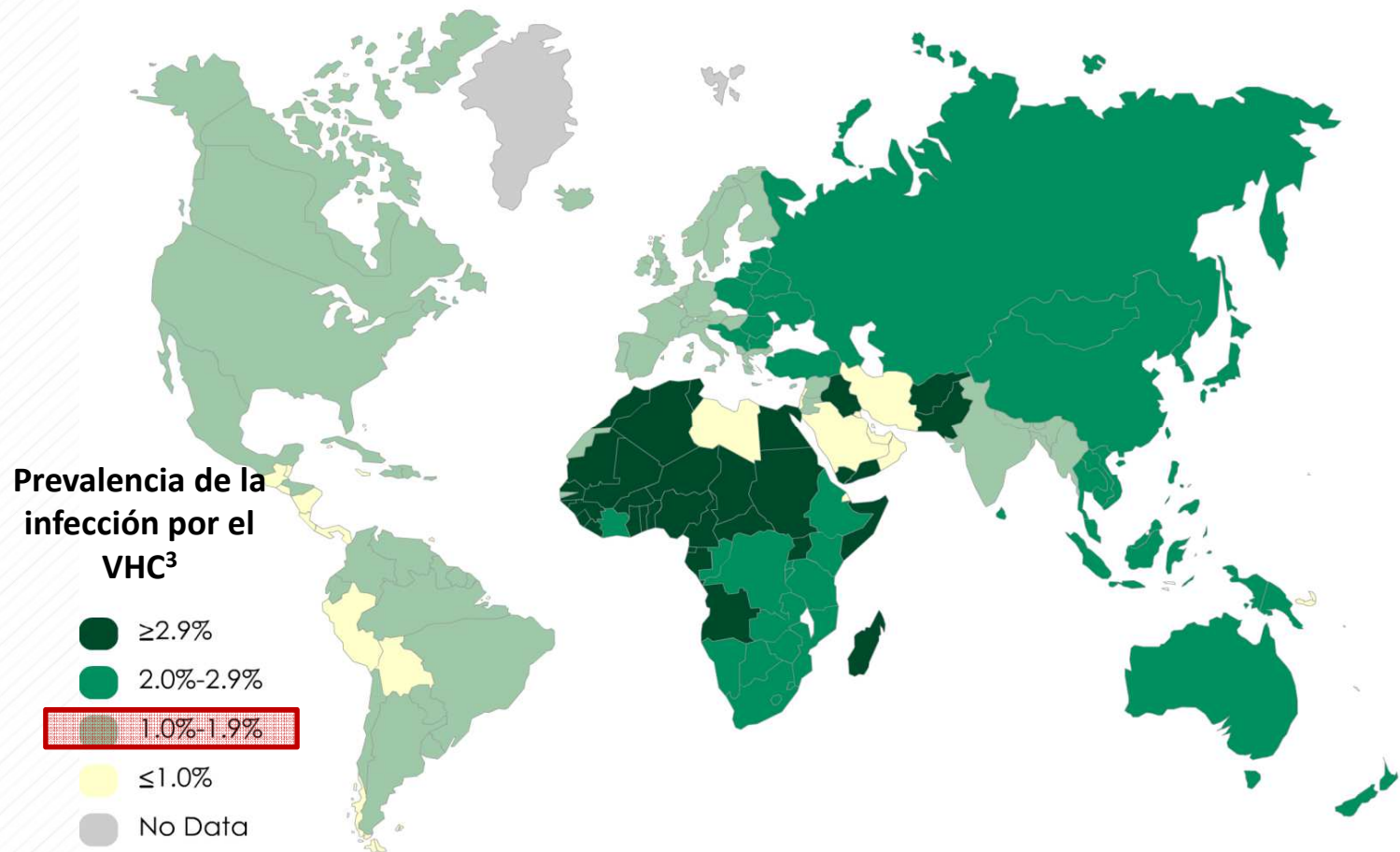# Futuro de la Epidemiologia y del Tratamiento del VHC. ¿Caminando hacia la erradicación?

Rafael Esteban

Hospital Universitario Valle Hebron. Barcelona, Spain

Hepatitis C es un problema de salud

130–170 millones de personas están infectadas con el virus de la hepatitis C (VHC)[1,2]

Prevalencia de la infección por el VHC[3]

- ≥2.9%
- 2.0%-2.9%
- 1.0%-1.9%
- ≤1.0%
- No Data

1. Lavanchy D *Liver International* 2009; 29:74-81
2. Averhoff FM, et al. *Clin Infect Dis.* 2012;55(S1):S10-S15.
3. Global Burden of Hepatitis C Working Group. *Journal of Clinical Pharmacology.* 2004;44:20-29
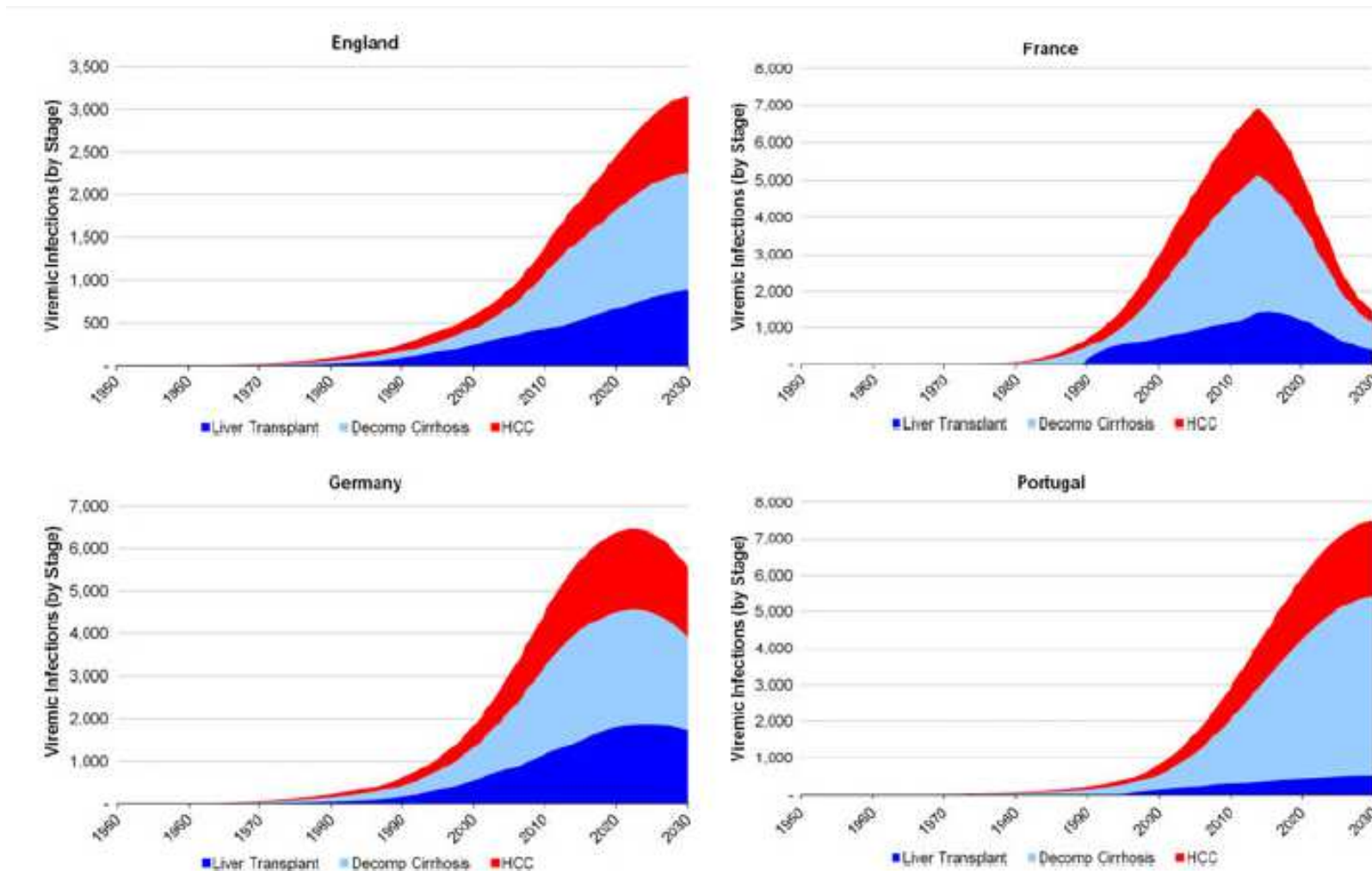
Estimated HCV prevalence, diagnosis rate and treatment uptake

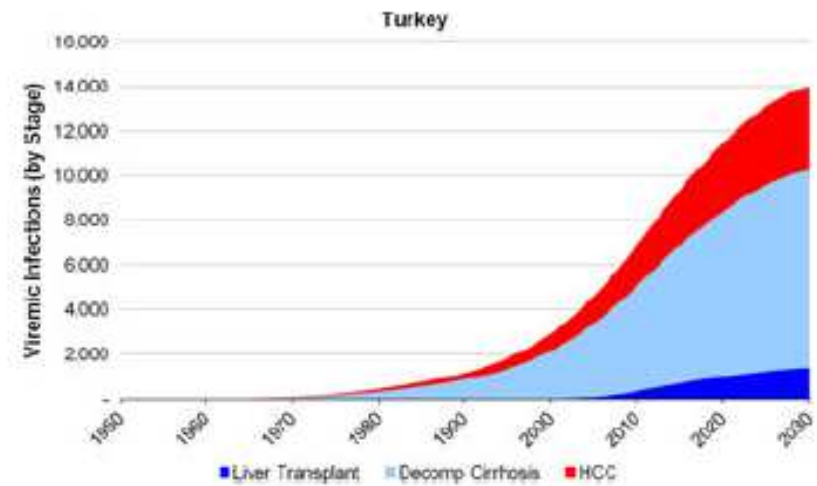- **Prevalencia estimada de la HCC, tasa de diagnóstico y tasa de tratamiento en 2013**

Dore GJ, Ward J and Thursz M. Journal of Viral Hepatitis 2014, 21 (Suppl 1): 1-4.
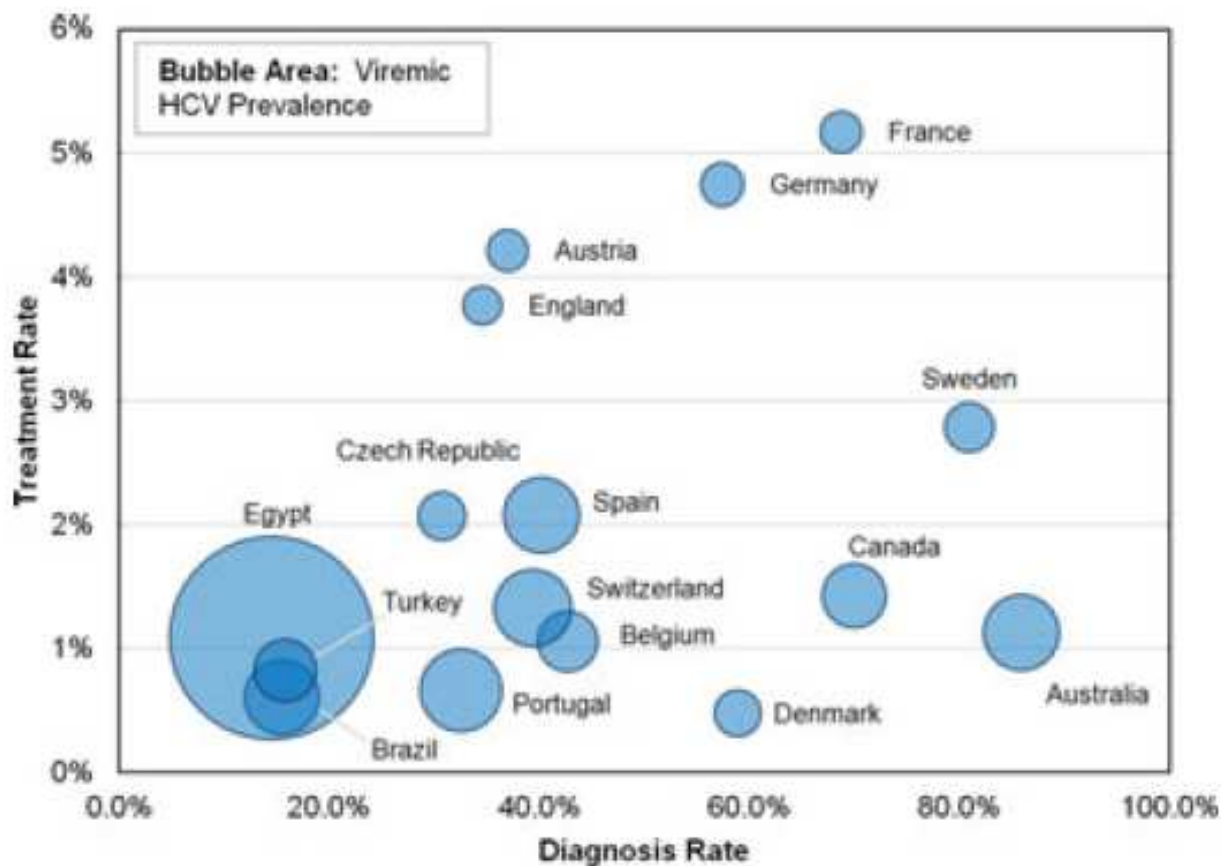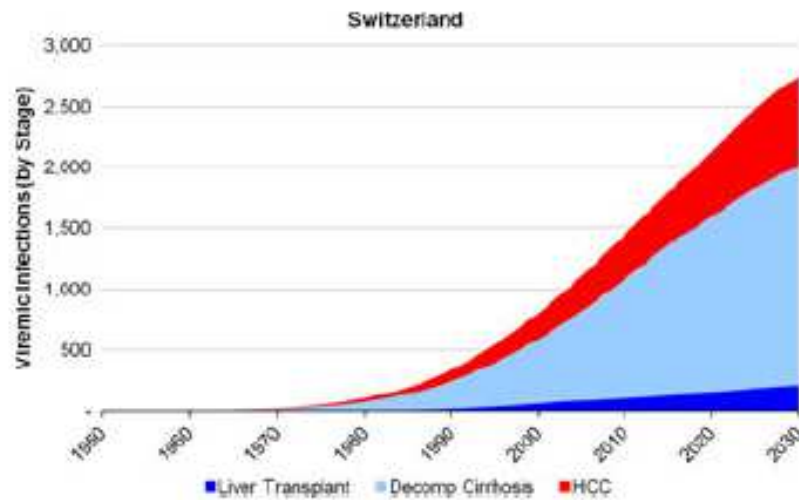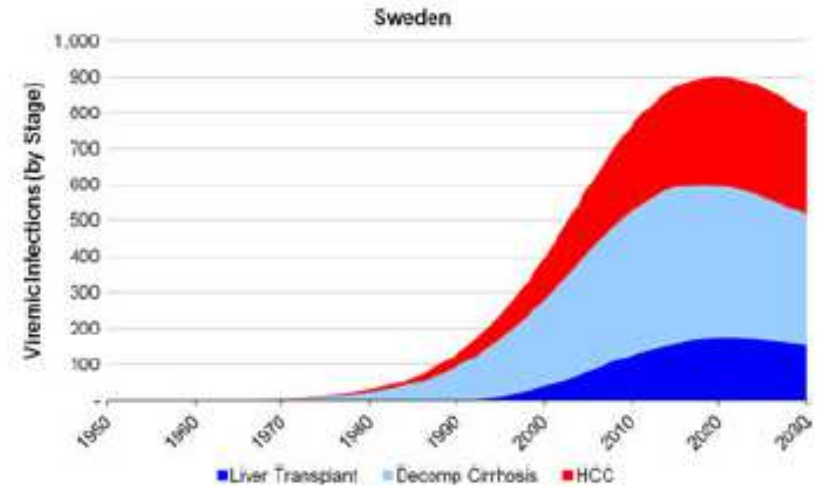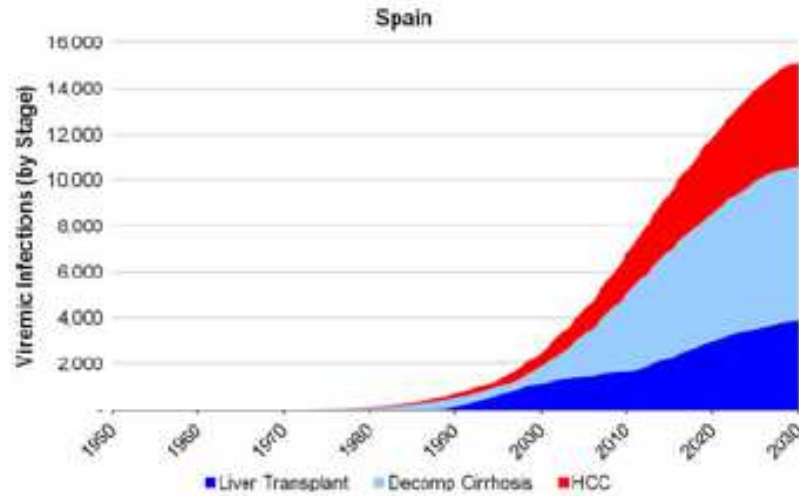
Mortality projection related to HCV In Europe

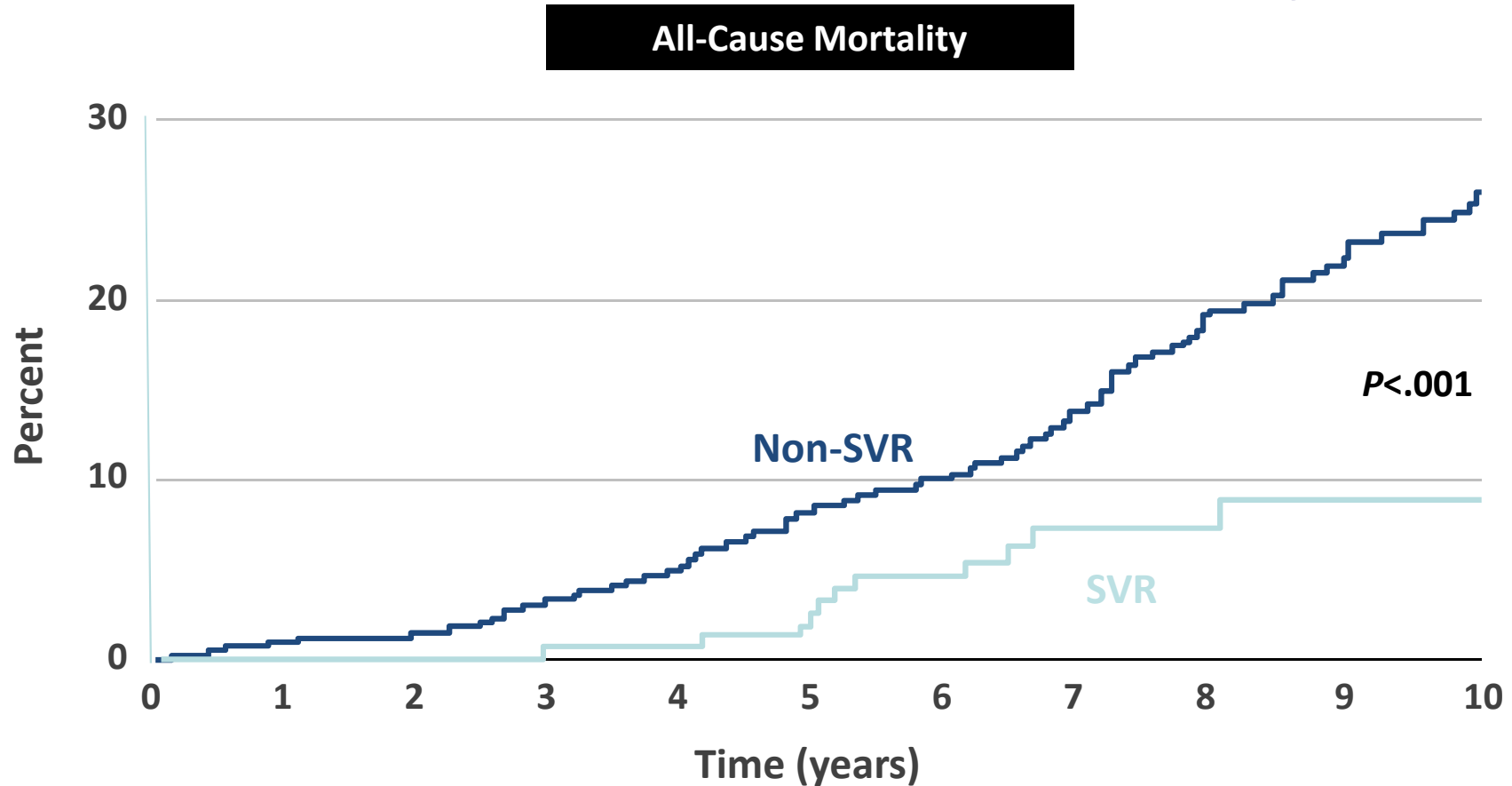**Changes in the number of liver transplants, decompensated cirrosis and HCC cases over time**

Mortality projections related to HCV

SVR Was Associated With Reduced Long-Term Risk of All-Cause Mortality in HCV Patients with cirrhosis
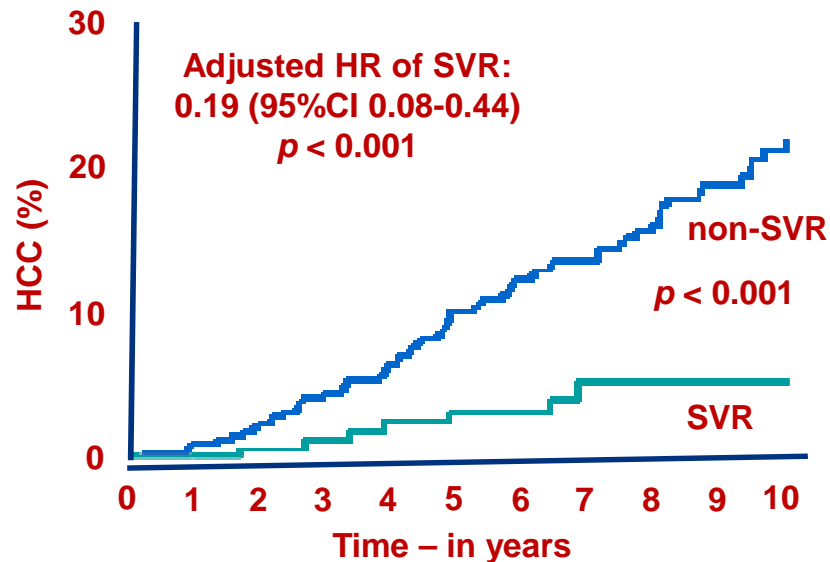## Results of an International, Multicenter Study

All-Cause Mortality

Non-SVR

SVR

P<.001

Percent

Time (years)

Liver-related Mortality and Morbidity
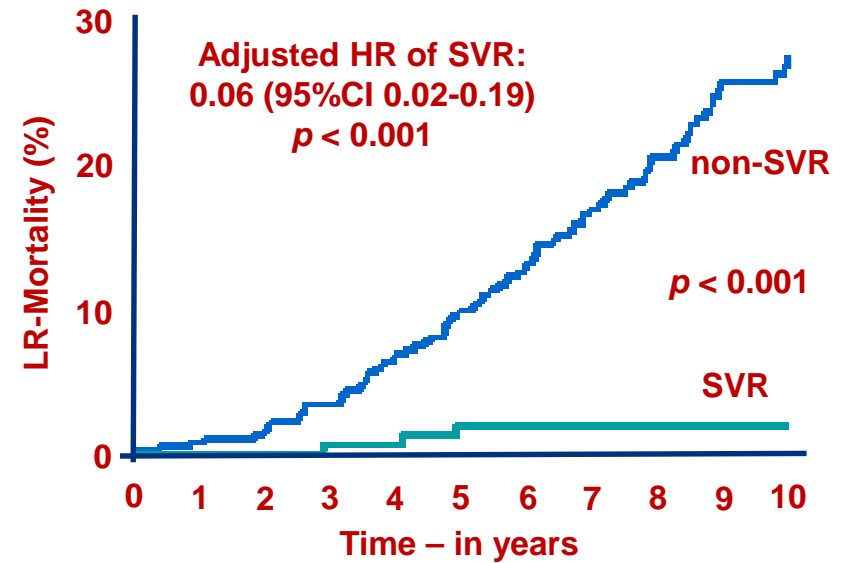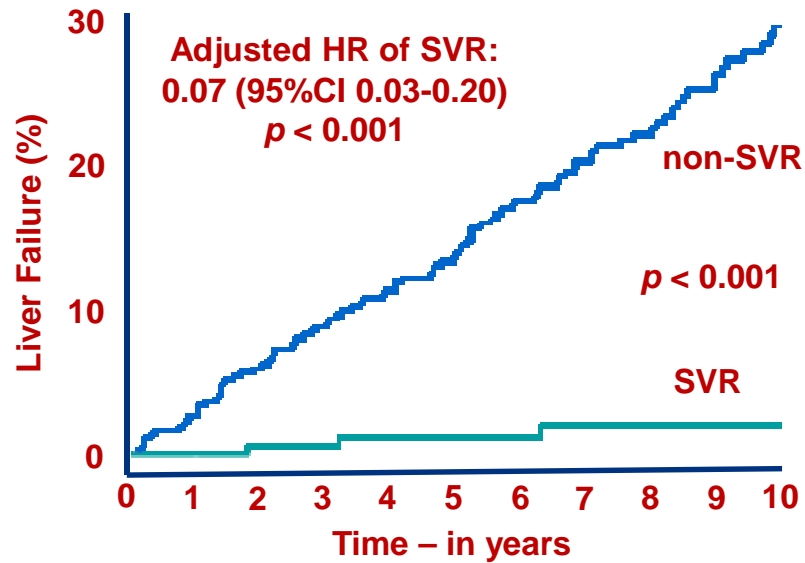
n=530

Median Follow-up 8.4 yrs

Spain Hepatitis C Action Plan

Aim of the Plan:

To Reduce HCV morbidity/mortality in the Spanish population

Objective

Make Prevention/Diagnosis/Treatment and Follow up of the patients

Intervention

Euros 1.000 million additional investment 2015-17

Phase 1

2015-2017

PATIENTS TREATED IN THE NATIONAL STRATEGIC PLAN 2015

TOTAL
- 3154
- 24491
- 27645

VIEKIRAX/EXVIERA
- 6292
- 6292

HARVONI
- 11450
- 11450

SOVALDI/OLYSIO/DAKLINZA
- 2475
- 5932
- 8407

OLYSIO+INTERFERON
- 679
- 817
- 1496
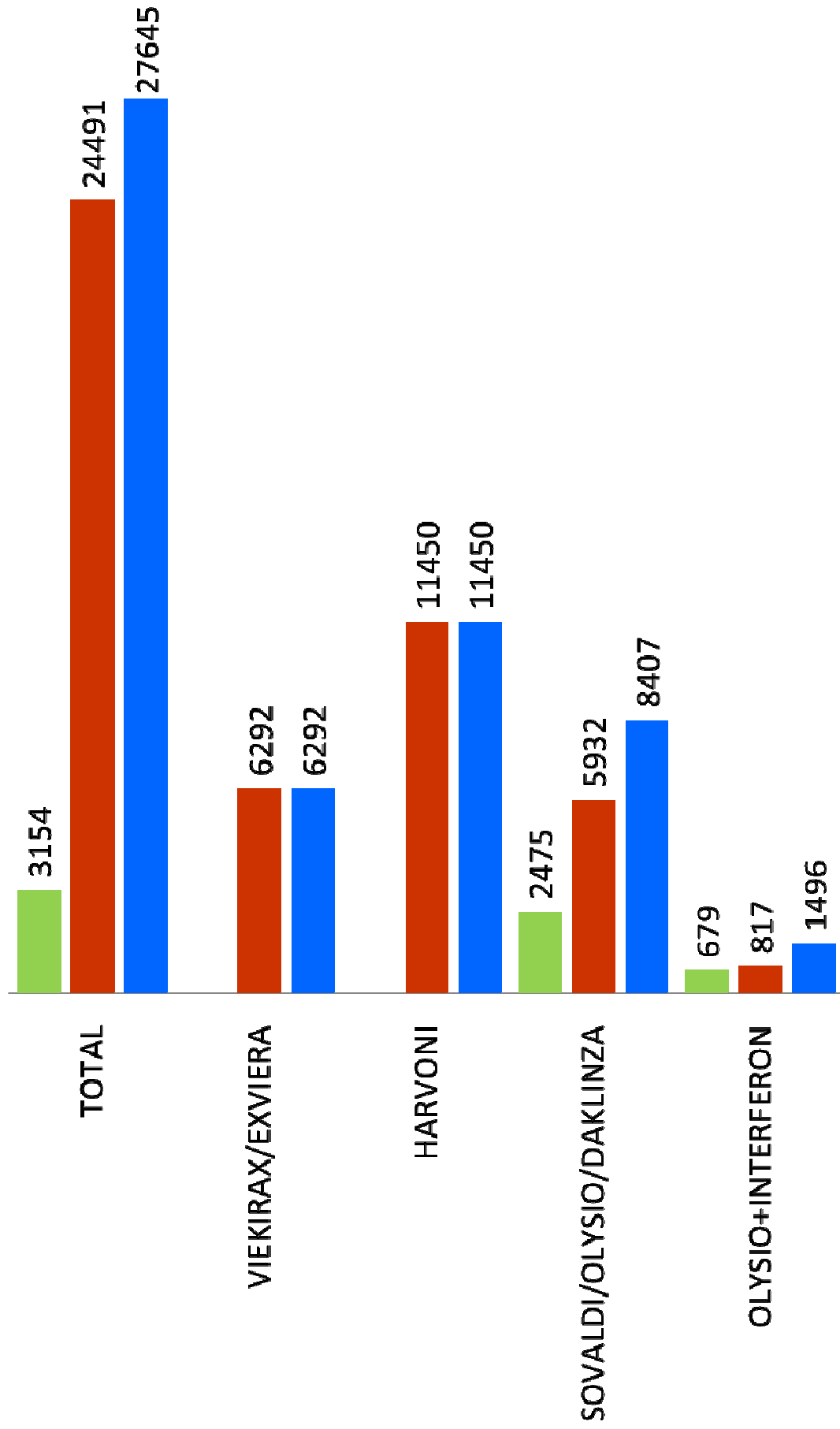
- PACIENTES TRATADOS ENERO -31 DE MARZO
- PACIENTES TRATADOS 1 ABRIL-30 DE SEPTIEMBRE
- PACIENTES TRATADOS 1 ENERO - 30 DE SEPTIEMBRE

MINISTERIO
DE SANIDAD, SERVICIOS SOCIALES
E IGUALDAD

GOBIERNO
DE ESPAÑA

C-EDGE TN: GZR/EBR for 12 Weeks in TN GT 1, 4, or 6 Patients

Study Design and Demographics

Phase 3, randomized study of grazoprevir (GZR, NS3/4A inhibitor) / elbasvir (EBR, NS5A inhibitor)

Wk 0		12	16	24	28

n=316 — GZR / EBR ◆ SVR12

n=105 — Placebo GZR / Placebo EBR → GZR / EBR // ◆ SVR12

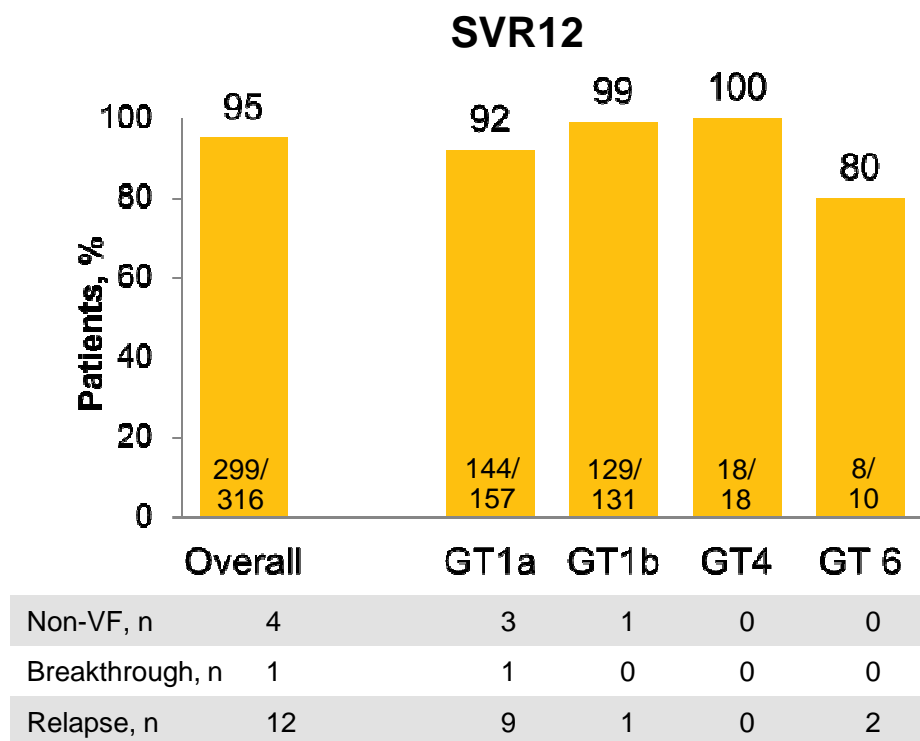Once daily dosing of GZR 100 mg / EBR 50 mg
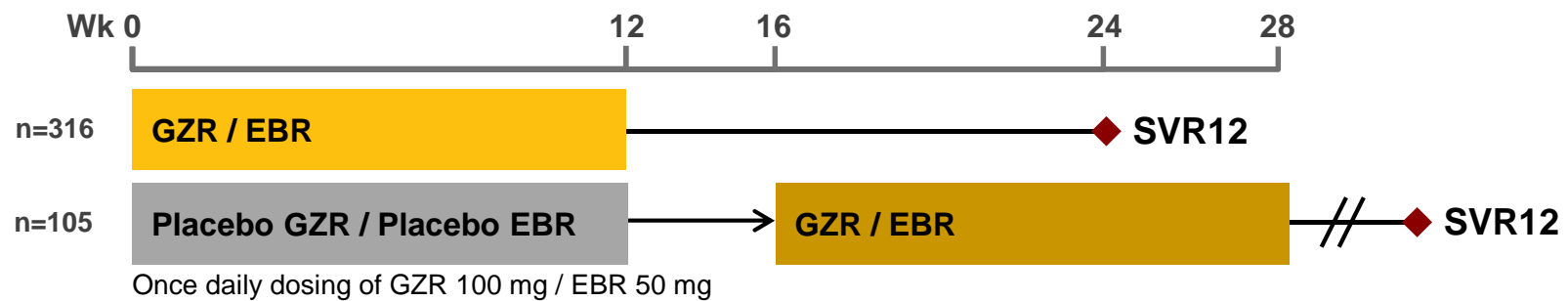
Patients	GZR + EBR n=316	Placebo n=105	Total n=421
Age, years, mean (SD)	52.2 (11.1)	53.8 (11.2)	52.6 (11.2)
Male, n (%)	171 (54)	56 (53)	227 (54)
HCV genotype, n (%)			
1a	157 (50)	54 (51)	211 (50)
1b	131 (42)	40 (38)	171 (41)
4	18 (6)	8 (8)	26 (6)
6	10 (3)	3 (3)	13 (3)
Baseline HCV RNA > 800,000 IU/mL, n (%)	222 (70)	66 (63)	288 (68)
Cirrhosis, n (%)	70 (22)	22 (21)	92 (22)

Zeuzem, EASL, 2015, G07;
Zeuzem, et al. Ann Intern Med
Published Online April 2015

Efficacy and Safety

SVR12

	Overall	GT1a	GT1b	GT4	GT 6
Non-VF, n	4	3	1	0	0
Breakthrough, n	1	1	0	0	0
Relapse, n	12	9	1	0	2

Safety Overview

	GZR/EBR n=316	Placebo N=105
SAE, n (%)	9 (3)	3 (3)
D/C due to AE, n (%)	3 (1)	1 (1)
Death	2 (<1)*	0

*1 autopsy documented coronary disease (presumed arrhythmia); 1 strangulated hiatal hernia

- Relapse primarily occurred in GT 1a and GT 6 patients
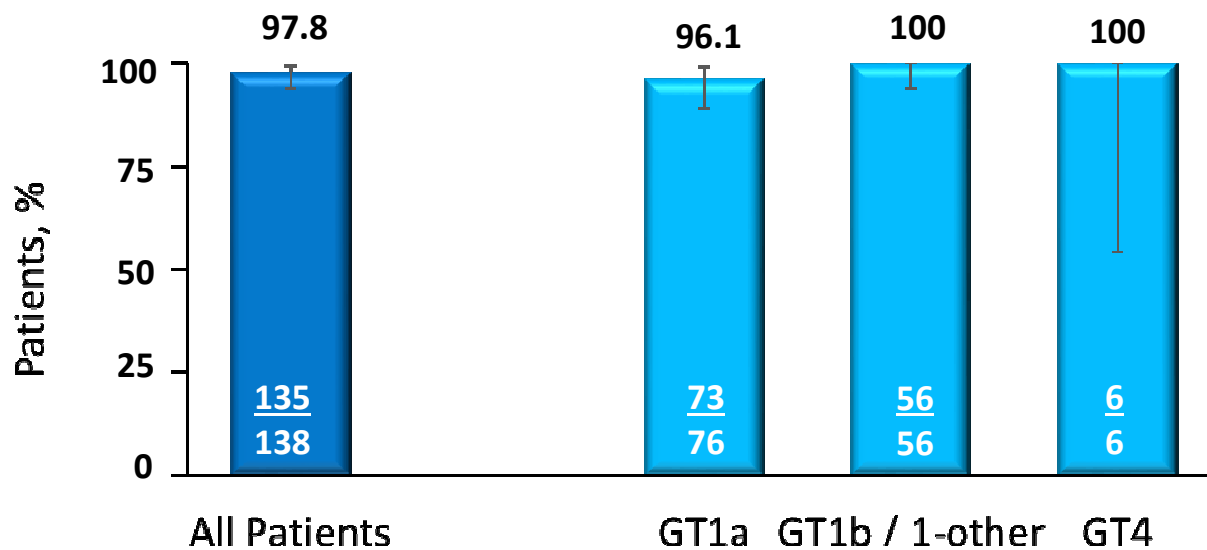- Most common AEs: headache, fatigue, nausea, arthralgia

SVR12: TREATMENT-NAIVE
12 WEEKS, NO RBV (FULL ANALYSIS SET)

	All Patients		GT1a	GT1b / 1-other	GT4
LTFU/Early Discon.	1*		1*	0	0
SVR12 (mFAS§)	98.5% (135/137)		97% (73/75)	100% (56/56)	100% (6/6)
Breakthrough	1		1	0	0
Relapse	1		1	0	0

*Death (coronary artery disease)
§mFAS (modified full analysis set) excludes patients who discontinued treatment for reasons unrelated to study medication
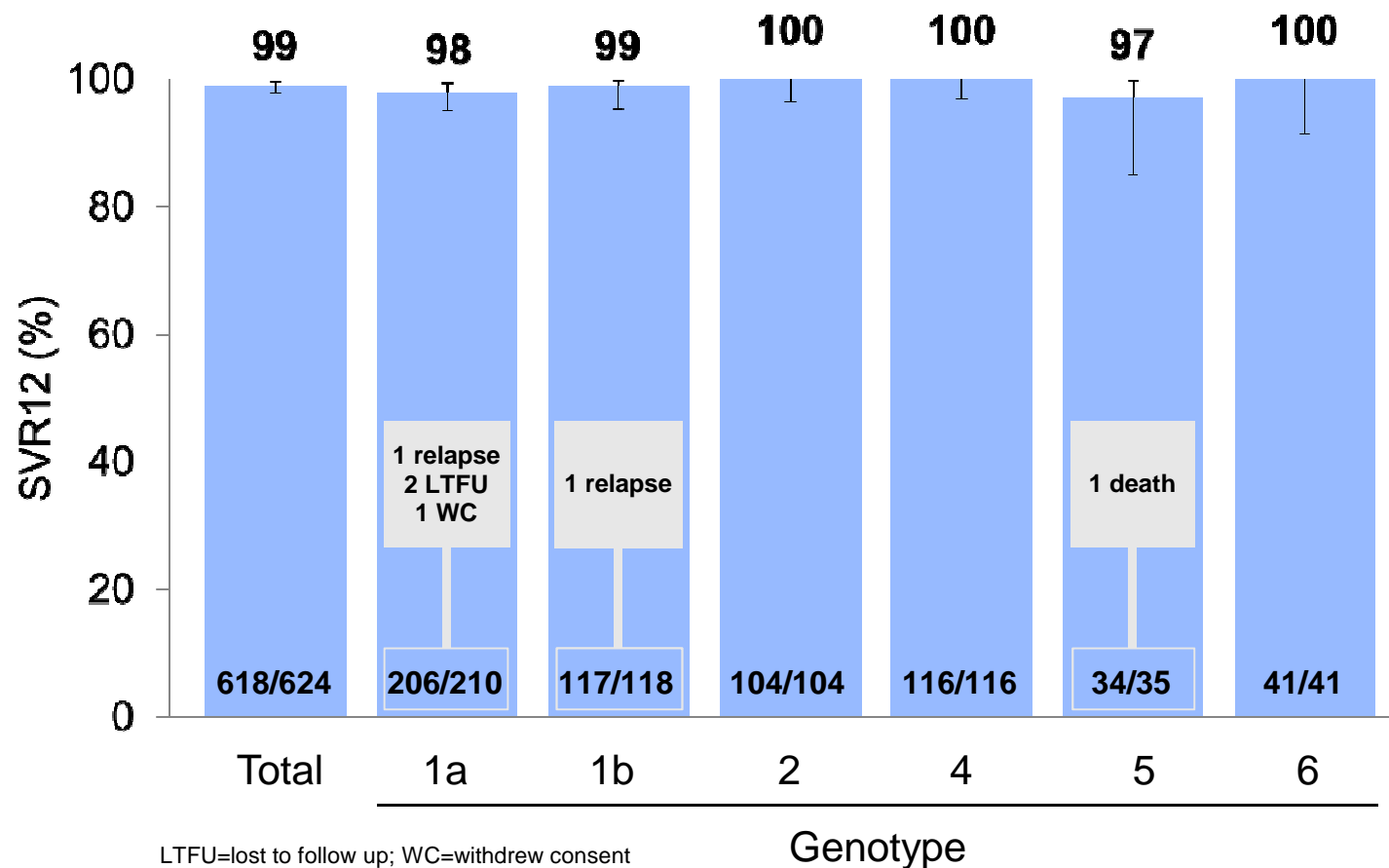
GZR/EBR ± RBV for 12 weeks in G1/4 patients who previously failed PegIFN/RBV: C-EDGE treatment-experienced trial
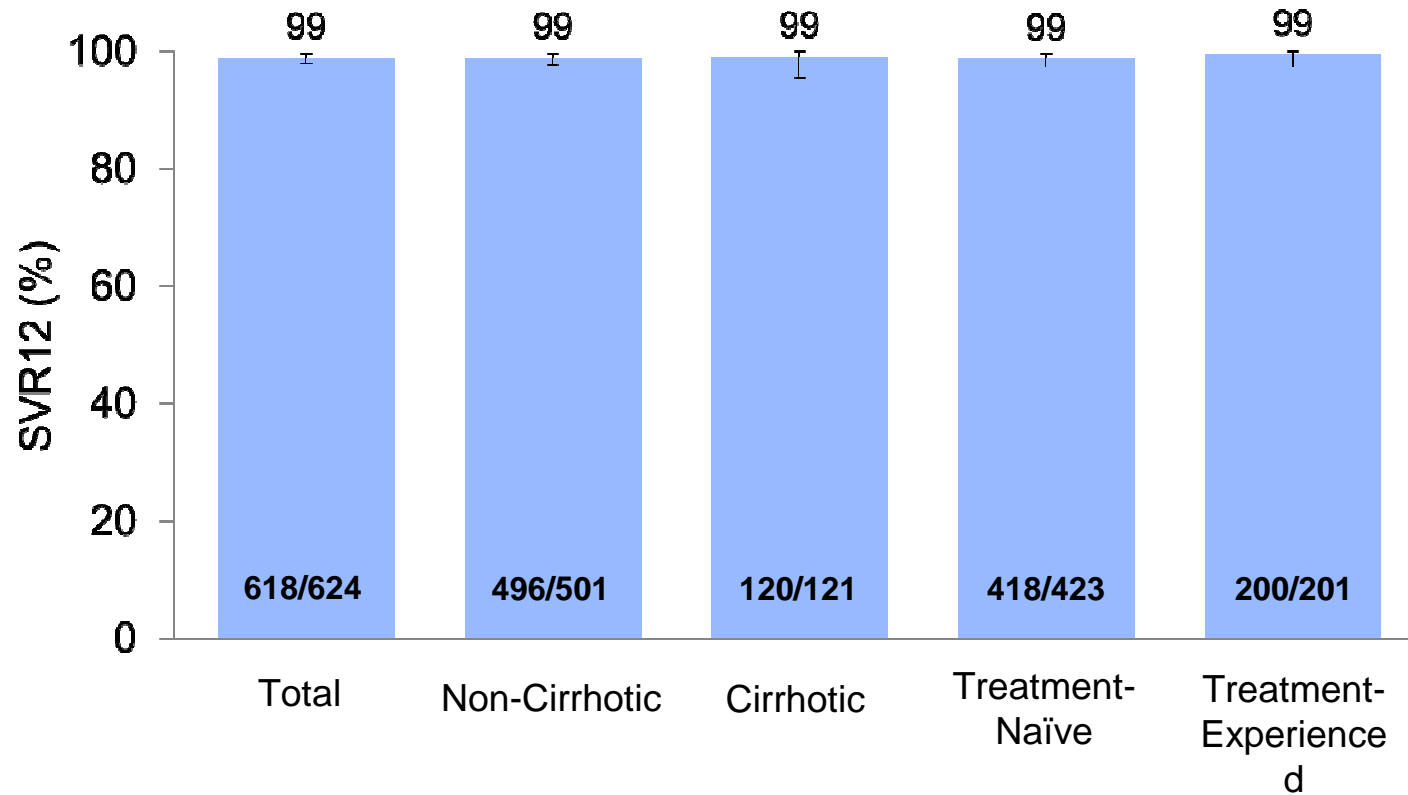
SVR according to baseline factors

Kwo P, et al. EASL 2015, Vienna. #P0886
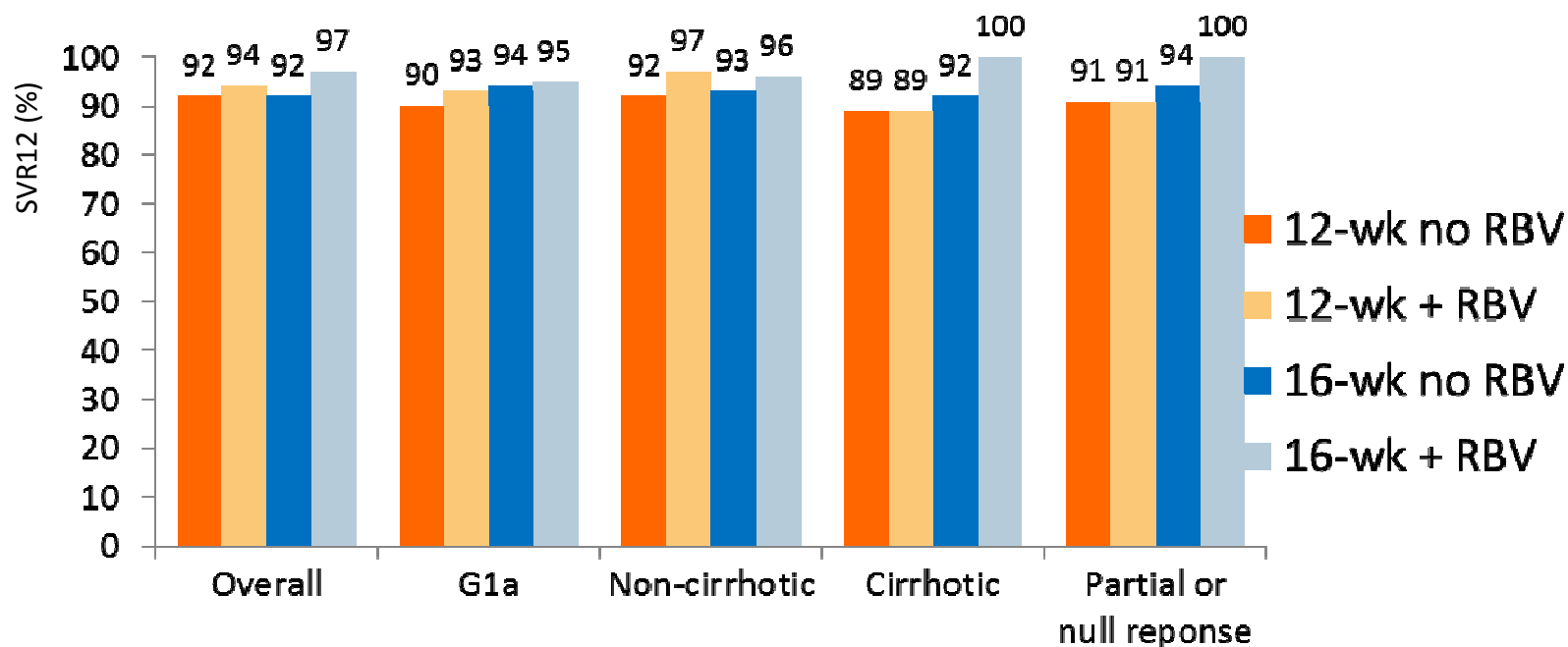
ASTRAL-1: SOF/VEL STR for 12 Weeks in GT 1, 2, 4, 5, 6 HCV-Infected Patients
SVR12 by Genotype

LTFU=lost to follow up; WC=withdrew consent

SVR12 by Cirrhosis Status or Treatment History

ASTRAL-1: SOF/VEL STR for 12 Weeks in GT 1, 2, 4, 5, 6 HCV-Infected Patients

Error bars represent 95% confidence intervals.

Feld, AASLD, 2015, LB-2. Feld JJ, et al. *N Engl J Med.* 2015. DOI: 10.1056/NEJMoa1512610

The Real Problem:
Under-diagnosis & Under-treatment

- **In wealthy countries - >50% of infected individuals remain undiagnosed!**
  - **USA 72%[1]**
  - **France 44-55%[2]**

- **In resource-poor countries – the figures are much more discouraging**
  - **Minimal data but very low diagnosis rates**

1. Rein Ann Int Med 2012 2. Defossez Eur J Gastro Hep 2008 3. Shah CMAJ 2013