# STATISTICS FOR ONCOLOGY

A Course for Scottish Trainees

by… The Edinburgh Cancer Informatics Research Group

https://edin.ac/oncology-statistics

# HEALTH ECONOMICS

PETER HALL

University of Edinburgh

# Outline

- Healthcare expenditure and health
- Health Economics
- Reimbursement decision making
- Cost-effectiveness analysis
- Decision making in the NHS
- Evidence for cost-effectiveness

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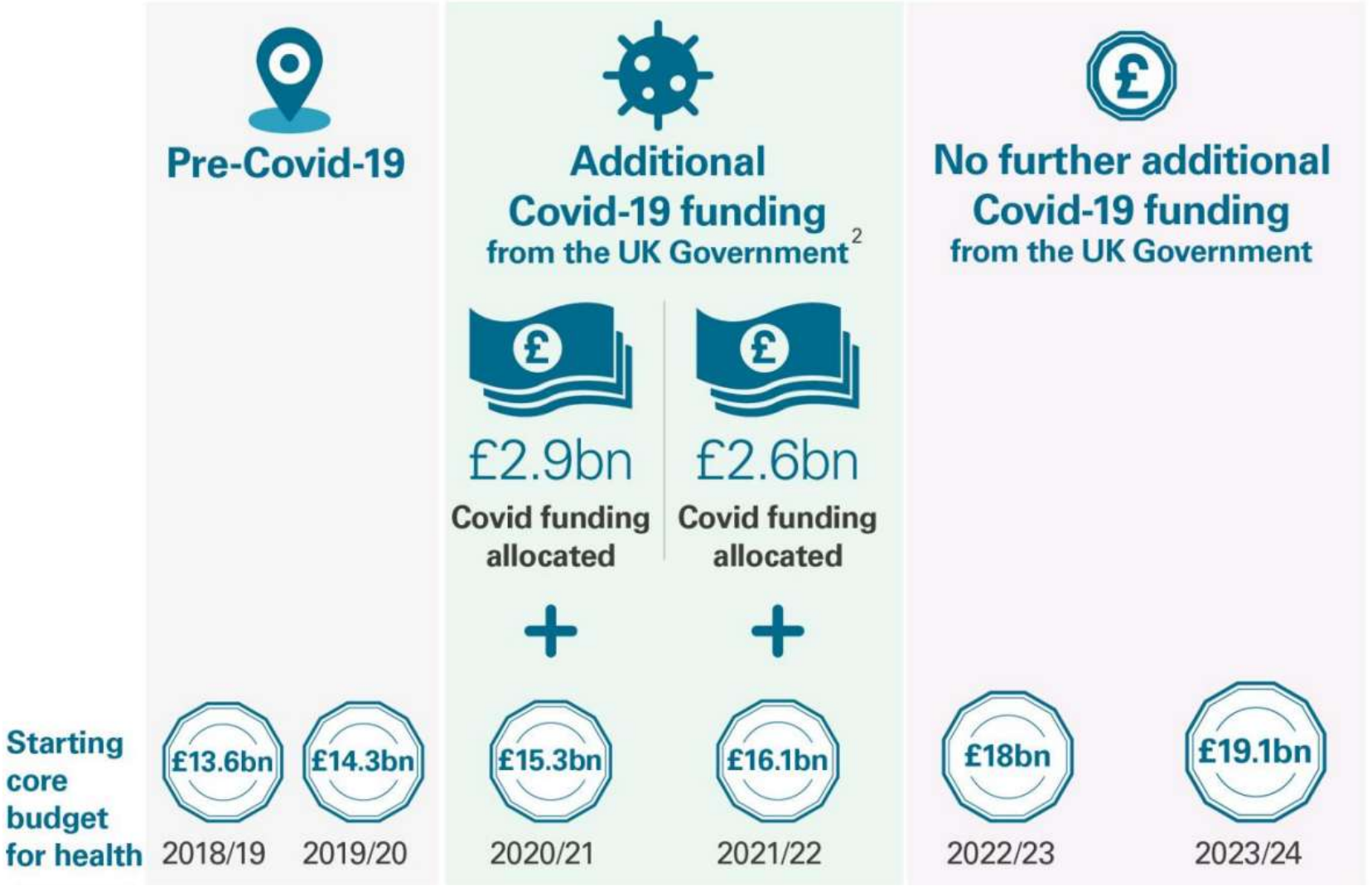
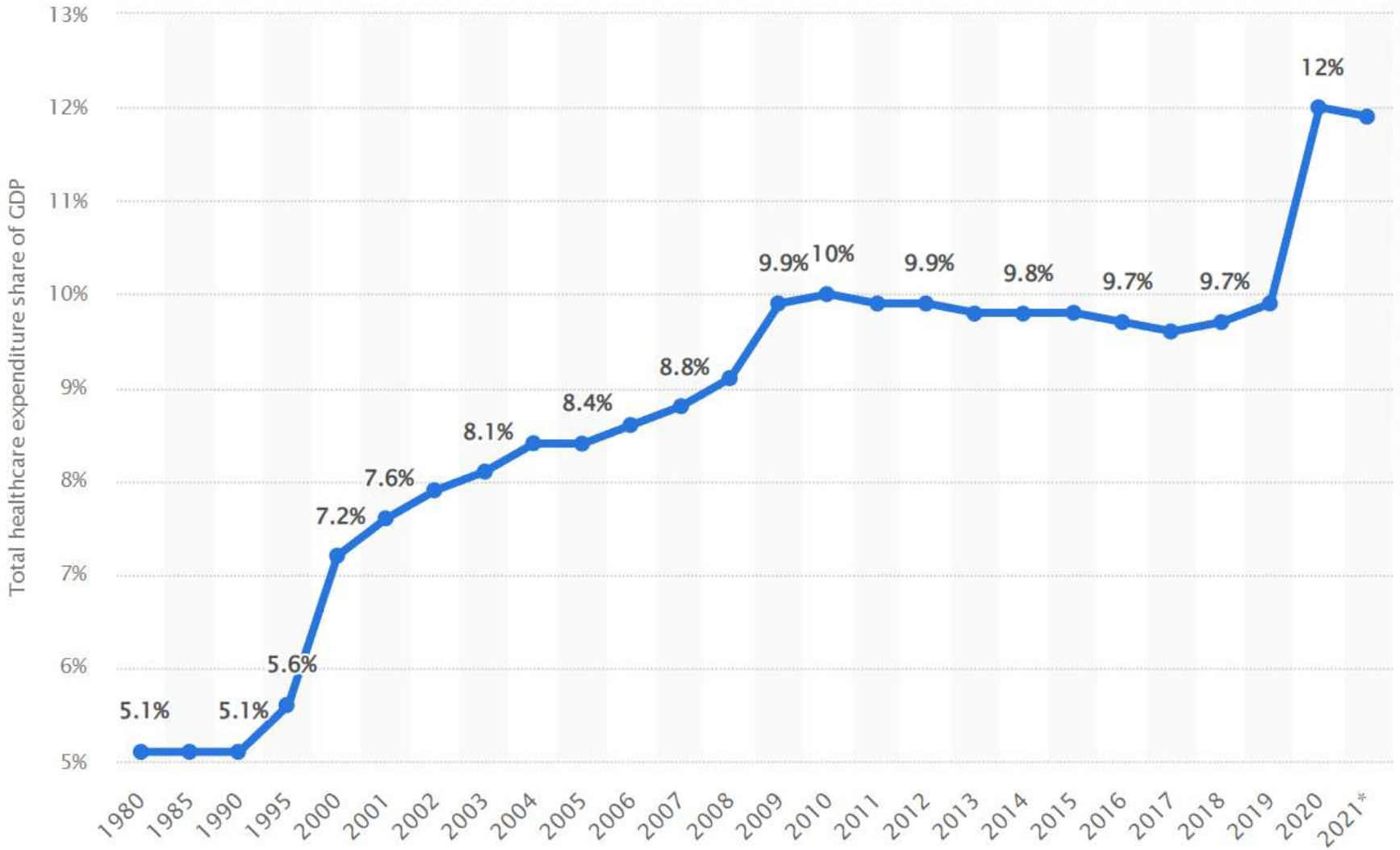
## Health funding in Scotland 2018/19 to 2023/24[1]




Source: Scottish Government

# Total UK healthcare expenditure as % of GDP

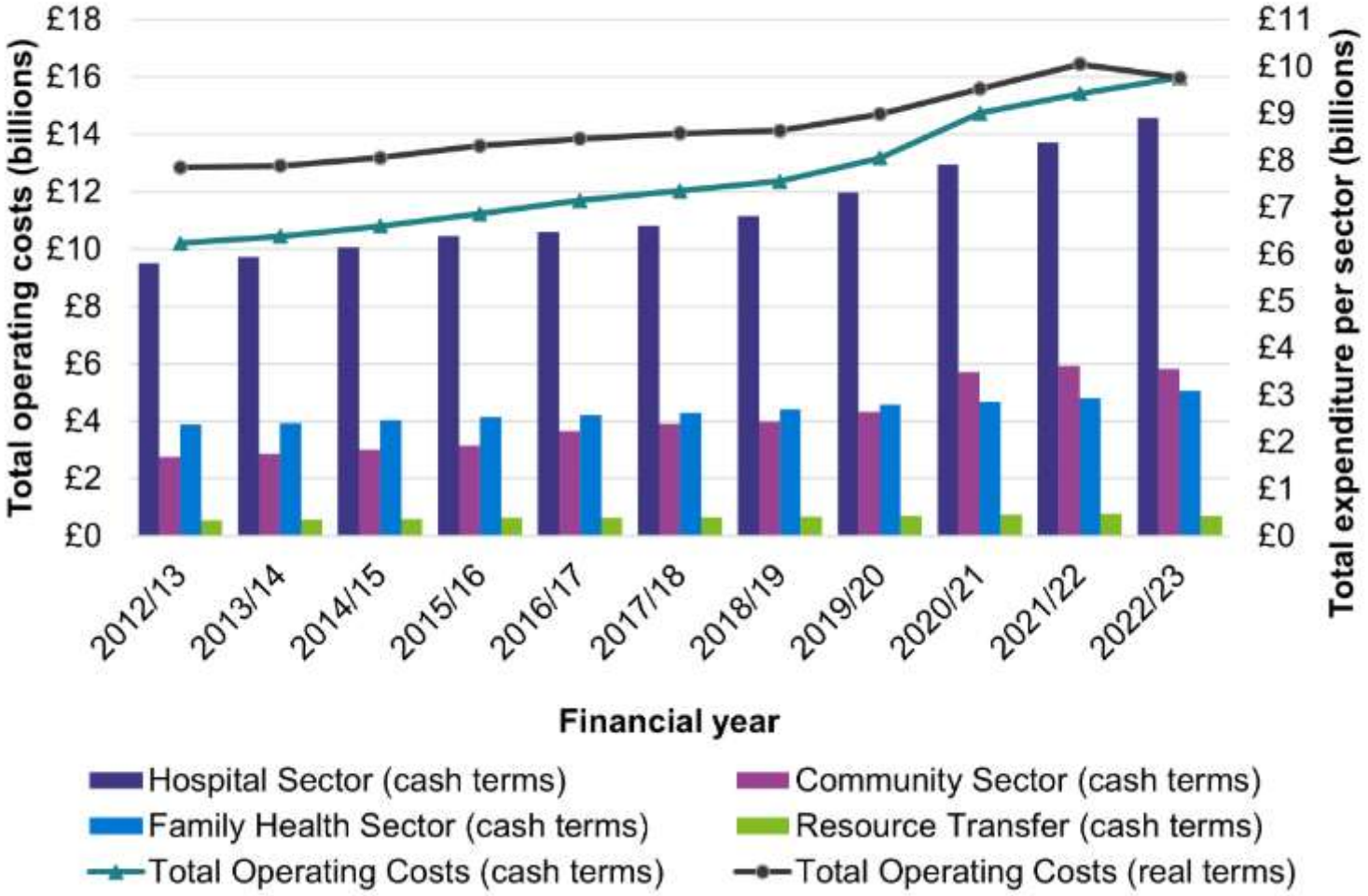



© Statista 2022

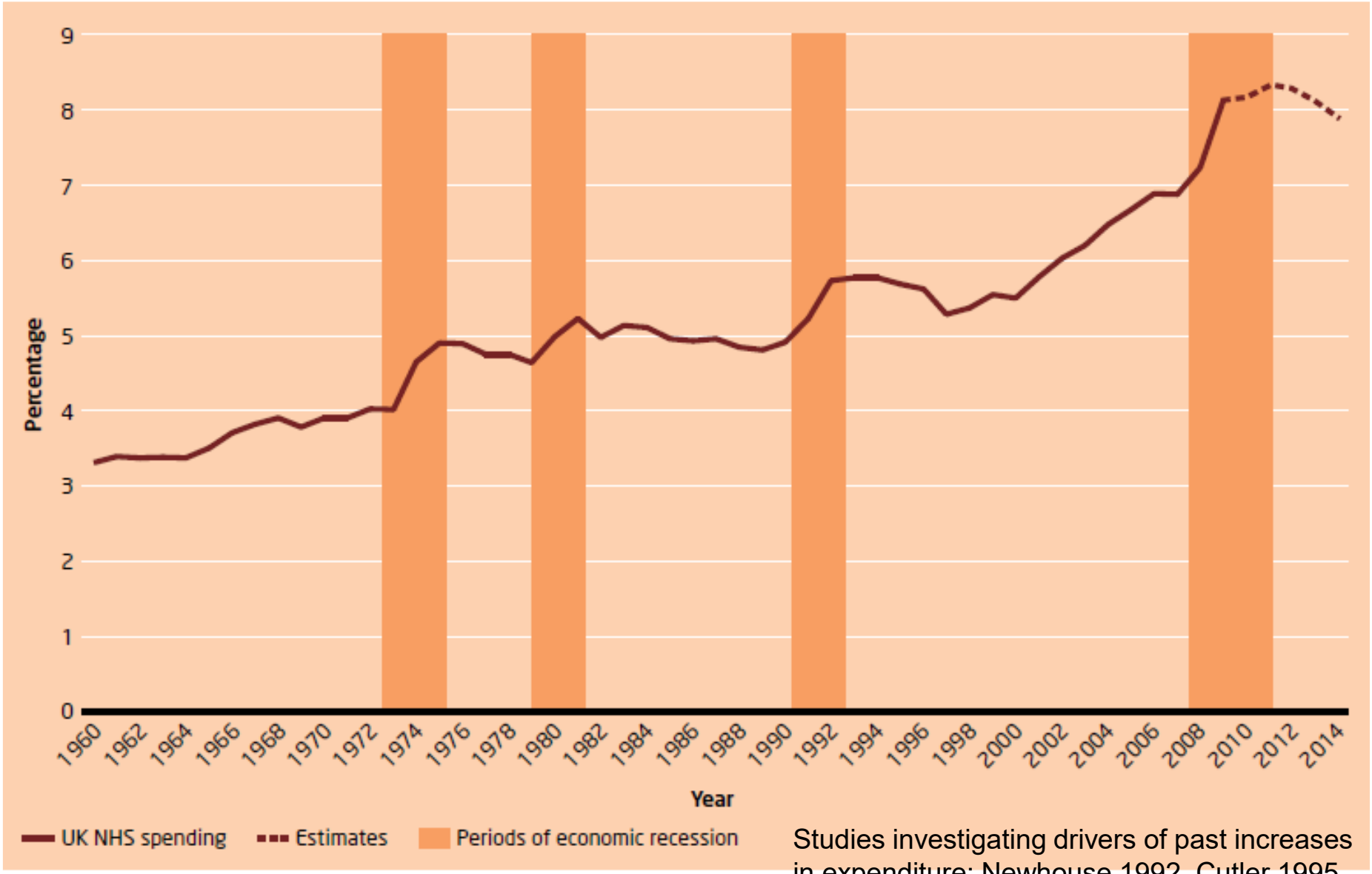
Additional Information

Show source

Figure 1: Trend in expenditure, 2012/13 to 2022/23



# NHS spending as a percentage of GDP 1960-2014

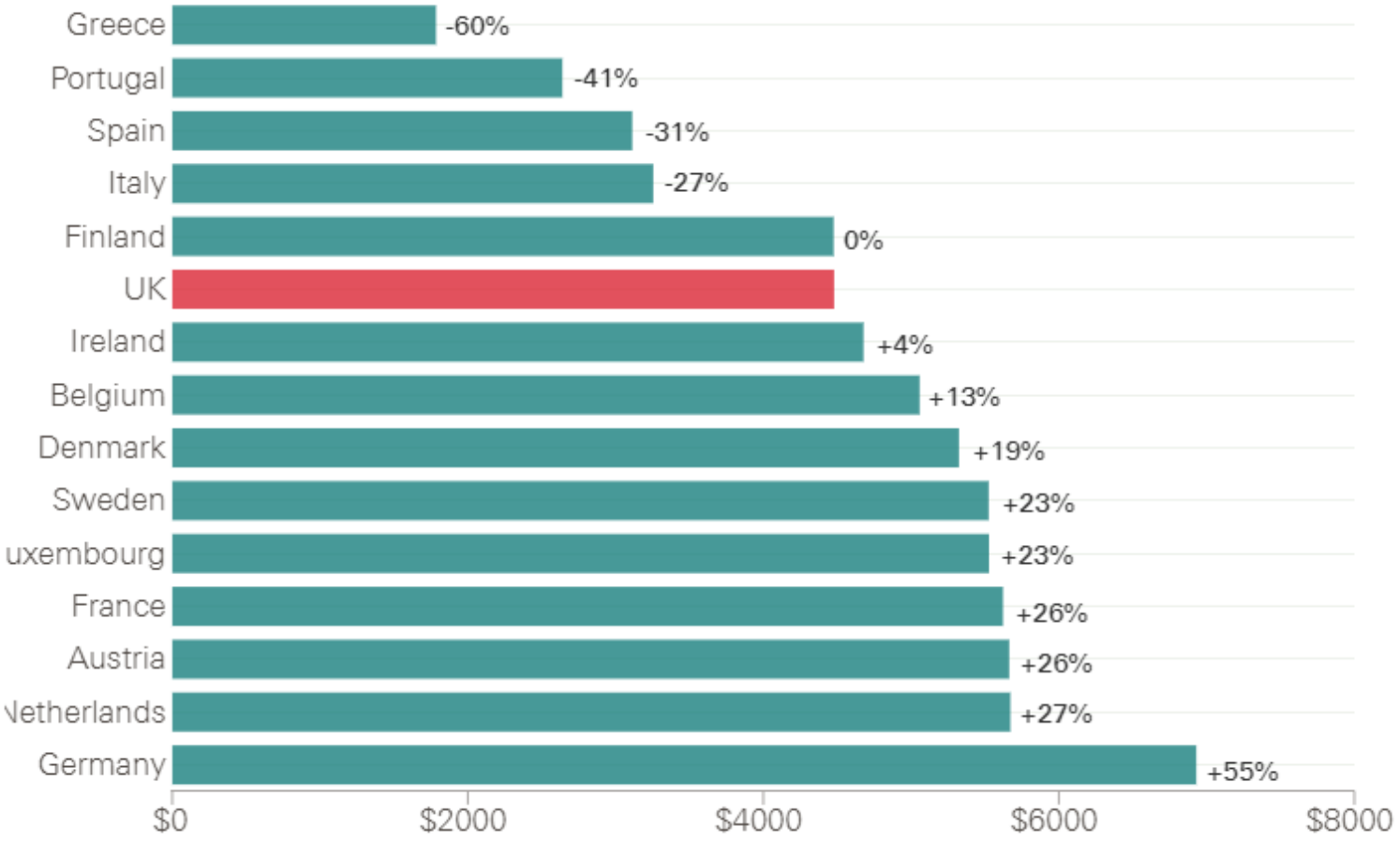



Source: Appleby, King's Fund, 2013

Studies investigating drivers of past increases in expenditure: Newhouse 1992, Cutler 1995 and Smith et al 2009

## Publicly funded health spend per capita in 2022, with comparison to UK (%)

**USD, purchasing power parity**




**REAL Centre**

The Health Foundation © 2024

Source: Government/compulsory schemes, all providers, per capita, current prices, current purchasing power parity (USD), 2022. OECD (2024), 'Health expenditure and financing: Health expenditure indicators', OECD Health Statistics (database), https://doi.org/10.1787/data-00349-en (accessed on 20 June 2024). • The percentages at the end of the bars give the percentage difference between a country's spending per capita and UK spending per capital in 2022.

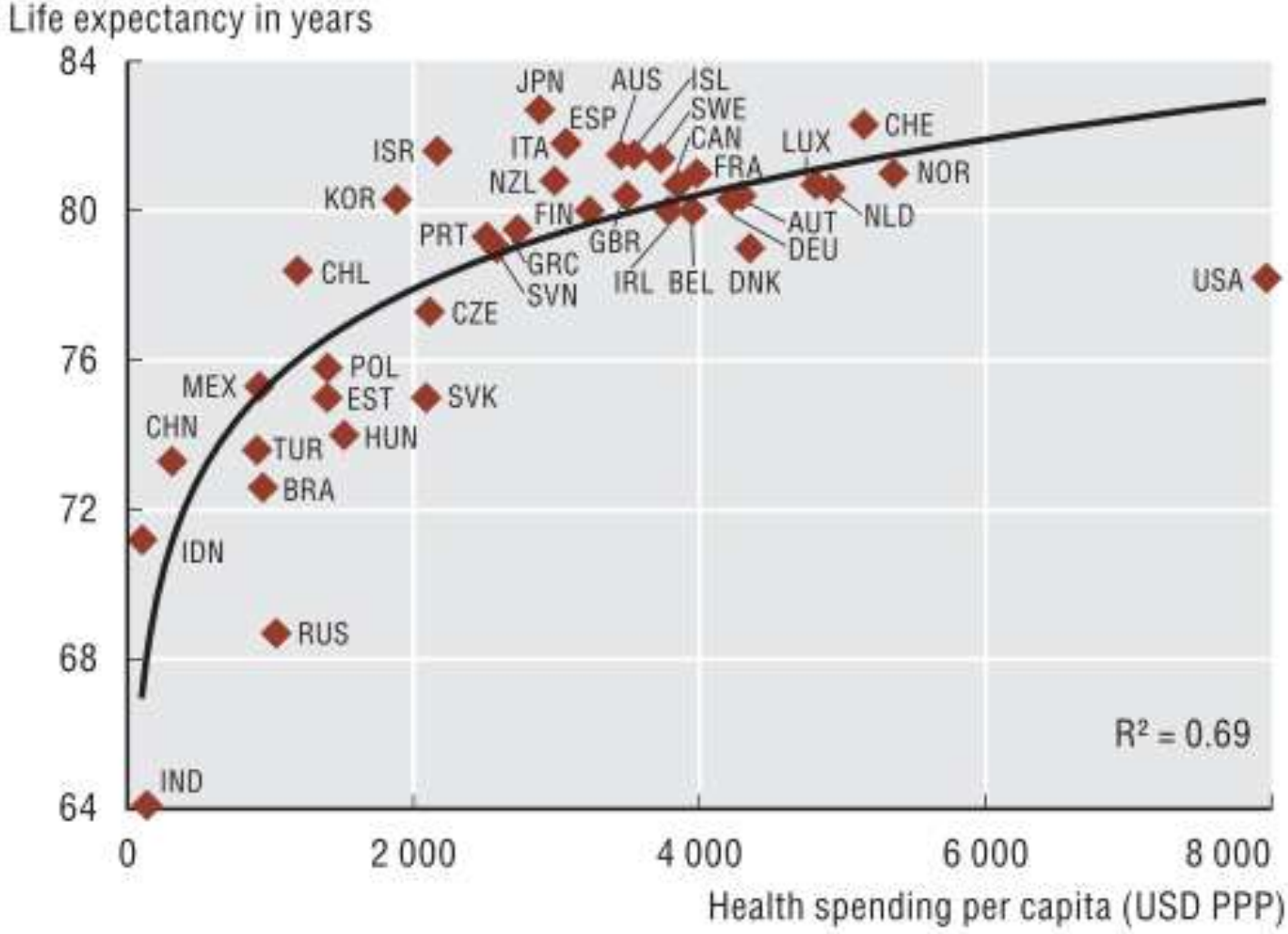
# What fuels healthcare inflation?

- Life expectancy, people living longer
  - by 2035 over 85's increase from 2% to 5% of population
- Technology and scientific advances, emergence of new treatments and drugs
- Patient expectation, less deferential more demanding- extrovertocracy (David Jones)
  - Political consumerism
  - Healthcare as a commodity
- 'Free' no constraints, no financial disincentive to seek care
- Heavy reliance on labour, staff cost run over inflation
- Building infra-structure run over inflation
- Compliance (CQC England/Care Inspectorate Scotland)
- Negligence

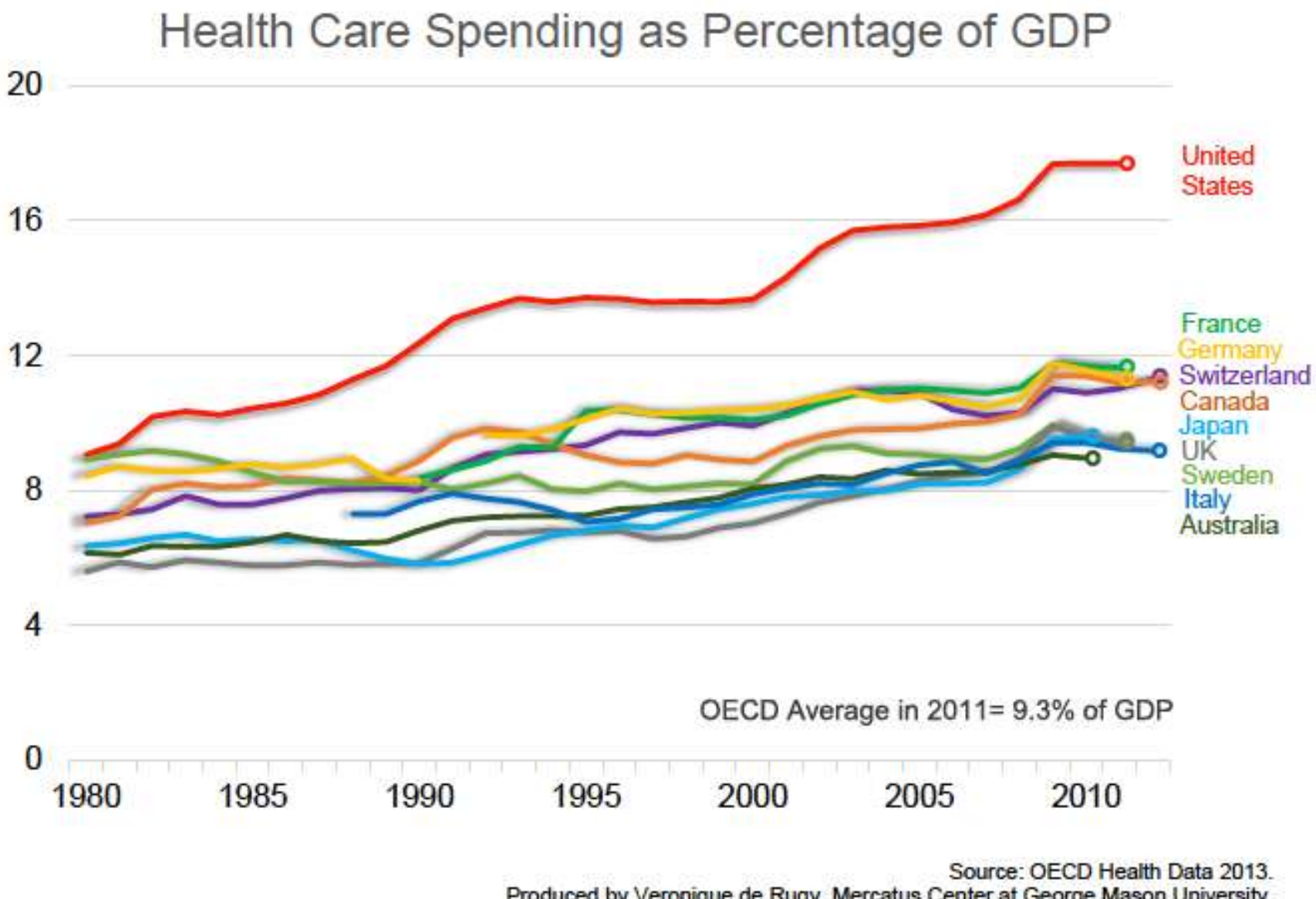
# Healthcare expenditure

- Is more expenditure a good thing?
- Does it work?
  - Is population health improved?
- Are there more important things to spend money on?
  - Education, social security, tax cuts, etc

## 1.1.3 Life expectancy at birth and health spending per capita, 2009 (or nearest year)




*Source:* *OECD Health Data 2011*; World Bank and national sources for non-OECD countries.




Source: OECD Health Data 2013.
Produced by Veronique de Rugy, Mercatus Center at George Mason University.

TOTAL NATIONAL HEALTH EXPENDITURES

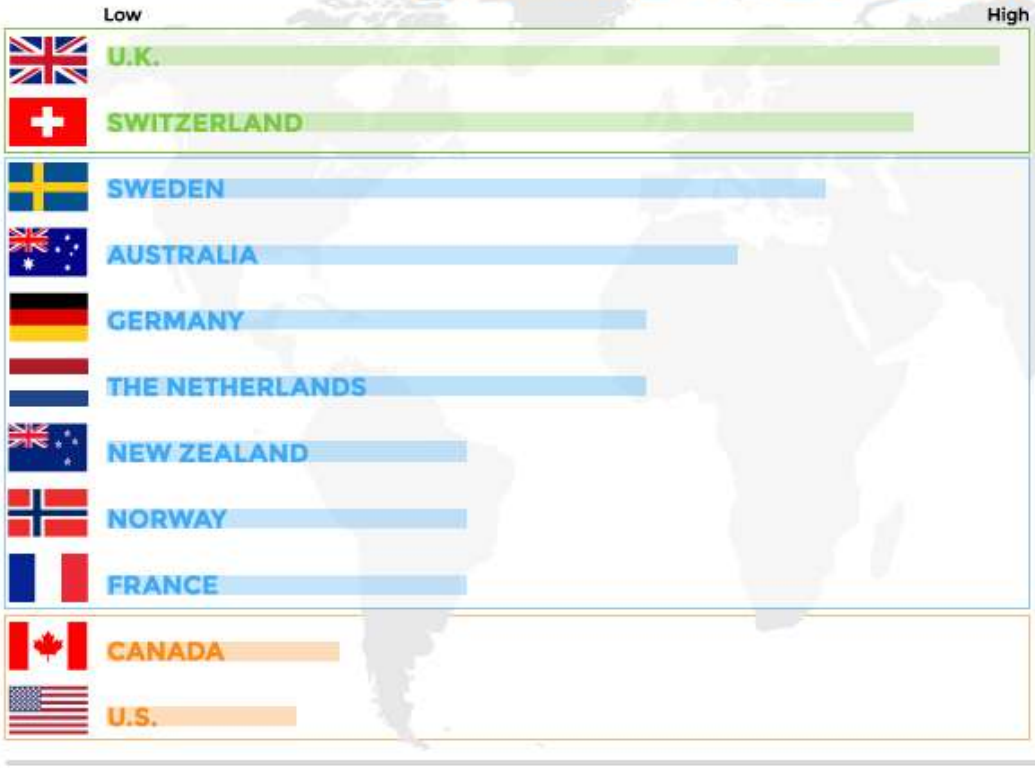
# USD 2.6 TRILLION

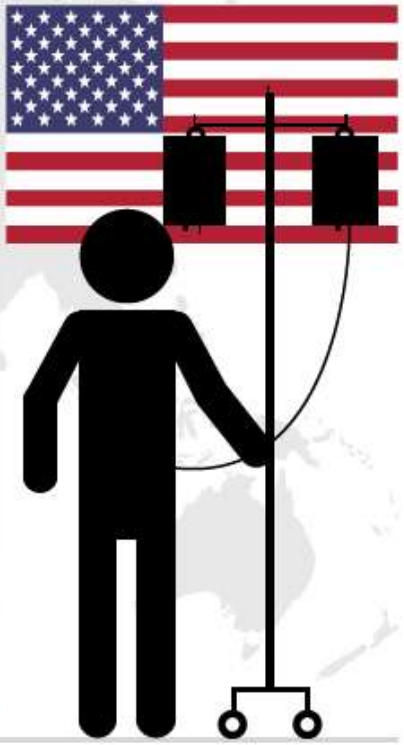
=17.9 percent of US GDP

# U.S. HEALTH CARE RANKS LAST AMONG WEALTHY COUNTRIES

A recent international study compared 11 nations on health care quality, access, efficiency, and equity, as well as indicators of healthy lives such as infant mortality.

## Overall Health Care Ranking



Source: K. Davis, K. Stremikis, D. Squires, and C. Schoen, *Mirror, Mirror on the Wall: How the Performance of the U.S. Health Care System Compares Internationally, 2014 Update*, The Commonwealth Fund, June 2014.

The COMMONWEALTH FUND

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- Evidence for cost-effectiveness

# What is economics?

$$
\begin{aligned}
&(m-2)^{i-1}\left\{(m-2)A_1\binom{n+i-1}{2i+1}+(A_2-A_1)\binom{n+i-1}{2i}\right\}\\
&\binom{n-1}{1}+\sum(m-2)^{i-1}\left\{(m-2)A_1\binom{n+i-1}{2i+1}+(A_2-A_1)\binom{n+i-1}{2i}\right\}\\
&(m-2)^{i-2}\left\{(m-2)A_1\binom{n+i-2}{2i-1}+(m-2)(A_2-A_1)\binom{n+i-1}{2i}\right\}\\
&(m-2)^{i-1}\left\{A_2\binom{n+i-2}{2i-1}+(A_2-A_1)\binom{n+i-2}{2i}\right\}\\
&(m-2)^{i-1}\left\{A_2\binom{n+i-3}{2i-1}+A_2\binom{n+i-3}{2i-2}+(A_2-A_1)\binom{n+i-2}{2i}\right\}\\
&\binom{-2}{0}+\sum(m-2)^{i-1}\left\{A_2(m-2)\binom{n+i-2}{2i}+A_2\binom{n+i-3}{2i-1}+(A_2-A_1)\binom{n+i-2}{2i}\right\}\\
&\binom{}{2}+\sum(m-2)^{i-1}\left\{(A_2(m+1)-2A_2-A_1)\binom{n+i-2}{2i}+A_2\binom{n+i-3}{2i-1}\right\}\\
&\binom{-2}{0}+\sum(m-2)^{i-1}\left\{(A_2(m+1)-2A_2-A_1)\binom{n+i-3}{2i}+\right.\\
&\qquad\left.+(A_2m+A_2-2A_2-A_1+A_2)\binom{n+i-3}{2i-1}\right\}
\end{aligned}
$$

# What is economics?

*"Economics is a science which studies human behaviour as a relationship between ends and scarce means which have alternative uses."*

*Lionel Robbins,LSE,1932*

= *the science of choice*

# Why do we need to choose?

- Resource are finite
- We choose how to allocate our resources to maximise happiness
- Sacrifice necessary – benefit foregone

- **SCARCITY**
- **UTILITY**
- **OPPORTUNITY COST**

# Opportunity cost

SCARSE RESOURCE

?

= UTILITY

= OPPORTUNITY COST

# Opportunity cost - healthcare

# Opportunity cost - healthcare

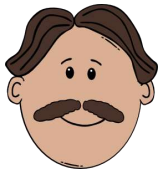
?

Opportunity cost not identifiable

Need a measurement of value to inform funding decisions

# Why should clinicians care?

- Duty to individual patient



- Duty to society?

Expertise?

- Reimbursement decisions are made at a higher level…
  - Guidelines / policy makers

Scottish Medicines Consortium
Providing advice about the status of all newly licensed medicines
www.scottishmedicines.org.uk
Delta House 50 West Nile Street Glasgow G1 2NP Tel 0141 225 6999 Chairman: Professor Jonathan G Fox
NHS SCOTLAND

NHS
National Institute for Health and Clinical Excellence

# Perspectives on healthcare expenditure

## Macro or aggregate level

- How much health care should be provided for a population?
- Can the organisation of health care become more efficient?
- Should health care be allowed to squeeze out other economic sectors?

## Micro or individual level

- How should new (and old) interventions be tested and evaluated?
- How can we compare competing interventions?
- Who should live and who should die?

Tools of the trade from health economics

# Opportunity cost!

=

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# Opportunity cost!

=

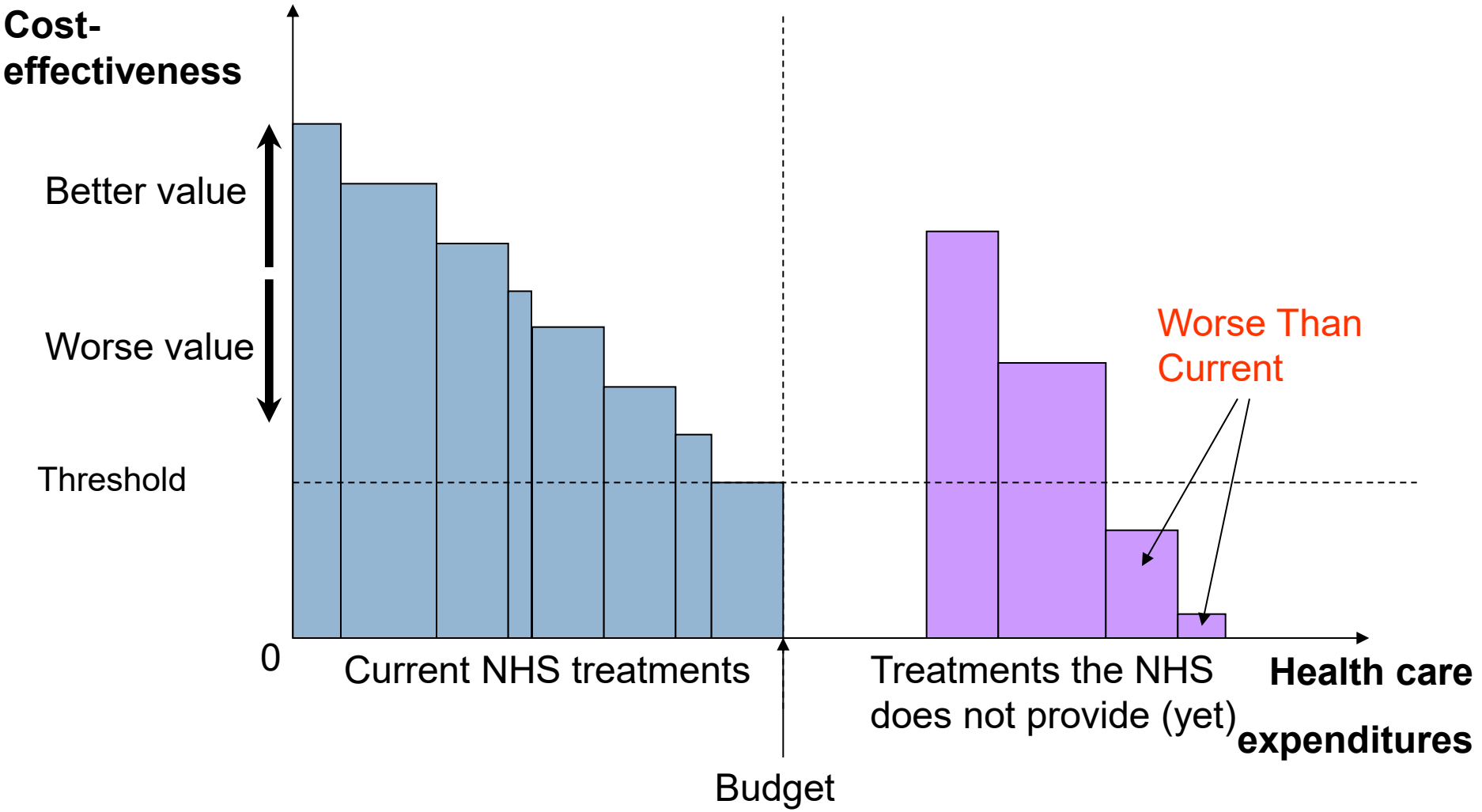
# Acceptable opportunity cost?

- Health economics
  - Measuring opportunity cost
  - Valuing healthcare
  - Cost-effectiveness analysis

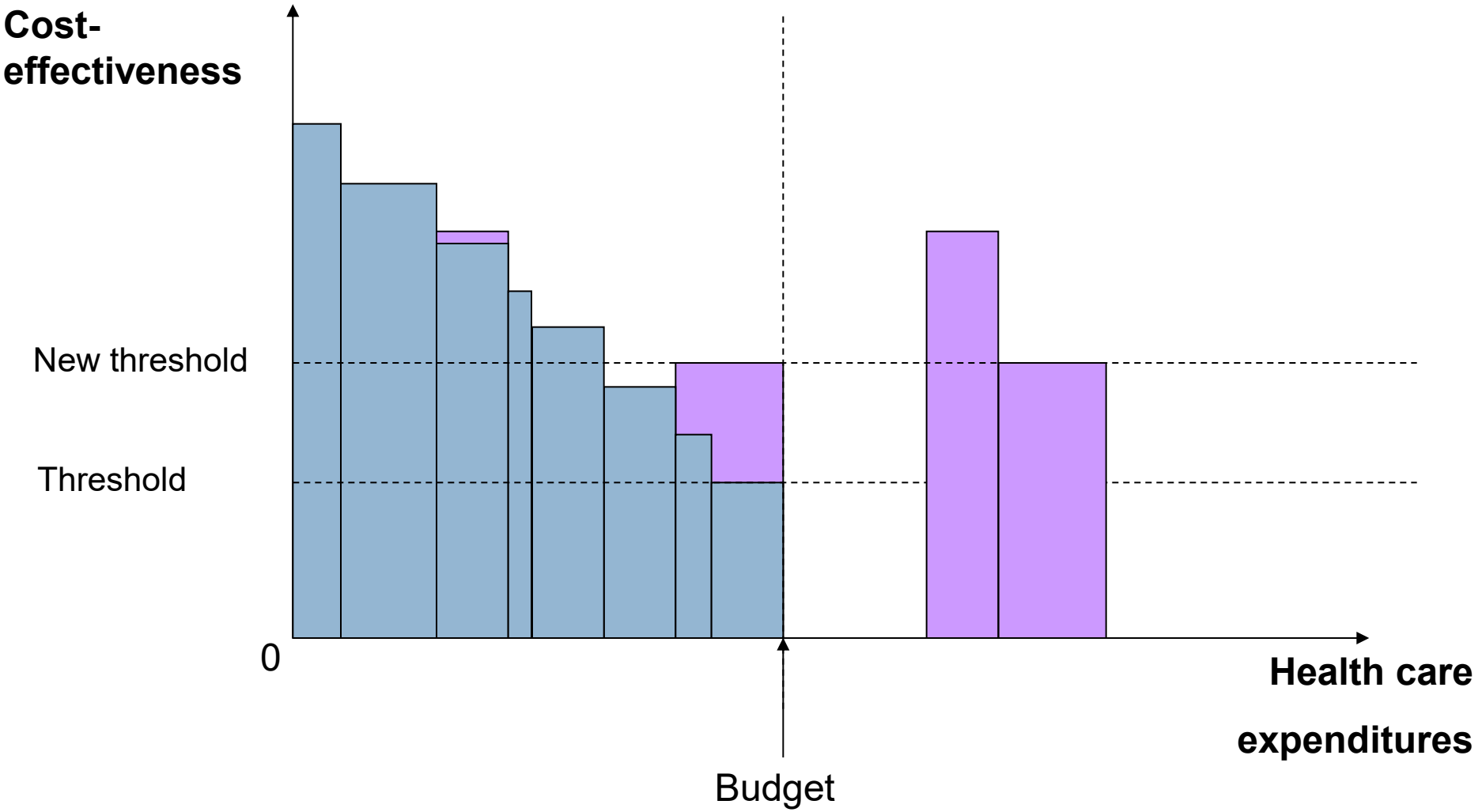
  - = cost-effectiveness threshold
  - (=willingness to pay threshold)

  - Health economists don't set the threshold!

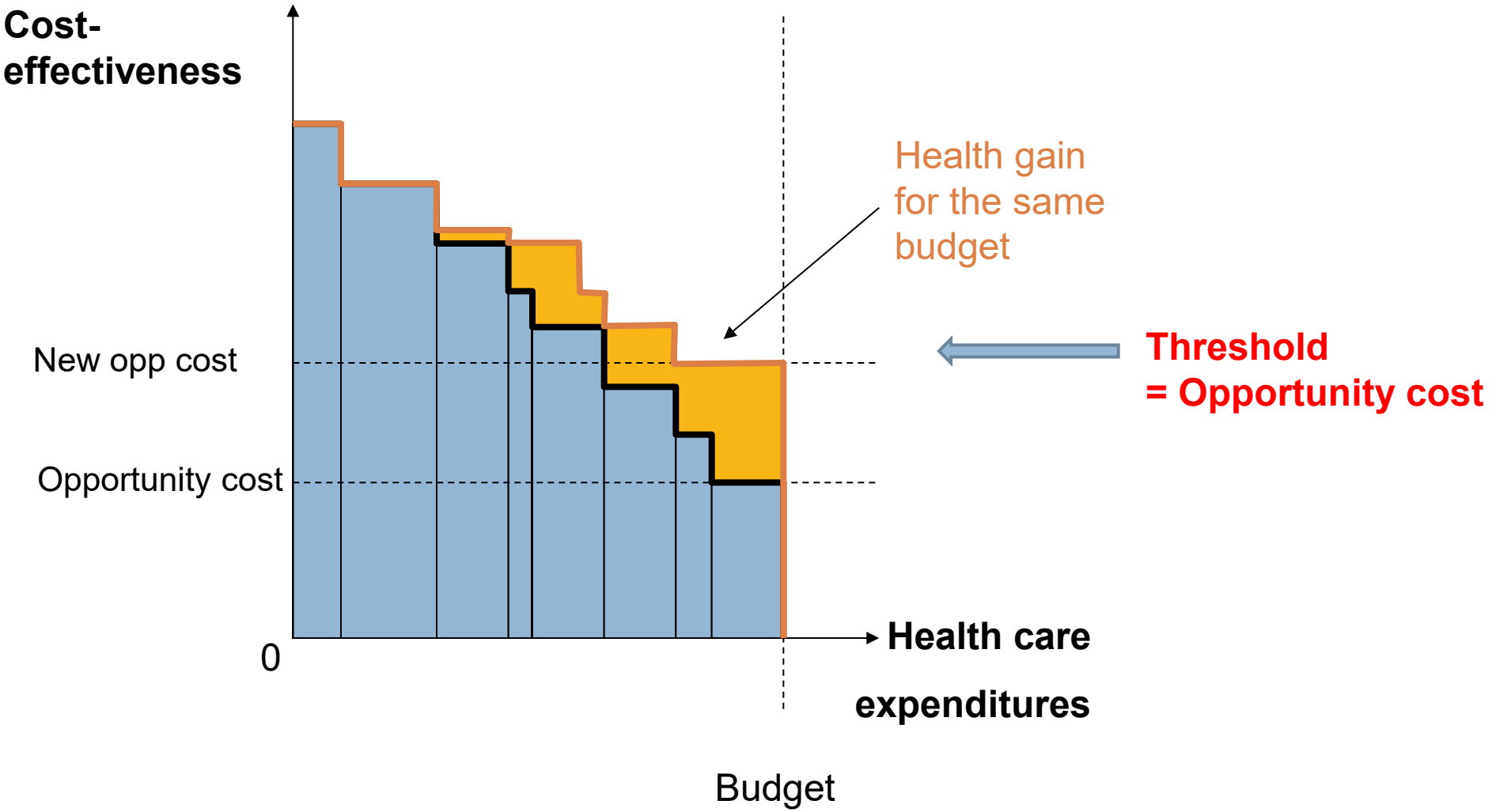
# Opportunity cost and cost effectiveness analysis



# Opportunity cost and cost effectiveness analysis



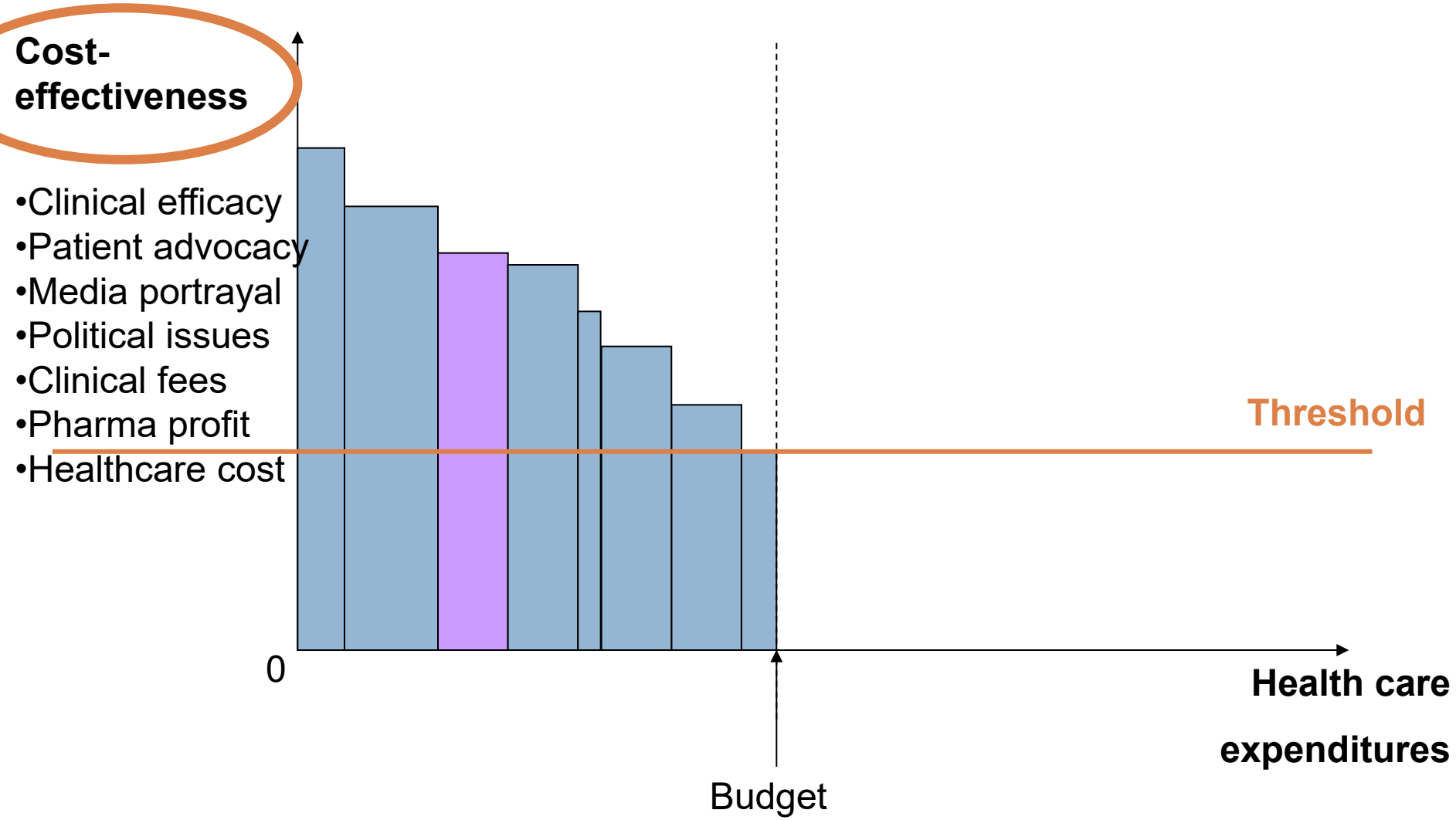
# Opportunity cost and cost effectiveness analysis



# The cost effectiveness threshold

- The cost effectiveness threshold is the maximum amount the health service will pay per unit of health gained.
  - It represents the maximum *opportunity cost* consistent with improving population health by introducing a new intervention.

# Opportunity cost and cost effectiveness analysis



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# Cost-effectiveness analysis

- Budget = £100,000
- Option 1
  - New asthma inhaler = £50
  - Can treat 2,000 children
  - Will prevent 10 hospital admissions
  - Cost per admission prevented = £10,000
- Option 2
  - New antihistamine medication = £100 per course
  - Can treat 1,000 children
  - Will prevent 20 hospital admissions
  - Cost per admission prevented = £5,000

# Cost-effectiveness analysis

- Budget = £100,000
- Option 2
  - New antihistamine medication = £100 per course
  - Can treat 1,000 children
  - Will prevent 20 hospital admissions
  - Cost per admission prevented = £5,000
- Option 3
  - New pain killer = £10 per course
  - Can treat 10,000 back pain sufferers
  - Will prevent 5,000 days stuck on a sofa
  - Cost per sofa-day prevented = £20

# Measuring health

- Length of life (= Life years)
- Quality of life (QoL weight [utility])
  - 1 = full health
  - 0 = death

# QALY calculation

QALYs = LYs x QoL weight

e.g.

10 LYs

QoL weight = 0.8

10 x 0.8 = 8 QALYs

# Measurement of cost-effectiveness

- **ICER** (Incremental Cost-effectiveness Ratio)
  - new intervention vs standard care

Additional costs : Additional health benefit

$$\text{ICER} = \frac{(C_1 - C_0)}{(E_1 - E_0)}$$

# Some ICERs

- **Cost per QALY less than £3,000**
  - Neurosurgery for benign brain tumours
  - Laser treatment for diabetic retinopathy
  - Folic acid fortification of cereal grain products
- **Cost per QALY £3,000 to £30,000**
  - CABG for left main vessel disease
  - Neonatal ITU for very low birth weight
  - Haemodialysis
- **Cost per QALY > £30,000**
  - Anticholinesterases in mild AD
  - New drugs for Renal Cell Cancer
- **More harm than good**
  - Antiarrhythmics after MI
  - PSA Screening

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# Who are the decision makers?

- Scotland
  - Regional Health Boards (14)
  - Scottish Government
  - Healthcare Improvement Scotland

# Scottish system

- Medicines and Healthcare Products Regulatory Agency (MHRA)
- NHS Scotland
  - Health Care Improvement Scotland (HIS)
    - Scottish Medicines Committee (licensed indications)
      - New Drugs Committee
      - Appraisal Committee
      - PACE
    - National Cancer Medicines Advisory Group (NCMAG)
    - Scottish Health Technologies Group (SHTG)
    - Scottish Intercollegiate Guidelines Network (SIGN)

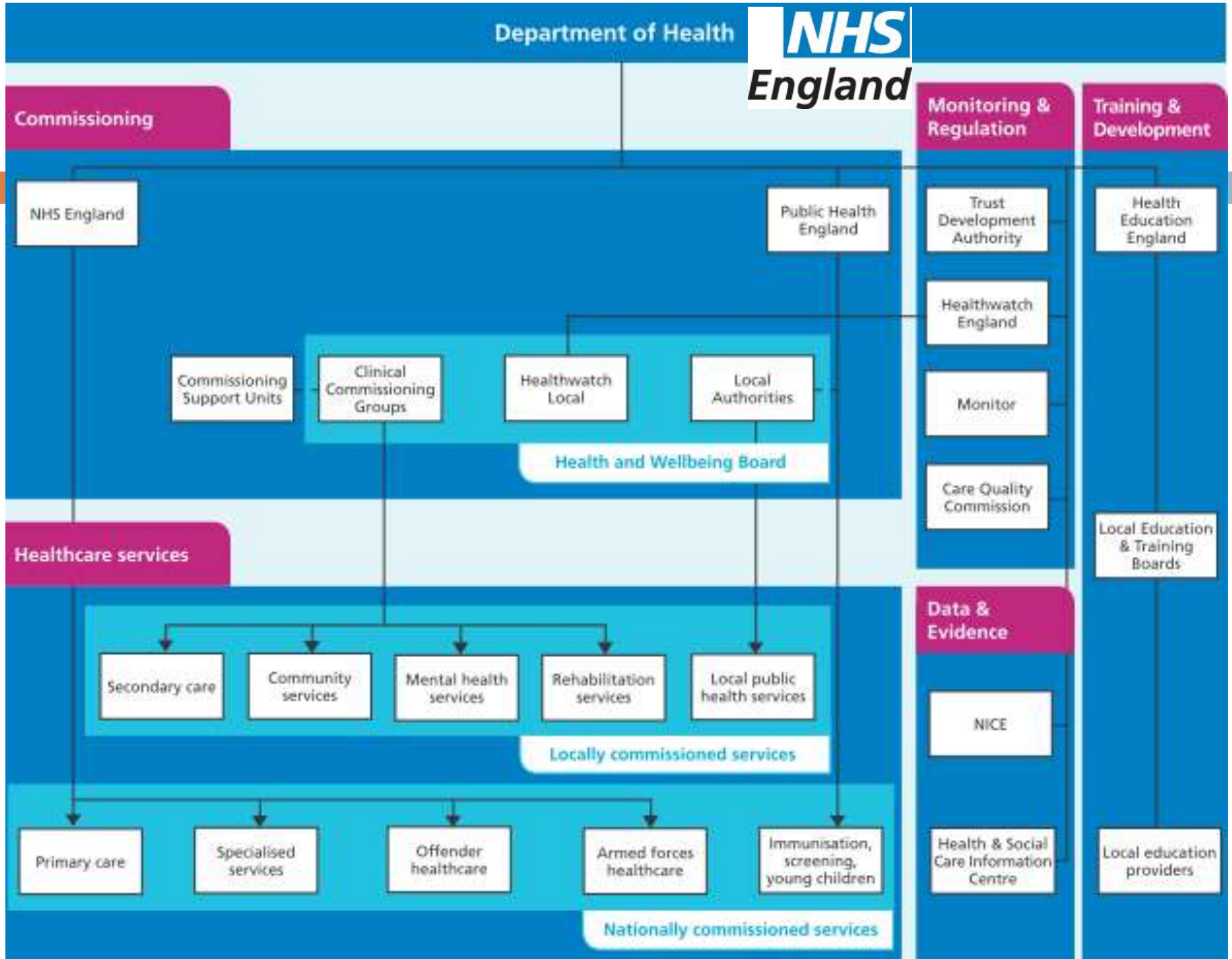
Scottish Medicines Consortium

Scottish Health Technologies Group

SIGN

# Scottish system

- Health Board (NHS Lothian and SCAN)
  - Joint Regional Formulary (via FAF)
  - Area Drugs and Therapeutics Committee (ADTC)
  - Cancer Medicines Management Committee MMC
  - Peer Approved Clinical System (PACS, ex-IPTR)
  - Early Access to Medicines Schemes (EAMS)


Department of Health
NHS England
Commissioning
NHS England
Public Health England
Commissioning Support Units
Clinical Commissioning Groups
Healthwatch Local
Local Authorities
Health and Wellbeing Board
Healthcare services
Secondary care
Community services
Mental health services
Rehabilitation services
Local public health services
Locally commissioned services
Primary care
Specialised services
Offender healthcare
Armed forces healthcare
Immunisation, screening, young children
Nationally commissioned services
Monitoring & Regulation
Trust Development Authority
Healthwatch England
Monitor
Care Quality Commission
Data & Evidence
NICE
Health & Social Care Information Centre
Training & Development
Health Education England
Local Education & Training Boards
Local education providers

# NICE National Institute for Health and Care Excellence

- Started in 1999
- Objective to end the postcode lottery
- Reduce inequality (inequity?)

# NICE Technology appraisal

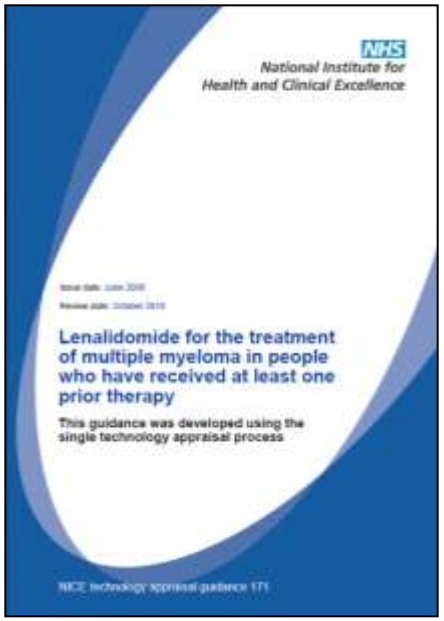
• Provide guidance on selected health technologies

- Pharmaceuticals
- Medical devices

• Considers the evidence on health benefits and costs

- Impact on quality of life
- Effects on mortality
- Associated costs, particularly on costs to the NHS and personal social services

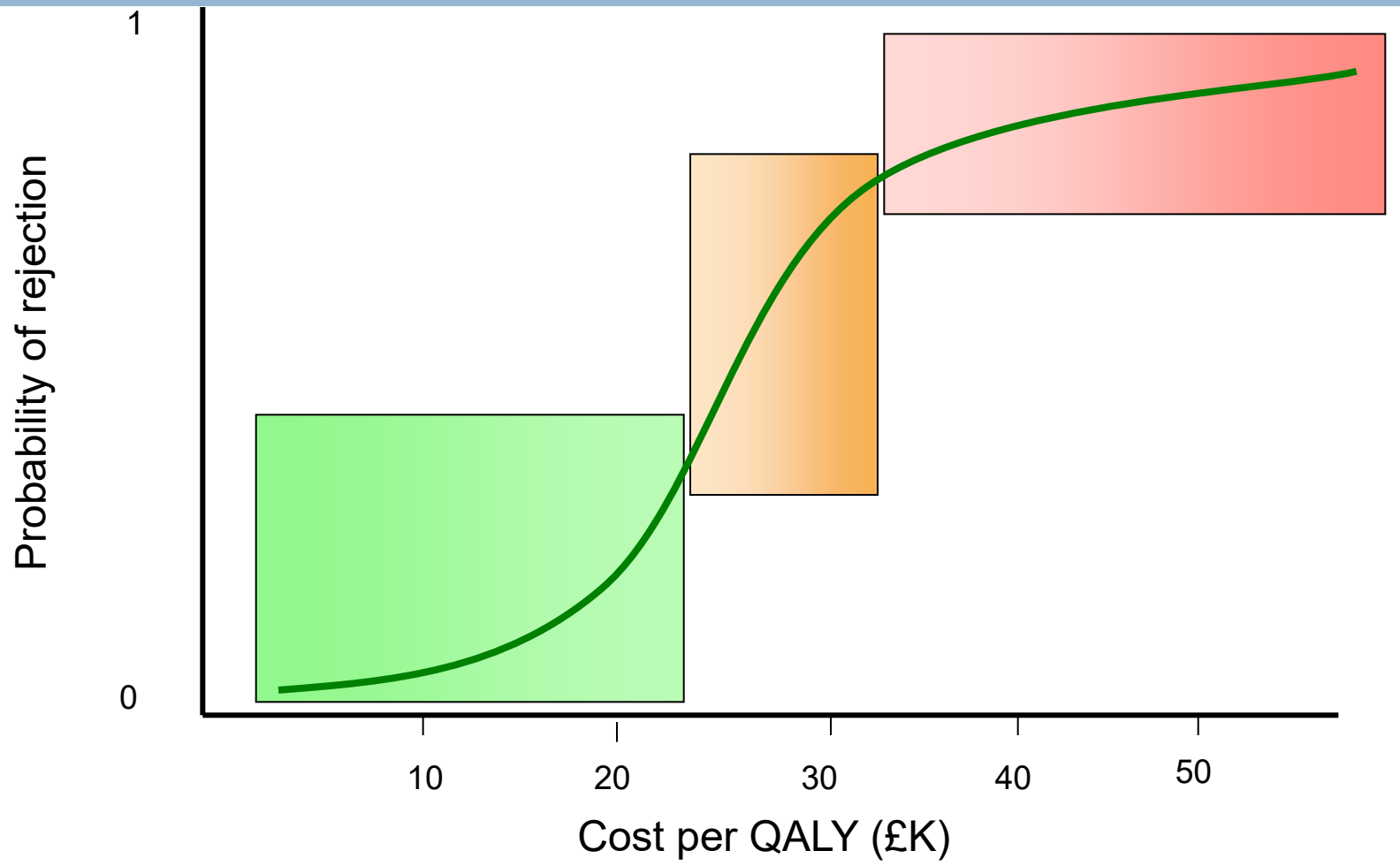
• Department of Health direction to NHS to make funding and resources available within 3 months



# NICE Technology Appraisal

- Deliberative value assessment
  - expert **clinical** opinion
  - **public/patient** opinion
  - expert **statistical** opinion
  - expert health **economic** opinion
  - **industry** / **economy** considerations
  - safety
  - efficacy
  - cost-effectiveness

# Seeking the threshold

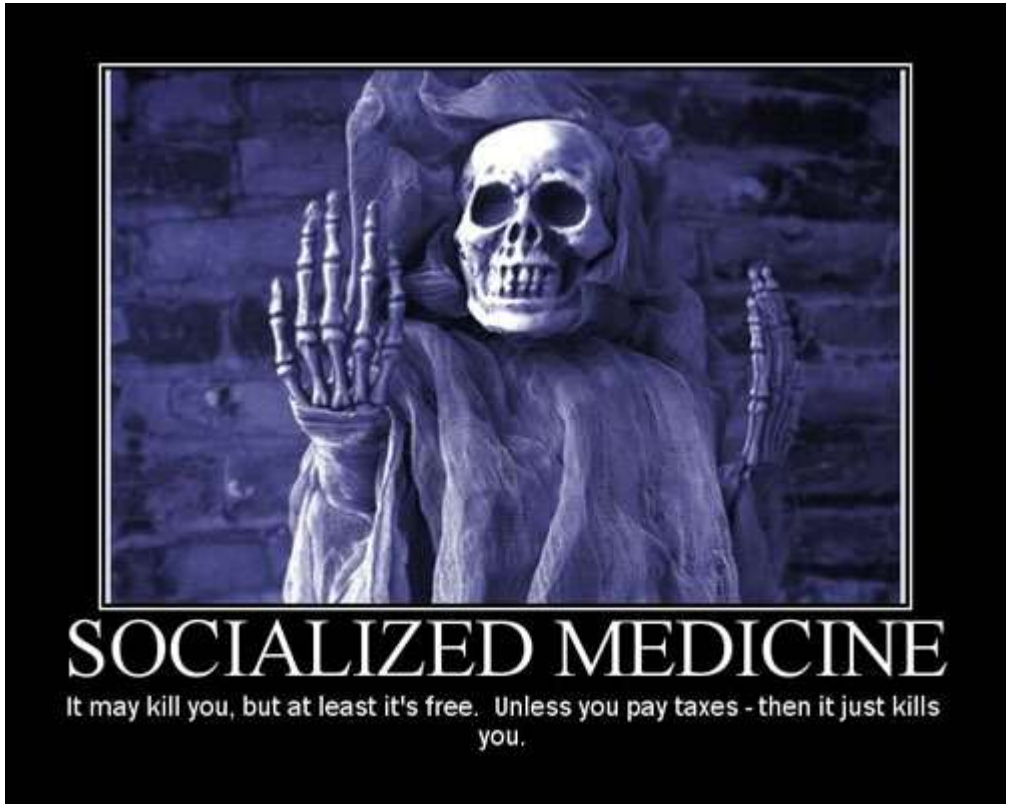


# Global demand for NICE's expertise

# NICE and politics

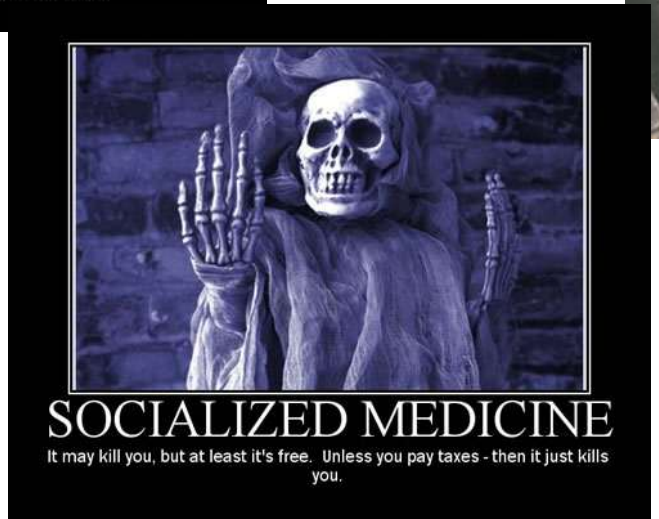
NHS

National Institute for
Health and Clinical Excellence



NHS

National Institute for Health and Clinical Excellence



# Test case 2006

- New expensive drugs for advanced kidney cancer
  - Sunitinib
  - Bevacizumab
  - Everolimus
- Control cancer for an extra 6 months
- ICER ~ £50,000 per QALY

→ REJECT

# Test case 2006

**Mother of two Nikki Phelps fought the NHS decision to deny her the life prolonging drug sunitinib**

# Rule changes

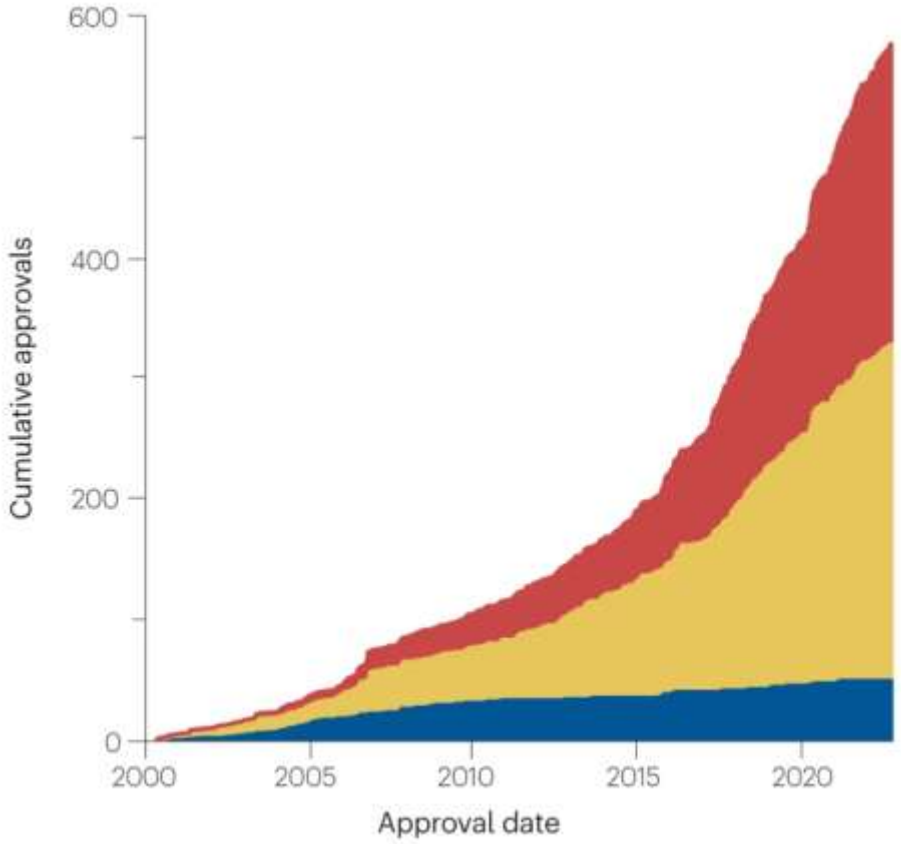
- Special situations
  - End of life
  - Burden of disease
  - Small patient population (orphan drugs)
  - Unmet need
  - Particularly innovative technology

Kidney cancer drugs approved

# 2010 – The Cancer Drugs Fund

- £200 million per year until 2014
- In 2012 – overspent £280m
- By 2015 – annual budget £340m
- 2015 – 25 drugs dropped from fund
- 2016 – CDF 2.0  Access with Evidence Development

# PROLIFERATION OF NEW TECHNOLOGIES




## FDA DRUG APPROVALS

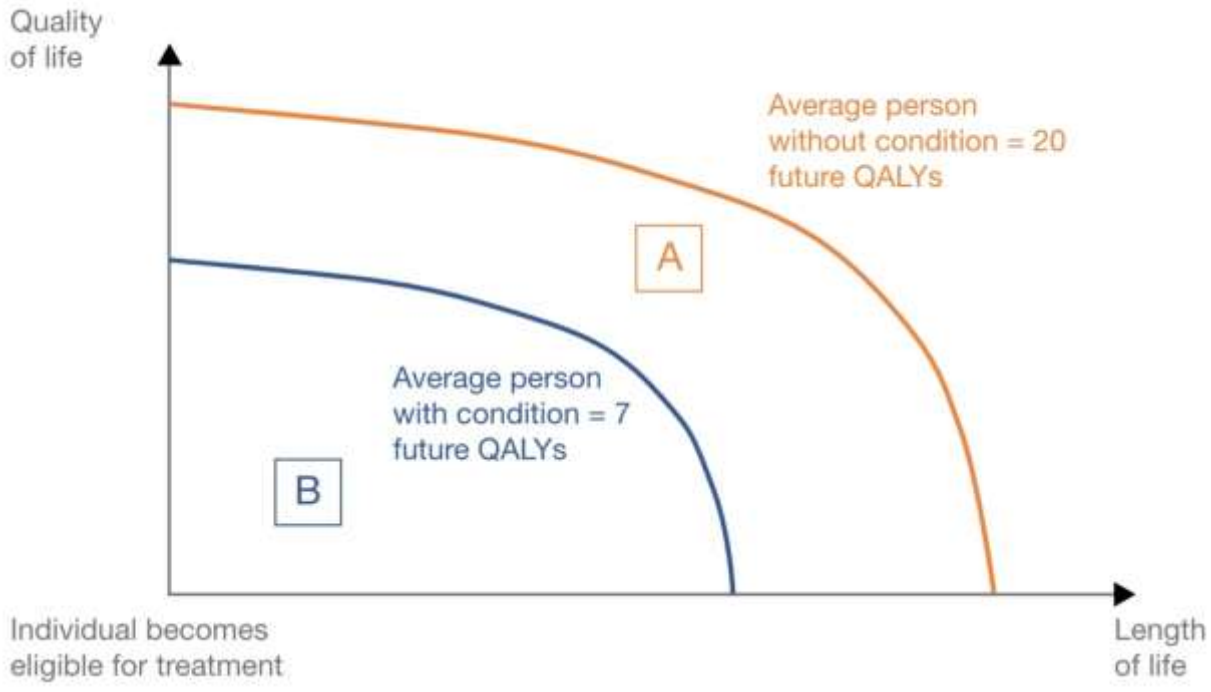
Cytotoxic drugs

Targeted drugs

Targeted biologics

Scott, E.C., Baines, A.C., Gong, Y., Moore Jr, R., Pamuk, G.E., Saber, H., Subedee, A., Thompson, M.D., Xiao, W., Pazdur, R. and Rao, V.A., 2023. Trends in the approval of cancer therapies by the FDA in the twenty-first century. *Nature Reviews Drug Discovery*, *22*(8), pp.625-640.

# NICE Severity Weight




| QALY weight | Proportional QALY shortfall | Absolute QALY shortfall |
|---|---|---|
| 1 | Less than 0.85 | Less than 12 |
| 1.2 | 0.85 to 0.95 | 12 to 18 |
| 1.7 | At least 0.95 | At least 18 |

Abbreviations: QALY, quality-adjusted life year.

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# Evidence from clinical trials

Getting the ICER from the evidence

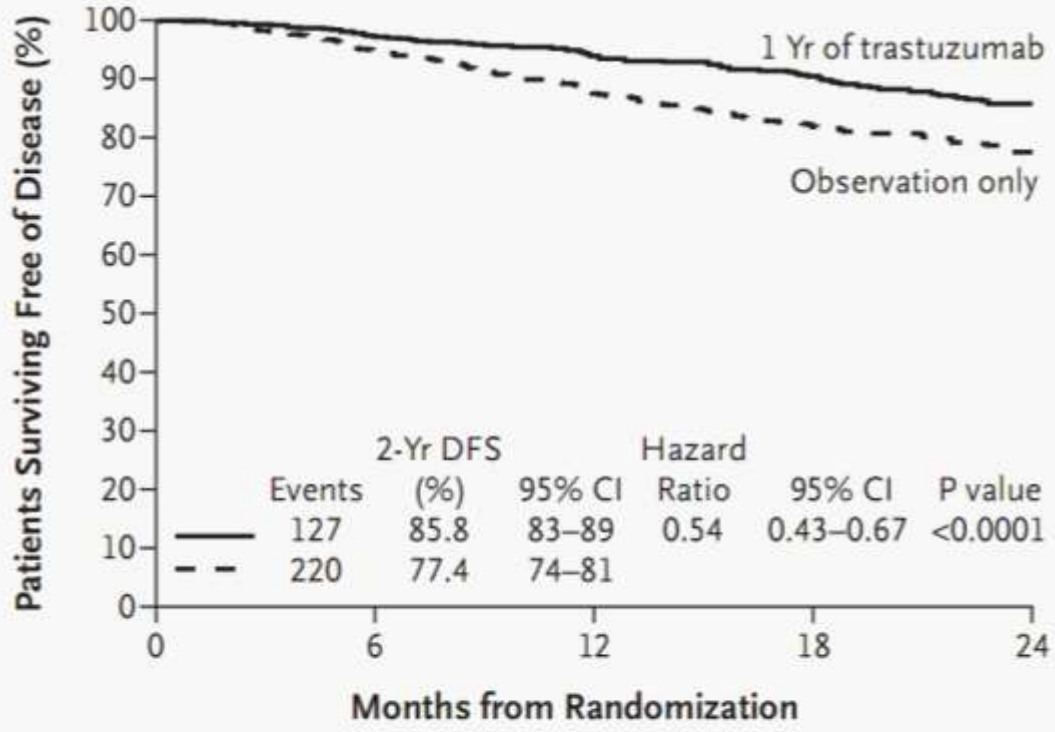
# Example: Trastuzumab for early breast cancer

- Registration trial (HERA) reported in 2005

Piccart-Gebhart. NEJM 2005, 353:1659-1672

# Efficacy

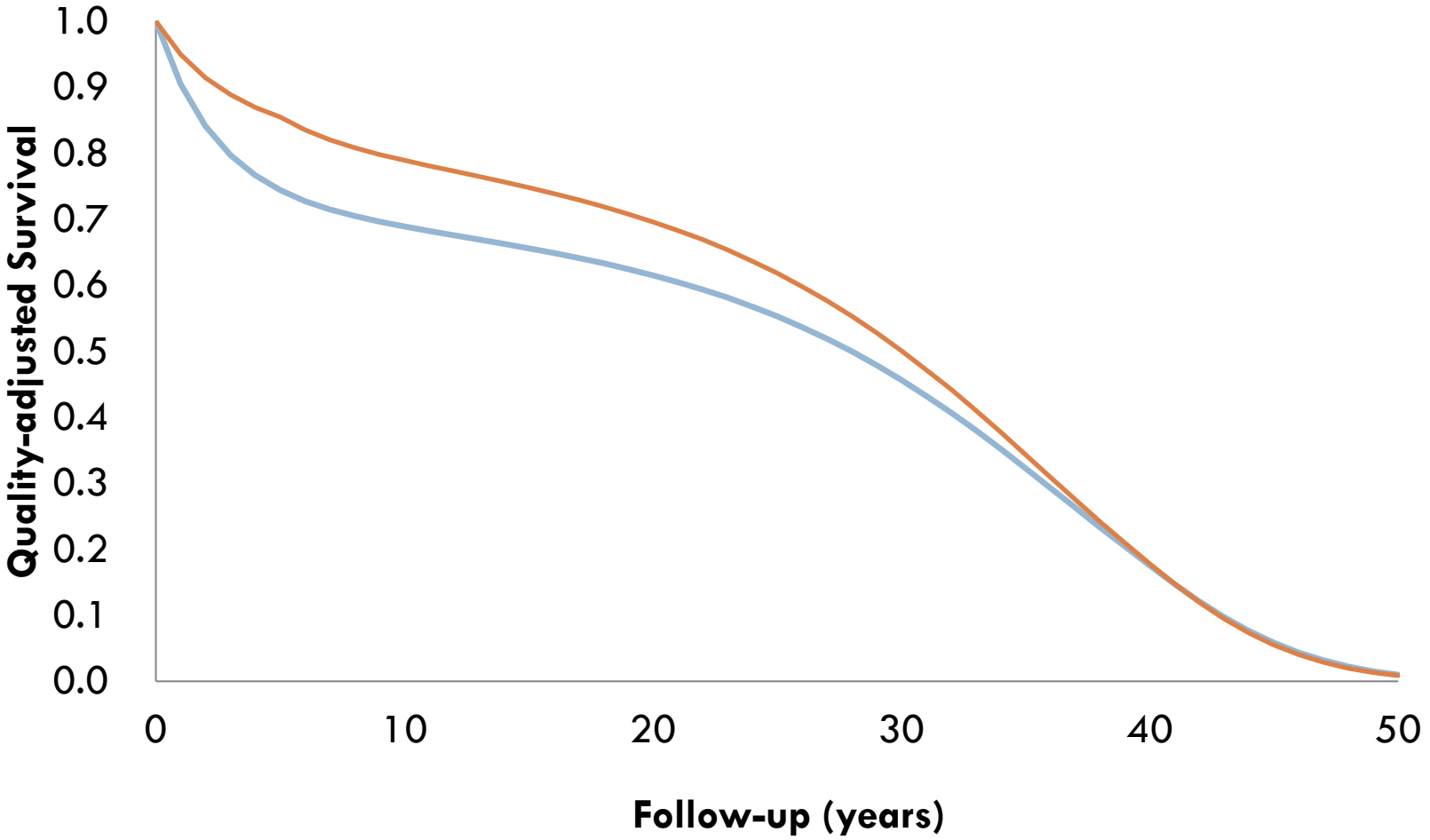
Primary endpoint = disease free survival



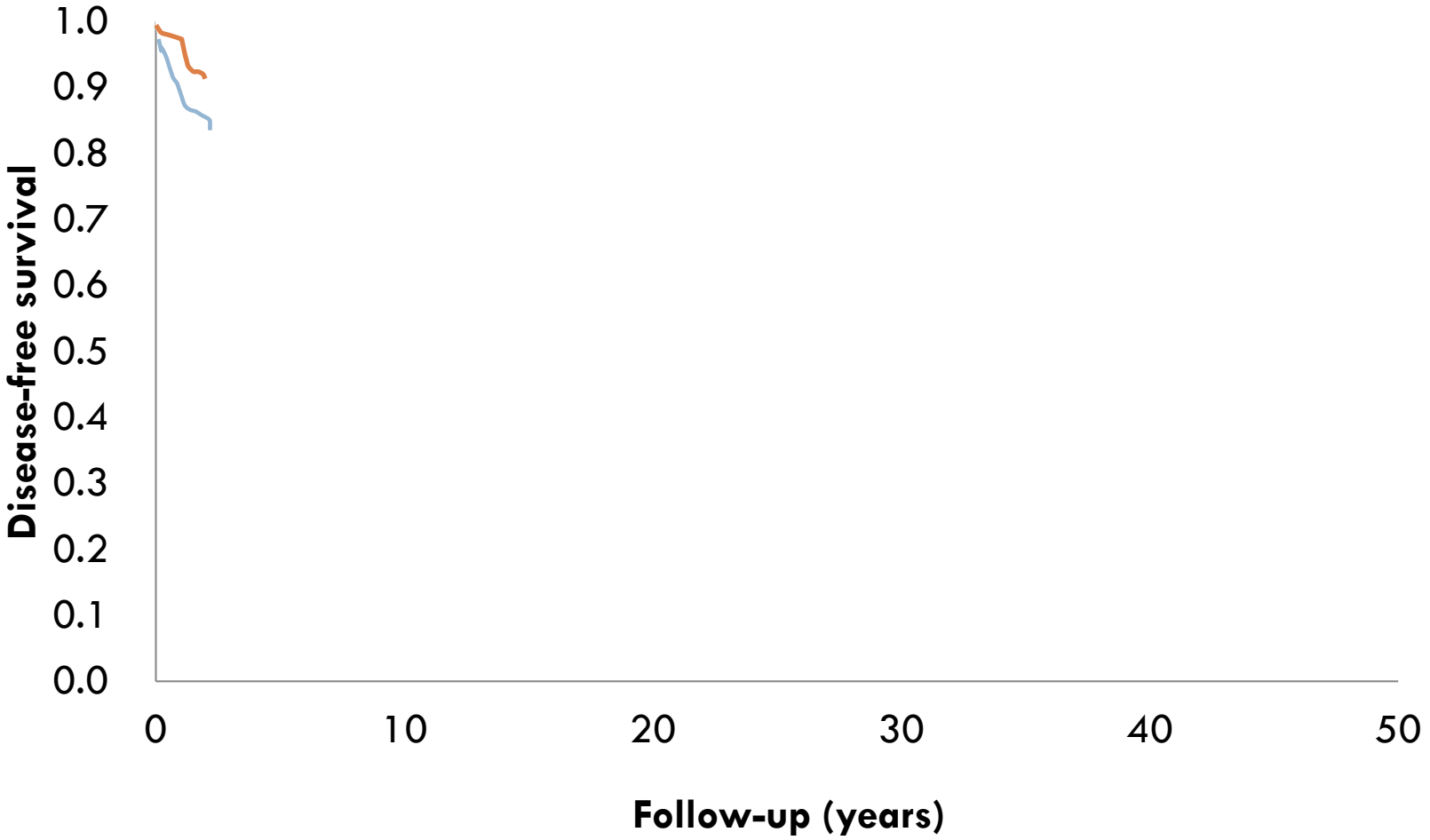

| | Events | 2-Yr DFS (%) | 95% CI | Hazard Ratio | 95% CI | P value |
|---|---|---|---|---|---|---|
| 1 Yr of trastuzumab | 127 | 85.8 | 83–89 | 0.54 | 0.43–0.67 | <0.0001 |
| Observation only | 220 | 77.4 | 74–81 | | | |

| No. at Risk | | | | | |
|---|---|---|---|---|---|
| 1 Yr of trastuzumab | 1694 | 1172 | 885 | 532 | 268 |
| Observation only | 1693 | 1108 | 767 | 445 | 224 |

# Cost-effectiveness?



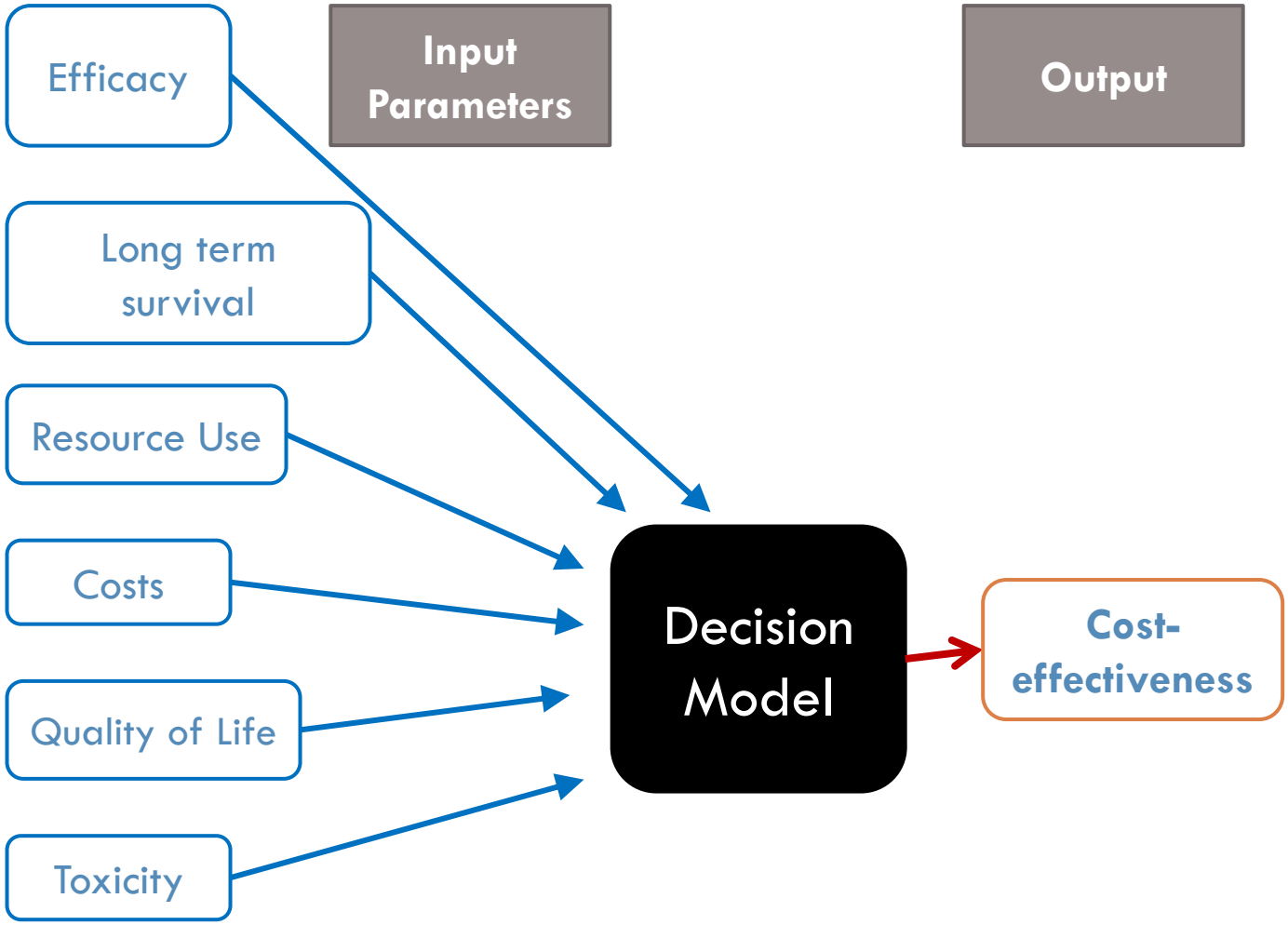
# Disease-free survival



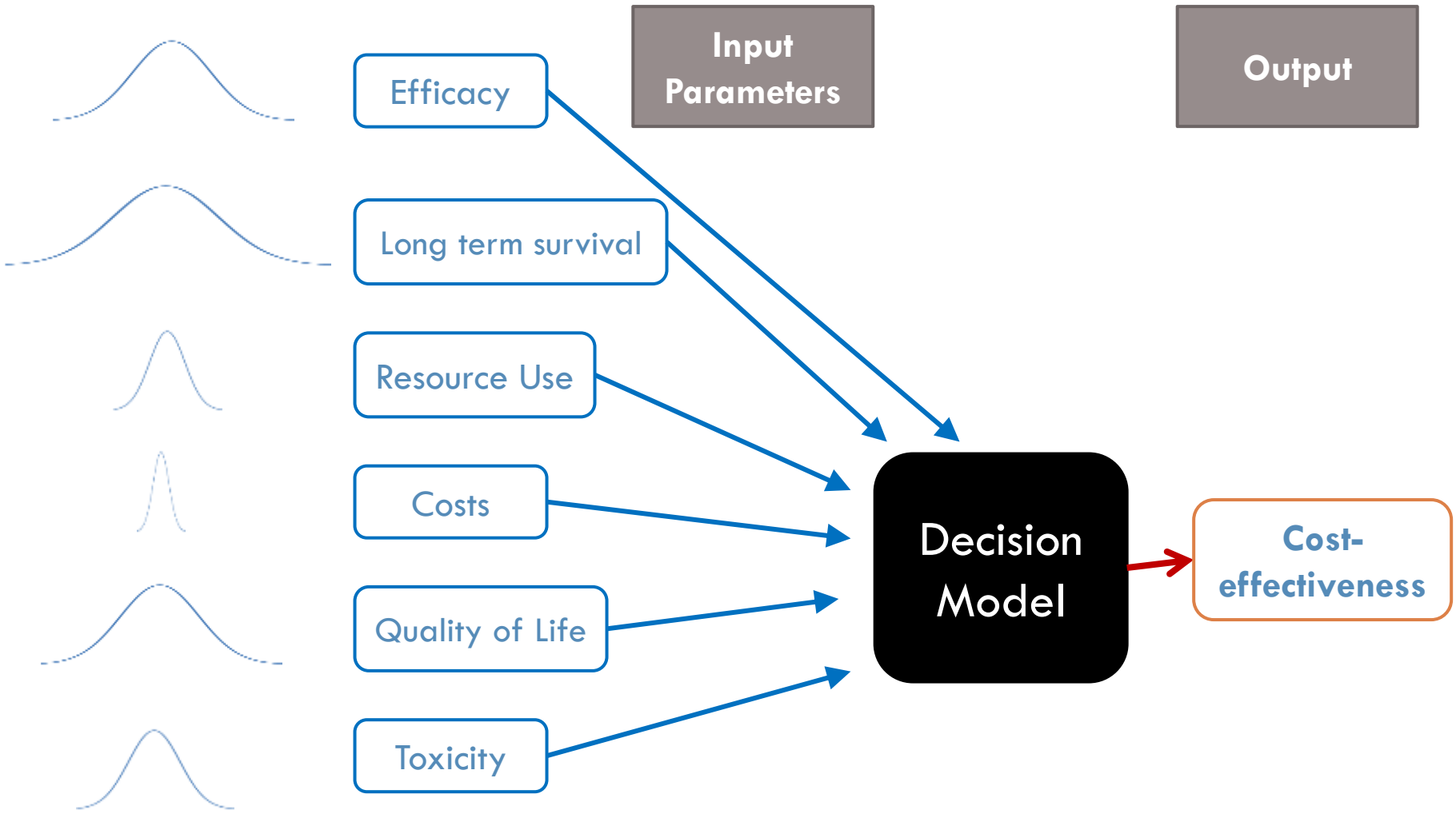
# 2 year DFS → lifetime QALY

1. Extrapolate DFS over 50 years
2. → Overall survival (control)
3. → Overall survival (treatment)
4. → QALYs
5. **Costs**
   - **Short term costs**
   - **Long term costs**

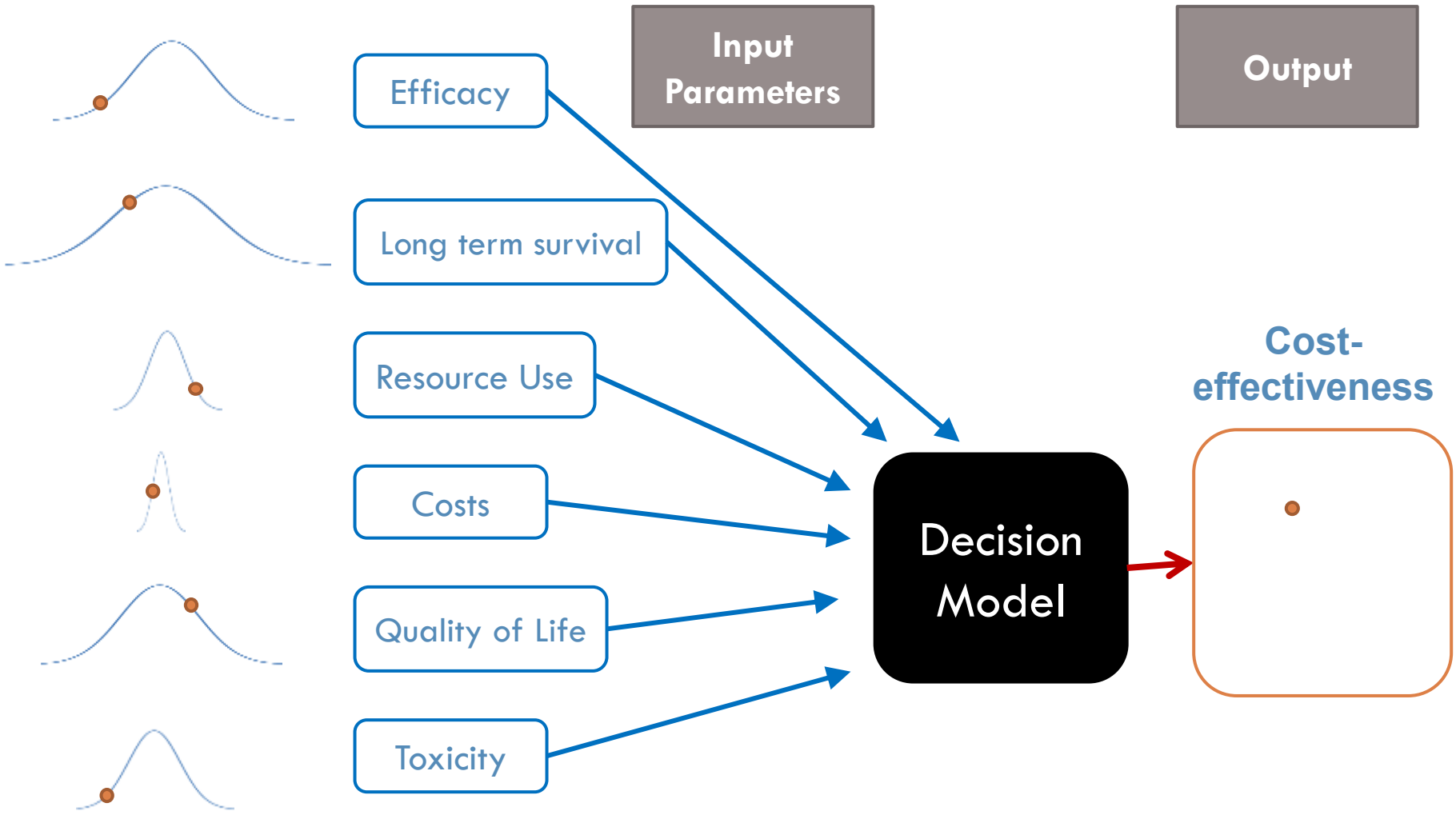
# Model


Efficacy
Input Parameters
Output
Long term survival
Resource Use
Costs
Quality of Life
Toxicity
Decision Model
Cost-effectiveness

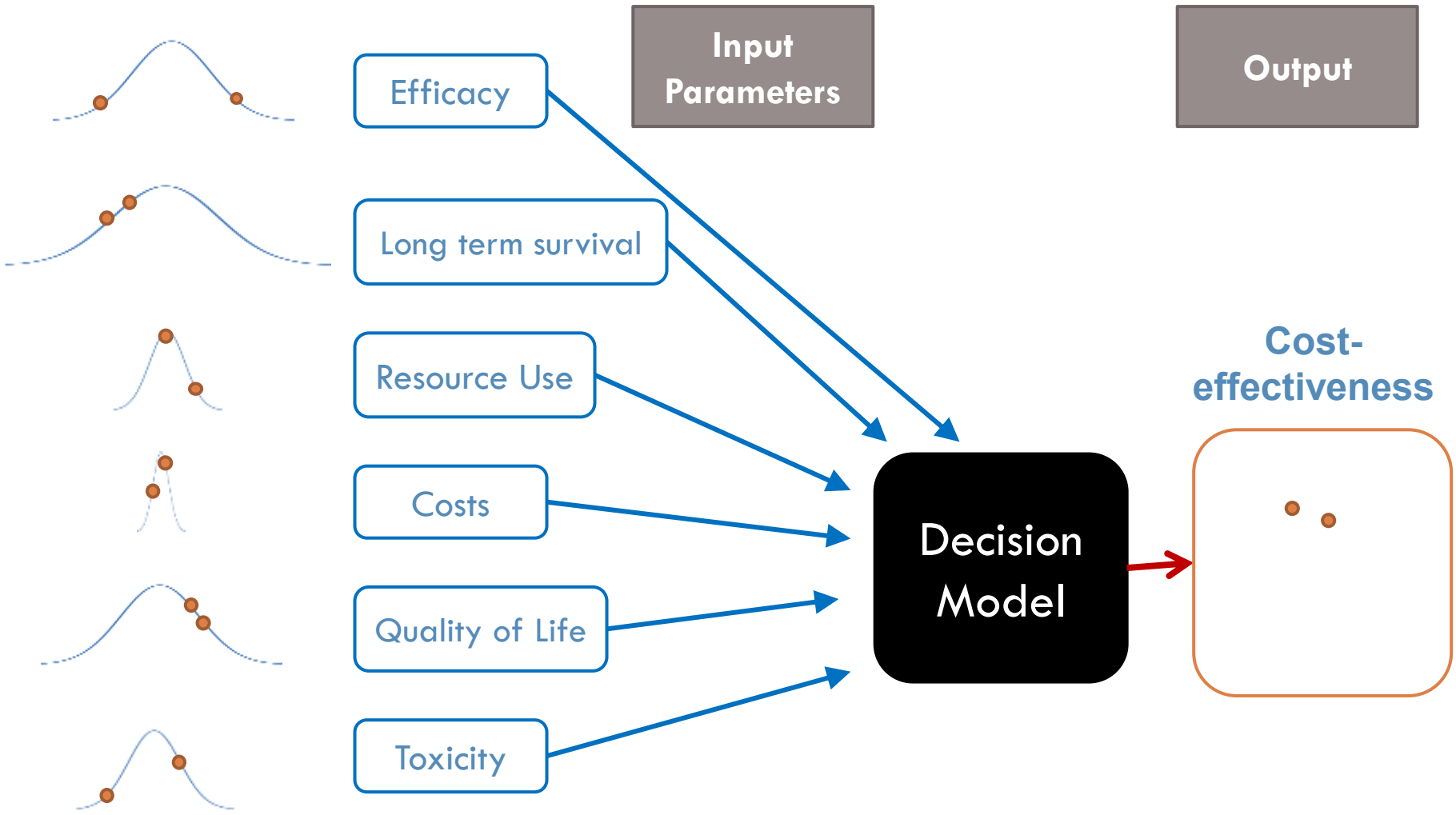
# Uncertainty



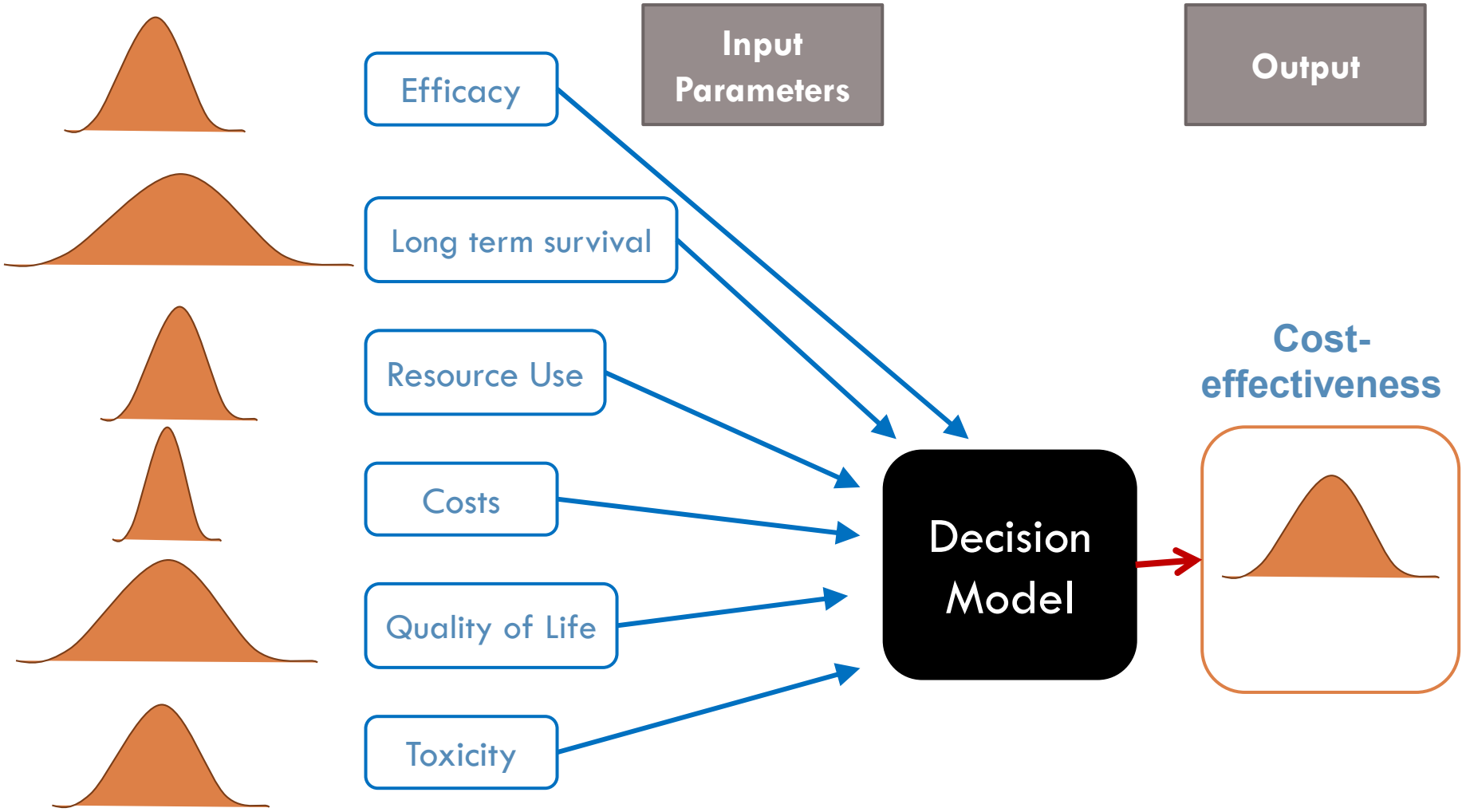
# Monte Carlo Simulation



# Monte Carlo Simulation

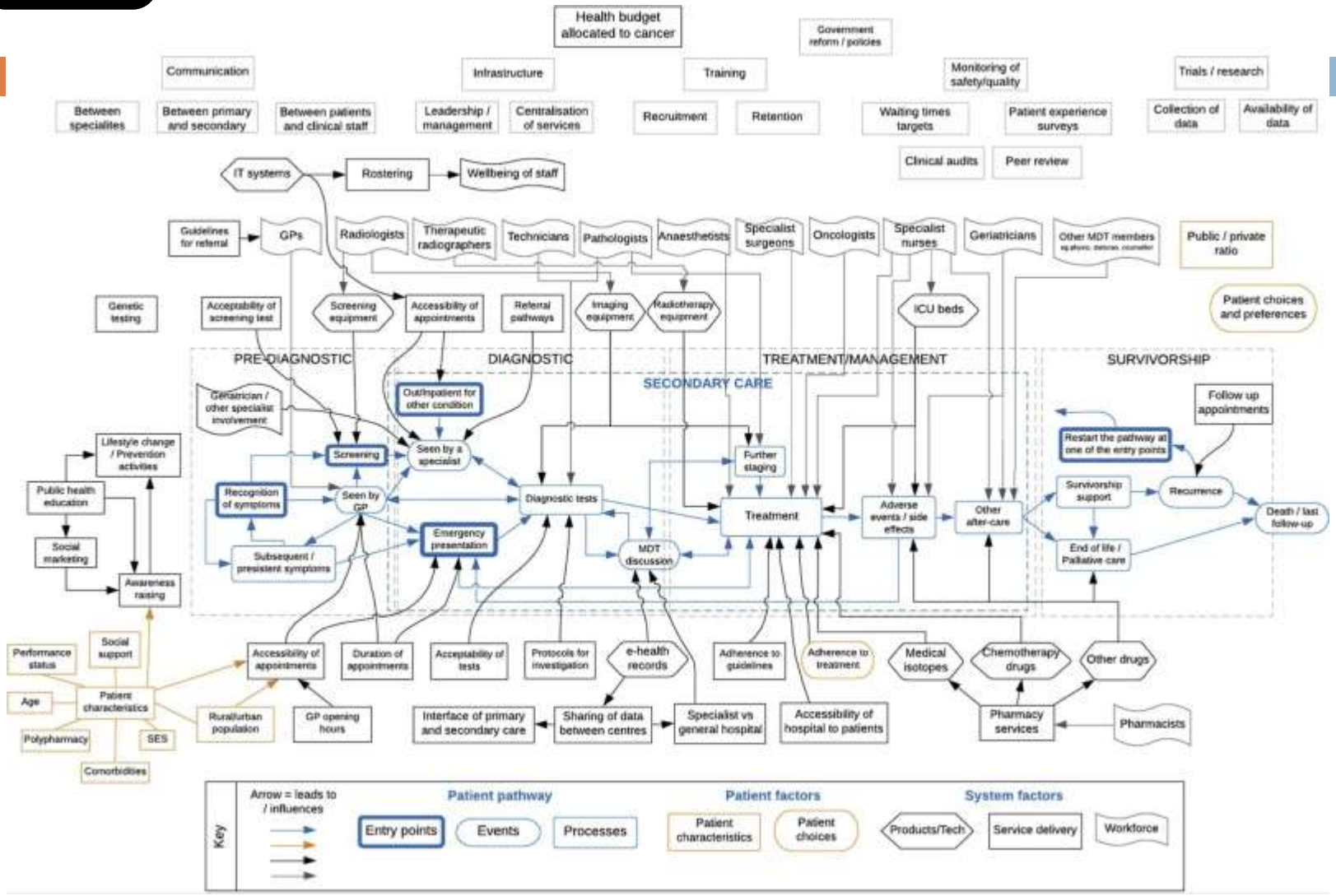


# Monte Carlo Simulation



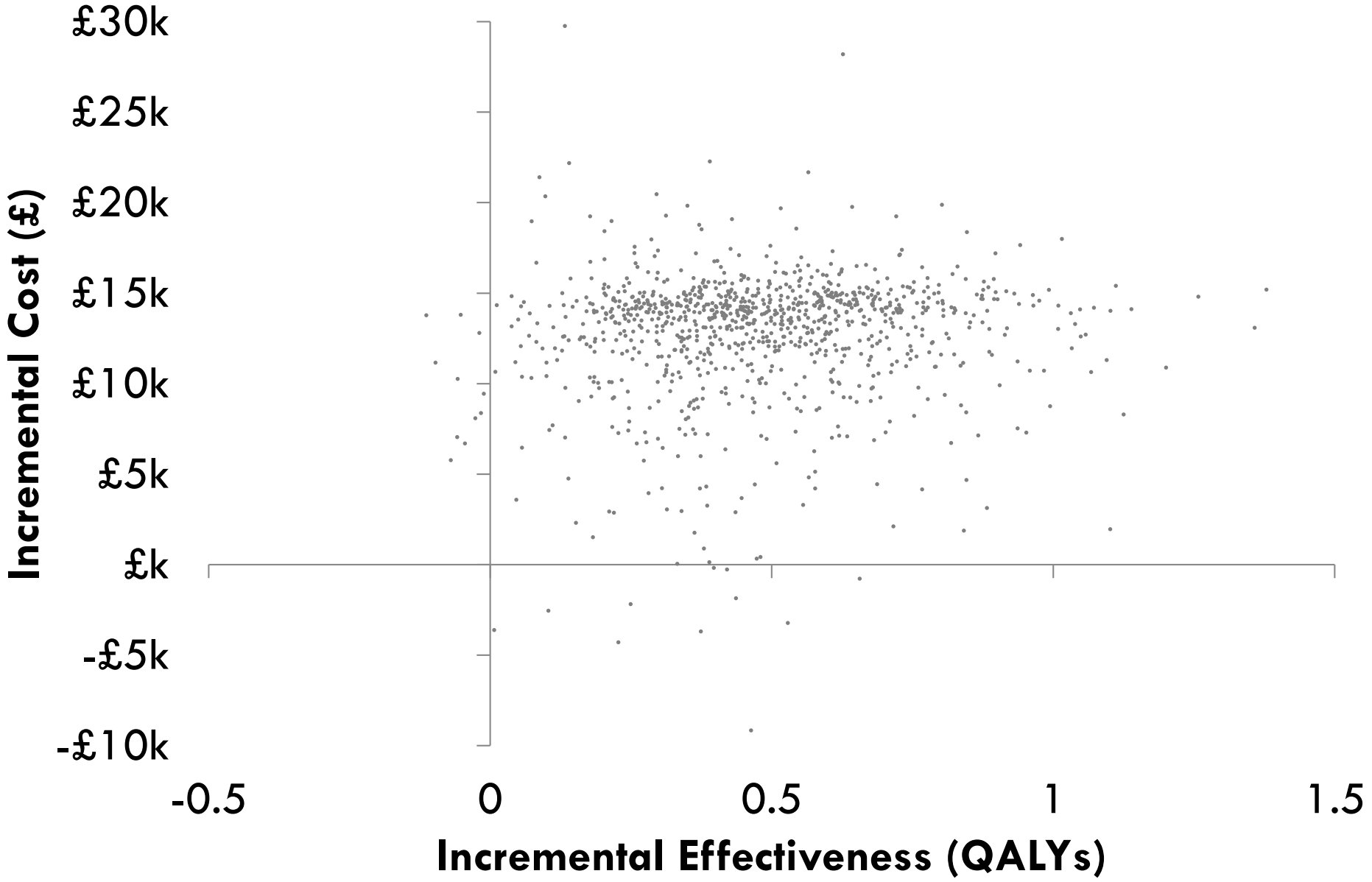
Decision Model

# = Clinical care pathway

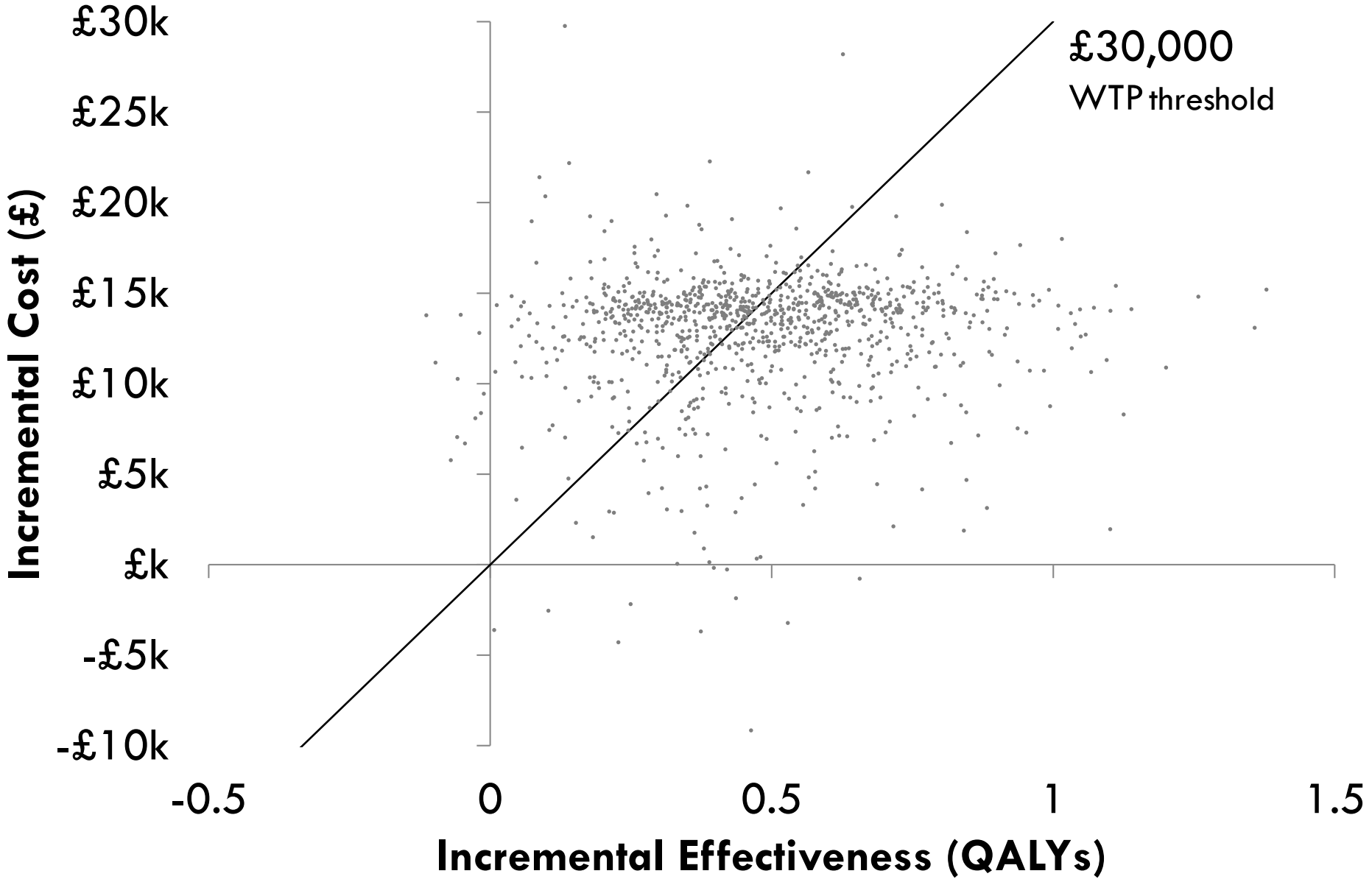



Morris, M., et al. 2020. *Journal of Cancer Policy*, *25*, p.100233.

# Uncertainty around the Incremental cost-effectiveness ratio



# Uncertainty around the Incremental cost-effectiveness ratio



# Is Trastuzumab Cost-effective?

- 2006 estimate accepted by NICE:
  - **ICER = £18,500** per QALY (threshold £20 – 30k)
  - 90% CI £12,250 - >£50,000

- 2011 update* :
  - **ICER = £25,803** per QALY
  - 90% CI £15,000 - £59,000

*Hall et al. Pharmacoeconomics 2011 29(5);415-432

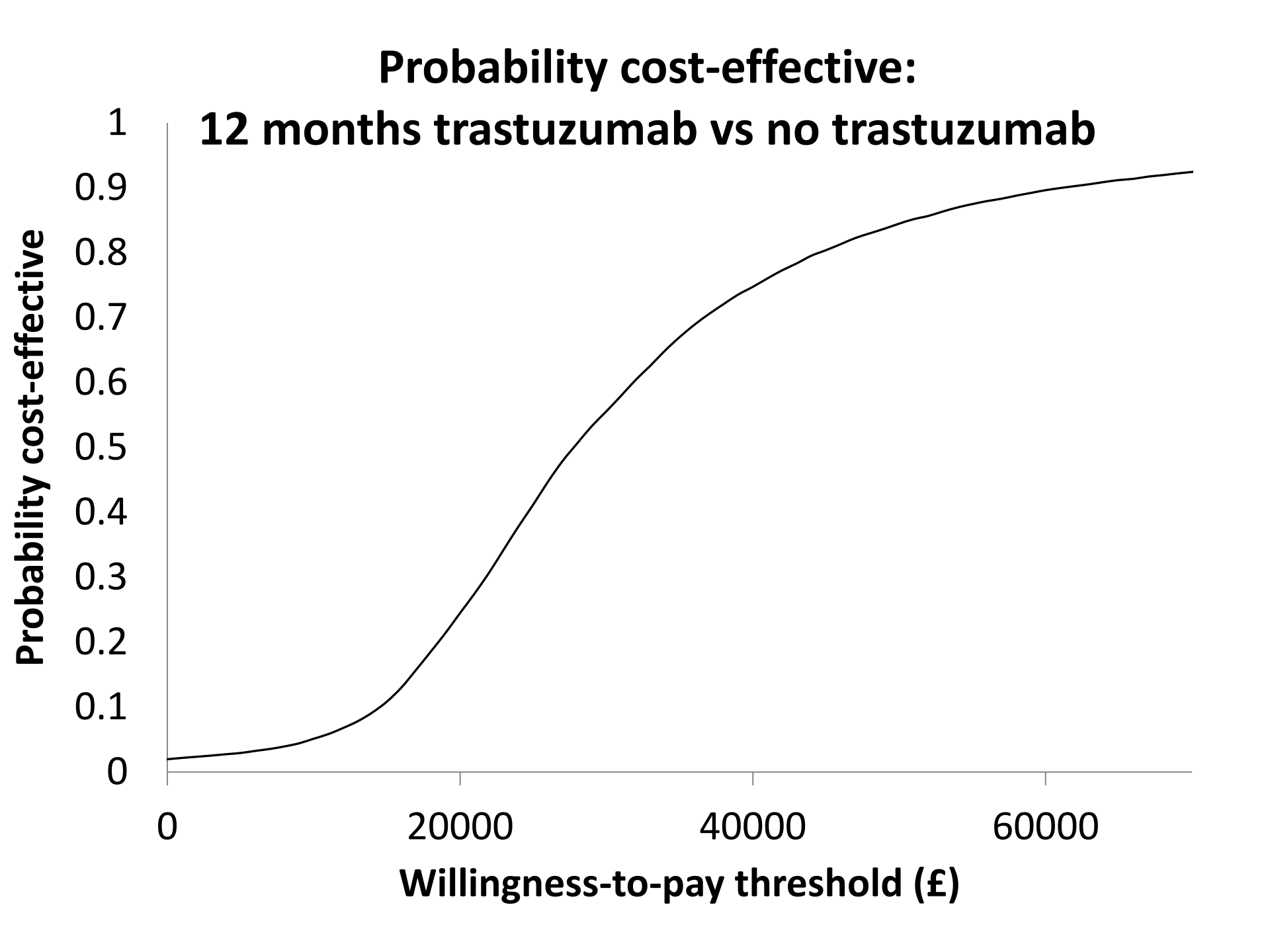
# Irrelevance of inference

- Probability cost-effective = 56%

  (threshold £30,000 per QALY)

- Is this certain enough?
  - Probability no trastuzumab cost-effective = 44%
  - Probability trastuzumab cost-effective = 56%

- Optimal decision?
  - Adopt trastuzumab and do more research


Probability cost-effective:
12 months trastuzumab vs no trastuzumab
Probability cost-effective
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0
20000
40000
60000
Willingness-to-pay threshold (£)

# Is Trastuzumab Cost-effective?

- 2006 estimate accepted by NICE:
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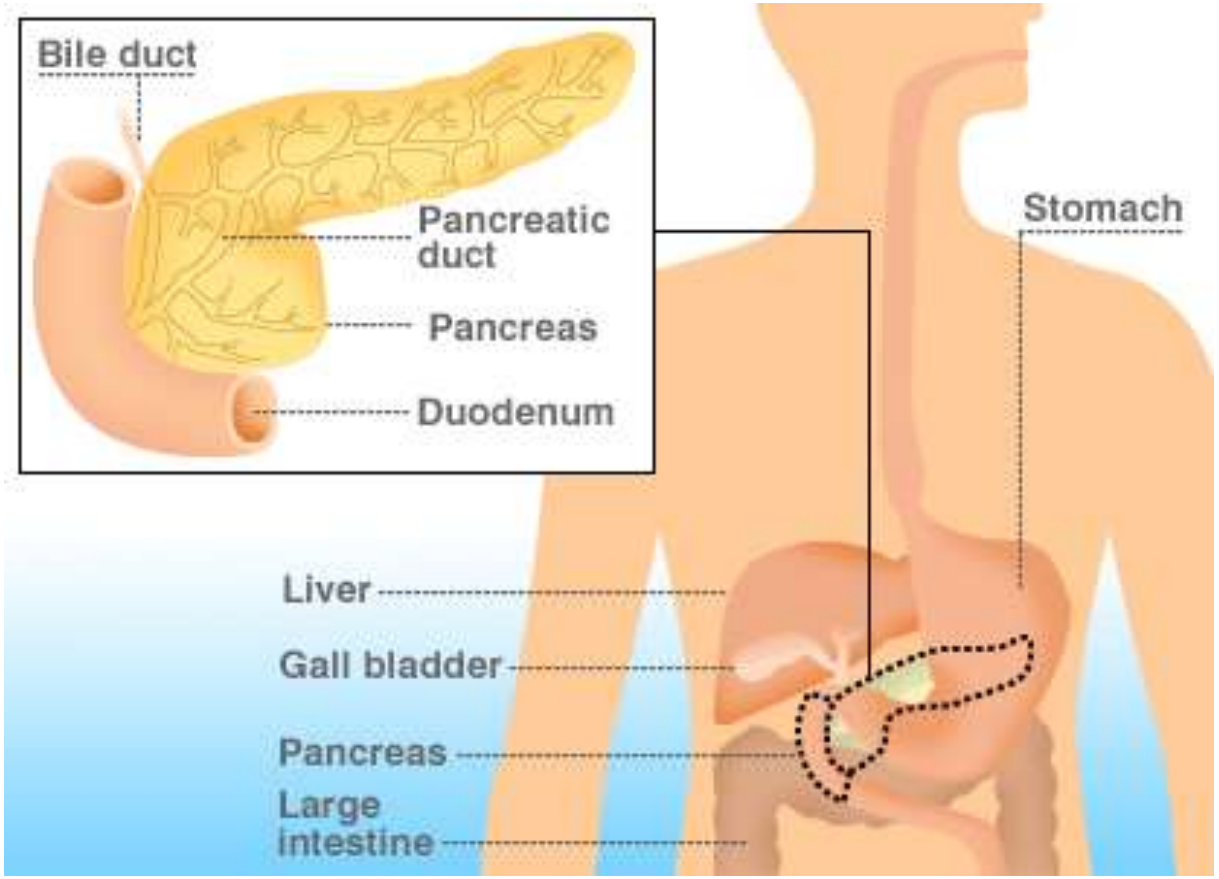
*Hall et al. Pharmacoeconomics 2011 29(5);415-432

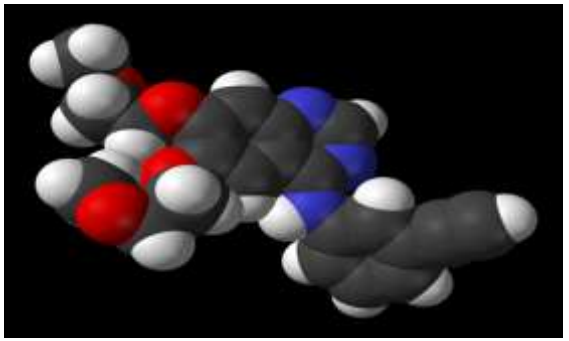
# Example:
# Early HER2 +ve breast cancer

# Advanced cancer

## Pancreatic cancer

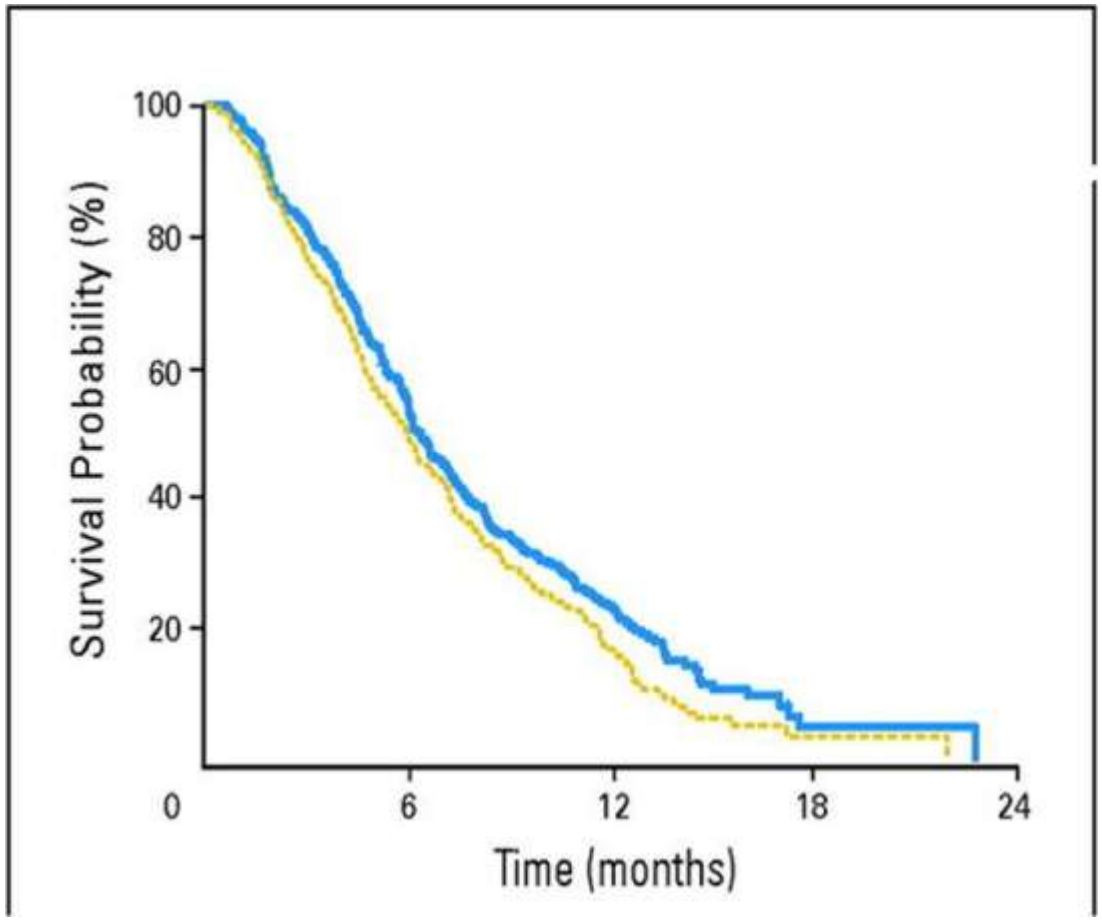



Erlotinib (Tarceva)



# Advanced cancer Overall survival

Erlotinib for advanced pancreatic cancer




HR 0.82
95% CI 0.69 to 0.99
p=0.038

**= success!**

**→ positive licensing decision**

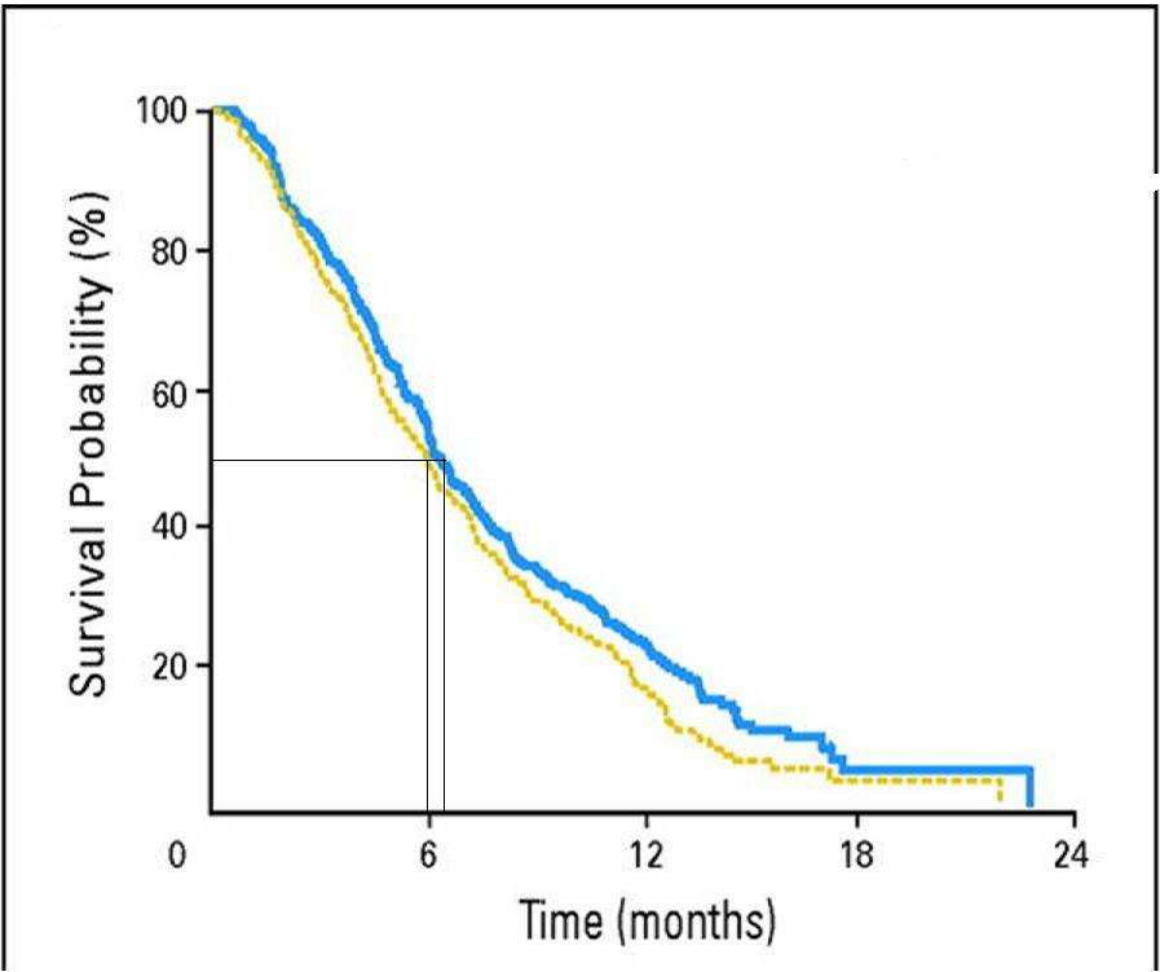
# Advanced cancer Overall survival

Erlotinib for advanced pancreatic cancer

Reimbursement decision?

# Advanced cancer Overall survival

## Erlotinib for advanced pancreatic cancer




HR 0.82
95% CI 0.69 to 0.99
p=0.038

Median survival =
6.24 months vs.
5.91 months

increase in median survival
=11 days

# Advanced cancer Overall survival

Erlotinib for advanced pancreatic cancer

- mean incremental LY per patient = 0.037
- Cost
  - incremental drug costs = £4000 (mean 3.75 months)
  - incremental side effect costs = £400

- ICER = £4400/0.037
  = **£118,919** per LY gained

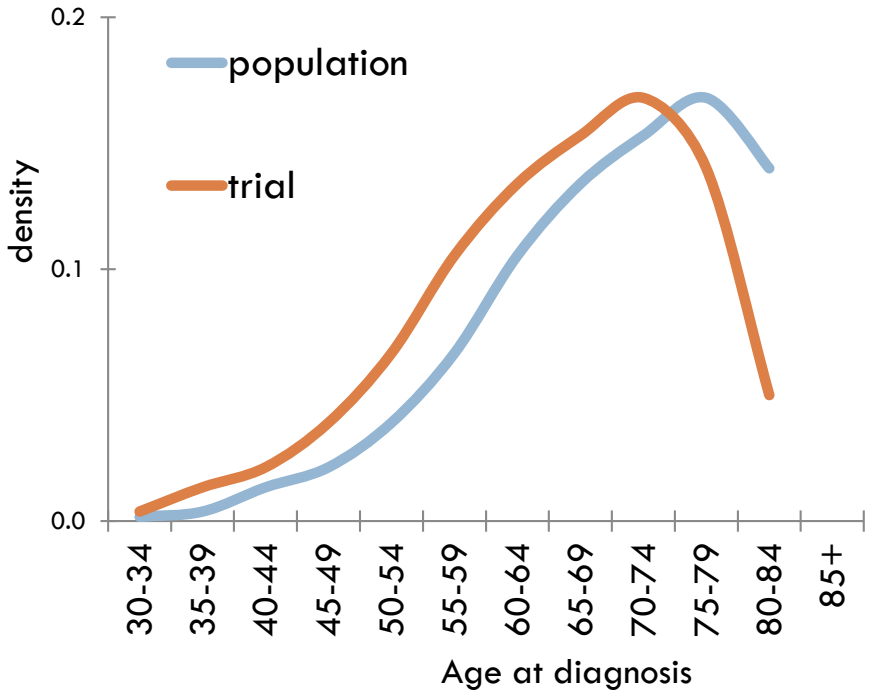
# Advanced cancer Overall survival

Erlotinib for advanced pancreatic cancer

QoL / cost per QALY ??

# Advanced cancer Overall survival

## Erlotinib for advanced pancreatic cancer – age distribution



# Erlotinib – NICE decision

- £118,919 per LY gained
- £ ??.?? per QALY gained
- wrong patient population

→ **rejected**

**Remember opportunity cost?**

# Summary

- Rising healthcare costs
- Fixed budget
- Efficient resource allocation is key
  - **OPPORUNITY COST**
- Cost-effectiveness analysis is a tool for improved healthcare
- Need better evidence for cost-effectiveness