Economic Evaluation in Practice

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Learning objectives

- Describe measurement of costs and quality-adjusted life-years alongside a randomised controlled trial.
- Explain need for decision modelling in economic evaluations.
- Outline key elements of model-based economic evaluation.
- Present and interpret cost-effectiveness results.

Alec Miners and Manuel Gomes. Economic evaluation in practice. Health Care Evaluation (second edition), chapter 11, Carmen Tsang and David Cromwell (Editors), Open University Press, 2016.

Framing an economic evaluation

- Decision problem
- Costs
- Outcomes
- Perspective
- Time horizon
- Discounting

Decision problem

- Identifying the research question of the economic evaluation

- Intervention scope
  - What?
  - How?
  - When?
  - Where?
  - By whom?
  - For whom?

- Economic evaluation approach
  - Clinical trial-based
  - Model-based
  - combination of the two

Costs - healthcare & non-healthcare

- Health service costs
  - Direct costs of intervention:
    - Staff time, medical devices, clinic overheads etc
    - Future related (and unrelated) health service costs - typically future events in the same (different) disease category
- Non-health service costs
  - Direct
    - travel costs
    - accommodation
    - meals
  - Indirect
    - Patient’s time and informal care costs (other’s time)
    - Productivity costs (impact on patient’s work and leisure time)

Costs - financial & economic

- Financial costs
  - Actual expenditure on goods and services.
- Economic costs
  - Includes the full value of all resources used in the intervention
  - Differs from actual expenditure when market rate is not paid for resource:
    - Donated or subsidised goods and/or volunteer time

Costs - capital & recurrent

- Capital costs
  - items with long lives (often defined as over one year)
    - buildings
    - equipment
    - vehicles
    - etc…
- Recurrent costs
  - resources that produce benefits for one year or less
  - incurred on a continual basis
    - supplies
    - personnel
    - etc...

Perspective

- Which costs should be included?
- Ideally, we should consider all costs above, irrespective of who incurs them (societal perspective)
  - But quantifying the costs of everyone affected by the intervention is challenging
- Often payer perspective (e.g. UK NHS) is adopted, resources incurred by the health service only.
- Sensitivity analysis can help assess whether cost-effectiveness results are sensitive to cost perspective

Time horizon

- Should be sufficiently long to capture all costs and outcomes associated with the interventions under comparison.
- May require decision-analytical models to extrapolate beyond the trial follow-up
  - For example, evaluation of alternative treatments for chronic conditions usually require modelling costs and outcomes over patient’s lifetime

Discounting

- Cost and outcomes related to the interventions usually occur over a long period of time
- Need to discount future costs and outcomes to their net present value to allow a fair comparison
- Time preferences: people prefer benefits earlier and costs later.
  - £432 invested now at 3% will be worth £500 five years later
  - Represents the real return on investment of resources (not inflation!)
- Net present value = future value / (1 + r)^t
  - where r is the discount rate and t is time in years

Measuring costs

- Costs are quantitative measures of resource use related to the interventions under comparison
- Ideally, costs should represent the value of the next best use of resources (opportunity cost) – not necessarily the price!
- Costing involves:
  - Identifying all relevant resource use components
  - Measuring the resource use
  - Valuing (assign unit costs) each resource use item

Measuring costs

- Consider importance of costs (which costs might differ by a large amount across comparators)

- Macro or micro costing?
  - Macro – apply a fixed cost per episode (eg NHS reference cost for hip replacement)
  - Micro – detailed study to record all staff time input and resources consumed
  - Mixed – combine fixed costs for components i.e. theatre costs plus length of stay multiplied by bed day cost

Measuring costs

- Cost adjustments
  - Inflation
    - When comparing costs occurring in different years
    - Convert costs to same year using inflation indices such as Hospital and Community Health Services index
  - Different currencies
    - Convert using Purchasing Power Parity rates (PPPs)
      - “Bundle of goods”
      - Available on OECD website http://www.oecd.org/sdd/prices-ppp/

Measuring outcomes

- QALY is a generic measure incorporating both quality of life (QOL) and ‘quantity’ of life (longevity)

- Measure QOL
  - Typically generic ‘pre-scored’ instrument are used (E.g. EQ-5D):
  - Patients describe their functional status across different health domains (corresponding to a distinct health state)
  - Preferences (valuations) from the general population are placed on the different health states, generating a QOL score (“utility”)

By placing a tick in one box in each group below, please indicate which statements best describe your own health state today

Mobility

I have no problems in walking about ☐

I have some problems in walking about ☐

I am confined to bed ☐

Self-Care

I have no problems with self-care ☐

I have some 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 with performing my usual activities ☐

I have some problems with performing my usual activities ☐

I am unable to perform my usual activities ☐

Pain/Discomfort

I have no pain or discomfort ☐

I have moderate pain or discomfort ☐

I have extreme pain or discomfort ☐

Anxiety/Depression

I am not anxious or depressed ☐

I am moderately anxious or depressed ☐

I am extremely anxious or depressed ☐

Source: adapted from the EuroQol Group: www.euroqol.org

This is the utility score

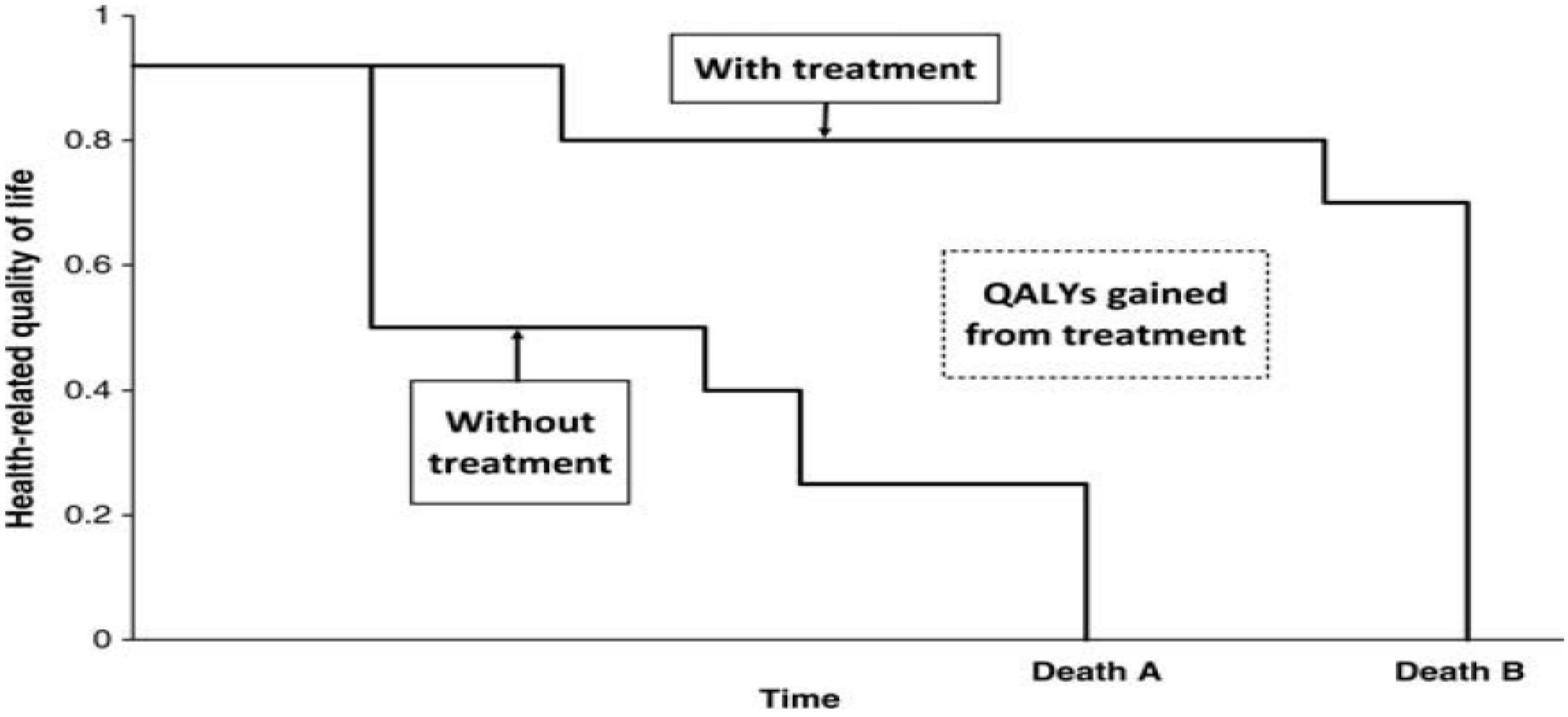


Fig. 1 QALYs gained from treatment.

Incremental cost-effectiveness ratio (*ICER*)

$$ICER = \frac{\text{Cost}_{\text{new intervention}} - \text{Cost}_{\text{control}}}{\text{Effectiveness}_{\text{new intervention}} - \text{Effectiveness}_{\text{control}}}$$

- Change in cost (numerator)
  - New intervention
  - Control
- Change in effectiveness (denominator)
  - New intervention
  - Control

$$\boxed{\frac{(\text{Cost}_{\text{new}} - \text{Cost}_{\text{old}})}{(\text{Effectiveness}_{\text{new}} - \text{Effectiveness}_{\text{old}})} = \textbf{ICER}}$$

$$\textbf{ICER} = \Delta \textbf{C} / \Delta \textbf{E}$$

Incremental resources **required** by the intervention

Incremental health effects gained by using the intervention

Uncertainty in cost-effectiveness analysis

- Parameter uncertainty
- Structural uncertainty
  - modelling and extrapolation
- Methodological uncertainty
  - Perspective
  - discount rate
  - etc

- Decision uncertainty
  - joint implication of uncertainties (above)

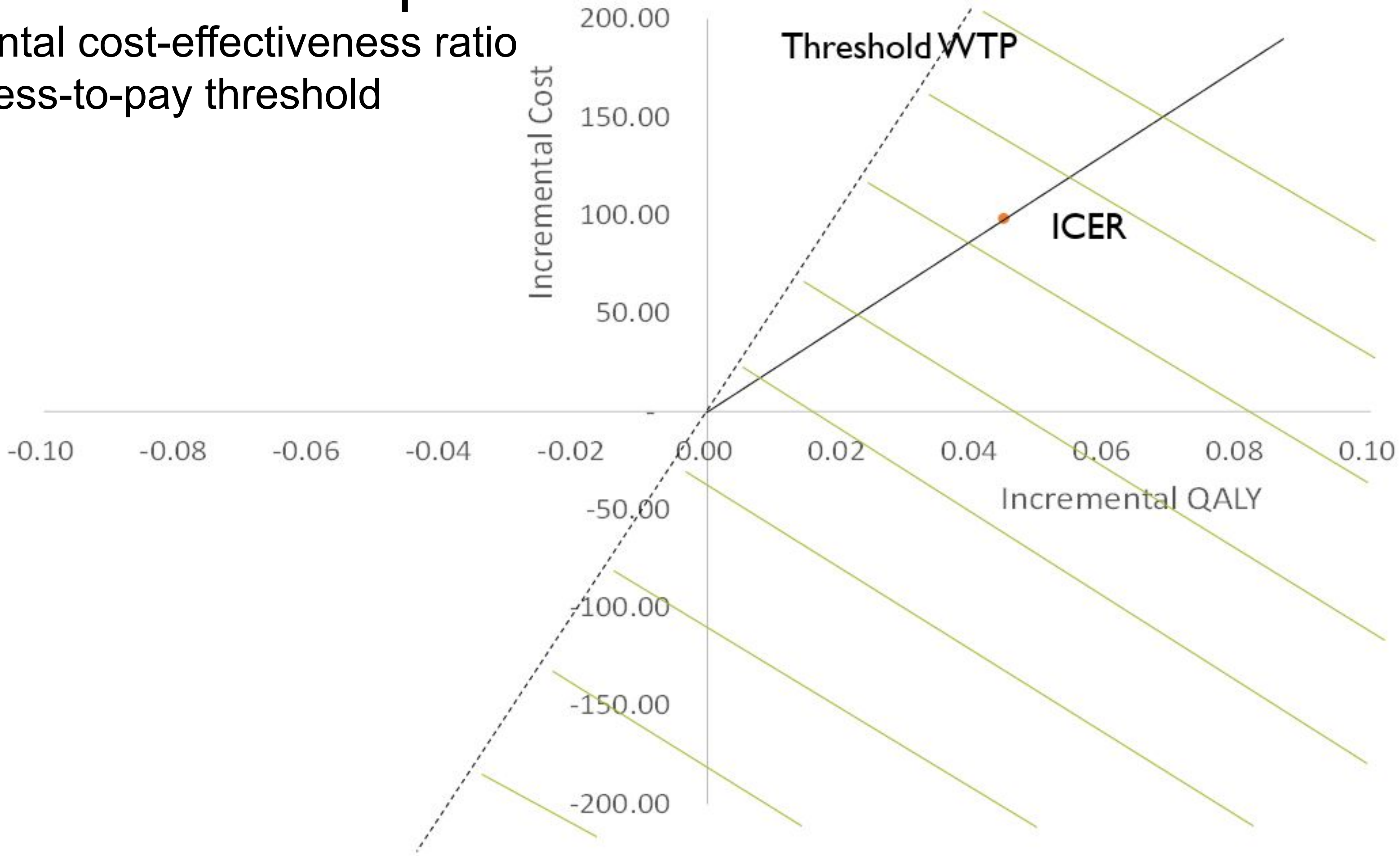
Sensitivity analysis

- Deterministic sensitivity analysis
  - univariate sensitivity analysis
  - multivariate sensitivity analysis
- Probabilistic sensitivity analysis
  - Impact of joint uncertainty of all input parameters on the outputs
  - quantify the level of confidence in the output of the analysis, in relation to uncertainty in the model inputs

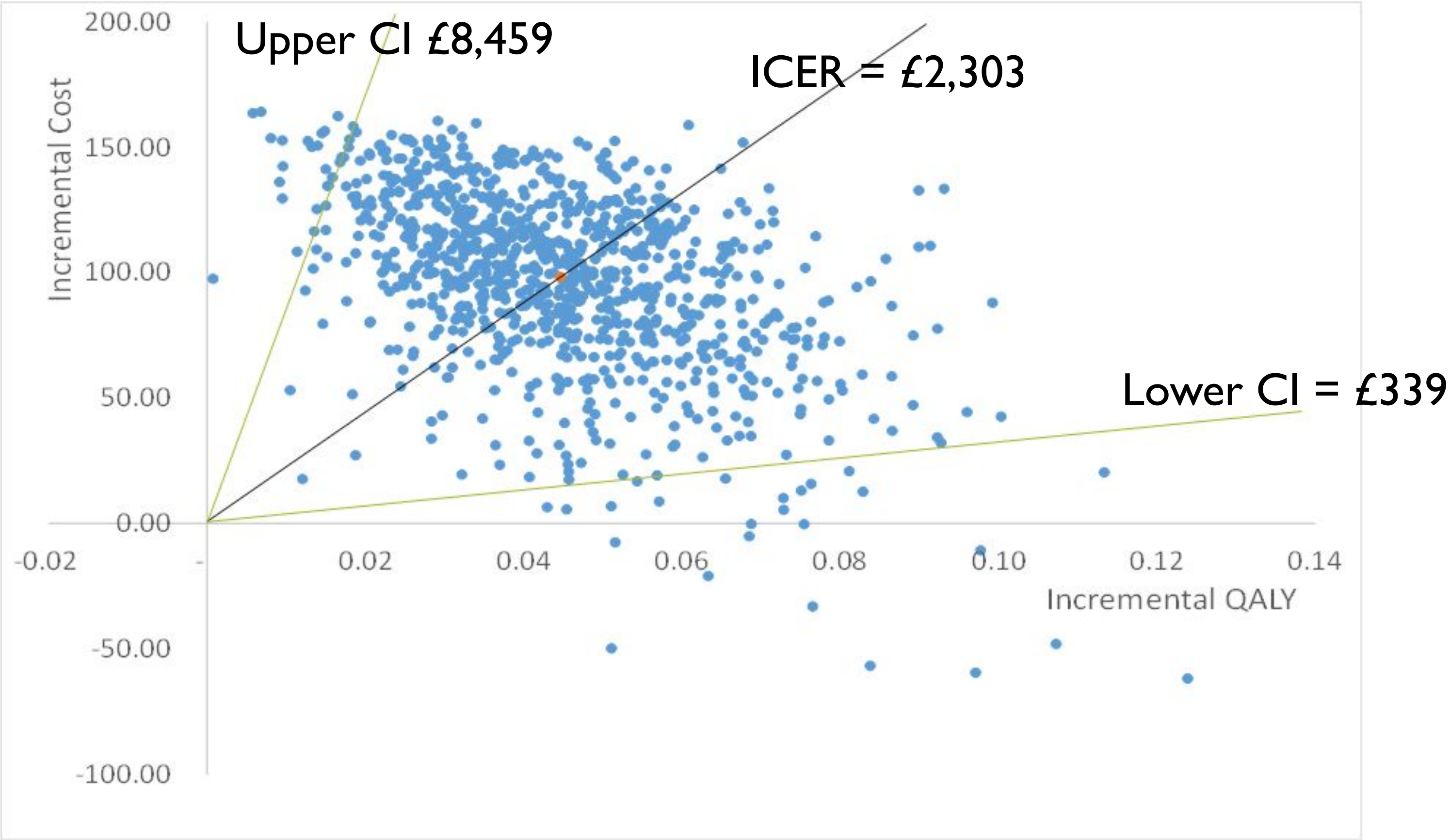
- How to conduct PSA (Probabilistic Sensitivity Analysis)?
  - Draw a value from an appropriate distribution describing each parameter
  - ‘Run’ decision model using selected parameter values
  - Repeat process n times (e.g. n = 10000)
  - Average costs and outcomes across all runs

Cost-effectiveness plane

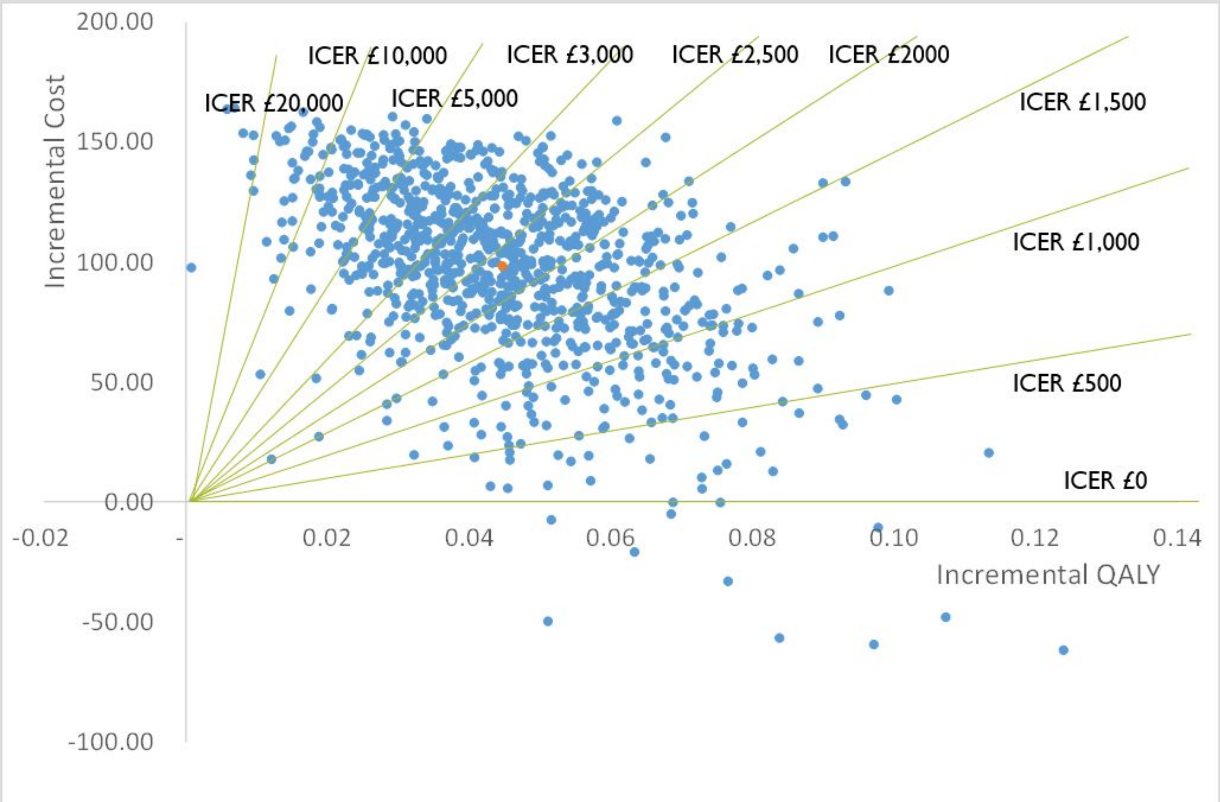
- Incremental cost-effectiveness ratio
- Willingness-to-pay threshold



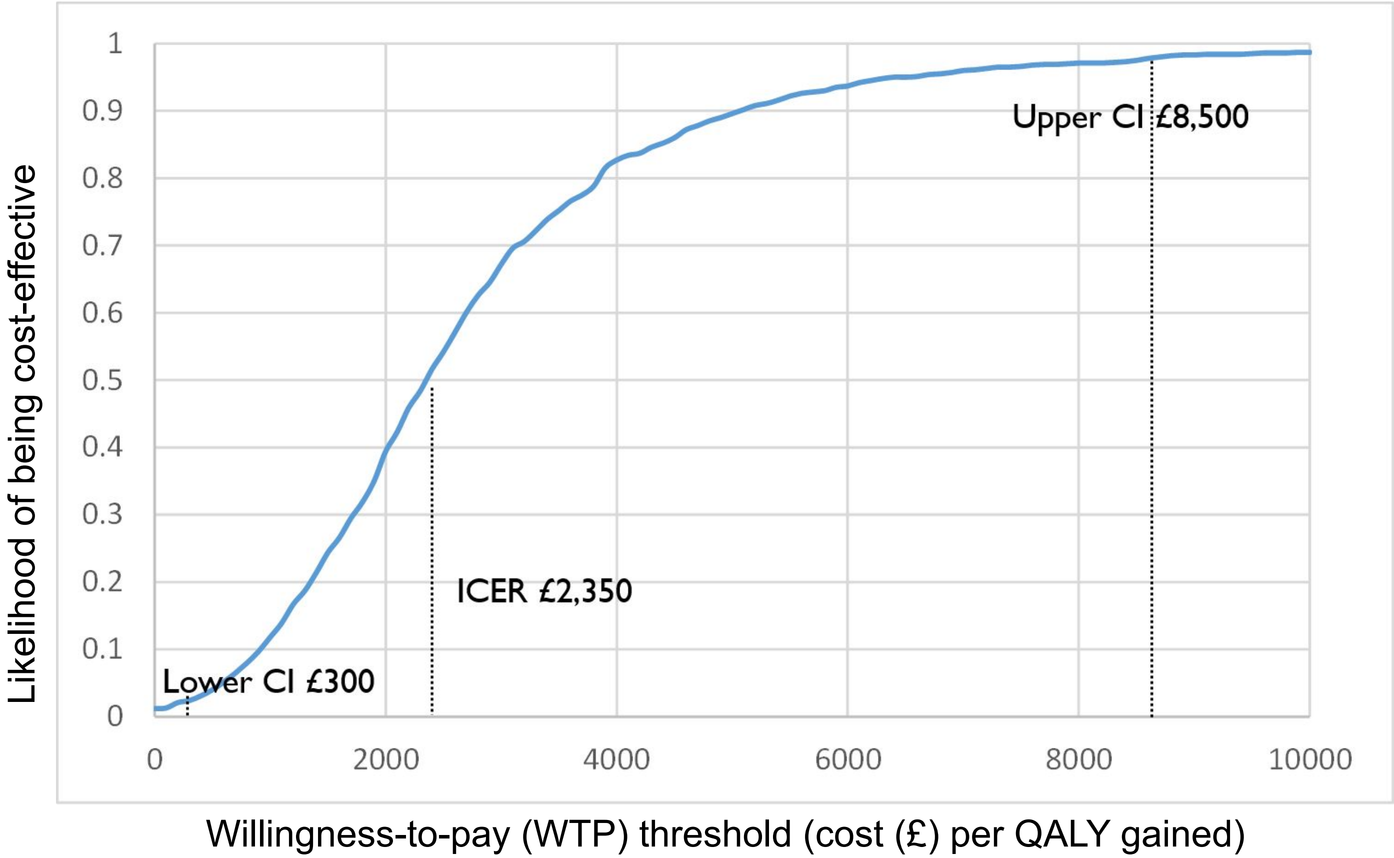
Probabilistic simulations on the cost-effectiveness plane



Varying cost-effectiveness thresholds



Cost-effectiveness acceptability curve



Activity 11.1

Consider a randomized controlled trial comparing two different surgical procedures to treat patients with an emergency abdominal aortic aneurysm.

(1) Outline the key resource components that you would need to consider up to one year post-randomization using the UK health service perspective.
(2) What units of measurement could you use to measure the use of these resources?
(3) How would you value each of these resources?
(4) Table 11.1 provides details of the aggregated costs (£) associated with each intervention (open and endovascular repair). Calculate the incremental cost of endovascular repair versus open repair using a health service perspective.
(5) Should a societal perspective be adopted in this economic evaluation?

Table 11.1 Key costs of resource components associated with each intervention (per patient)

Resource components	*Open repair (£ GBP)*	*Endovascular repair (£ GBP)*
Medical devices and consumables	4 000	7 000
Primary hospital stay	18 500	15 000
Re-admissions	1 000	1 500
Community care	2 000	1 000
Informal care	500	250

(1–3) Table 11.2 summarizes some important resource use components, the appropriate measuring unit, and potential sources for the unit costs.

Table 11.2 Main resource use components according to the health service perspective

Resource use components	*Measurement unit*	*Source of unit costs*
Hospital inpatient care		
Emergency room	Minute	Published studies
Theatre		
Medical devices	Patient	Manufacturer list prices
Consumables	Unit	Manufacturer list prices/published studies
Staff	Minute	Health and social care costs
Critical care		
ITU/HDU	Bed-day	NHS reference costs
Stroke unit	Bed-day	NHS reference costs
Outpatient and community care		
Outpatient visit	Visit	Health and social care costs
Nursing home	Bed-day	Health and social care costs
GP and nurse visits	Visit	Health and social care costs

(4) Under the health service perspective, informal care should be excluded from the calculations:

$$Cost_{open\ repair} = 4500 + 18{,}500 + 1000 + 2000 = 26{,}000$$

$$Cost_{endovascular\ repair} = 7000 + 15{,}000 + 1500 + 1000 = 24{,}500$$

$$Incremental\ Cost_{endovascular\ vs.\ open\ repair} = 24{,}500 - 26{,}000 = -1500$$

(5) Most of the costs associated with both open and endovascular repair for the treatment of patients with ruptured aneurysms are incurred by the health service. For example, the proportion of informal care not covered by the health and social care services is small and unlikely to be a driver of the cost differences between the two interventions (as suggested in Table 11.1). Other indirect costs such as potential earnings lost due to illness may be small in this setting, as most patients are likely to be elderly and retired.

Activity 11.2

(1) Outline the potential limitations of using QALYs to inform decisions about resource allocation.

(2) Table 11.4 lists EQ-5D values associated with a new treatment and standard care for treating patients with arthritis. Calculate the QALY gain of the new treatment compared with standard care.

Table 11.4 EQ-5D values associated with the new treatment and standard care at different follow-up periods

	New treatment	*Standard care*
Baseline	0.1	0.1
6 months	0.5	0.3
12 months	0.8	0.6
18 months	1	0.8
24 months	1	1

1 Possible limitations of using QALY in informing decisions about resource allocation include:

- As a generic measure, QALY may be less sensitive to small changes in health than disease-specific measures, particularly in less severe health conditions. In addition, it may not be possible to capture all the benefits of a health intervention into a single index.
- The valuation of each health state at a particular point in time is assumed not to depend on the time spent in that health state or the heath states preceding it (also known as the inter-temporal utility independence).
- Preferences elicited from the general public on different health states may not reflect those of the population for whom the interventions are being evaluated. For example, (healthy) people may value health states differently when these are hypothetical, compared with how they would value them if they actually experienced them (experienced preferences).
- Maximizing population health (greatest number of QALYs) for a given budget implies that all QALYs have the same social value irrespective of who benefits (patient characteristics or health conditions). Therefore, the use of QALY may lead to the failure to treat a small number of patients with rare diseases or in terminal stages, possibly raising equity and ethical issues.

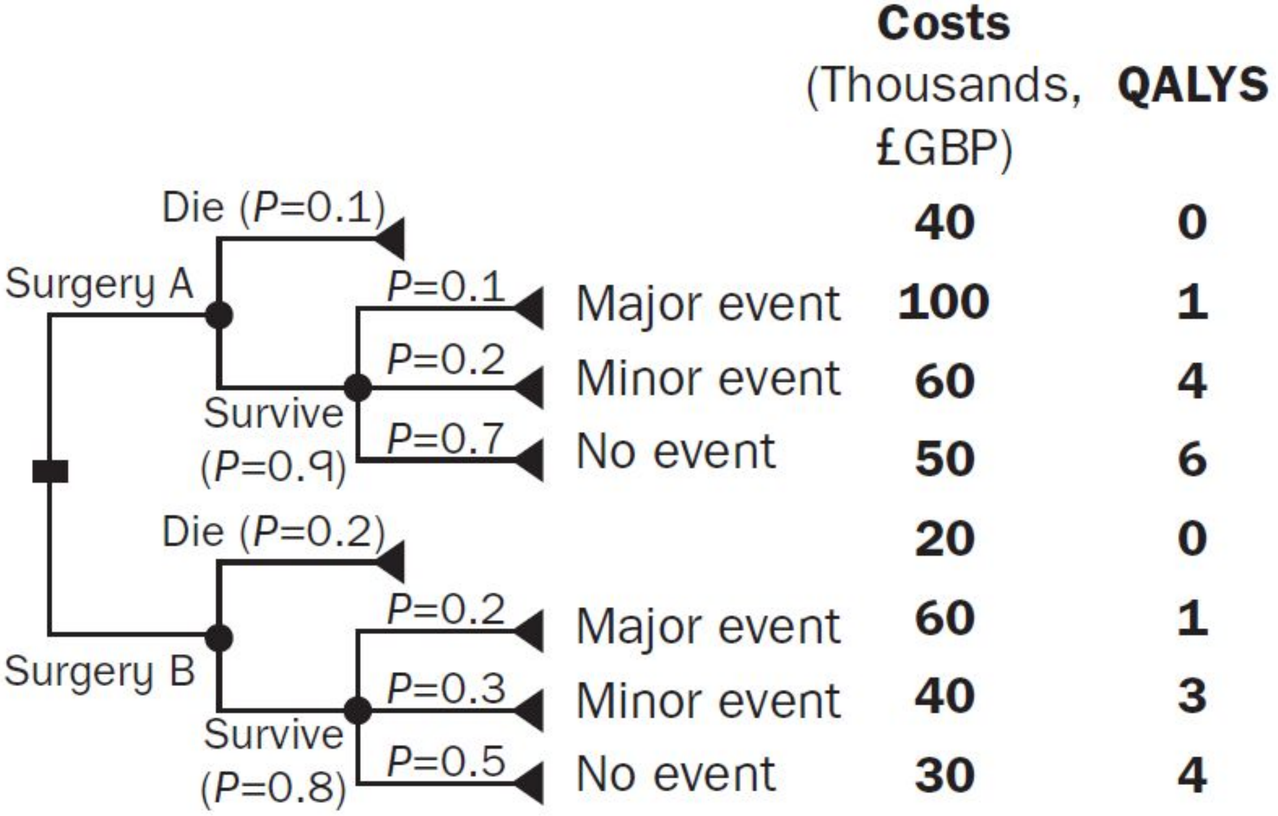
2 QALY gain of new treatment (NT) versus standard care (ST):

$$QALY_{NT} = \frac{0.1 + 0.5 + 0.8 + 1}{2} = 1.2$$

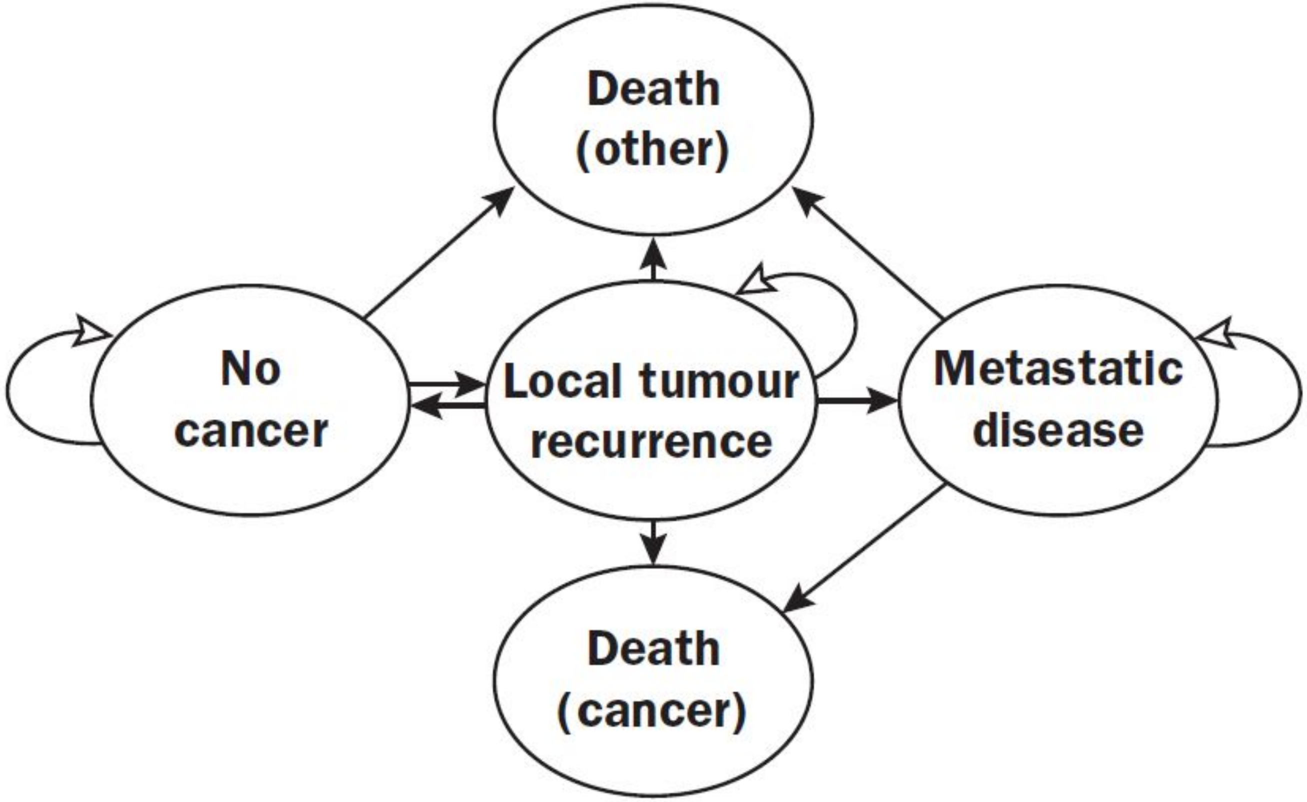
$$QALY_{ST} = \frac{0.1 + 0.3 + 0.6 + 0.8}{2} = 0.9$$

$$QALY_{gain} = 1.2 - 0.9 = 0.3 \text{ QALYs}$$

(A) Decision tree: Surgery A vs. Surgery B after traumatic brain injury



(B) Markov model: Prostate cancer stages after initial treatment



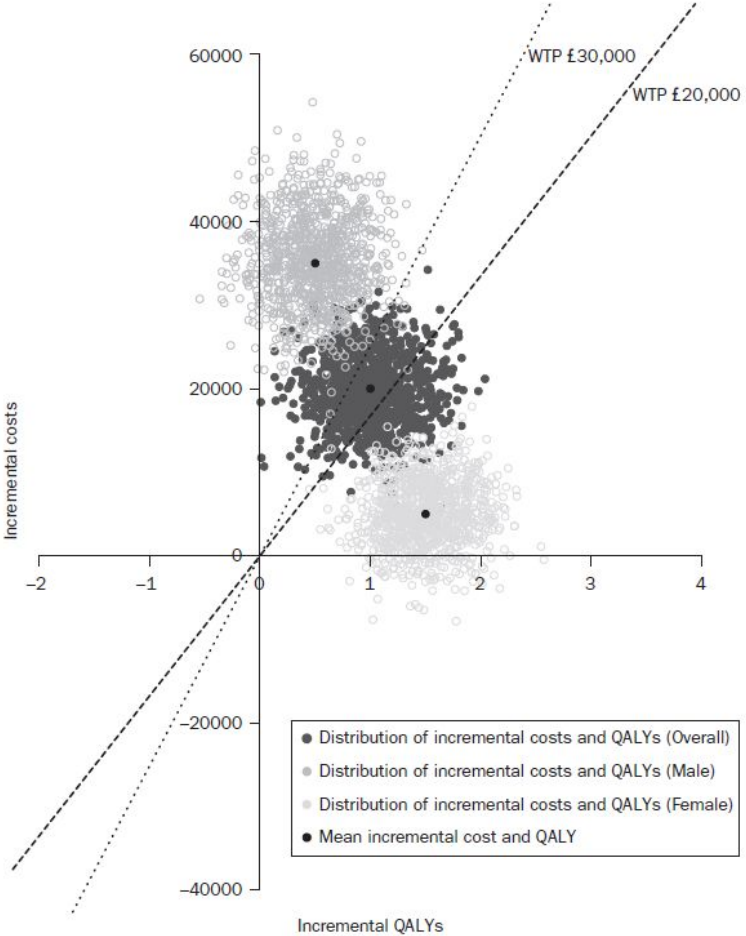


Figure 11.2 Distribution of incremental costs and incremental QALYS in an evaluation of surgery A versus surgery B for traumatic brain injury.

Case Studies

Cost effectiveness analysis & cost utility analysis

Cost effectiveness and cost-utility analysis of a group-based diet intervention for treating major depression - the HELFIMED trial.
Segal L, Twizeyemariya A, Zarnowiecki D, Niyonsenga T, Bogomolova S, Wilson A, O'Dea K, Parletta N. https://www.ncbi.nlm.nih.gov/pubmed/30570386

BACKGROUND/OBJECTIVES:
Major depression has a negative impact on quality of life, increasing the risk of premature death. It imposes social and economic costs on individuals, families and society. Mental illness is now the leading cause globally of disability/lost quality life and premature mortality. Finding cost-effective treatments for depression is a public health priority. We report an economic evaluation of a dietary intervention for treating major depression.

METHODS:

This economic evaluation drew on the HELFIMED RCT, a 3-month group-based Mediterranean-style diet (MedDiet) intervention (including cooking workshops), against a social group-program for people with major depression. We conducted (i) a cost-utility analysis, utility scores measured at baseline, 3-months and 6-months using the AQoL8D, modelled to 2 years (base case); (ii) a cost-effectiveness analysis, differential cost/case of depression resolved (to normal/mild) measured by the DASS. Differential program costs were calculated from resources use costed in AUD2017. QALYs were discounted at 3.5%pa.

RESULTS:

Best estimate differential cost/QALY gain per person, MedDiet relative to social group was AUD2775. Probabilistic sensitivity analysis, varying costs, utility gain, model period found 95% likelihood cost/QALY less than AUD20,000. Estimated cost per additional case of depression resolved, MedDiet group relative to social group was AUD2,225.

CONCLUSIONS:

A MedDiet group-program for treating major depression was highly cost-effective relative to a social group-program, measured in terms of cost/QALY gain and cost per case of major depression resolved. Supporting access by persons with major depression to group-based dietary programs should be a policy priority. A change to funding will be needed to realise the potential benefits.

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Cost utility analysis

From Research to Policy Implementation: Trastuzumab in Early-Stage Breast Cancer Treatment in Thailand.

Kongsakon R, Lochid-Amnuay S, Kapol N, Pattanaprateep O.

https://www.ncbi.nlm.nih.gov/pubmed/30428405

OBJECTIVES:

To evaluate the adjuvant therapy of trastuzumab cost and quality-adjusted life-years (QALYs) in lifetime horizon and describe the use of an economic evaluation in supporting policy-making decisions in the treatment of early-stage breast cancer in Thailand.

METHODS: A Markov model was used to evaluate the cost effectiveness of 1-year adjuvant trastuzumab for patients with early-stage breast cancer who were considered human epidermal growth factor receptor 2/neu-positive with a societal perspective and lifetime horizon. The research variables were probability of health state change, health utility, and cost of treatment. A sensitivity analysis was conducted using probabilistic methods. A budget impact analysis was also performed.

RESULTS: The results revealed that the treatment cost and QALYs in the trastuzumab group yielded 4.59 QALYs. The incremental cost-effectiveness ratio was $3387 (THB 118 572; THB = Thai baht) per QALY gained. On the basis of the willingness-to-pay threshold in Thailand, a 1-year adjuvant trastuzumab treatment for breast cancer was a cost-effective therapy.

CONCLUSIONS: A combination therapy that includes trastuzumab is a preferable choice and should be used in early-stage breast cancer treatment. The Thai government has listed trastuzumab on the National List of Essential Medicines to be used for the early stages of breast cancer since 2014.

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Cost benefit analysis

A cost-benefit analysis of smoking cessation prescription coverage from a US payer perspective.

Baker CL, Ding Y, Ferrufino CP, Kowal S, Tan J, Subedi P.

https://www.ncbi.nlm.nih.gov/pubmed/30038510

INTRODUCTION: Smoking drives substantial direct health care spending, comprising 8.7% ($168 billion) of annual United States aggregated spending. Smoking cessation (SC) prescription use is an effective strategy to improve health outcomes, increase quit rates, and reduce economic burden. However, patient out-of-pocket costs may limit the use. Health care payers play a vital role in driving use through formulary decisions and copayment policies but must consider both the near-term financial investment as well as downstream effects of increased coverage on health care budgets. This study estimates the return on investment (ROI) of providing Affordable Care Act (ACA)-recommended prescription SC coverage.

METHODS:

A cost-benefit analysis (CBA) estimates the ROI of providing prescription SC coverage, based on pharmacy costs and savings from smoking-attributable medical expenditures among Medicare, Medicaid, and commercial plan enrollees over 10 years. The CBA incorporated national-level population demographics, smoking prevalence estimates, proportion of smokers attempting to quit, and the utilization of SC products. A five-state Markov chain model simulated patterns of quit attempts, relapse, and cessation assuming two quit attempts per year, no patient cost-sharing, and 25.4% utilization of prescription SC aids. Results include number of quitters, annual pharmacy and smoking-attributable medical costs, and ROI.

RESULTS:
After initial investment in SC treatment, smoking-attributable medical benefits accrue over time, generating a positive ROI by year 4 for commercial (11.3%) and Medicaid (78.4%) plans and by year 3 for Medicare (30.6%). Over 10 years, an average return of $1.18, $2.50, and $3.22 savings per dollar spent on SC prescriptions for commercial, Medicaid, and Medicare plans, respectively, may be realized.

DISCUSSION:
Given the proven efficacy of SC pharmacotherapy, near-term investments in supporting ACA-recommended SC coverage translate into a positive ROI. As smoking is a leading cause of morbidity and mortality, increased access to prescription SC medications may improve health outcomes and reduce smoking-attributable costs to payers over time.

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CBA

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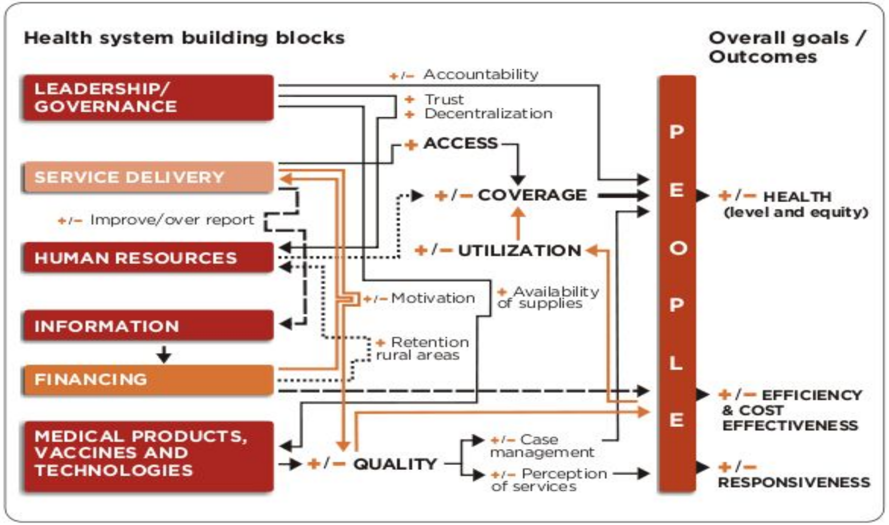

STEEPLES Analysis

- **S**ocial
  - **T**echnology
    - **E**conomics
      - **E**nvironment
        - **P**olitics
          - **L**egal
            - **E**thics
              - **S**ecurity

Economic evaluation for health:

Effectiveness & Efficiency (& Equity?)