Economic evaluation alongside clinical trials

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Learning objectives

The George Institute for Global Health Australia

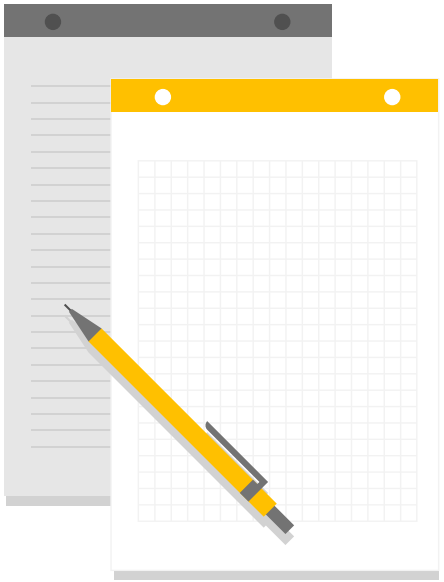
- Identify when economic evaluation alongside trial is useful
- Consider relevant perspective for the decision maker
- Identify methods for collecting costs and outcomes
- Describe when modelling may be beneficial

Do I need to consider an economic evaluation?

- Yes!
- Start early – include in grant app and include in your budget
- Why? We do trials to improve care – this care is delivered in a space with constrained resources. Generating evidence to support implementation (or not) can help guide decision makers.
- Not needed for consumer products (e.g. fitbit) – each individual decides for themselves if they think it's worth the cost

Perspective

- What kind of intervention, where, who would decide if it is implemented?
- Helps to decide what costs and outcomes you collect and how



Power and sample size

- Important for hypothesis testing in clinical trials
- Economic evaluation is interested in the estimate of cost-effectiveness and uncertainty around that estimate
- Powering for a joint distribution of costs and effects usually requires larger sample and longer follow-up
- Pragmatically - trials funded through grants have tight budgets and timelines
- EVPI may help guide this if precision needed

Where to find costs

Intervention costs

- Financial statements
- Interviews/ time and motion studies

Downstream costs

- Trial records (case report forms / adverse event reporting)
- Participant questionnaires (including diagries)
- Hospital records
- Linked administrative data (e.g., regional or national records of public health insurance or social services claims)

Examples:

Health Service Utilisation	
Since the last assessment, how many times has the participant seen the following practitioners	
Practice nurse	
GP	
Doctor in pu	
Doctor in pu	
Doctor in pri	

E. Health Services and/or Hospital Admissions in the PAST 2 MONTHS

a. **IN THE PAST 2 MONTHS** have you used any health services and/or been admitted to hospital (including day-only procedures) for **any reason**?

Yes No (Please circle one)
If Yes, please detail below

Type of service	For what condition or reason?	Number of Visits	Start Date
1.			
2.			
3.			
4.			

NOTE: On the reverse side plea
Thank you fo
Please

February 2017

Mon	Tue	Wed	Thu	Fri	Sat	Sun
		1	2	3	4	5
6	7	8	9	10	11	12
13	14	15	16	17	18	19
20	21	22	23	24	25	26
27	28					

Please mark the calendar each day with a letter:
GP = primary care doctor visit
S = specialist doctor (eg. cardiologist, nephrologist, surgeon)
N = nurse visit
T = heart test or scan
B = blood test
E = emergency room visit
H = hospital stay (put an H in each day you spent in hospital)

Leave day blank if none of these things occurred.

Types of outcomes

- Natural units: person achieving blood pressure target, strokes prevented, lives saved
- Utilities: quality adjusted life year (QALY), disability adjusted life year (DALY) averted
- Service outputs: time to first appointment, number of assessments completed, number of reports reviewed
- Monetary units: benefits are given monetary value (e.g., AUD)

Which outcomes?

- What are the outcomes of interest?
  - To patients and families?
  - To clinicians?
  - To decision makers?
- Are there multiple outcomes? How do you measure it?
  - Natural units – clinical standards, research standards
  - Utilities – DALY published disability weights and mortality data, QALY published norms and event weights, or self-reported EQ-5D or SF36

Plan from the start

- Protocol, consent forms, and case report forms
- Visit schedule
- Length of visit (How much time spent completing extra Qs?)
- Data linkage – hospital, ambulance, births, deaths, MBS, PBS, education, justice, housing?
  - What is important and relevant?
  - When do you think the effect of the intervention will impact service use?

Example: QUARTET trial CEA

- Included a brief description of the CEA in the protocol
- Planned for short-term data collection of resource use at 6 and 12 weeks using CRFs ("Since last visit…")
- Major events (unplanned admissions) are captured as SAEs
- Planned for data linkage of PBS and MBS data for longer term (fixed dates on consent form)

Chow CK, et al. Heart Journal. 2021;231:56-67.

Challenges

- Timing and funding: my fellowship funding to do the CEA began and ended while the trial was still recruiting
- Collecting up hard-copy DHS consent forms (during a pandemic)
- Database functions and exportable data

QUARTET CEA: within trial results

- Trial's primary outcome was change in a particular systolic blood pressure measurement – gold standard for blood pressure trials
- Sense check on the outcome: $/mmHg what does that mean?

Results The within-trial analysis showed no clear difference in cost per mm Hg BP lowering between randomised treatments at 3 months ($A10 (95% uncertainty interval (UI) $A –18 to $A37) per mm Hg per person) for quadpill versus monotherapy. The

Atkins ER, et al. Heart 2023;0:1–8. doi:10.1136/heartjnl-2022-322300

Moving beyond the trial

- RCTs have fixed duration and limited scope – great for answering the question "Does this work?"
- When looking at whether something is cost-effective in a population, we usually need a bigger picture, and that's where modelling comes in to help

Modelled cost-effectiveness

Models vary in complexity

- Simple risk equation (e.g., Framingham and Globorisk cardiovascular risk calculators)
- Cohort (Markov)
- Microsimulation (individual)

Tasks

- Translation (data from elsewhere)
- Extrapolation (over time and populations)
- Transformation (intermediate e.g., BMI and rates of smoking to disease events, mortality and QALYs)

Modelled cost-effectiveness

Advantages

- Uses best available evidence rather than single study (systematic review and meta-analysis to derive effectiveness data)
- Enables the evaluation to be tailored to policy question
- Ability to assess cost-effectiveness at a population level (scaling up)

Cons

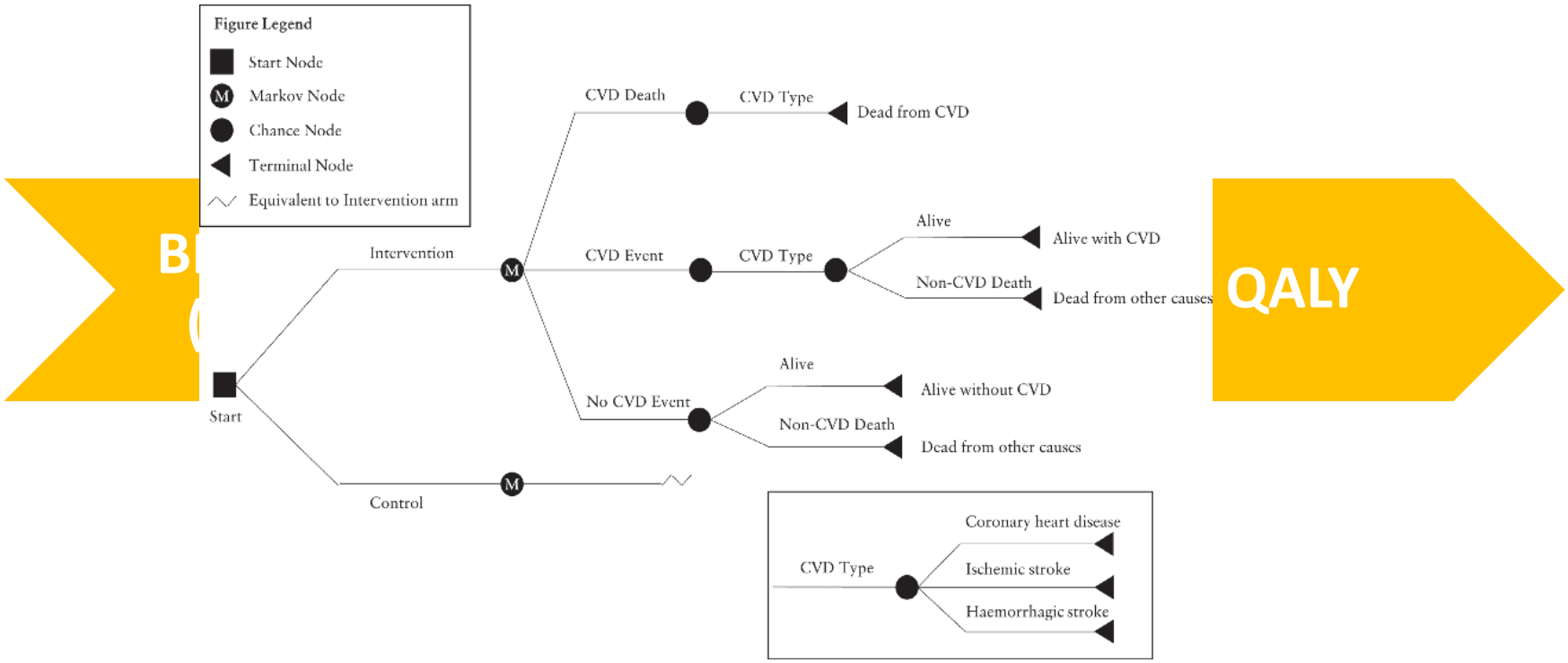
- Relies on assumptions
- 'Black box'; amenable to manipulation

Nevertheless, strong regulatory support (e.g. PBAC, UK NICE)

What kind of model?

- Meet the needs of decision makers
- Pragmatic
  - Data available
  - Computational capacity and software

QUARTET CEA: model



QUARTET CEA: model

Table 3 Base case (constant quadpill effect for first year, and then 10% p.a. decline until zero effect for a lifetime)

Mean total cost (95% UI)		Mean incr cost (95% UI)	Mean total QALYs (95% UI)		Mean incr QALY (95% UI)	ICER	Probability of cost-effectiveness (% at different $A/QALY)		
Quadpill	Irbesartan		Quadpill	Irbesartan			$A10 000	$A25 000	$A50 000
$A10 398 ($A10 158–$A10 649)	$A10 133 ($A9874 to $A10 395)	$A265 ($A166 to $A357)	10.01 (9.94 to 10.08)	9.99 (9.92 to 10.06)	0.02 (0.01 to 0.03)	$A14 006	10%	95%	100%

Table shows the results of probabilistic sensitivity analysis of 500 samples of 10 000 bootstrapped patients from the initial QUARTET trial data, simulated over a lifetime (death by 100 years of age). The UIs show the 2.5 to 97.5 percentiles for the incr differences in costs and QALYs. The uncertainty for the ICER (cost per QALY gained) is calculated as the probability of cost-effectiveness (proportion of cost-effective replications) under different willingness-to-pay thresholds.
ICER, incremental cost-effectiveness ratio; incr, incremental; p.a., per annum; QALY, quality-adjusted life year; QUARTET, Quadruple UltrA-low-dose tReaTment for hypErTension; UI, uncertainty interval.

Impact

- So, for the QUARTET example there's a few more hurdles to overcome before implementation because it's a pharmaceutical product
- However, other types of interventions e.g. changes in service delivery, can be implemented in local area health services quite quickly when there is need and appetite for change

Thank you!

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