



Designing Economic Evaluation Alongside Clinical Studies

Health Economics Short Course

For more information and course dates, please visit our website

<http://mdhs-study.unimelb.edu.au/short-courses/mspgh-short-courses/designing-economic-evaluation-alongside-clinical-studies/overview>

Or email us : health-economics@unimelb.edu.au



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Module 4 – Economic evaluation, uncertainty & modelling

Centre for Health Policy
Melbourne School of Population and Global Health



Economic Evaluation



Purpose of economic evaluation

- **Inform decisions!**
 - Is the intervention cost-effective?
 - How does it compare to other interventions?
- **Helps translate study results into information for:**
 - Decision makers at your hospital
 - Evidence base within your field
 - Government funding agencies

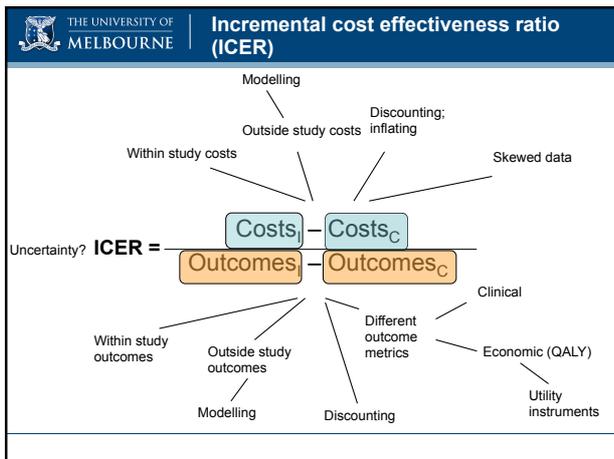


Incremental cost effectiveness ratio (ICER)

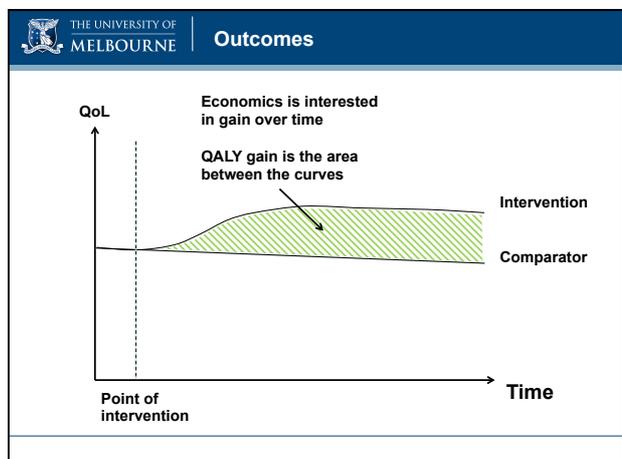
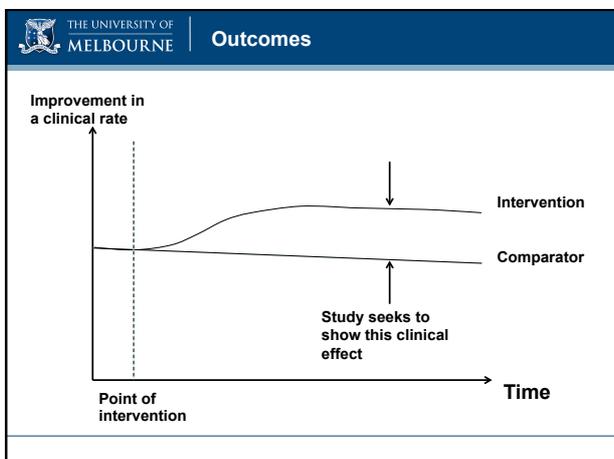
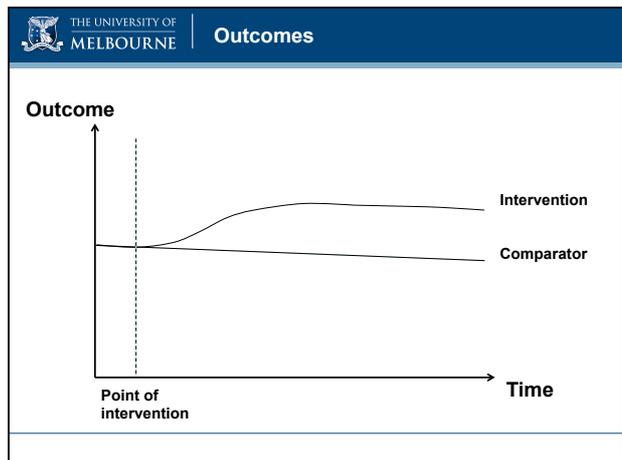
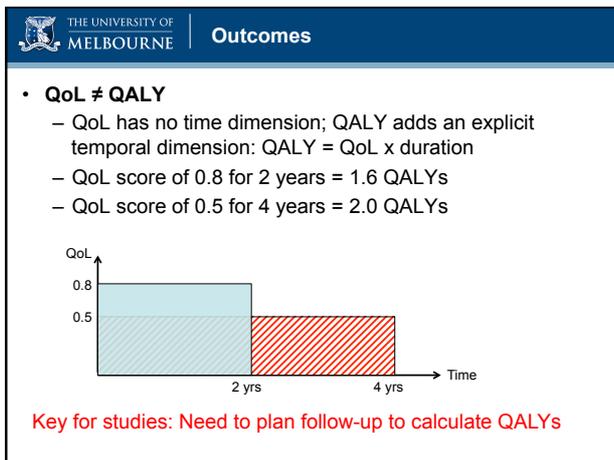
- **How?** Bring **costs** and **benefits** together to allow comparisons

$$ICER = \frac{\text{Costs} - \text{Costs}_C}{\text{Outcomes} - \text{Outcomes}_C}$$

- Incremental; common outcome measures
- **CEA** → maximisation of health outcomes within given funding/budgets



- Outcomes**
- **Clinical**
 - typically primary outcomes
 - consider translation to other outcomes?
 - **Economic**
 - Standard metric is the Quality Adjusted Life Year (QALY)
 - **Key for studies? Perspective differences**
 - Clinical 'success' at point in time
 - Economics interested in gains over time



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- Likely to be skewed
- Wide confidence intervals
- Missing versus zero values

```

-> group = 'Placebo'
Variable | Obs   Mean   Std. Dev.  Min   Max
-----+-----
post_cost | 196  5416.211 15398.42   0 144454.3

-----+-----
-> group = 'Vasectomy'
Variable | Obs   Mean   Std. Dev.  Min   Max
-----+-----
post_cost | 196  8017.515 23776.2   0 221384.1
  
```

- Key for studies? Costs unlikely to be powered (uncertainty around costs)

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Within study results: the ADVANCE study

	Perindopril-indapamide	Placebo/standard practice	Difference
Costs	\$21,001	\$20,499	\$502
Years of life	4.17	4.14	0.03
Eq-5D	0.8	0.8	-
QALY	3.33	3.31	0.02

CEA= \$502/0.03 = \$16,733 per life year saved
 CUA= \$502/0.02 = \$25,100 per QALY saved

Key for studies: Could we estimate this prior to study?

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Economic Modelling

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Why is it necessary?

Clinical studies are limited in **scope and duration**: they do not contain all the information required by decision makers

- Need to **extrapolate** beyond study follow-up period
- Need to **generalise** from one setting/population to another
- Need to link between intermediate and final outcomes (**transform**)
- Need to **evaluate uncertainty**

THE UNIVERSITY OF MELBOURNE | **Extrapolation: costs**

- Within study versus long-term costs

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Economics is interested in gain over time

QALY gain is the area between the curves

QALY gain continues post study

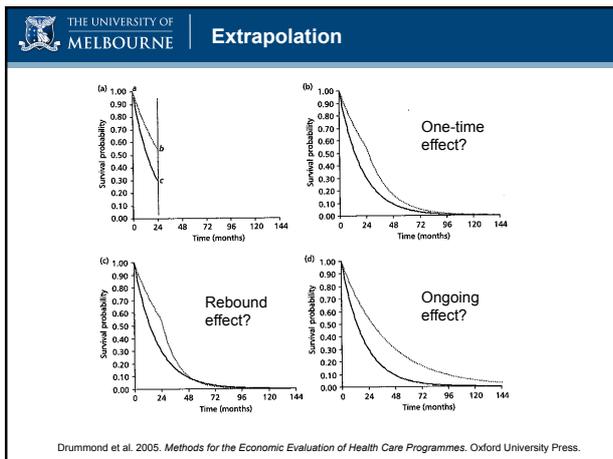
Intervention

Comparator

Point of intervention

End of study

Time



THE UNIVERSITY OF MELBOURNE | **Cost effectiveness analysis**

Full results: the ADVANCE study

	Within study	Within study + modelling	Difference
Costs	\$502	\$502	-
Years of life saved	0.03	0.05	-40%
QALYs saved	0.02	0.03	-33%
\$/years of life saved	\$16,733	\$10,040	67%
\$/QALY saved	\$25,100	\$16,733	50%

- **Key for study: within study results may underestimate cost effectiveness**
 - Consider how you expect the outcomes to vary

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- Discounting (time preferences)
 - Both costs and outcomes
- Inflation (changes in prices over time)
 - 1986 = \$1.75
 - 2016 = \$5.30
 - Costs

- THE UNIVERSITY OF MELBOURNE** | **Generalisability**
- An RCT finds folic acid during pregnancy improves birth outcomes
 - Should the Department of Health fund a folic acid program to all pregnant women?
 - What do we need to know?
 - How many pregnant women each year?
 - How did the treatment effect vary across covariates? Ethnicity? Age? Income? Education?
 - **Key for studies?**
 - Design your study sample to be representative or measure how it is different
 - Consider power for sub-cohorts

- THE UNIVERSITY OF MELBOURNE** | **Transformation**
- An RCT is used to highlight how a new intervention can improve the glycemic control in type 1 diabetes patients
 - What are the long-term implications of this?
 - Simulation model transforms change in risk factor (e.g. blood glucose) to change in outcomes (e.g. fewer strokes)
 - **Key for studies?**
 - Final outcomes could be immeasurable within study: do models exist to transform your intermediate outcomes to final outcomes?

- THE UNIVERSITY OF MELBOURNE** | **Evaluating uncertainty**
- Studies aim to reduce uncertainty
 - Is the intervention effective?
 - Typically focus on randomisation and sample size (parameter uncertainty)
 - But still much uncertainty
 - Structural/model
 - Methodological
 - Combinations of primary and secondary data
-

Evaluating uncertainty

- Modelling can help systematically evaluate uncertainty: sensitivity analysis

Evaluating uncertainty

- Modelling can help systematically evaluate uncertainty: sensitivity analysis

One way

Evaluating uncertainty

- Modelling can help systematically evaluate uncertainty: sensitivity analysis

Multi way

Evaluating uncertainty

- Modelling can help systematically evaluate uncertainty: sensitivity analysis

Probabilistic

Evaluating uncertainty

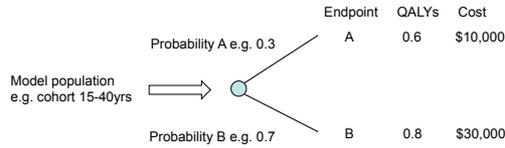
- Key for studies?
 - Many areas of uncertainty
 - Not just parameter uncertainty!
 - Try to capture rather than ignore uncertainty
 - Identify likely sources of uncertainty
 - Use modelling to help evaluate the impact of uncertainty

Demystifying modelling

- What actually is modelling??
- Relationships (e.g. CVD events related to obesity)
- Data (e.g. population projections)
- Computing power
 - Many equations, many calculations

"all models are wrong, but some are useful"
George E.P. Box

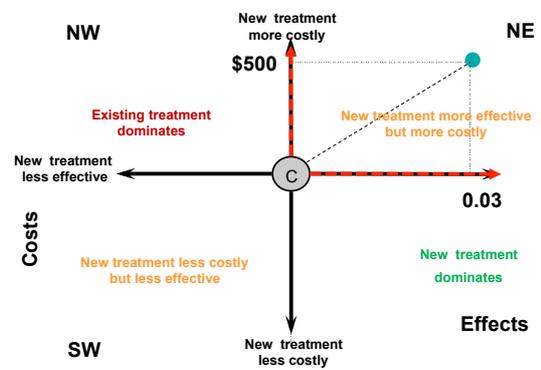
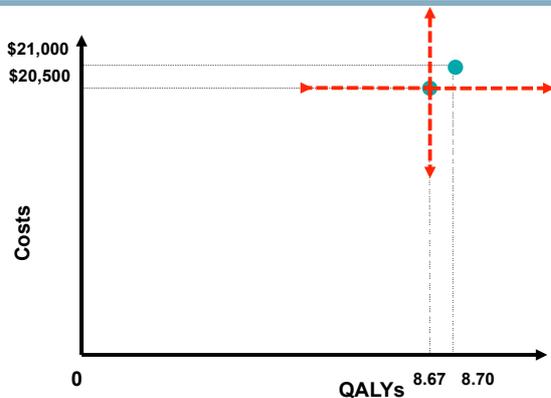
- Different types of modelling?
 - Survival analysis
 - Decision analysis, Markov
 - Microsimulation



- Analysis and manipulation of costs
 - Skewed data
 - Inflation, discounting
- Analysis of outcomes
 - Clinical data
 - Calculation of QALYs
 - Discounting
- Out-of-study costs and outcomes?
 - Modelling

Interpreting economic evaluations

- How can economic evaluations be interpreted?
- How do they feed into decisions?
- What exactly are we trying to show?
- **Key for studies? How will the study influence a decision? Start with the end in mind**



Decision rules for CEA

- Recommend
 - If new intervention dominates
- Reject
 - If new intervention is dominated
- Develop a decision rule for NE & SW quadrants
 - Compare to established threshold
- Key for studies? Where do you expect the intervention to lie? What's the 'pitch'?



How do I know if it is cost effective?

- What is the maximum amount society is willing to pay for an extra unit of health gain?
- Varies across countries
 - Australia \$40K-\$70K per life year¹
 - UK, NICE states £20-30K per QALY²
 - US \$50,000 per QALY as a minimum³

1. George B, Harris A, Mitchell A (2001) Cost Effectiveness Analysis and the Consistency of Decision Making: Evidence from Pharmaceutical Reimbursement in Australia 1991-96, *Pharmacoeconomics* 19(11):1103-9
 2. Devlin (2004) Does NICE have a cost-effectiveness threshold and what other factors influence its decisions? A binary choice analysis. *Health Economics* 13(5):437-52
 3. Neumann, P.J., Cohen, J.T., and Weinstein, M.C. (2014). Updating cost-effectiveness – the curious resilience of the \$50,000-per-QALY threshold. *N Engl J Med* 2014; 371:796-797

Considerations with thresholds

- In practice in Australia, thresholds vary
 - Medical versus lifestyle interventions
 - Treatment versus screening objectives
 - Child versus adult target populations

HEALTH ECONOMICS
 Health Econ. 19: 445-451 (2001)
 Published online: 20 April 2009 in Wiley InterScience (www.interscience.wiley.com). DOI: 10.1002/hec.1483

FIXING THE GAME: ARE BETWEEN-SILO DIFFERENCES IN FUNDING ARRANGEMENTS HANDICAPPING SOME INTERVENTIONS AND GIVING OTHERS A HEAD-START?

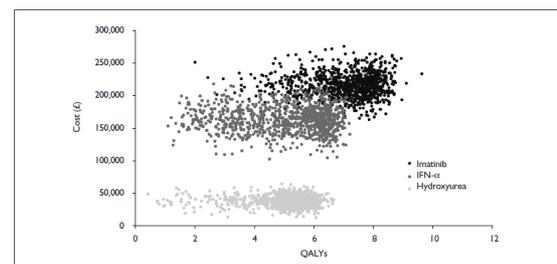
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SUMMARY

Given resource scarcity, not all potentially beneficial health services can be funded. Choices are made, if not explicitly, implicitly as some health services are funded and others are not. But what are the primary influences on these choices? We sought to test whether funding decisions are linked to cost effectiveness and to quantify the influence of funding arrangements and community values arguments. We used this via empirical analysis of 245 Australian healthcare interventions for which cost-effectiveness estimates had been published. The likelihood of government funding was modelled as a function of cost effectiveness, patient-target group characteristics, intervention characteristics and publication characteristics, using multiple regression analysis. We found that higher

Probabilistic sensitivity analysis

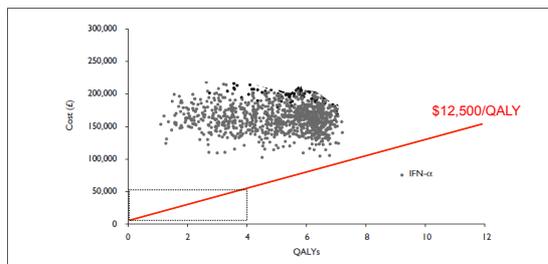
Cost-effectiveness plane



Dalziel, K, Round, A, Garside, R & Stein K 2005. 'Cost effectiveness of Imatinib compared with Interferon-alpha or Hydroxycarbamide for first-line treatment of Chronic Myeloid Leukaemia', *Pharmacoeconomics*, vol. 23, no. 5, pp. 515-26.

Probabilistic sensitivity analysis

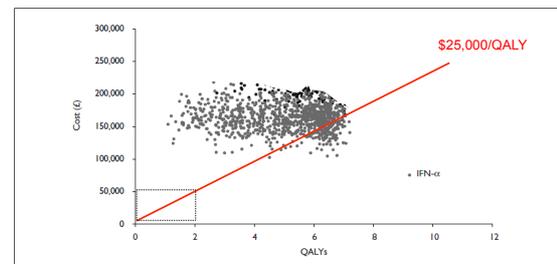
Cost-effectiveness plane



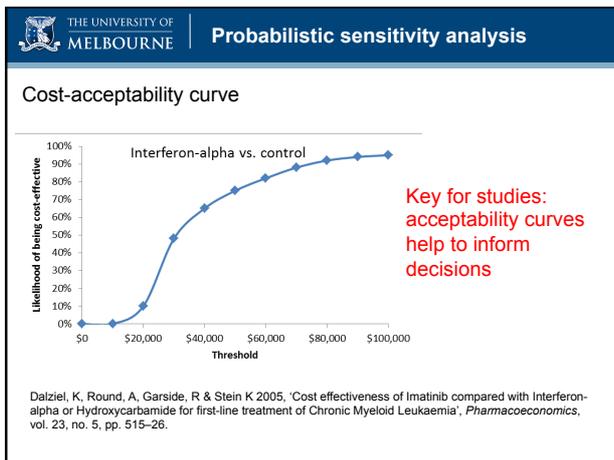
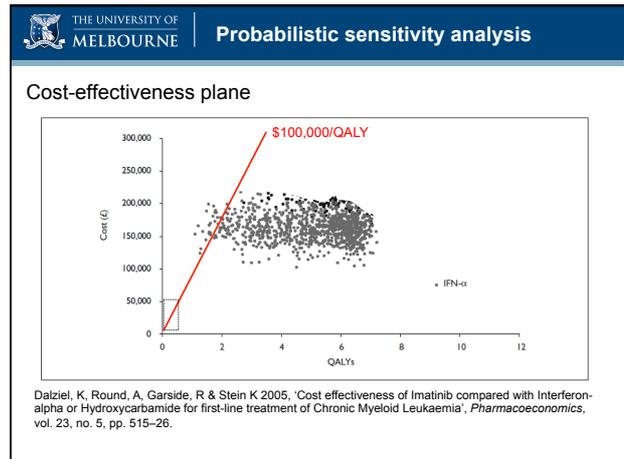
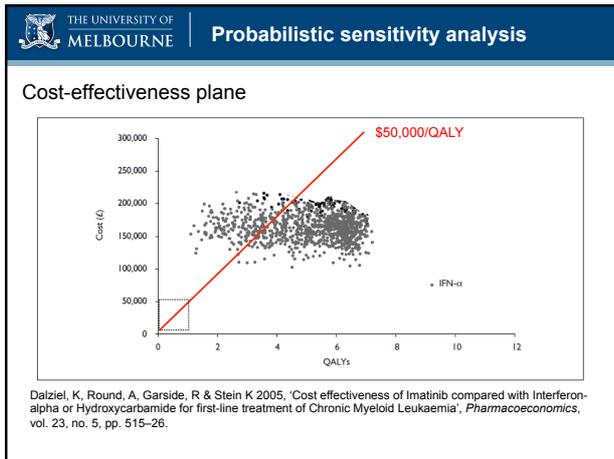
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Probabilistic sensitivity analysis

Cost-effectiveness plane



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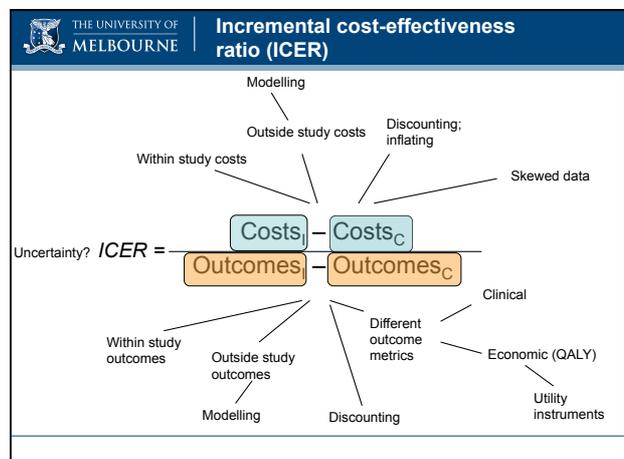


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- Guidelines available to apply across the research cycle
 - Informing protocol development
 - Citing in funding applications
 - Using in practice
 - Reporting results
- Key for studies: helps guide smooth path for acceptance

THE UNIVERSITY OF MELBOURNE Incremental cost-effectiveness ratio (ICER)

$$\frac{\text{Costs}_I - \text{Costs}_C}{\text{Outcomes}_I - \text{Outcomes}_C}$$



Key points for studies

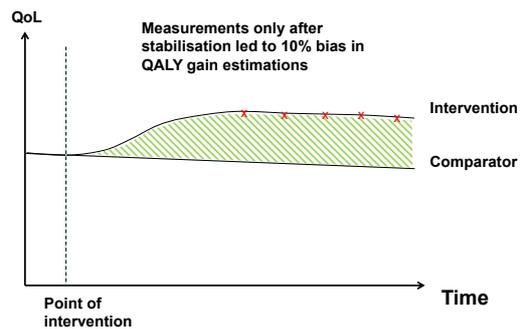
- Differences between clinical and economic outcomes
 - Plan follow-up measurements
- Within study results might underestimate cost-effectiveness
 - Think about how outcomes might vary
- Many areas of uncertainty
 - Don't ignore, but evaluate
- Study should help to inform a decision
 - Estimate cost-effectiveness prior to study
 - Use guidelines and standard economic evaluation methods

Other contributions from economics

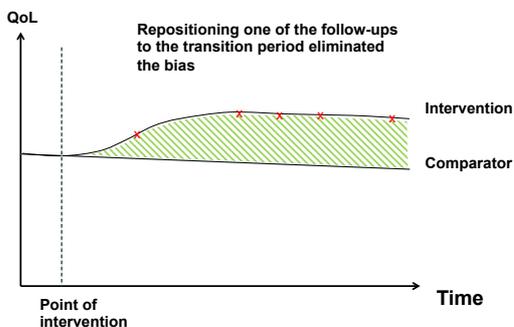
Informing decisions

- Economics is essentially a tool to help make decisions, of which there are plenty in study design:
 - Economics of recruitment
 - Economics of follow-up timing
 - Economics of site selection
 - Economics of duration of study
 - Etc!

Follow-up scheduling example



Follow-up scheduling example



Efficiency of clinical studies example

- Current grant application to investigate drivers of recruitment and cost. What makes for more efficient studies?
 - Location
 - Accreditation
 - Ethics
 - Type of centre
 - Staff expertise and experience
 - Centre experience in running studies
 - Scale
 - Clinician engagement

- Fundamentally, economics considers marginal (incremental) costs and benefits
- Key for studies? Does the marginal benefit outweigh the marginal cost?
 - An extra follow-up point?
 - A larger sample?
 - Including more outcome measures?
 - Including different sites?