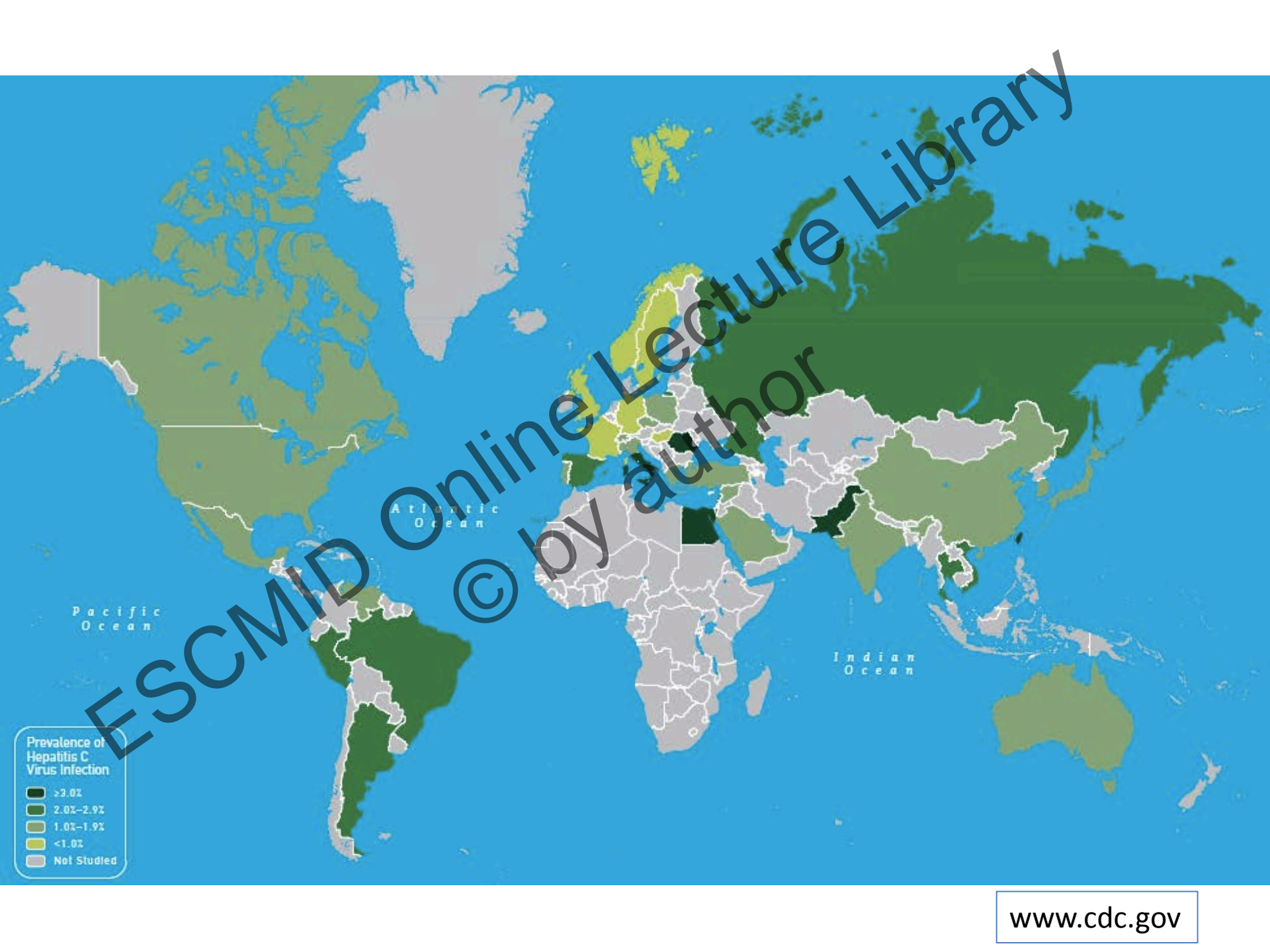


Hepatitis C Treatment in Developing Countries: Economic Perspectives

Resat Ozaras, MD, Professor
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- Chronic HCV infection: a considerable economic burden on health services



HCV is costly

- Diagnosis
- Treatment
- Management of complications

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Strategy 1

Community

No screening

No mild cases

No cost for community



Hospital

Cirrhosis

HCC

Strategy 2

Community

More screening
(for exp.: screen 100
individuals for 1 patient)

More mild cases

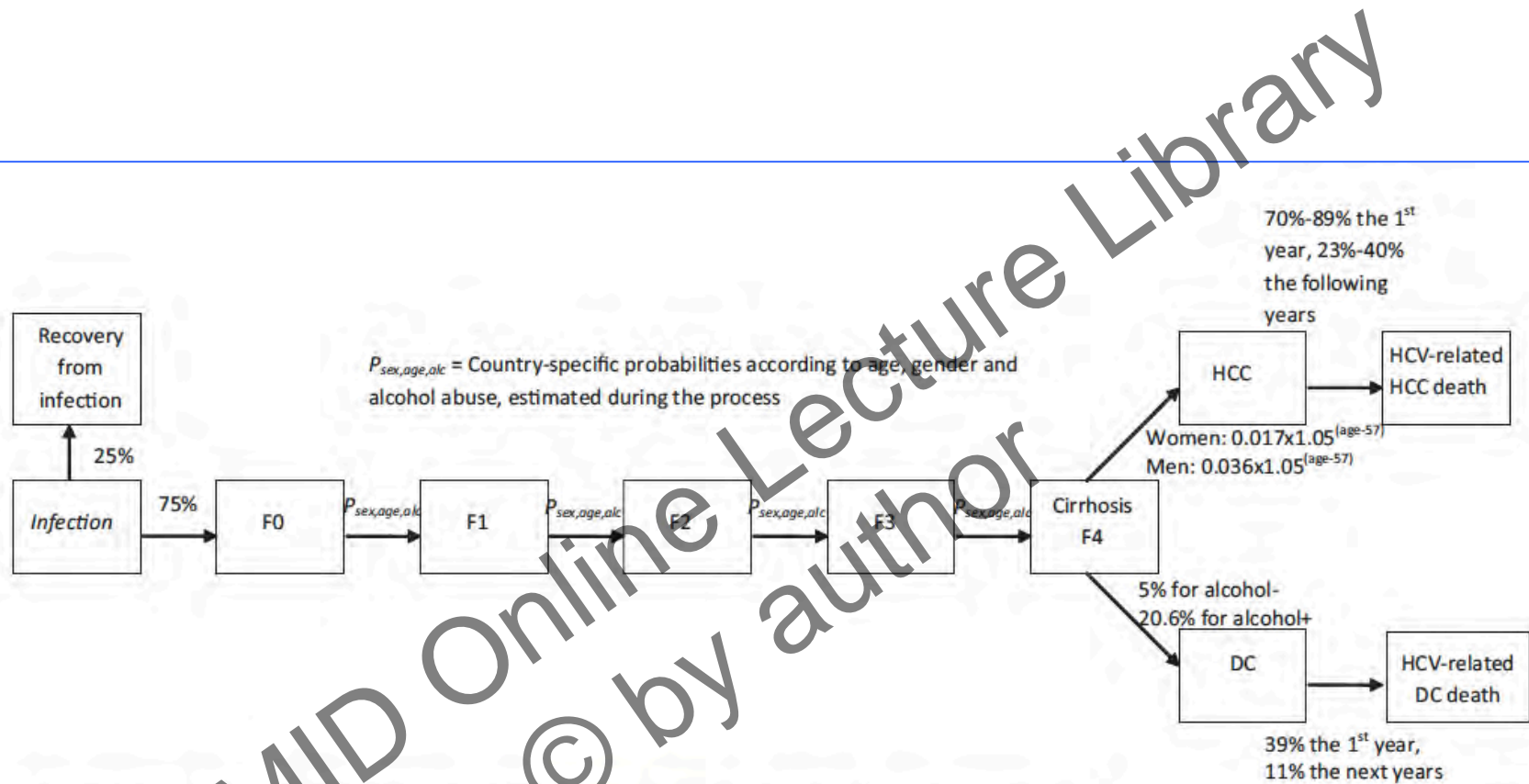
Higher treatment rate



Hospital

Less cirrhosis

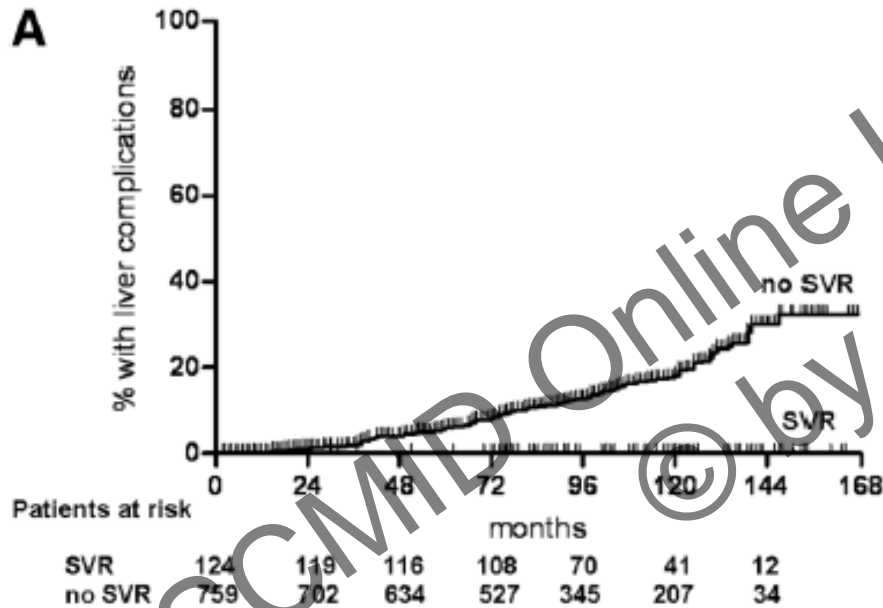
Less HCC



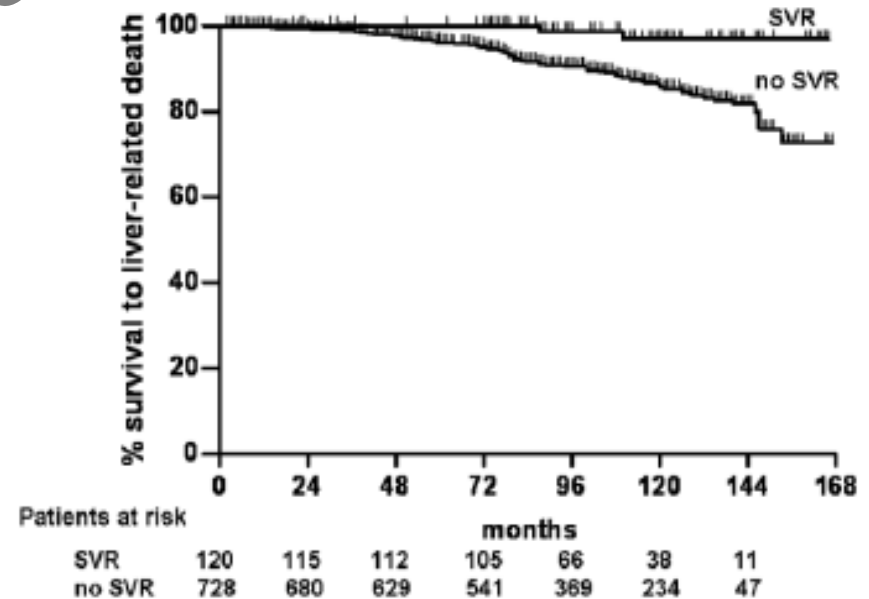
Supplementary Figure 1. Natural history of HCV disease. Annual probability of fibrosis progression, $P_{sex,age,alc}$, for each country was estimated according to sex, age, and alcohol abuse status (see Supplementary Table 3 for country-specific estimates).

SVR Saves Lives Even in Cirrhotics

Complications



Liver-related Death





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Economic Assessment of an Anti-HCV Screening Program in Italy

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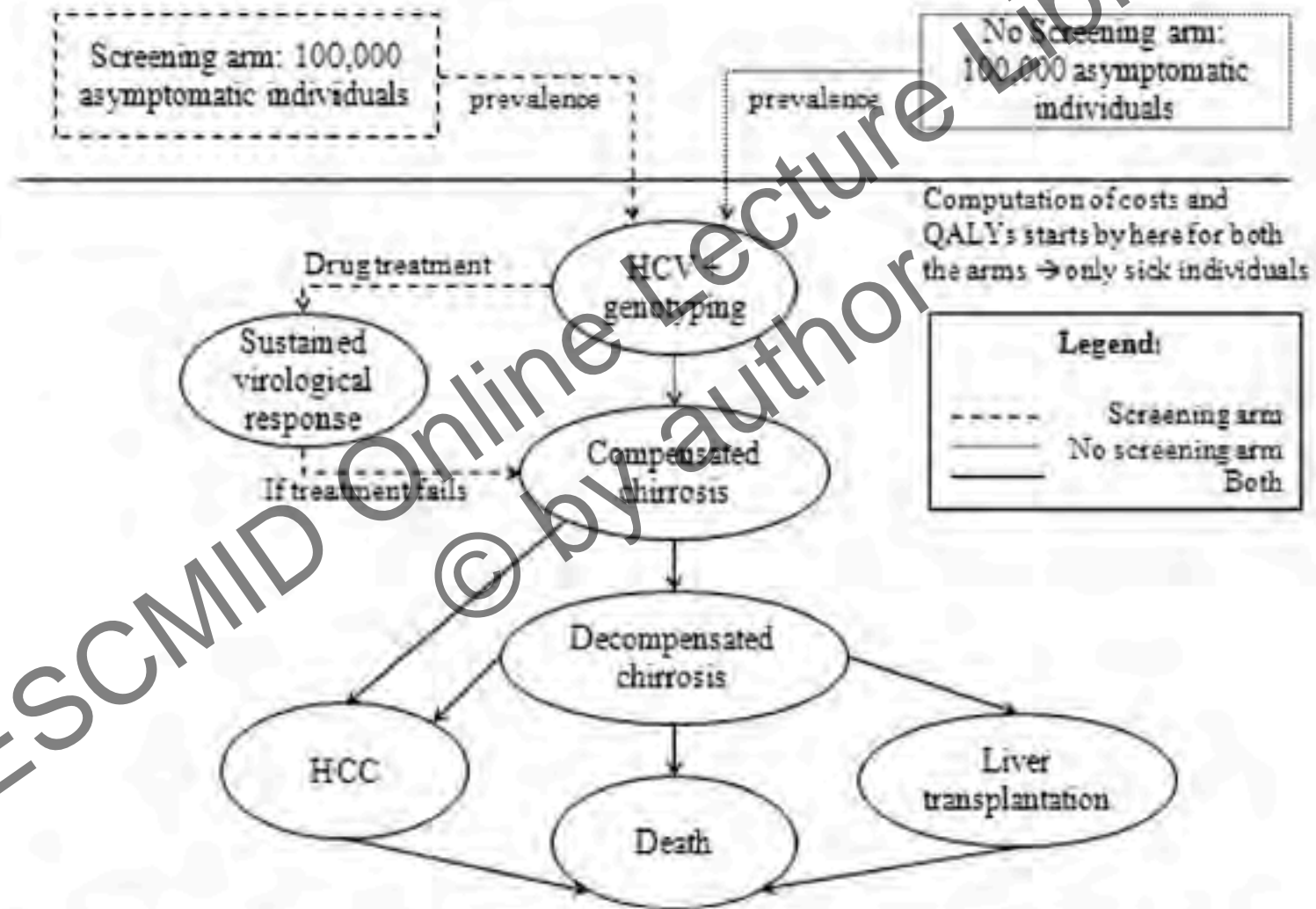


Fig. 1 - Model structure. HCC, hepatocarcinoma; HCV, hepatitis C virus.

Table 6 – Heterogeneity of results with respect to age: anti-HCV screening.

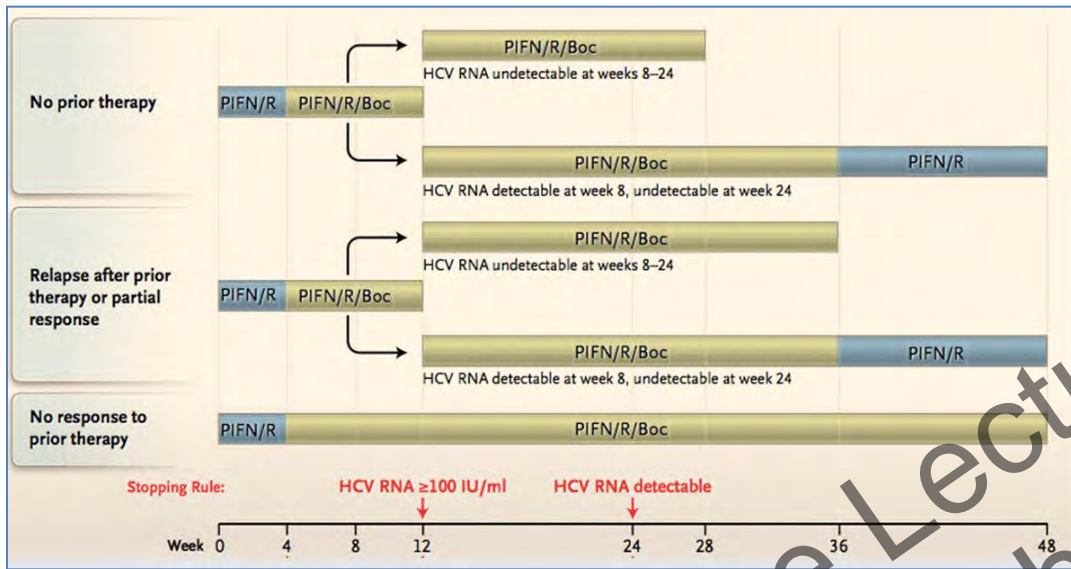
	Costs (€)	QALYs	Incremental costs (€)	Incremental QALYs	ICER
Base case					
Screening	25,341.07	27.31			
No screening	15,661.57	25.43	9,679.51	1.87	5,171.23
People aged 35 y					
Screening	31,041.24	31.03			
No screening	27,563.59	28.51	3,477.65	2.51	1,384.14
People aged 45 y					
Screening	27,688.07	28.80			
No screening	19,704.13	26.79	7,983.94	2.01	3,971.88
People aged 55 y					
Screening	23,540.91	23.77			
No screening	11,859.92	22.28	11,680.99	1.49	7,829.85
People aged 65 y					
Screening	19,525.23	25.42			
No screening	4,261.80	23.96	15,263.43	1.46	10,432.86

HCV, hepatitis C virus; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life-year.

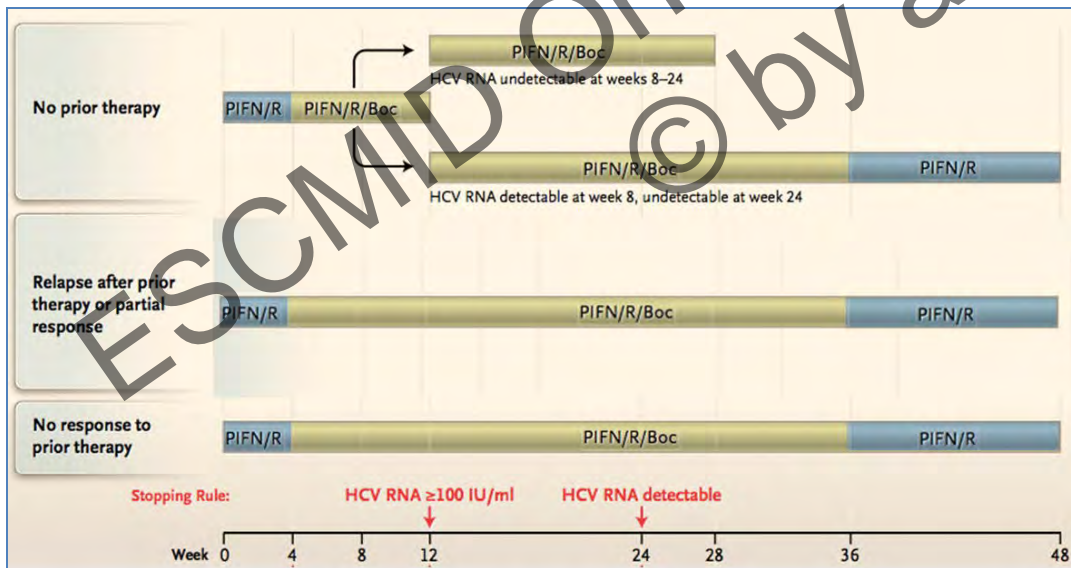
- Early diagnosis of HCV infection through testing followed by prompt treatment of subjects testing positive has a favorable ICER in the population
- The anti-HCV screening program is a valid health-related investment
 - improving patients' quality of life and survival
 - with an acceptable expenditure increase

Cost of treatment

- Drugs
 - Peg-IFN, ribavirin, telaprevir, boceprevir,
 - Sofosbuvir, daclatasvir, simeprevir,...
- Monitoring the treatment
 - HCV-RNA
 - Biochemistry
 - CBC
- Management of side effects



Liang&Ghany NEJM 2013;368:1907



Ozars R, Yemisen M, Balkan I. NEJM 2013;369:679

Telaprevir: Treatment Algorithms

Chronic HCV Genotype 1, telaprevir 750 mg (two 375 mg tablets) orally 3 times daily (7-9 hrs apart with food (~ 20 gm fat¹))

Treatment Decision Points (wks) 0 4 8 12 16 20 24 28 32 36 40 44 48
 End of 4 Wks End of 12 Wks End of 24 Wks End of 48 Wks

Initiate antiviral treatment

Telaprevir + PEG-IFN + RBV

PEG-IFN + RBV

PEG-IFN + RBV

RESPONSE-GUIDED THERAPY

Tx-Naïve & Prior Relapse Patients

4-wk HCV-RNA

12-week HCV-RNA

For telaprevir, HCV-RNA at week 4 and week 12 determine duration of therapy

eRVR Undetectable at Wks 4 & 12

Detectable ≤ 1000 IU/mL at Wks 4 and/or 12

Treatment-naïve with Cirrhosis[†]

Treatment Complete at 24 Wks

Treatment Complete at 48 Wks

48

Tx of Prior Partial & Null Responders

Triple therapy for 12 wks

Treatment Complete at 48 Wks

48

No RBV in partial and null responder patients with TVR

¹Largest food within 30 min prior to dose. ~20 gm fat: Bagel w/cream cheese; 1/2 cup nuts; 3 Tbs peanut butter; 1 cup ice cream; 2 oz American or cheddar cheese; 2 oz potato chips; 1/2 cup trail mix.

[†]Treatment-naïve patients with cirrhosis who have undetectable HCV-RNA at weeks 4 and 12 may benefit from an additional 36 weeks of PEG-IFN/RBV (48 weeks total)

© See stopping rules. Standard stopping rules still apply (Wk 4, 12, and 24 for telaprevir).

Immediate versus delayed treatment

- Resource-limited setting (Egypt)
- Markov model
- Lifetime cost
- Quality-adjusted life expectancy (QALE)
- Incremental cost-effectiveness ratio (ICER)

- Immediate treatment of patient at stages F1/F2/F3 is less expensive and more effective than delaying treatment until more severe stages or not treating
 - QALE: 18.3 years for F1
 - QALE: 18.2 years for F2
 - Wait till F3 when in F1: QALE:17.3 years
 - Wait till F3 when in F2: QALE:14.6 years

F4 patients

- Treatment is more effective than no treatment at all
 - QALE: 10.3 years versus 8.77 years
- Cost-effective
 - ICER: \$1915/QALY

HCV Treatment

- Delaying treatment in F1 patients until F2 then treating all patients regardless of their disease stage is cost-effective
 - ICER: \$33/QALY

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HCV Treatment

- Immediate treatment of F1/F2/F3: less expensive, more effective
- Immediate treatment of F1 versus waiting F1 to F2: only slightly more effective (sensitive to new drugs)
- Immediate treatment F4: highly effective and cost-effective

Cost-Effectiveness of Adding DAAs

- An analysis from US
 - The Veterans Health Administration (the largest single provider of care for HCV infection)
- 102,831 patients with untreated genotype 1 infection
- Decision-analytic Markov model to examine:
 - Standard dual therapy (PR)
 - PR+boceprevir
 - PR+telaprevir
 - No treatment

Estimated costs

- PR: \$8000
- PR+boceprevir: \$31,300
- PR+telaprevir: \$ 41,700

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- Liver-related death reduction

- PR: 5.2%

- PR+boceprevir: 10.9%

- PR+telaprevir: 11.5%

Incremental Cost-effectiveness Ratios

- PR+boceprevir vs PR: \$29,184/QALY
- PR+telaprevir vs PR: \$44,247/QALY

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- Despite substantial up-front costs with DAAs, each regimen
 - Improves QAL
 - Extends life expectancy
 - Reduces liver-related mortality

- Successful treatment of index case decreases the rate of HCV transmission

The State of Hepatitis B and C in the Mediterranean and Balkan Countries: Report from a Summit Conference

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Table 3 Comparative HBV and HCV screening policies in the non-EU Mediterranean countries

	Algeria	Egypt	Israel	Jordan	Lebanon	Libya	Morocco	Tunisia
Antenatal screening					HBV	HBV		HBV
Blood and organ donors	Both	Both	Both	Both	Both	Both	Both	Both
Blood transfusion or products prior to 1992 in EU, or any transfusion outside EU			Both	Both				
Clinical signs or laboratory signs (including cirrhosis and HCC)	Both	Both	HCV	Both	Both	Both		Both
Candidates for chemotherapy or immunosuppressive treatment			HBV		HBV	HBV		Both
Haemophiliacs who received concentration factors prior to 1987			Both		Both			
Haemodialysis	Both	Both	Both	Both	Both	Both	HBV	Both
History of shared injecting equipment	Both	Both	Both	Both	Both	Both		
History of long-term imprisonment	Both							
Hospital surgery patients							Both	
Household contacts	Both		Both	Both			Both	
HIV	Both				Both			
IVF candidates			Both				Both	
Men who have sex with men								
Migrants from high prevalence countries			Both					
Military recruits	Both	Both		Both	Both			Both
Organ or tissue transplants prior to 1992 in EU or outside EU			Both		Both			
Pre-employment		Both	HCV, health care	Both				
Pregnant women and newborns			Selective risk groups: HBV	HBV	HBV	HBV		HBV
Pre-nuptial	Both				HBV			HBV
STI clinic patients			Both	HBV	Both	HCV		
Traditional medicine exposure	HBV							
Unvaccinated healthcare workers	Both		HBV	Both				HBV
Occupational exposure and/or carrying out exposure-prone procedures	Both	Both	Both	Both	Both	HBV		HBV

EU, European Union; HBV, hepatitis B virus; HCV Ab, hepatitis C virus.

Table 4 Comparative HBV and HCV screening policies in the non-EU Balkan countries

	Bosnia-Herzegovina	Croatia	Kosovo	Serbia
Antenatal screening	HBV	HBV		HBV
Blood and organ donors	Both	Both	Both	Both
Blood transfusion or products prior to 1992 in EU, or any transfusion outside EU	HCV	Both		
Clinical signs or laboratory signs (including cirrhosis and HCC)	Both	Both		Both
Candidates for chemotherapy or immunosuppressive treatment		Both		
Haemophiliacs who received concentration factors prior to 1987		Both		HCV
Haemodialysis	Both	Both		Both
History of shared injecting equipment	Both	Both		Both
History of long-term imprisonment		Both		Both
Household contacts	Both	Both		HBV
HIV		Both		Both
IVF candidates		Both		
Military recruits				HBV
Organ or tissue transplants prior to 1992 in EU or outside EU		Both		
Pregnant women and newborns	HBV	HBV		Both
Traditional medicine exposure	HBV			
Unvaccinated healthcare workers	Both			
Occupational exposure and/or carrying out exposure-prone procedures	Both	Both recommended as a part of postexposure procedures		Both

EU, European Union; HBV, hepatitis B virus; HCV Ab, hepatitis C virus.

Country	GDP per capita, 2011, USD*	HCV drug costs (euro)†
Algeria	\$5244	PEG-IFN alpha-2a/rib: €16 412
Egypt	\$2781	Peg-IFN/rib: €2000
France	\$42 377	PEG-IFN/rib: €16 000 Triple therapy: €16 000 + €27 180 (telaprevir) €16 000 + €36 452 (boceprevir)
Greece	\$25,622	PEG-IFN/rib: €10 680-€13 812
Israel	\$31,282	PEG-IFN: €9010 Ribavirin: €5308 Telaprevir: €18 552 Boceprevir: €20 165
Italy	\$36,103	PEG-IFN/rib: €12 000-€18 000 DAA: €12 000-€50 000 PEG-IFN/rib: €12 000 Protease inhibitor: €27 300
Morocco	\$3054	PEG-IFN/rib: €12 000 protease inhibitor: €27 300
Serbia	\$6310	PEG-IFN/rib: €3500-7000
Spain	\$31943	

*Source: World Bank GDP per capita. <http://data.worldbank.org/indicator/NY.GDP.PCAP.CD>, accessed 29 March 2013.

†Source: Country representative presentations, Conference on Hepatitis B and C in the Mediterranean and Balkan Countries.

‡Ibid.

Turkish Experience

- HCV positivity is 0.5%,
- 90-95%: genotype I (1b is the most prevalent)
- Screening before
 - Blood & organ donation
 - Operations
 - Marriage
- Screening in special groups
 - Hemodialysis
 - Hemophiliacs, ...
- Screening programs by Liver & ID associations

- Peg-IFN and ribavirin are reimbursed
 - HCV-RNA positivity and genotyping are needed
 - Bx is not mandatory

- PR+Telaprevir or PR+Boceprevir are reimbursed to
 - Relapser
 - Naïve, advanced fibrosis (4-6/6 fibrosis)
- Sofosbuvir is registered (not reimbursed yet)

- HCV-RNA \$50
- HCV genotyping \$100
- Peg-IFN+RIBA \$8,000-10,000
- Telaprevir \$ 30,000
- Boceprevir \$ 24,000-30,000
- Liver Tx: \$60,000-100,000

Conclusion

- HCV diagnosis and management: costly
- Screening people (especially those having higher risk), giving more potent (yet more “expensive”) drugs: cost-effective

- Eradication: big goal
 - Preventive measures
 - Recognizing undiagnosed ones
 - Treating them effectively