Funding Innovation in Hepatitis C Treatment

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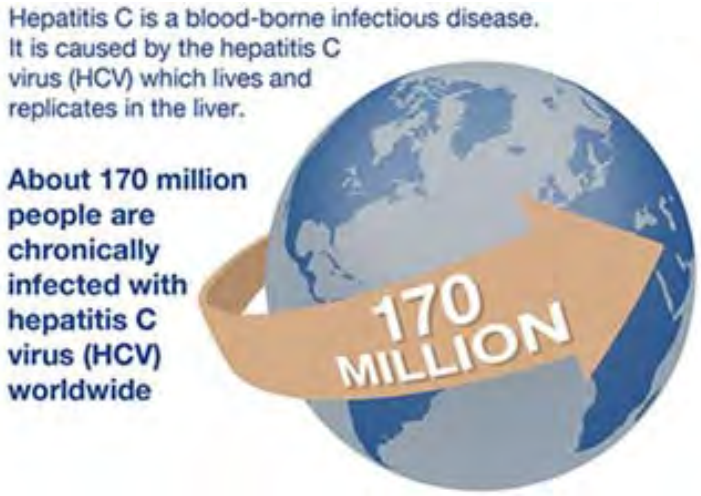
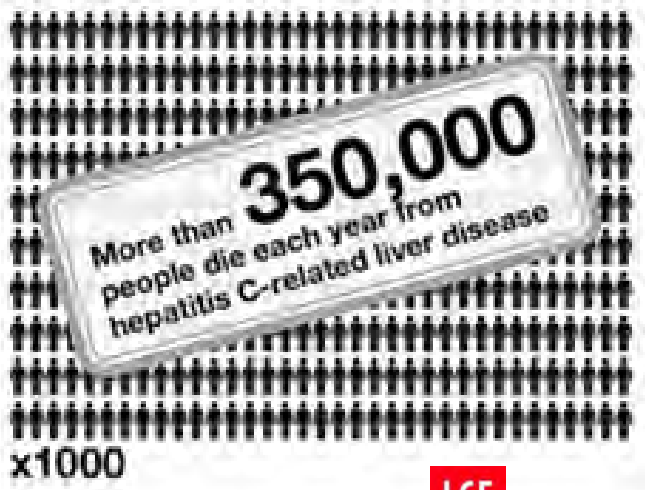
LSHTM, 5 June 2015

Outline

- The economic and social impact of Hepatitis C
- New treatments in Hepatitis C
- Funding models for new hepatitis C treatments
  - From efficacy to effectiveness
  - Funding models and using innovative approaches

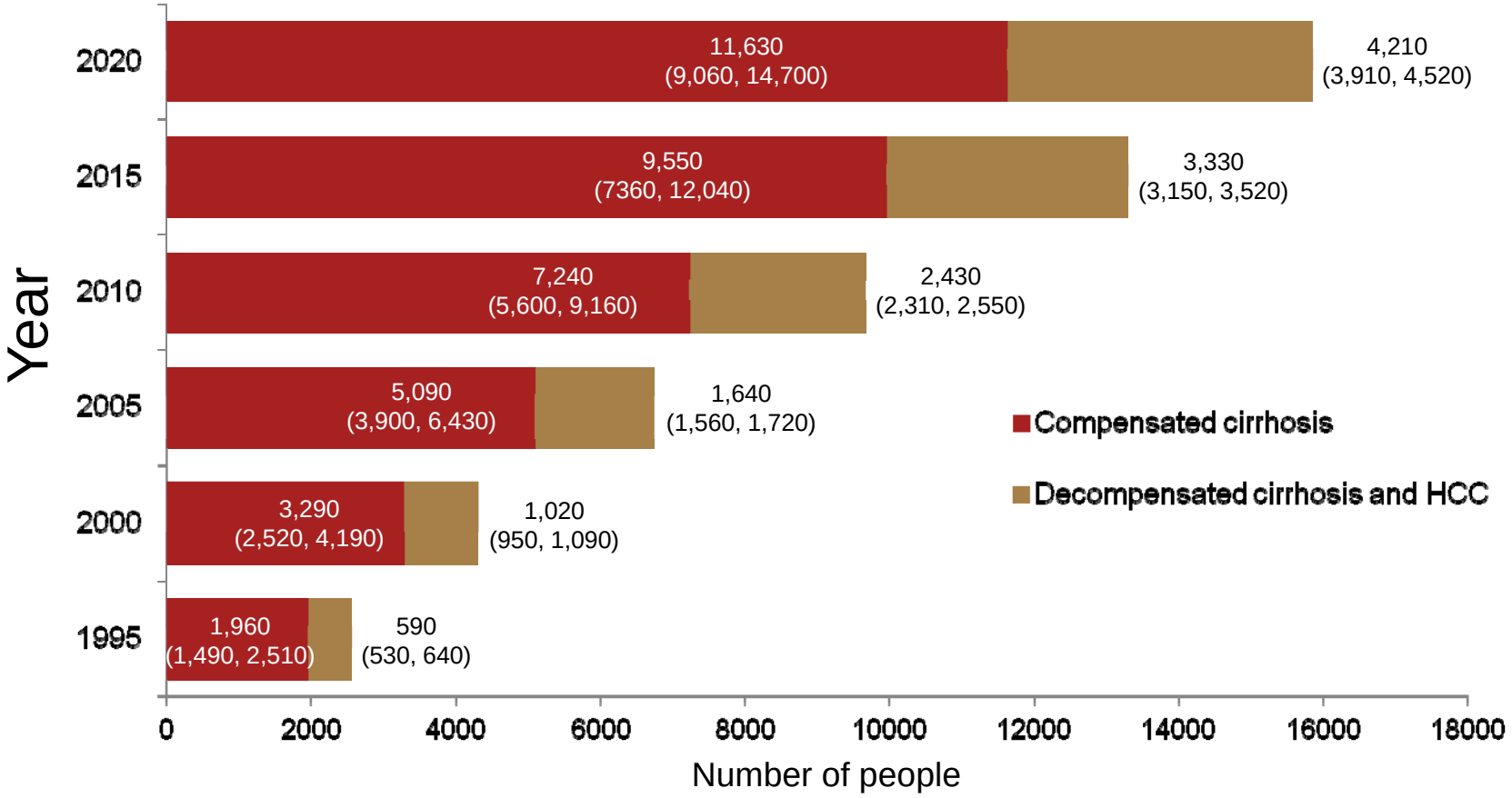
HCV is a major public health issue





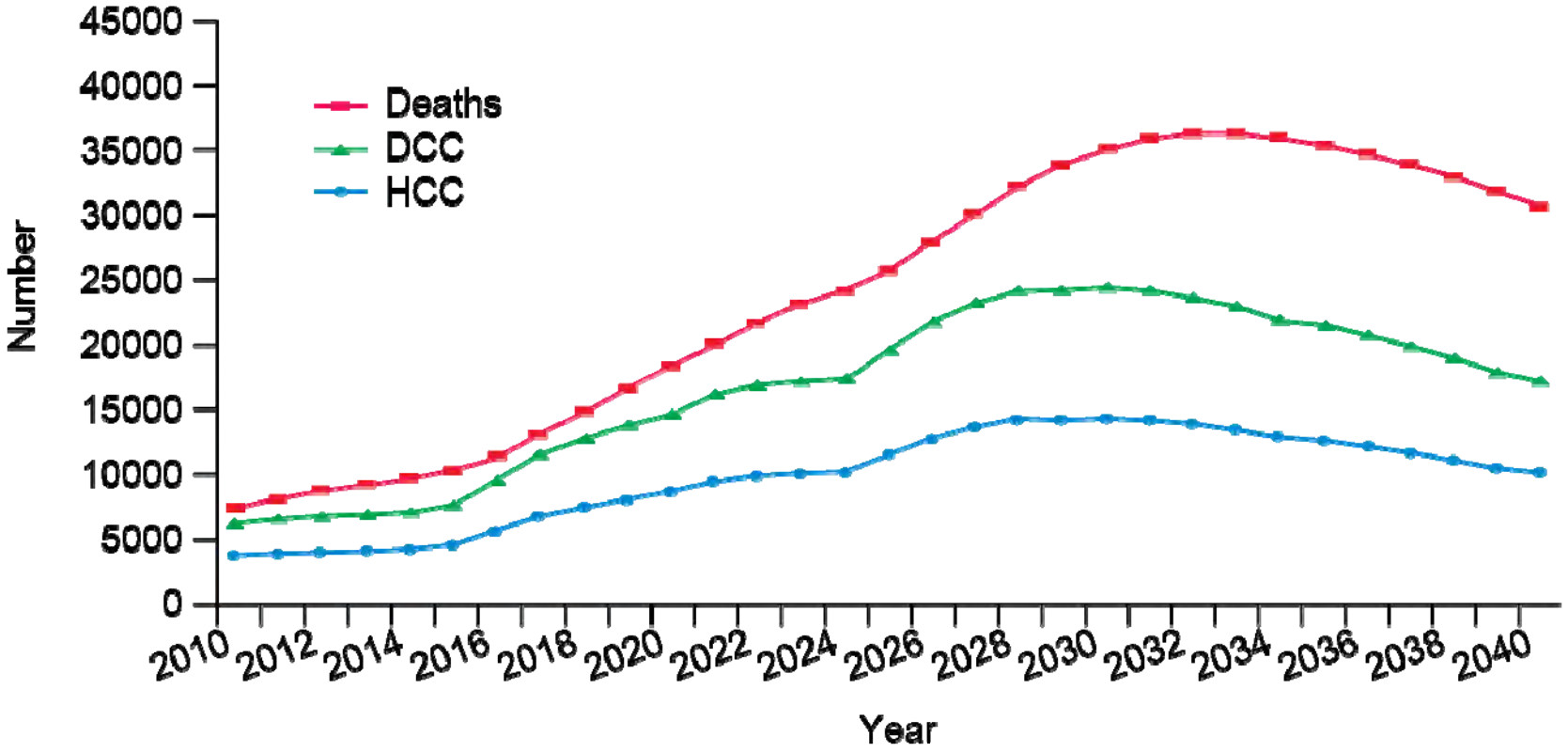
A growing number of people are living with HCV-related sequelae

Estimated number of people living with HCV-related cirrhosis and decompensated cirrhosis/HCC in England 1995–2020 (95% CI)



Health Protection Agency. Hepatitis C in the UK 2012.
Available from: http://www.hpa.org.uk/HPAwebfile/HPAweb_C/1317135237219. Accessed August 2013.

The incidence of HCV-related liver cancer and death is also expected to peak in the coming decades



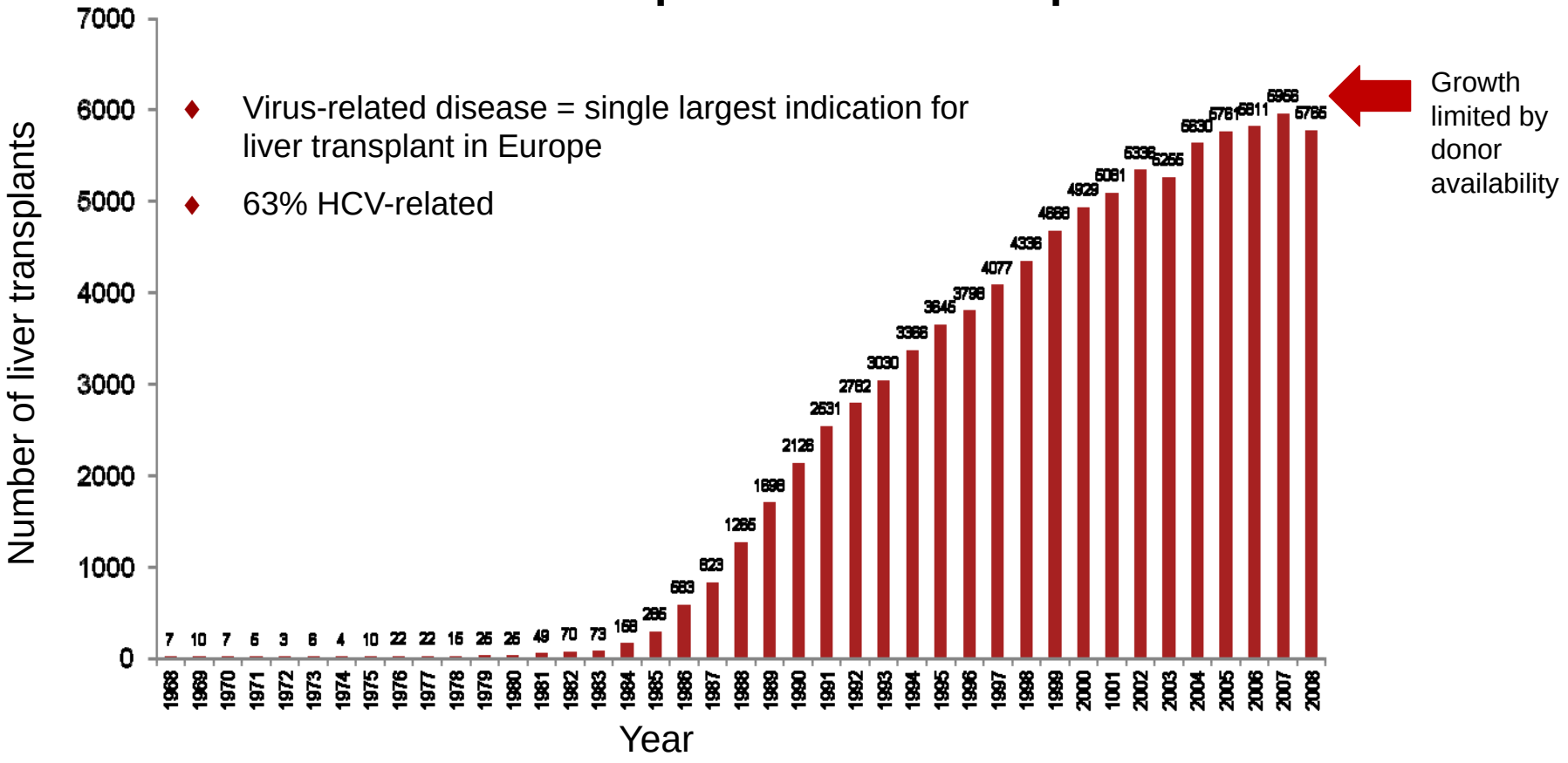
- At peak in the USA:
  - 38,600 cases of end-stage liver disease; 3,200 referrals for transplant; 36,100 deaths

Rein DB, et al. Dig Liver Dis 2011;43:66–72.

DCC: decompensated cirrhosis

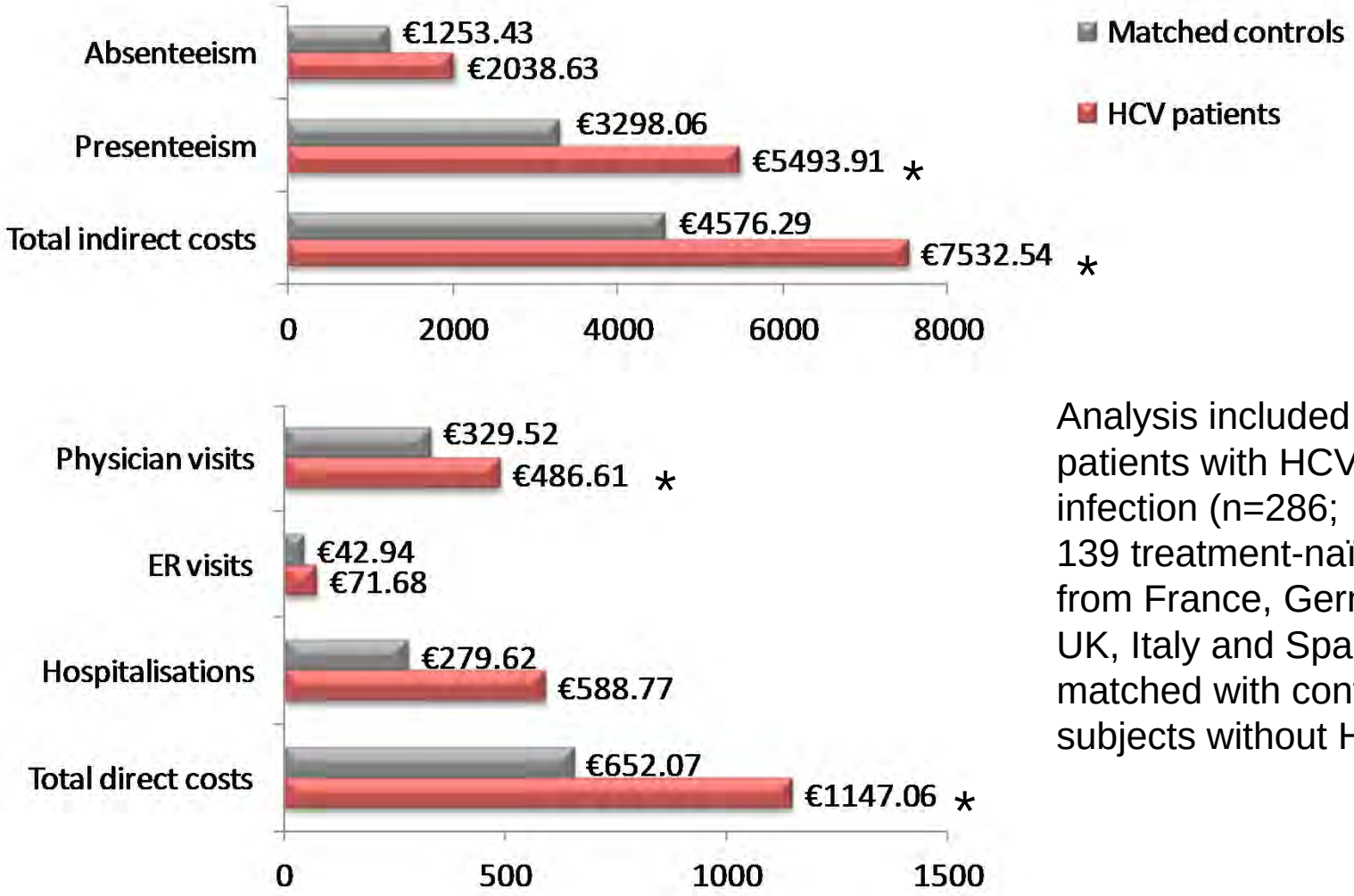
Numbers of liver transplants have been increasing in Europe over the past two decades

HCV-related cirrhosis is the commonest indication for liver transplantation in Europe



European Association for the Study of the Liver (EASL). The burden of liver disease in Europe. Available at: http://www.easl.eu/assets/application/files/54ae845caec619f_file.pdf. Accessed August 2013.

At a substantial cost for treating consequences of chronic HCV



Analysis included patients with HCV infection (n=286; 139 treatment-naïve) from France, Germany, UK, Italy and Spain, matched with control subjects without HCV

Vietri J, et al. BMC Gastroenterol 2013;13:16.

*P≤0.002
ER: emergency room

Whilst, unlike HIV and HBV, HCV can be cured and this can be achieved faster and with fewer side effects

Unlike chronic infection with HBV or HIV, where a reservoir of virus always remains once the infection is established, HCV can be eradicated in the vast majority of patients[1]

- SVR is defined as undetectable HCV RNA in the blood after completion of therapy[2]
  - SVR24 has been the gold standard measure of treatment success in the past
  - SVR12 is now an established primary endpoint and measure of treatment success accepted by clinical and regulatory agencies

1. Soriano V, et al. J Antimicrob Chemother 2008;62:1–4;
2. Chen J, et al. Gastroenterology 2013;144:1450–5.

New therapies are recommended by leading organisations

World Health Organization

Media centre

WHO issues its first hepatitis C treatment guidelines

News release

9 APRIL 2014 | LONDON, UNITED KINGDOM - WHO has issued its first guidance for the treatment of hepatitis C, a chronic infection that affects an estimated 130 million to 150 million people and results in 350 000 to 500 000 deaths a year.

The publication of the "WHO Guidelines for the screening, care and treatment of persons with hepatitis C infection" coincides with the availability of more effective and safer oral hepatitis medicines, along with the promise of even more new medicines in the next few years.

"The WHO recommendations are based on a thorough review of the best and latest scientific evidence," says Dr Stefan Wiktor, who leads WHO's Global Hepatitis Programme. "The new guidance aims to help countries to improve treatment and care for hepatitis and thereby reduce deaths from liver cancer and cirrhosis."

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But at what cost?

By KIM PETERSON / MONEYWATCH / April 3, 2014, 8:27 AM

$1,000-a-day miracle drug shocks U.S. health care system

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Sovaldi, a new hepatitis C treatment, can cure up to 90 percent of patients within three months. There's just one problem: The drug costs $1,000 a day. That price tag has thrown the biotechnology world into turmoil, as lawmakers and insurance companies complain that Sovaldi's maker is trying to milk desperate patients.

SundayReview | EDITORIAL

How Much Should Hepatitis C Treatment Cost?

By THE EDITORIAL BOARD MARCH 15, 2014

HealthlineNews

Healthline → Healthline News → New Hep C Drug Sovaldi Ignites Fierce Pricing Debate

New Hep C Drug Sovaldi Ignites Fierce Pricing Debate

Written by Kristen Fischer
Published on 11 Απρίλιος 2014

A new drug that successfully treats Hepatitis C is being hailed as
breakthrough, but is also stirring fierce debate for it's $84,000 pr

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New treatments for Hepatitis C, a great hope for people infected with HCV, but accessible for how many?

Publication of a study on strategies for achieving universal access to HCV treatments

Patient segments and potential interventions

1. Prisoner populations: Prevention treatment
   - ① Assure access for an undertreated segment, leverage closed system to improve public health and cure by release from prison
   - ② Support routine diagnosis of high-risk population
   - ③ Early intervention in closed system to reduce long-term cost burden
2. Methadone maintenance programs: Prevention treatment
   - ① Assure access for an undertreated segment and decrease HCV transmission to society
   - ② Support routine diagnosis of high-risk population
   - ③ Cure and prevention of transmission in high-risk population
3. Non-marginalised populations: Develop integrated care models
   - ① Rapid cure with limited side-effects
   - ② Higher societal benefits
4. An EU-wide HCV prevention program
   - ① Target key causes of spread by supporting IC programs

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How do we pay for all this?

1. Are treatments effective (not only efficacious)?
2. What are the target populations and in what ways can we target them?

Evidence development:

The importance of registries in showcasing benefit and effectiveness and some evidence of how it can be used to gauge effectiveness and promote efficiency

Example: Monitoring registries in Italy

Clinical and anthropometric baseline data of cases analyzed

	Exenatide (n=16,761)	Liraglutide (n=20,149)	Saxagliptin (n=11,625)	Sitagliptin (n=16,382)	Sitagliptin/Met (n=7,690)	Vildagliptin (n=5,358)	Vildagliptin/Met (n=6,511)
	42,7%			57,3%			
Gender (M/F)	8,196/8,565	10,436/9,713	6,427/5,198	8,835/7,847	4,211/3,479	2,790/2,568	3,671/2,840
Age in years, mean	57.4	58.0	62.8	61.0	61.1	61.5	61.1
Body Mass Index (Kg/m^2), mean	36.2	39.0	29.9	30.9	30.9	30.7	30.8
Fasting glucose (mg/dl), mean	187.8	179.4	162.0	169.7	166.2	178.2	168.0
HbA_{1c} (%), mean	8.8	8.5	8.0	8.2	8.1	8.3	8.1

Total treatment costs and mean cost/patient from the Antidiabetics AIFA Monitoring Registry

	Total costs (Thousand €)	% of total cost	Mean treatment duration (days)	Mean cost per patient (€)
Exenatide	22,184.60	26.4%	272.0	1,323.60
Liraglutide	26,851.30	32.0%	282.7	1,332.60
Saxagliptin	6,550.90	7.8%	255.0	563.52
Sitagliptin	15,093.90	18.0%	351.0	921.40
Sitagliptin/Met	4,313.50	5.1%	229.1	560.90
Vildagliptin	4,467.60	5.3%	351.0	833.80
Vildagliptin/Met	4.506.40	5.4%	232.7	692.12

HCV patient population – Overview

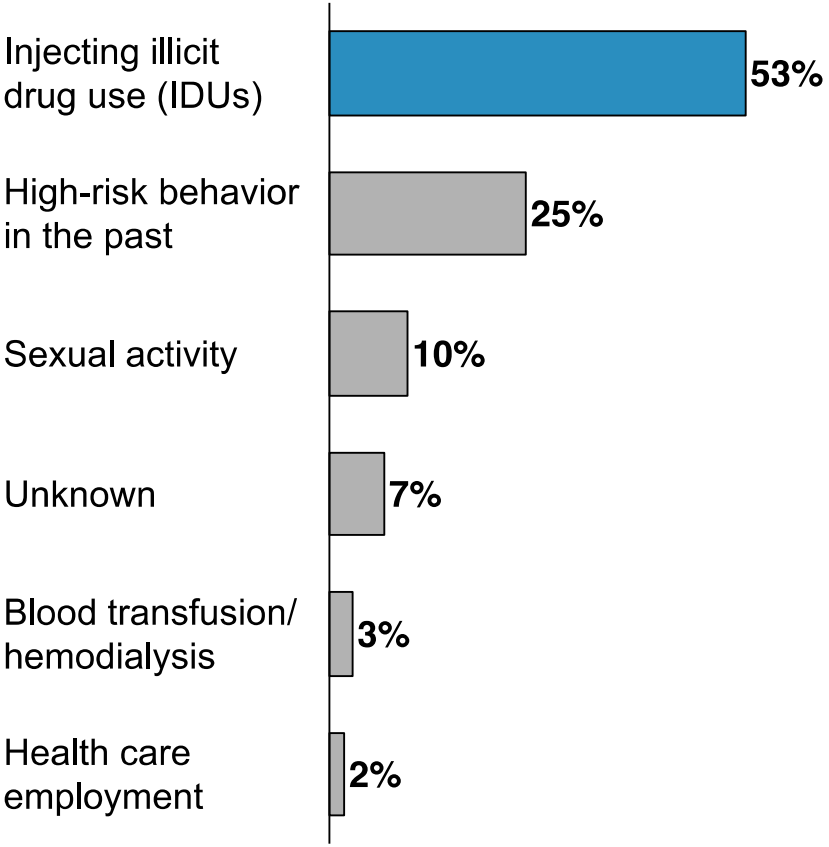
Example: In Spain 1/3 of the HCV population is F3-F4 with patient management mainly taking place by specialists

Mode of transmission[1)] / *Patient setting*	Prisoners	Active and past IDUs	BT infected	HCP	Other[2)]	All
1. *Stage F1-F2*	≈ 70%	≈ 70%	≈ 70%	≈ 70%	≈ 70%	≈ 30%
2. *Stage F3-F4*	≈ 30%	≈ 30%	≈ 30%	≈ 30%	≈ 30%	≈ 70%
Primary attention	**23k**	**7k**	**27k**	**13k**	**58k**	**~130k**
Specialists (Office based and Uni. clinics)	**n.a.**	**30k**	**110k**	**51k**	**232k**	**~421k**
Total	**23k**	**37k**	**137k**	**63k**	**290k**	**~550k**

Other: Incl. other high-risk groups (e.g. men-having sex with men and unknown mode of transmission)

Most new cases of HCV arise from IDU
Applying filters to set treatment priorities: Treatment decisions contingent on patient willingness to comply

Risk factors for acute HCV infection



Treatment decision – HCV

Treat	Wait	Don't treat
▪ Rehabilitated IDUs ▪ Patients with symptoms of liver disease ▪ GT/GT3 patients	▪ Recovering IDUs ▪ Young patients ▪ GT1 patients	▪ Current IDUs ▪ Elderly ▪ Decompensat-ed liver disease ▪ Psychiatric illness
Motivated and committed patients	**Unwilling/ unable patients**	**Marginal patients**

Decision levers

1. **Ability** of patient to comply with treatment
2. **Willingness** of patient to undergo treatment
3. **Likelihood** of treatment success (e.g. genotype)

Payment models: Paying for value

- Clinical benefit assessment
    - Ranking of technologies based on their clinical benefit in relation to current standards of care
- Clinical and cost effectiveness
    - New treatments can be highly cost-effective driven by high clinical benefit or QALY gain
- But, high budget impact
    - Treating entire patient population could require expenditure 3-5 times greater than total drug spend
- And, uncertainty about outcome in the community

Financing models for HCV innovation

A mix of models to suit different patient populations

① Social/Health impact bonds

- A financing mechanism where investor returns are aligned with social outcomes
- Based on contract with public sector in which it commits to pay for improved social outcomes (re-payments from public sector plus a financial return)
- Adolescent Behavioral Learning Experience (US/NYC): evidence-based intervention to adolescents after release in the community

Outcome Improvement[2] [%]	IRR[3] [%]	City net savings [USD m]
≥ 20.0	8.1	20.5
≥ 16.0	5.3	11.7
≥ 13.0	3.1	7.2
≥ 12.5	2.7	6.4
≥ 12.0	2.3	5.6
≥ 11.0	2.0	1.7
≥ 10.0	0.0	≥ 1.0
≥ 8.5	-25.9[4]	≥ 1.0

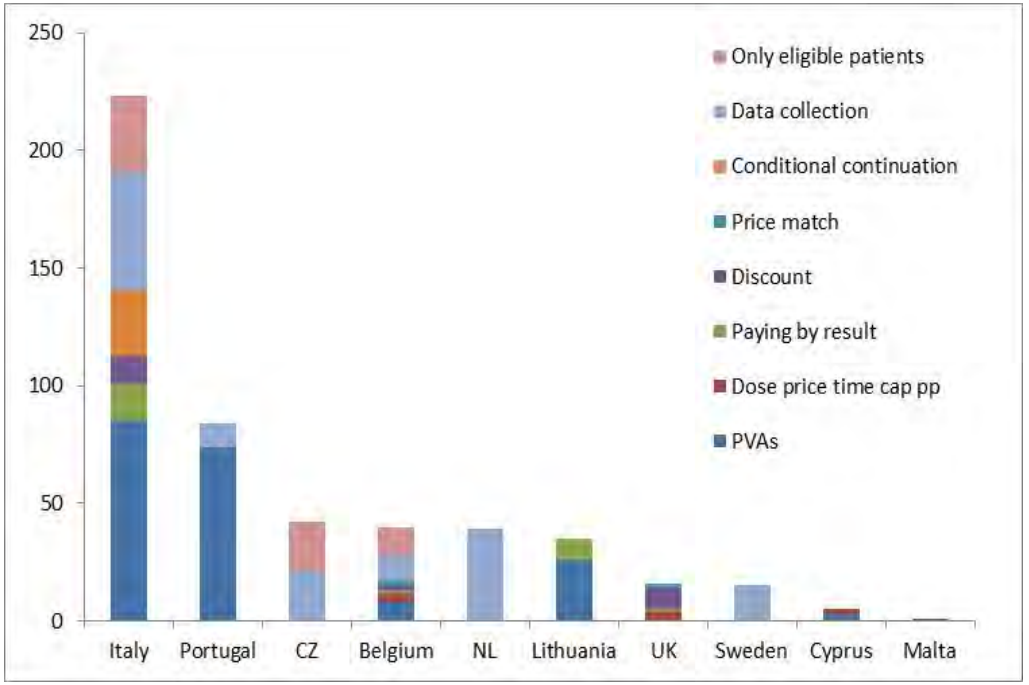
Financing models for HCV innovation

A mix of models to suit different populations: Non-marginalised populations

① Risk sharing and Managed Entry Schemes

- Disagreement or uncertainty on therapeutic value
- Very high cost and budget impact
- Uncertainty as to who might benefit most and possibly larger patient numbers
- Reduce decision uncertainty, enable effectiveness evidence to enter decision-making, improve affordability (through P/Q or discounting, etc.)

Risk sharing options



Examples of risk sharing types and risks addressed by individual schemes

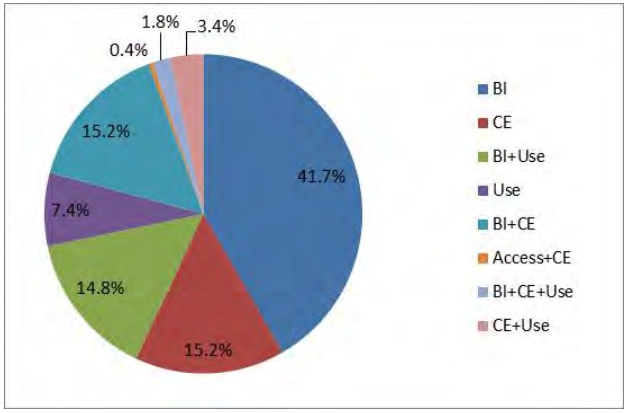
	Right patients	Uncertain clinical value	Low cost effectiveness	Budget overspend
Coverage with ED	Yes	Yes	Yes	x
Conditional coverage	Yes	Yes	Yes	Yes
Outcome guarantee	Yes	Yes	Yes	x
Price-volume deal	x	x	X	Yes

“Innovative” payor schemes

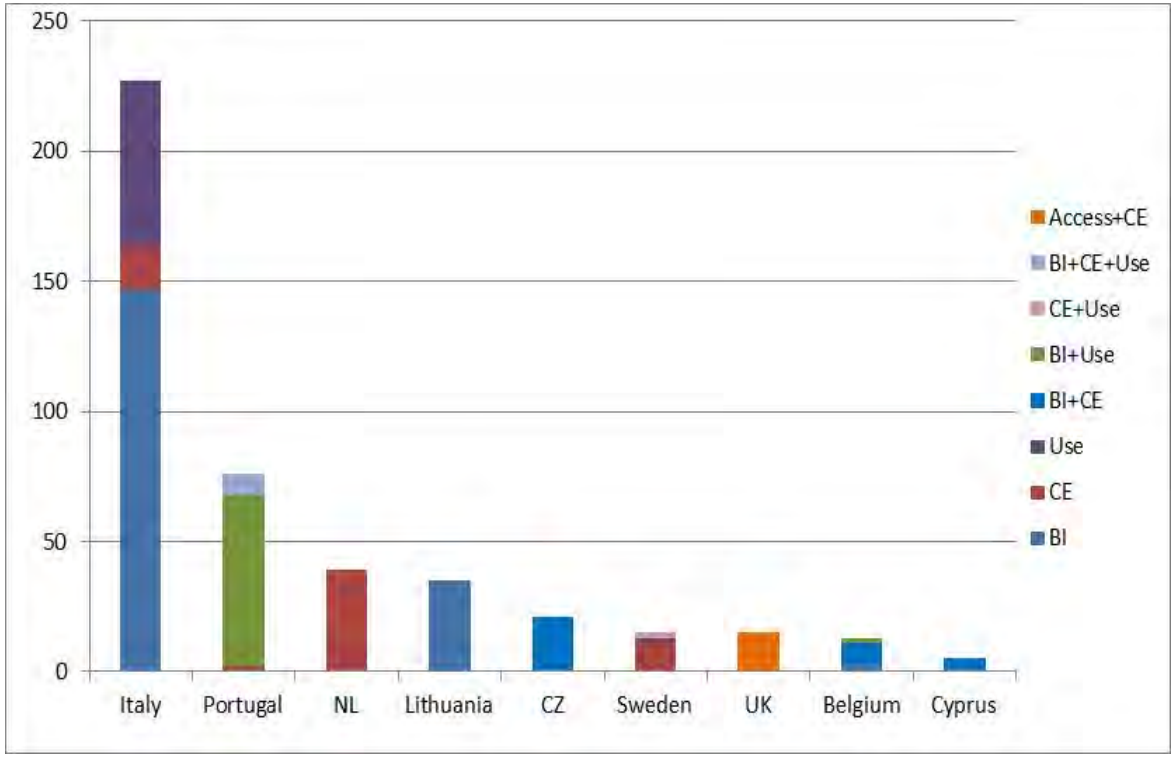
- Why?
  - Disagreement or uncertainty on therapeutic value
  - Uncertainty on dose in daily practice
  - Possibility to drive to larger patient access
- Main types of strategies
  - Portfolio deals
  - One price per patient
  - Targeting the patient out-of-pocket burden
  - **Disease management, integrated care and service agreements**

The role of Managed Entry Schemes in delivering value to health systems: Evidence of how Risk Sharing and Managed Entry Schemes are used in practice

Main objectives of MEAs

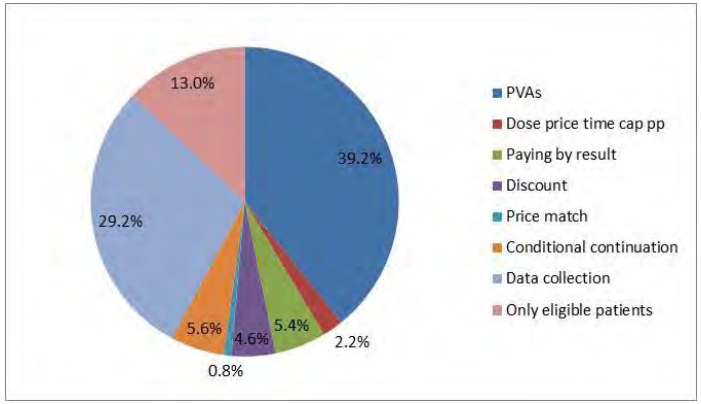


BI: Budget impact
CE: Cost-effectiveness
Use: utlisation
U: Uncertainty of treatment

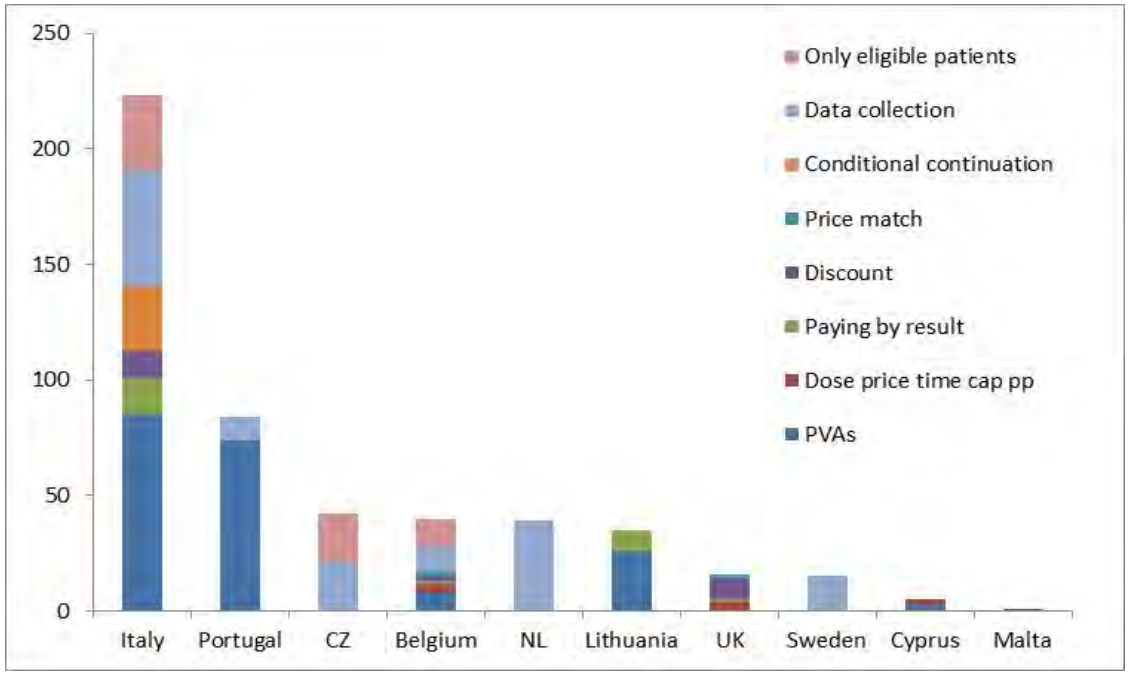


Ferrario & Kanavos, 2013

Common elements of MEAs

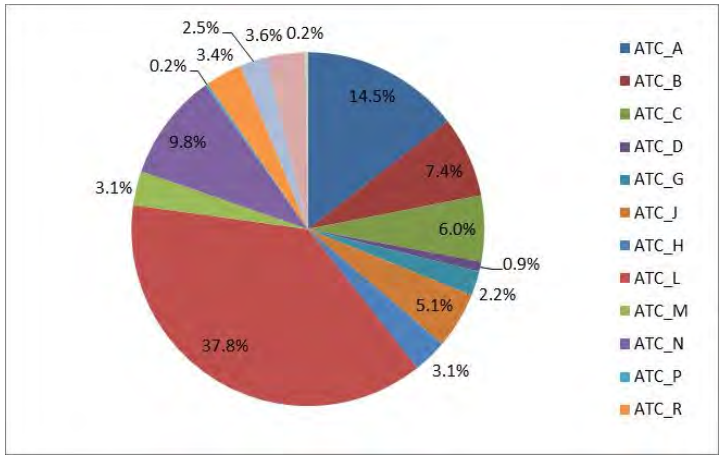


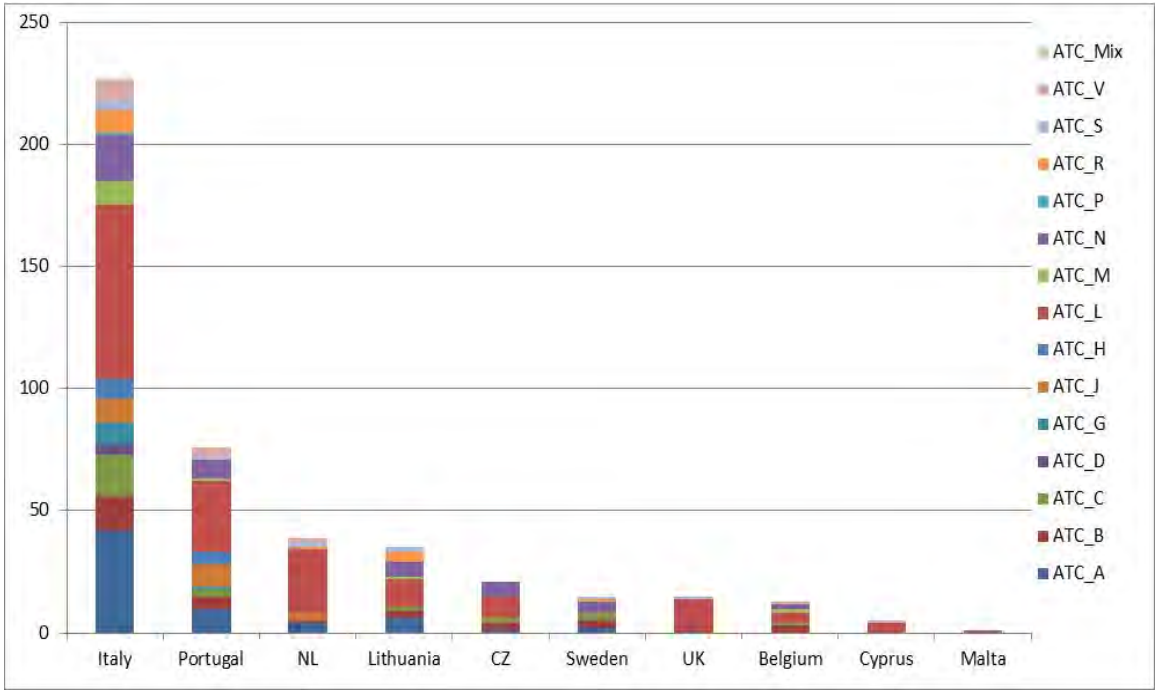
PVAs: Price-volume agreements
pp: per person



Ferrario & Kanavos, 2013

Therapeutic classes





ATC groups (according to ATC-index 2011)
A: Alimentary tract and metabolism
B: Blood and blood forming organs
C: Cardiovascular system
D: Dermatologicals
G: Genito urinary system and sex hormones
H: Systemic hormonal preparations, excl. sex hormones and insulins
J: Anti-infectives for systemic use
L: Antineoplastic and immuno-modulating agents
M: Musculo-skeletal system
N: Nervous system
R: Respiratory system
S: Sensory organs;
V: Various
ATC_Mix: There was one case in Italy where a particular AIFA-note contained medicines from different ATC-groups.

Ferrario & Kanavos, 2013

Conclusions

- HCV: a big public health concern
- The importance of prevention, also at EU level
- New funding models for certain populations
- Risk sharing and Managed Entry Schemes
- From Efficacy to Effectiveness & registries
- Bold moves in policy terms, but evidence that they can happen