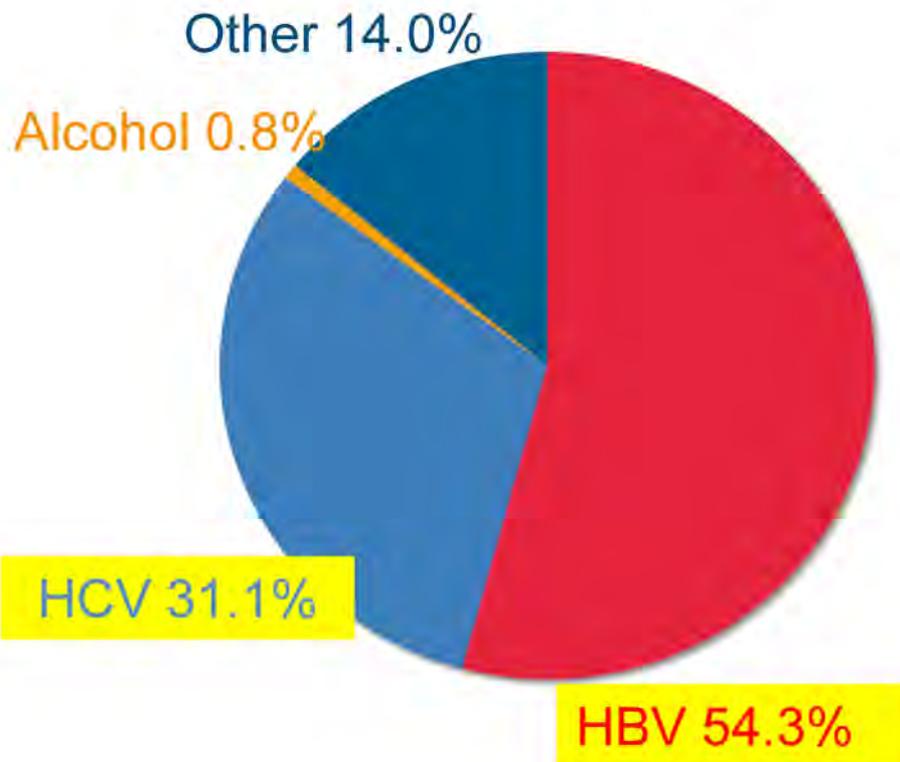
HCV accounted for 48% of viral hepatitis-related mortality in 2013

DALYs for HCV have more than doubled since 1990

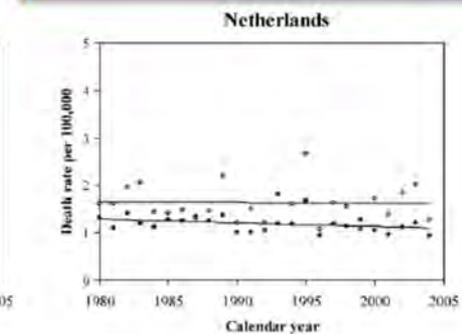
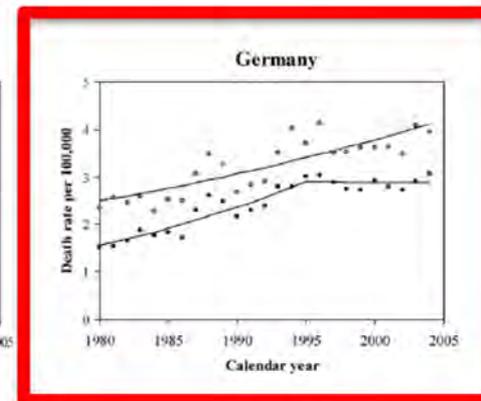
*COPD, chronic obstructive pulmonary disease; DALY, disability-adjusted life-year (the number of years lost due to ill health, disability, or early death).
** Age-standardized mortality rate.

The Increasing Incidence of Hepatocellular Carcinoma

Worldwide etiology



Mortality due to HCC in men 1970-2002



HCV is the leading cause of liver cirrhosis and hepatocellular carcinoma (HCC), which causes over 700,000 hepatitis C related deaths annually

Global deaths HCV in 1990 and 2013 for all ages and both sexes combined and age-standardised death rates

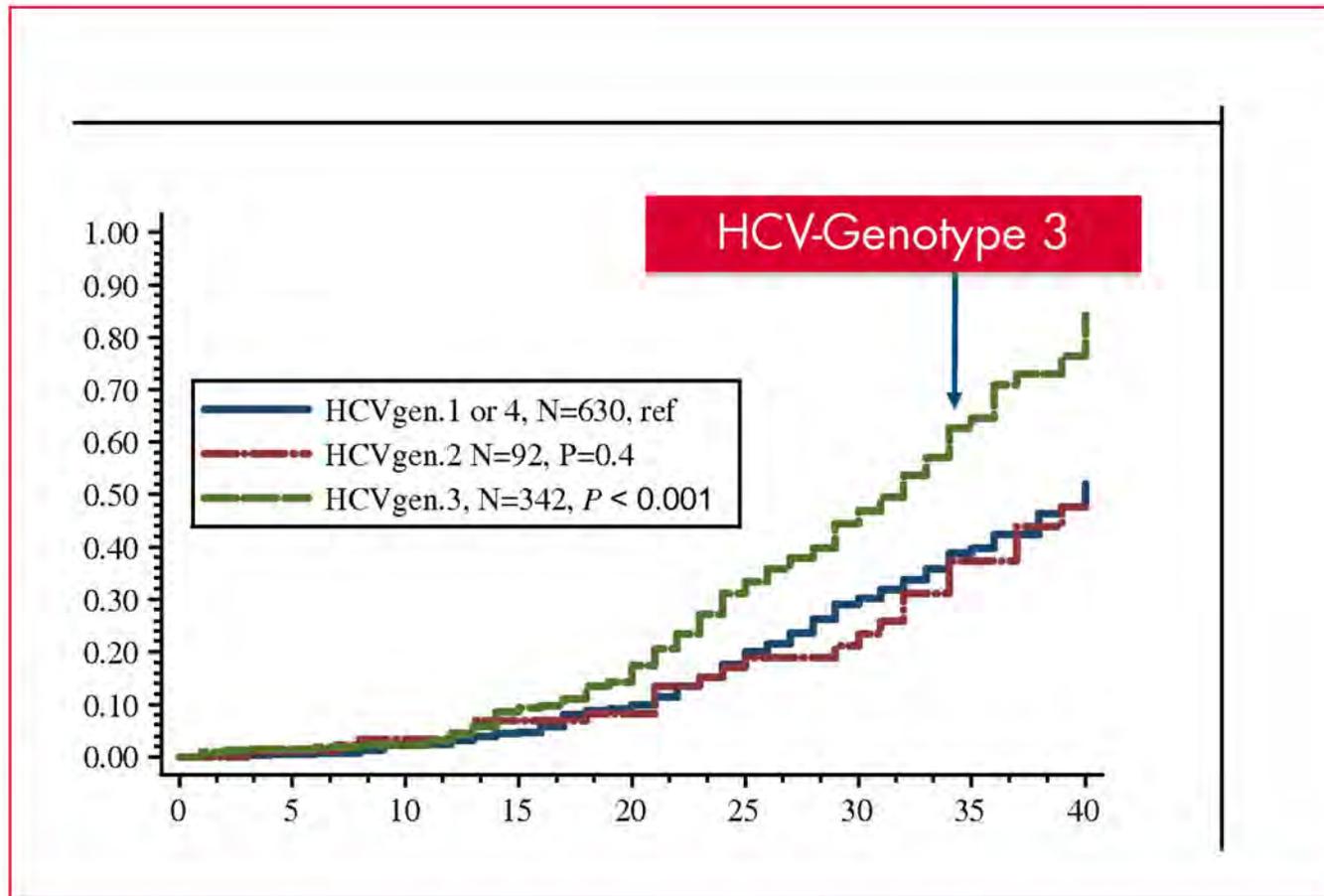
All ages deaths (thousands)

	1990	2013	Median % change
Hepatitis C	2.3 (0.5 to 5.3)	3.5 (0.7 to 8.2)	51.0 (24.40 to 86.56)
Liver cancer secondary to hepatitis C	87.4 (79.5 to 94.7)	342.5 (317.1 to 375.3)	290.8 (251.46 to 342.52)
Cirrhosis of the liver secondary to hepatitis C	213.1 (200.4 to 226.7)	357.8 (334.3 to 386.1)	67.3 (54.60 to 83.86)
	302.8	703.8	

Factors influencing the rate of fibrosis progression in chronic hepatitis C.

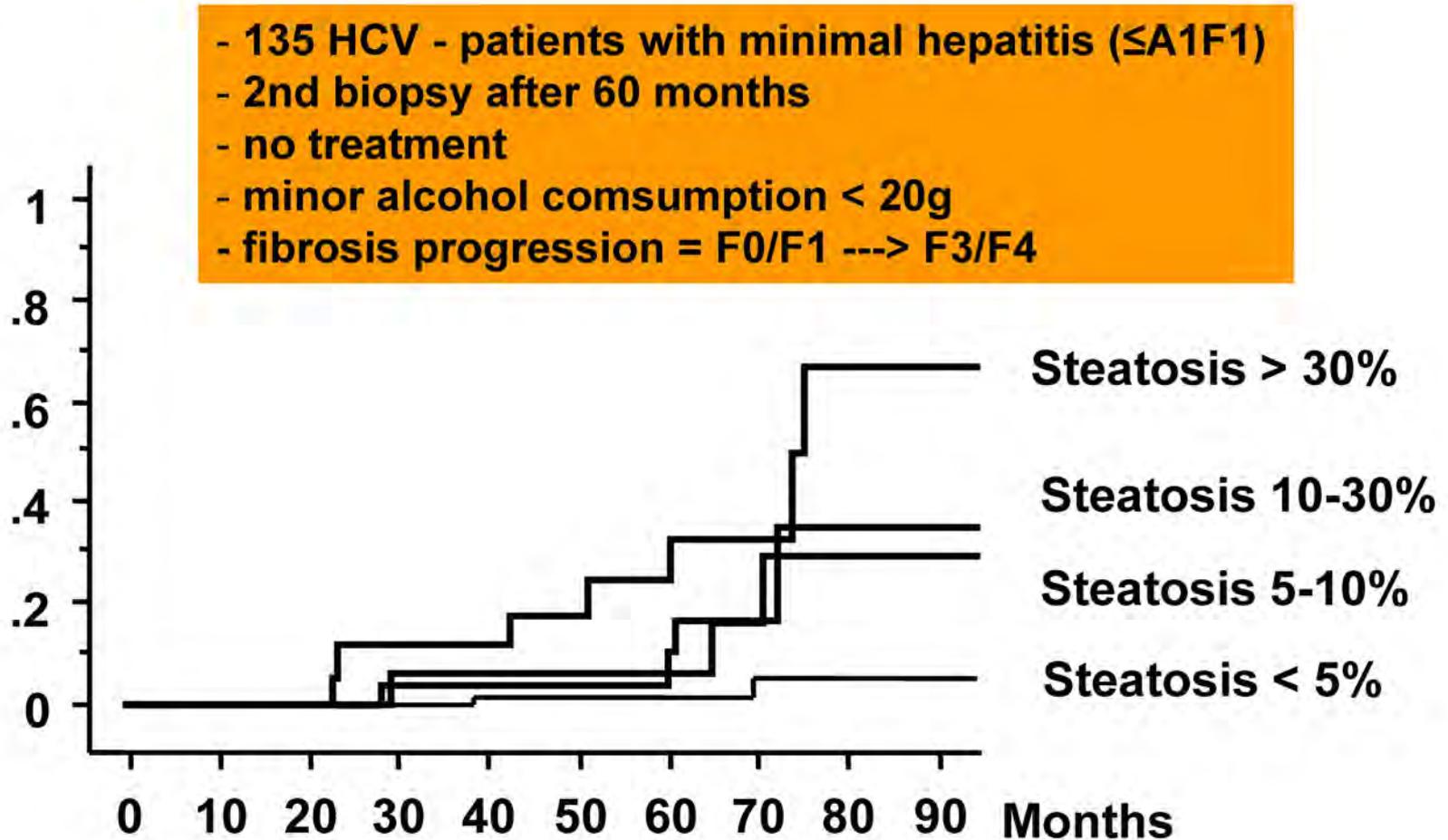
- **Alcohol**
- **Age >50 years**
- **HCV Genotype**
- **Steatosis**
- **Insulin resistance**
- **Male gender**
- **Genetics**
- **Smoking**
- **Co-infections (HBV, HDV, HIV)**

HCV-Genotype 3 is associated with faster fibrosis progression



Progression of HCV infection depends on the grade of steatosis

Probability of fibrosis progression
between paired liver biopsies



Cox Model: Steatosis is an independent factor of fibrosis progression

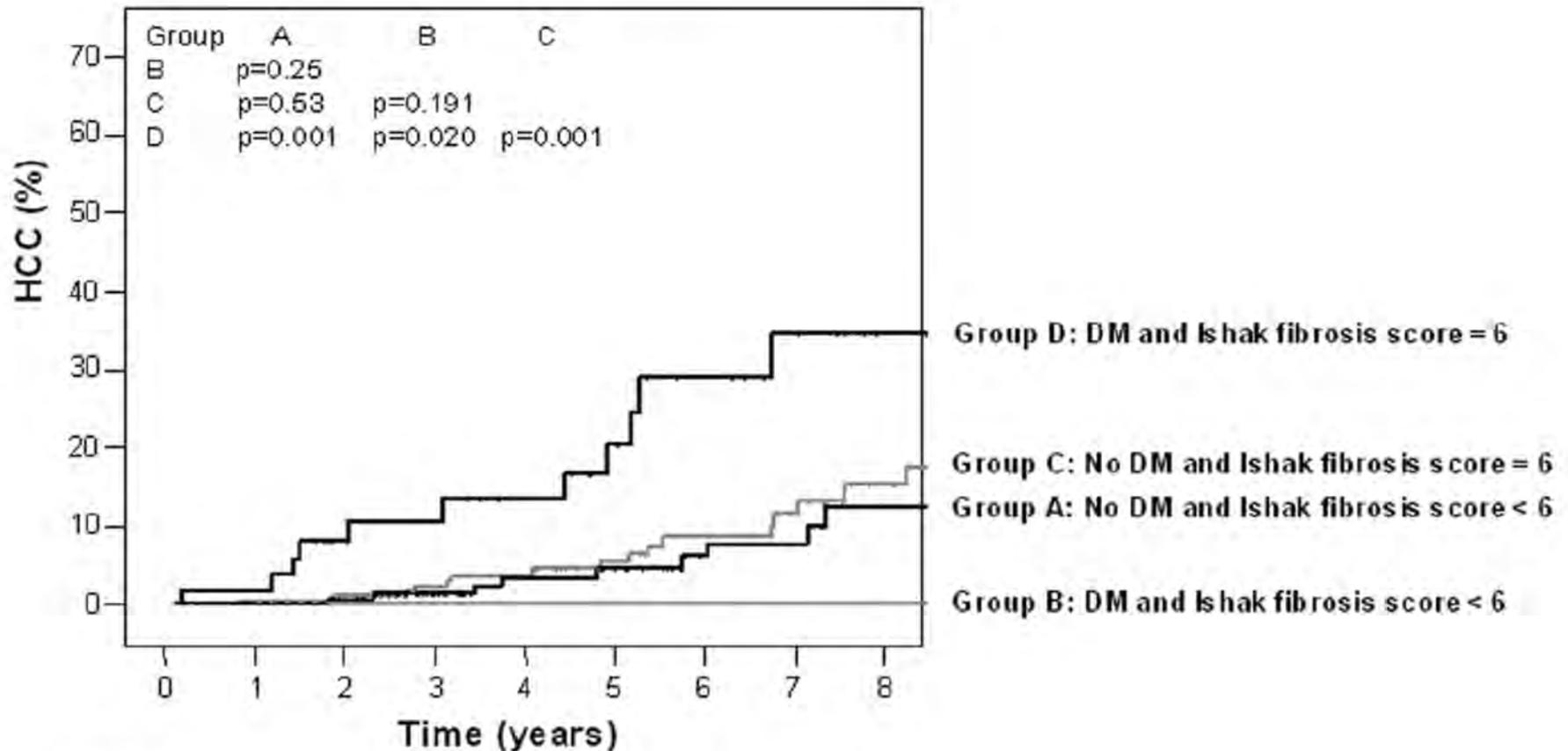
USA NHANES III cohort
13.004 Personen anti-HCV negativ; 264 anti-HCV positiv



Overall mortality (AHR=2.80, 2.79-2.81),
Liver-related mortality (AHR=17.96, 17.80-18.12),

In HCV patients, increases mortality was associated with
DM (AHR=2.139, 2.11-2.16),
higher BMI (AHR=1.054, 1.53-1.055)
Hypertension (AHR=1.408, 1.394-1.422)

HCV infection and Diabetes mellitus increase the risk of HCC development



At risk	0	1	2	3	4	5	6	7	8
A:	210	197	152	119	95	70	57	43	30
B:	27	24	22	16	12	10	6	6	4
C:	246	227	189	145	126	99	79	55	41
D:	58	49	38	31	27	21	15	11	6

REVIEWS IN BASIC AND CLINICAL GASTROENTEROLOGY AND HEPATOLOGY

Robert F. Schwabe and John W. Wiley, Section Editors

Extrahepatic Morbidity and Mortality of Chronic Hepatitis C



Francesco Negro,¹ Daniel Forton,² Antonio Craxi,³ Mark S. Sulkowski,⁴
Jordan J. Feld,⁵ and Michael P. Manns⁶

Ulcerative keratitis

Idiopathic pulmonary fibrosis

Insulin resistance
Diabetes mellitus

Porphyria cutanea tarda

Autoimmune thrombocytopenic purpura



Fatigue, depression, anxiety,
cognitive impairment

Thyroid autoimmune stigmata

Mixed cryoglobulinemia

Non-Hodgkin Lymphoma

Pruritus

....

BRAIN FOG



Patients with advanced fibrosis who clear HCV infection have
a survival similar to the general population!

Figure 2. Overall survival of patients without SVR compared to the age- and sex-matched Dutch population

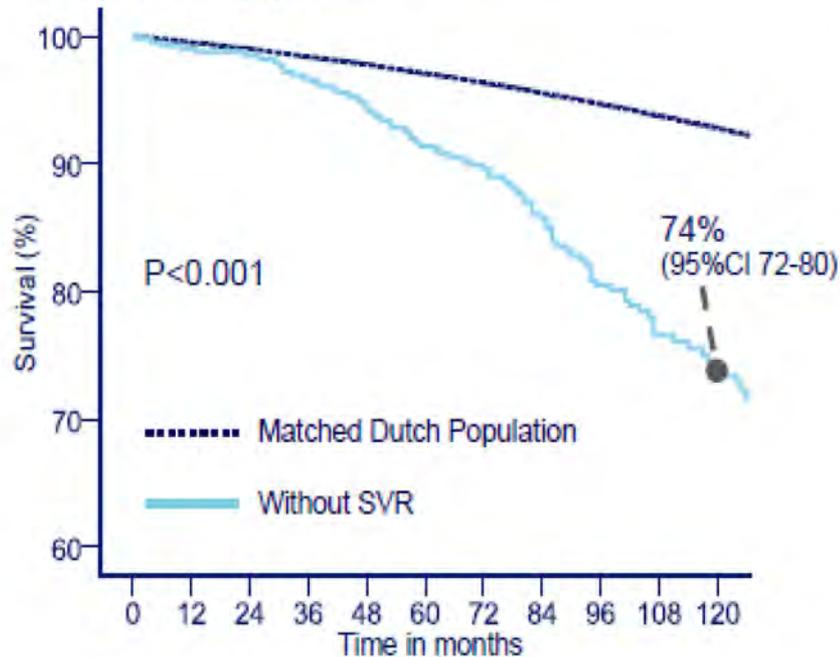
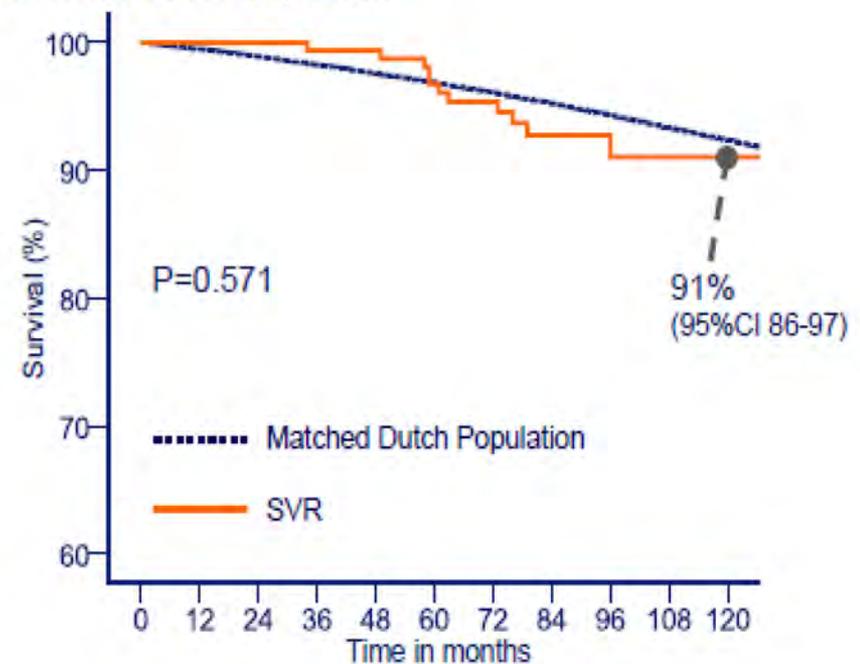
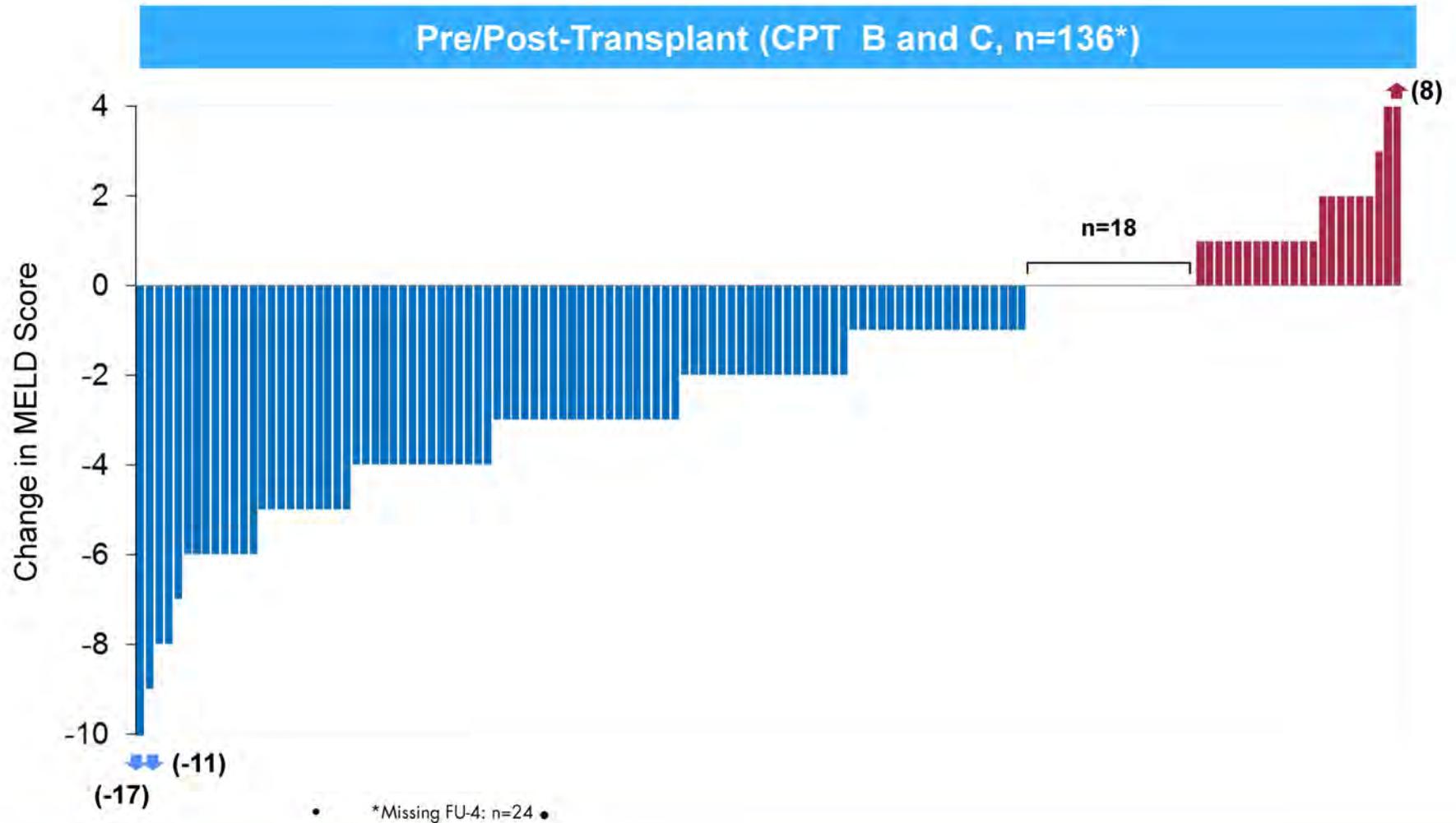


Figure 3. Overall survival of patients with SVR compared to the age- and sex-matched Dutch population

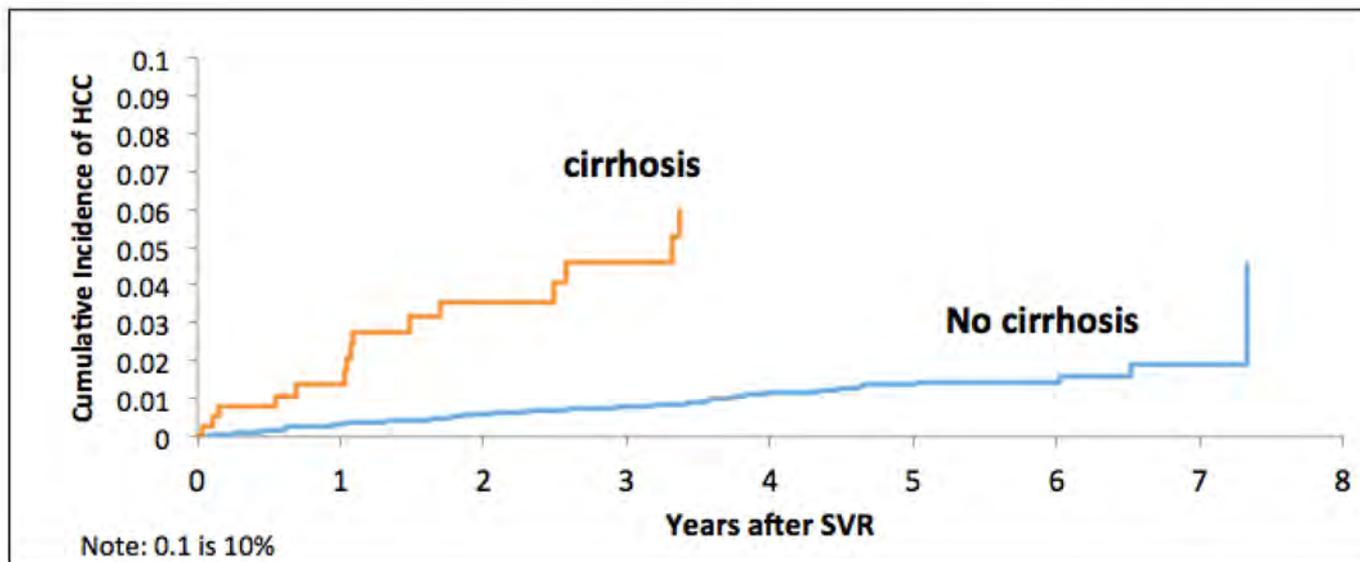


Ledipasvir, Sofosbuvir, Ribavirin (SOLAR- 2 Study):

Improvement of liver function with DAA treatment

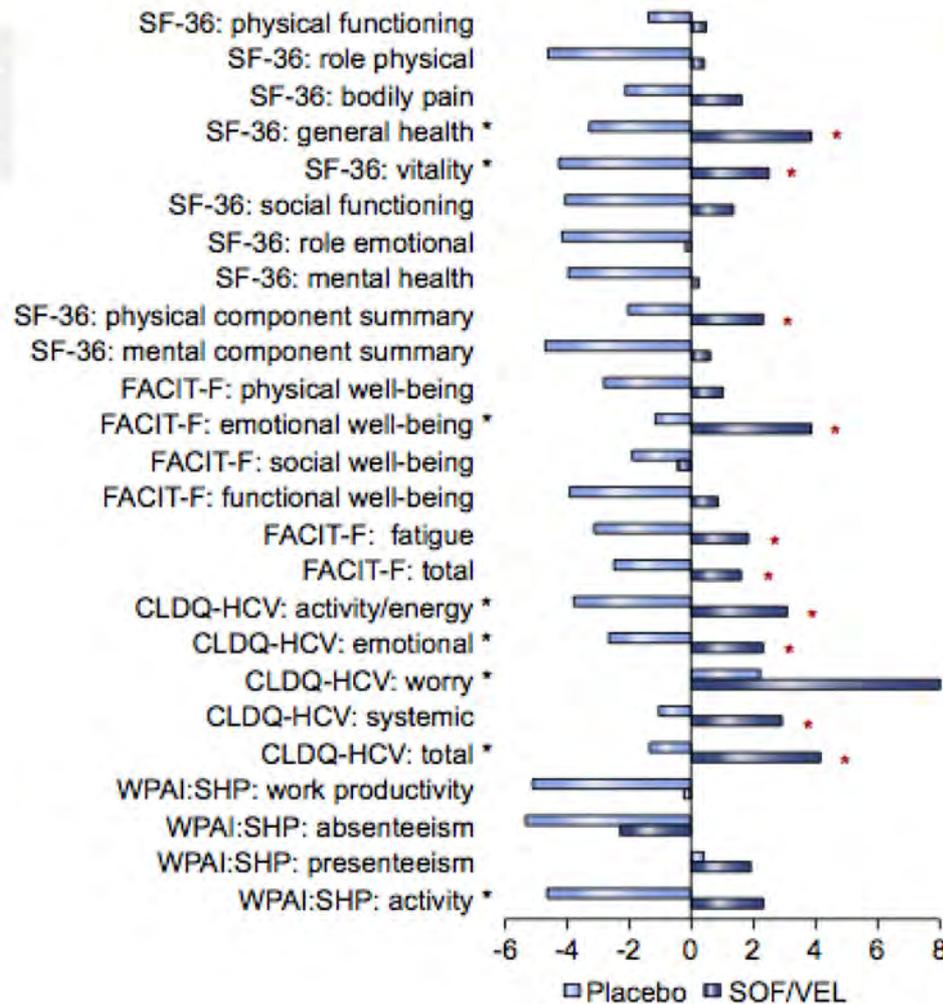


HCC Incidence Following SVR: by Cirrhosis



Improvement of quality of life

SOF/VEL
vs.
Plazebo



**Fast alle Personen sind
krankenversichert.**

**Wir können bei Verdacht
alle Personen auf HCV untersuchen.**

**Wir können alle HCV-Patienten
behandeln
- unabhängig von Alter und Fibrose.**

