Introduction to Cost-Effectiveness Analysis in Health

THE UNIVERSITY OF MELBOURNE

Health Economics Short Course

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Module 4 – Policy Use and Interpretation of Cost-Effectiveness Analysis

THE UNIVERSITY OF MELBOURNE

Centre for Health Policy
Melbourne School of Population and Global Health

Purpose of economic evaluation

- In a resource constrained environment, provide information on the costs and benefits of options for intervening
- Inform decisions regarding the allocation of scarce resources, including information on opportunity cost
- Inform maximisation of health outcomes with given funding/budgets
- Use explicit criteria for choices

Types of economic evaluation analysis

TYPE	COSTS	OUTCOMES	DECISION
Cost Minimisation	Dollars	Not compared, assumed ***identical in all aspects***	Least cost alternative
Cost Effectiveness/ Cost Consequences	Dollars	Comparison based on **a common measure *on health***, eg LY's gained, blood pressure reduction	Incremental cost per **natural** unit of consequence gained
Cost Utility	Dollars	A ***summarised measure*** of impacts ***on health related quality of life***, *Valued* as "utility", eg QALY	Incremental cost per **preference adjusted** unit of consequence gained
Cost Benefit	Dollars	A **summarised measure** of impacts on ***health and non health benefits*** valued in monetary term (i.e., Dollars)	Net $; Cost/benefit ratio

Example CEA

RESEARCH

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

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Reducing the vascular complications of type 2 diabetes mellitus is a global health priority; worldwide the number of people with diabetes is projected to rise from 171 million in 2000 to 366 million in 2030.[1] Most people with diabetes will die from or be disabled by macrovascular and microvascular complications that can be reduced by blood pressure (BP)-lowering therapy.[2] Traditional strategies have set BP thresholds and targets for treatment. While effective, these strategies are resource intensive, requiring multiple

ABSTRACT

Objective: To determine the cost-effectiveness of routine administration, irrespective of blood pressure (BP), of a fixed-dose combination of perindopril and indapamide to patients with type 2 diabetes mellitus.

Design, setting and participants: Prospective cost-effectiveness analysis within the Action in Diabetes and Vascular Disease: Preterax and Diamicron-MR Controlled Evaluation (ADVANCE) trial, an international, multicentre, randomised controlled trial of 11 140 participants with type 2 diabetes randomly allocated to receive perindopril plus indapamide (4 mg–1.25 mg/day) or placebo.

Main outcome measures: Health-related quality-of-life measured by the EuroQol-5D, resource utilisation, and cost-effectiveness (cost per death averted at 4.3 years' average follow-up, and estimated cost per life-year gained, by extrapolation).

Main economic evaluation

- Comparison: Perindopril-Indapamide versus placebo for lowering blood pressure in Type 2 Diabetes
- Data: Patient level data on costs and LYs and QALYS from ADVANCE trial
- Time period: 4.3 years follow up
- Perspective: Australian health care purchaser

Costs and resource use

1 Australian unit costs and their sources for the major cost items

Resource item	Unit cost 2007 (A$)	Source
Standard single GP visit	28.30	MBS
Perindopril–indapamide (4 mg–1.25 mg daily), per month	29.83	PBS
Other drugs	Cost per item	PBS
The four most frequently used DRGs	**Cost per hospital episode**	
K60B: Diabetes episode without severe complication	3556	NHCDC
B70C: Stroke without other complication	5810	NHCDC
F62B: Heart failure and shock without catastrophic complication	4314	NHCDC
F66B: Coronary atherosclerosis without complication	1560	NHCDC

DRG = diagnosis-related group. GP = general practitioner. MBS = Medicare Benefits Schedule. NHCDC = National Hospital Cost Data Collection. PBS = Pharmaceutical Benefits Schedule. ◆

Outcomes and survival

Outcomes and survival

All-cause mortality and cardiovascular mortality from the clinical trial have previously been reported.[8] We calculated the survival time within the study for each treatment group from survival curves. Life expectancy of survivors beyond the close of the study was based on multistate life tables under the assumption of no continuing benefits from the within-trial treatment. These life tables were constructed from parametric survival models, and estimates were based on information about all ADVANCE participants who were alive 2 years after randomisation, including age, sex, smoking status, duration of diabetes and history of major cardiovascular disease.

Outcomes (LYs)

6 Life expectancy and life-years gained, from the within-trial effect of treatment with fixed combination of perindopril and indapamide

Type of outcome	Mean (95% CI) life expectancy (years) per patient: Perindopril–indapamide	Mean (95% CI) life expectancy (years) per patient: Placebo	Mean life-year gain per patient (95% CI)
Within-trial	4.17 (4.15–4.18)	4.14 (4.12–4.16)	0.03 (0.00–0.05)
Total life expectancy	14.97 (13.77–16.44)	14.88 (13.69–16.35)	0.09 (0.06–0.12)
3% discount per year	12.28 (11.48–13.23)	12.22 (11.42–13.17)	0.06 (0.04–0.07)
5% discount per year	10.88 (10.27–11.60)	10.84 (10.23–11.56)	0.05 (0.03–0.06)
10% discount per year	8.36 (8.04–8.72)	8.34 (8.01–8.70)	0.02 (0.02–0.03)

Costs

2 Summary of outcomes and mean costs per patient over the follow-up period and mean cost differences, for perindopril–indapamide compared with placebo, by cost category*

Outcome	Perindopril–indapamide (n = 5569)	Placebo (n = 5571)	Difference (95% CI)†
Cardiovascular mortality, no. (%)	211 (3.8%)	257 (4.6%)	0.8% (0.1% to 1.6%)
All-cause mortality, no. (%)	408 (7.3%)	471 (8.5%)	1.1% (0.1% to 2.1%)
	Mean (SD) cost per patient for Australian participants		
Hospital costs‡	7 913 (11 826)	8 323 (12 957)	−410 (−2007 to 1187)
Outpatient visit costs§	5 317 (3 583)	5 389 (3 807)	−72 (−547 to 404)
Intervention costs	1 368	0	1 368
Other drug therapies§	8 616 (6 212)	8 948 (5 678)	−332 (−1092 to 428)
Total costs (undiscounted)	23 214 (16 155)	22 660 (17 002)	555 (−730 to 1580)
Total costs (discounted at 3%)	21 811 (15 159)	21 281 (15 984)	529 (−1476 to 2535)
Total costs (discounted at 5%)	21 001 (14 565)	20 499 (15 377)	502 (−1425 to 2431)
Total costs (discounted at 10%)	19 223 (13 284)	18 775 (14 070)	447(−1314 to 2209)

Cost-effectiveness

- Comparative (intervention A vs B)
- Common outcome measure
- Incremental cost-effectiveness ratio (ICER)
- ICER= difference in costs (C_A-C_B) divided by the difference in effects (E_A-E_B)

Cost-effectiveness analysis

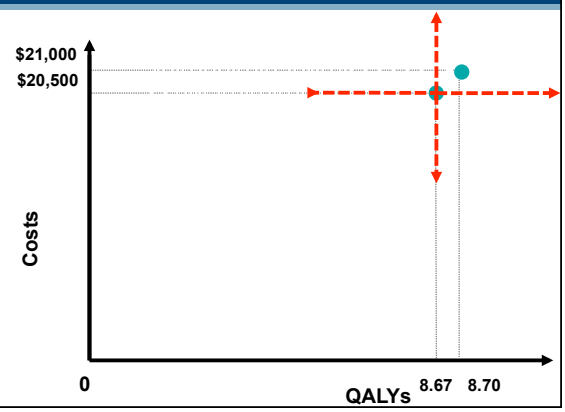
From the ADVANCE trial

	Perindopril-indapamide	Placebo/ standard practice	Difference
Costs	$21,001	$20,499	$502
Years of life	10.88	10.84	0.05
EQ-5D	0.8	0.8	-
QALY	8.70	8.67	0.03

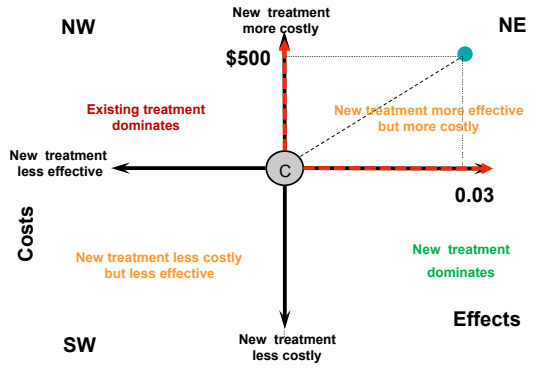
CEA= $502/0.05 = $10,040 per life year saved

CUA= $502/0.03 =$16,733 per QALY saved

Graphing costs and effects



Cost-effectiveness plane



Decision rules for CEA

- Recommend
  - If new intervention dominates
- Reject
  - If new intervention is dominated
- Develop a decision rule for NE & SW quadrants
  - Use a league table to compare with other interventions
  - Compare to established ceiling ratio

League tables

- Involves ranking of options for intervening/treating with most cost-effective on top of list
- Allocated a fixed budget down the list until budget is expended
- Method to prioritise activities that generate greater health gains per dollar invested

Priority setting example

Program	Cost of mal-treatment avoided /100 families	Cost of program minus cost of control /100	ICER
The Safe Environment for Every Kid (SEEK) Model	5.9	$79,700	$13,537
Triple P – Positive Parenting Program	0.31	$6,560	$21,438
Parents under Pressure (PUP)	19.8	$820,100	$41,327
Child FIRST	12	$1,000,400	$83,366
Special Families Care Project	19	$3,006,600	$158,244
Healthy Families New York	1.05	$706,300	$672,684

Problems with league tables

- Concept
  - Too simplistic, what about other factors?
  - Conceptually difficult to compare very different interventions (e.g. high cost life saving to low cost screening)
  - Context may not translate across countries settings
  - May not match funding structures (e.g. different state/federal health responsibilities)
- Methodology
  - Similarity of comparators
  - Perspective of costs may differ
  - Mutually exclusive options

Problems with league tables

- Size of financial impact not considered
- Very important to disaggregate costs and outcomes
- Example:

Programs	Cost of mal-treatment avoided /100 families	Cost of program	ICER	Financial impact
Parents under Pressure (PUP)	19.8	$8,201	$41,327	1,000 families $8.2 million
Triple P – Positive Parenting Program	0.31	$65.60	$21,438	500,000 families $32.8 million

Ceiling cost effectiveness ratio

- The maximum amount society is willing to pay for an extra unit of health gain
- Australian estimates
  - No official statement of 'thresholds'
  - between $42K-$76K per life year (George et al, 2001)
- UK
  - NICE states £20k to £30k (McCabe, 2008)
  - Upper threshold £47-50K per QALY (Devlin and Parkin, 2004)
  - 50% probability of funding £39k to £43k (Dakin, 2014)
- Developing countries = 1-3 x GDP

Considerations with ceiling ratios

- Vary across countries
  - Prices change
  - Different budgets
  - Different finance/government structures
- Decision makers may prefer different thresholds for different types of interventions
  - e.g. life saving versus prevention
- Difficulties determining threshold relative to absolute budget, hard to change once set
- Can lead to uncontrolled expenditure growth

Uncertainty

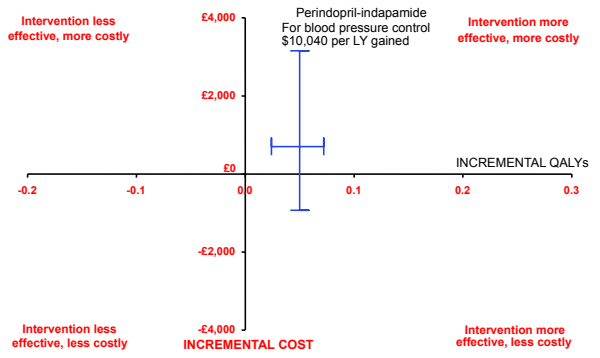
- By nature economic evaluation is uncertain
  - All inputs potentially uncertain (clinical effectiveness, utilities, resource costs, downstream cost savings, long term outcomes, disease progression)
  - Combinations of primary/ secondary data
  - Assumptions

- Types of uncertainty
  - Parameter (precision of estimates)
  - Structural
  - Methodological

Sensitivity analysis

- Type of sensitivity analysis
  - One-way
    - To determine largest sources of uncertainty i.e. what your economic evaluation is most sensitive to
  - Multi-way
    - Combined impact of a couple of main drivers of uncertainty
  - Probabilistic
    - Combined simulated impact of parameter uncertainty, able to be graphed, produce CIs

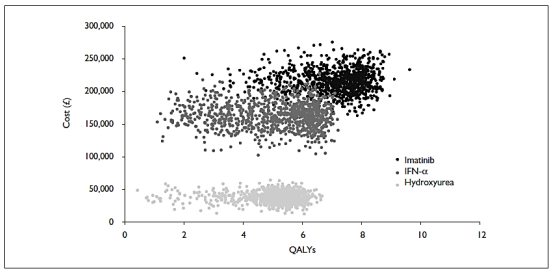
Cost-utility results



Costs & QALYs discounted at 3.5% p.a.

Probabilistic sensitivity analysis

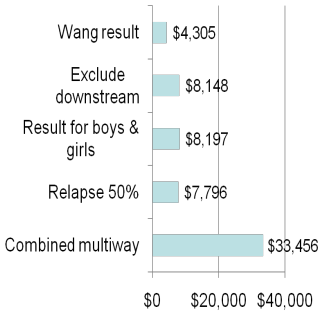
CE plane



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.

Example: impact of uncertainty

- **Wang et al (2003) Economic analysis of a school-based obesity prevention program**
- **Key assumptions**
  - **Weight loss maintained into adulthood**
  - **No structural possibility of relapse**
  - **Full downstream cost savings of obesity applied**



Dalziel K, Segal L, 'Uncertainty in the economic analysis of school-based obesity prevention programs: urgent need for quality evaluation, *Obesity Research 2006*;14(9):1481-82

Guidelines for reporting

- PBAC and MSAC guidelines
  - http://pbac.pbs.gov.au/
  - http://www.msac.gov.au/internet/msac/publishing.nsf/Content/applicants
- Journal guidelines
  - BMJ : http://www.bmj.com/about-bmj/resources-authors/article-types/research
- ISPOR
  - https://www.ispor.org/Health-Economic-Evaluation-Publication-CHEERS-Guidelines.asp

CHEERS – ISPOR

Limitations of CEA

- Tells us relative efficiency, not absolute
- Doesn't consider total cost
- Not helpful in assessing a single programme
- Narrow uni-dimensional measure of success
- Cannot compare disparate alternatives
- Only as strong as the underlying evidence

Other factors informing decisions

Ross 1995 survey of Australian decision makers

- 58% political factors
- 58% nature of existing policies
- 47% administrative feasibility
- 47% equity
- 23% availability of resources
- 20% opinions of influential groups

Factors associated with funding

- Quality and certainty of evidence (Mason and Drummond, 2009; Devlin and Parkin, 2004)
- Severity/burden of disease (Cookson et al, 2008; Devlin and Parkin, 2004)
- Life extension (Foy et al, 1999)
- Availability of other options (Devlin and Parkin, 2004)
- Cost-effectiveness (Segal et al, 2010; Bryan et al, 2007; Dakin et al, 2014)
- Total cost to government (Harris et al, 2008)

Assessment of Australian C/E results

- 245 interventions that had been subject to cost-effectiveness analysis and reported a cost/LY or cost/QALY to 2005
- Median CE: $18,100 per LY/QALY gained
- Diagnostics higher, children higher, drug and alcohol and metabolic syndrome lower ICERs
- For any given condition, modality or setting are likely to be examples of interventions that are cost-effective
- Need decision based on the individual merits of an intervention rather than rely on broad generalisations

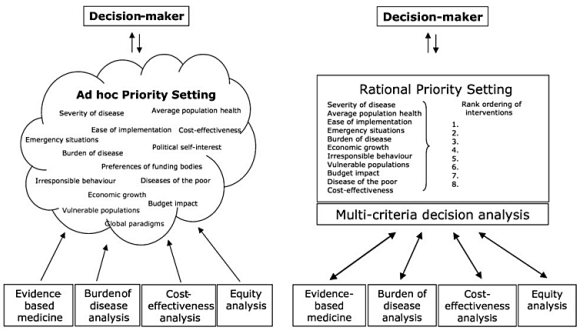
Dalziel, K, Segal, L & Mortimer, D 2008, 'Review of Australian Health Economic Evaluation– 245 interventions: What can we say about cost-effectiveness?' *Cost Effectiveness and Resource Allocation*, vol. 6, no. 9.

Segal, L, **Dalziel, K** & Mortimer, D 2010, 'Fixing the game: Are between-silo differences in funding arrangements handicapping some interventions and giving others a head-start?' *Health Economics*, vol. 19, no. 4, pp. 449–465.

Factors predicting funding

- Australian study of 245 published economic evaluations and their funding outcomes
- Predictors of funding (model correctly classified 85% of funded programs)
  - Lower ICER
  - Eligible for subsidy under MBS/PBS
  - Medical treatment interventions (compared to lifestyle, screening, diagnosis)
  - Interventions where individual could not reduce their own risk of disease
  - Interventions aimed at averting or slowing disease

Multi criteria decision analysis (MCDA)



MCDA example (Baltussen & Niessen, 2006)

Options	Cost-effectiveness	Severity of disease	Disease of the poor	Age
Antiretroviral treatment in HIV/AIDS	US$200 per DALY	••••	√	15 years and older
Treatment of childhood pneumonia	US$20 per DALY	••••	√	0–14 years
Inpatient care for acute schizophrenia	US$2000 per DALY	••		15 years and older
Plastering for simple fractures	US$50 per DALY	•		all

Options	Cost-effectiveness	Severity of disease	Disease of the poor	Age	Total
Antiretroviral treatment in HIV/AIDS	50	100	100	0	70
Treatment of childhood pneumonia	100	100	100	100	100
Inpatient care for acute schizophrenia	0	50	0	0	5
Plastering for simple fractures	100	25	0	50	48
Weights	40	10	40	10	

Preference scores for 'cost-effectiveness' are obviously inverse to its values, and are based on three categories: it scores 0 if the cost-effectiveness is higher than US$300 per DALY, 50 if between US$100 and US$300, and 100 if below US$100 per DALY. For 'disease of the poor', if the feature is present, it scores 100, otherwise 0. Preference scores for 'severity of disease' are scaled between 0 and 100 in proportion to their stars. Assuming decision makers have a preference to treat young people over old, '0–14 years' receives a score of 100, '15 years and older' a score of 0, and 'all ages' a score of 50. Preference scores are presented here for illustrative purposes only, and are arbitrary.