Masterclass: Health economic studies in liver diseases: challenges and opportunities

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Outline

- Misconceptions about health economics
- Outcomes and costs: how are they combined
  - Cost effectiveness
  - Cost utility
- Examples in liver disease
  - Treatments
  - Diagnostics
- What next

Misconceptions in health economics

- The first word in ‘health economics’ is ‘health’ which means that it is not only about costs
- It is not therefore just a cost calculation
- It is not a calculation of hospital profitability
- It is not about reducing health care expenditures (or it would be a spectacular failure)
- It is not better if patients die (“then they do not cost anything” ?)

How is health economics relevant to your practice?

- Because you need to understand the articles dealing with health economics in your specialty journals
- Because it is now a household topic (drug prices for example), your relatives will ask you about it, and expect an enlightening answer
- As healthcare professionals you will be involved in decisions about formularies, pricing and reimbursement at the local, regional and national levels
- The pharma representatives increasingly present health economics data which you need to be able to critically appraise

An ad campaign in France, 2016 (withdrawn after formal complaints)

- *« leukemia means on average a 20,000% markup »,*
- *« a well invested cancer can bring over 120,000 euros RoI. »,*
- *« What is a melanoma? 4 billion euros in revenue. »*
- *« breast cancer? The more advanced, the more lucrative »*

Hepatitis C can be cured. So why aren't more people getting treatment?

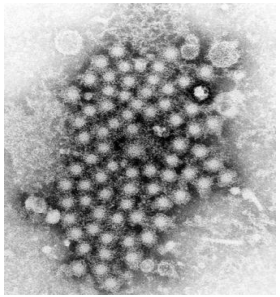
June 29, 2023Heard on Morning Edition

Improving Access to High-Value, High-Cost Medicines: **The Use of Subscription Models to Treat Hepatitis C Using Direct-Acting Antivirals in the United States**

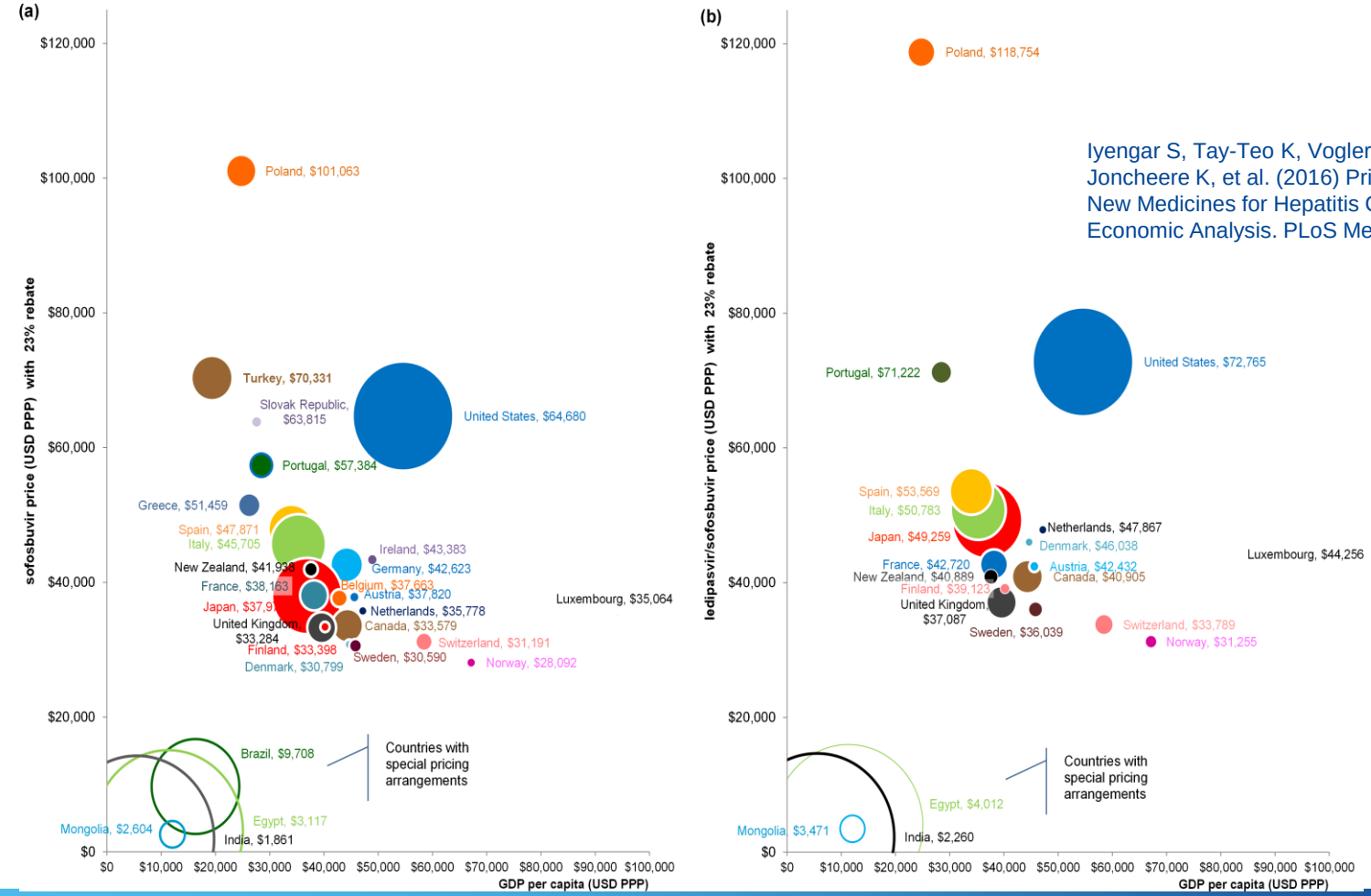
J Health Polit Policy Law (2022) 47 (6): 691–708.

Are New Hepatitis C Drugs Too Expensive?

For millions of Americans the upcoming release of two new hepatitis C drugs, Sovaldi and Olysio, offer an appealing alternative to the current treatment regimen. Along with excitement over the new releases also comes controversy. In comparison, a twelve week course of Sovaldi costs roughly $84,000 and a twelve week course of Olysio costs upwards of $66,000. Accordingly, a "firestorm of objection" has arisen in response to the extremely high prices of these potentially life saving new drugs.



Jennifer Wall, who works for the Pharmaceutical Research and Manufacturers of America, explains that "on average, to research and develop just one medicine takes 10 to 15 years and more than one billion dollars." The company behind Sovaldi, Gilead, announced that it will charge less for its product in countries outside the United States in response to the growing criticism over cost.



Iyengar S, Tay-Teo K, Vogler S, Beyer P, Wiktor S, de Joncheere K, et al. (2016) Prices, Costs, and Affordability of New Medicines for Hepatitis C in 30 Countries: An Economic Analysis. PLoS Med 13(5): e1002032.

What is health economic evalaution?

- Measuring the resources that need to be committed in order to achieve health outcomes

- Why is it necessary

The objective is to maximize the amount of health produced by the healthcare system under budget constraint

Not unlike what you seek with your family budget: maximize the satisfaction (utility) of the family under budget constraint

- How do we measure health outcomes
- Which are the resources that are measured

Health econmics vs market economy
General principles, 1

- You choose between:

Insert here a picture of the most beautiful sweater you can find

Insert here a picture of the ugliest sweater you can find

- For usual goods: you decide, you pay, you wear it
- Whow much MORE would you be ready to pay for the Vuitton hoodie with Swarovski rather than the Father christmas ?

In health care sytems

- There is no market (in EU countries)
- 3 stakeholders
  - Payers (state or social health insurance) = they pay
  - Health care professionals = they decide
  - Patients/ population = they consume

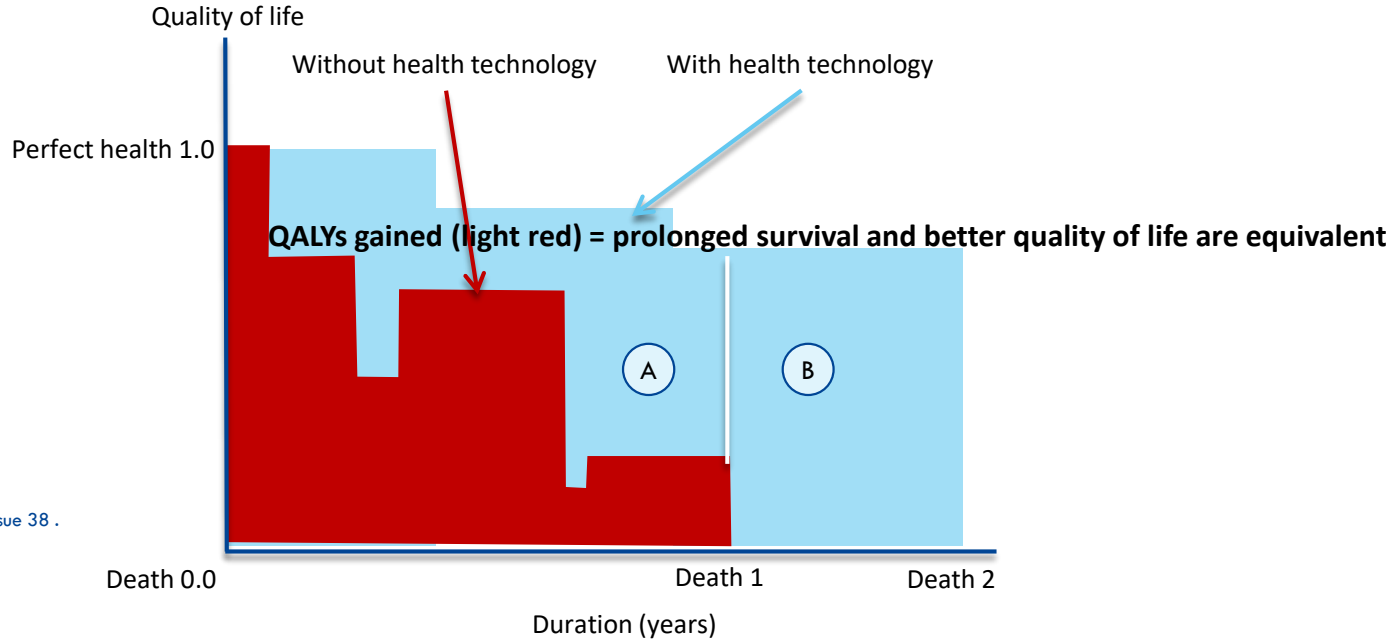
- Health economics attempts to re create a transparent market where payers know what they pay for, ie how much health does the population get for a given amount of money spent on a health intervention

Outcomes: how to we measure the quantity of health produced by an intervention

- Disease-specific outcomes (clinical endpoints in a trial):
  - Good face validity
  - Do not allow comparisons between medical specialties
  - Ex: ophthalmology, rheumatology, ACLF, ICU, oncology

- Need to have a measure of health that is common to all specialties= the invention of QALYs
  - Not disease specific= generic
  - Combines quantity and quality of health
  - Each has the same value

Quality of life: What are QALYs?
We combine duration and quality of survival



QALY; quality-adjusted life-years.

García-Altés A. *CAHTA Newsletter* 2006 Issue 38 .

How do we obtain the weights (values) for QoL= the EQ5D (3L or 5L)

Figure 1: EQ-5D-5L (UK English sample version)

Under each heading, please tick the **ONE** box that best describes your health **TODAY**

MOBILITY
- I have no problems in walking about ❑
- I have slight problems in walking about ❑
- I have moderate problems in walking about ❑
- I have severe problems in walking about ❑
- I am unable to walk about ❑

SELF-CARE
- I have no problems washing or dressing myself ❑
- I have slight problems washing or dressing myself ❑
- I have moderate problems washing or dressing myself ❑
- I have severe problems washing or dressing myself ❑
- I am unable to wash or dress myself ❑

USUAL ACTIVITIES *(e.g. work, study, housework, family or leisure activities)*
- I have no problems doing my usual activities ❑
- I have slight problems doing my usual activities ❑
- I have moderate problems doing my usual activities ❑
- I have severe problems doing my usual activities ❑
- I am unable to do my usual activities ❑

PAIN / DISCOMFORT
- I have no pain or discomfort ❑
- I have slight pain or discomfort ❑
- I have moderate pain or discomfort ❑
- I have severe pain or discomfort ❑
- I have extreme pain or discomfort ❑

ANXIETY / DEPRESSION
- I am not anxious or depressed ❑
- I am slightly anxious or depressed ❑
- I am moderately anxious or depressed ❑
- I am severely anxious or depressed ❑
- I am extremely anxious or depressed ❑

No problem= 1
Extreme/unable= 5

Check a box for each dimension,
You obtain a string of 5 figures
Ex: 11122
Go to the country's value set
Find the corresponding QoL value

Example French value set

Health state	Utility
11111	1
11112	.97954
11113	.95317
11114	.79995
11115	.74197
11121	.97802
11122	.95756
11123	.93119
11124	.77797
11125	.71999
11131	.95296
11132	.9325
11133	.90613
11134	.75291
11135	.69493
11141	.73626
11142	.7158
11143	.68943
11144	.53621
11145	.47823

Pharmacoeconomics

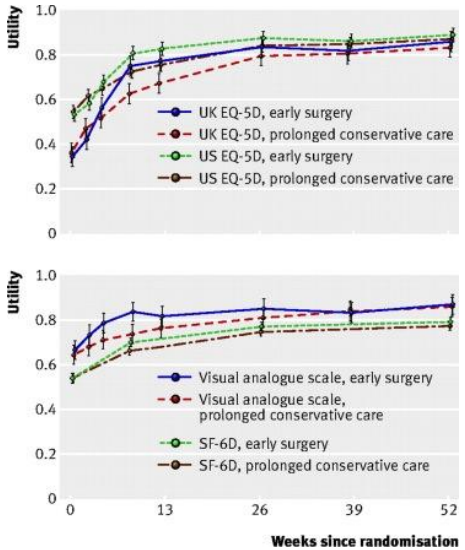
A French value set for the EQ-5D-5L

Luiz Flavio Andrade[1], Kristina Ludwig[2], Juan Manuel Ramos Goni[3], Mark Oppe[3], Gérard de Pouvourville[1].

QALYs calculation

- In a clinical trial
  - Patients fill out the EQ 5D (declare your study on EuroQol website) at each follow up visit
  - Calculate the weights
  - Use the area under the curve approach to calculate QALYs

Fig 1 Utilities according to UK and US EQ-5D, SF-6D, and visual analogue scale.



Hout W B v d et al. BMJ 2008;336:1351-1354

Costs, prices and tariffs

- Costs= production costs

- Price= when a list price is available eg for drugs or devices that can be purchased

- Tariffs= what the payer will pay to healthcare providers, eg medical fees

Endless discussions about ‘fair pricing’:

- price = production costs (central planning in former communist countries) or
- price = value (market-based economy)
- Price = Ability to pay = discriminating monopoly

What is a cost (academic défition)

- Simple definition:
- it is the value of resources that are used to achieve a goal and therefore are foregone for anything else

- It works for material resources and for time

Cost in health economics

	Medical	Non-Medical
Direct	Consultations, drugs, hospital admissions, tests, imaging…	Transportation (non-medical) Informal carers Home alterations
Indirect	Prolonged life	Lost productivity: sick leave, presenteeism, premature death

Costs in economic evaluations

- National authorities have provided guidance on which costs to use for economic evaluations in healthcare
- Not always consistent (price and costs)

- In international trials there are some problems:
  - Quantities (eg length of stay) and unit cost are not independant variables
  - It is therefore not very correct to put French costs on German quantities and decide it makes the cost of the treatment in France
  - In federal countries there might not be a national cost available

NICE guidance:
Are the unit costs of resources from the best available source?

- “Resources should be valued using the prices relevant to the national or local government (depending on who delivers the intervention) for health costs
- and in prices relevant to the respective sectors responsible for other costs. “

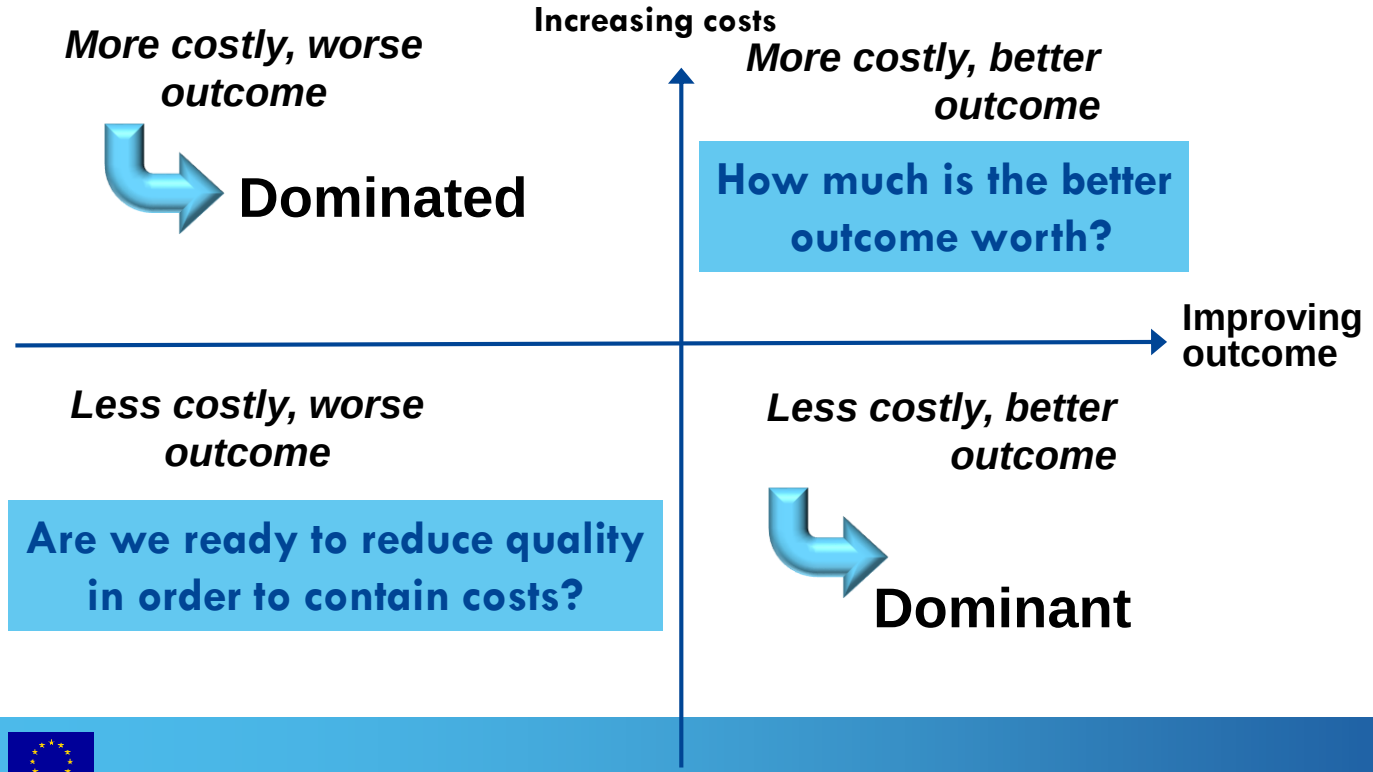
French guidance:
Favours production cost whenever possible

For economic evaluations in healthcare

- We will consider the value (or price) of resources used to produce care for patients
- In a clinical trial=
  - Estimate the cost of the innovative strategy vs the cost of the reference strategy
  - ALL relevant costs during the follow up period (no censoring)= intervention, side effects, complications ..
  - Via the eCRF or claims database whenever possible
  - Estimate the difference in costs

Combining outcomes and costs: The cost-effectiveness plane[1,2]

- Adapted from: 1. Laupacis A et al. Can Med Assoc J. 1992;146:473–81; 2. NICE Guide to the methods of technology appraisal 2008.

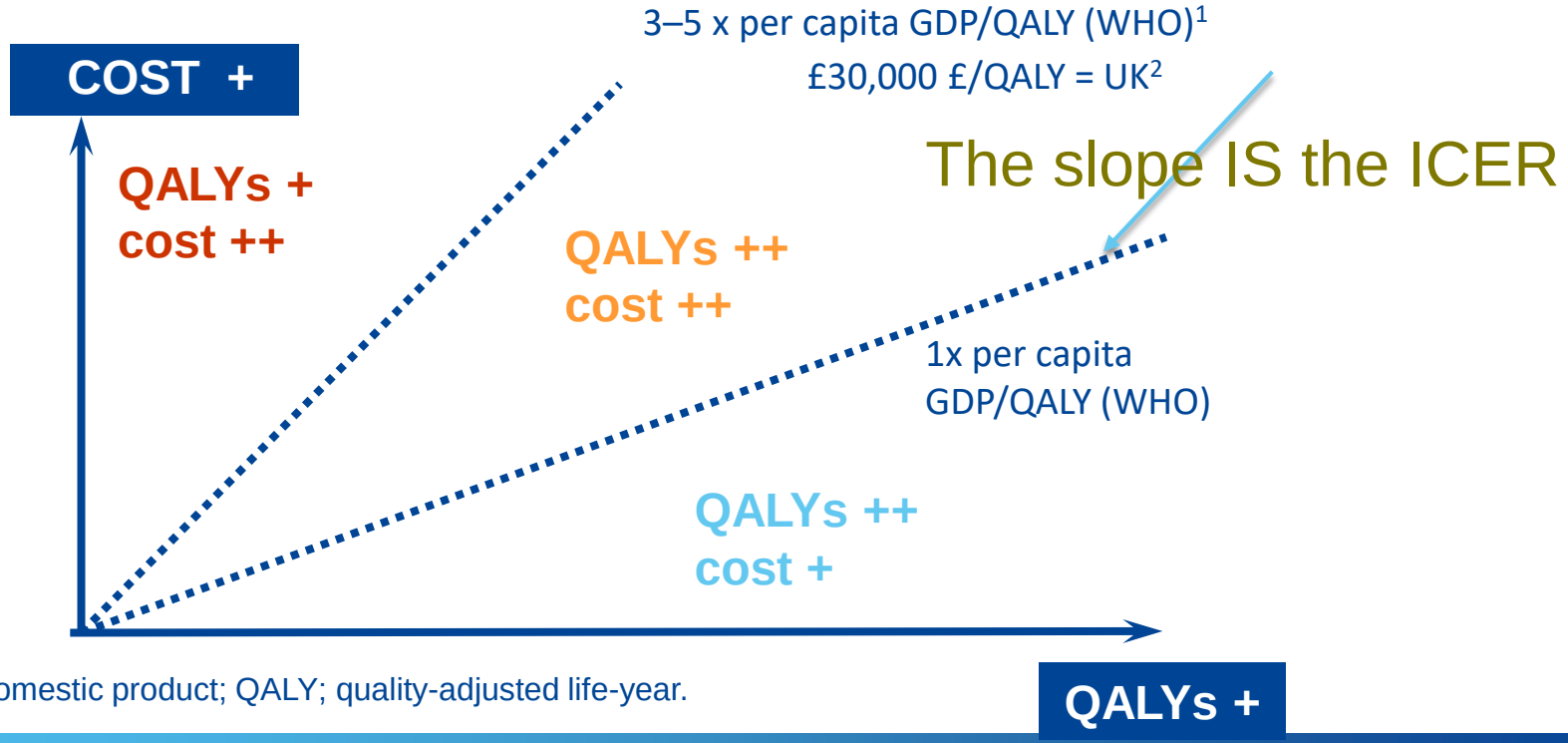


ICER= difference in costs /difference in outcomes

What is ‘too expensive’?

Adapted from: Laupacis A et al. Can Med Assoc J. 1992;146:473–81.

1. WHO Threshold values for intervention cost-effectiveness by region. Available at: http://www.who.int/choice/costs/CER_levels/en/ (Accessed May 2014); 2. NICE Guide to the methods of technology appraisal 2008.

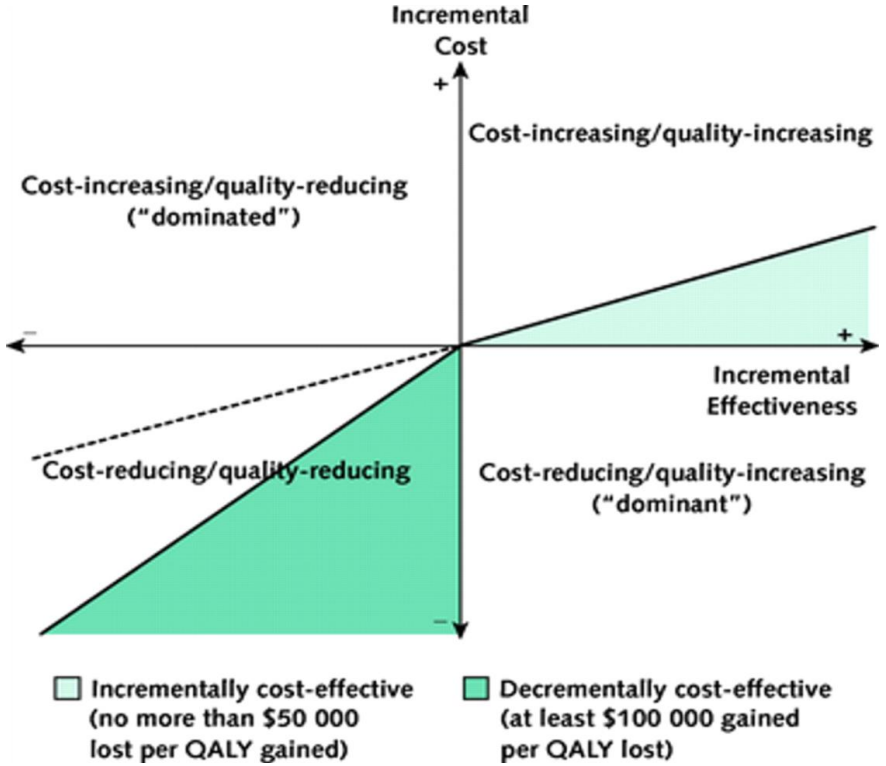


GDP, Gross domestic product; QALY; quality-adjusted life-year.

Where nobody wants to go: the SW quadrant

- QALY; quality-adjusted life-year.

  Nelson A, et al. Ann Intern Med. 2009;151(9):662–667.



EU.AB.2014.092 Date of preparation January 2015

Example of an economic evaluation for a treatement= trial based and model based

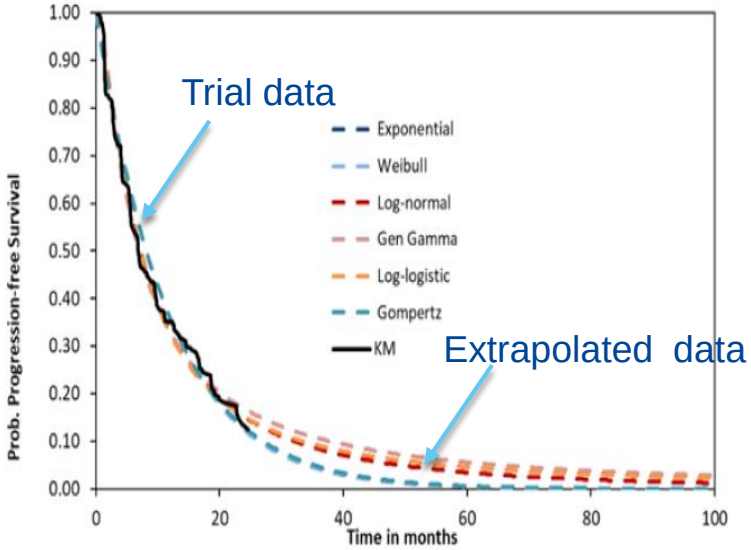
- Tecentriq (atezolizumab&bevacizumab) for HCC
- Point estimate of the ICER= 144 156 €/QALY versus sorafenib

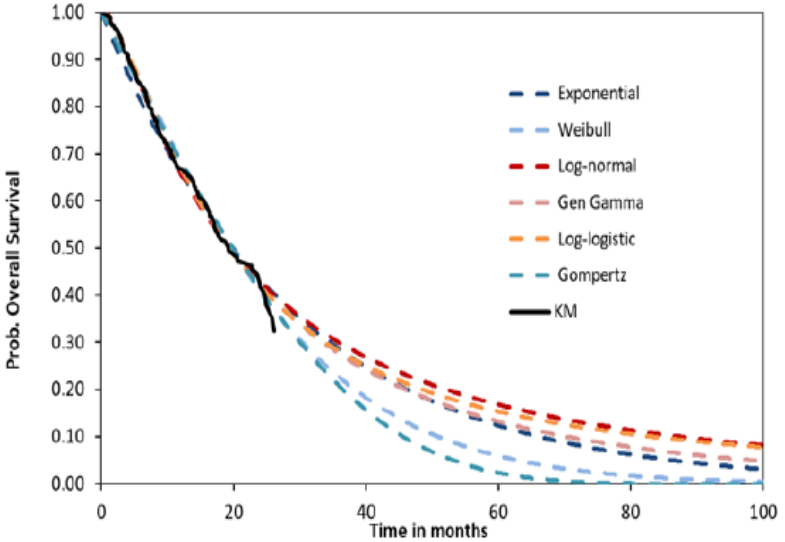
Stratégie	Coûts (€)	QALYs	AV	RDCR (€/AV)	RDCR (€/QALY)
Sorafenib	37 478	1,35	1,57	-	-
Atezolizumab + bevacizumab	124 838	1,95	2,26	126 095	144 156

https://www.has-sante.fr/upload/docs/application/pdf/2021-06/tecentriq_13042021_avis_economique.pdf

How do you get 5-10 year results with a 2-year trial?

- Partitioned survival models (& extrapolation)



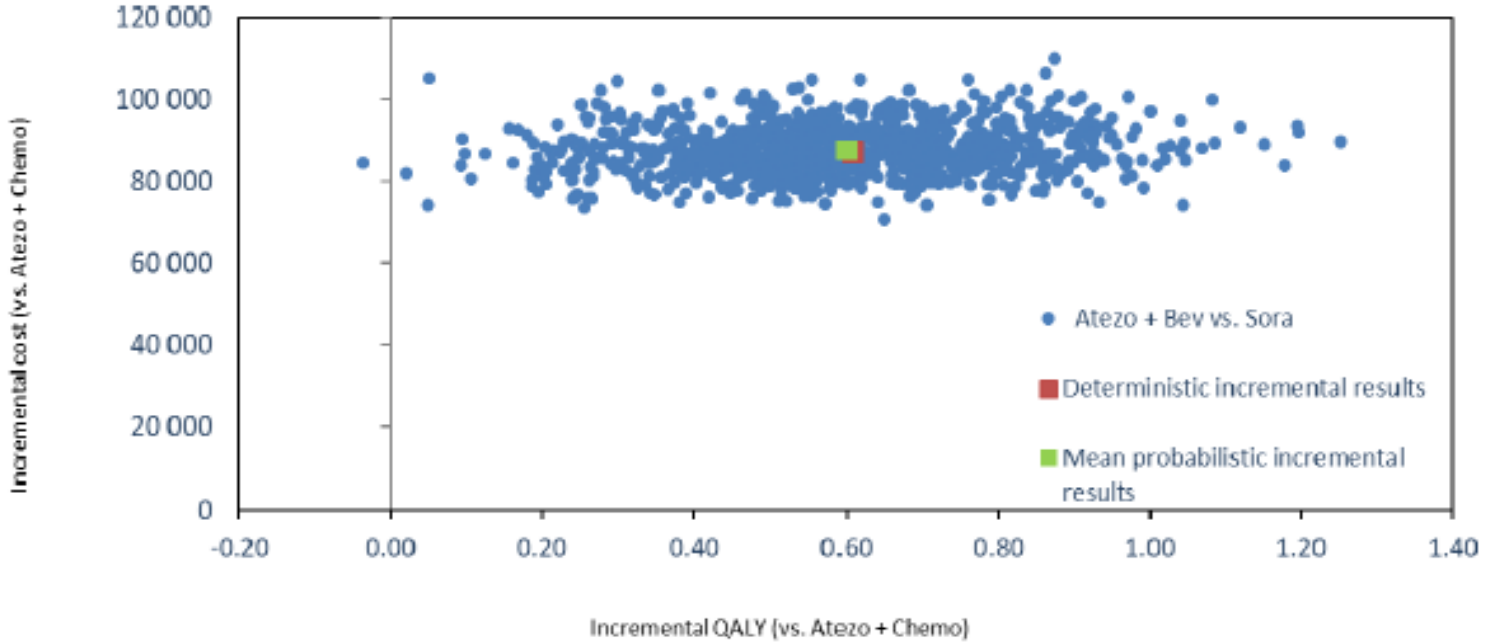


Partitioned survival models (very common in cancer)

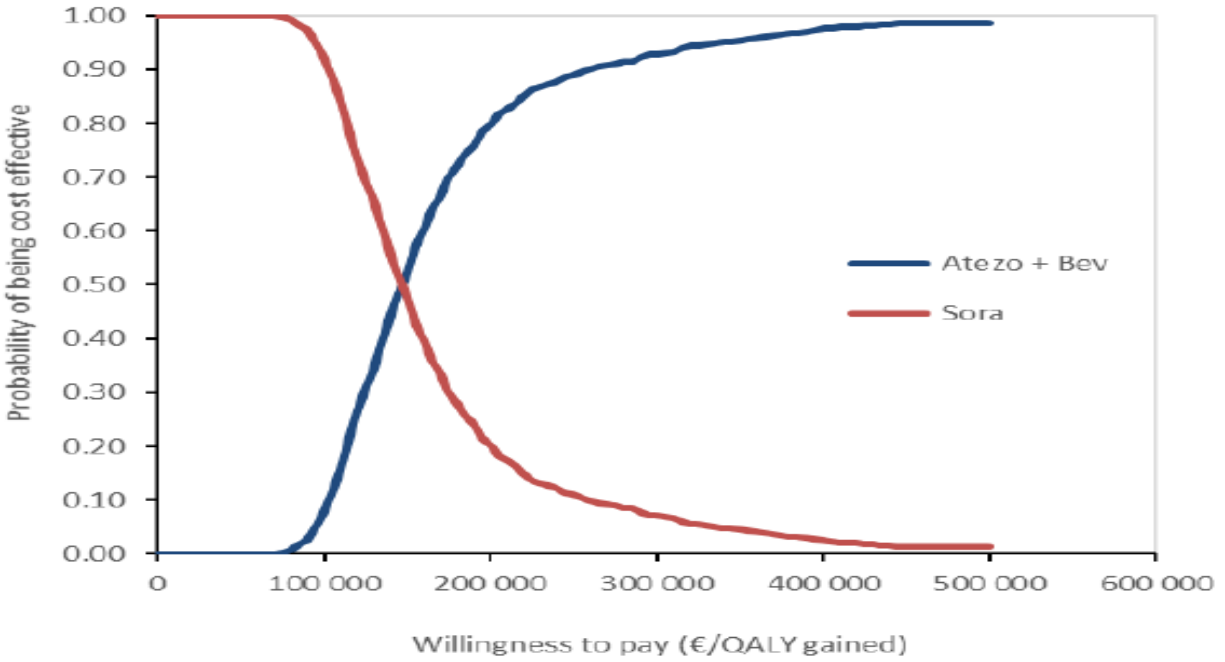
- 3 states: pre progression, progression, death
- For each state:
  - Quality of life
    - Pre progression = 0.75
    - Post progression= 0.6
  - Costs

Representing uncertainty in 2 dimensions and non normal distributions

Scatterplot on the C/E plane

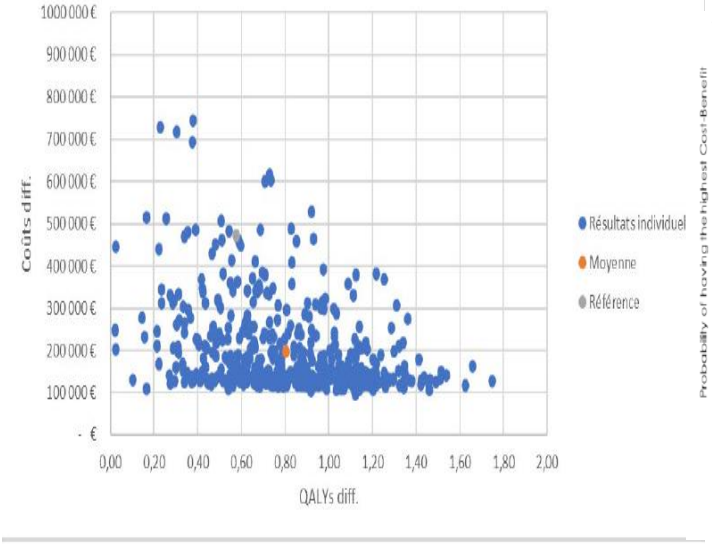


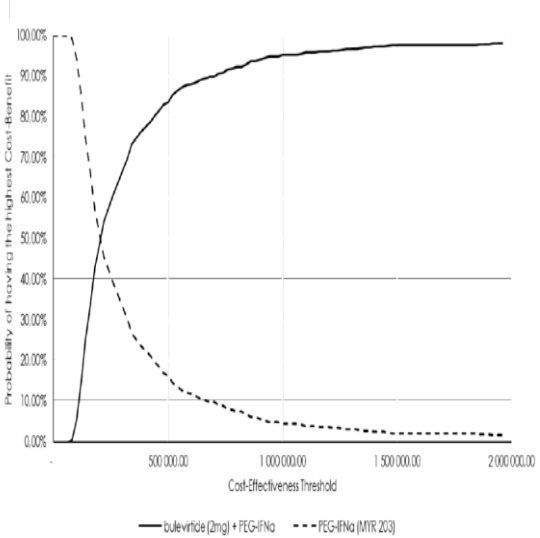
Acceptability curve

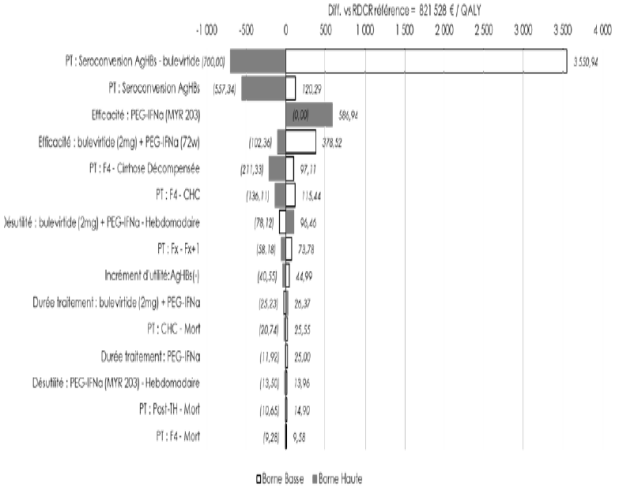


Hepatitis delta & Hepcludex= another uncertainy analysis

The tornado diagram

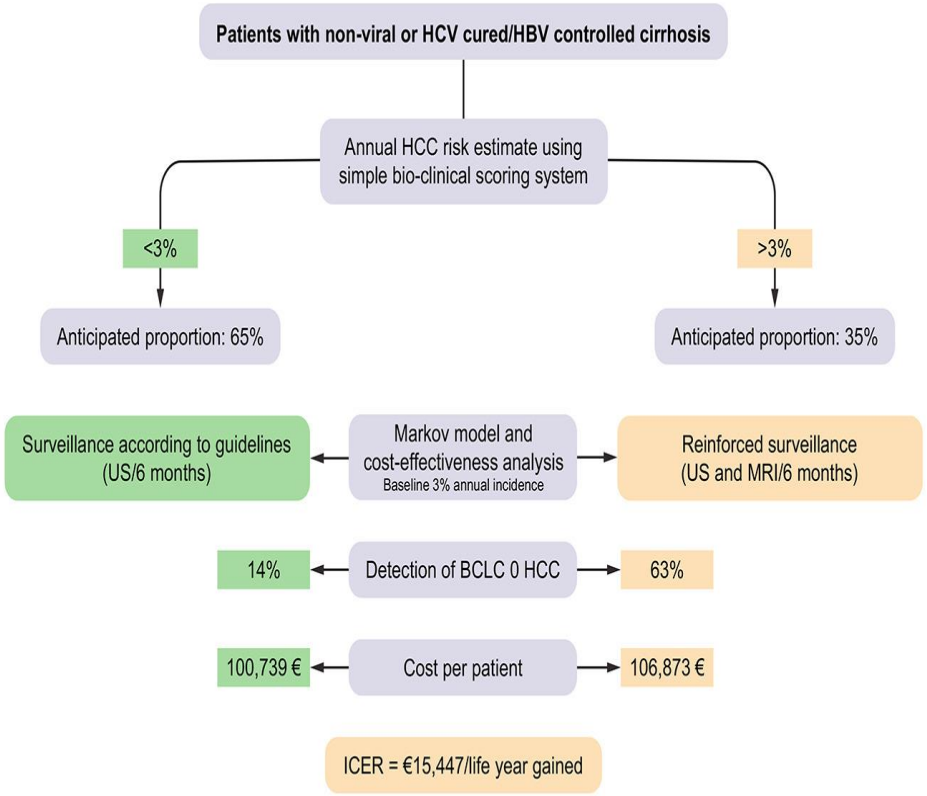






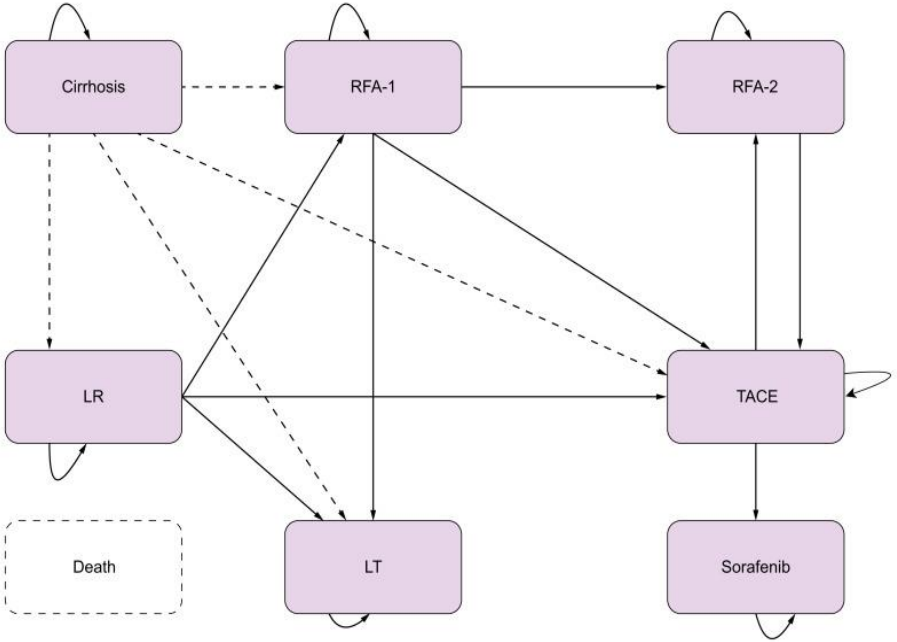
https://www.has-sante.fr/upload/docs/application/pdf/2021-03/hepcludex_12012021_avis_economique.pdf.pdaf

Model only

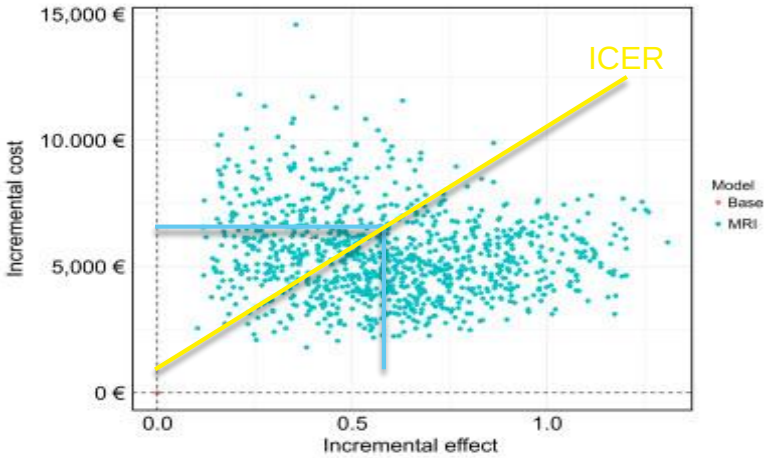


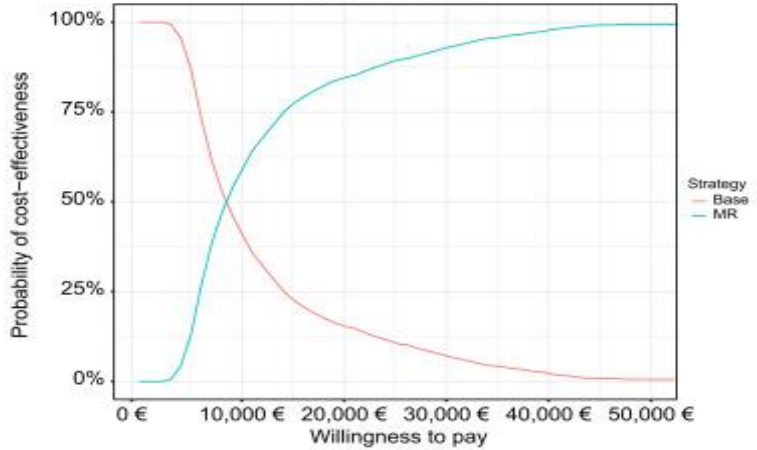
JHEPReport 2022 4DOI: (10.1016/j.jhepr.2021.100390)

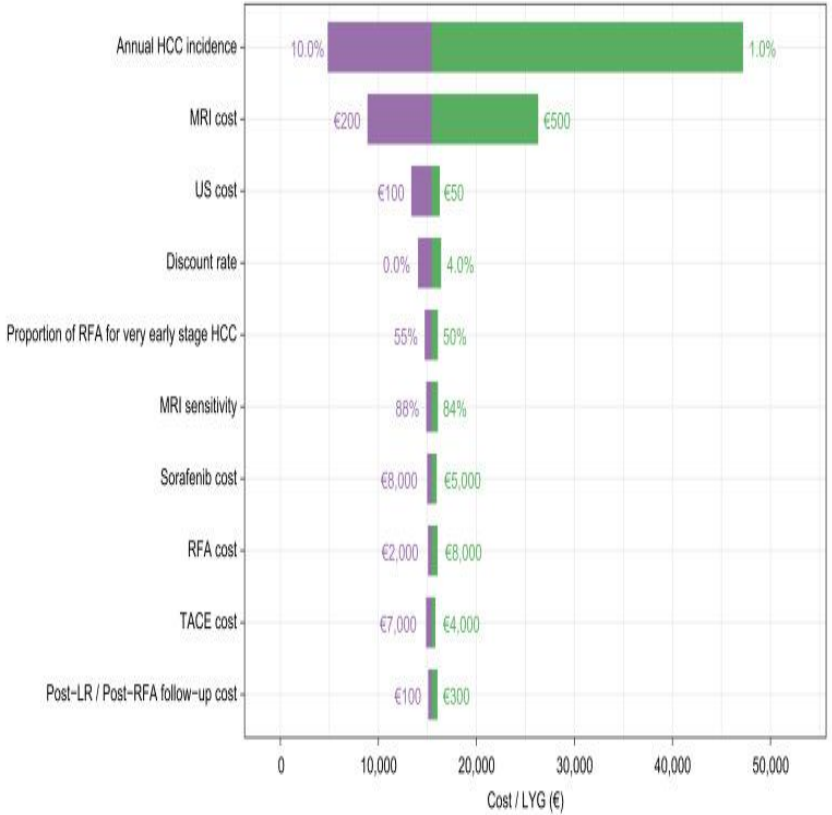
Diagnostic of HCC= MRI vs US



RFA= radiofrequency ablation
LR= liver resection
TACE= transarterial chemoembolization
LT= liver transplant


15,000 €
10,000 €
5,000 €
0 €
Incremental cost
0.0
0.5
1.0
Incremental effect
ICER
Model
Base
MRI


100%
75%
50%
25%
0%
Probability of cost−effectiveness
0 €
10,000 €
20,000 €
30,000 €
40,000 €
50,000 €
Willingness to pay
Strategy
Base
MR


Annual HCC incidence
10.0%
1.0%
MRI cost
€200
€500
US cost
€100
€50
Discount rate
0.0%
4.0%
Proportion of RFA for very early stage HCC
55%
50%
MRI sensitivity
88%
84%
Sorafenib cost
€8,000
€5,000
RFA cost
€2,000
€8,000
TACE cost
€7,000
€4,000
Post−LR / Post−RFA follow−up cost
€100
€300
0
10,000
20,000
30,000
40,000
50,000
Cost / LYG (€)

Economic evalaution in context =external validity

- Resources (facilities, staff, training)
- Funding
- Availablity of drugs
- Referral and care pathways
- Values and expectations
- Financial incentives or disincentives

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