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

Module 1 – What is economics and economic evaluation?

Centre for Health Policy
Melbourne School of Population of Global Health

Overview of the day

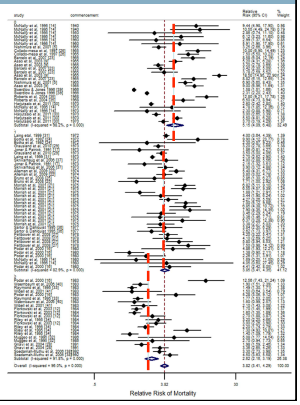
- **Module 1:** What is economics and economic evaluation?
- **Module 2:** Measuring health-related quality of life and use of clinical outcomes
- **Module 3:** Collecting relevant health system and patient cost data
- **Module 4:** Economic evaluation, uncertainty and modelling
- **Module 5:** Examples & getting projects funded
- **Workshop of selected case studies**

Insulin: A case study

- The discovery of insulin by Banting & Best turned a fatal disease (Type 1 Diabetes) into a chronic condition
- The first commercial insulin preparations contained numerous impurities
- 1930: Long acting insulins
- 1980s: Purified pork insulin/recombinant human insulin
- 1996: Diabetes Control and Complication trials demonstrated that intensive blood glucose control could reduce the complications of Type 1 Diabetes
- 2000s: Analogue insulins

Lung 2014 (PLOS One)

- The relative mortality of people with Type 1 Diabetes has improved
- Relative risk (pre-1971): 6 times general population
- Relative Risk (post-1990) : 3 times general population
- There is still a life expectancy gap of 11-13 years



Lung, PLOS One 2014

Insulin analogues

Insulin analogues "afford more flexible treatment regimens with a lower risk of the development of hypoglycemia" (NEJM 2005)

Short acting insulin (taken at meal time)

Long acting insulin (taken daily)

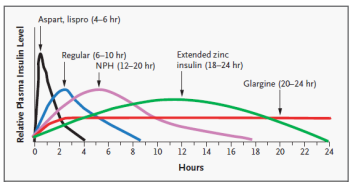


Figure 2. Approximate Pharmacokinetic Profiles of Human Insulin and Insulin Analogues.
The relative duration of action of the various forms of insulin is shown. The duration will vary widely both between and within persons.

What are the benefits of insulin analogues?

- It is necessary to focus on the incremental benefit relative to a comparator (human or animal insulin)
- Rapid acting analogues reduce postprandial hyperglycemia (high blood sugar after meals)
- Long acting analogues reduce the risk of hypoglycemia (low blood sugar, which impact on judgment and can lead to a diabetic coma)

What are the benefits of reducing "hypos"?

1) Quality of life
   - Patients value not having hypoglycemic episodes – they have reduced quality of life during an episode and in the long-term due to increased complications
   - Perhaps all people with Diabetes are affected by a "fear of hypos"

2) Clinical impact
   - There is emerging evidence of increased mortality (particularly after cardiovascular events)

Recent evidence of survival post CVD event

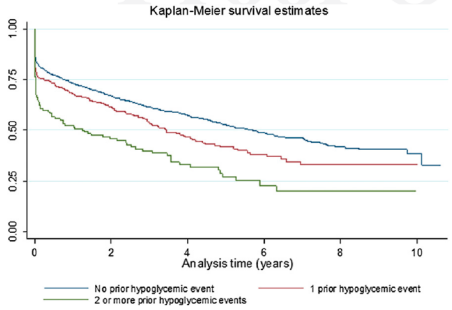


Figure 1—Survival after a CVD event, stratified by prior hypoglycemic events. (A high-quality color representation of this figure is available in the online issue.)

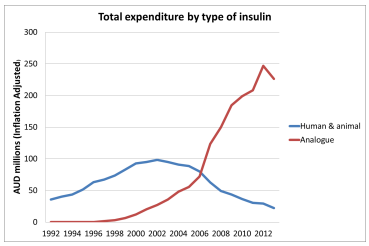
Lung et. al., Diabetes Care, 2014

Now a look at the cost…

- **Australian prices:**

  Insulin Isophane Human :
  $224 per script

  Insulin Glargine:
  $433 per script



- **The increase in expenditure reflects:**
  Expanded use for people with Type 2 Diabetes
  The higher price of insulin analogues

Are Analogues "value for money"?

- **In Australia these decisions are made by the Pharmaceutical Benefits Advisory Council (PBAC) on the basis of cost-effectiveness.**
- Example of Insulin Glargine:
  - Considered 5 times by the economic sub-committee of the PBAC
  - First considered by the PBAC in 2003
  - Finally listed in 2006
  - Company projected to cost $145 million over first four years (actual cost $263 million)

What the PBAC thought…

Comments from Oct 2005 Meeting:
"A number of problems with this analysis were identified during the evaluation, and the PBAC considered that the trial-based incremental costs per extra hypoglycaemic event avoided could be higher than estimated in the submission"

"The PBAC did not accept other assumptions in the economic model"

Recommendation:
Reject

What evidence do we need to make a decision?

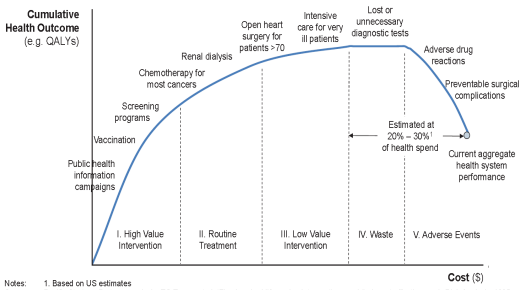
Information on:

- **Outcomes** – including assessment of Quality of Life (Module 2)
- **Costs** – not only of the therapy, but any savings (e.g. reduced hospitalisations caused by "hypos" at the time of event and subsequent secondary complications; e.g. organ damage) (Module 3)
- How would we **extrapolate** the long-term effects of a "hypo" on mortality? How do we bring it all together? (Module 4)
- **Practical applications** (Final session)

Food for thought: health system performance

Health outcomes are driven by productivity and cost-effectiveness of interventions

Health System Performance



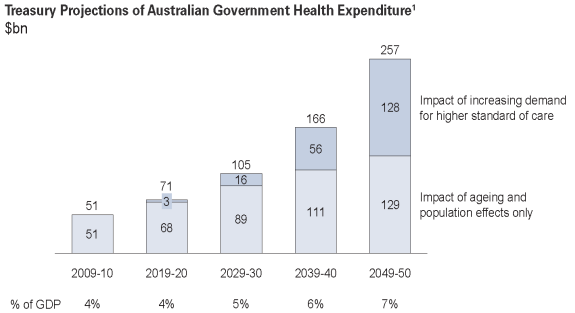
Notes: 1. Based on US estimates
Source: Pacific Strategy Partners analysis; TO Tengs, et al, 'Five-hundred life saving interventions and their cost effectiveness', *Risk Analysis*, 1995, 15(3):369–484; Institute of Medicine of the National Academies, *Best Care at Lower Cost: The Path to Continuously Learning Health Care in America*, 2012; DM Berwick & AD Hackbarth, 'Eliminating Waste in US Health Care', *Journal of the American Medical Association*, 2012, 307(14):1513-1516; Pricewaterhouse Coopers (PWC) Health Research Institute, *The Price of Excess: Identifying Waste in Healthcare Spending*, 2008

Source: McKeon Review

Food for thought: health expenditure

Projected Australian Government health expenditure is unsustainable

Treasury Projections of Australian Government Health Expenditure[1]



Notes: 1. Excludes state and territory government health expenditure
Source: Australian Government, *Intergenerational Report 2010*, Canberra, 2010

Source: McKeon Review

What is economics?

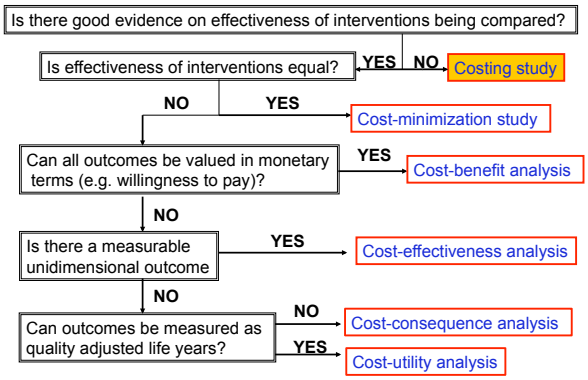
- Economics is concerned with the allocation of scarce resources
- Resources (labour, materials, natural resources etc.) are broadly fixed at any moment in time
- Therefore, choices have to be made concerning how to use these resources:
  - more on housing or more on a car
  - more health care or tax cuts

What is economic evaluation?

- Premise: scarce (health care) resources
- Aim: to maximise health gain with the available resources
- Method: compare the cost and effectiveness of therapies
- Balance: about costs and effects

Economic evaluation provides explicit criteria to aid in making choices

Types of economic evaluation

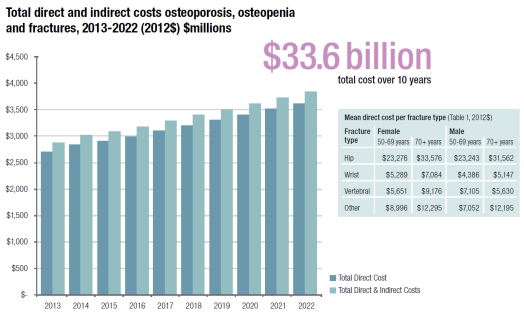


Cost of illness

- A form of cost analysis
- It attempts to quantify burden – lost productivity, costs of health care, social services, courts etc.
- It is often used for advocacy
- It tells you the size of the problem, but not what you should do about it
- It provides a partial analysis and rarely provides the context of the cost in relation to overall expenditure

Osteoporosis - An Australian Example

Osteoporosis Costing Data for Australia

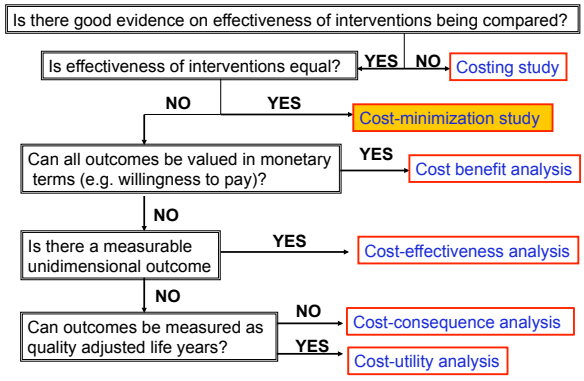


Mean direct cost per fracture type (Table 1, 2012$)

Fracture type	Female 50-69 years	Female 70+ years	Male 50-69 years	Male 70+ years
Hip	$23,276	$33,576	$23,243	$31,562
Wrist	$5,289	$7,084	$4,386	$5,147
Vertebral	$5,651	$9,176	$7,165	$5,630
Other	$8,996	$12,295	$7,052	$12,195

Watts et al, 2013

Types of economic evaluation



Cost-minimisation

- A special form of cost effectiveness analysis
- It compares **at least two** treatments
- Outcomes are measured using same measure (e.g. number of stroke events)
- Outcomes are statistically equivalent (with sufficient power to say that they are the same, not just to say that there is no evidence of difference)
- Cost-effectiveness analysis is preferable

Cost of illness in 1906

*"TUBERCULOSIS causes annually more than 150,000 deaths in the United States… If we assume that the net value of a year of human life … is at least $50, the real loss to the Nation… may be estimated at **$240,000,000 per annum**. These astounding and almost incomprehensible figures are far from being an exaggeration…"*

($50 in 1906 ~ $1200 in 2008)

Source: Huber, Consumption: It's relation to man (1906)

A century later…

*"In addition to the tremendous human cost, chronic diseases exact a tremendous financial toll on our health care resources. Care for patients with diabetes costs **$130 billion each year** alone, and this amount is growing. Tackling chronic diseases is also straining our public health departments…"*

Barack Obama, Health Care Plan, 2008

Cost-minimisation - Example

Cost minimisation analysis for prostate resection

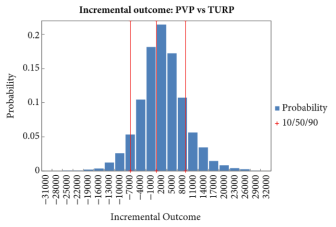


Fig. 2 Distribution of incremental cost from the simulations in the probabilistic sensitivity analysis. + Incremental costs PVP compared with TURP: 10th percentile AU$ −6933; 50th percentile AU$ 568; 90th percentile AU$ 8879.

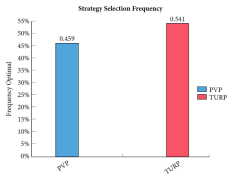


Fig. 3 Frequency each intervention is optimal.

Whitty et al, 2014

Cost-minimisation - Example

Cost-minimisation analysis for prostate resection

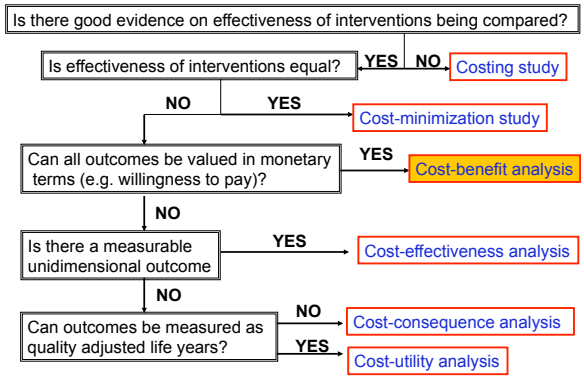
*"Two systematic reviews based on the literature to December 2006 and February 2012, including up to nine randomised controlled trials using the PVP 80-W (five trials) or 120-W system (four trials) and with up to 36-month follow-up, suggest PVP **can generally be considered non-inferior** to TURP for the management of symptomatic BPH."*

However,

*"**Despite the apparent overall non-inferiority** of PVP in functional and safety outcomes, **there is some recent data suggesting that PVP may result in higher re-operation rates** in some patient subgroups, particularly those with a larger prostate volume. Although Thangasamy et al. reported no statistically significant difference in unplanned re-operation rates between PVP and TURP in their review, there was a clear trend for a difference favouring TURP (RR 1.87, 95% CI 0.65–5.39). **If true, this would likely have cost implications**."*

Whitty et al, 2014

Types of economic evaluation



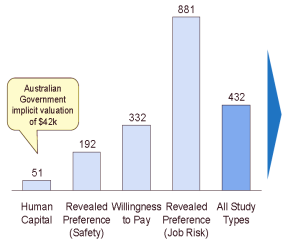
Cost-benefit analysis

- Measures inputs and outcomes in dollars
- Enables comparisons across sectors and different clinical outcomes
- Addresses issues such as net gain to society
- Addresses the question of whether the program is worthwhile to society

Cost-benefit analysis

The value of a quality-adjusted life year is estimated at ~$432,000

Value of a Quality-Adjusted Life Year[1]
$000s



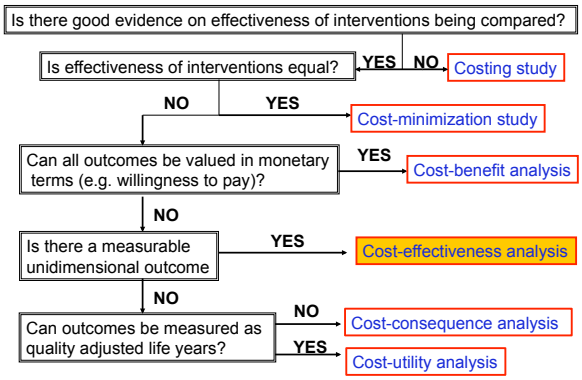
- There are four main methodologies to measure the value of a QALY:
  - **Human capital** – reflects ability to generate earnings, but does not capture value to individual
  - **Revealed preference (safety)** – based on value of life in relation to non-occupational safety risks
  - **Willingness to pay** – value individuals place on their life contingent upon their ability to pay
  - **Revealed preference (job risk)** – reflects wage premium required to attract the most risk-averse worker to accept a risky job
- The median value across all studies is $432,000

Notes: 1. Median values from a literature review encompassing 42 studies that were deemed appropriate. Values originally based on 1997 US$ converted to A$ assuming an exchange rate of US$1 = A$0.74 and inflation adjusted to 2012 values

Source: R Hirth, M Chernew, E Miller, A Fendrick & W Weissert, 'Willingness to Pay for a Quality-Adjusted Life Year: in Search of a Standard', *Medical Decision Making*, 2000, pp.332-342; S Mak, *Evaluation of Health Programs: Application of Social Cost Benefit Analysis in the Pharmaceutical Benefits Scheme Listing of Australia*, Dissertation, 2005; ABS, *Consumer Price Index, Australia, December 2012*

Source: McKeon Review

Types of economic evaluation



Cost-effectiveness analysis (CEA)

- The most commonly used method of economic evaluation
- Compares costs and outcomes
- Requires a common, unambiguous outcome measure
- Outcomes measured in natural unit:
  - cases detected
  - deaths prevented
  - life years gained

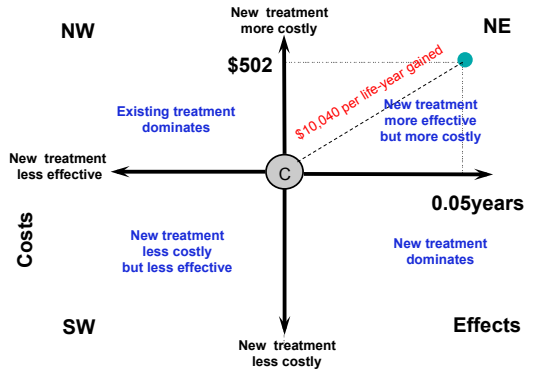
CEA example

Cost-effectiveness of lowering blood pressure with a fixed combination of perindopril and indapamide in type 2 diabetes mellitus: an ADVANCE trial-based analysis

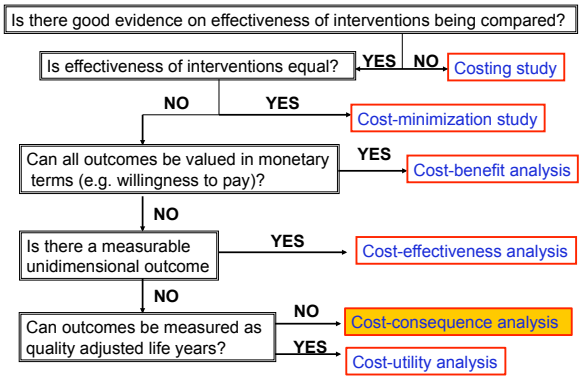
Paul P Glasziou, Philip Clarke, Jan Alexander, Mohana Rajmokan, Elaine Beller, Mark Woodward, John Chalmers, Neil Poulter and Anushka Patel

- The intervention involved the use of blood pressure drugs in diabetes
- The intervention cost $1350 (over four years)
- The intervention group experienced lower hospital & other health care costs (~$800 in savings)
- The net cost was approximately $502.
- There was an increase in life expectancy of 0.05 life years over remaining lifetimes

Cost-effectiveness plane



Types of economic evaluation



Cost- consequence analysis (CCA)

- This is a form of economic evaluation in which the multi-dimensional outcomes are reported separately from costs.
- Provide information to the decision maker on the costs and consequences of an intervention
- Does not explicitly value outcomes relative to costs
- Mainly applied in complex public health interventions with multiple outcomes

Example Evaluation of Two Implantable Cardiac Monitors

Consequences

Table 2 Expected number of events

	Number of events per 1000 patients over 10 years					
	Undiscounted			Discounted		
	HM	CFU	Difference (%)	HM	CFU	Difference (%)
Death and cardiovascular events						
Death (all cause)	596	596	0 (0)	542	542	0 (0)
Stroke	26	26	0 (0)	22	22	0 (0)
ADHF	796	796	0 (0)	724	724	0 (0)
Sustained ventricular arrhythmia	2313	2313	0 (0)	2035	2035	0 (0)
AF	983	983	0 (0)	865	865	0 (0)
Shock events						
Inappropriate shock (total)	116	237	−121 (−51)	102	209	−107 (−51)
Due to lead issues*	12	52	−40 (−77)	10	46	−36 (−78)
In AF*	104	185	−81 (−44)	92	163	−71 (−44)
Appropriate shock for SVA*	364	364	0 (0)	320	320	0 (0)
Device-related events						
Battery replacement	467	502	−35 (−7)	367	409	−42 (−10)
Lead issues	87	87	0 (0)	76	76	0 (0)
Follow-up services						
Number of visits (total)	11 355	22 328	−10 973 (−49)	10 018	19 699	−9681 (−49)
Unscheduled	4976	3190	1786 (56)	4390	2814	1576 (56)
Scheduled	6379	19 138	−12 759 (−67)	5628	16 885	−11 257 (−67)

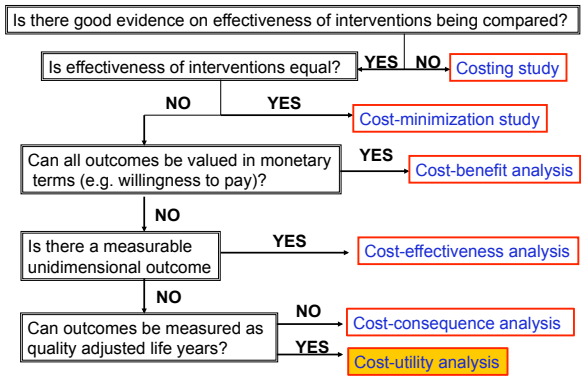
Costs

Table 3 Costs results

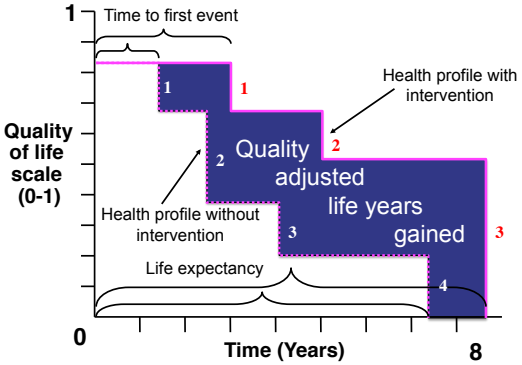
	Cost per patient over 10 years (GBP)					
	Undiscounted			Discounted		
	HM	CFU	Difference (%)	HM	CFU	Difference (%)
Costs						
Total	13 608	13 660	−52 (−0.4)	11 452	11 486	−34 (−0.3)
Device and patient management	10 091	10 143	−52 (−0.5)	8356	8389	−33 (−0.4)
CV events	3517	3517	–	3096	3097	–

Burri et al, 2013

Types of economic evaluation



Using QALYs to measure outcomes



CUA Example – Cardiac Devices

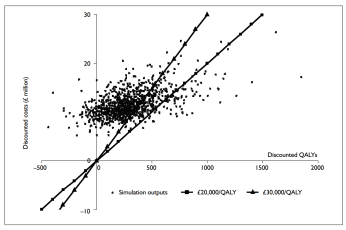


FIGURE 60 Simulation output (cohort based, 1000 trials) for the cost-effectiveness of CRT-D in comparison with CRT-P

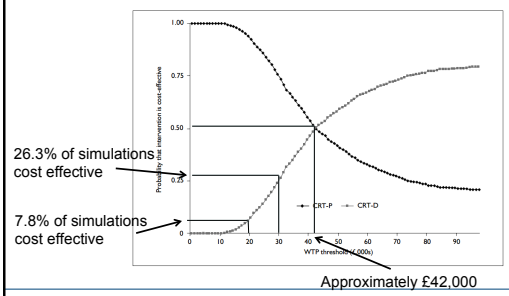
- Comparison of implantable cardiac resynchronization devices with (CTR-P) and without defiburillation (CTR-D)

- CTR-D was more costly: £11,689
- CTR-D was however more effective: 0.29 QALYs

Fox, 2007

CUA Example – Cardiac Devices

Cost-effectiveness acceptability curve



Fox, 2007