Chronic viral hepatitis and liver disease in Belgium

Pierre Deltenre

Brussels, November 7, 2017

Hepatitis B and C in Belgium
What we need to know

1. Who is at risk of infection?
2. What is the natural history?
3. What are the risk factors for disease progression and which risk factors can we correct?
4. How we can reduce mortality related to viral hepatitis?

WHO IS AT RISK OF INFECTION?

Hepatitis B virus and hepatitis C virus infections in Belgium: similarities and differences in epidemics and initial management

Bénédicte De Vroey[a], Christophe Moreno[b], Wim Laleman[h], Marc van Gossum[c], Isabelle Colle[i], Chantal de Galocsy[d], Philippe Langlet[e], Geert Robaeys[j], Hans Orlent[k], Peter Michielsen[l], Jean Delwaide[m], Hendrik Reynaert[f], François D'Heygere[n], Dirk Sprengers[o], Stefan Bourgeois[p], Collins Assene[g], Bertrand Vos[q], Réginald Brenard[r], Michael Adler[b], Jean Henrion[a] and Pierre Deltenre[a]

387 newly diagnosed HBV infections – 268 newly diagnosed HCV infections

	HBsAg-positive patients (n=387)	HCV patients with detectable HCV RNA (n=268)	P-value
Age (years)[a]	36 (34–37)	45 (43–46)	<0.0001
Sex ratio (male/female) [n (%)]	266/121 (69/31)	150/118 (56/44)	0.0008
Origin [n (%)]			
Known	386 (100)	252 (94)	<0.0001
White	165 (43)	214 (85)	
Black African	123 (32)	25 (10)	
Asia	44 (11)	1 (0.4)	
Maghreb	52 (13)	8 (3)	
Other	2 (1)	4 (1.6)	
Unknown	1 (0)	16 (6)	
Risk factor for infection [n (%)]			
Known	139 (36)	196 (73)	<0.0001
Transfusion	12 (9)	66 (34)	
Intravenous drug use	8 (6)	86 (44)	
Surgery	4 (3)	14 (7)	
Sexual transmission	56 (40)	2 (1)	
Familial transmission	42 (30)	1 (0.5)	
Other	17 (12)	27 (14)	
Unknown	248 (64)	72 (27)	

De Vroey B, *et al*. EJGH 2013;25:613-19

Hepatitis B virus and hepatitis C virus infections in Belgium: similarities and differences in epidemics and initial management

Bénédicte De Vroey[a], Christophe Moreno[b], Wim Laleman[h], Marc van Gossum[c], Isabelle Colle[i], Chantal de Galocsy[d], Philippe Langlet[e], Geert Robaeys[j], Hans Orlent[k], Peter Michielsen[l], Jean Delwaide[m], Hendrik Reynaert[f], François D'Heygere[n], Dirk Sprengers[o], Stefan Bourgeois[p], Collins Assene[g], Bertrand Vos[q], Réginald Brenard[r], Michael Adler[b], Jean Henrion[a] and Pierre Deltenre[a]

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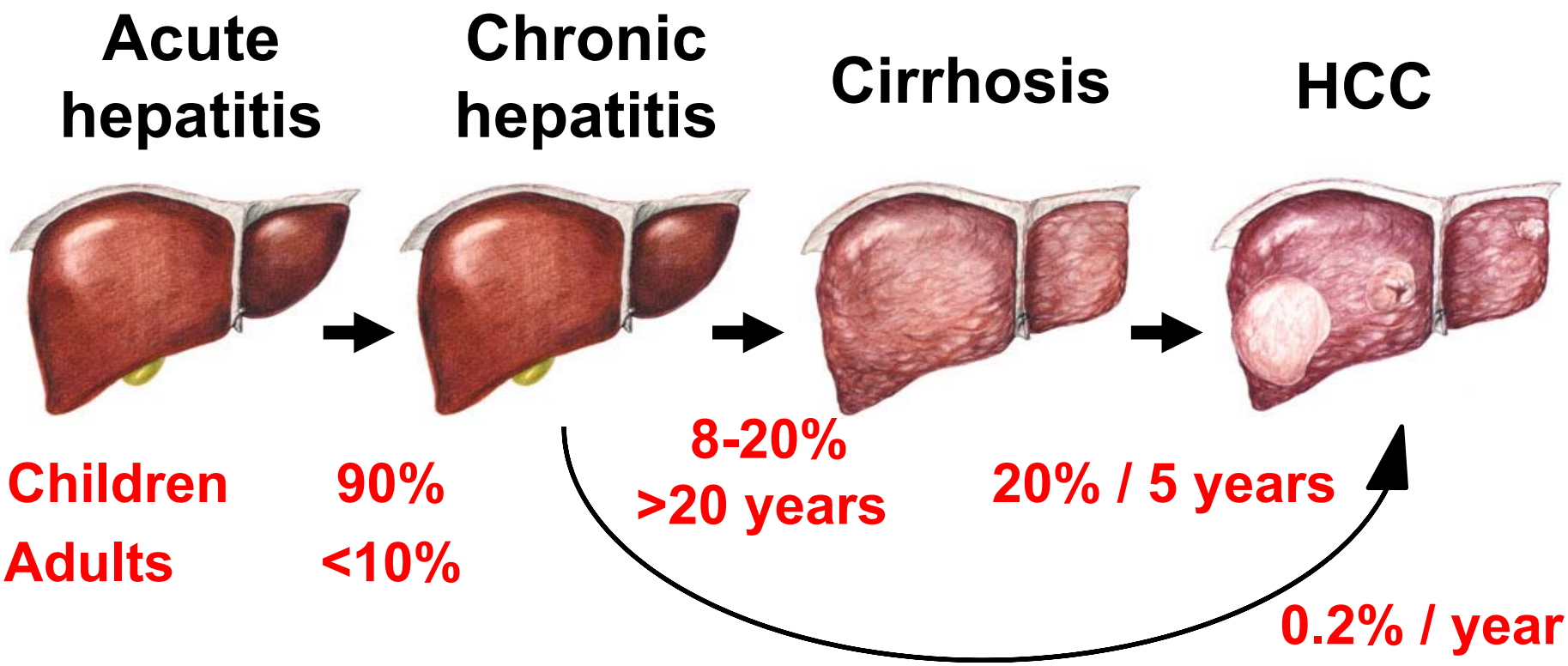
De Vroey B, *et al*. EJGH 2013;25:613-19

WHAT IS THE NATURAL HISTORY?

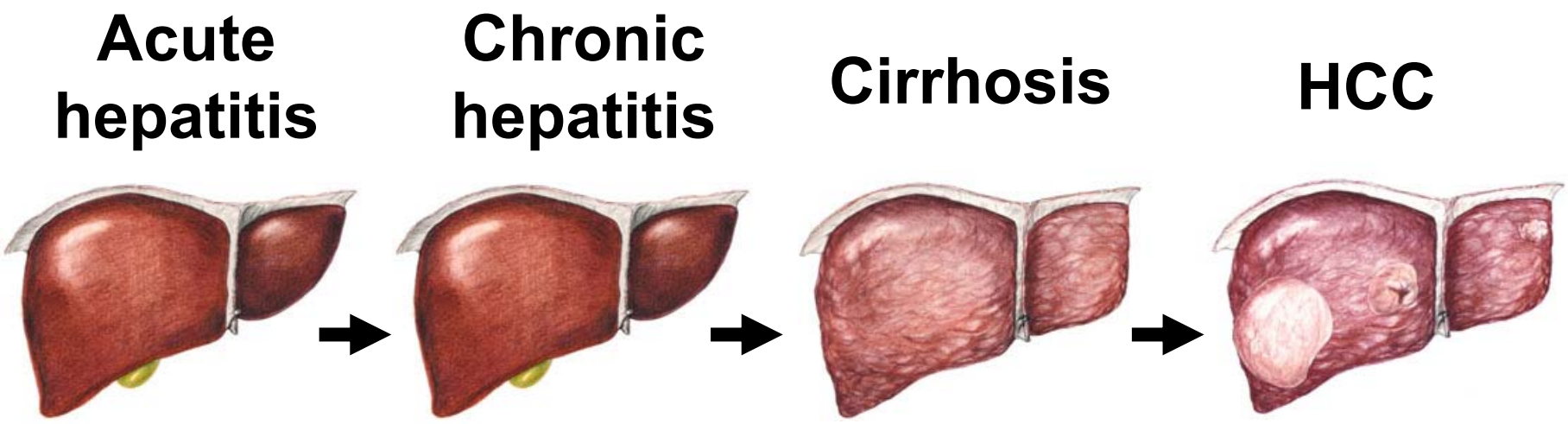
Natural history

HBV infection



Natural history

HCV infection



EASL Clinical Practice Guideline. J Hepatol 2011;55:245-264
AASLD Practice Guideline. Ghany M, *et al*. Hepatology 2011;54:1527-1537

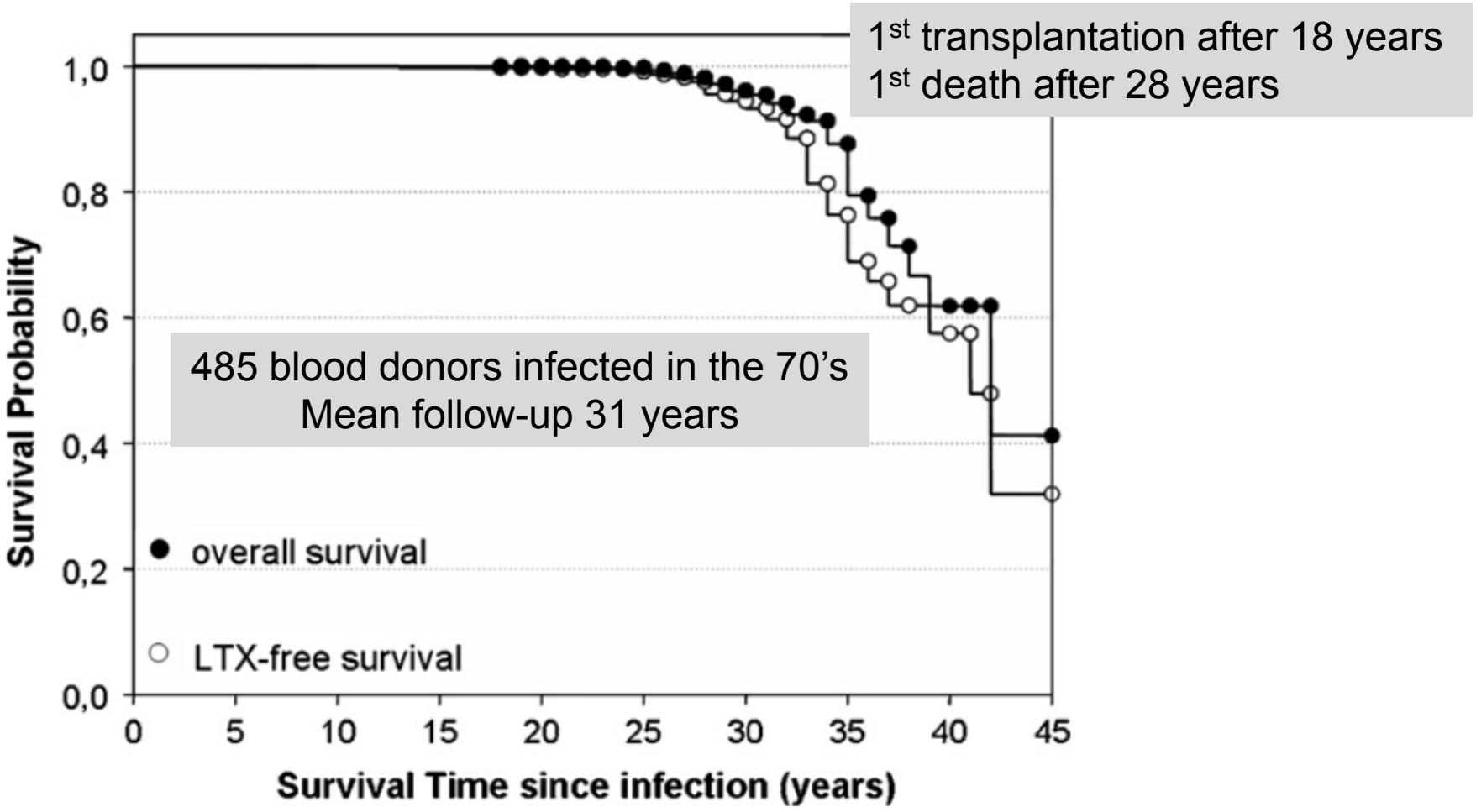
Natural history

	Hepatitis B	Hepatitis C	HBV and HCV co-infection
Number of patients	39109	75834	2604
Follow-up (years)	5.3	4.6	3.5
Mortality rate *	1.4	3.1	5.6
Liver-related mortality rate *	12.2	16.8	32.9
HCC-related mortality rate *	27.8	16.7	39.7

* Compared to mortality rate in the general population

Amin J, *et al*. Lancet 2006;368:938-45

Natural history
HCV infection



Ferenci P, *et al*. J Hepatol 2007;47:31-36

Risk factors for HCC

GEOGRAPHICAL DISTRIBUTION OF MAIN RISK FACTORS FOR HCC WORLDWIDE

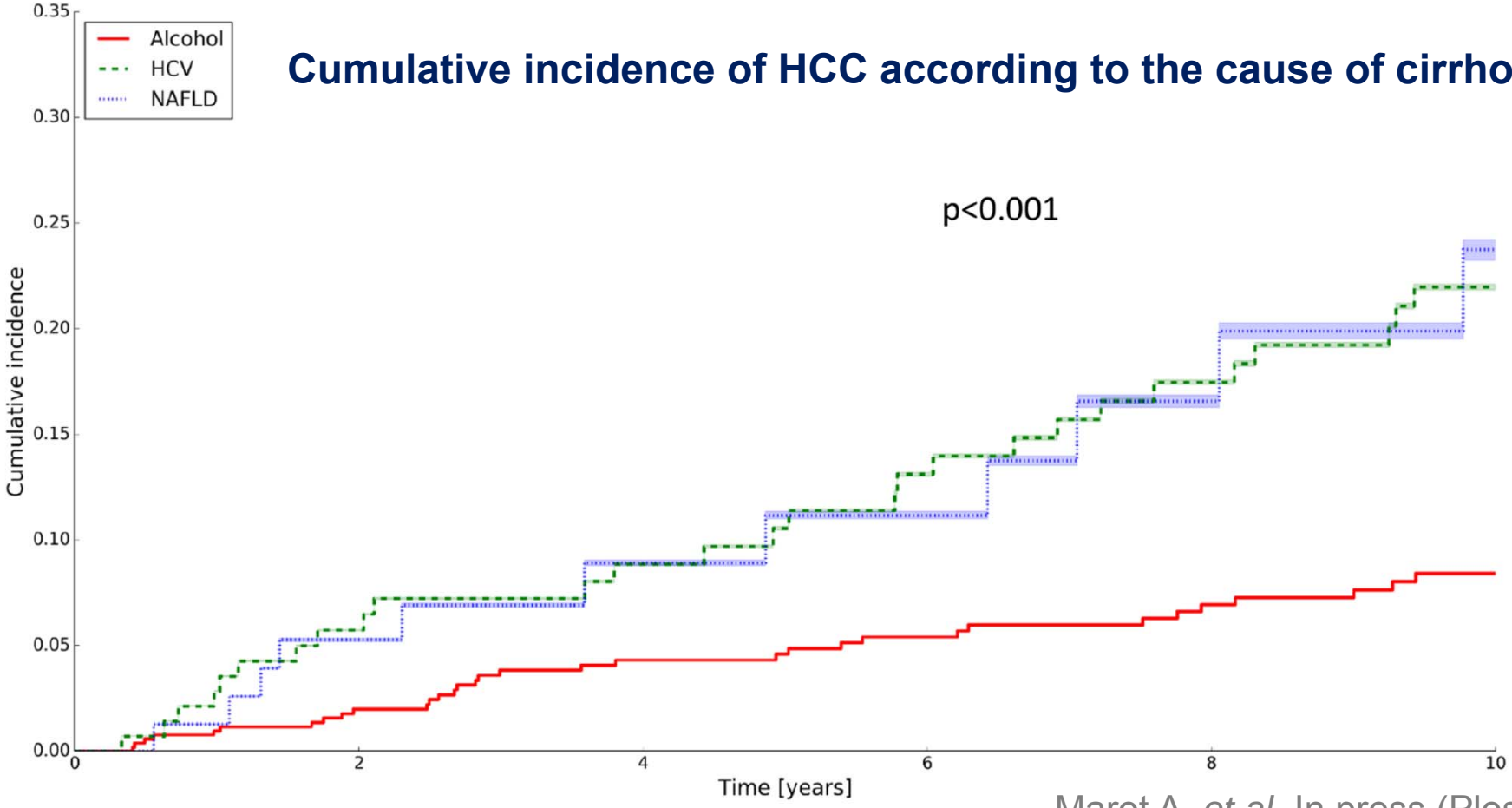
Geographic area	AAIR	Risk factors		Alcohol	Others
	M/F	HCV (%)	HBV (%)	(%)	(%)
Europe	6.7/2.3	60-70	10-15	20	10
Southern	10.5/3.3				
Northern	4.1/1.8				
North America	6.8/2.3	50-60	20	20	10 (NASH)
Asia and Africa		20	70	10	10 (Aflatoxin)
Asia	21.6/8.2				
China	23/9.6				
Japan	20.5/7.8	70	10-20	10	10
Africa	1.6/5.3				
WORLD	16/6	31	54	15	

EASL Guidelines. J Hepatol 2012;56:908-43

Alcoholic liver disease confers a worse prognosis than HCV infection and non-alcoholic fatty liver disease among patients with cirrhosis: An observational study

Astrid Marot[1], Jean Henrion[2], Jean-François Knebel[3,4], Christophe Moreno[5], Pierre Deltenre[1,5]*

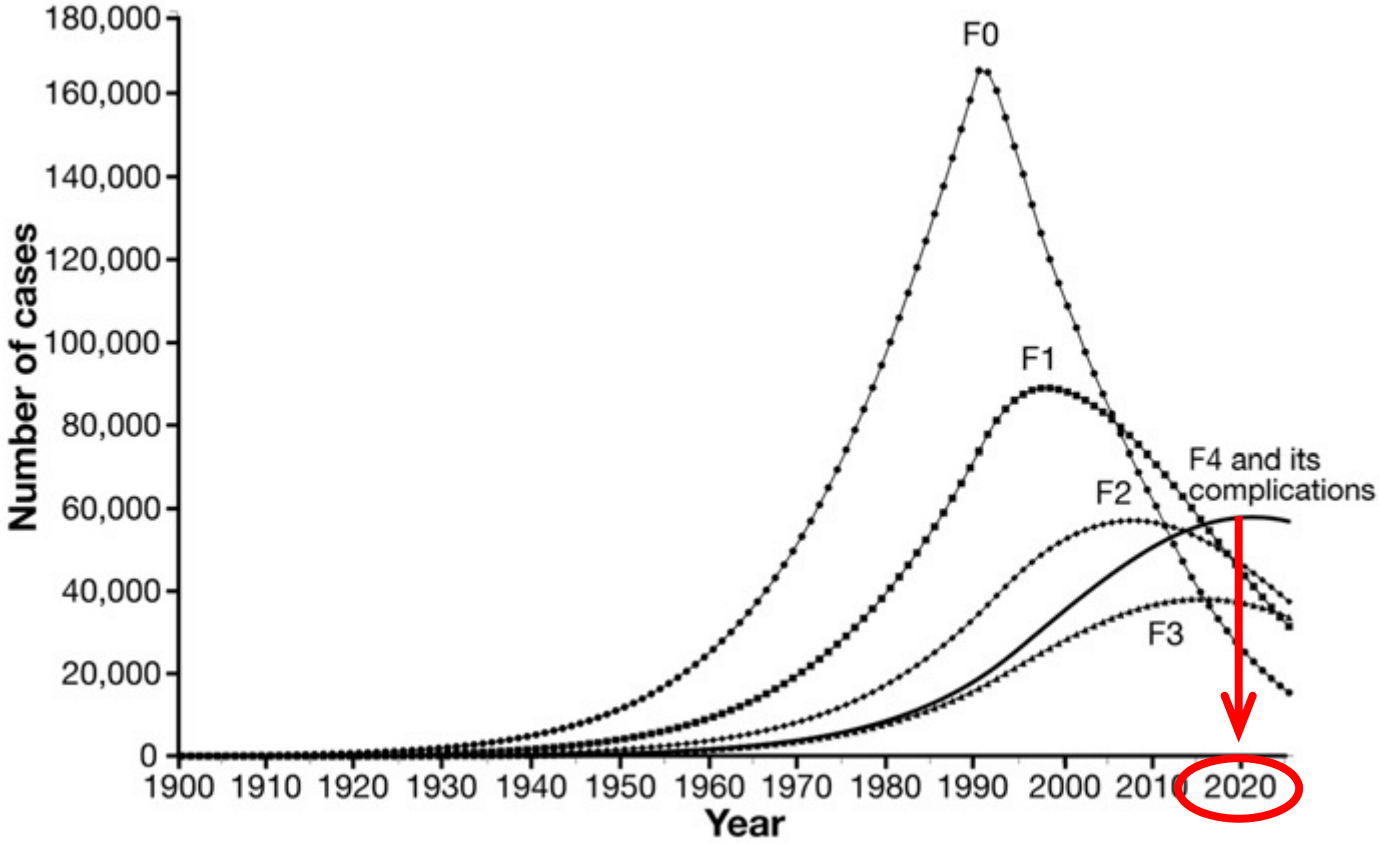
Cumulative incidence of HCC according to the cause of cirrhosis



Marot A, *et al*. In press (Plos One)

Dynamics of HCV infection

DISTRIBUTION OF FIBROSIS STAGES IN THE ABSENCE OF TREATMENT IN FRANCE

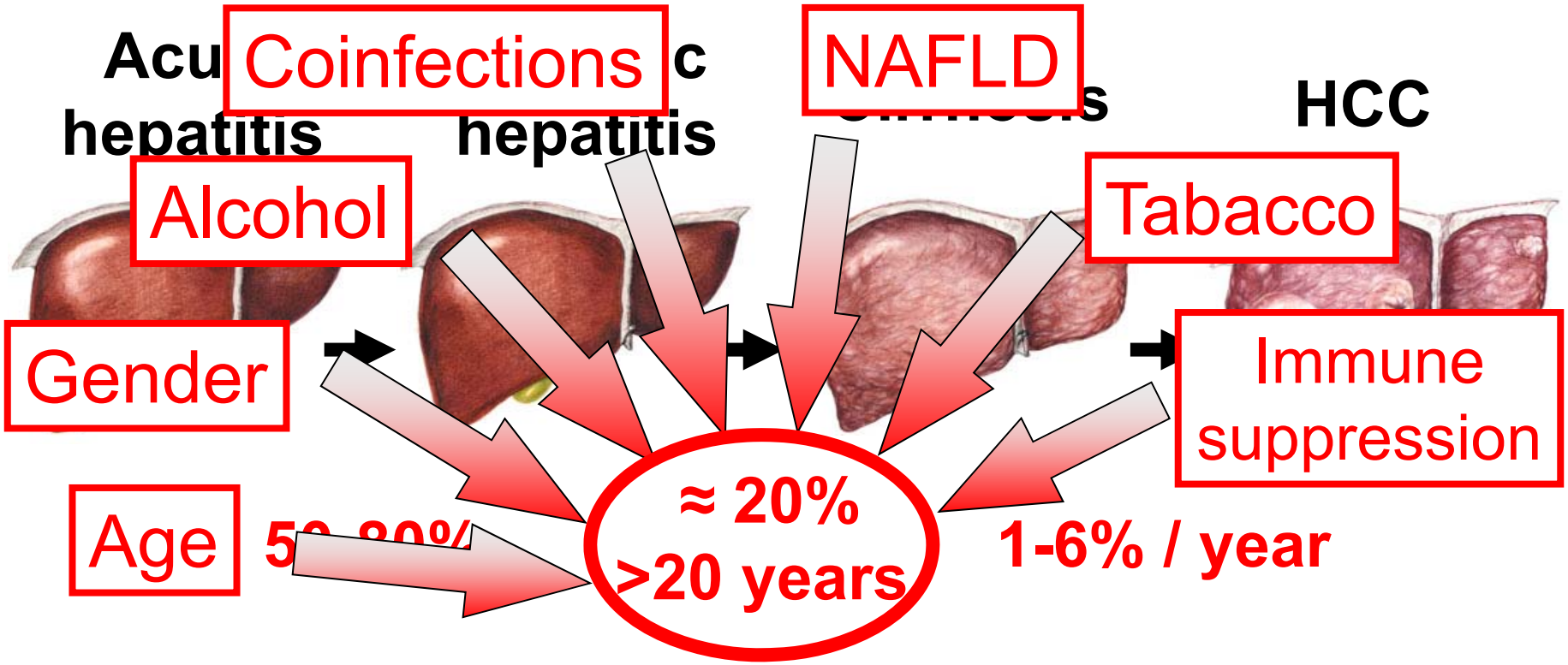


Deuffic-Burban S, Deltenre P, *et al.* Gastroenterology 2012;143:974-985 e914

WHAT ARE THE RISK FACTORS FOR DISEASE PROGRESSION AND WHICH RISK FACTORS CAN WE CORRECT?

Natural history

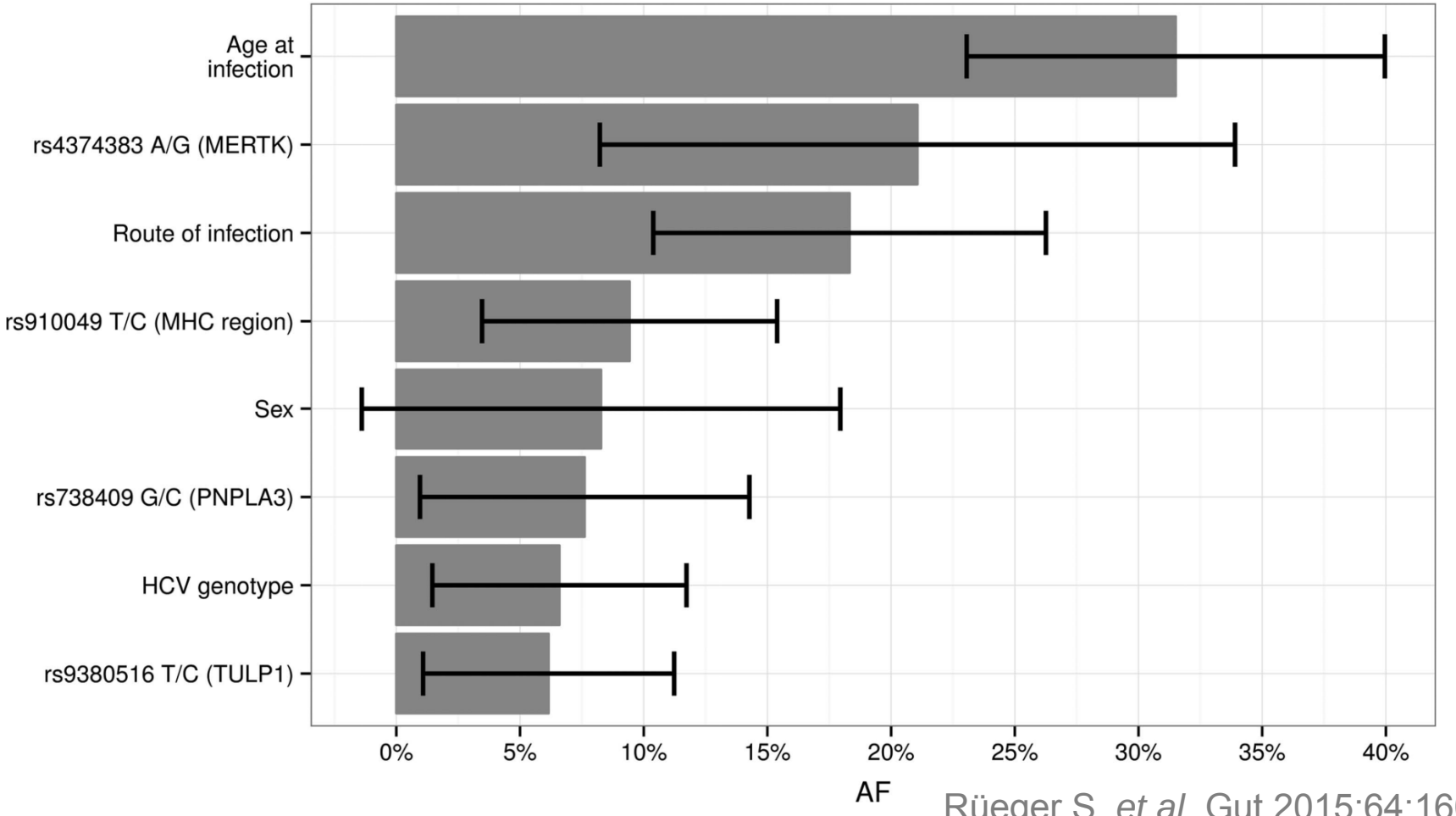
HCV infection



Missiha SB, *et al*. Gastroenterology 2008;134:1699-1714

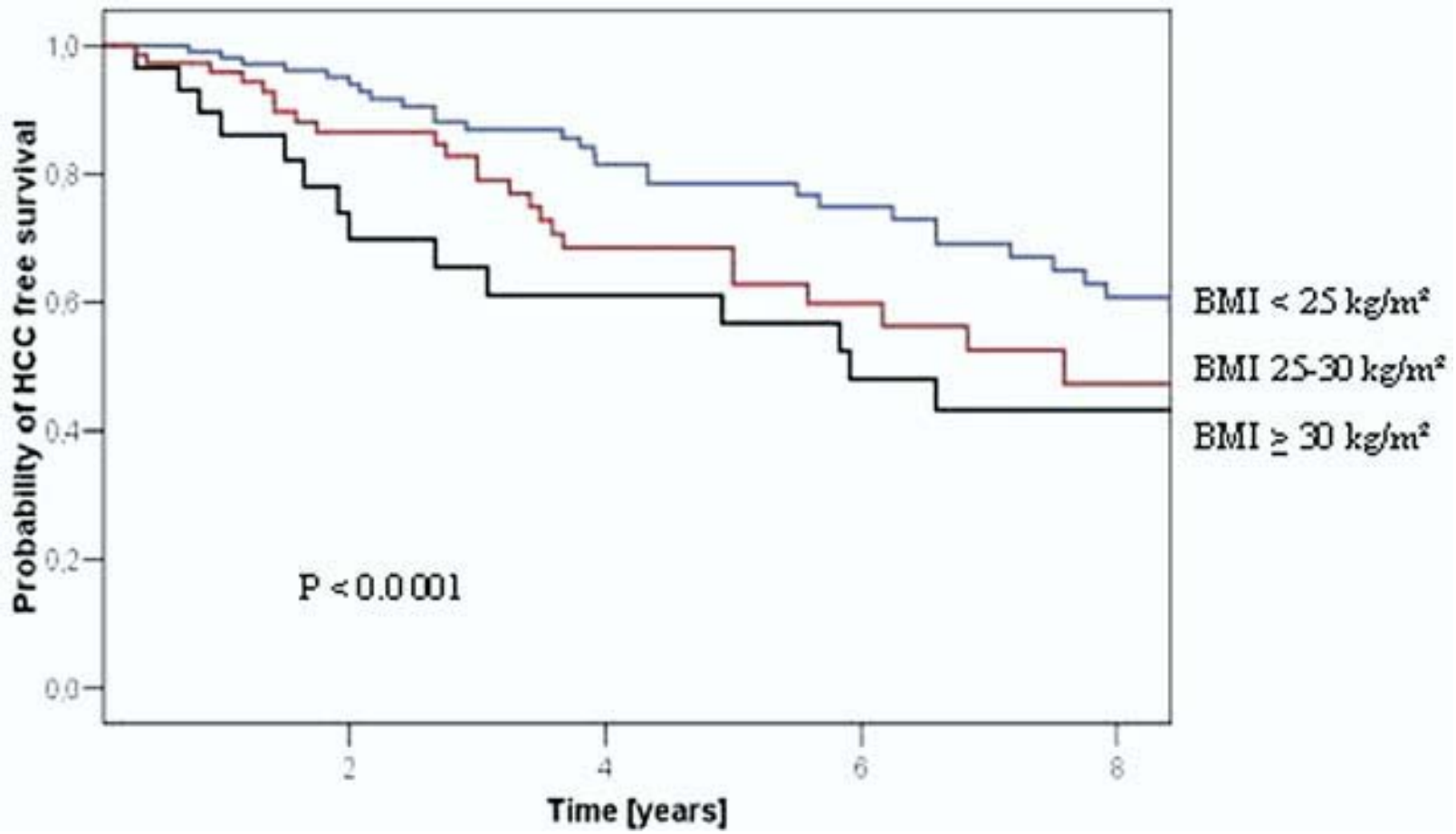
Most factors accelerating liver fibrosis progression in chronic hepatitis C are non modifiable

Attributable fraction of risk for accelerated progression rate



Rüeger S, *et al*. Gut 2015;64:1605-15

Risk of HCC according to metabolic factors

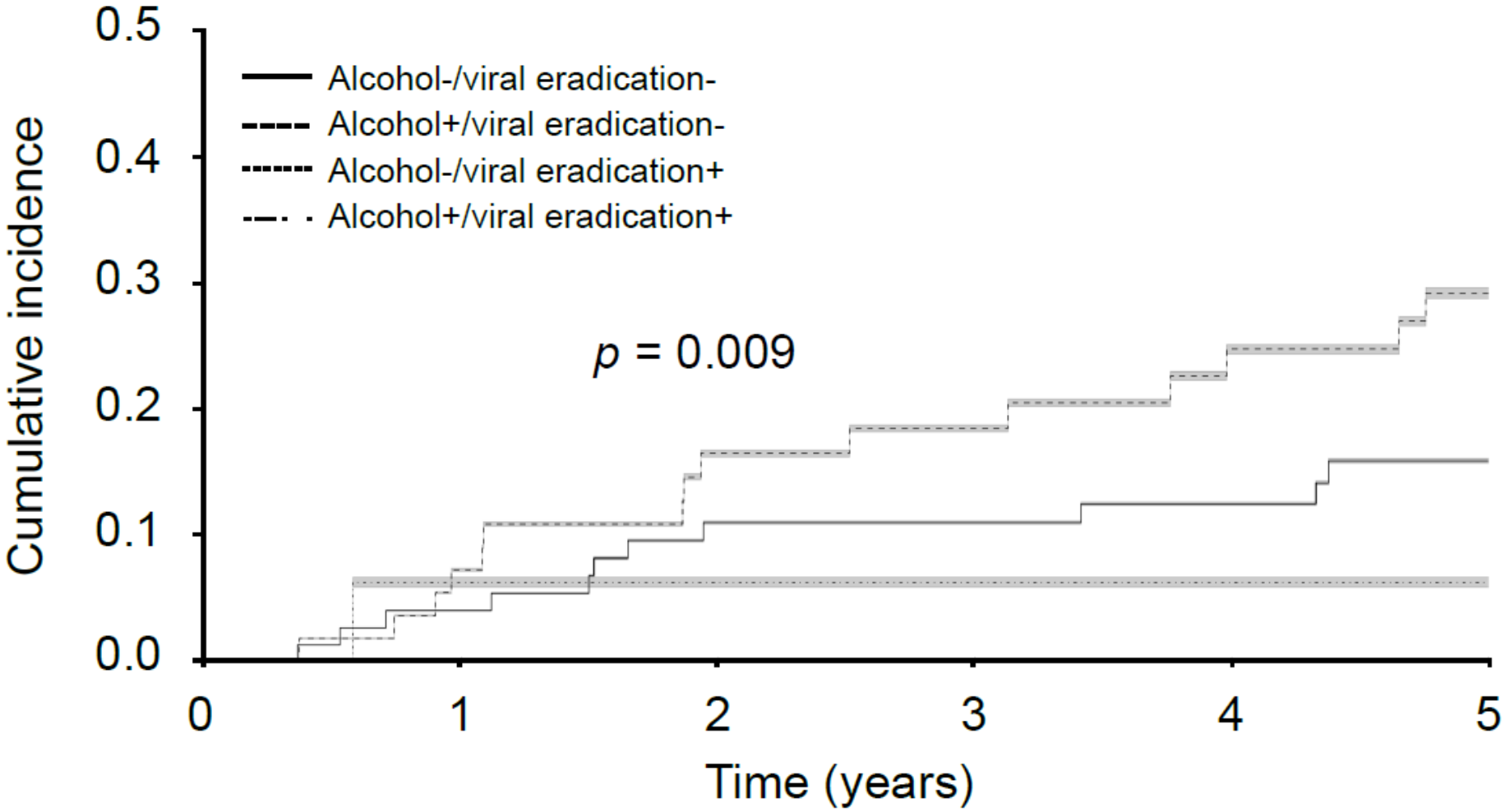


N'Kontchou G, *et al*. CGH 2006;4:1062-68

Alcohol intake increases the risk of HCC in hepatitis C virus-related compensated cirrhosis: A prospective study

EASL JOURNAL OF HEPATOLOGY

Hélène Vandenbulcke[1], Christophe Moreno[2], Isabelle Colle[3], Jean-François Knebel[4,5], Sven Francque[6], Thomas Sersté[7], Christophe George[8], Chantal de Galocsy[9], Wim Laleman[10], Jean Delwaide[11], Hans Orlent[12], Luc Lasser[13], Eric Trépo[2], Hans Van Vlierberghe[3], Peter Michielsen[6], Marc van Gossum[7], Marie de Vos[1], Astrid Marot[14], Christopher Doerig[14], Jean Henrion[1], Pierre Deltenre[2,14,*]



Vandenbulcke H, *et al*. J Hepatol 2016;65:543-61

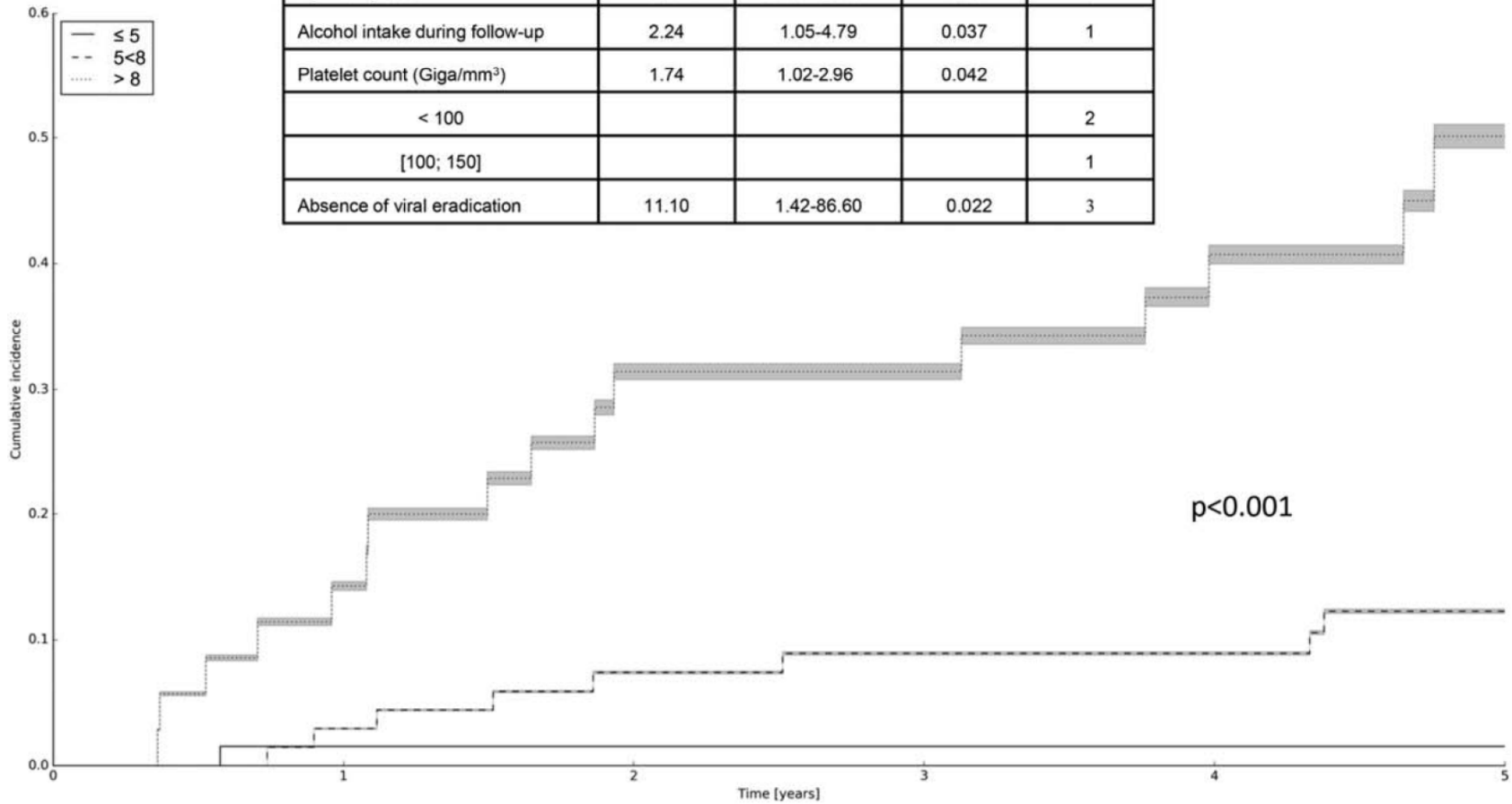
HEPATOLOGY

AASLD
AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES

External Validation of the Nomogram for Individualized Prediction of Hepatocellular Carcinoma Occurrence in Patients With Hepatitis C Virus–Related Compensated Cirrhosis

Astrid Marot, M.D.[1]
Hélène Vandenbulcke, M.D.[2]
Jean-François Knebel, M.D.[3,4]
Christopher Doerig, M.D.[1]
Christophe Moreno, M.D., Ph.D.[5]
Pierre Deltenre, M.D., Ph.D.[1,5]

Variables	HR	95% HR CI	p-Value	Risk score
Age >50 years	15.58	1.95-124.70	0.01	4
Alcohol intake during follow-up	2.24	1.05-4.79	0.037	1
Platelet count (Giga/mm^3)	1.74	1.02-2.96	0.042	
< 100				2
[100; 150]				1
Absence of viral eradication	11.10	1.42-86.60	0.022	3



Marot A, *et al*. Hepatology 2017;65:1419-21

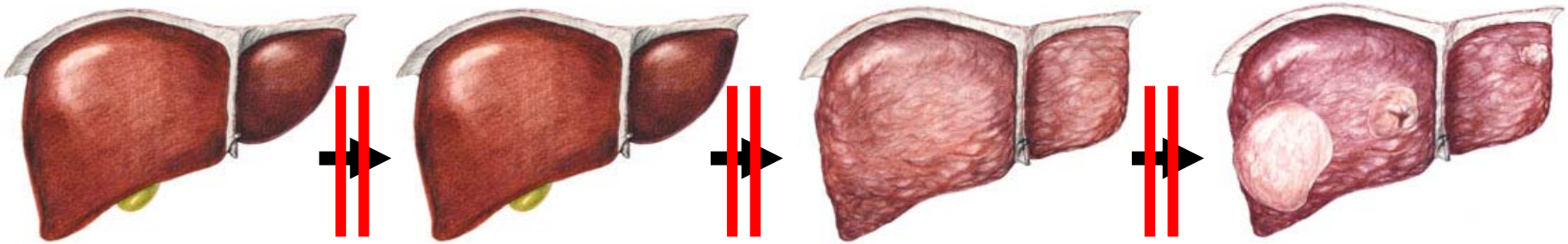
HOW WE CAN REDUCE MORTALITY RELATED TO VIRAL HEPATITIS?

1. CONTROLLING OR CURING THE INFECTION

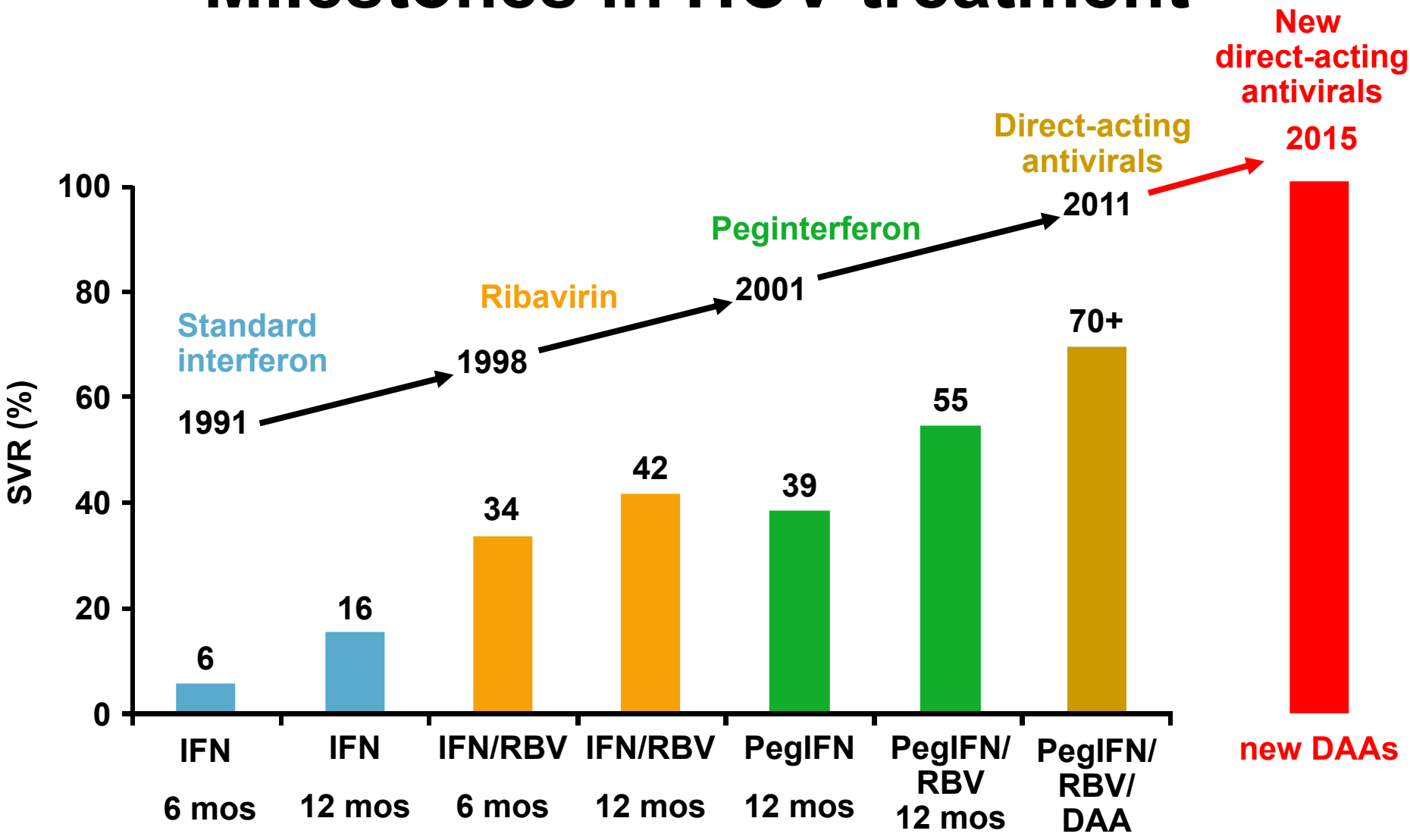
Natural history

ANTIVIRAL TREATMENT

Acute hepatitis → **Chronic hepatitis** → **Cirrhosis** → **HCC**

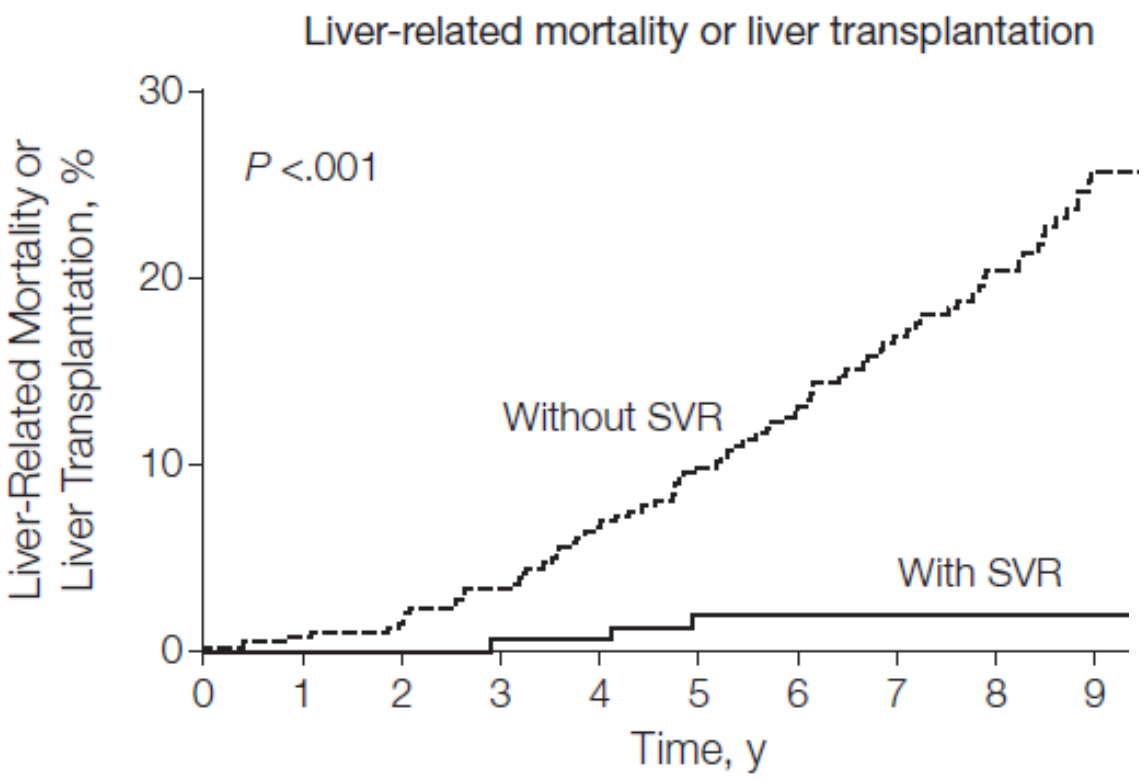


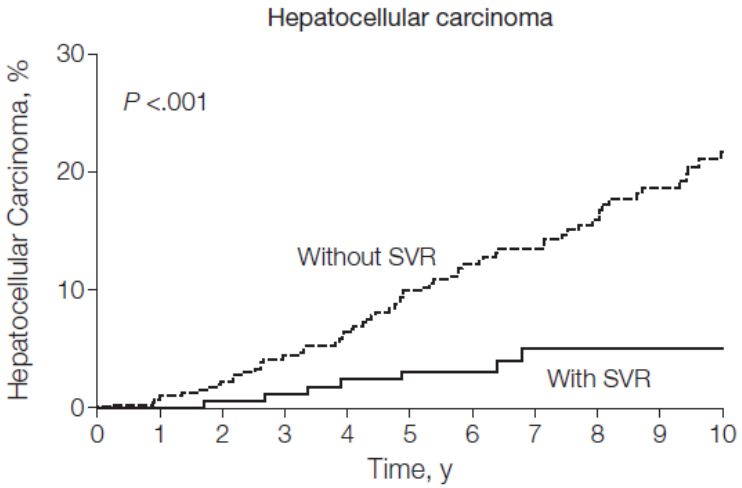
Milestones in HCV treatment

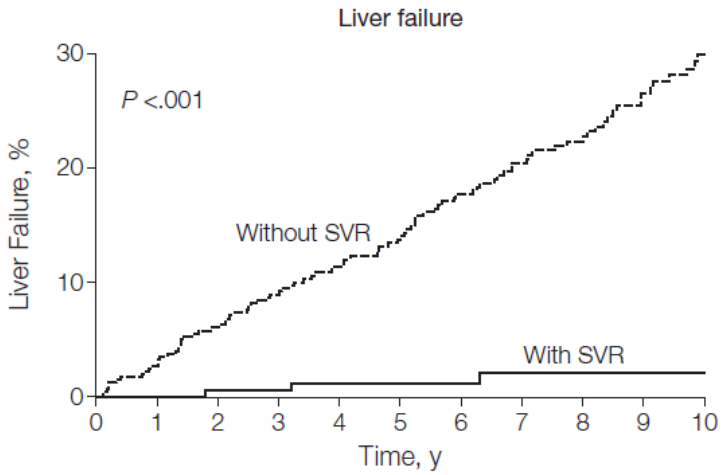


SVR is the only way to increase survival of HCV patients

530 HCV patients with extensive fibrosis or cirrhosis







Van der Meer AJ, *et al*. JAMA 2012;308:2584-93

HOW WE CAN REDUCE MORTALITY RELATED TO VIRAL HEPATITIS?

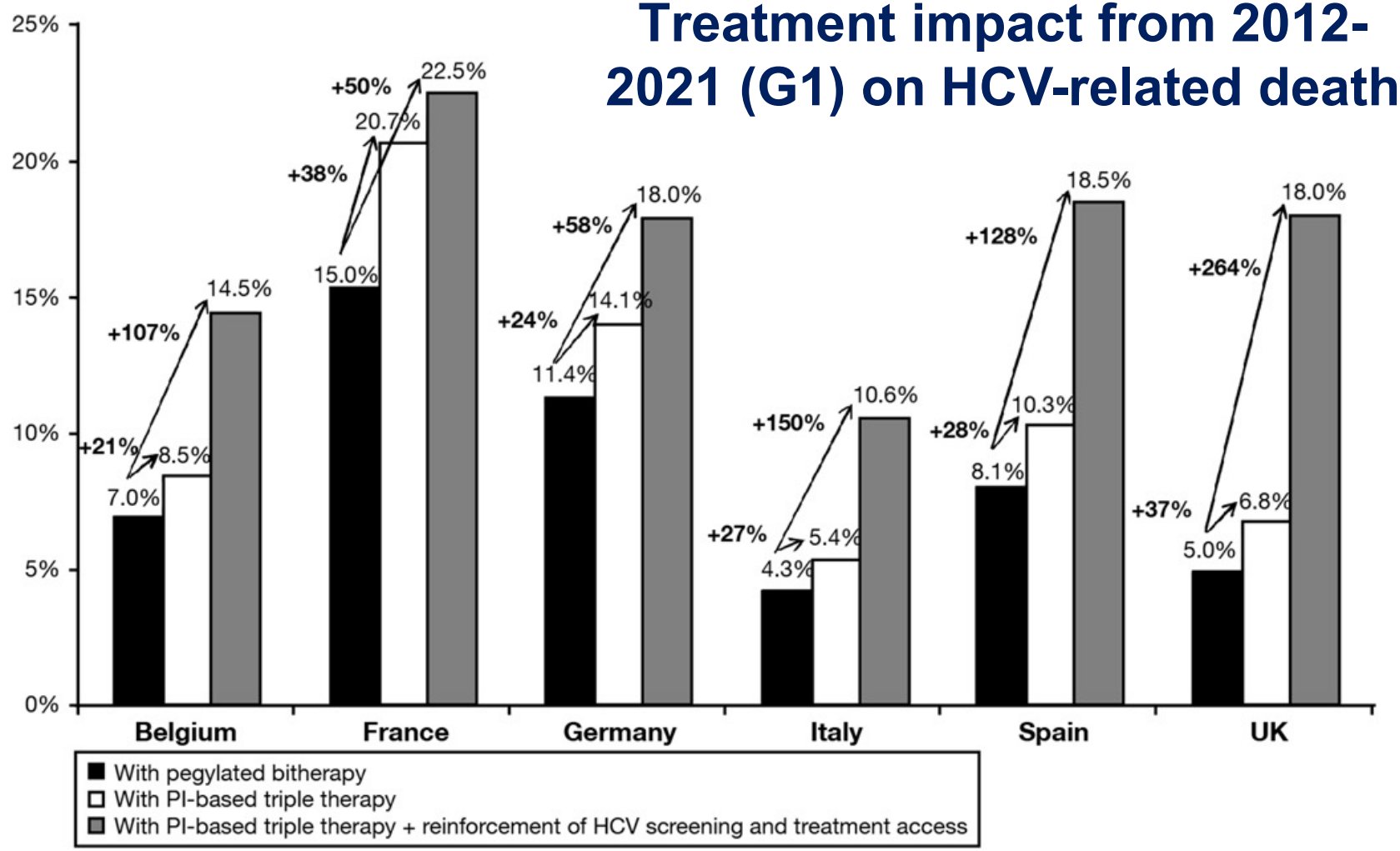
2. TREATING MORE PEOPLE

THE EXAMPLE OF HCV INFECTION

Predicted Effects of Treatment for HCV Infection Vary Among European Countries

SYLVIE DEUFFIC–BURBAN,[*,‡] PIERRE DELTENRE,[§,‖] MARIA BUTI,[¶] TOMMASO STROFFOLINI,[#] JULIE PARKES,[**] NIKOLAI MÜHLBERGER,[‡‡] UWE SIEBERT,[‡‡,§§,‖‖] CHRISTOPHE MORENO,[¶¶] ANGELOS HATZAKIS,[##] WILLIAM ROSENBERG,[***] STEFAN ZEUZEM,[‡‡‡] and PHILIPPE MATHURIN[§,§§§]

Treatment impact from 2012-2021 (G1) on HCV-related death



Deuffic-Burban S, Deltenre P, *et al.* Gastroenterology 2012;143:974-985 e914

Screening strategies

Screening strategies have a deep impact on HCV-related mortality

→ **We definitely need new screening strategies able to increase the number treated patients**

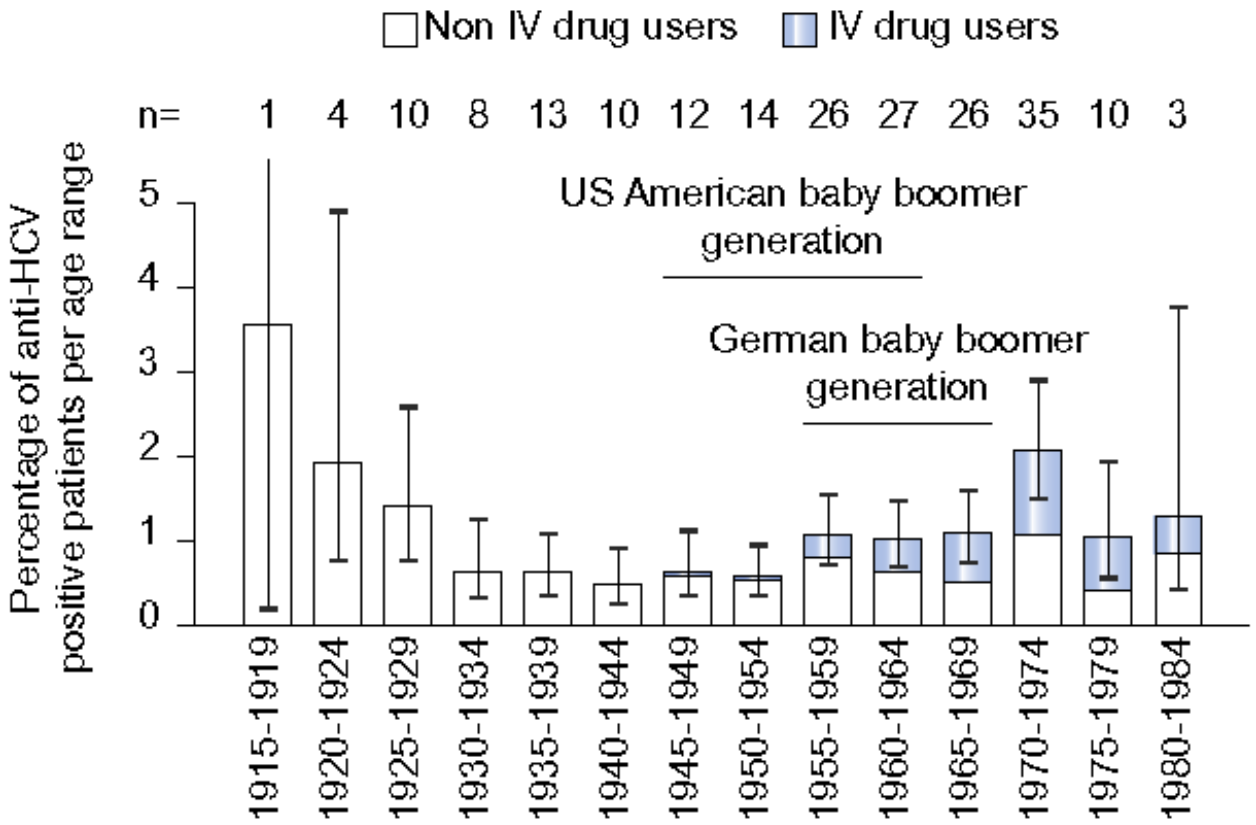
Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Recommendations and Reports / Vol. 61 / No. 4
August 17, 2012

Recommendations for the Identification of Chronic Hepatitis C Virus Infection Among Persons Born During 1945–1965

- Persons born between 1945 and 1965 account for ¾ of all HCV infections in the US
- 11% HCV Ab pos in a recent survey performed in 1287 individuals

Smith BD, *et al*. MMWR Recomm Rep 2012;61(RR-4):1-32
Galbraith JW, *et al.* Hepatology 2015;61:776-82

However…



"Check-Up 35+": 21,008 patients, 51 primary care private practices
Selection bias: patients had to consult a primary care physician in order to have a chance of being included

Wolffram I, *et al.* J Hepatol 2015;62:1256-64

However…

Birth Cohort Screening for Chronic Hepatitis During Colonoscopy Appointments

Dawn M. Sears, MD[1,2], Dan C. Cohen, MD[1,2], Kimberly Ackerman, DO[1,2], Jessica E. Ma[1,2] and Juhee Song, PhD[1,2]

OBJECTIVES: More than 70% of infections with hepatitis C viruses (HCV) occur among people born between 1945 and 1965 (baby boomers). The US Centers for Disease Control estimate that 70% of people with chronic hepatitis are not aware that they are infected with a virus. We performed a prospective trial to determine whether people born during this time period would accept testing for chronic viral infection (hepatitis B virus (HBV) and HCV) during routine colonoscopies. We also evaluated acceptance and efficacy of screening for immunity to hepatitis A (HAV) and B viruses.

METHODS: During a 3-month period, 500 people, 50–65 years old, who received a colonoscopy were offered a test for viral hepatitis. Patients answered questions about vaccination, exposure, diagnoses, and risk factors related to viral hepatitis, and blood samples were collected. Patients who tested positive for antibodies to HCV or hepatitis B surface antigen (HBsAg) were contacted for further testing and possible therapy. Patients without immunity to HAV or HBV were offered vaccinations.

RESULTS: Three hundred and seventy-six people (158 men) agreed to be tested. Four were found to have antibodies against HCV and one had detectable virus. None of the patients tested positive for HBsAg; 136 (36%) had at least one risk factor for chronic hepatitis and 31 (8%) had multiple risk factors. Three hundred and fifteen patients (84%) were not immune to HAV, HBV, or both viruses.

CONCLUSIONS: It is possible to screen patients for viral hepatitis during visits for routine colonoscopy. This approach can identify individuals with undiagnosed chronic HBV and HCV infections who could benefit from education, vaccination, or therapy.

Sears M, *et al.* AJG 2013;108:981-89

Large-scale screening is not useful to identify individuals with hepatitis B or C virus infection: Results of an Interim Analysis

Astrid Marot[1*], Aicha Trabelsi[1*], Cyril André[2], Pierre Deltenre[1,3]

[1] Division of Gastroenterology and Hepatology, Centre Hospitalier Universitaire Vaudois, University of Lausanne, Lausanne, Switzerland , [2] Division of immunology and allergology, Centre Hospitalier Universitaire Vaudois, Lausanne, Suisse,[3] Department of Gastroenterology, Hepatopancreatology and Digestive Oncology, CUB Hôpital Erasme, Université Libre de Bruxelles, Brussels, Belgium (* Equal contribution)

PREVALENCE 0.4%

	Whole cohort (n=1345)	Anti-HCV negative (n=1256)	Anti-HCV positive (n=5)	*p-Value*
Age (years) *	44 (43-45) *	44 (43-45) *	49 (39-54) **	0.14
Gender (n of male, %)	678/1345 (50%)	632/1256 (50%)	3/5 (60%)	0.7
Swiss patients	900/1318 (68%)	848/1233 (69%)	4/5 (80%)	0.6
Previous screening for HBV infection	256/1275 (20%)	241/1193 (20%)	4/5 (80%)	< 0.001
Previous vaccination for HBV infection	378/992 (38%)	356/931 (38%)	2/4 (50%)	0.6
Previous screening for HCV infection	146/1188 (12%)	133/1112 (12%)	5/5 (100%)	< 0.001
Risk factors for infection (n, %)				
Intravenous drug use	6/1268 (0.5%)	2/1184 (0.2%)	4/5 (80%)	< 0.001
Nasal drug use	82/1240 (6.6%)	74/1160 (6.4%)	4/5 (80%)	< 0.001
Cannabis use	93/1271 (7.3%)	87/1186 (7.3%)	4/5 (80%)	< 0.001

* Data expressed in median (95% CI) ** Data expressed as range

Marot A, *et al*. International Liver Congress 2017

Large-scale screening is not useful to identify individuals with hepatitis B or C virus infection: Results of an Interim Analysis

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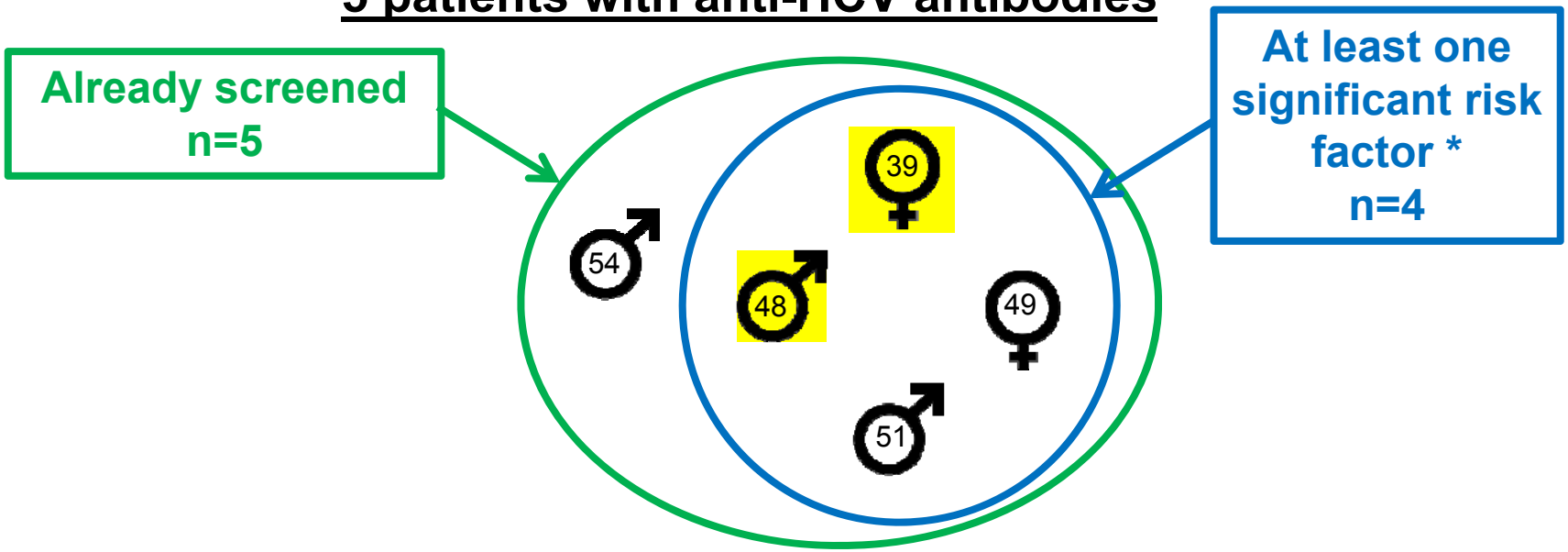
[1] Division of Gastroenterology and Hepatology, Centre Hospitalier Universitaire Vaudois, University of Lausanne, Lausanne, Switzerland , [2] Division of immunology and allergology, Centre Hospitalier Universitaire Vaudois, Lausanne, Suisse,[3] Department of Gastroenterology, Hepatopancreatology and Digestive Oncology, CUB Hôpital Erasme, Université Libre de Bruxelles, Brussels, Belgium (* Equal contribution)

5 patients with anti-HCV antibodies



* Risk factors considered as significant
- Transfusion before 1992 (n=0)
- Intravenous drug use (n=4)
- Intranasal drug use (n=4)
- Tattoo or piercing with non-sterile material (n=0)

NB. Patients underlined in yellow had detectable HCV RNA

Marot A, *et al*. International Liver Congress 2017

Conclusions

What we need to know when a patient has viral hepatitis B or C

1. HBV and HCV chronic infections kill people --- don’t underestimate the risk
2. Pay attention to avoidable risk factors
3. Available treatments highly effective --- should be used in any case at risk of disease progression
4. Find undiagnosed infected people --- effective screening strategies still need to be defined