A-TANGO

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

Isabelle Durand-Zaleski
APHP

3rd General Assembly and 7th Steering Committee
26th of September 2023 – Remote

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 945096.

Outline

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

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 945096.

A-TANGO

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)

This project has received funding from the European Union’s Horizon 2020 research and innovation programme under grant agreement No 945096.

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

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 945096.

An ad campaign in France, 2016 (withdrawn after formal complaints)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

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 945096.

“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.

This project has received funding from the European Union’s Horizon 2020 research and innovation programme under grant agreement No 945096.

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?

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 945096.

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 ?

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 945096.

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

This project has received funding from the European Union’s Horizon 2020 research and innovation programme under grant agreement No 945096.

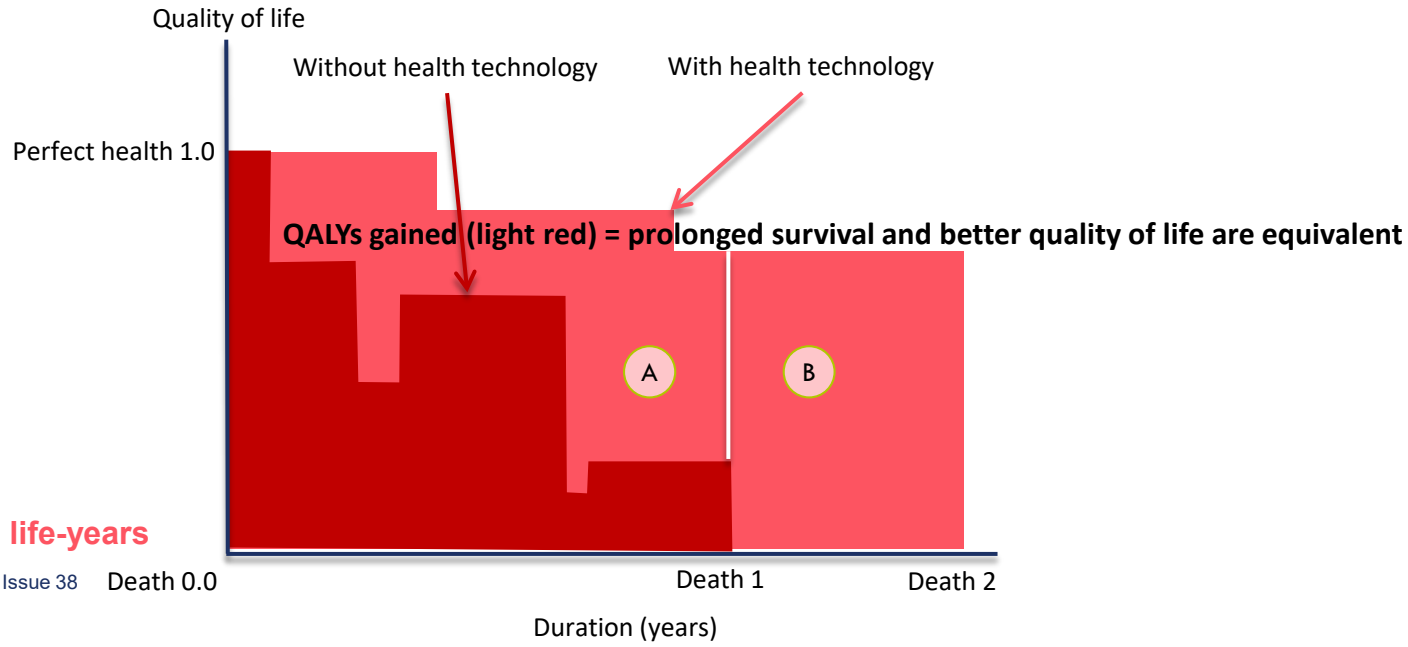
Outcomes: How to we measure the quantity of health produced by an intervention?

- 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 <u>same value</u>

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 945096.

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

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 945096.

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

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 945096.

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 ❑

SAMPLE

A-TANGO

No problem = 1
Extreme / unable = 5

EQ-5D

- 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

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 945096.

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

Pharmacoeoconomics

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

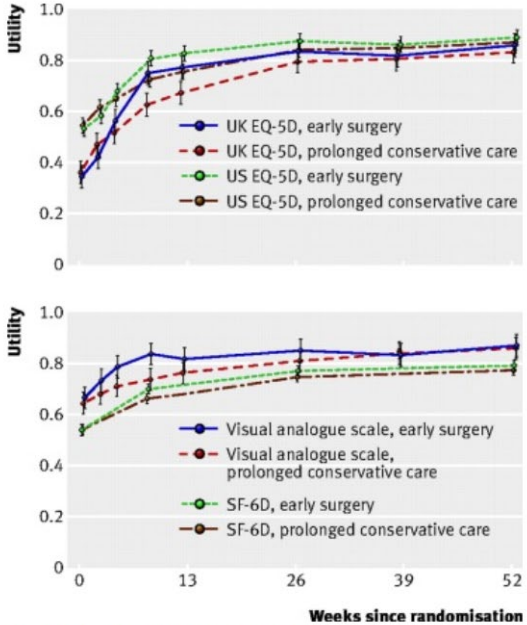
Luiz Flavio Andrade[1], Kristina Ludwig[2], Juan Manuel Ramos Goni[3], Mark Oppe[3], Gérard de Pouvourville[1].

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 945096.

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

©2008 by British Medical Journal Publishing Group

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 945096.

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

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 945096.

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

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 945096.

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

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 945096.

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

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 945096.

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

This project has received funding from the European Union’s Horizon 2020 research and innovation programme under grant agreement No 945096.

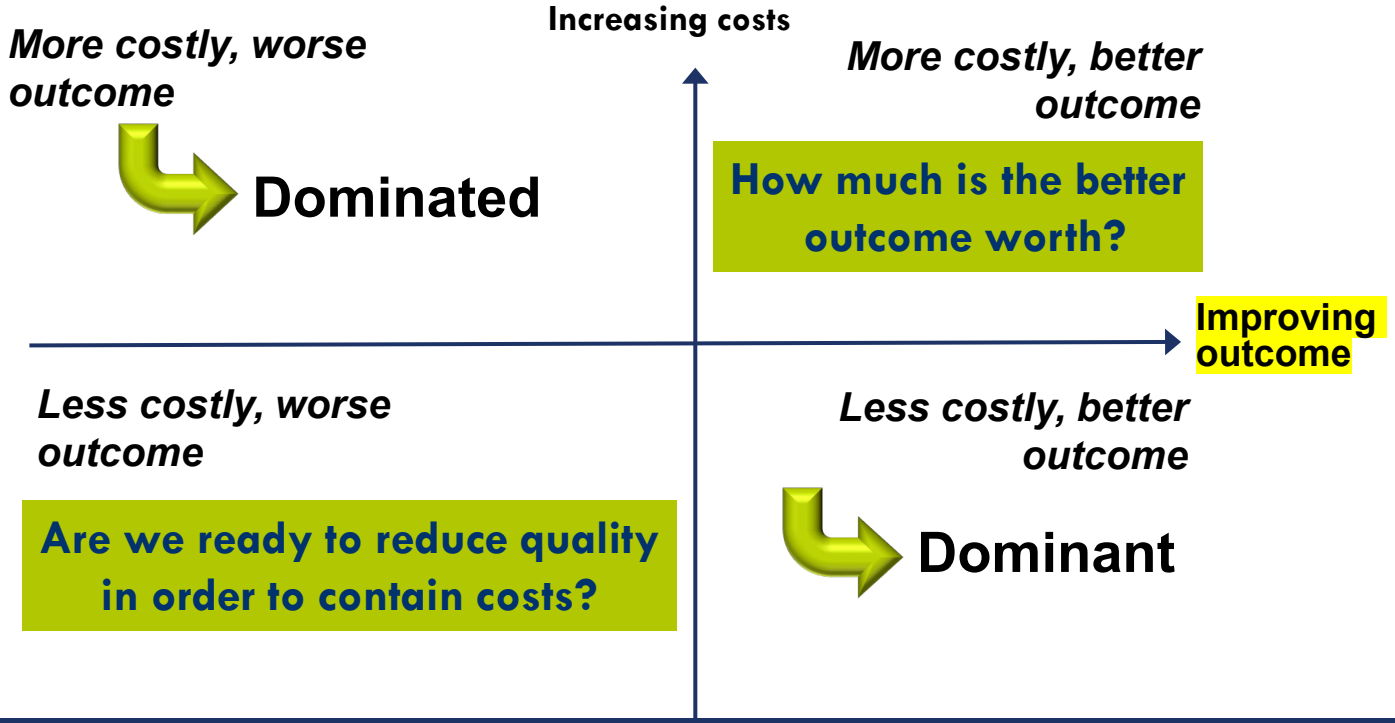
For economic evaluations in healthcare

- 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

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 945096.

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.



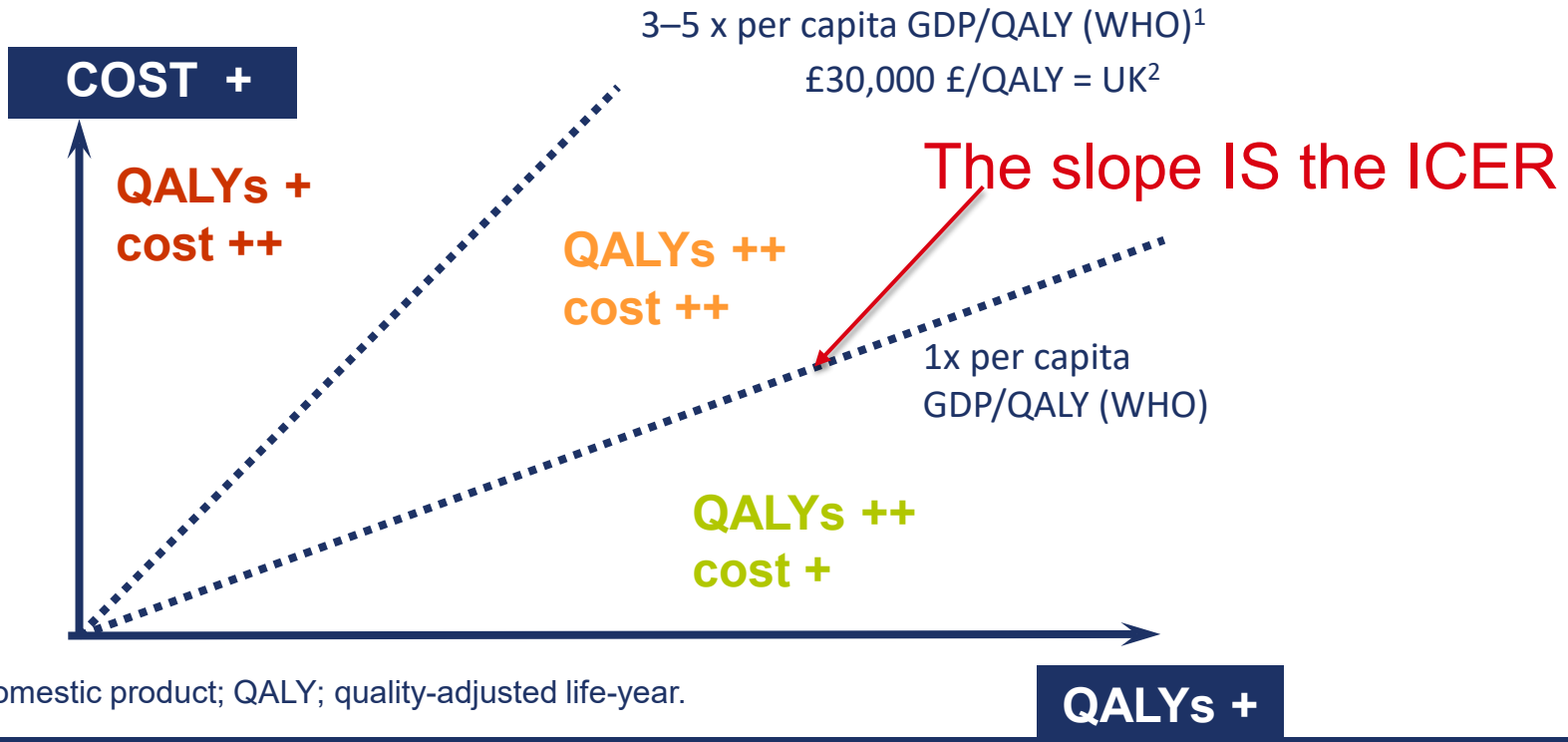
ICER= difference in costs / difference in outcomes

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 945096.

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.



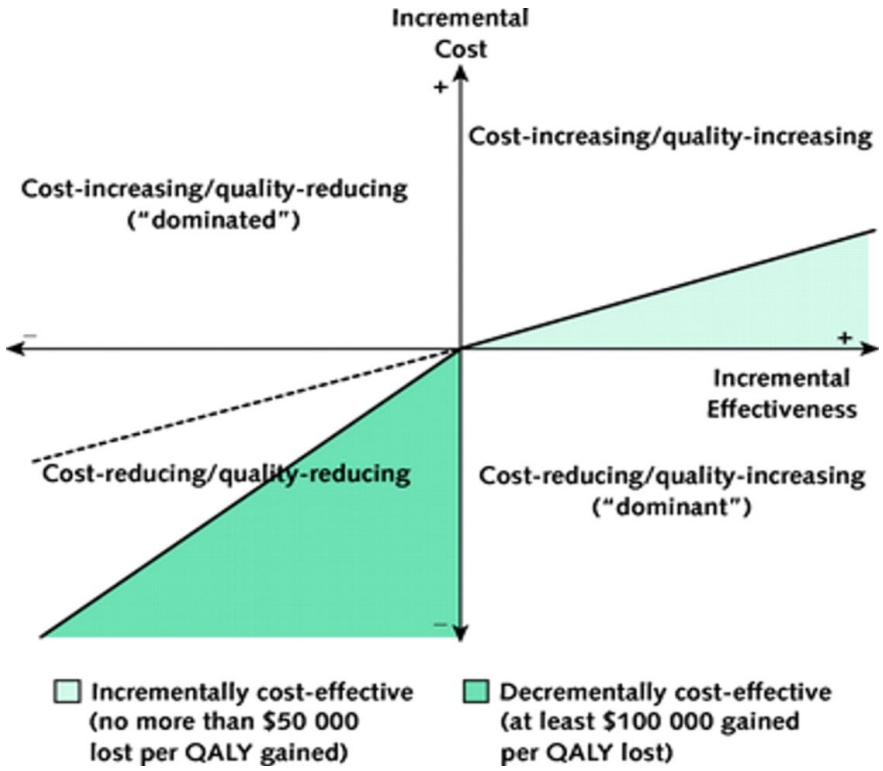
GDP, Gross domestic product; QALY; quality-adjusted life-year.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 945096.

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

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 945096.

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

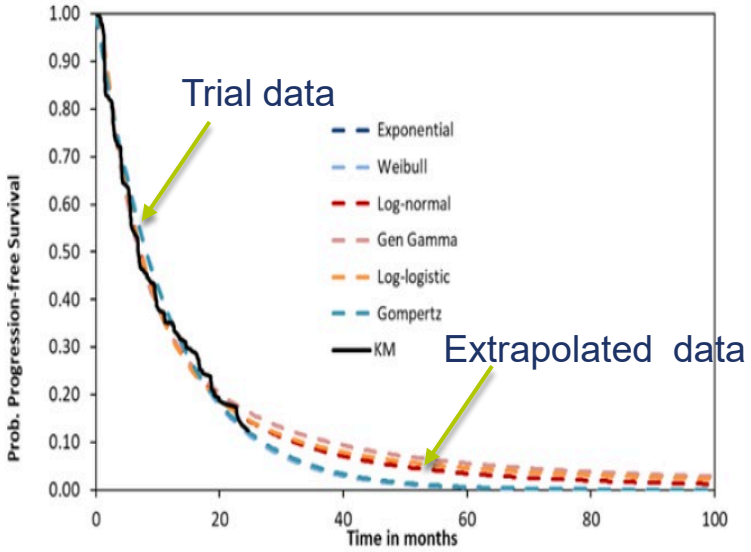
Stratégie	Coûts (€)	QALYs	AV	RDCR (€/AV)	RDCR (€/QALY)
Sorafenib	37 478	1,35	1,57	-	-
Atezolizumab + bevacizumab	124 838	1,95	2,26	126 095	144 156

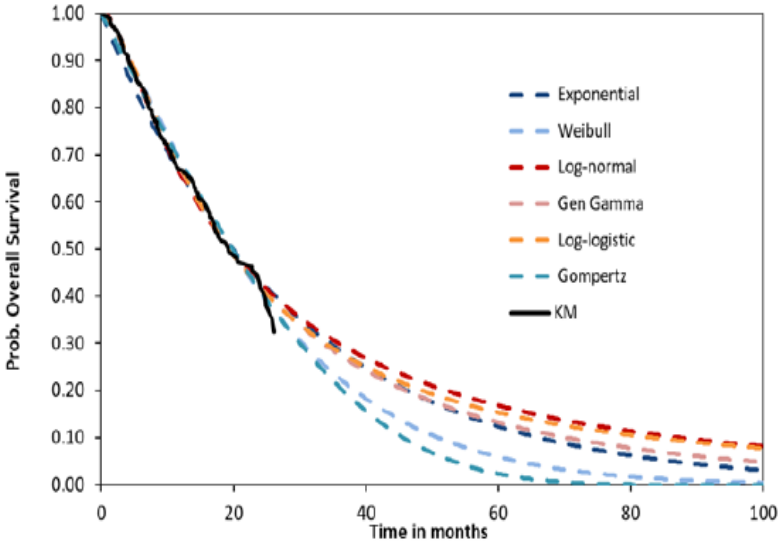
Source: https://www.has-sante.fr/upload/docs/application/pdf/2021-06/tecentriq_13042021_avis_economique.pdf

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 945096.

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

- Partitioned survival models (& extrapolation)





This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 945096.

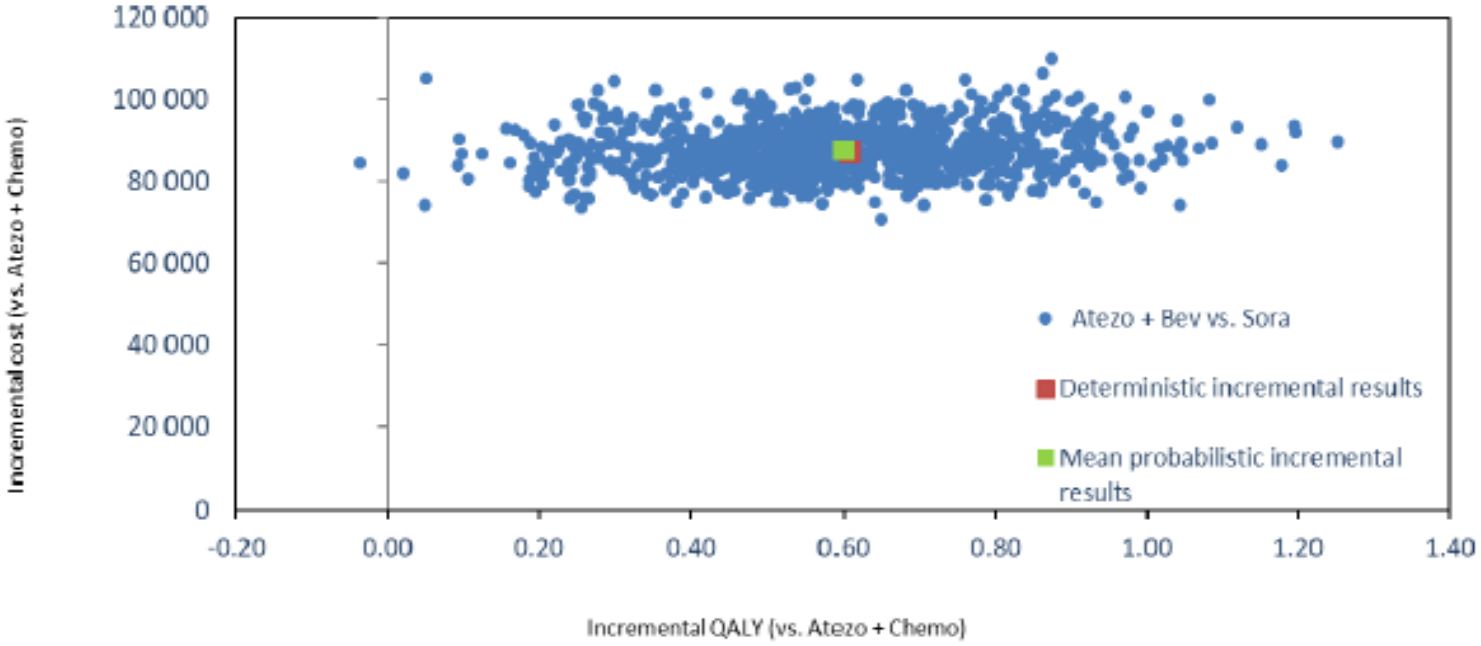
Partitioned survival models (very common in cancer)

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

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 945096.

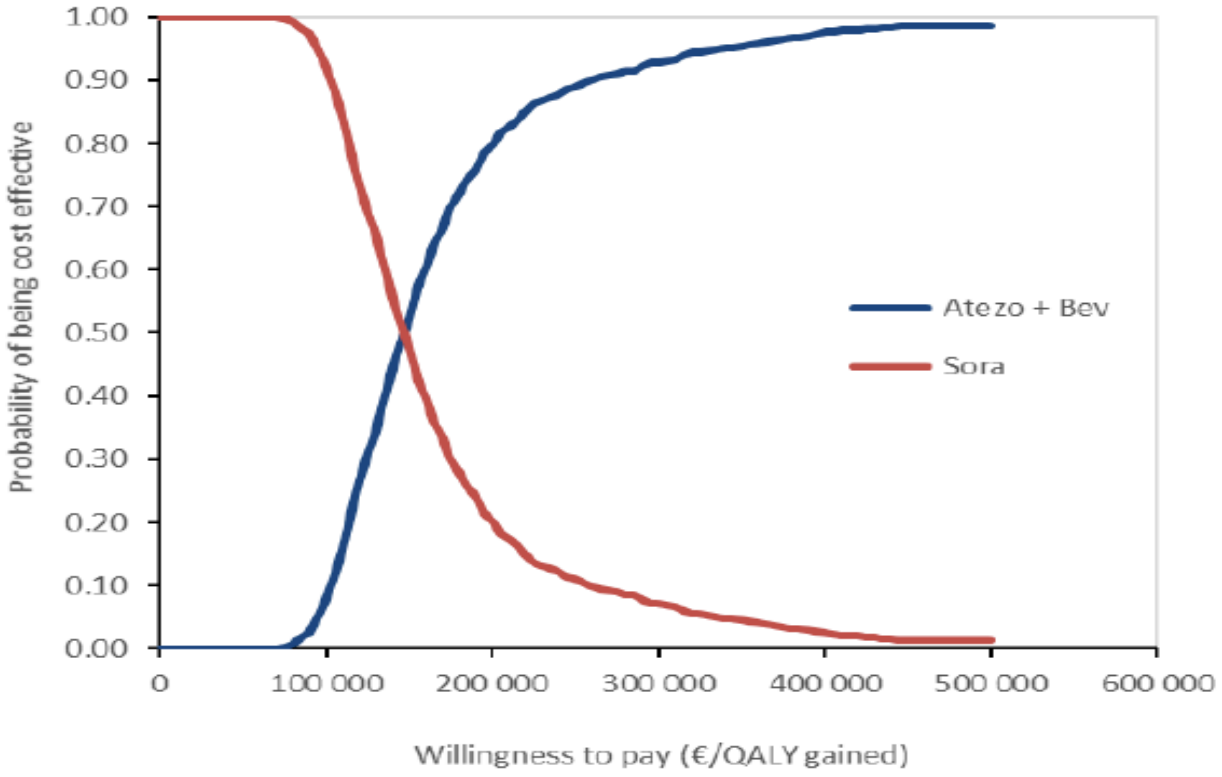
Representing uncertainty in 2 dimensions and non-normal distributions

Scatterplot on the C/E plane



This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 945096.

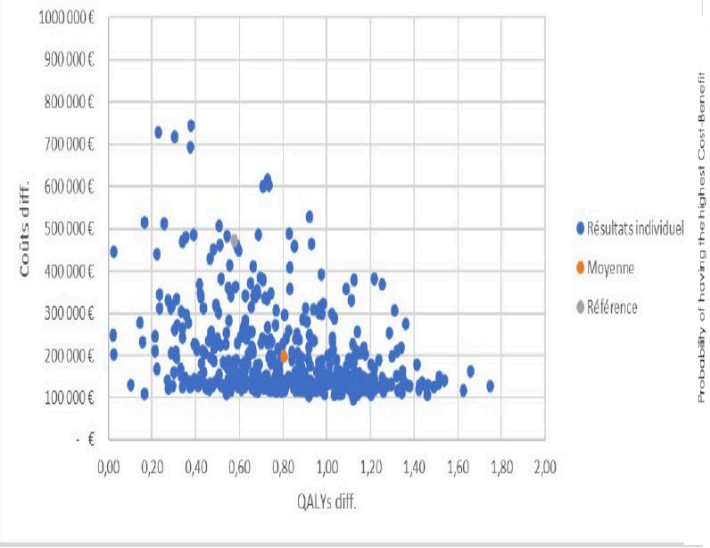
Acceptability curve

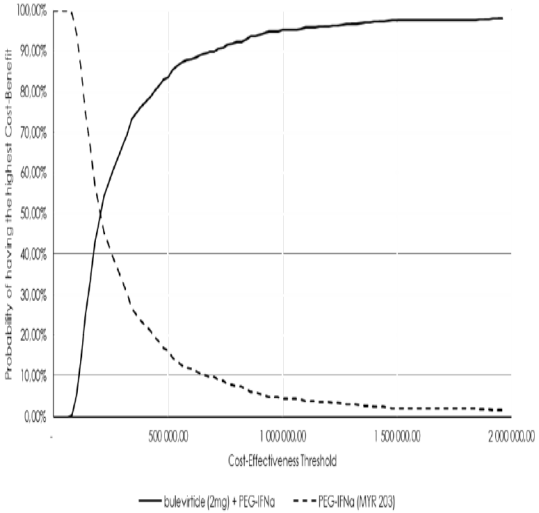


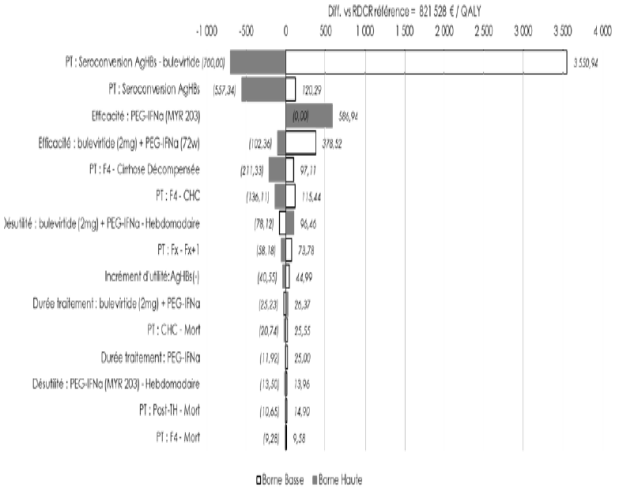
This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 945096.

Hepatitis delta & Hepcludex = another uncertainy analysis

The "tornado" diagram





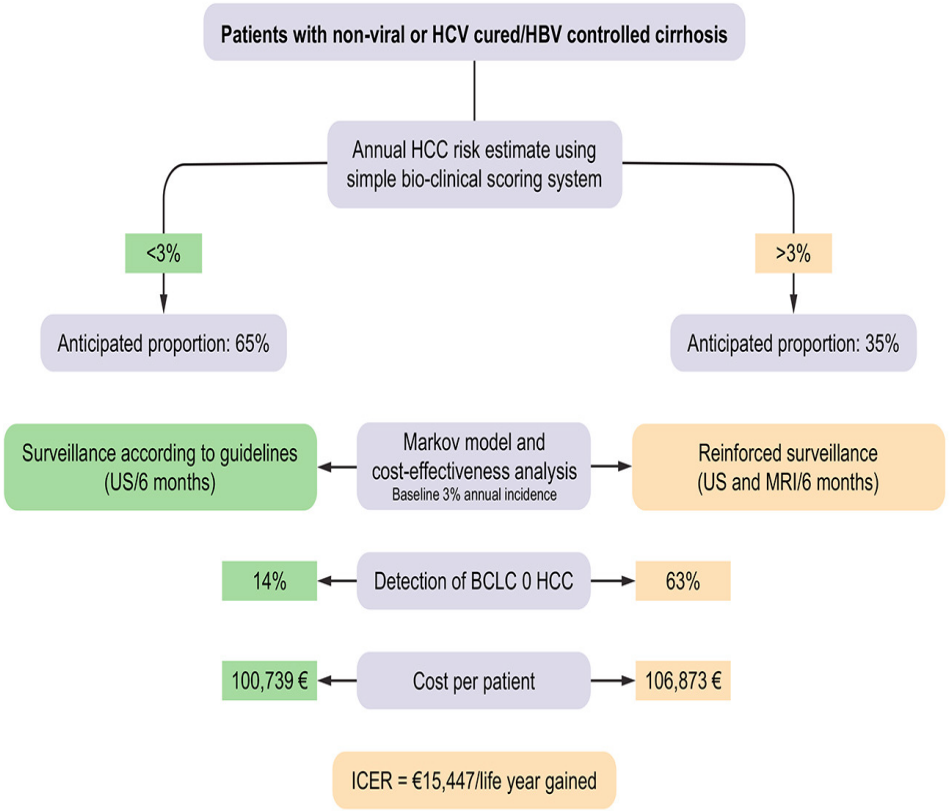


Source: https://www.has-sante.fr/upload/docs/application/pdf/2021-03/hepcludex_12012021_avis_economique.pdf.pdaf

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 945096.

Assessing cost-effectiveness of 2 surveillance strategies based on HCC risk stratification

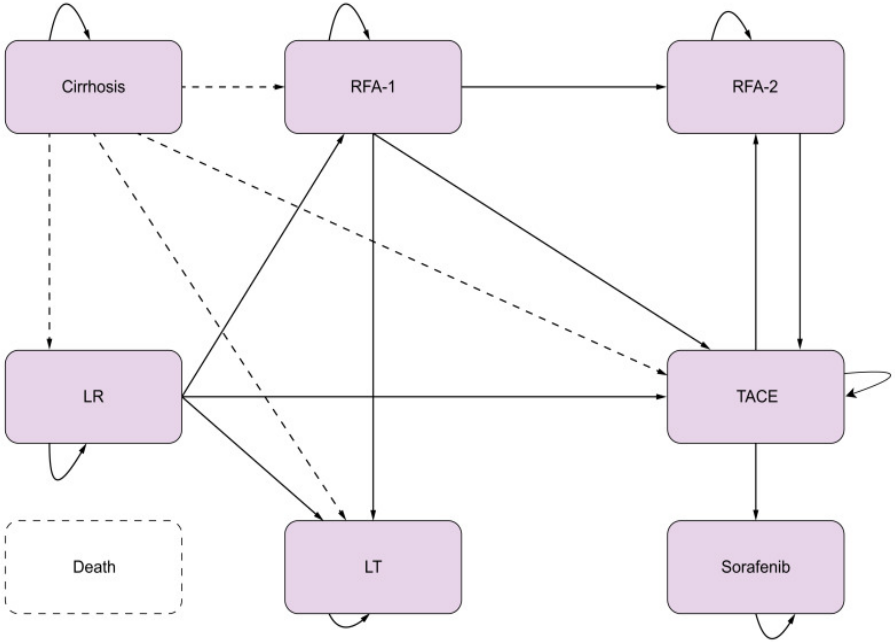
Model only



JHEPReport 2022 4DOI: (10.1016/j.jhepr.2021.100390)
Copyright © 2021 The Author(s) Terms and Conditions

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 945096.

Diagnostic of HCC= MRI vs US



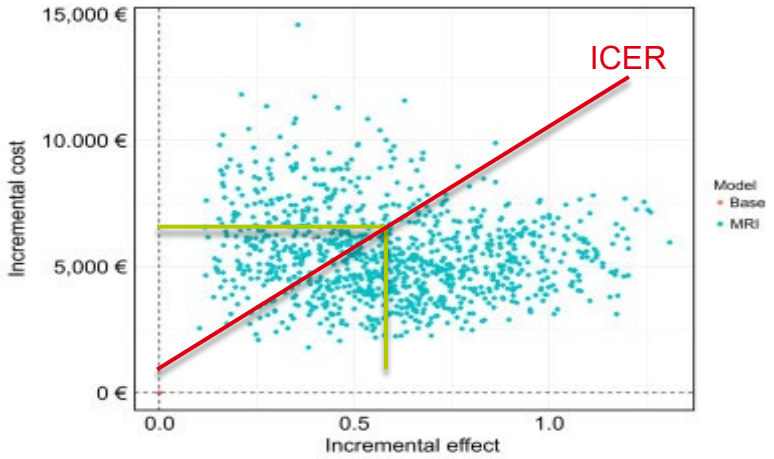
RFA = radiofrequency ablation

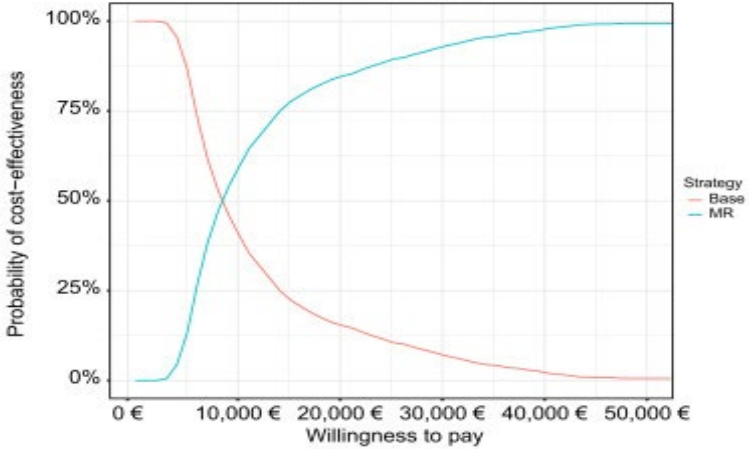
LR = liver resection

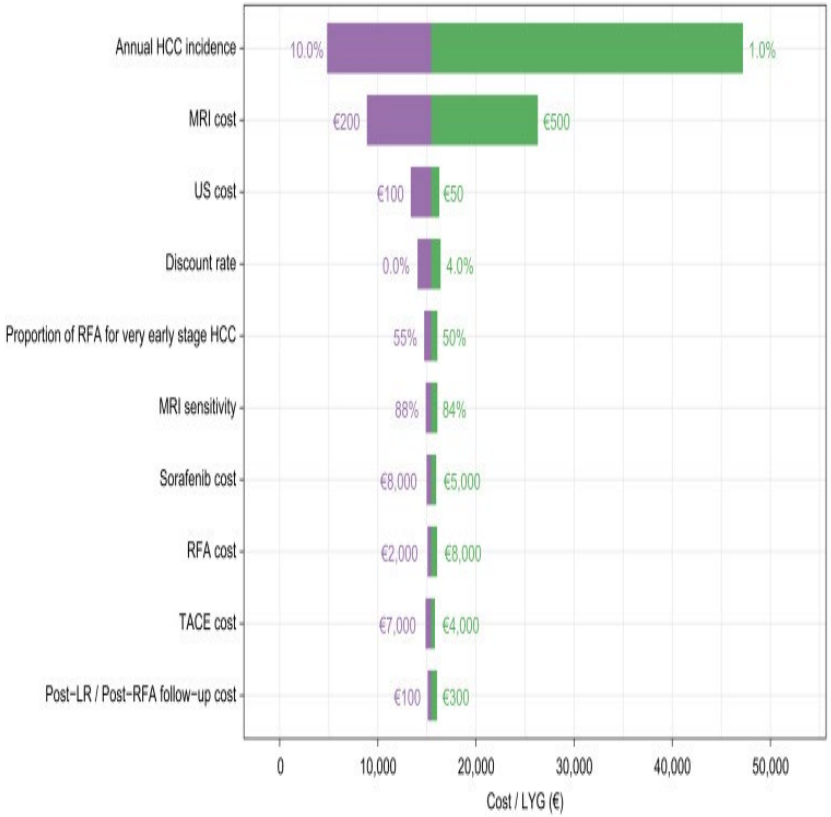
TACE = transarterial chemoembolization

LT= liver transplant

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 945096.







This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 945096.

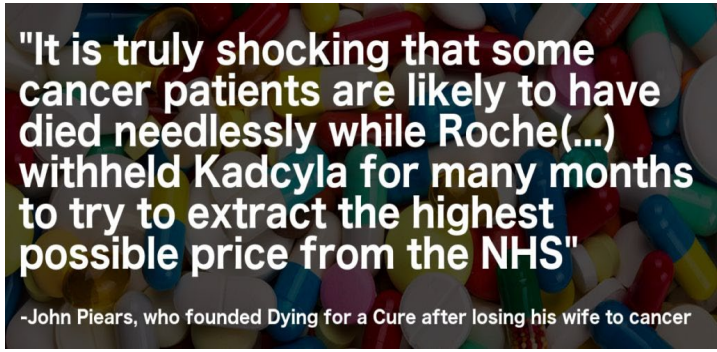
Summary: Health Economics Practical

- 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

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 945096.

Back to the Kadcyla case

- **Richard Erwin, General Manager at Roche**, said: "Close collaboration between Roche, NHS England and NICE has resulted in NICE recommending Kadcyla 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."..."



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)

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 945096.