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Regione Lombardia
ASST Fatebenefratelli Sacco

GIORNATE INFETTIVOLOGICHE "LUIGI SACCO"

Milano, 25-26 Maggio 2017

Epatite acuta C: trattare o non trattare?

L. Milazzo

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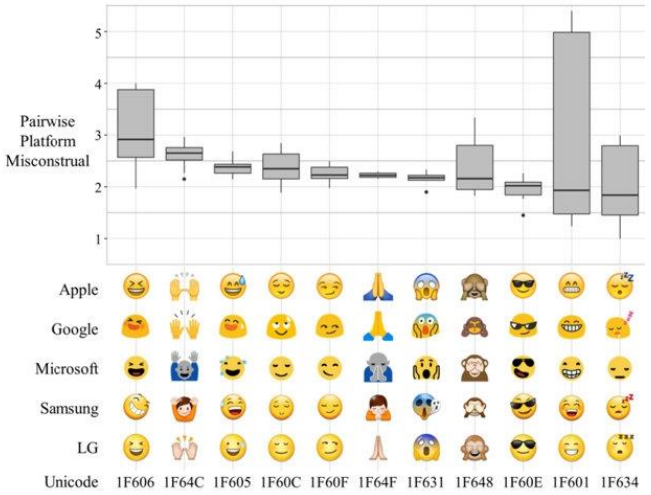

✓ Le dimensioni del problema

✓ quando trattare

✓Perché trattare (o non trattare) in fase acuta

- Prevenire l'evoluzione della malattia nel singolo
- Prevenire la diffusione dell'infezione nella popolazione

✓ per quanto tempo trattare

✓Le dimensioni del problema

INCIDENZA EPATITE ACUTA C IN ITALIA

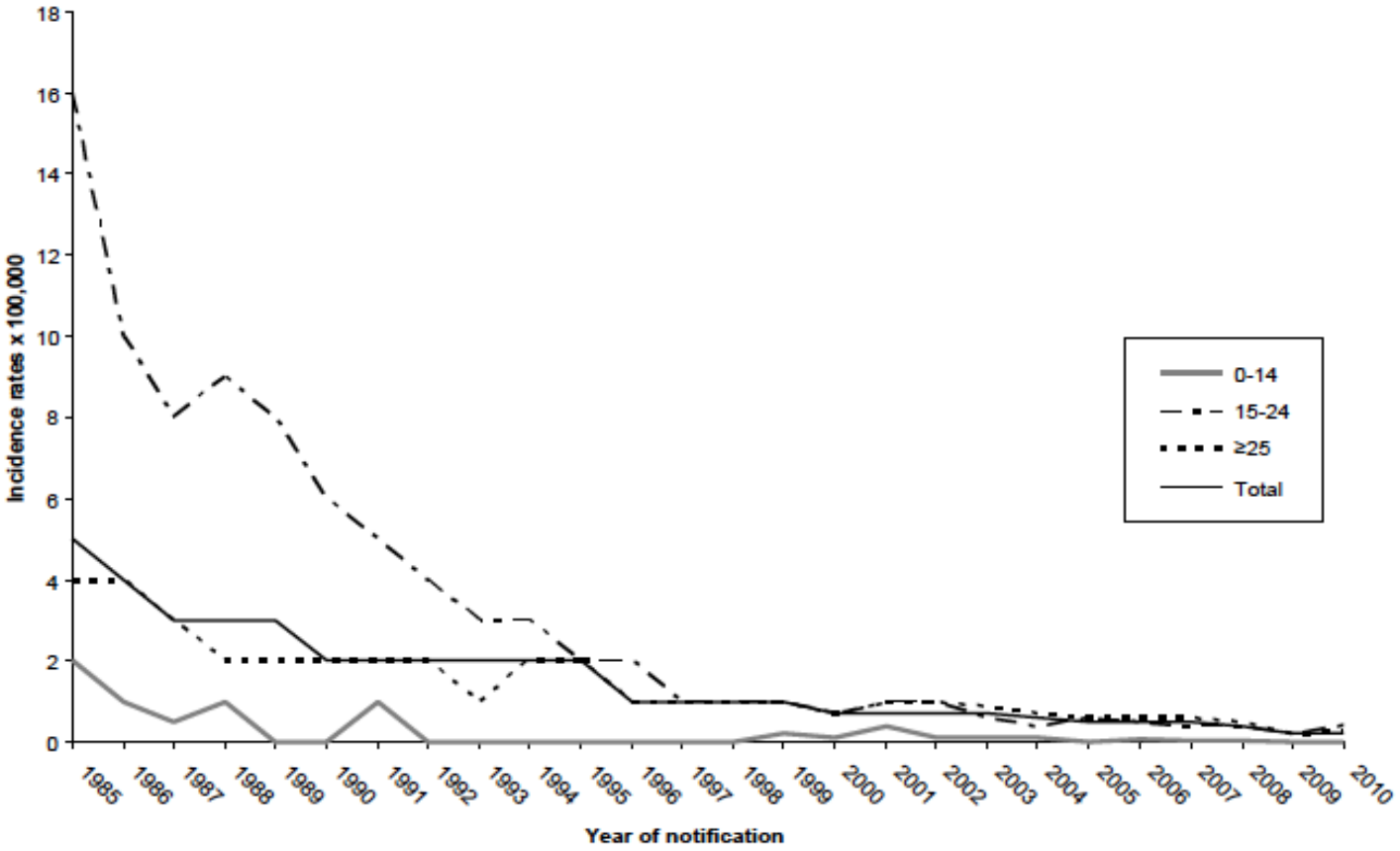

Figure 12. Incidence of reported acute HCV infection, by year and age group. (SEIEVA 1985-2010)

Tassi annuali/100.000 per età, sesso, ed area geografica. SEIEVA 2015

	Nord-centro*			Sud-isole**			Italia		
Epatite C									
Età	**Maschio**	**Femmina**	**Totale**	**Maschio**	**Femmina**	**Totale**	**Maschio**	**Femmina**	**Totale**
0-14	0,00	0,05	0,02	0,00	0,00	0,00	0,00	0,03	0,02
15-24	0,11	0,18	0,15	0,00	0,17	0,08	0,08	0,18	0,13
25-34	0,19	0,12	0,15	0,15	0,00	0,07	0,18	0,09	0,14
35-54	0,39	0,27	0,33	0,15	0,07	0,11	0,34	0,23	0,28
≥55	0,16	0,09	0,13	0,17	0,07	0,11	0,16	0,09	0,13
Totale	0,21	0,15	0,18	0,11	0,06	0,09	0,19	0,13	0,16

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Casi notificati di epatite C in Italia con fattore di rischio identificato. SEIEVA 2015

		Fascia di età										TOTALE	
		0-14		15-24		25-34		35-54		55+			
	Fattore di rischio	N.	%	N.	%	N.	%	N.	%	N.	%	N.	%
Parenterale o sessuale	Trasfusione sangue	0	0,0	1	16,7	0	0,0	0	0,0	3	20,0	4	6,1
	Interventi chirurgici	1	100,0	2	33,3	0	0,0	11	30,6	8	47,1	22	32,4
	Ospedalizzazione	0	0,0	0	0,0	0	0,0	1	2,9	2	11,1	3	4,4
	Altre esposizioni parenterali**	0	0,0	1	20,0	0	0,0	10	27,8	6	35,3	17	25,4
	Terapia odontoiatrica	1	100,0	0	0,0	0	0,0	16	44,4	5	29,4	22	32,8
	Uso di droghe E.V.	0	0,0	2	40,0	5	62,5	3	8,3	0	0,0	10	14,7
	Convivente tossicodipendente	0	0,0	0	0,0	1	12,5	1	2,9	0	0,0	2	3,1
	Contatto con itterico nei 6 mesi	0	0,0	0	0,0	0	0,0	3	8,8	0	0,0	3	4,9
	Partner sessuali (>1 nell'ultimo anno)	0	0,0	2	50,0	2	66,7	9	45,0	0	0,0	13	40,6
	Convivente di soggetto HCV+	0	0,0	0	0,0	4	57,1	3	10,7	0	0,0	7	13,0
	TOTALE CASI***	1		6		9		37		18		71	

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In ogni caso la punta di un iceberg

Recent data from the UK have shown that of all **3811 HIV-negative MSM** attending a London clinic for sexual health screening, **only 565 (14.82%)** were tested for HCV although there are data also from the UK describing a cohort of 36 HIV-negative MSM with AHC

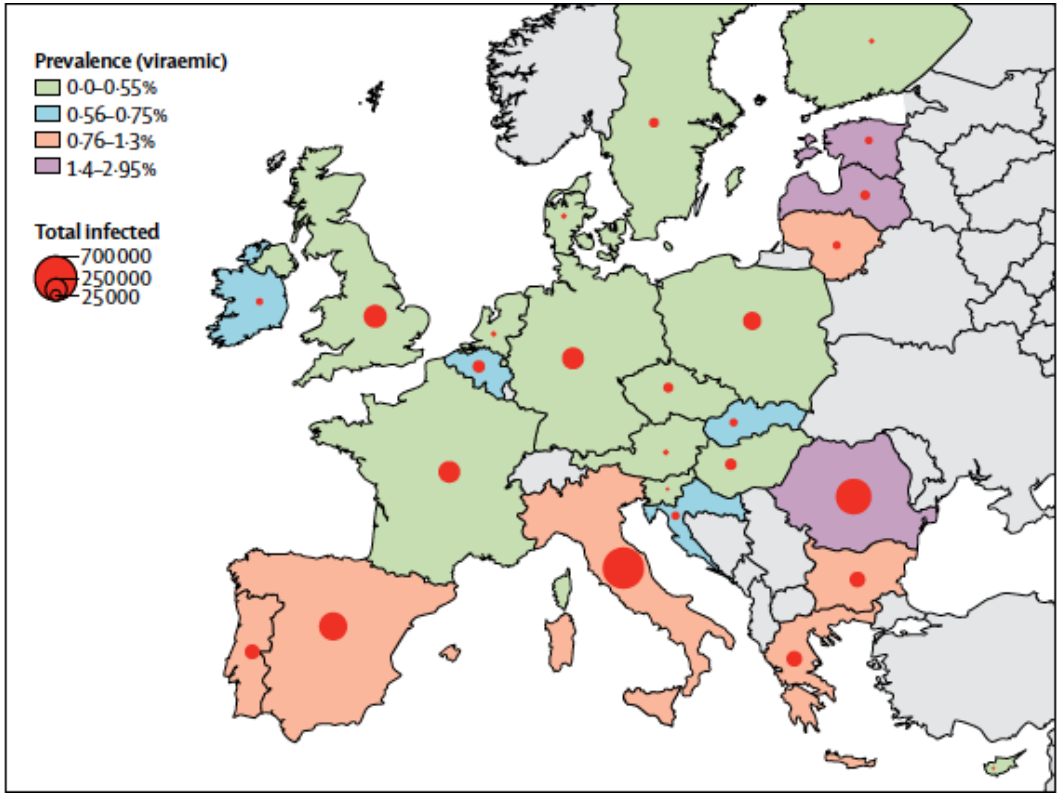
At least annual **anti-HCV antibody and 6-month ALT measurements** followed by **HCV RNA** testing in cases of suspected AHC seem to be a reasonable approach for AHC screening in HIV-positive individuals.

Boesecke C, et al. J Viral Hepatitis 2015;22:2-7

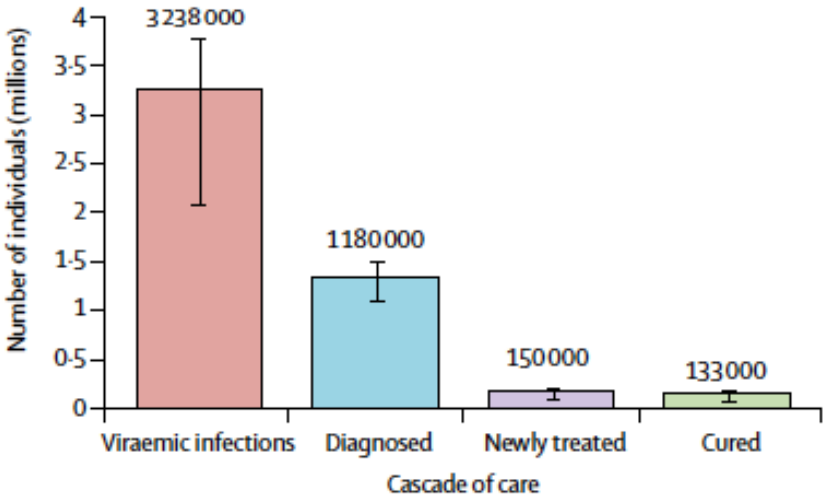
WHO targets by 2030:

- 65% reduction of liver-related deaths
- 90% reduction of new infections
- 90% of pts with viral hepatitis being diagnosed

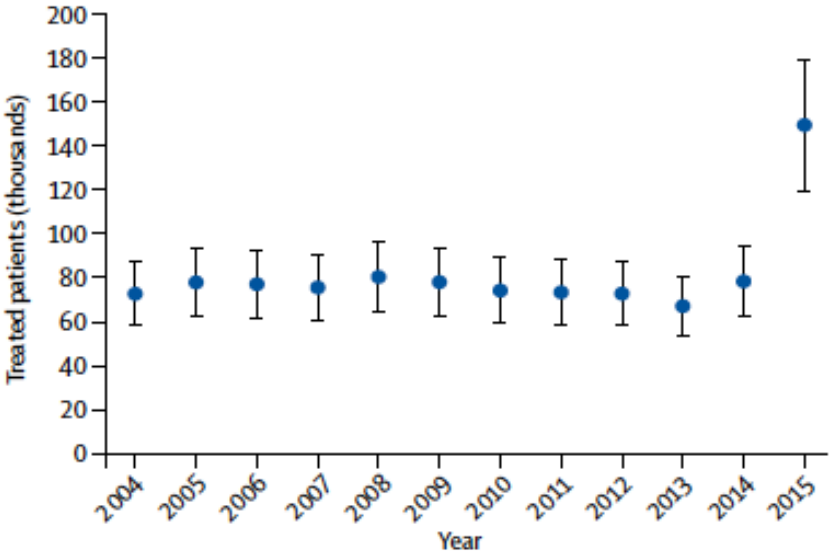
Hepatitis C viraemic prevalence and total infcted in EU



Cascade of care in EU 2015

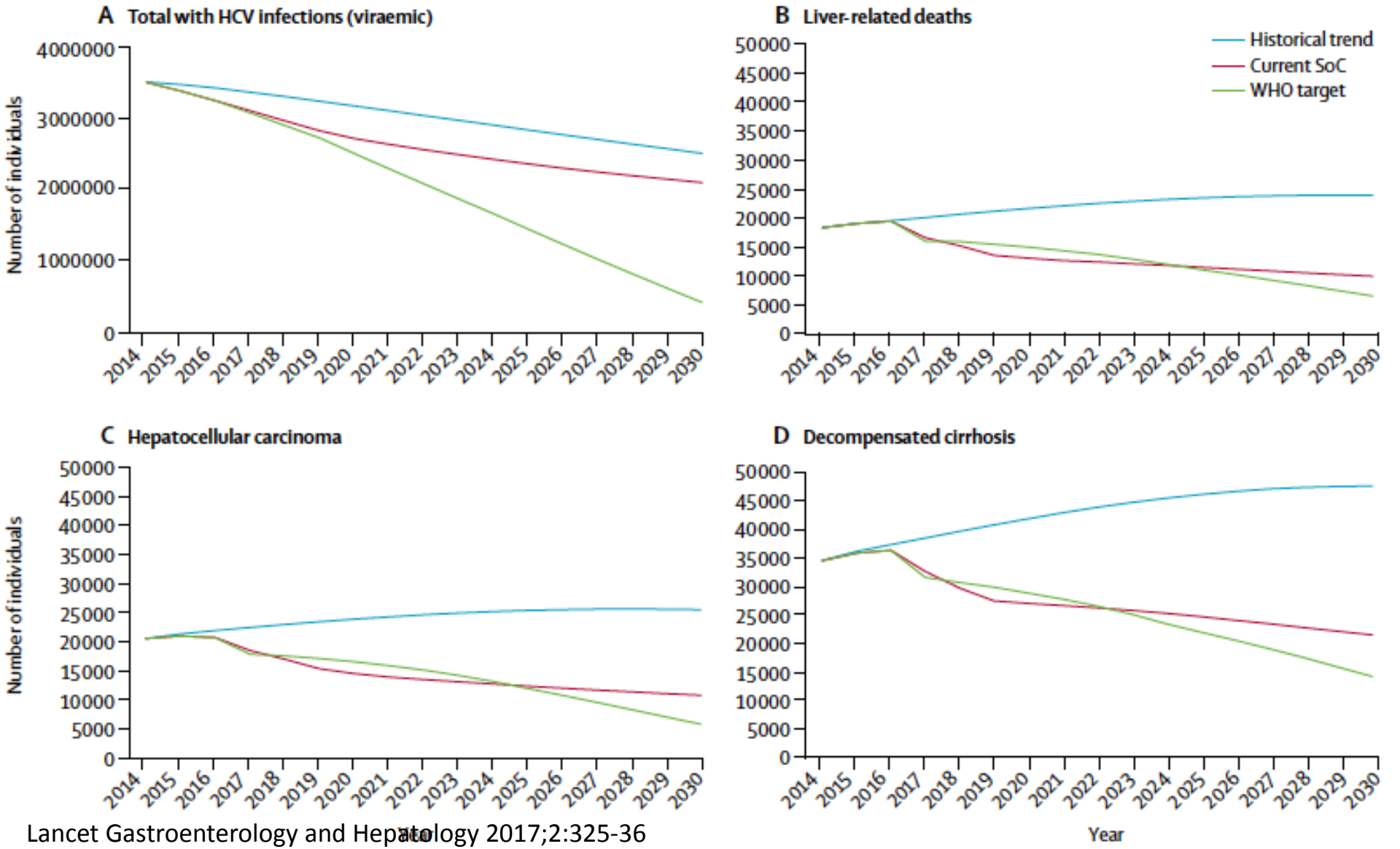


Annual number of pts treated in EU, 2004-15



Lancet Gastroenterology and Hepatology 2017;2:325-36

Projection of HCV morbidity and mortality, by diagnosis and treatment strategy, 2014-30



Lancet Gastroenterology and Hepatology 2017;2:325-36

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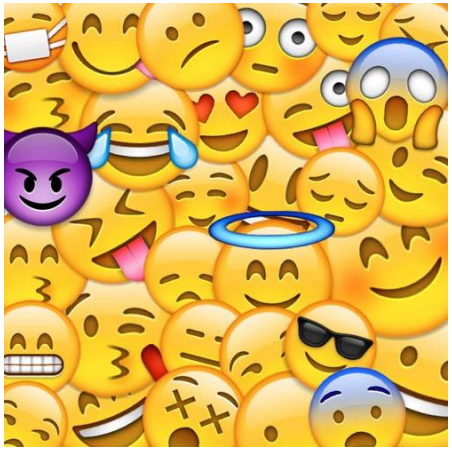
Who Should Be Treated for HCV Infection?

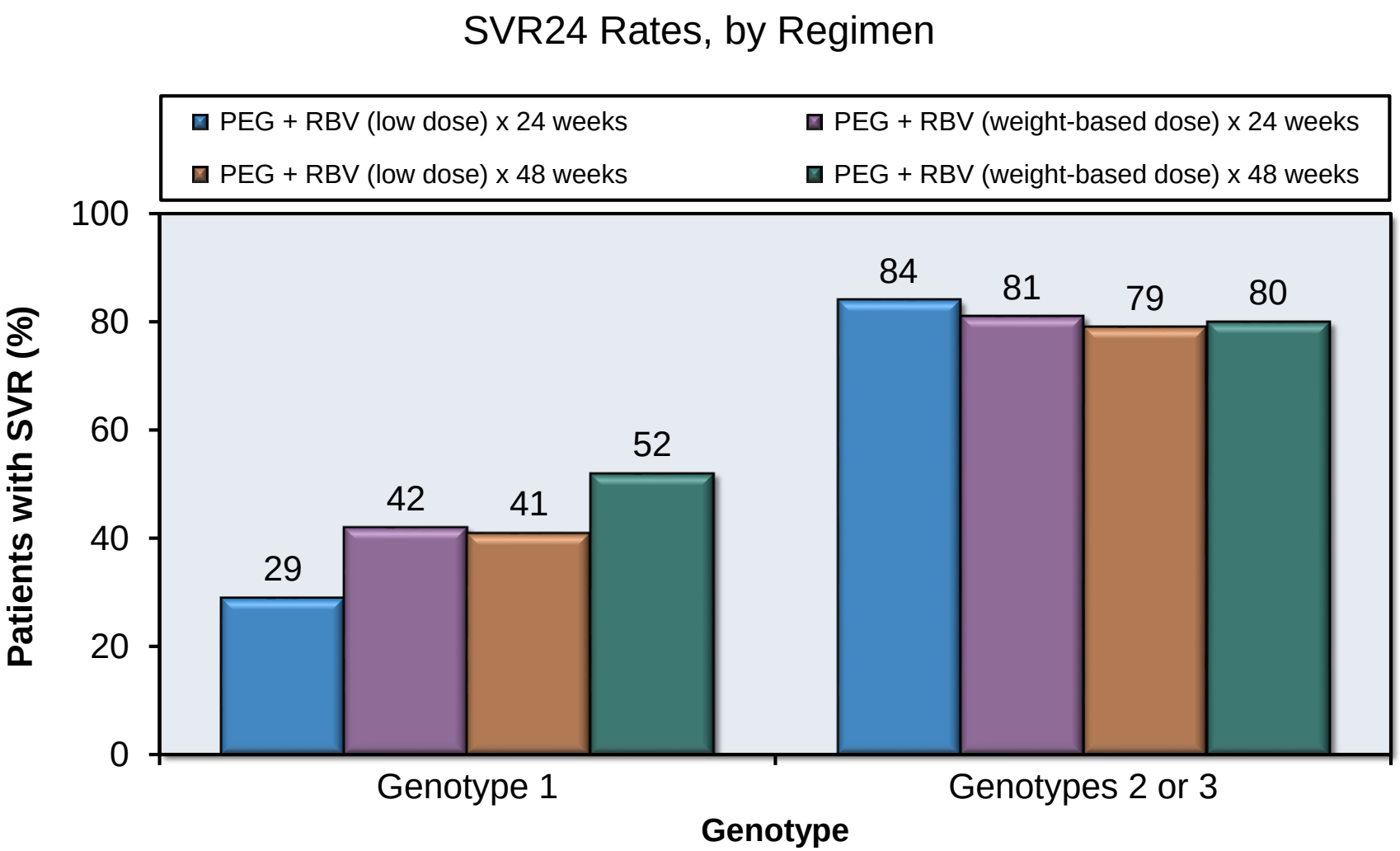
- Short answer: everyone



- AASLD/IDSA: "the panel continues to recommend treatment for all pts with chronic HCV infection, except those with short life expectancies who cannot be remediated by treating HCV, by transplantation, or by other directed therapy"

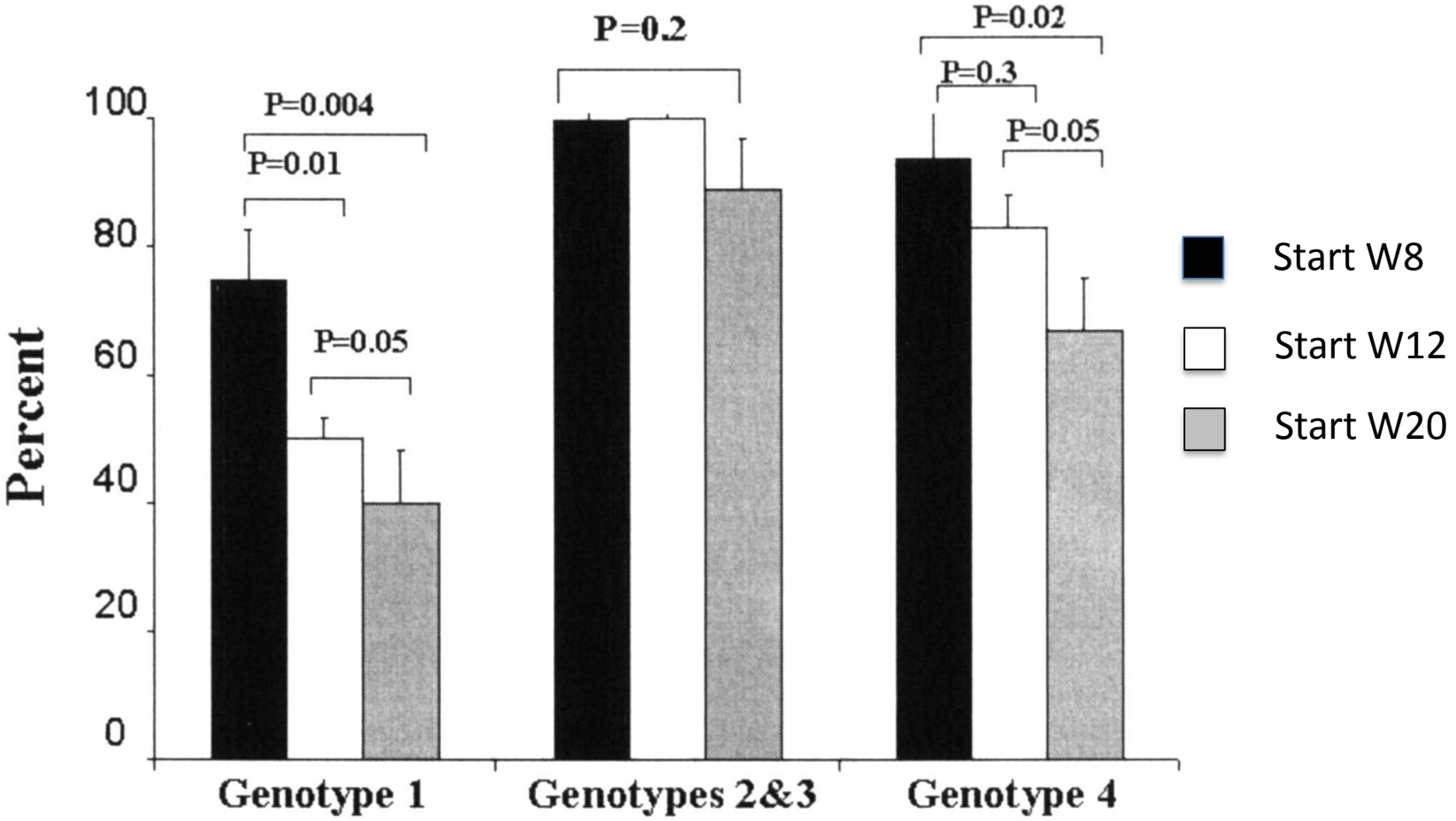
AASLD/IDSA. HCV guidance. September 2016.

Peginterferon alfa-2a + Ribavirin for Chronic HCV Treatment Duration and Ribavirin Dose



Hadziyannis SJ, et. al. Ann Intern Med. 2004;140:346-55.

Peginterferon Alfa-2b Therapy in Acute Hepatitis C: Impact of Onset of Therapy on Sustained Virologic Response



Kamal SM, et al. Gastroenterology 2006;130:632-8

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✓Quando e quanto trattare

The ideal time point for starting therapy has not been firmly established.
The SVR rates with SOF/LDV were**: 93%** (13/14) after **4 weeks** of treatment in injection drug users [181**], 77% (**20/26) after **6 weeks** of treatment in HIV-positive individuals, and **100%** (20%) after **6 weeks** of treatment in HIV-negative, non-injection drug users. Because of the small number of patients included in these trials, of the differences in their results, and by analogy with chronic hepatitis C for which **at least 8 weeks** of therapy are required to maximize SVR rates, patients with acute hepatitis C should be treated with the combination of sofosbuvir and an NS5A inhibitor for 8 weeks

EASL guidelines 2016

Basu PP, et al. Hepatol Int 2016;10:S14–S15.

Rockstroh JK, et al. Conference on Retroviruses and Opportunistic Infections (CROI), February 22–25, Boston, Massachusetts.

Deterding K, et al. J Hepatol 2016;64:S211.

Recommended Treatment for Patients with Acute HCV Infection

If the practitioner and patient have decided that a delay in treatment initiation is acceptable, monitoring for spontaneous clearance is recommended for a minimum of 6 months.

Rating: Class IIa, Level C

If a decision has been made to initiate treatment during the acute infection period, monitoring HCV RNA for at least 12 weeks to 16 weeks before starting treatment is recommended to allow for spontaneous clearance.

Rating: Class IIa, Level C

Recommended Regimens for Patients with Acute HCV Infection.

Owing to high efficacy and safety, the same regimens that are recommended for chronic HCV infection are recommended for acute infection.

Rating: Class IIa, Level C

There are instances, however, where clinicians may decide that the benefits of early treatment outweigh waiting for HCV clearance. These include situations where importance is placed on the prevention of HCV transmission (eg, **surgeon, IVDU, and or HIV+ MSM with sexual transmission**), **mitigation of clinical consequences (eg, patient with cirrhosis who is acutely superinfected with HCV**), or **reduction in likelihood of loss-to-follow-up** in patients who may not be engaged in care in 3-to-6 months.

AASLD treatment guidelines

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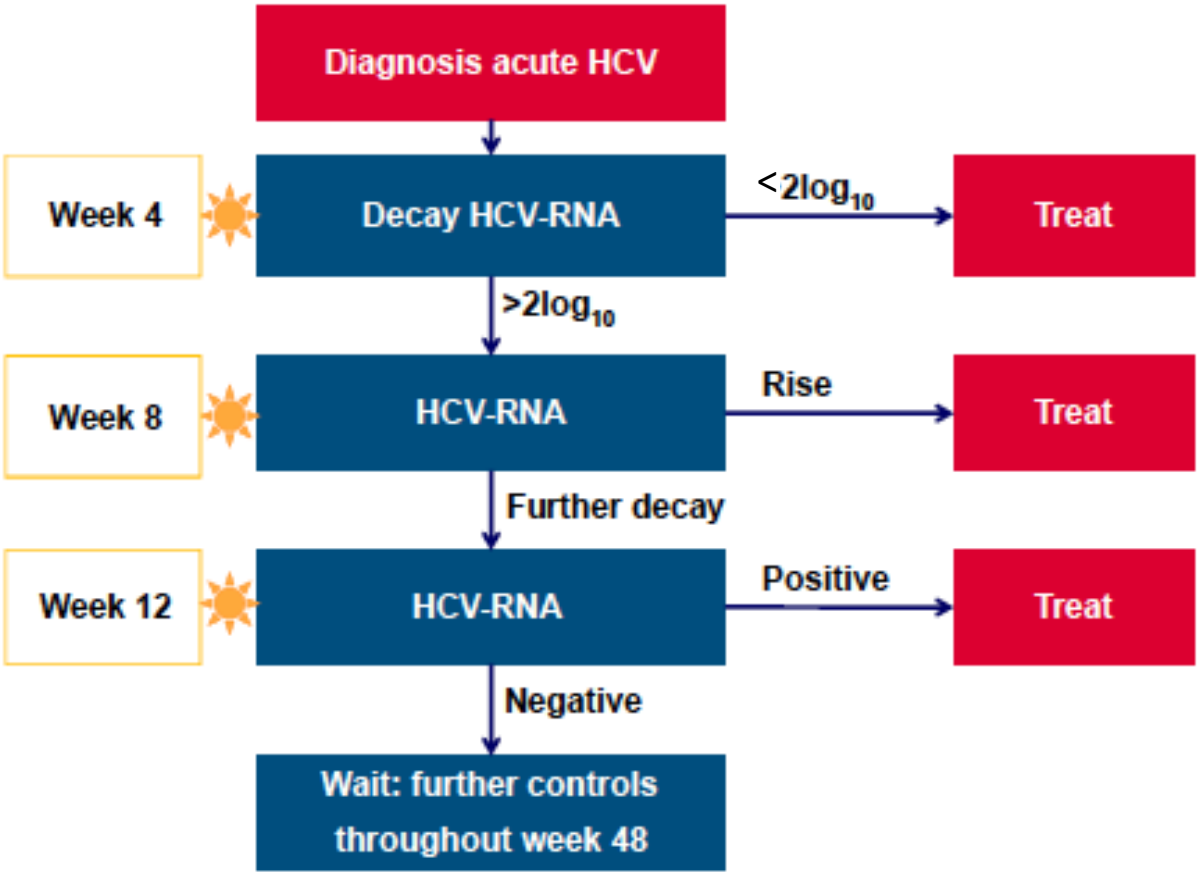
Acute HCV infection: starting antiviral therapy according to the course of hepatitis C virus RNA in HIV coinfection



Boesecke C, et al. J Viral Hepatitis 2015;22:2-7

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✓Eradicazione?

Comparison of HCV disease burden in 2013 and 2030

	Australia	Austria	Belgium	Brazil	Canada	Czech Republic	Denmark	Egypt	England	France	Germany	Portugal	Spain	Sweden	Switzerland	Turkey
Viremic HCV infections																
2013 Est.	233 000	25 400	67 100	1 940 000	252 000	42 500	20 900	5 980 000	144 000	195 000	267 000	125 000	473 000	40 600	82 700	514 000
2030 Est.	251 000	13 900	47 700	1 250 000	209 000	42 200	17 200	4 420 000	83 700	85 100	121 000	87 400	285 000	31 900	63 200	352 000
% Change	5	(45)	(30)	(35)	(15)	0	(20)	(25)	(40)	(55)	(55)	(30)	(40)	(20)	(25)	(30)
HCC cases																
2013 Est.	590	110	300	9710	730	90	90	16 100	410	1770	1530	1150	2210	270	400	2230
2030 Est.	2030	150	640	18 900	2090	170	210	18 300	920	300	1640	2050	4500	290	740	3770
% Change	245	35	110	95	190	85	140	15	125	(85)	10	80	105	10	85	70
Liver related mortality																
2013 Est.	530	100	290	9000	720	80	80	33 000	390	1570	1300	890	1940	170	380	2020
2030 Est.	1740	130	570	16 620	1800	160	180	36 500	770	380	1430	1700	3750	170	650	3420
% Change	230	25	95	85	150	90	130	10	100	(75)	10	90	95	1	70	70
Decompensated cirrhosis																
2013 Est.	1430	200	820	27 500	1790	190	230	137 000	860	3650	2430	2410	4230	430	1140	5590
2030 Est.	4150	180	1400	45 000	3370	390	480	136 000	1370	760	2200	4910	6710	360	1790	8820
% Change	190	(10)	70	65	90	100	110	(1)	60	(80)	(10)	105	60	(15)	55	60
Compensated cirrhosis																
2013 Est.	13 800	2450	7060	222 000	18 500	1830	1870	626 000	9500	29 100	31 100	17 900	46 200	3890	8520	51 100
2030 Est.	37 900	2010	11 500	323 000	36 100	3740	3670	611 000	14 700	5770	24 400	25 600	72 700	3430	12 700	71 200
% Change	175	(20)	65	45	95	105	95	(2)	55	(80)	(20)	45	55	(10)	50	40

Razavi H, et al. J Viral Hepat 2014;21:34-59

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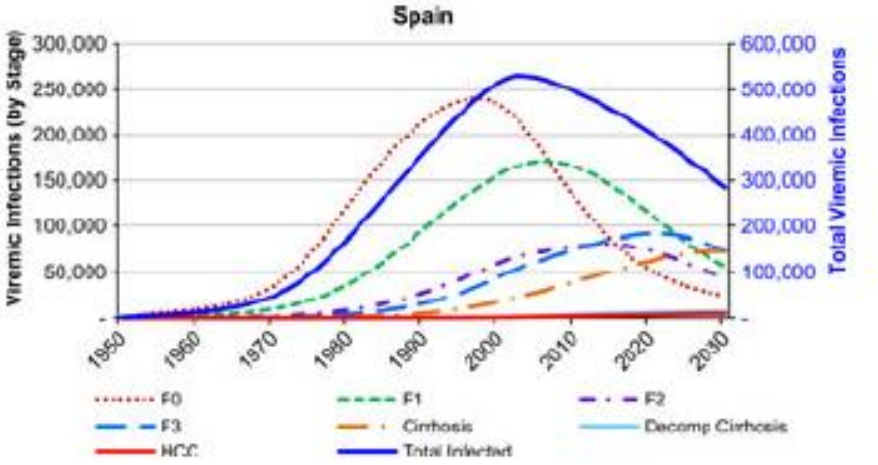
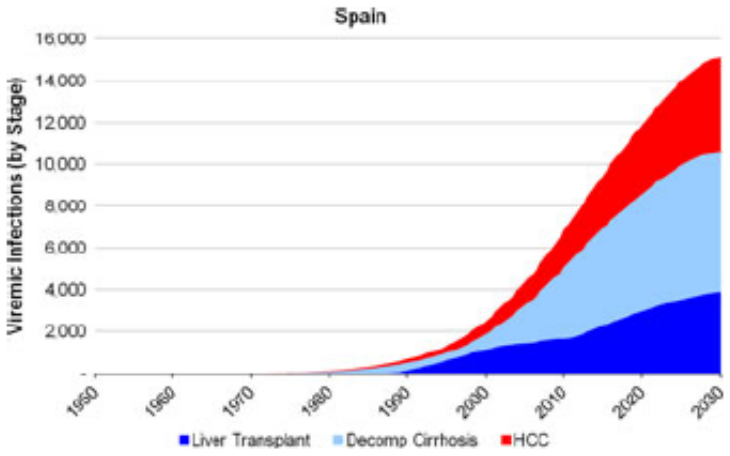
Impact of HCV: What Happens If We Do Nothing?

A) Change in HCV disease burden over time
B) Change in the number of liver transplant, decompensated cirrhosis and HCC cases over time

A



B



Razavi H, et al. J Viral Hepat 2014;21:34-59

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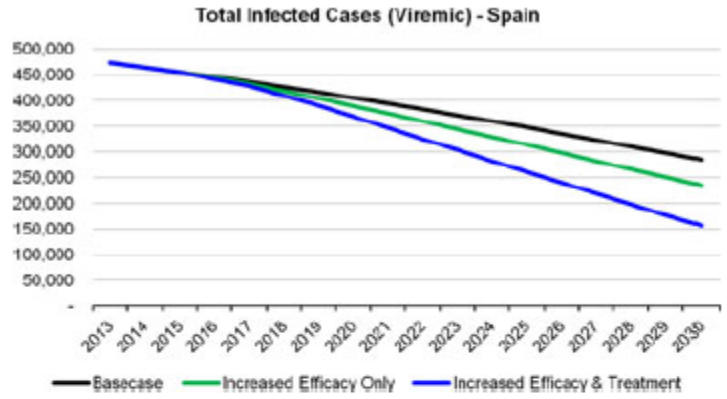
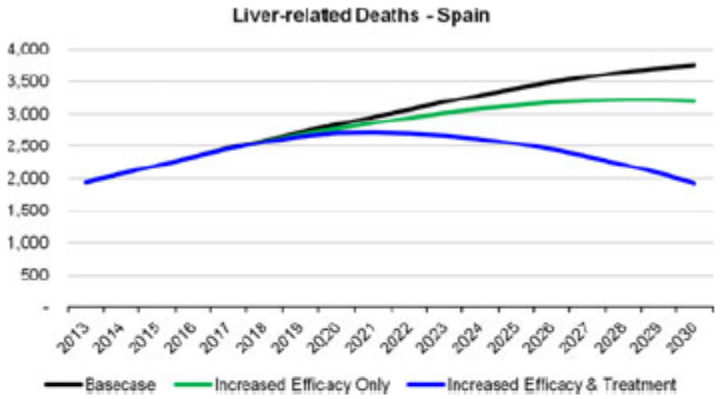
Change in HCV morbidity and mortality, by scenario, 2013-2030

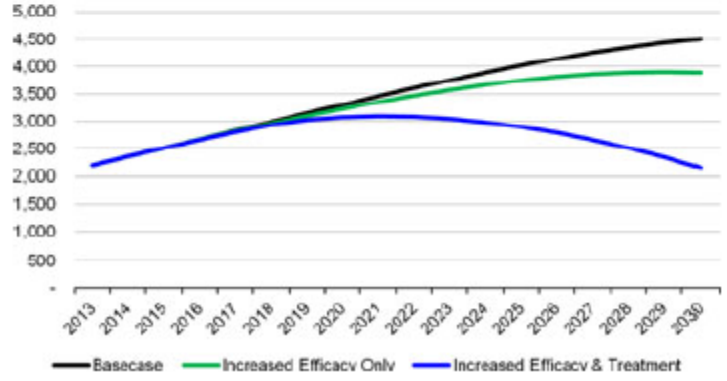
- 20%
- 45%

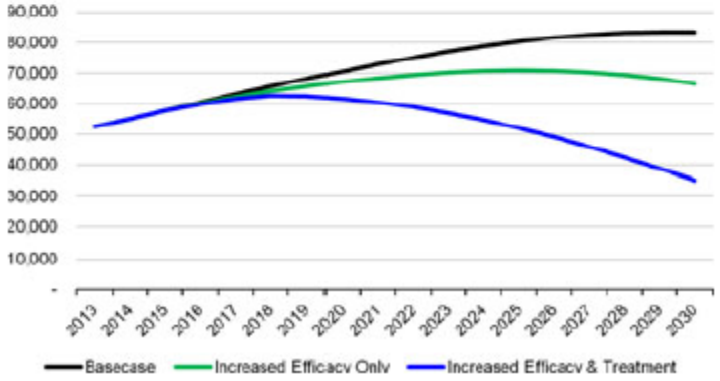




- 15%
- 50%

- 15%
- 50%





- 20%
- 60%

Wedemeyer H, et al. J Viral Hepat 2014;21:60-89

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Can Hepatitis C Virus (HCV) Direct-Acting Antiviral Treatment as Prevention Reverse the HCV Epidemic Among Men Who Have Sex With Men in the United Kingdom? Epidemiological and Modeling Insights

Table 1. Cumulative Prevalence (Antibody or RNA Positive) of Hepatitis C Among Human Immunodeficiency Virus (HIV)-Positive Men Who Have Sex With Men in the UK Collaborative HIV Cohort Study

Year	Total No. of MSM Under Follow-up in That Year in UK CHIC	Total No. of MSM Under Follow-up in That Year With a Reported Test by End of Year	% With an HCV Test Reported by End of That Year	Cumulative No. HCV Infected (Ab or RNA Positive)	Cumulative HCV Prevalence (Ab or RNA Positive), %
2004	11 012	6774	61.51	492	7.26
2005	11 765	8398	71.38	641	7.63
2006	12 335	9550	77.42	752	7.87
2007	12 895	10 808	83.82	896	8.29
2008	13 262	11 799	88.97	1049	8.89
2009	13 693	12 607	92.07	1195	9.48
2010	14 147	13 369	94.50	1293	9.67
2011	13 101	12 789	97.62	1261	9.86
Ever	17 574	16 533	94.08	1673	10.12

Martin NK, et al. CID 2016;62:1072-80

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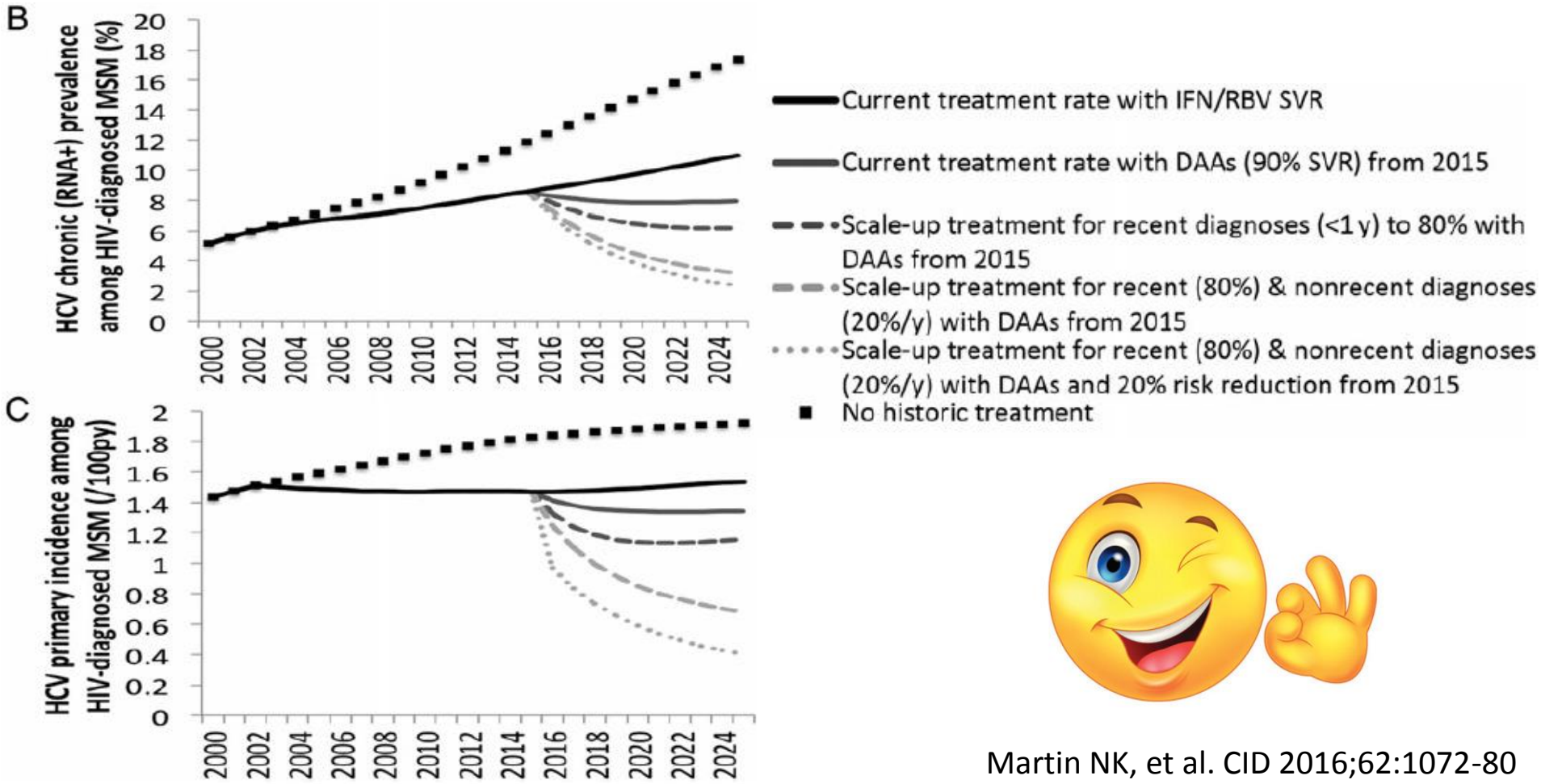
Model projections with various treatment scenarios in UK



Martin NK, et al. CID 2016;62:1072-80

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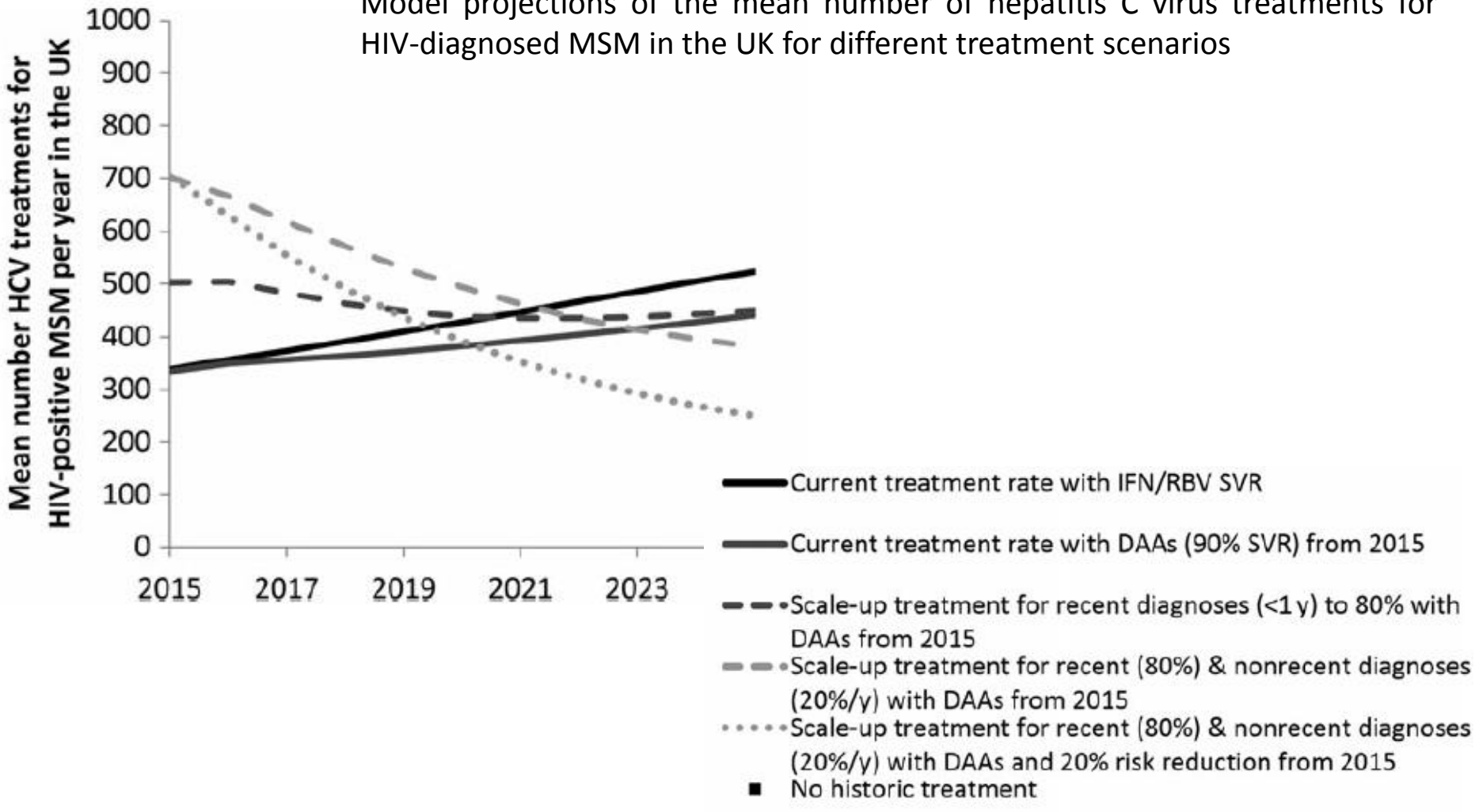
Model projections of the mean number of hepatitis C virus treatments for HIV-diagnosed MSM in the UK for different treatment scenarios



Martin NK, et al. CID 2016;62:1072-80

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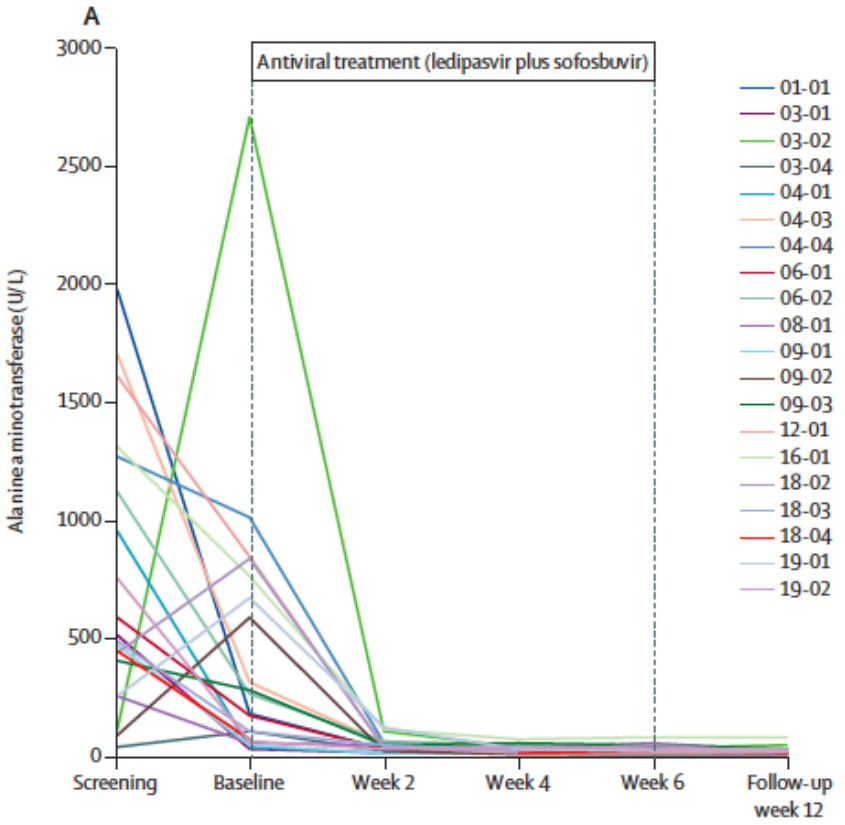
✓efficacia

Ledipasvir plus sofosbuvir fixed-dose combination for 6 weeks in patients with acute hepatitis C virus genotype 1 monoinfection (HepNet Acute HCV IV): an open-label, single-arm, phase 2 study

20 patients (enrolled by 10 centers in Germany) with acute hepatitis C genotype 1 treated with ledipasvir/sofosbuvir for 6 weeks.

SVR 12: 100%



Deterding K, et al; Lancet Inf Dis 2017;17:215-22

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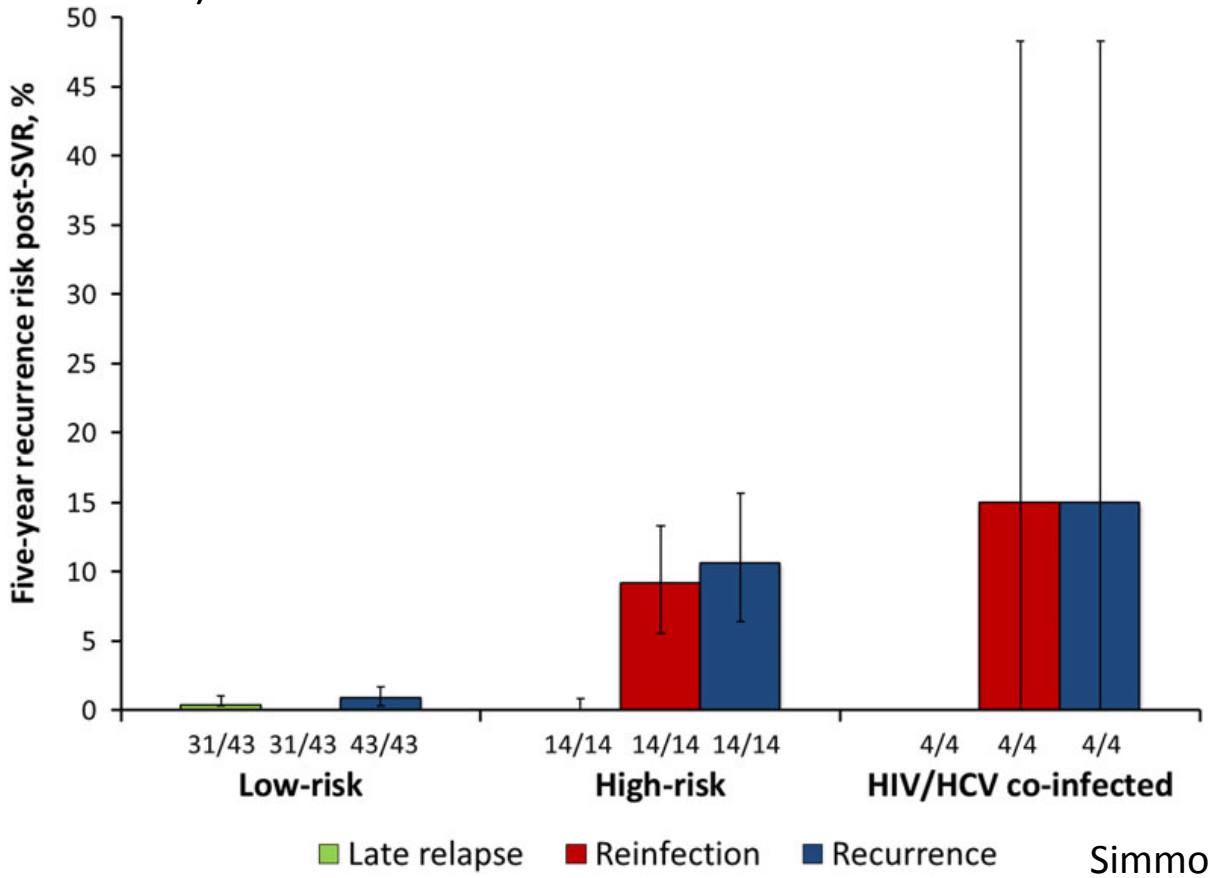
✓reinfection

Low-risk population: 5-year late relapse and reinfection rates of 0.40% (95% CI, .35%–1.05%) and 0.00% (95% CI, .00%–.00%), respectively

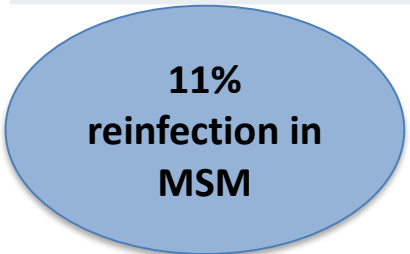
High-risk population: 5-year recurrence rate of 10.67% (95% CI, 6.38%–15.66%), mainly reinfection HIV/HCV coinfected population: 5-year risk of reinfection of 15.02% (95% CI, .00%– 48.26%)

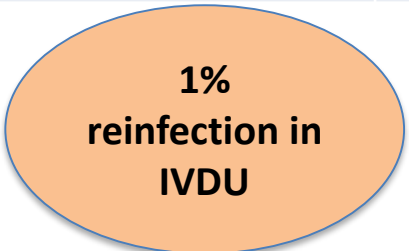


Simmons B, et al . CID 2016;62:683-94

24/1417 (1.7%) patients had a reinfection after DAA successful therapy

	Reinfection n. 24
Median age, years (IQR)	49 (42-54.5)
Male, n. (%)	24 (100)
Mode of HCV transmission IVDU, n. (%) MSM, n. (%) MSM+IVDU, n. (%)	 5 (21) **14 (58)** **5 (21)**
HIV-coinfection, n. (%)	20 (83)
Median time to reinfection, weeks (IQR)	41 (25-67)
Previous HCV treatment SOF-PEG-RBV, n. (%) SOF/LDV, n. (%) PTV/r/OBV+/-DSV+/-RBV, n. (%) SOF/RBV, n. (%) SOF/DCV, n. (%) SOF/SIM, n. (%)	 7 (29) 11 (46) 2 (9) 1 (5) 2 (9) 1 (5)





German Hepatitis C cohort (GECCO): CROI 2017

Grazie dell'attenzione