Fair prices for new direct-acting antiviral agents (DAAs) to make treatment affordable

Sylvie Deuffic-Burban
Inserm, IAME, UMR1137, Univ Paris Diderot, Paris
Inserm, LIRIC-U995, Univ Lille 2, Lille
FRANCE

New HCV treatment paradigm

- Past IFN-based therapies
  - Suboptimal cure rates
  - High toxicity
  - Treatment monitoring required
  - Prolonged duration of treatment
- New all-oral IFN-free therapies
  - Higher cure rate
  - Fewer side effects
  - Less on-treatment monitoring
  - Shorter duration of treatment
- No medical reasons to withhold therapy

New HCV treatment paradigm

- Past IFN-based therapies
  - Suboptimal cure rates
  - High toxicity
  - Treatment monitoring required
  - Prolonged duration of treatment
- New all-oral IFN-free therapies
  - Higher cure rate
  - Fewer side effects
  - Less on-treatment monitoring
  - Shorter duration of treatment
- No medical reasons to withhold therapy

New therapies are expensive whereas available resources are limited

Cost containment

Increased medical costs *vs.*
Limited resources

Medico-economic evaluation

To evaluate the optimal conditions of resources use and optimize the use of available resources

MEDICO-ECONOMIC EVALUATION

- To provide more than a simple evaluation of individual benefit for each patient, by providing the decision maker an evaluation of the service to the community

- To assist in choosing from among competing alternatives, not only policy makers, but also developers of evidence-based clinical guidelines, public health officials, health-care providers and other decision makers

MEDICO-ECONOMIC EVALUATION

- Long-term evaluation = Cost-effectiveness analysis
  - To estimate the additional value to society of a new intervention relative to the current ones
  - To understand, prioritize and optimize the use of health care services

- Short-term evaluation = Budgetary impact analysis
  - To forecast the impact of new drugs/technologies on health care budgets
  - « Cost-effective doesn't mean cheap »

Long-term evaluation: CE analysis

- Two questions for any strategy
  - Is it effective?
  - Is it cost-effective?

  (If it's not effective, it's not cost-effective…)
- Two outcomes
  - Cost (Dollars, Euros…)
  - Effectiveness (life years=LY, quality adjusted life years = QALY…)
- More effective intervention is most-often more expensive
- Cost-effectiveness ratio = ICER
  - Δ Cost / Δ Effectiveness
  - Value of resources spent

Long-term evaluation: CE analysis

- Two questions for any strategy
  - Is it effective?
  - Is it cost-effective?

  (If it's not effective, it's not cost-effective…)
- Two outcomes
  - Cost (Dollars, Euros…)
  - Effectiveness (life years=LY, quality adjusted life years = QALY…)
- More effective intervention is most-often more expensive
- Cost-effectiveness ratio = ICER

Is the additional benefit worth the additional cost?

What are we willing to pay?

- NICE (UK)
  - 20,000-30,000 £/LY, QALY
- Sweden
  - Informal, according to the severity of the disease
    - Moderate ≈ 50,000/LY or QALY
    - Severe ≈ 100,000/LY or QALY
- France, Belgium, Germany
  - No thereshold
  - Efficiency frontier in Germany
- The Commission on Macroeconomics and Health (WHO)
  - CE ratios < 3 x GDP/capita = "cost-effective"
  - CE ratios < GDP/capita = "very cost-effective"

LONG-TERM EVALUATION

- Sofosbuvir-based regimens vs. SOC in United States
  - Chhatwal et al, 2015
    - $55,400 per qaly gained
    - Selected groups: $9,700 / qaly gained in G1-treatment naive patients with cirrhosis to $410,500 / qaly gained in G3-treatment-experienced patients without cirrhosis
  - Najafzadeh et al, 2015
    - IFN-based new regimens compared to SOC
      - G1: $21,528 / qaly gained
      - G2: $110,168 / qaly gained
      - G3: dominated
    - IFN-free regimens compared to SOC
      - G1: $12,825 (sof-ldv) to $71,445 (sof-smv) / qaly gained
      - G2: $691,574 (sof-dcv) / qaly gained
      - G3: $73,236 (sof-ldv-rbv) to $396,229 (sof-dcv) / qaly gained

Chhatwal et al, Ann Intern Med 2015;162:397-406; Najafzadeh et al, Ann Intern Med 2015;162:407-419

LONG-TERM EVALUATION

- Sofosbuvir-based regimens vs. SOC in United States
  - Chhatwal et al , 2015
    - $55,400 per qaly gained
    - Selected groups: $9,700 / qaly gained in G1-treatment naive patients with cirrhosis to $410,500 / qaly gained in G3

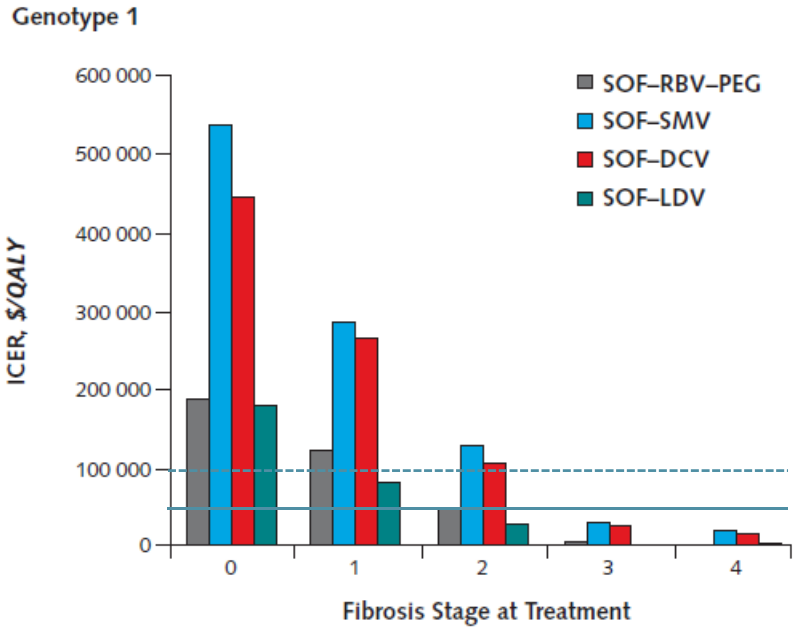
Substantial public health benefits at a reasonable cost per treated patients in selected groups

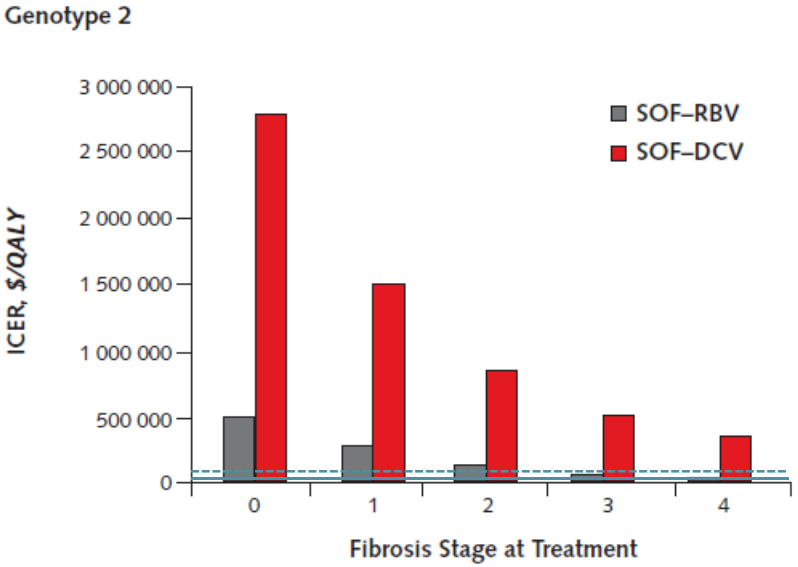
      - G1: $21,528 / qaly gained
      - G2: $110,168 / qaly gained
      - G3: dominated
    - IFN-free regimens compared to SOC
      - G1: $12,825 (sof-ldv) to $71,445 (sof-smv) / qaly gained
      - G2: $691,574 (sof-dcv) / qaly gained
      - G3: $73,236 (sof-ldv-rbv) to $396,229 (sof-dcv) / qaly gained

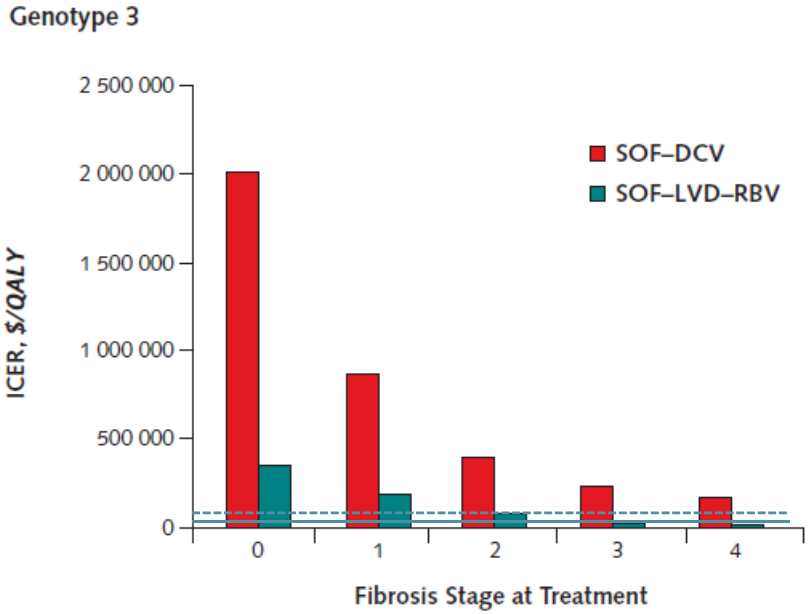
Chhatwal et al, Ann Intern Med 2015;162:397-406; Najafzadeh et al, Ann Intern Med 2015;162:407-419

Long-term evaluation

- Sensitive to the stage of fibrosis at treatment initiation



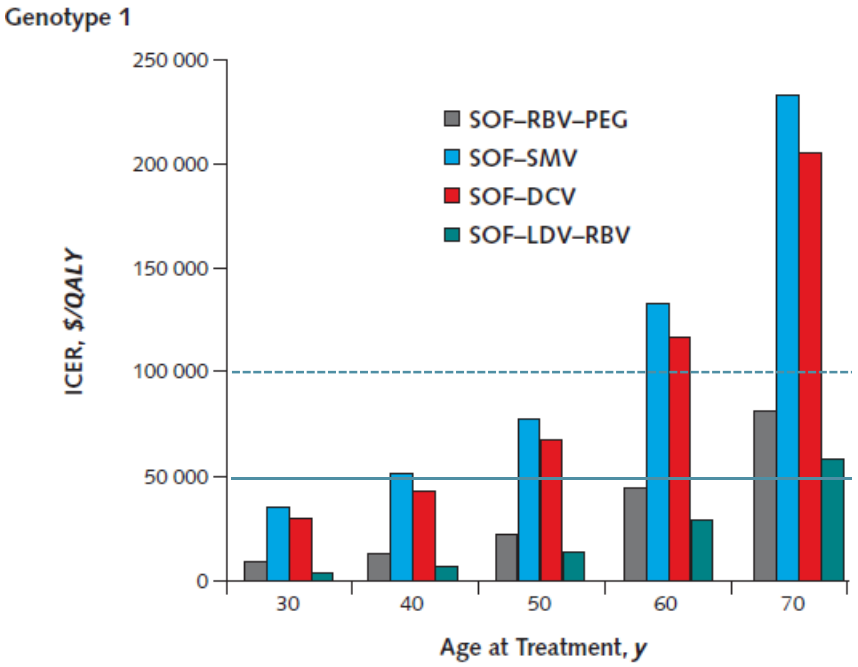


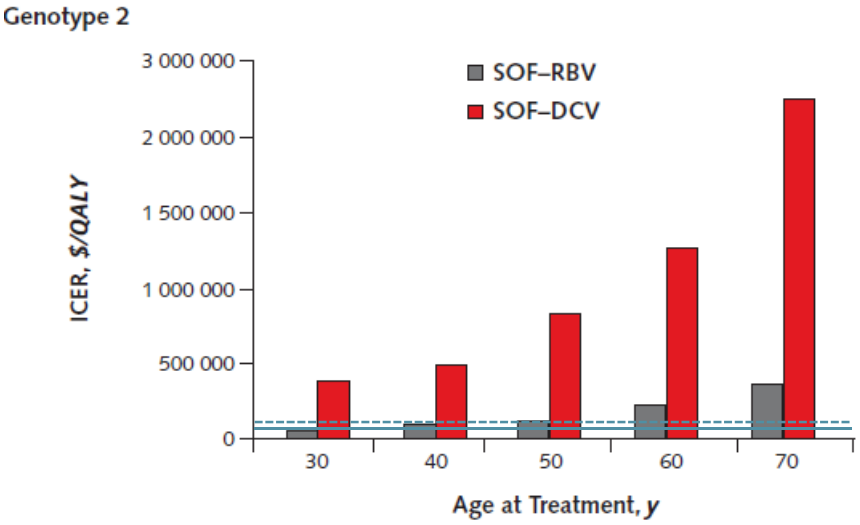


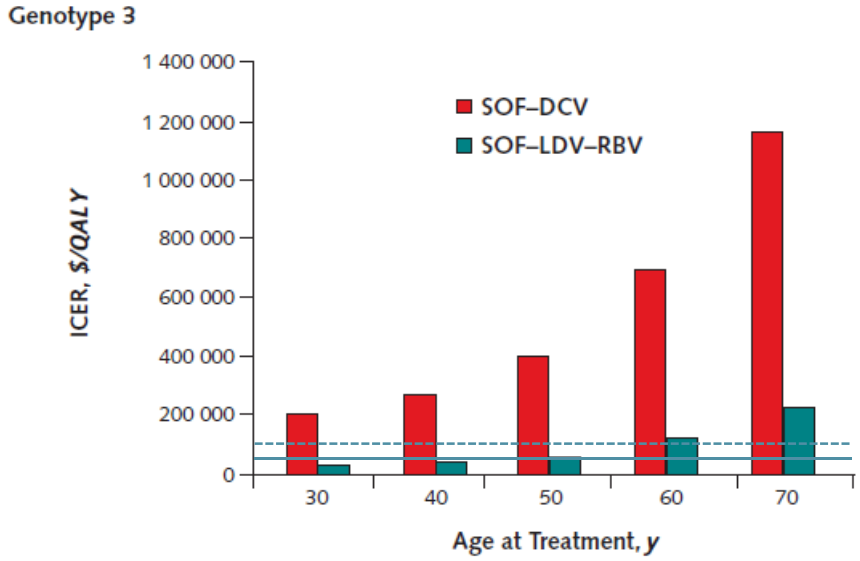
Najafzadeh et al, Ann Intern Med 2015;162:407-419

Long-term evaluation

- Sensitive to the age at treatment initiation



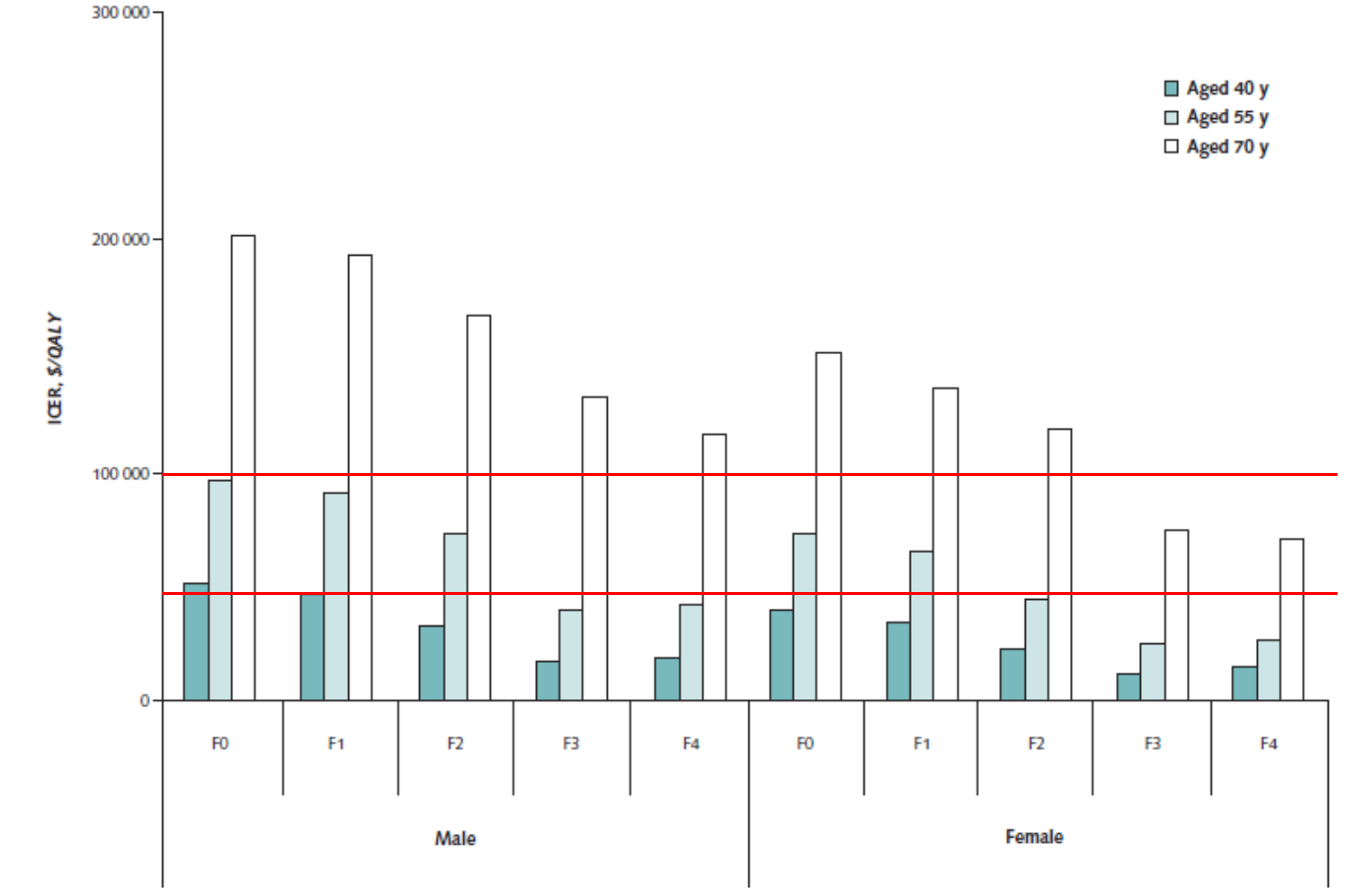




Najafzadeh et al, Ann Intern Med 2015;162:407-419

Long-term evaluation

- Sensitive to stage of fibrosis, age and gender

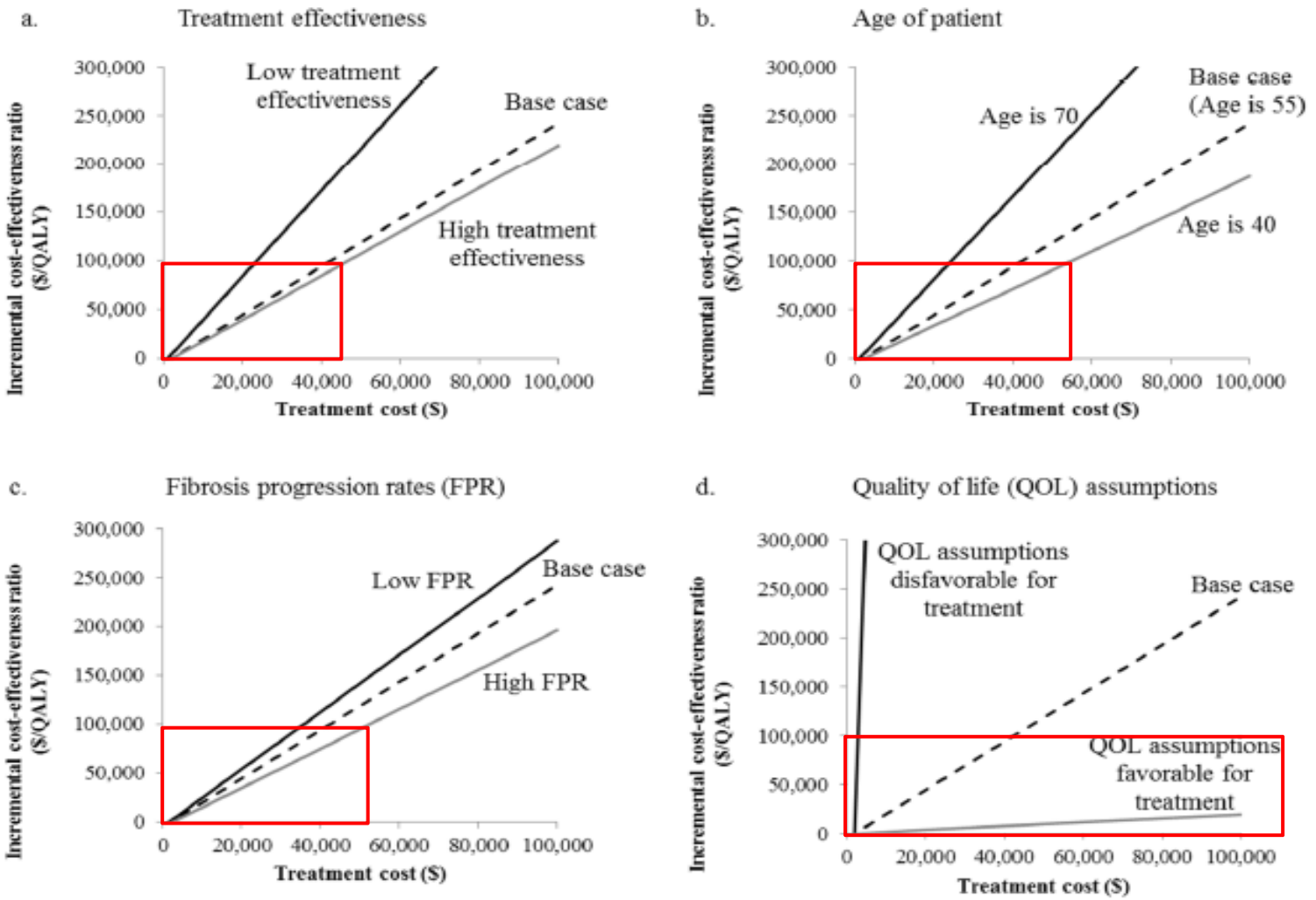


ICERs were higher for men because of their higher background mortality. ICER = incremental cost-effectiveness ratio; QALY = quality-adjusted life-year.

Chhatwal et al, Ann Intern Med 2015;162:397-406

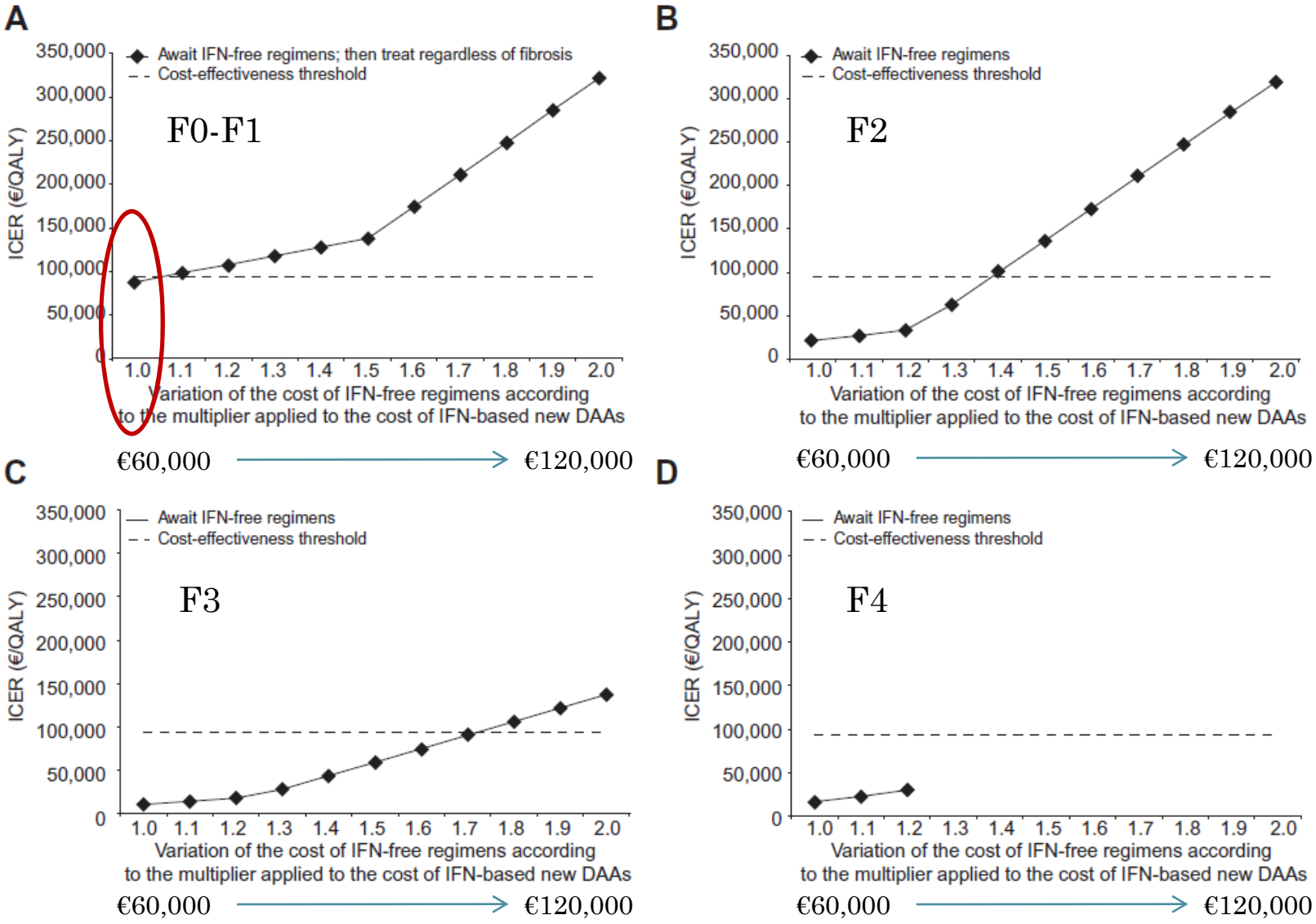
LONG-TERM EVALUATION

- Threshold analyses for treatment at F0 stage



Leidner et al, Hepatology 2015 epub

LONG-TERM EVALUATION



Deuffic-Burban et al, J Hepatol 2014;61:7-14

LONG-TERM EVALUATION

- The use of new combinations of DAAs is cost-effective
- A treat-all strategy mainly depends on the cost of new DAAs

⇨Treat in priority patients with advanced fibrosis, compensated or decompensated cirrhosis

"Cost-effective doesn't mean cheap"

- Need to evaluate the affordability and therefore the financial consequences of introducing a new intervention in a specific setting over the short to medium term

Short-term evaluation: France

- Over 3 years
- Only drug costs
  - 87€ for RBV
  - 41,000€ for 12-week SOF
  - 48,000€ for 12-week SOF+LDV
  - 35,000€ for 12- or 24-week DCV
- Assumptions
  - Treating persons aware of their infection when ≥ F2 with priority to ≥ F3
  - ≤ 20,000 patients treated/year
  - Scenarios
    1. Limited to 18-70 years old
    2. ≥ 18 without age limit

	Fibrosis stage at treatment initiation	Treatment history	Therapeutic option*	Duration (weeks)
Genotype 1	F2	All	Harvoni	12
	F3-4	Naive	Harvoni	12
		Non-naive	Harvoni	12
	Decompensated cirrhosis	All	Harvoni + RBV	12
Genotype 2	F2	All	SOF + RBV	12
	F3-4	Naive	SOF + RBV	12
		Non-naive	SOF + RBV	16
	Decompensated cirrhosis	All	SOF + DCV	24
Genotype 3	F2	All	SOF + RBV	24
	F3-F4	Naive	SOF + DCV†	24
		Non-naive	SOF + DCV + RBV†	24
	Decompensated cirrhosis	All	SOF + DCV + RBV†	24
Genotype 4	F2	All	Harvoni	12
	F3-F4	Naive	Harvoni	12
		Non-naive	Harvoni	12
	Decompensated cirrhosis	All	Harvoni	24

*Harvoni=Sofosbuvir+Ledipasvir, RBV=Ribavirin, SOF=Sofosbuvir, DCV=Daclatasvir ;

†Harvoni+RBV in sensitivity analysis

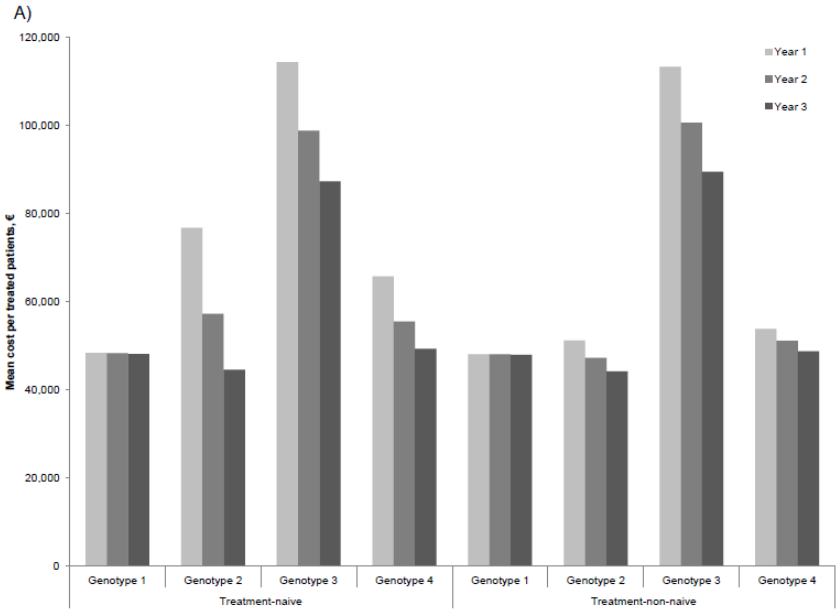
Deuffic-Burban et al, Hepatology 2014:1040A (AASLD 2014; poster 1749)

SHORT-TERM EVALUATION: FRANCE

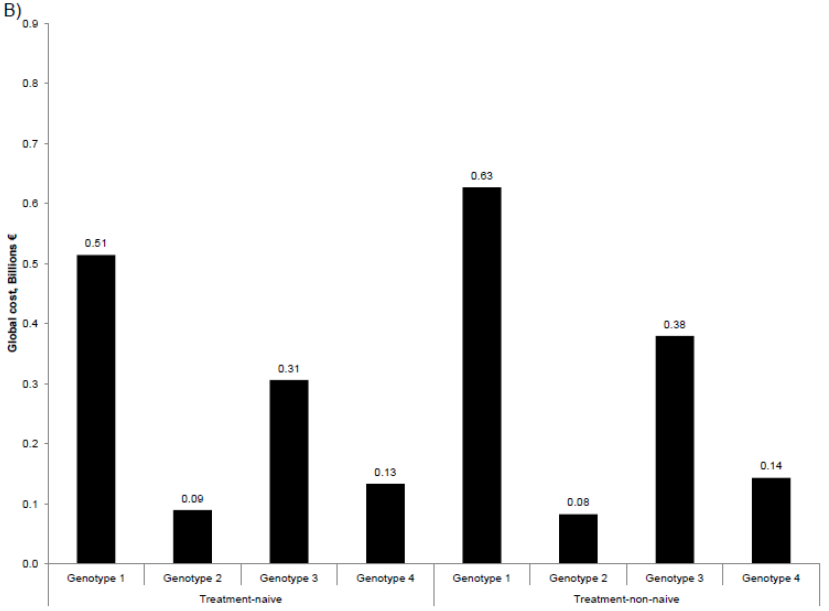
- Scenario 1 = Limited to 18-70 years old
  - 80% of DC and F3-F4, 20% of F2 during the 1st year
  - 100% of DC and F3-F4, 60% of F2 during the 2nd year
  - 100% of ≥ F2 during the 3rd year

  ⇨ 38,200 treated patients = 1.8-2.3 billion € = €47,120-60,209 / patient treated

Mean cost per treated patient



Global cost over 3 years



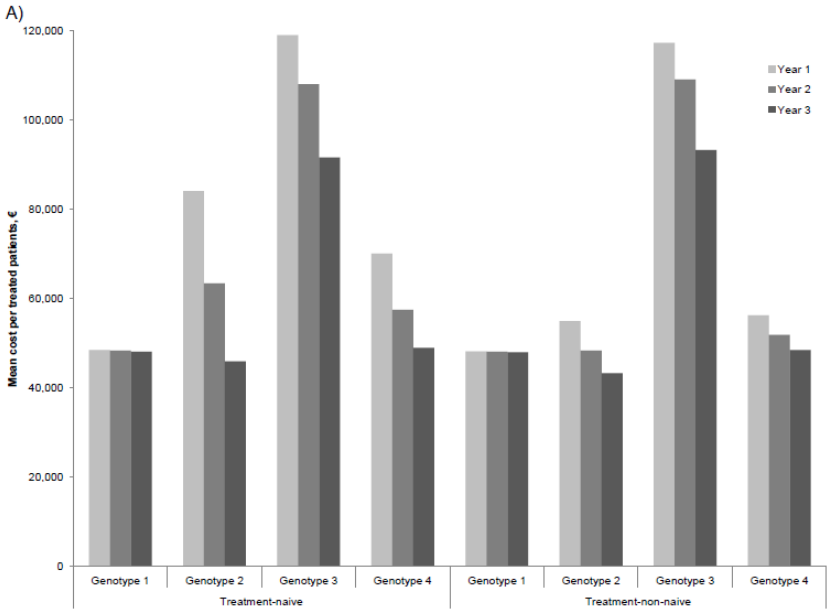
Deuffic-Burban et al, Hepatology 2014:1040A (AASLD 2014; poster 1749)

SHORT-TERM EVALUATION: FRANCE

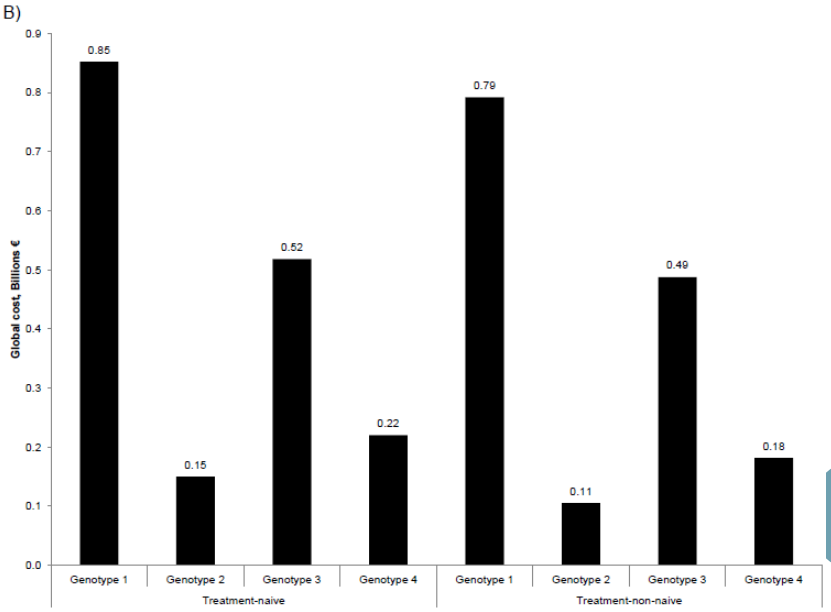
- Scenario 2 = over 18 years without age limit
  - 70% of DC and F4, 40% of F3 and 0% of F2 during the 1st year
  - 100% of DC and F4, 80% of F3 and 30% of F2 during the 2nd year
  - 100% of ≥ F2 during the 3rd year

  ⇨ 55,000 treated patients = 3.3 billion € = €60,000 / treated patient

Mean cost per treated patient



Global cost over 3 years



Deuffic-Burban et al, Hepatology 2014:1040A (AASLD 2014; poster 1749)

Short-term evaluation: United States

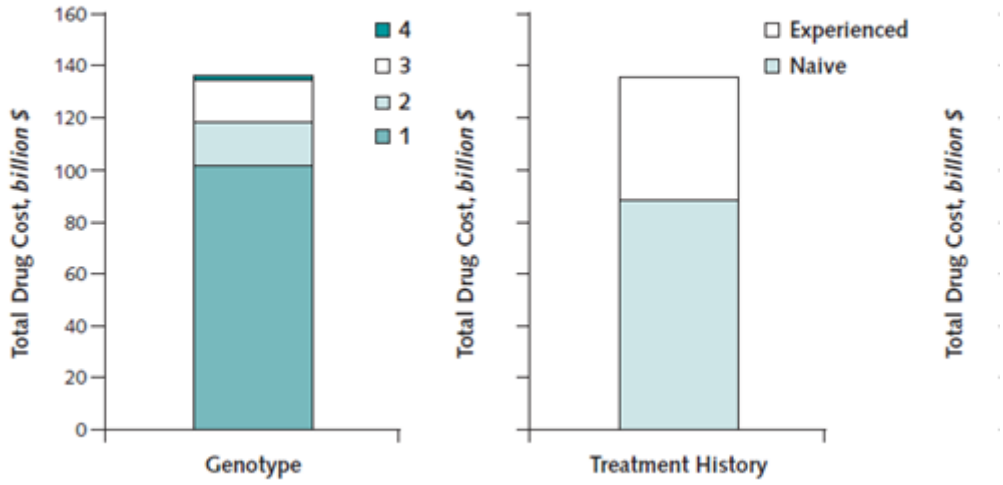
- Over 5 years
- Only drug costs ($/week)
  - Peg-RBV=$587
  - RBV=$309
  - BOC=$1100
  - TVR=$4100
  - SOF=$7000
  - LDV=$875
- Assumptions
  - 1.32 million treatment-naive and 450,000 treatment-experience persons aware of their HCV disease
  - 510,000 diagnosed in the 5 years

Chhatwal et al, Ann Intern Med 2015;162:397-406

Short-term evaluation: United States

- 1.60 million persons eligible for treatment during the next 5 years = $136 billion = $85,000 / treated patient

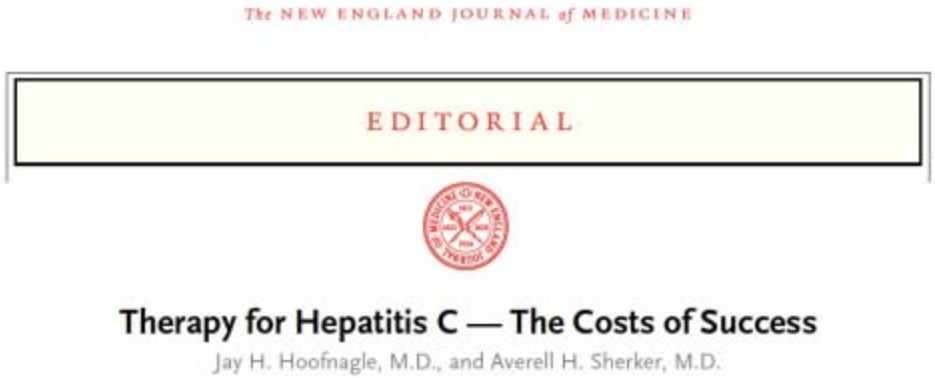
Figure 1. Total drug spending on sofosbuvir-ledipasvir to treat all HCV-infected



HCV = hepatitis C virus.

Chhatwal et al, Ann Intern Med 2015;162:397-406

SHORT-TERM EVALUATION

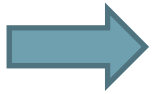


"With the present estimates of costs, however, treating even half the HCV-infected persons in the United States would add billions of dollars to an already overburdened medical care system. Costs alone cast a pall over the stunning success in achieving the long-hoped-for goal of a safe and effective therapy for hepatitis C."

Hoofnagle & Sherker, N Engl J Med 2014;370:1552-3

SHORT-TERM EVALUATION

- Treating all eligible patients with HCV would have an immense budgetary impact
- The challenges in the HCV field are moving to treatment access and delivery



Treatment scale up remains an unresolved public health challenge

- Even greater in low- and middle-income countries
- If prices of new regimens remain at current levels, additional resources and value-based patient prioritization will be needed to manage patients with HCV

High prices will continue to restrict access to treatment

Conclusion

- Even if the new HCV therapies are cost-effective, at their current prices, they are not cost-saving, and not affordable
- The most common strategy to address the cost is to limit access to therapy
  - Hard to rationalize
  - Difficult to accept for individuals
  - Delay progress towards elimination
  - Accurate fibrosis staging is required
- The simplest strategy to the price question may be to simply lower the costs of the drugs

Pawlotsky et al, J Hepatol 2015;62:S87-S99

Inserm IAME – UMR1137, DeSCID « Decision SCiences in Infectious Diseases, control and care »

Service des Maladies de l'Appareil Digestif – CHRU de Lille & Inserm LIRIC – UMR995