

A-TANGO

Health Economics: Why and how to perform economic evaluations in liver disease

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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

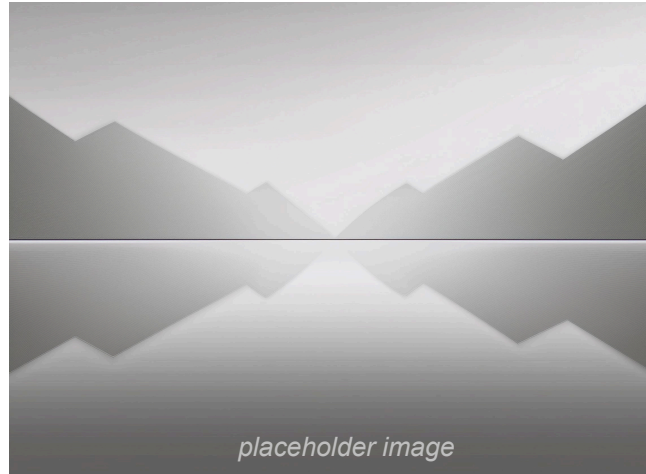
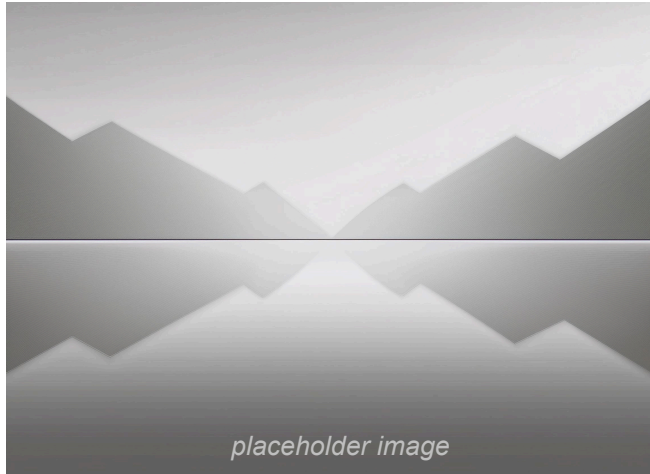
- The **first word** in 'health economics' is **'health'** which means that it is not only about costs
- Therefore, it is **not just a cost calculation**
 - It is not a calculation of hospital profitability
 - It is not about reducing health care expenditures (or it would be a spectacular failure)
 - 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 and your relations 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 the studies

An ad campaign in France, 2016 (withdrawn after formal complaints)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



*please note:
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“Breast cancer drug rejected for NHS use on cost-benefit grounds”



theguardian

- “Charities angered by guidance on **Kadcyla**, which costs **£90,000 per year per patient** and gives extra nine months on average”
- “**Kadcyla**, made by Roche Pharmaceuticals, was **rejected** by the National Institute for Health and Care Excellence. It has the highest price tag ever for a cancer medicine and was turned down because its benefits did not justify its cost, NICE said.”

NICE National Institute for
Health and Care Excellence

The company's base-case ICER for trastuzumab emtansine compared with lapatinib plus capecitabine was **£167,200 per QALY gained**.



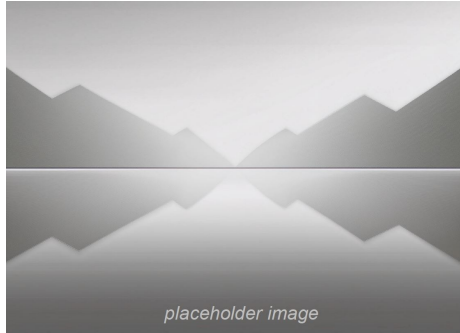
Health Economics - What is it?

- **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
- **What** are the types of resources that are measured?
- **How** do we measure health outcomes?

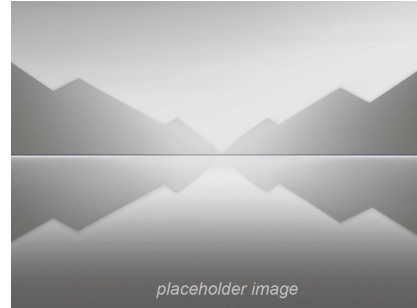
Health economics vs market economy

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
- How much MORE would you be ready to pay for the Vuitton hoodie with Swarovski rather than the Father Christmas ?

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In health care systems

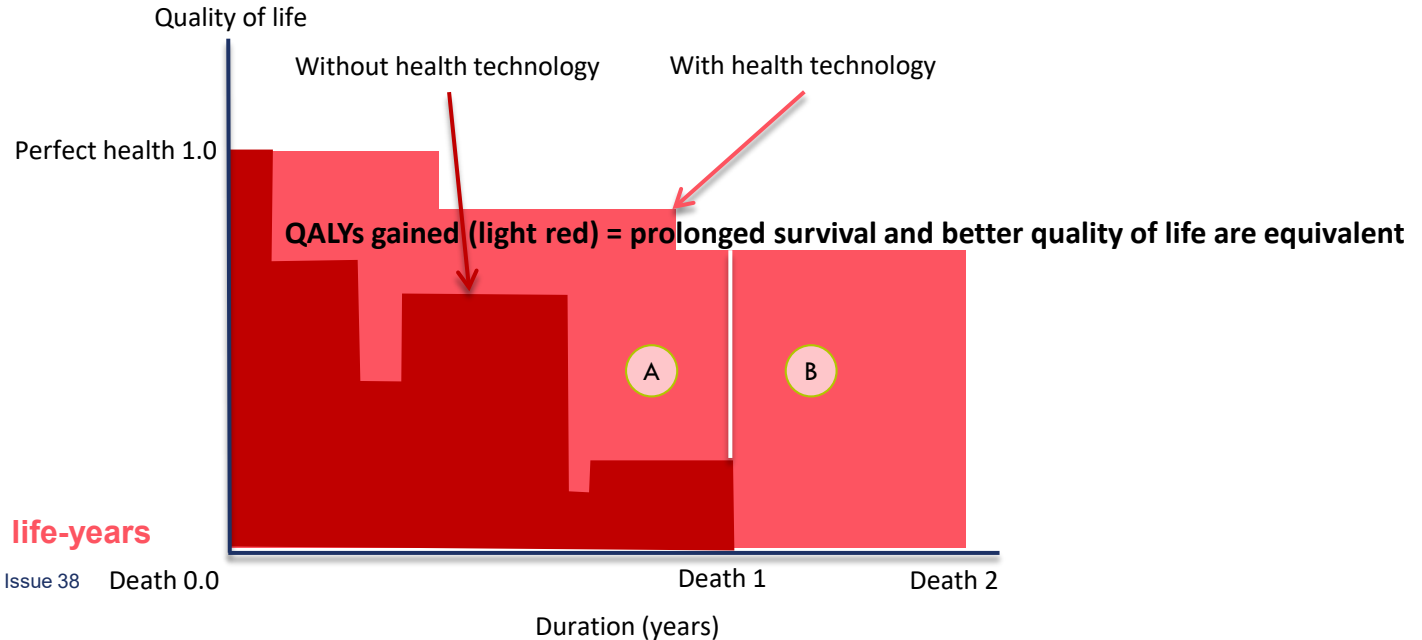
- There is no “market” (in EU countries)
- 3 key stakeholders
 - **Payers** (state or social health insurance) = they pay
 - **Health care professionals** = they decide
 - **Patients / General public** = they consume
- Health economics attempts to re-create a transparent market where payers know what they pay for, i.e. 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
 - Example: ophthalmology, rheumatology, ACLF, ICU, oncology
- Need to have a measure of health that is common to all specialties => leading to the invention of **QALYs**
 - Not disease- specific, but 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
- Example: 11122
- Go to the country's value set
- Find the corresponding QoL value



Example of 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

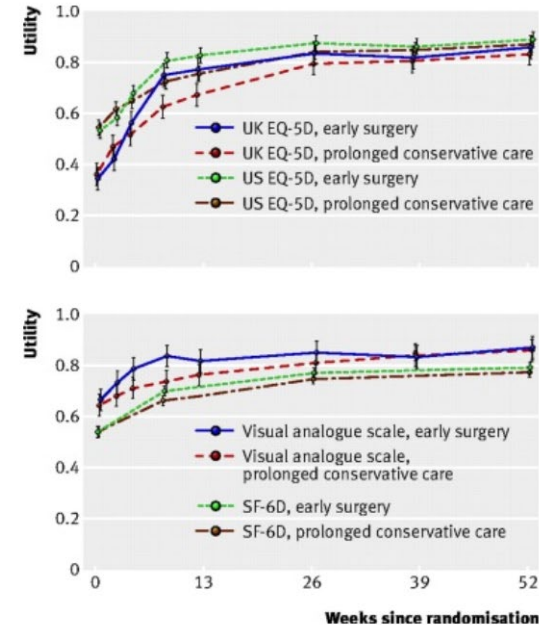
A French value set for the EQ-5D-5L

Luiz Flavio Andrade¹, Kristina Ludwig², Juan Manuel Ramos Goni³,
Mark Oppe³, Gérard de Pouvourville¹.

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
- **Prices** = when a list price is available, e.g. for drugs or devices that can be purchased
- **Tariffs** = what the payer will pay to healthcare providers, e.g. medical fees

What is a cost?

- Simple definition:

It is the **value of resources that are used** to achieve a goal
and therefore are foregone for anything else

- It applies to material resources and to 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 (e.g. length of stay) and unit cost are not independent variables
 - It is therefore not 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. “

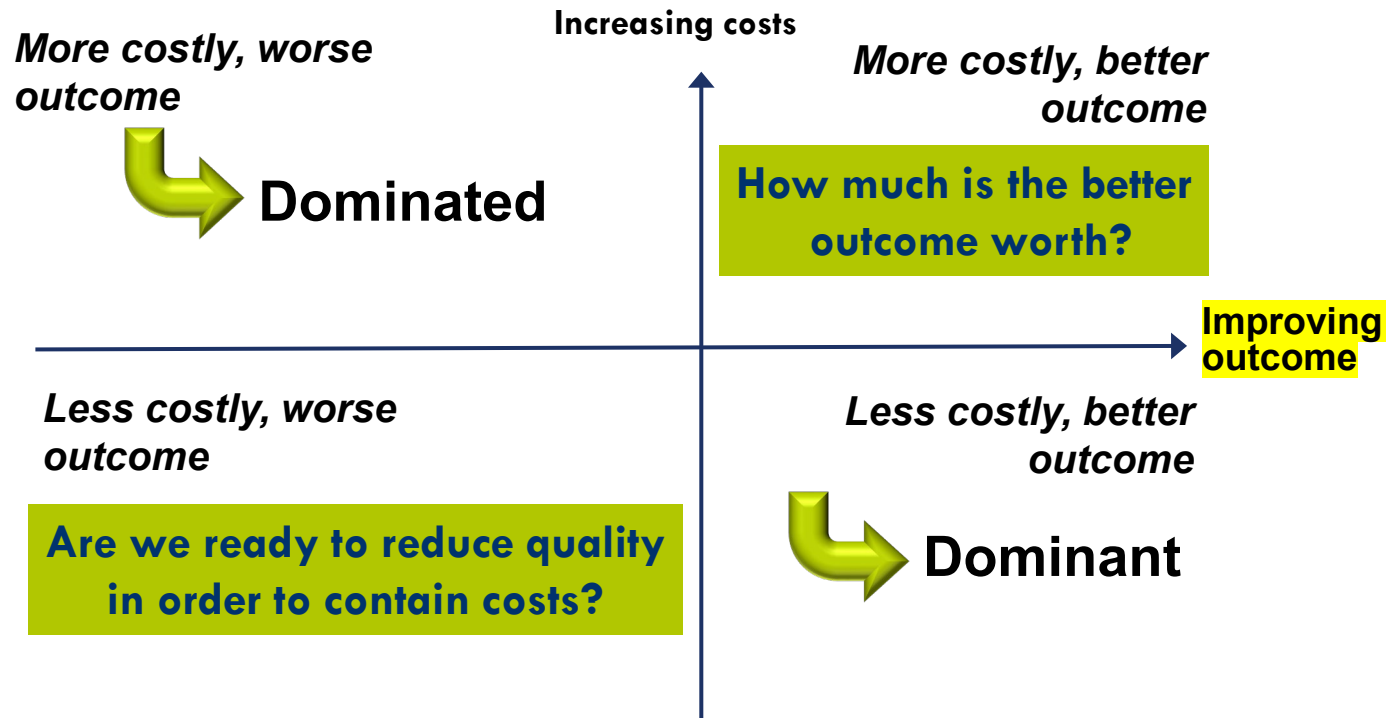
**French guidance:
Favours production cost
whenever possible**

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.



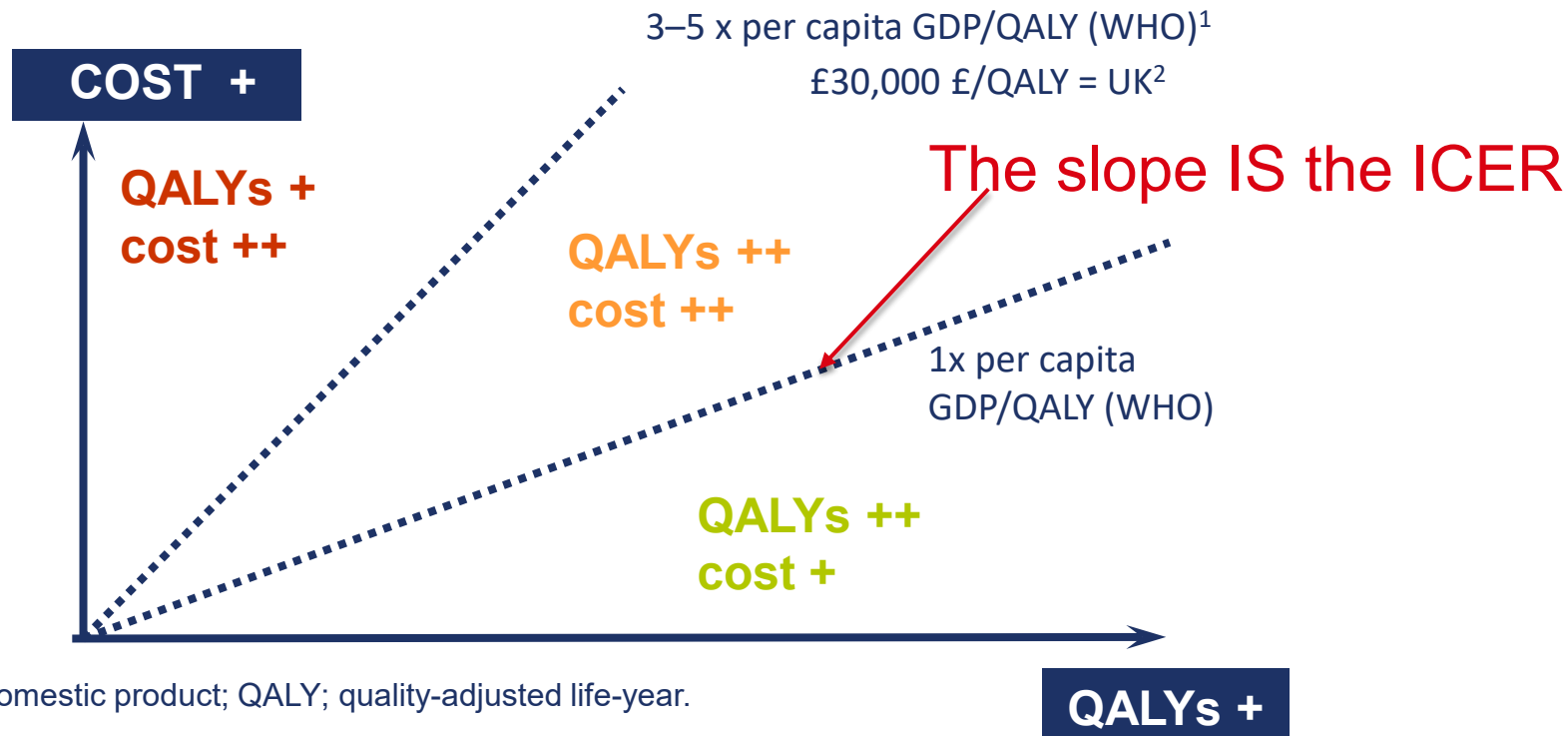
ICER=
difference in
costs /
difference in
outcomes

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.

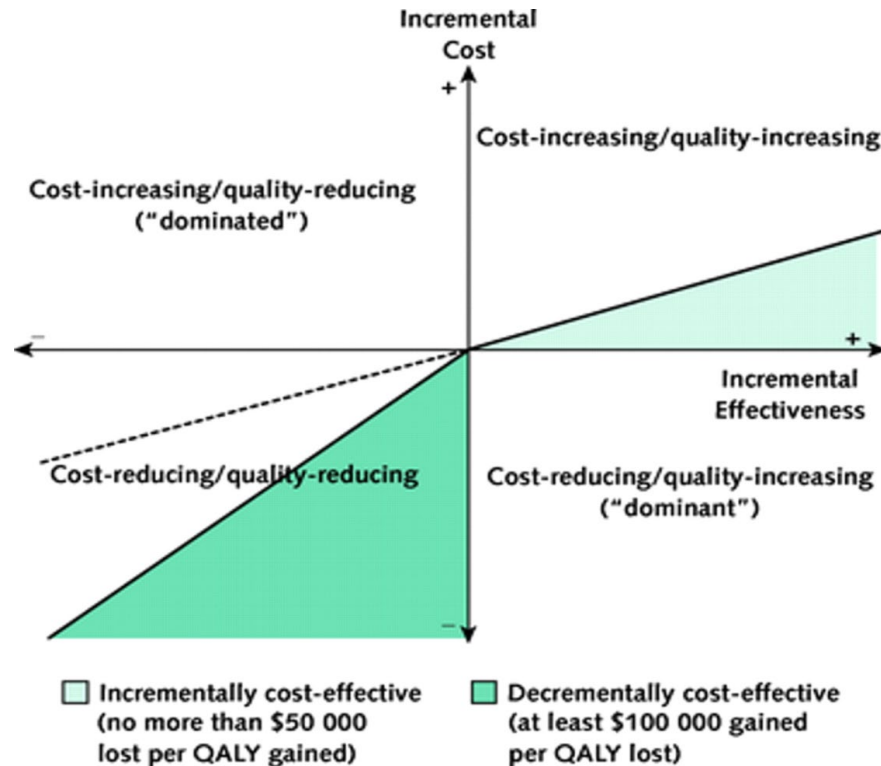


GDP, Gross domestic product; QALY; quality-adjusted life-year.

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 treatment= trial based and model based

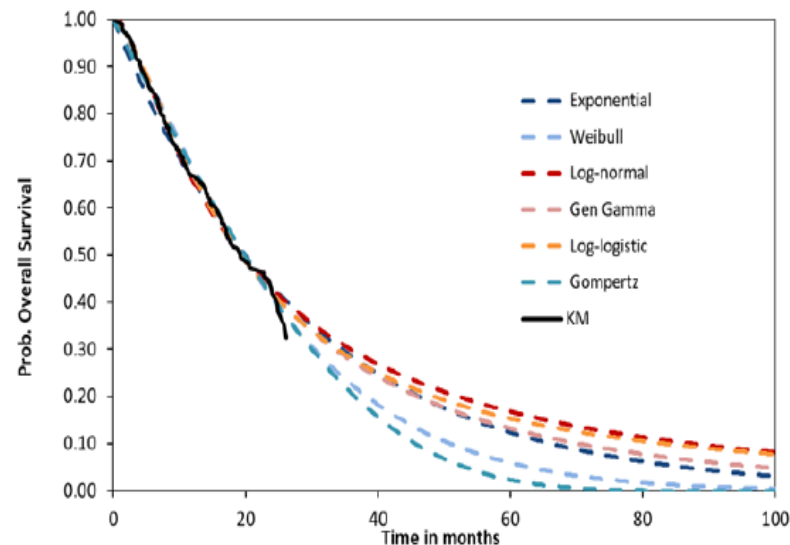
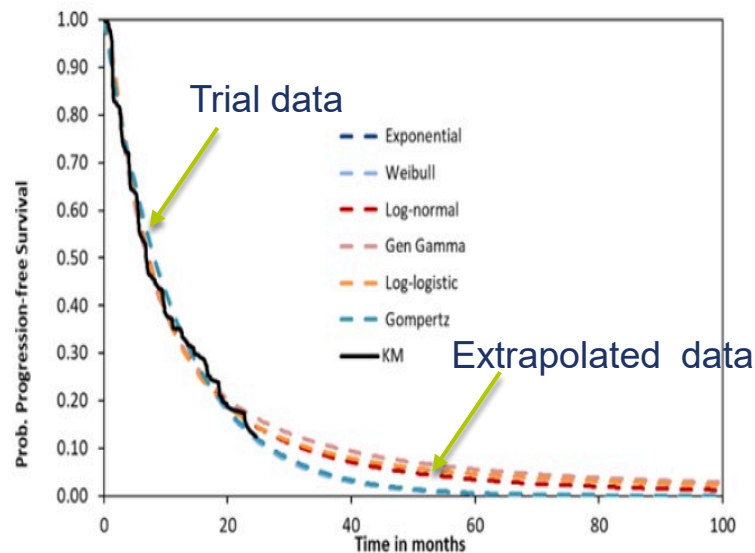
- Tecentriq (atezolizumab & bevacizumab) for HCC
- Point estimate of the ICER= 144,156 € / QALY versus sorafenib

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

Source: 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)

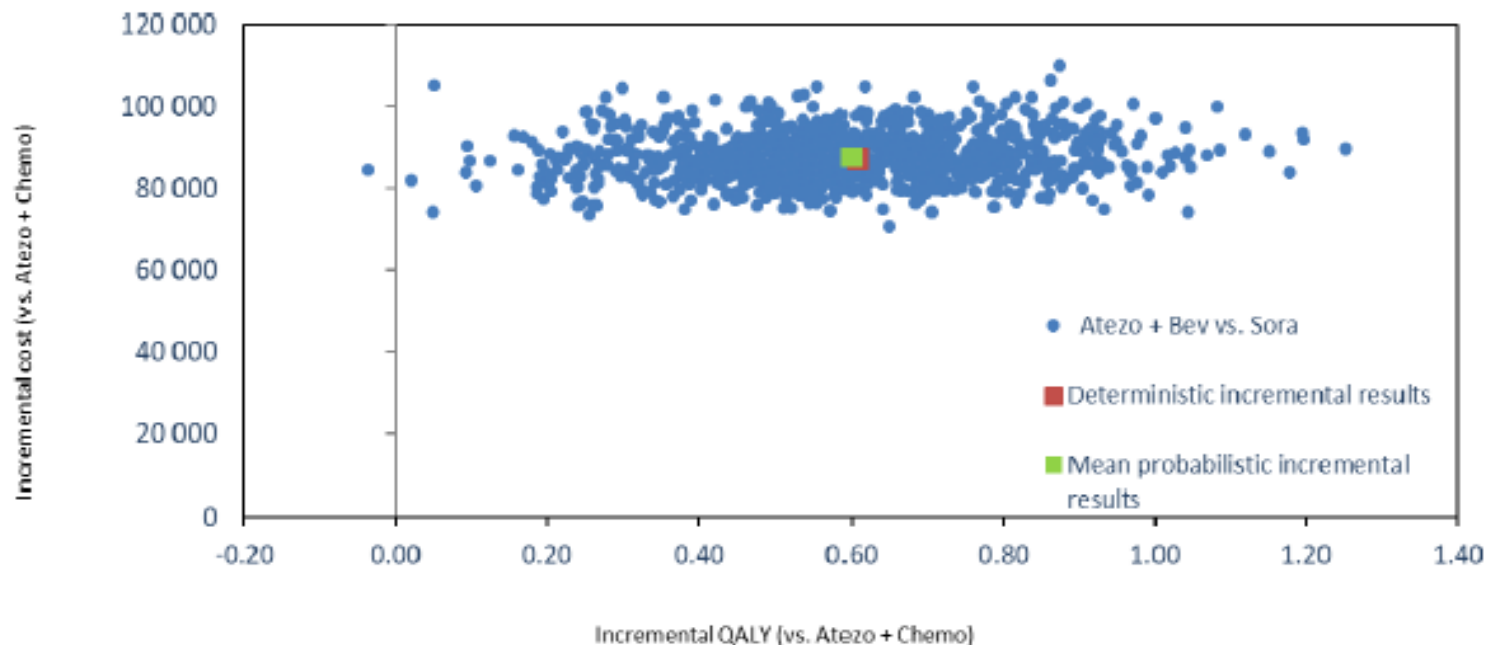


Partitioned survival models (very common in cancer)

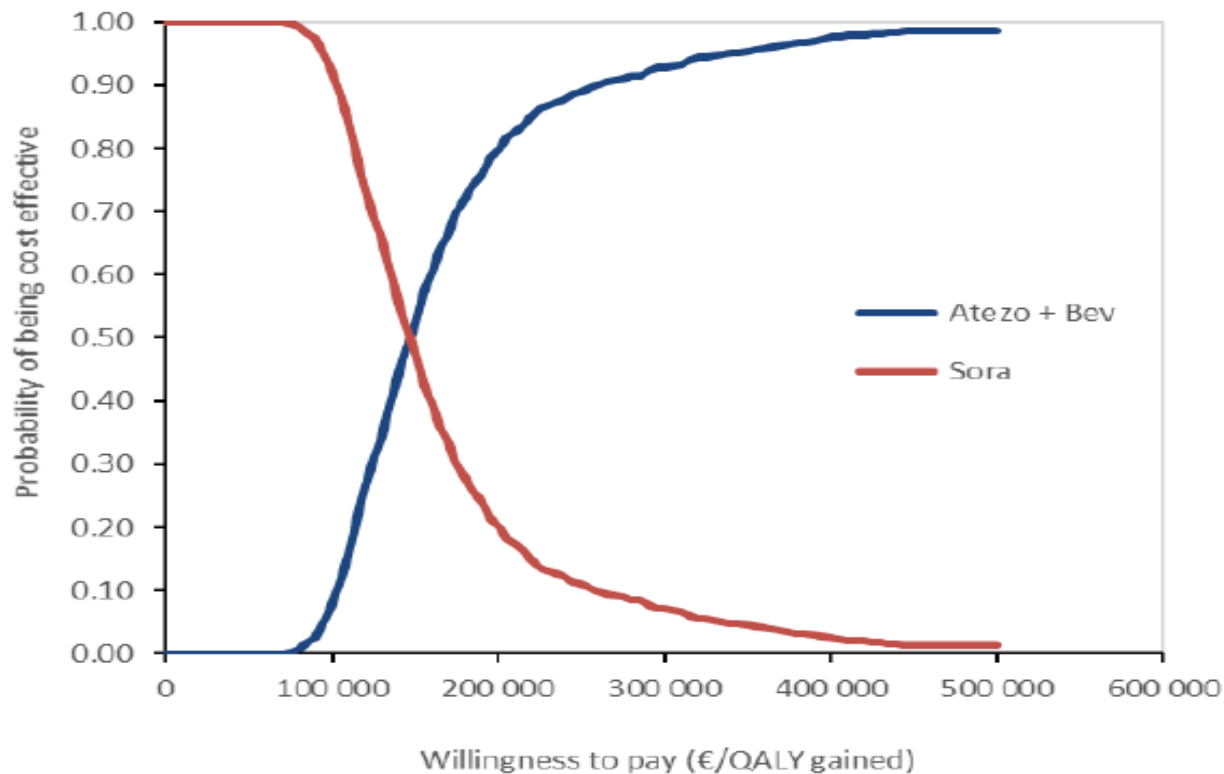
- 3 states: pre progression, progression, death
- For each state:
 - Quality of life
 - Pre progression = 0.75
 - Post progression = 0.6
 - Costs

Representing uncertainty in 2 dimensions and non-normal distributions

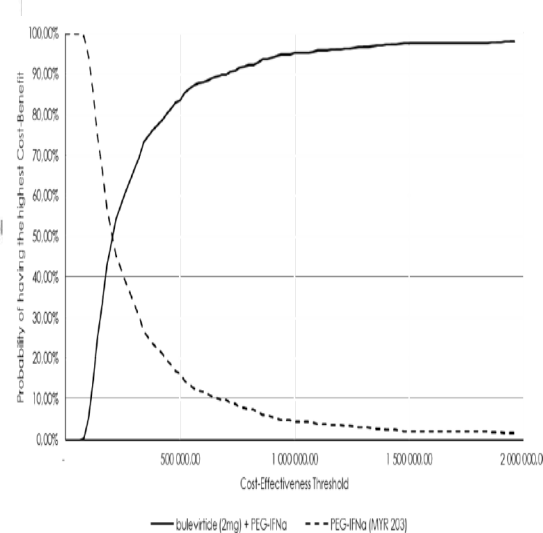
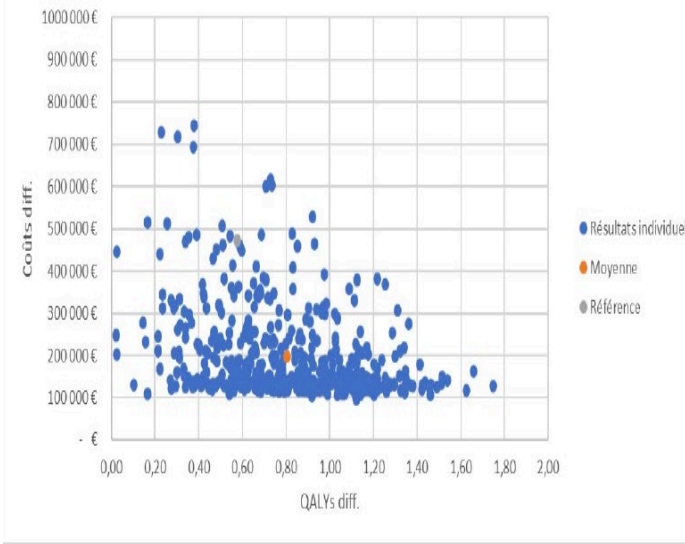
Scatterplot on the C/E plane



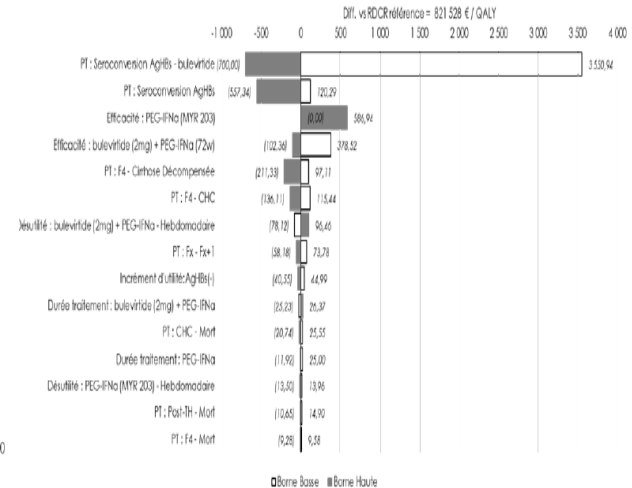
Acceptability curve



Hepatitis delta & Hepcludex = another uncertainty analysis

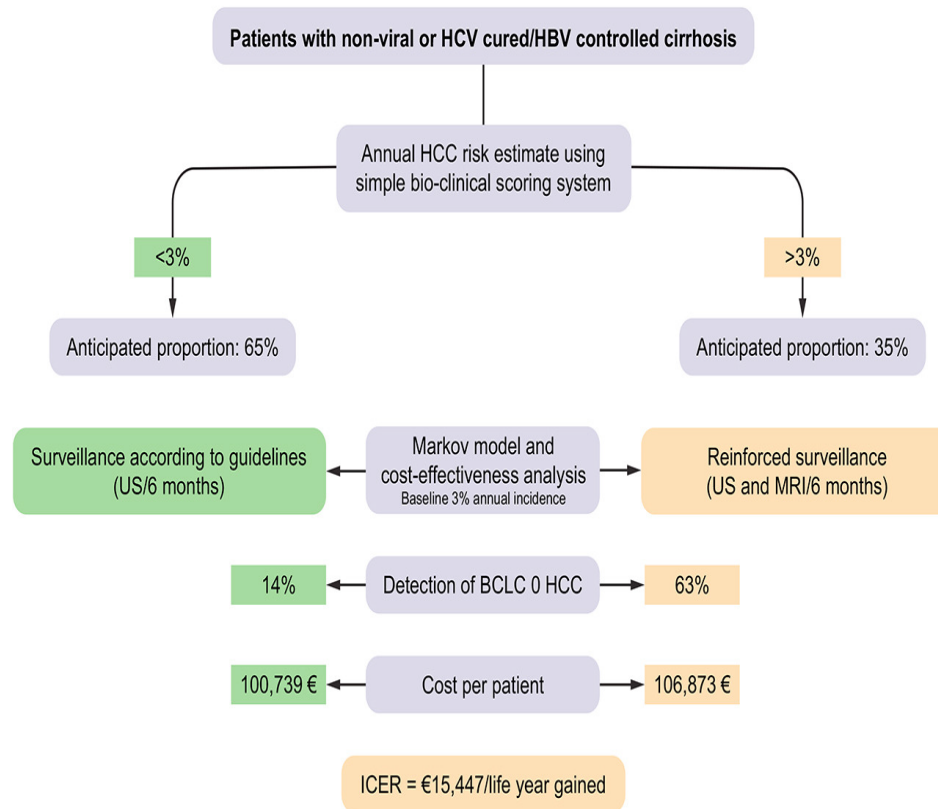


The “tornado” diagram

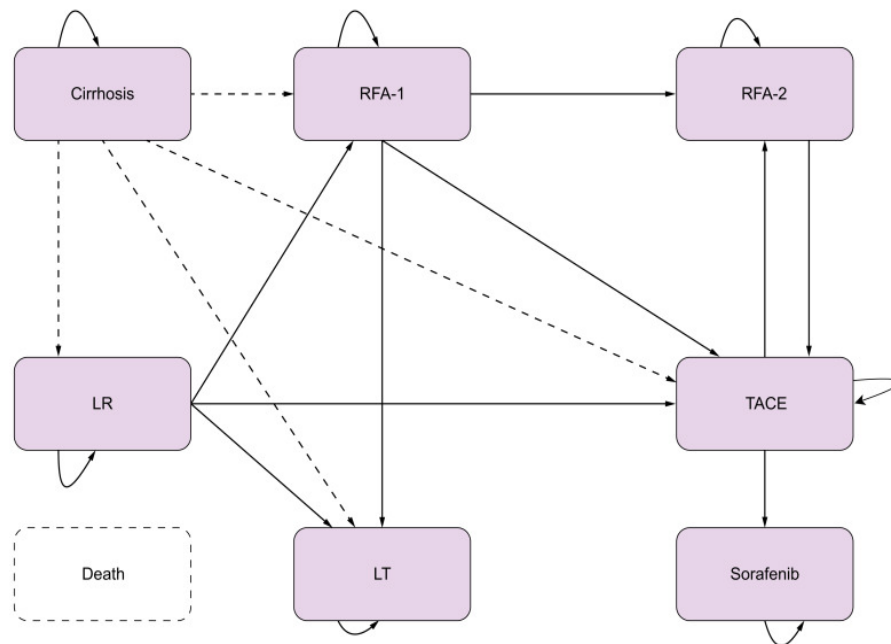


Source: https://www.has-sante.fr/upload/docs/application/pdf/2021-03/hepcludex_12012021_avis_economique.pdf.pdfaf

Model only



Diagnostic of HCC= MRI vs US

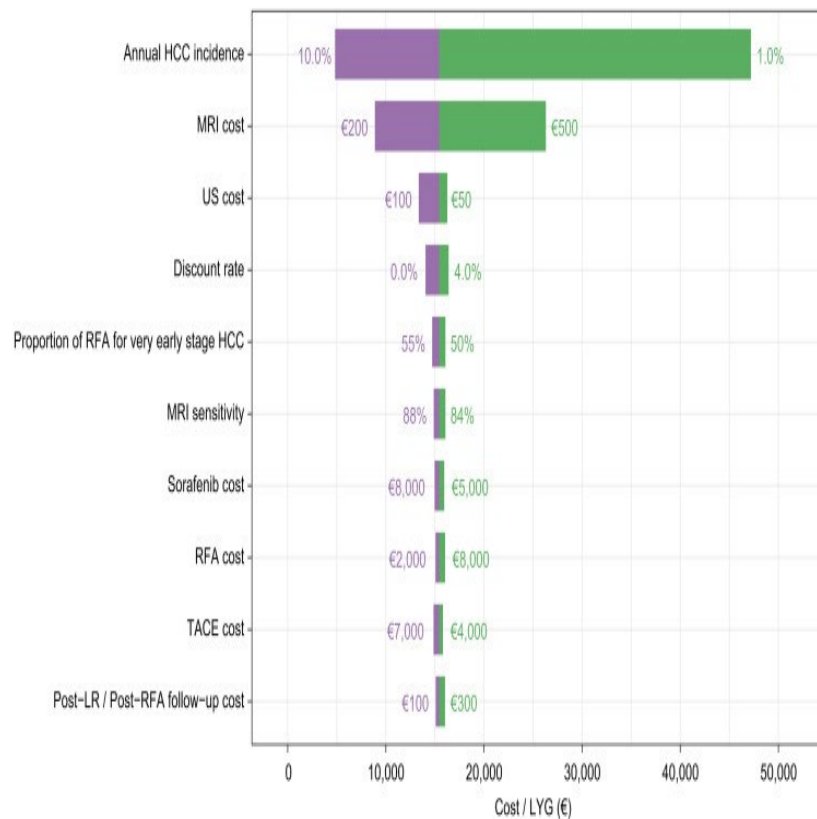
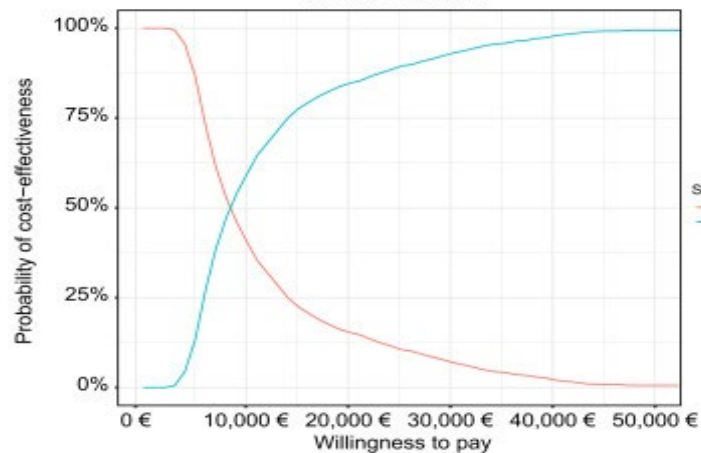
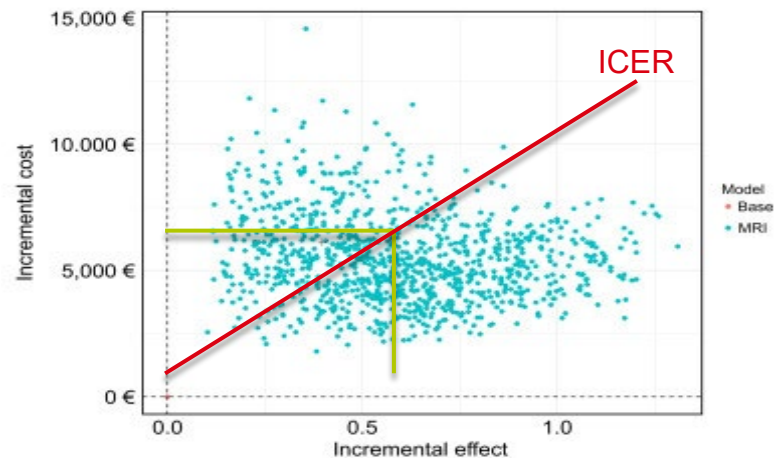


RFA = radiofrequency ablation

LR = liver resection

TACE = transarterial chemoembolization

LT= liver transplant



Summary: Health Economics Practical

- Methods are available to produce **robust economic evaluations**
- Need to contextualize with:
 - Local data
 - Local practices
 - Financial incentives
 - Budgeting vs budget impact
 - Long term impact assessment
 - Politics and stakeholders' values

Back to the Kadcylla case

- **Richard Erwin, General Manager at Roche**, said: “Close collaboration between Roche, NHS England and NICE has resulted in **NICE recommending Kadcylla as a cost effective treatment**. This is a positive example of how solutions can be reached when all parties show flexibility.”
- **Baroness Delyth Morgan, Chief Executive at Breast Cancer Now**, said: “We are absolutely delighted that tough negotiation and flexibility by NICE and NHS England, and the willingness of Roche to compromise on price, have ensured that thousands of women with incurable breast cancer will be given precious time to live.“...”

"It is truly shocking that some cancer patients are likely to have died needlessly while Roche(...) withheld Kadcylla for many months to try to extract the highest possible price from the NHS"

-John Pears, who founded Dying for a Cure after losing his wife to cancer

NICE has recently introduced new arrangements for taking into account the added value that society puts on treatments that extend life.

*These state that treatments with demonstrable benefits in terms of survival can be recommended for **patients who are not expected to live more than 24 months**, even if the incremental cost effectiveness ratio exceeds the current limit of £30 000 per QALY gained.(BMJ 2009;338:b3)*