

**Prof. Maribel Rodriguez Torres**

**12 August 1952 -  
28 December 2015**



# The Influence of Therapy on the Burden of Hepatitis C

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*of* NORTH CAROLINA  
*at* CHAPEL HILL

# Disclosures

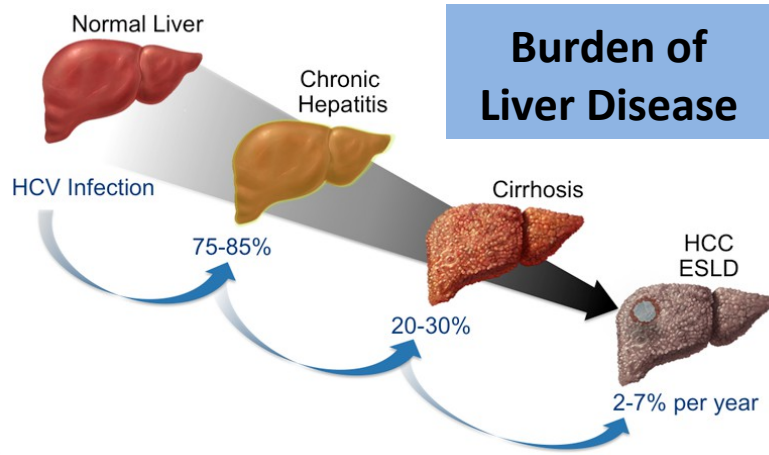
Michael W. Fried, M.D.

- **Grants/Research Support**
  - **Genentech, Merck, Vertex, Janssen, Bristol-Myers Squibb, AbbVie, Gilead,**
- **Consultant:**
  - **AbbVie, BMS, Gilead, Janssen, Merck, Vertex, Achillion**
- **Stock/Shareholder: None**
- **Speakers Bureau: None**
- **Other Financial Support: NIH Grants**
- **HCV-TARGET: Co-Principal Investigator**



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# The Influence of Therapy on the Burden of Hepatitis C

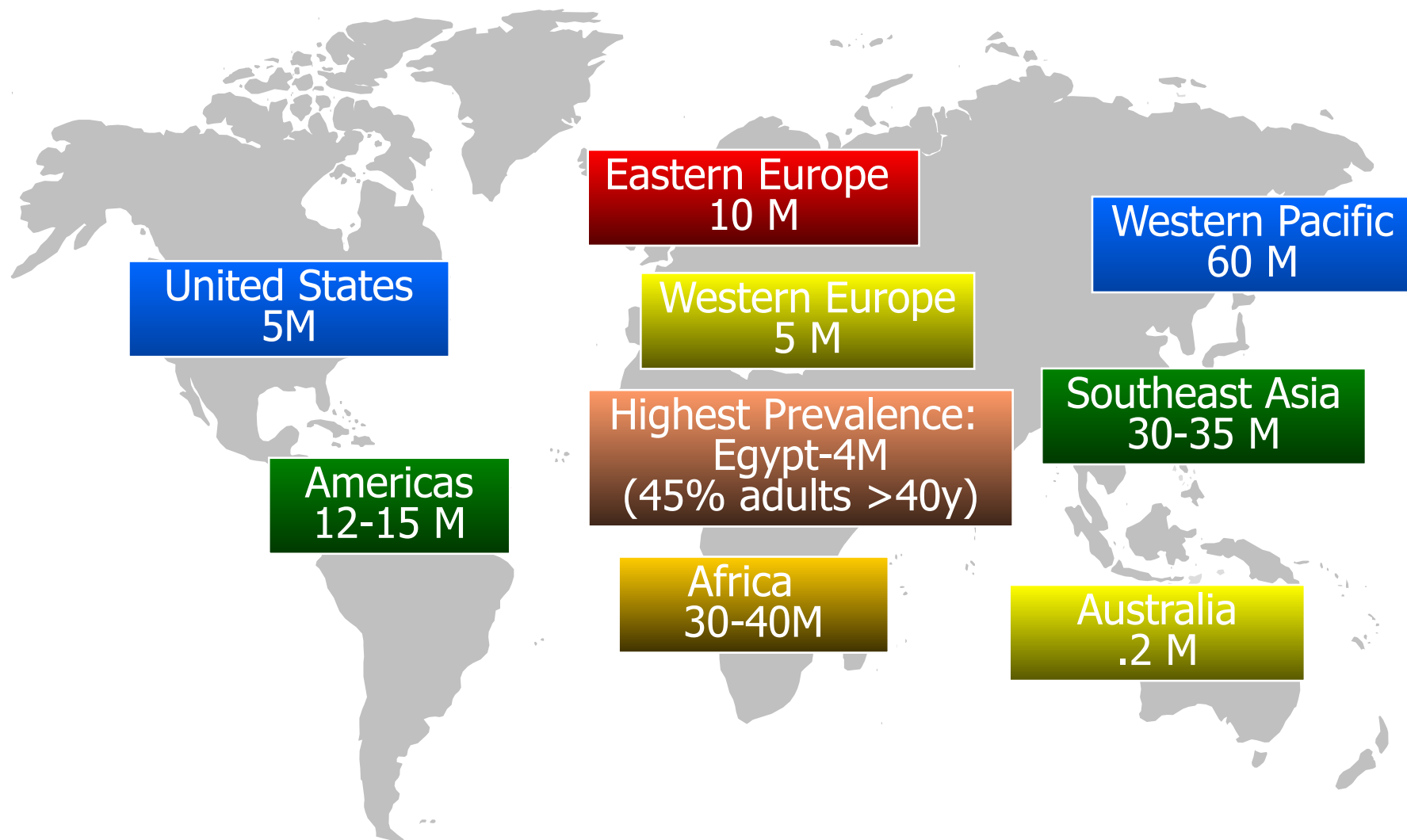


## Burden on Society

## Patient Burden



# Hepatitis C is a Global Problem: Seroprevalence of HCV

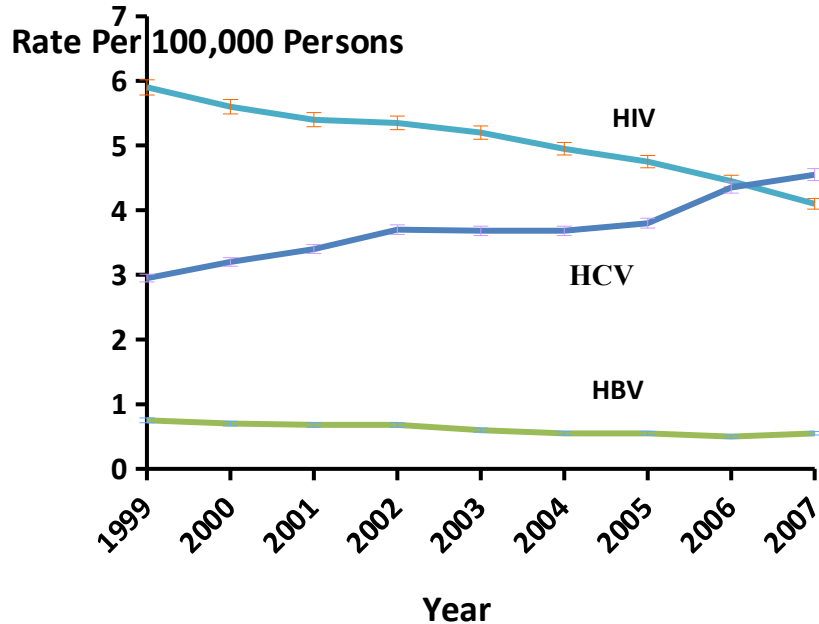


1. World Health Organization. *Wkly Epidemiol Rec.* 2000;75:17-28.

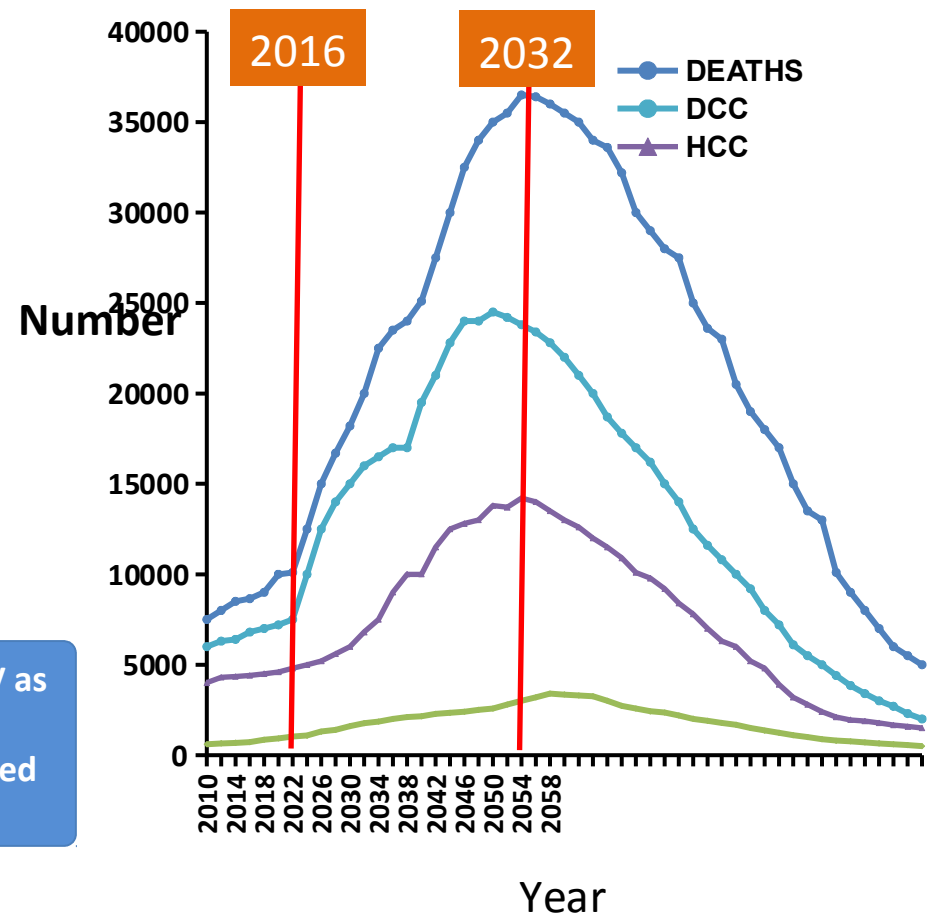
2. Edlin B et al. AASLD; November 11-15; 2005 San Francisco, California. Oral Presentation #44.

# Increased Morbidity and Mortality Due to HCV Now and in the Future

## Mortality Rates of HBV, HCV and HIV: 1999-2007



## Morbidity and Mortality Predictions2



- By 2007 hepatitis C-associated deaths had overtaken HIV as a cause of mortality in the United States.
- New policies and commitments to detect and link infected persons to care and successful treatment are needed.

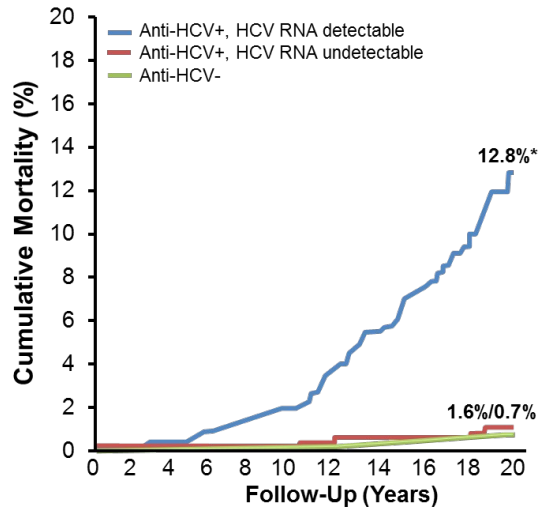
DCC, decompensated cirrhosis

Adapted from Ly KN et al. *Ann Intern Med.* 2012;156:271-278.

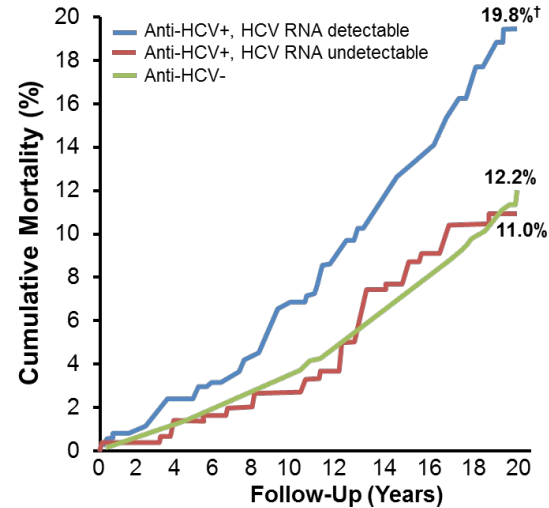
Adapted from Rein DB et al. *Dig Liver Dis.* 2011;43:66-72.

# Increased Mortality from Liver Cancer and Chronic Liver Diseases in HCV: REVEAL-HCV Study

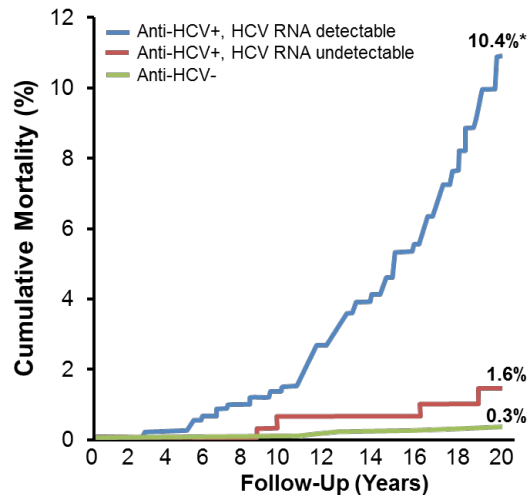
## Hepatic Diseases (n=195)



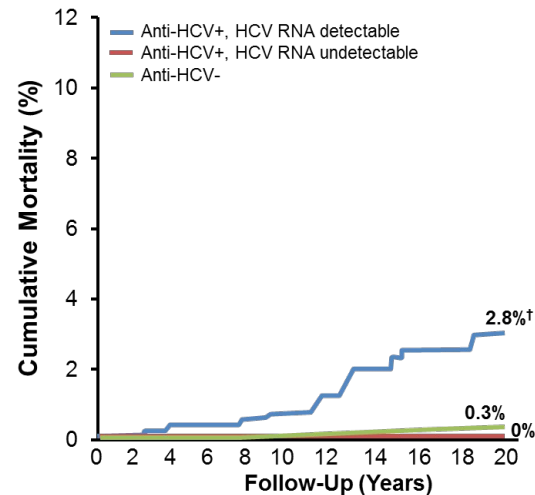
## Extrahepatic Diseases (n=2199)



## Liver Cancer (n=115)

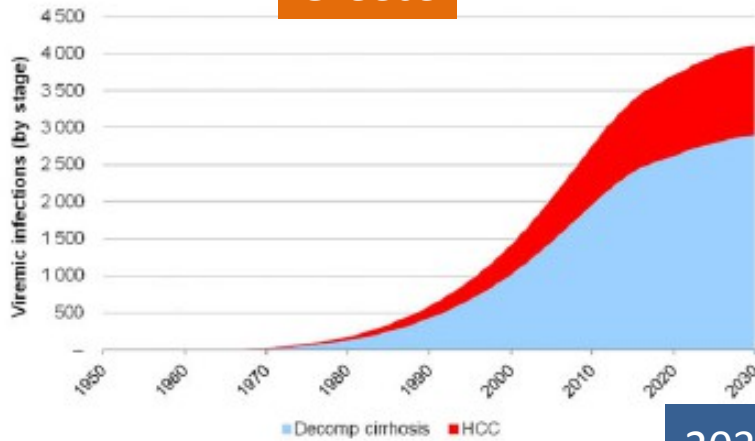


## Chronic Liver Diseases and Cirrhosis (n=76)



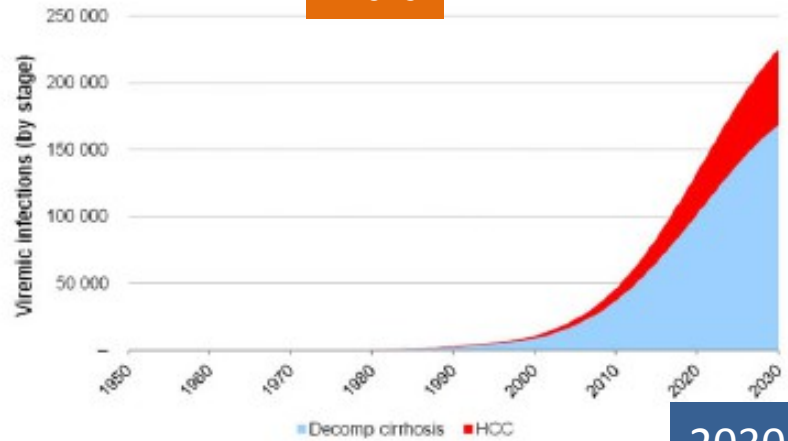
# Increasing Number of Cirrhosis and HCC Over Time is Occurring Everywhere

Greece



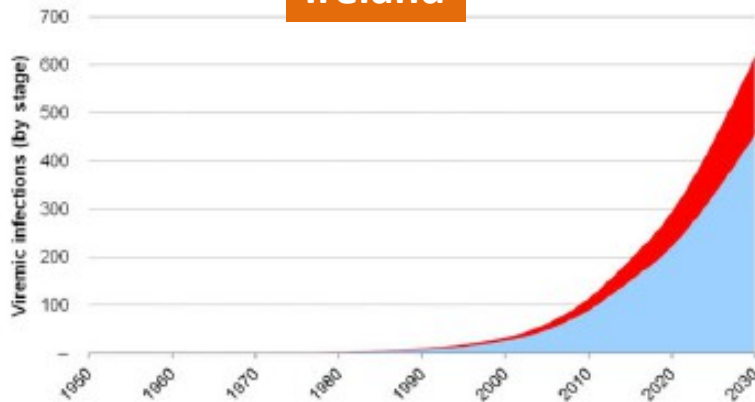
2030

India



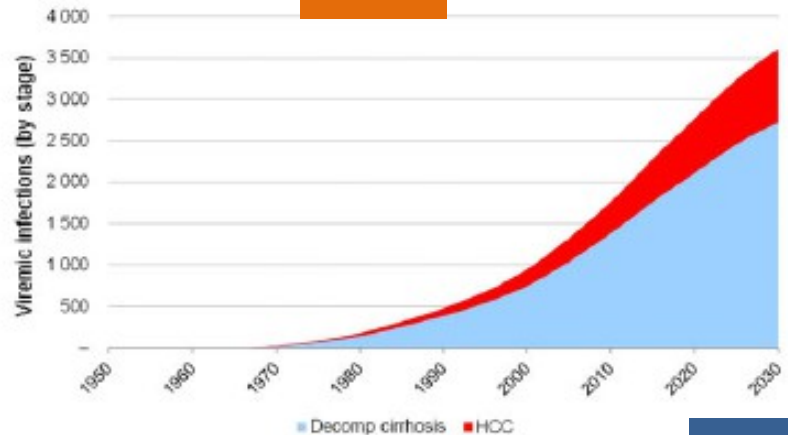
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Ireland



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Israel



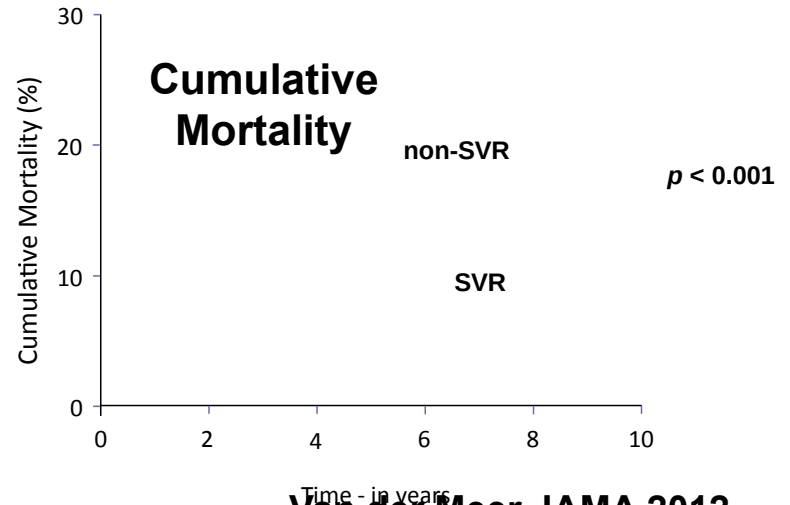
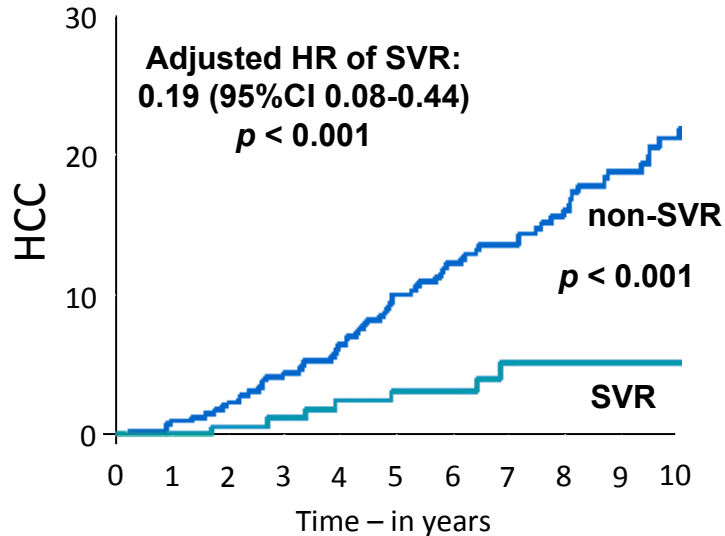
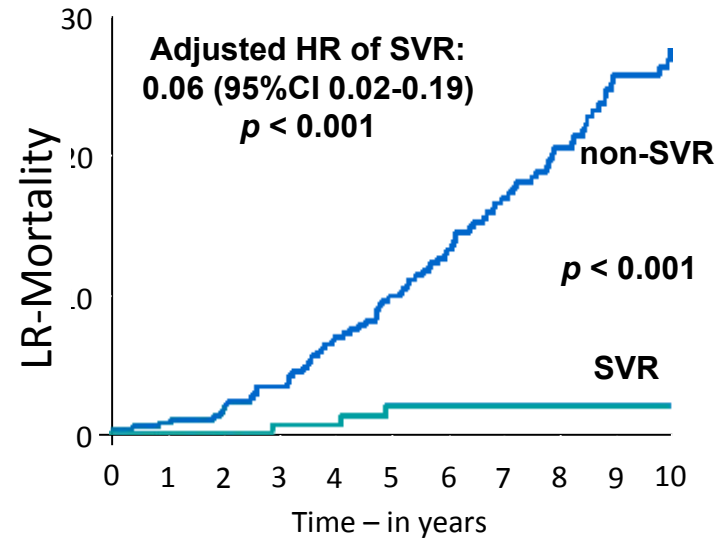
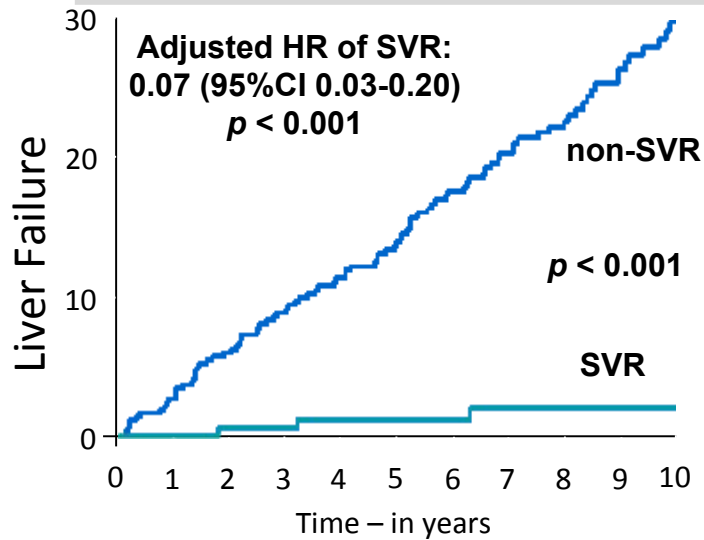
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Decompensated cirrhosis  
HCC

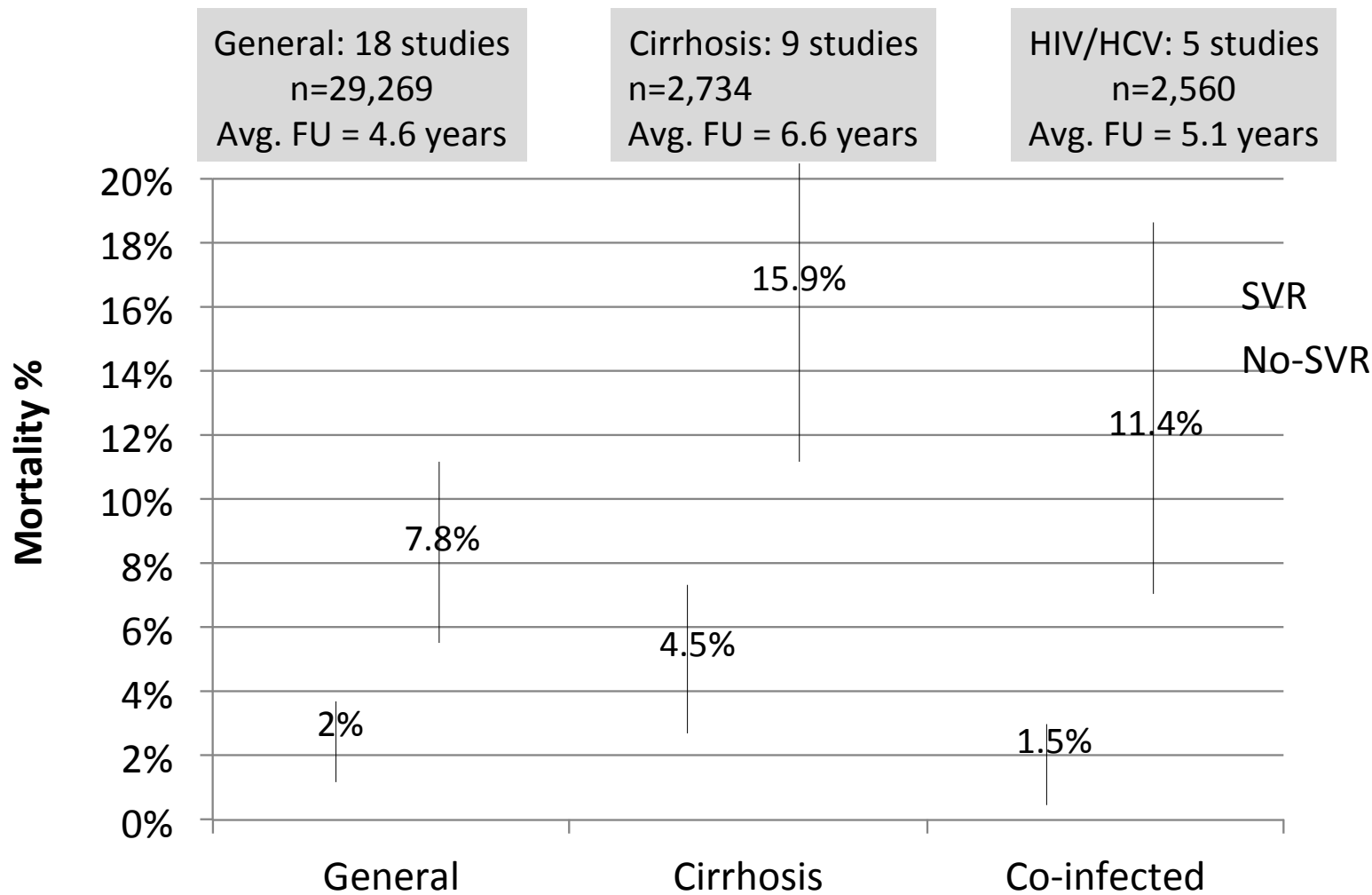


# Mortality and Morbidity Reduced with SVR

- 530 adults in Europe prospectively followed for median 8.4 years after HCV treatment
- 192 (36%) achieved SVR



## Decreased Five-year Mortality Rates in Multiple Populations Associated with SVR (Meta-analysis)



General= Studies that include all stages of liver disease

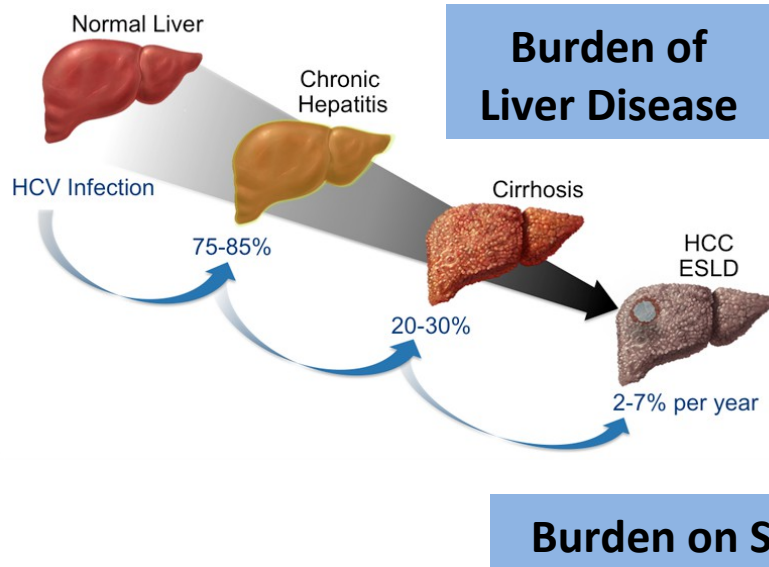
## Impact of Therapy on the Burden of Hepatitis C

- **HCV therapy with SVR unequivocally improves liver-related morbidity and mortality**
- **HCV therapy with SVR improves all-cause mortality**



**“The Happiest Place on Earth”**

# The Influence of Therapy on the Burden of Hepatitis C



## Patient Burden



# Patient-Reported Outcomes (PRO)

- “A **patient-reported outcome** or **PRO** is a method or questionnaire used in a clinical trial or a clinical setting, where the responses are **collected *directly* from the patient**” \*
  - Captures the patient experience related to treatment, side effects and outcomes that is **not** filtered through the lens of the healthcare provider
  - Must be validated to demonstrate that they measure and reflect the domain that they are trying to measure
    - Many validated instruments available
  - Can be administered via paper, telephone, computer, smartphone depending on resources of participants
  - Of increasing importance in clinical research and for demonstrating benefit of interventions

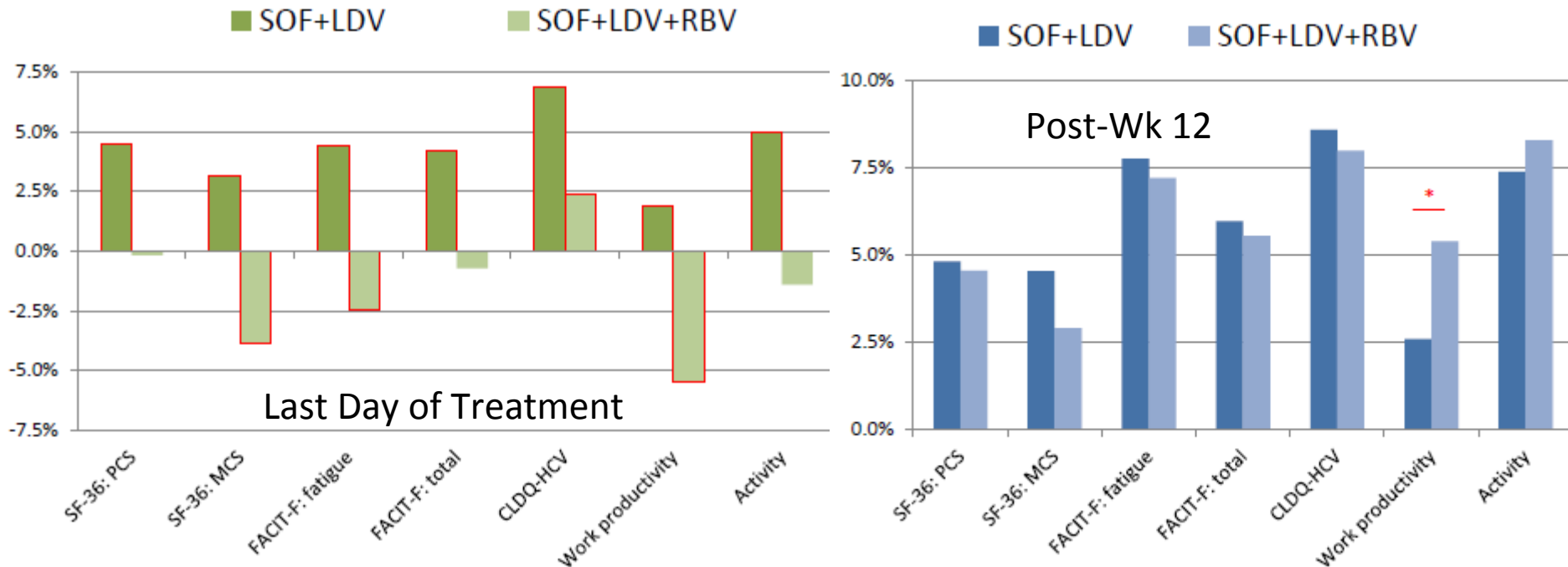
# Example of PRO for Fatigue (Excerpt from a Multiple Item Questionnaire)

In the past 7 days...

		Never	Rarely	Sometimes	Often	Always
FATEXP02	How often did you feel run-down?.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
FATEXP05	How often did you experience extreme exhaustion?.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
FATEXP06	How often did you feel tired even when you hadn't done anything?.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
FATEXP07	How often did you feel your fatigue was beyond your control?.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
FATEXP10	How often were you sluggish?.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
FATIMP05	How often were you less effective at work due to your fatigue (include work at home)?.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
FATIMP06	How often did your fatigue make you feel slowed down in your thinking?.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5

# Treatment with LDV/SOF Improves Patient-Reported Outcomes (PRO)

- PRO questionnaires administered at baseline, during, and post-treatment to patients treated with SOF+LDV regimens (n=1952): Baseline PROs were similar across regimens



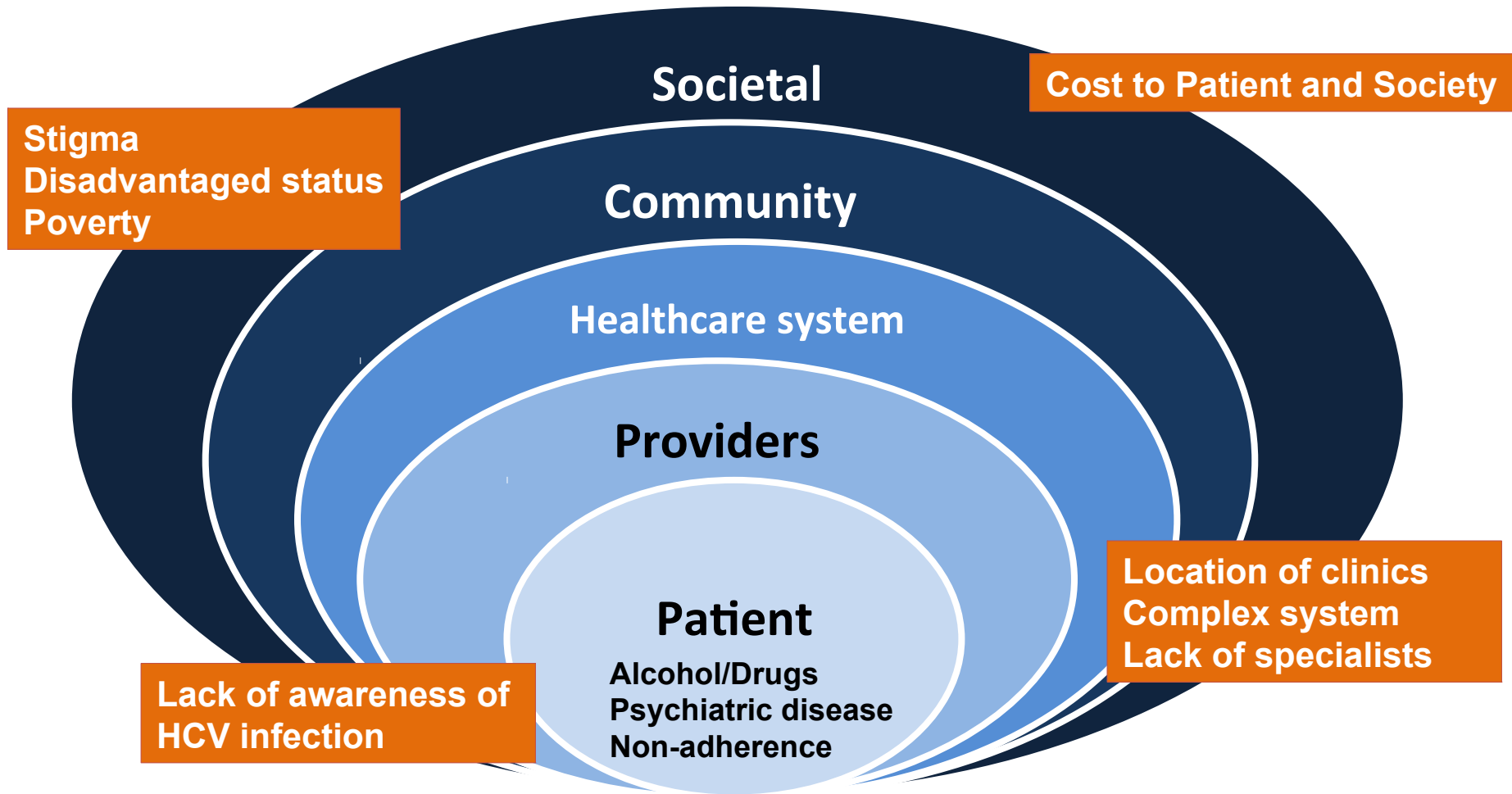
- SOF+LDV regimens were associated with significant improvement of PRO during treatment, as early as 2 weeks
- RBV was an independent predictor of PRO impairment in multivariate analysis
- Patients who achieved sustained viral eradication showed significant improvement of their PROs



## Impact of Therapy on the Burden of Hepatitis C

- HCV therapy unequivocally improves liver-related morbidity and mortality
- HCV therapy improves all-cause mortality
- **HCV therapy improves quality of life**
- **HCV therapy is associated with patients “feeling better”**
- **Rates of SVR (Cure of HCV infection) >95%** indicating that almost all patients will have these benefits of therapy
- **Why are we still debating the benefits of HCV therapy?**

# Many Barriers Exist to Treating HCV



# Focus on HCV Screening

2 1943 1944 1945 1946 1947 1948 1949 1950 1951 1952 1953 1954 1955 1956 1957 1958 1959 1960 1961 1962 1963 1964 1965 1966 1967

# BORN FROM 1945 TO 1965?

**AMERICANS BORN DURING THESE YEARS HAVE  
THE HIGHEST RATES OF HEPATITIS C.**

Talk to your doctor about getting tested. Early detection can save lives.



U.S. Department of  
Health and Human Services  
Centers for Disease  
Control and Prevention

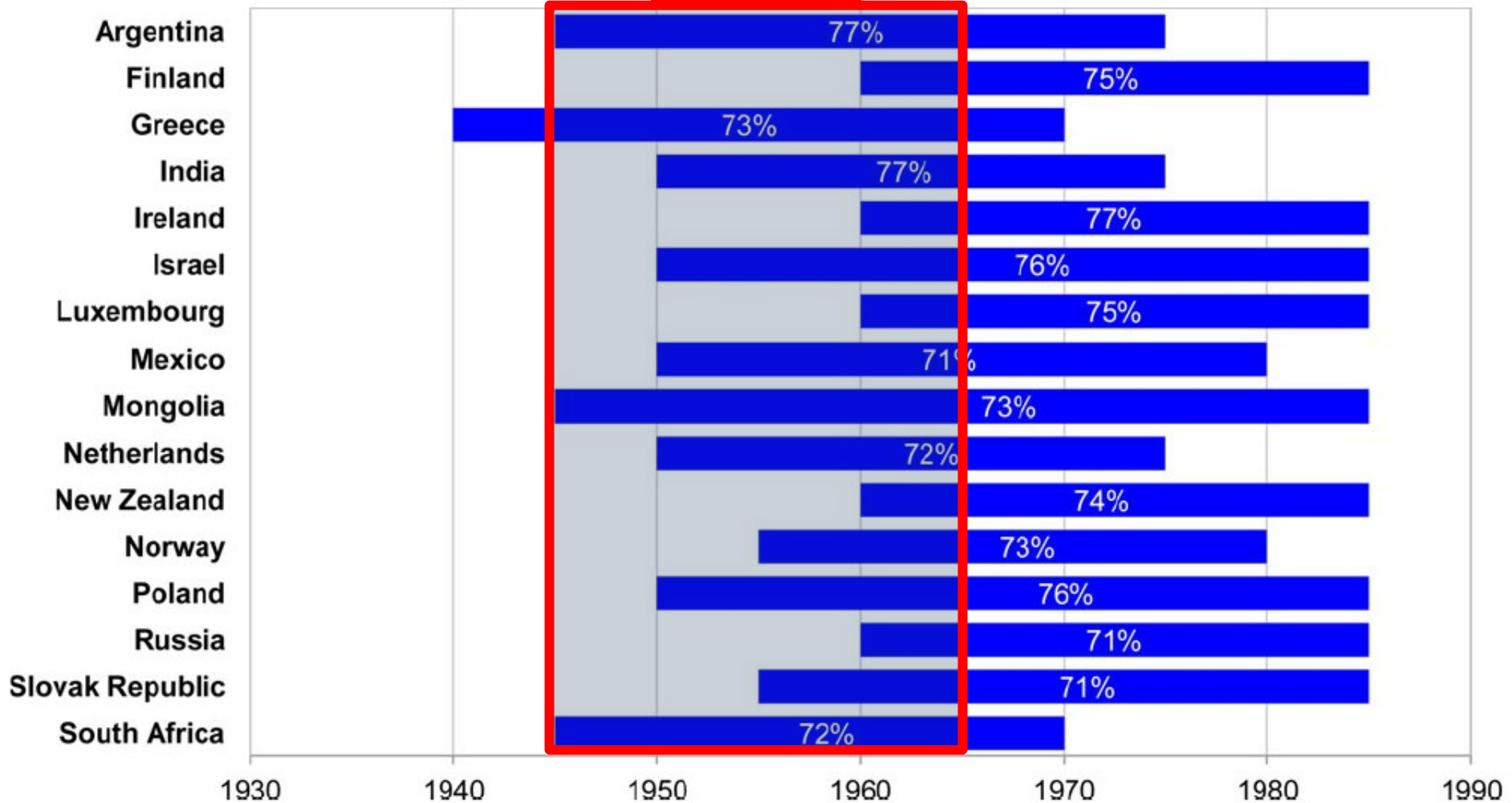
[www.cdc.gov/knowmorehepatitis](http://www.cdc.gov/knowmorehepatitis)



**KNOW  
MORE  
HEPATITIS™**

# Screening by Birth Year Cohort: Screening Strategies Must be Region-Specific

U.S Birth Year  
1945-1965



# Access to Care: Case 1

- **56 y/o man who injected drugs until 1980**
  - **Married, one daughter age 23**
  - **Not working, on state government health insurance plan**
  - **Asymptomatic, ALT= 37**
  - **FIBROSCAN = 14.5 kps c/w fibrosis stage F4**
- **Should this patient receive HCV therapy?**
- **This patient would be eligible for treatment in all of these cities except:**
  - Paris
  - Berlin
  - Chapel Hill, North Carolina
  - Detroit, Michigan

## Variable (and Arbitrary) Requirements for HCV Therapy Across State U.S. Medicaid Plans

**Table.** Prior Authorization Criteria for Sofosbuvir Prescription Under State Medicaid Fee-for-Service Programs

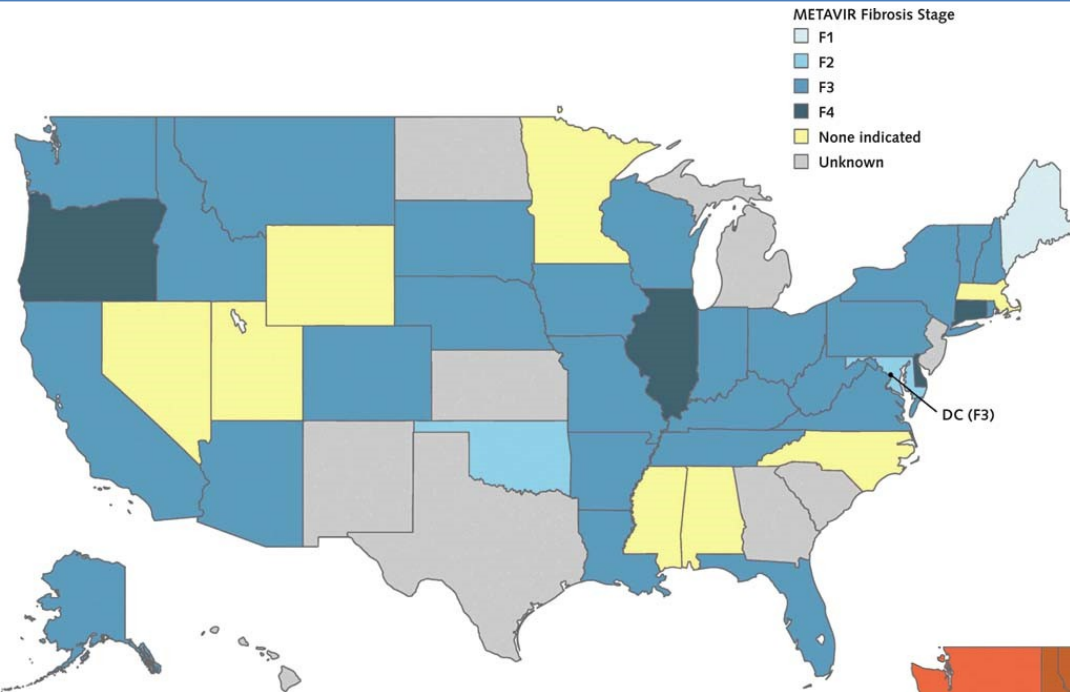
State	Status	Abstain From Alcohol Use Before Treatment	Abstain From Alcohol Abuse Before Treatment	Abstain From Drug Use Before Treatment	Abstain From Injection Drug Use Before Treatment	Minimum METAVIR Fibrosis Score	Specialist Prescriber
Alabama	NP	✓	✓	✓	✓	F2	-
Alaska	NP	✓	✓	✓	✓	F3*	-
Arizona	NP	-	✓	✓	✓	F3	✓
Arkansas	NP	-	✓	-	✓	F3*	-
California	NP	-	-	-	-	F3	-
Colorado	NP	-	✓	✓	✓	F3	✓
Connecticut	P†	-	-	-	-	-	-
Delaware	NP	✓	✓	✓	✓	F4	-
District of Columbia	NP	✓	✓	✓	✓	F2	✓
Florida	NP	✓	✓	✓	✓	F3	✓
Georgia	NP	-	-	-	-	F3	-
Hawaii	P	-	✓	✓	✓	F3	✓
Idaho	NP	-	✓	-	✓	F3	✓
Illinois	NP	✓	✓	✓	✓	F4	✓
Indiana	NP	-	-	-	-	F4	✓
Iowa	NP	✓	✓	✓	✓	F3*	✓
Kansas	NP	-	✓	✓	✓	F3	✓
Kentucky	P	-	✓	✓	✓	F3	✓
Louisiana	NP	-	✓	✓	✓	F3*	✓
Maine	P	-	-	-	-	F1	✓
Maryland	P	✓	✓	✓	✓	F2	✓
Massachusetts	P	-	-	-	-	NA	-
Michigan‡	NA	-	-	-	-	-	-
Minnesota	P	-	-	-	-	-	-
Mississippi	P	-	-	-	-	-	-
Missouri	P	-	-	-	-	-	-
Montana	P	-	-	-	-	-	-
Nebraska	P	-	-	-	-	-	-
Nevada	P	-	-	-	-	-	-
New Hampshire	P	-	-	-	-	-	-
New Jersey	P	-	-	-	-	-	-
New Mexico	P	-	-	-	-	-	-
New York	P	-	-	-	-	-	-
North Carolina	P	-	-	-	-	-	-
North Dakota	P	-	-	-	-	-	-
Ohio	P	-	-	-	-	-	-
Oklahoma	P	-	-	-	-	-	-
Oregon	P	-	-	-	-	-	-
Rhode Island	P	-	-	-	-	-	-
Tennessee	P	-	-	-	-	-	-
Texas	P	-	-	-	-	-	-
Utah	P	-	-	-	-	-	-
Vermont	P	-	-	-	-	-	-
Virginia	P	-	-	-	-	-	-
Washington	P	-	-	-	-	-	-
West Virginia	P	-	-	-	-	-	-
Wisconsin	P	-	-	-	-	-	-
Wyoming	P	-	-	-	-	-	-

**No patients on Michigan state health insurance have been treated with DAAs in 2015**  
 Update: Meeting on Dec 8: Coverage for F3-F4 will be allowed sometime in 2016

# Access to Care: Case 2

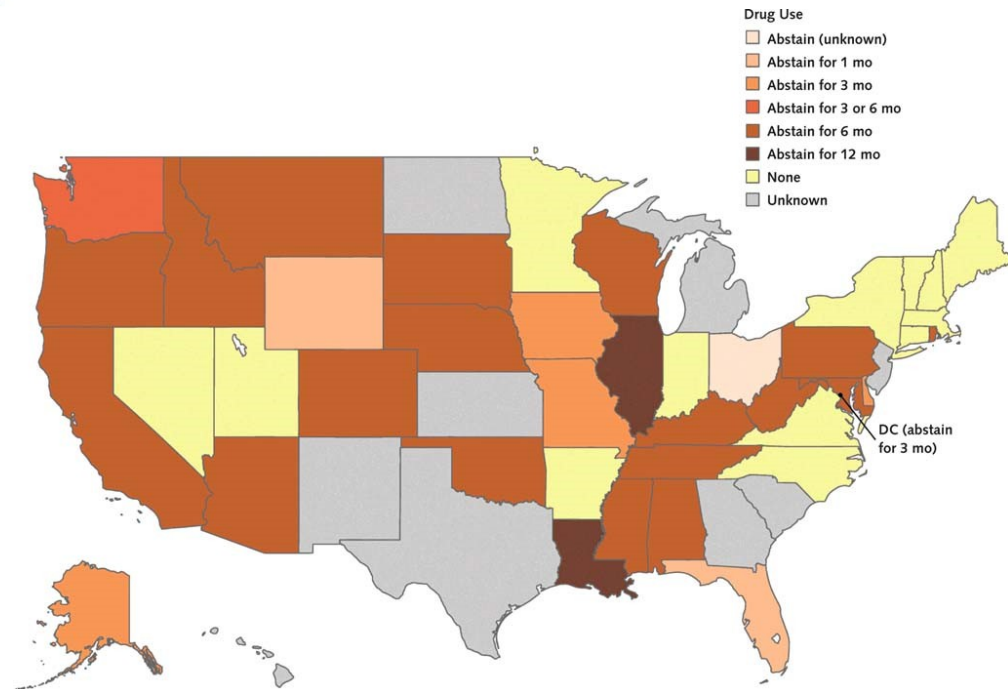
- **26 y/o woman previously addicted to prescription drugs and then heroin**
  - **Completed drug rehab program in 2012**
  - **Married, one daughter age 3**
  - **Recently graduated from college**
  - **Mild fatigue, ALT= 37**
  - **FIBROSCAN = 5.2 kps c/w fibrosis stage F1**
- **Should this patient receive HCV therapy?**
- **This patient would be eligible for treatment if she lived in which of these cities:**
  - Paris
  - Berlin
  - Chapel Hill
  - Warsaw

# Inconsistent Restrictions in State Medicaid Reimbursement for HCV Therapy



- Majority of state insurance plans require fibrosis stage  $\geq$  F3
- Liver biopsy required by 4 states!
- Reimbursement in most *countries* contingent upon advanced fibrosis

- Majority of state insurance plans require a defined period of abstinence from alcohol and/or drugs
- Some states require drug testing for **all** treatment candidates

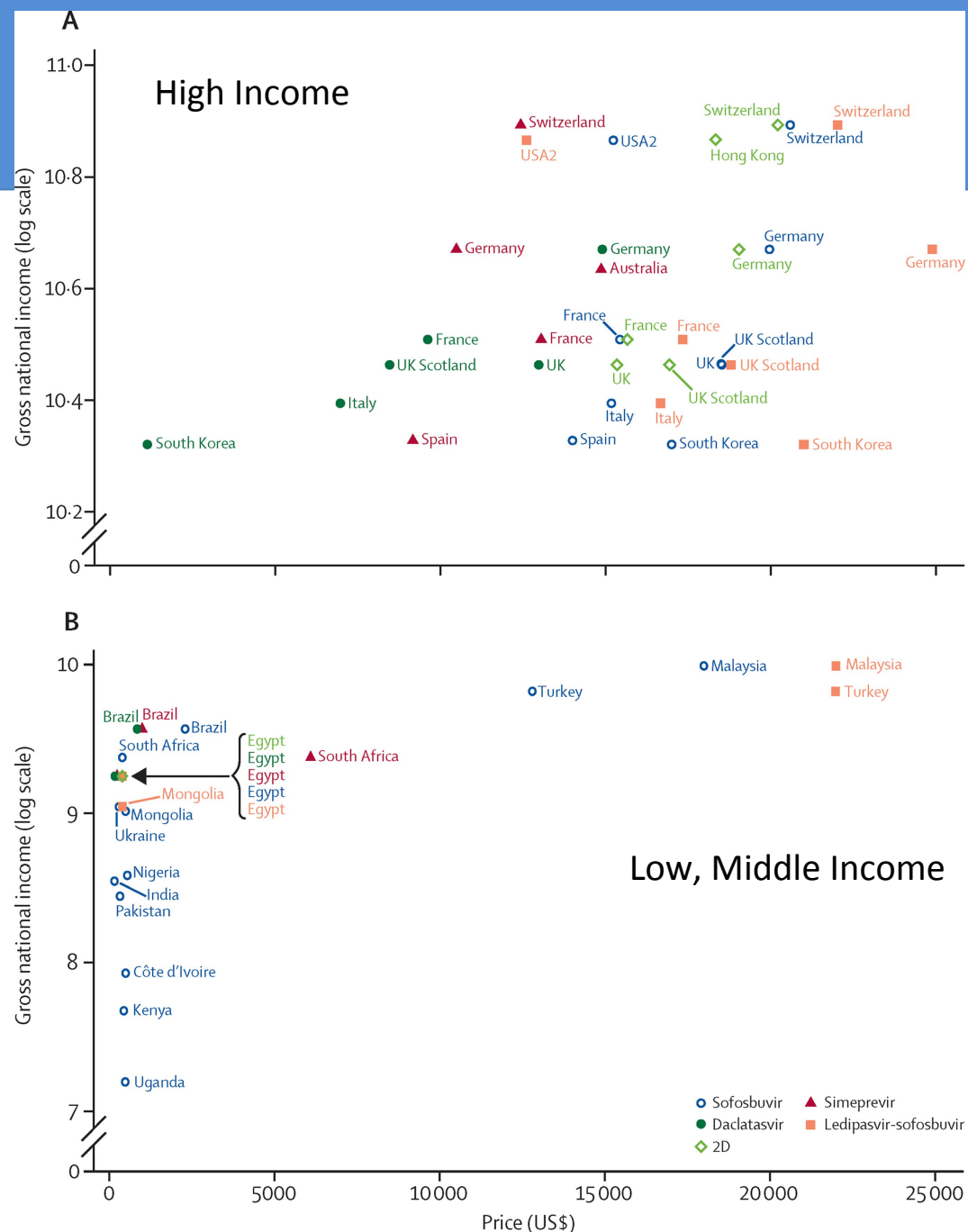




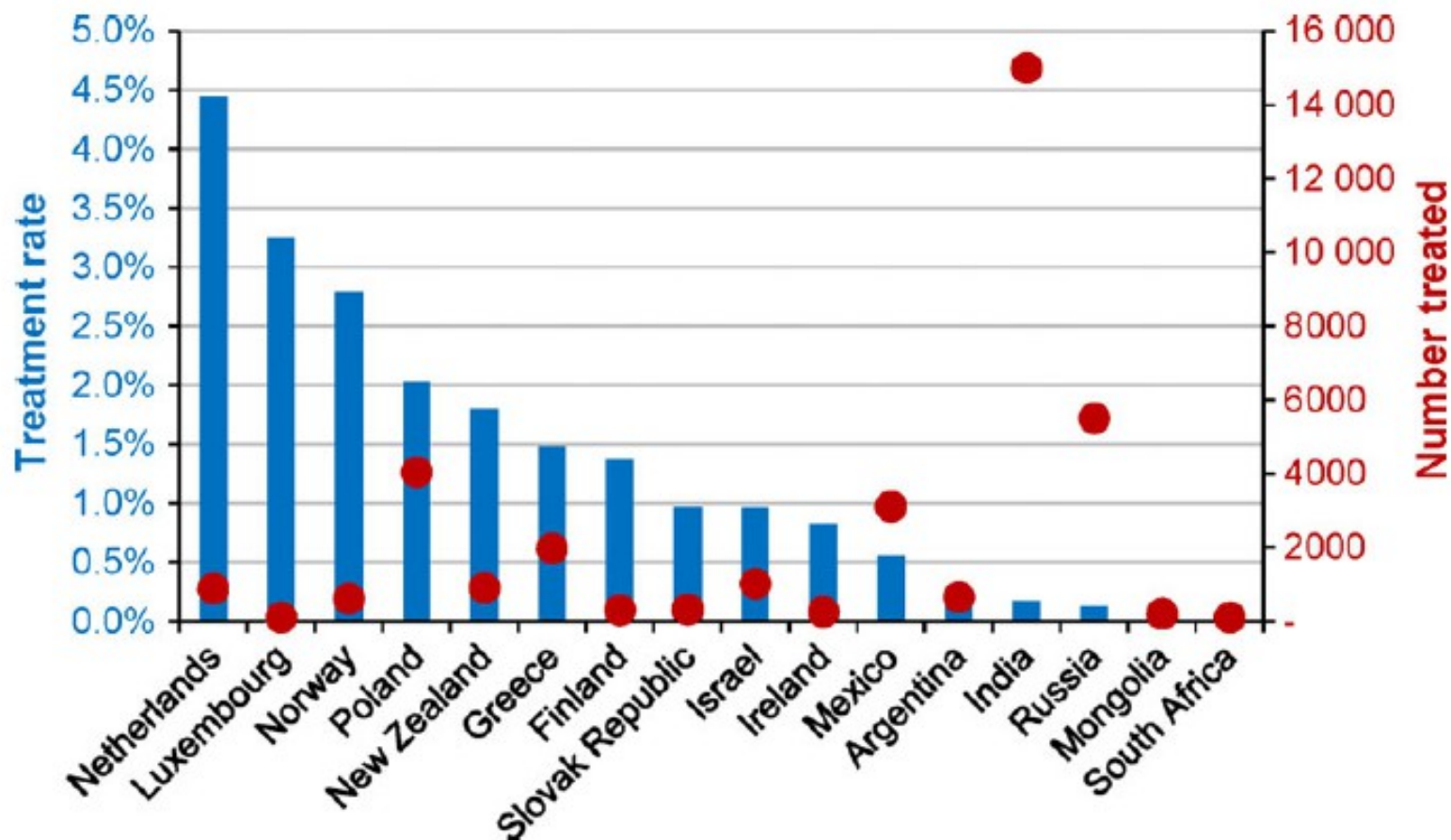
# Disparity in Market Prices for HCV DAA

Drug	Price per Bottle	
	Lowest (US\$)	Highest (US\$)
Sofosbuvir	300 India	20 590 CH
Daclatasvir	175 Egypt	14 899 Germany
Simeprevir	241 Egypt	14 865 Australia
SOF/LDV	400 Egypt	24 890 Germany
3D Regimen	400 Egypt	20 215 CH

- Pricing not related to manufacturing costs (<\$300/course)
- Prices generally related to gross national income
- Prices are lowest in lower and middle-income countries with some disparity
- Greatest variability noted across high-income countries (  $\Delta$  \$3000-\$6000)
- Voluntary licensing agreements (Gilead, BMS, AbbVie) decrease prices but often exclude middle-income countries.



## Estimated Treatment Rates Are Low in Most Countries

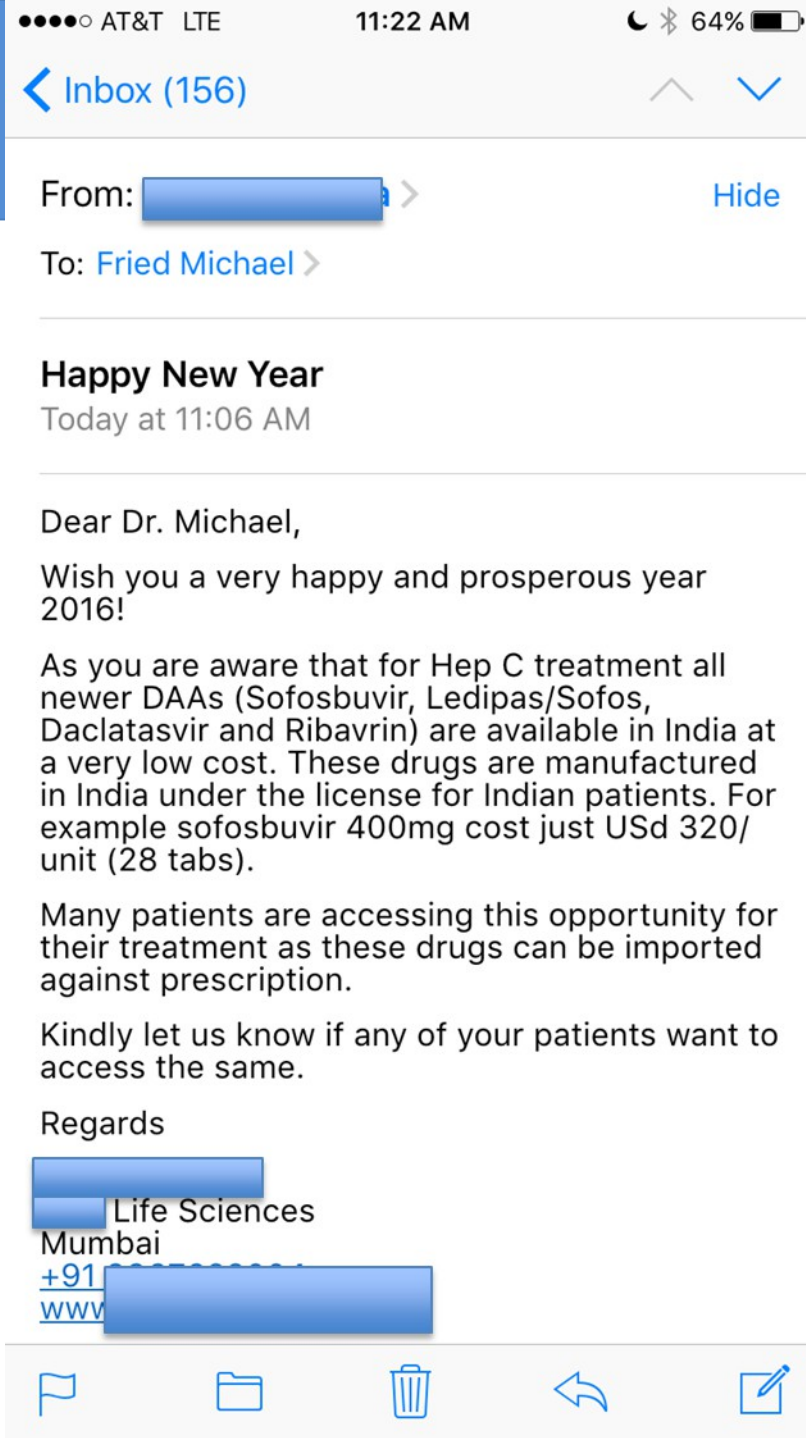


Treatment rate = # patients treated in a single year/Total chronic infections

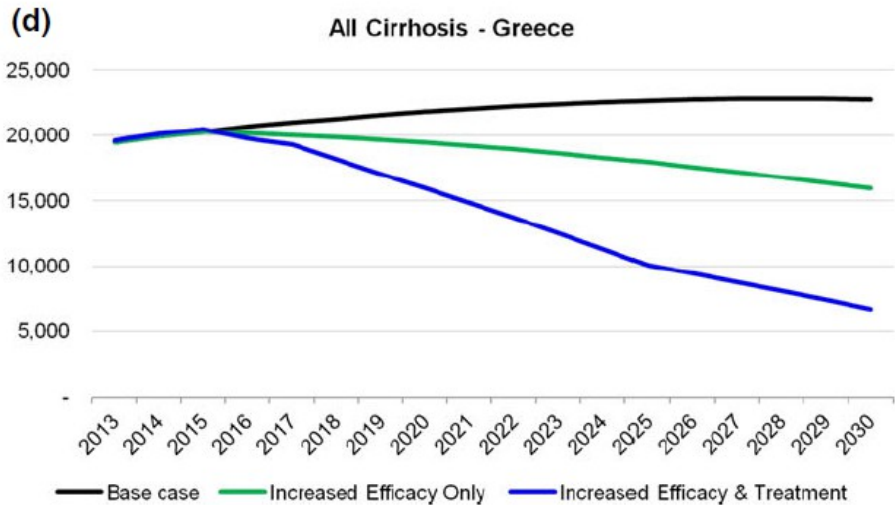
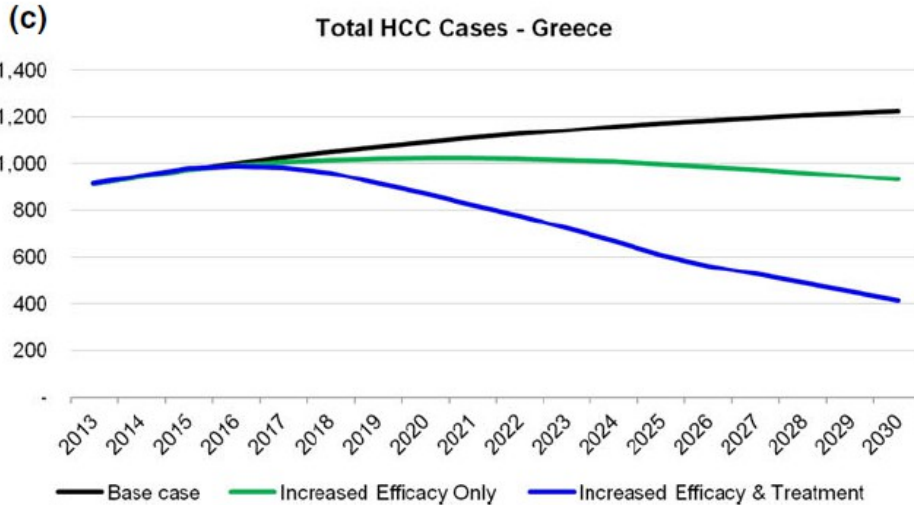
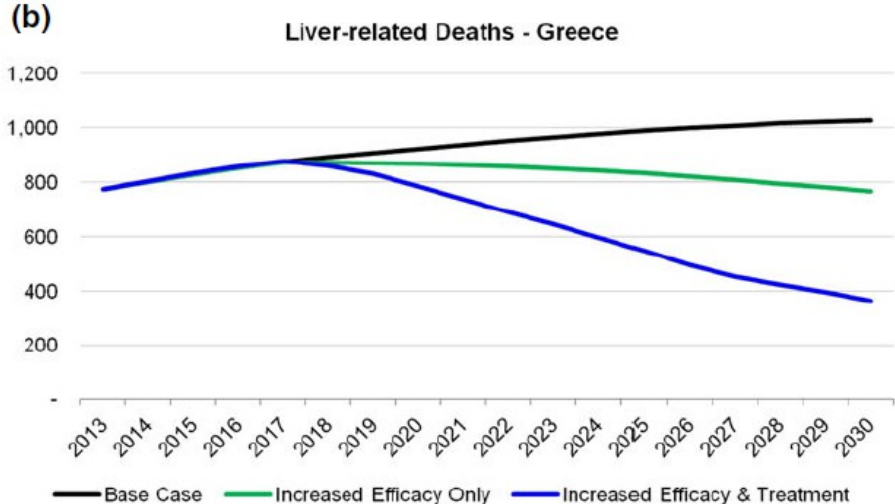
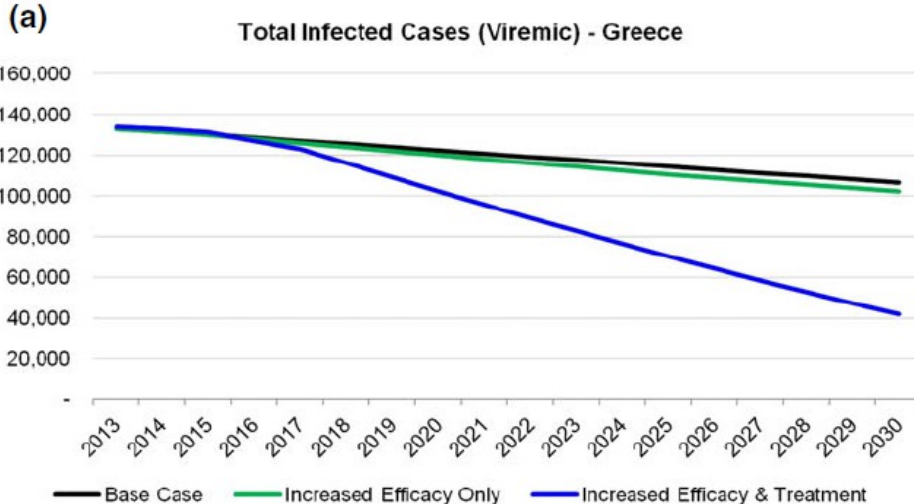
# Solicitation to Import Sofosbuvir from India to U.S.

**Sofosbuvir U.S. List Price = \$1000/day**

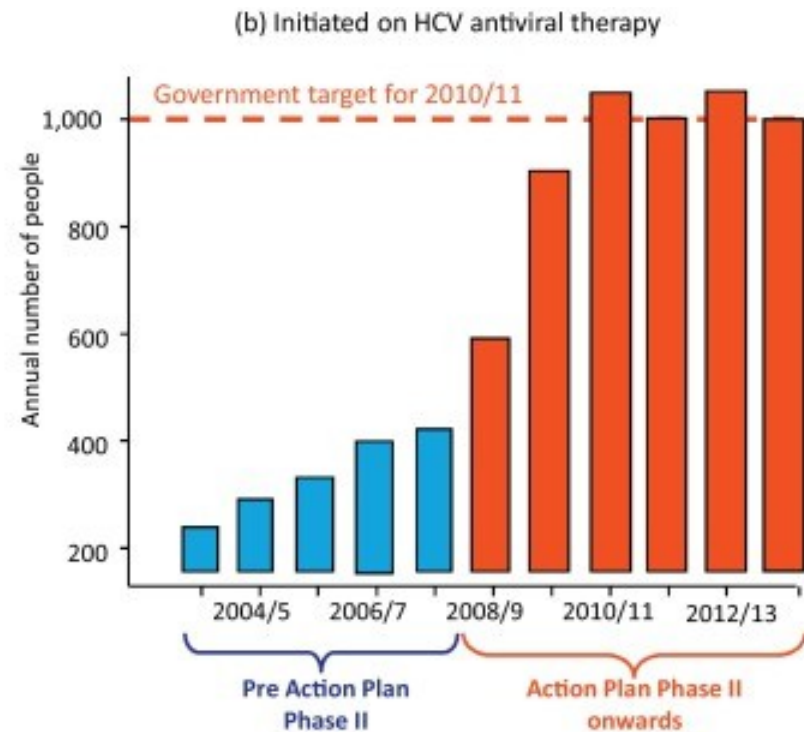
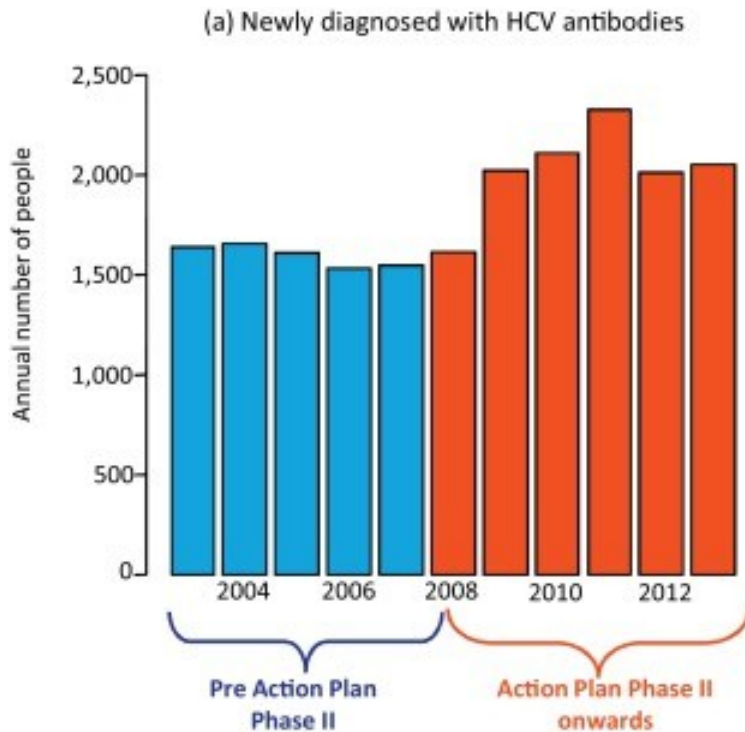
**Sofosbuvir 400mg = \$320/28 tabs or \$11.42 per day**



# Greatest Impact on Outcomes Requires Increased Efficacy AND Increased Treatment



# Scottish National HCV Action Plan



- Approximately 40,000 persons living with HCV in Scotland
- National Action Plan achieved initial goals:
  - Increased to 50% those diagnosed
  - More than doubled those treated annually (~1000/year)
  - Increased treatment rates among PWID
- Can this be scaled to larger geographic regions?

# The New York Times

## Curing Hepatitis C, in an Experiment the Size of Egypt

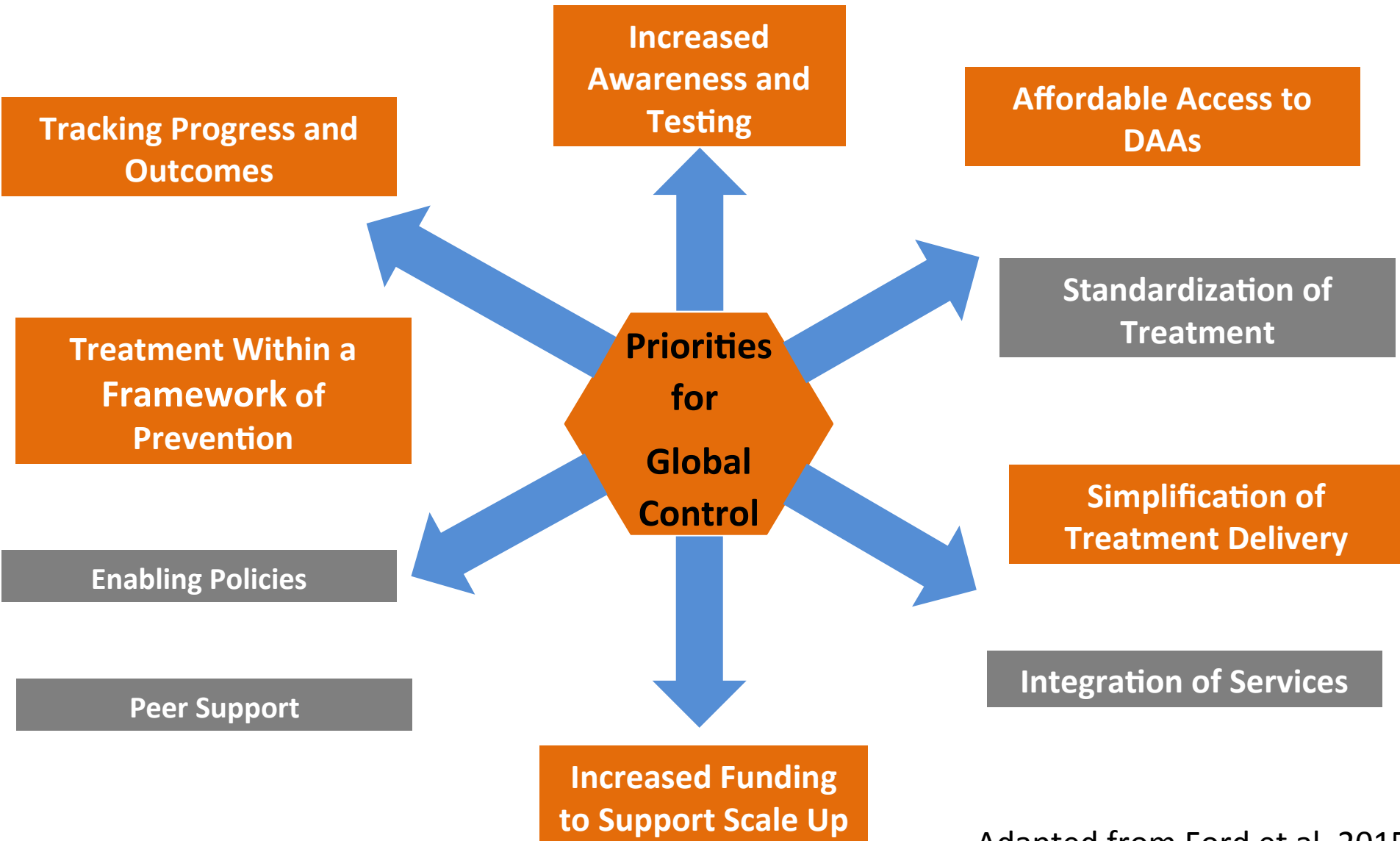
اقرأ المقال بالعربية | [Read in Arabic](#)

A new approach tested in Egypt could become the blueprint for providing cutting-edge medicines to the poor.

By DONALD G. McNEIL Jr. DEC. 15, 2015



# Top Ten Priorities for Global *Control* of HCV



# Prospects for Global *Eradiation* of HCV

- **Barriers to eradication:**
  - **Identification/diagnosis of patients with HCV is incomplete**
  - **Current treatments are too costly and access is severely limited in most countries**
  - **Few countries have devoted the resources to comprehensive national action plans**
  - **Continued occurrence of new infections and potential for reinfection**
- **Eradiation of HCV is unlikely to be accomplished without a prophylactic vaccination strategy**



# The Burden of Hepatitis C

## Summary

- **The burden of hepatitis C is immense and often underestimated**
- **Curing hepatitis C will have a positive impact by:**
  - **Decreasing the incidence of cirrhosis**
  - **Decreasing hepatocellular carcinoma**
  - **Improving overall quality of life for patients with HCV**
- **Multiple common barriers exist for implementation of focused programs to control HCV across low, middle, and high income countries**
- **We must continue to be the champions to effect change and to shape policies in our respective countries that will lead to greater access to care for all patients**



